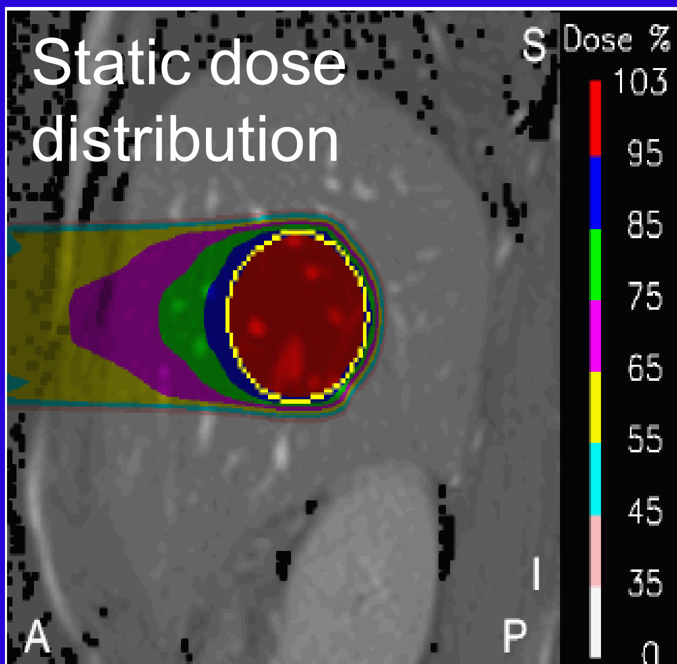
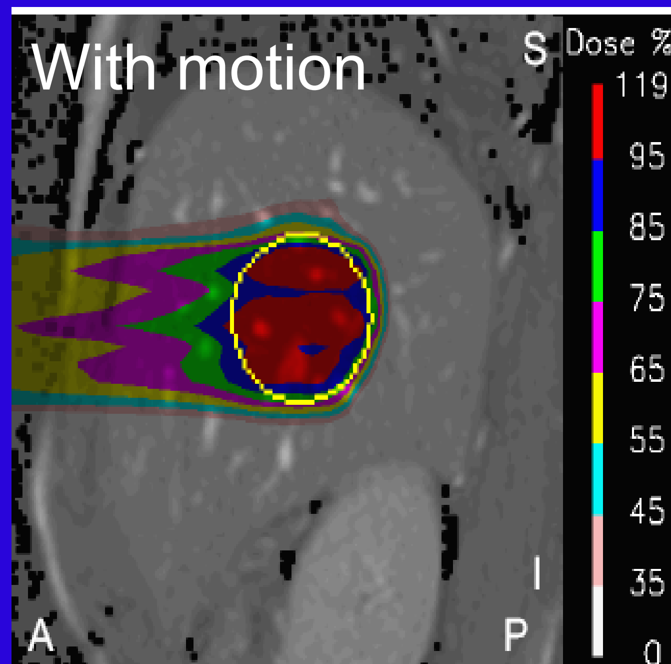
Future directions and current challenges of proton radiotherapy.

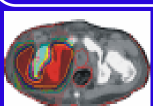




Tony Lomax
Centre for Proton Radiotherapy, Paul Scherrer Institute, Switzerland

Overview of presentation

- New developments in treatment delivery
- Current challenges
- Potential solutions
- Summary



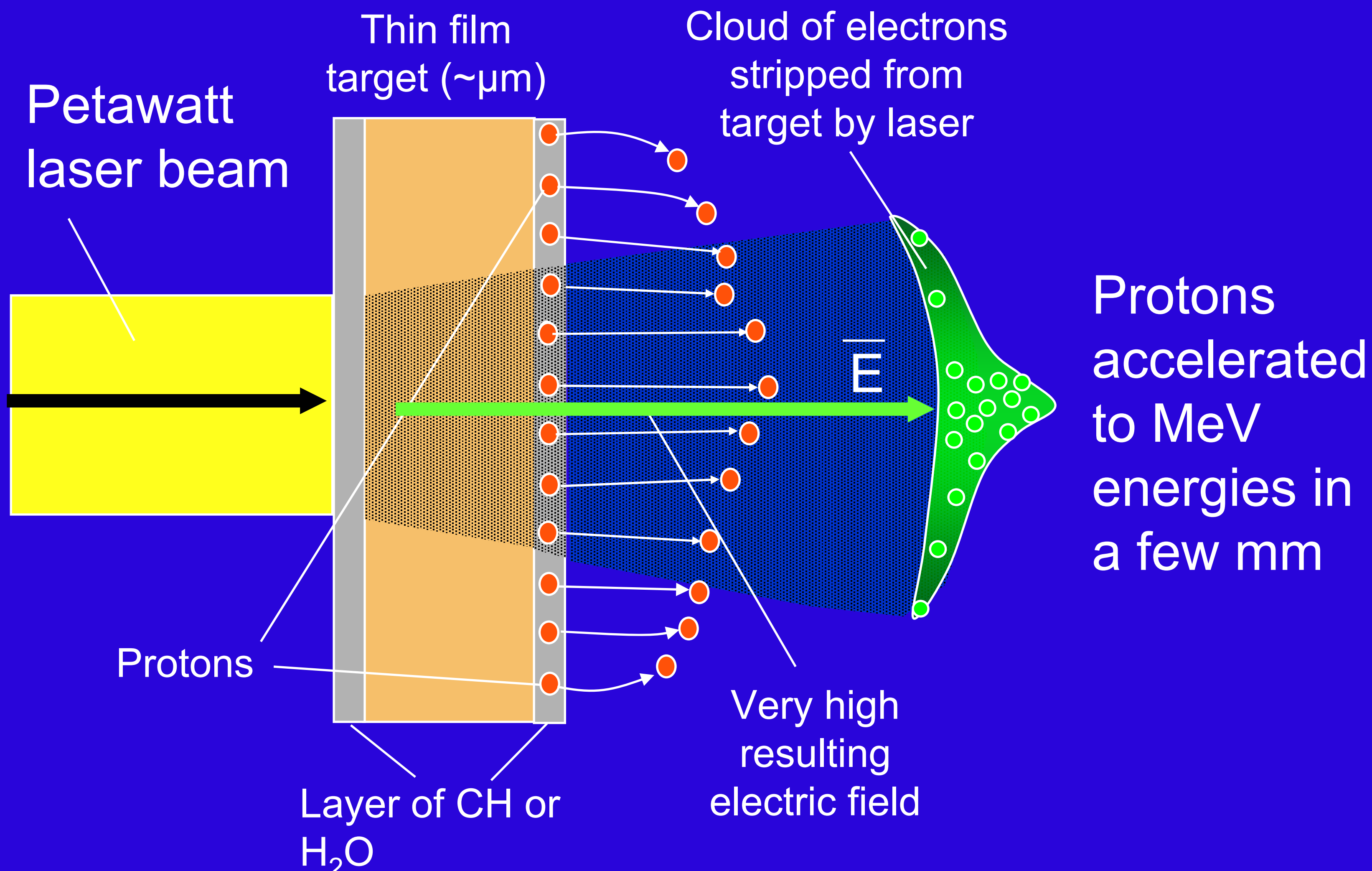
Industrial suppliers of radiotherapy equipment

Manufacturers currently offering photon therapy equipment	Manufacturers currently offering particle therapy equipment
	IBA*
Varian	Hitachi*
Elekta	Optivus*
Tomotherapy	Varian/Accell**
Siemens	Siemens**
	Still River systems

* Scanning option available

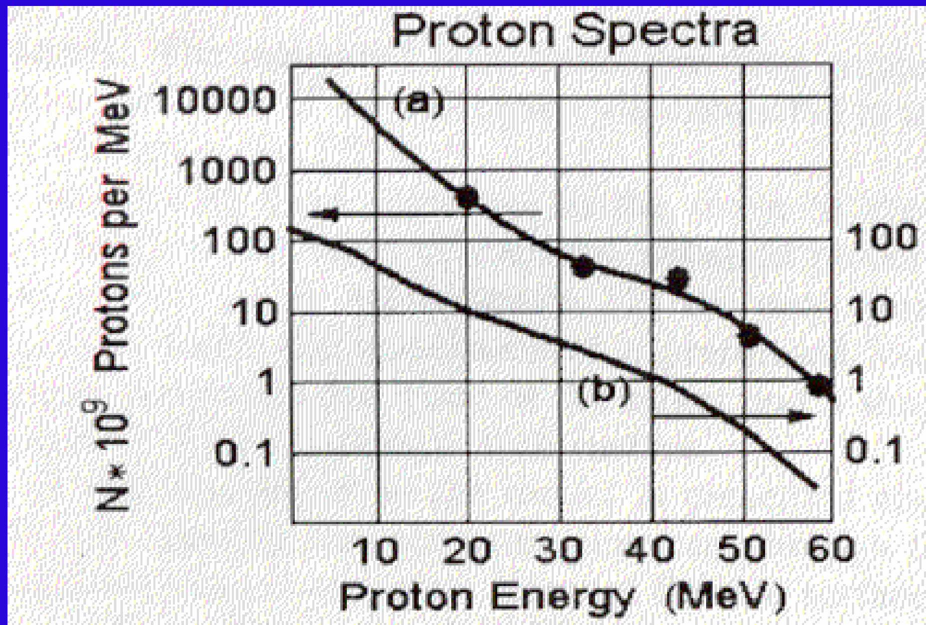
** Scanning only

Laser based acceleration



Laser based acceleration

Energy spectrum

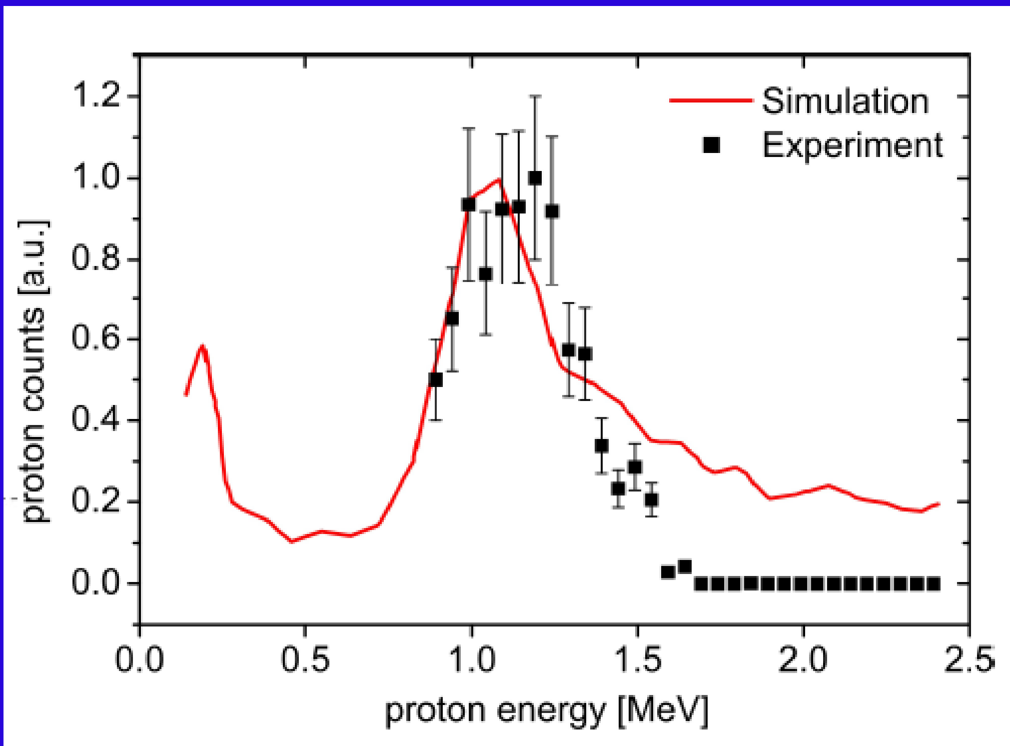


- <u>Maximum</u> proton energy reported so far is $E_p \approx 60$ MeV
- High intensity (10^9-10^{11} protons) in very short pulse (~ns)
- Very poor (broad) energy spectrum

R. A. Snavely, *et al., Phys. Rev. Lett.* Vol. 85, 2945, (2000)

Laser based acceleration

Achieving mono-energetic spectrums



$I = 3 \times 10^{19}$ W/cm^2

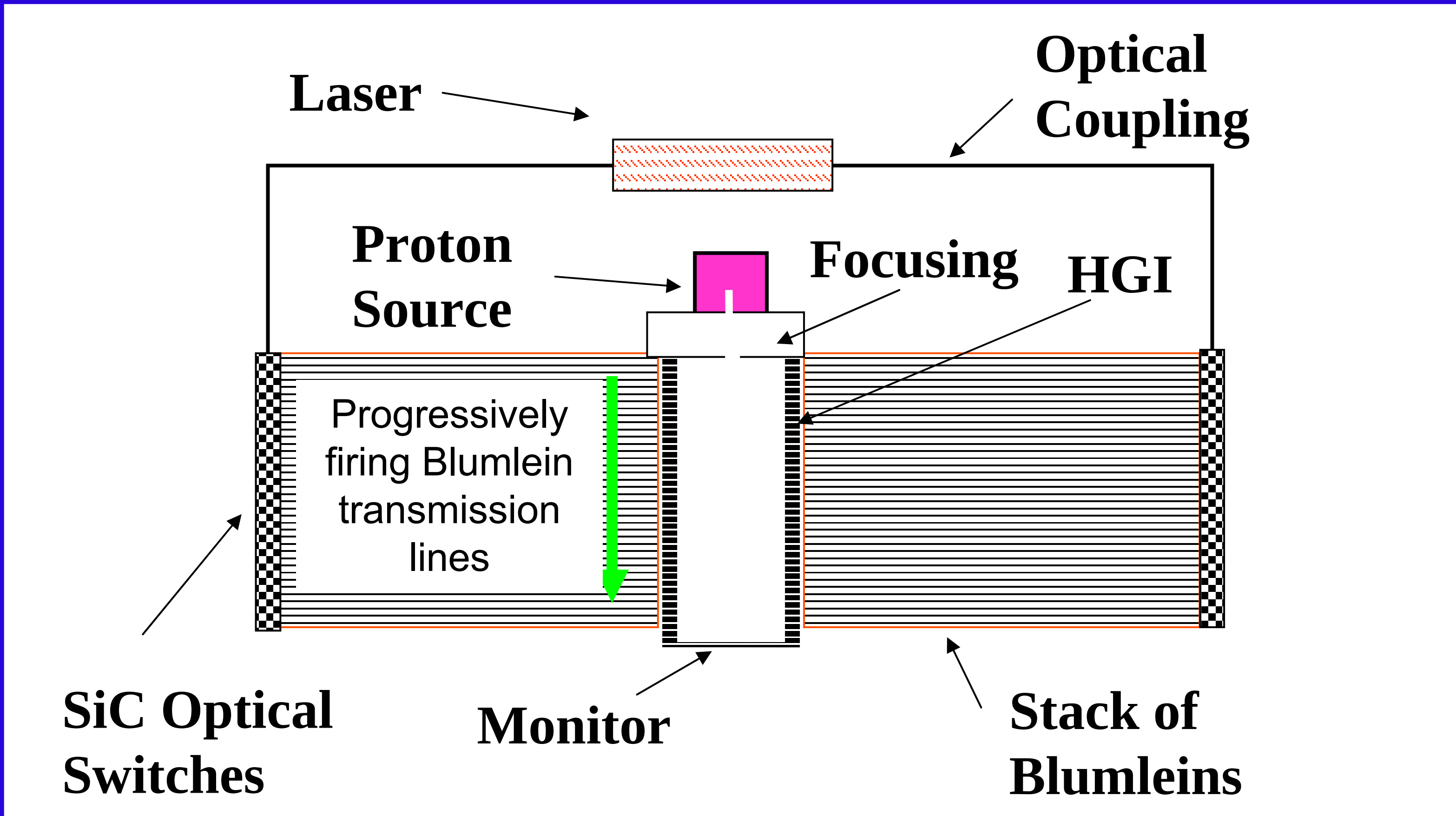
5µm thick Ti foil

0.5µm thick PMMA dot (20x20µm)

1.2 MeV ‘mono’-energetic protons produced

Schwoerer et al, Nature 439, 445 (2006)

Dielectric Wall Accelerators



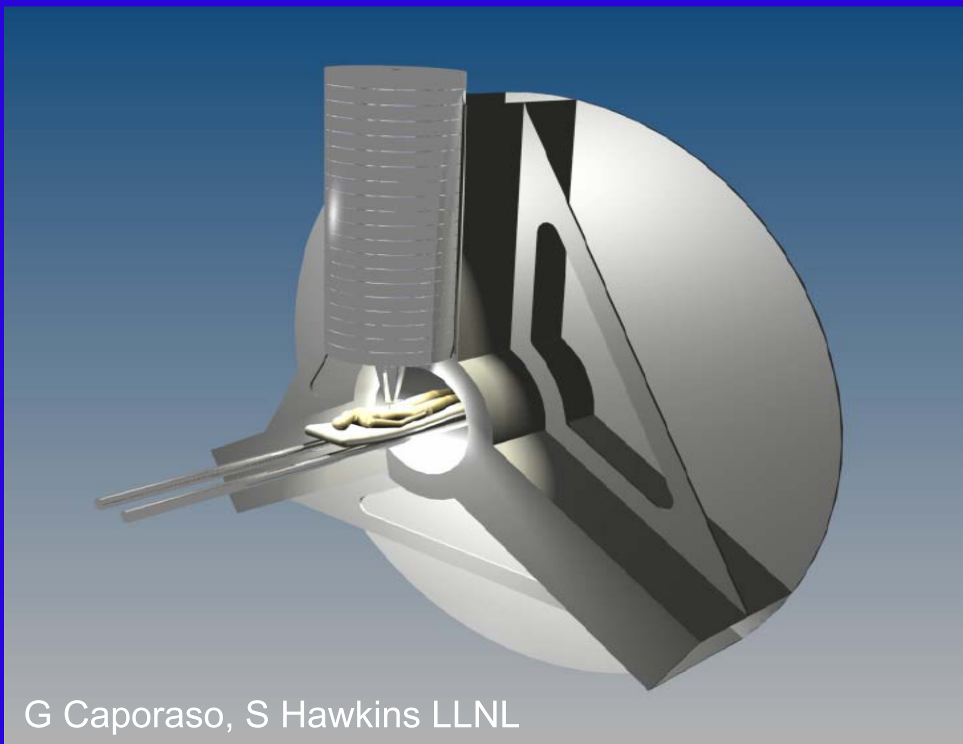
Thanks to Rock Mackie, UWisc/Tomotherapy Inc

Dielectric Wall Accelerators

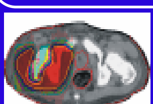
- DWA is a multi-stage inductive accelerator under development at Lawrence Livermore National Lab.
- Acceleration gradient of 100 MV/m possible.
- 200 MeV protons in 2 meters.
- This has been demonstrated in 'small' examples, with lengths of 2mm!
- Beam energy, intensity and spot size variable pulse-to-pulse.

Dielectric Wall Accelerators

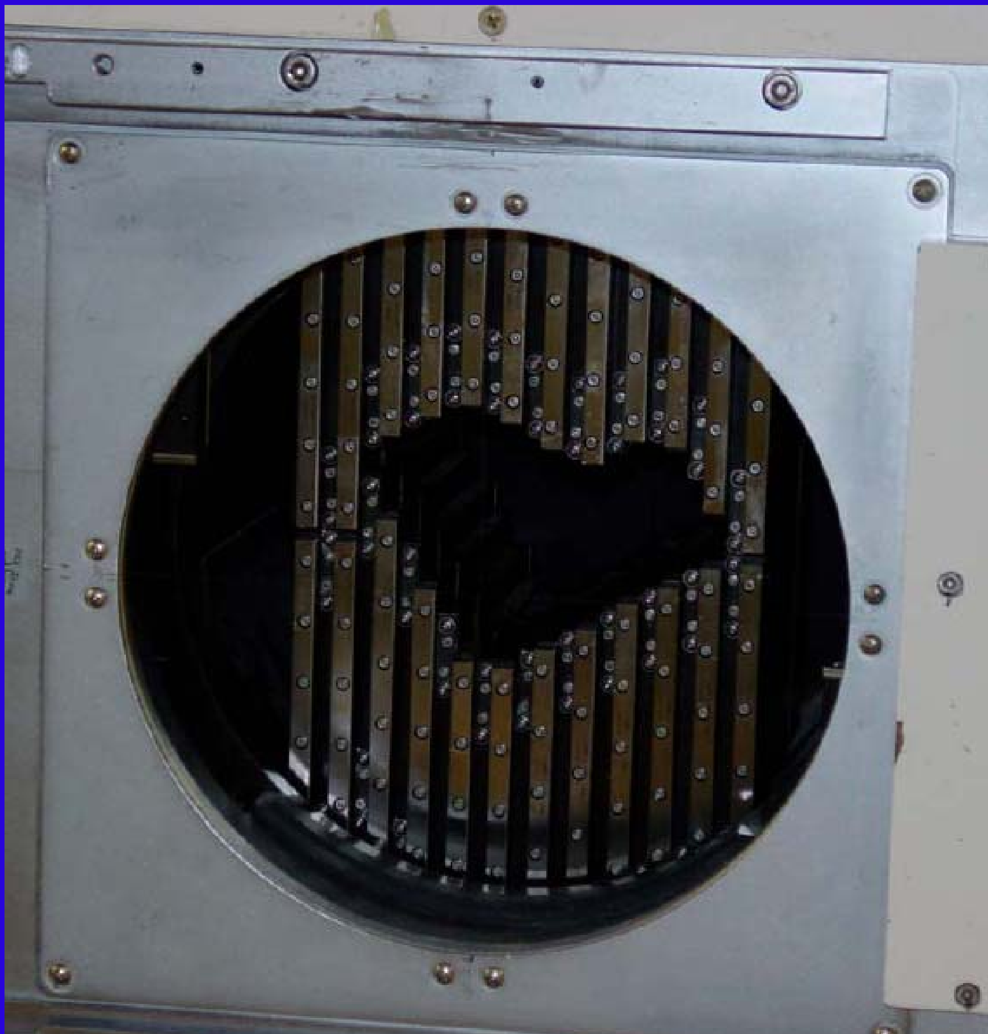
Proton tomotherapy



- Incorporation of DWA into a CT like treatment gantry for rotational delivery of proton therapy
- Single room facility
- Diameter ~ 5m
- Under investigation by Tomotherapy Inc. and LLNL



Proton Multi-leaf collimators



Particle MLC from Chiba (Japan)

- Saves changing collimators every field
- Can be used to 'simulate' scanning

Proton Multi-leaf collimators

Film dosimetry performed at Loma Linda using MLC and passively scattered proton beam

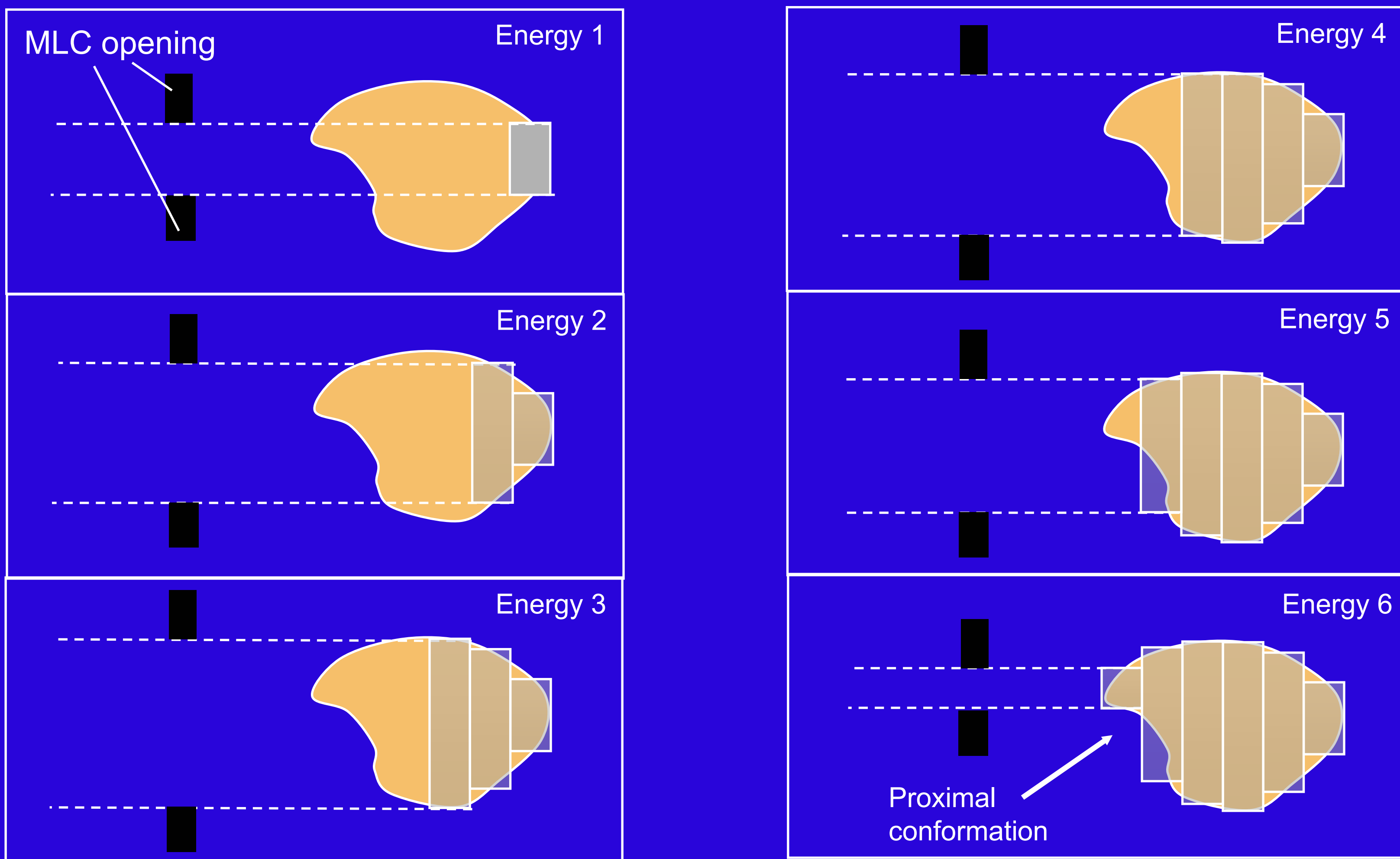
Shape at surface

Shape after 29cm water

Mike Moyers, Loma Linda

Proton Multi-leaf collimators

Simulated scanning using dynamic MLC's



Overview of presentation

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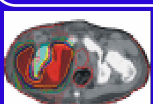
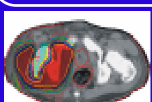
- Potential solutions
- Summary



Current challenges

- The neutron problem
- Range uncertainty
- Dealing with organ motion



Neutron dose during proton therapy: Is there a problem?

Hall, E. Intensity-modulated radiation therapy, protons, and the risk of second cancers. *Int J Radiat Oncol Biol Phys 2006 ; 65 : 1–7*

Neutron equivalent dose a factor 10 higher for passive protons than for IMRT?

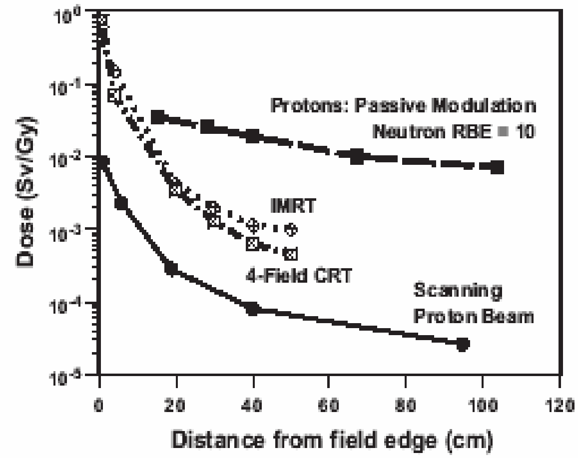
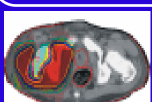


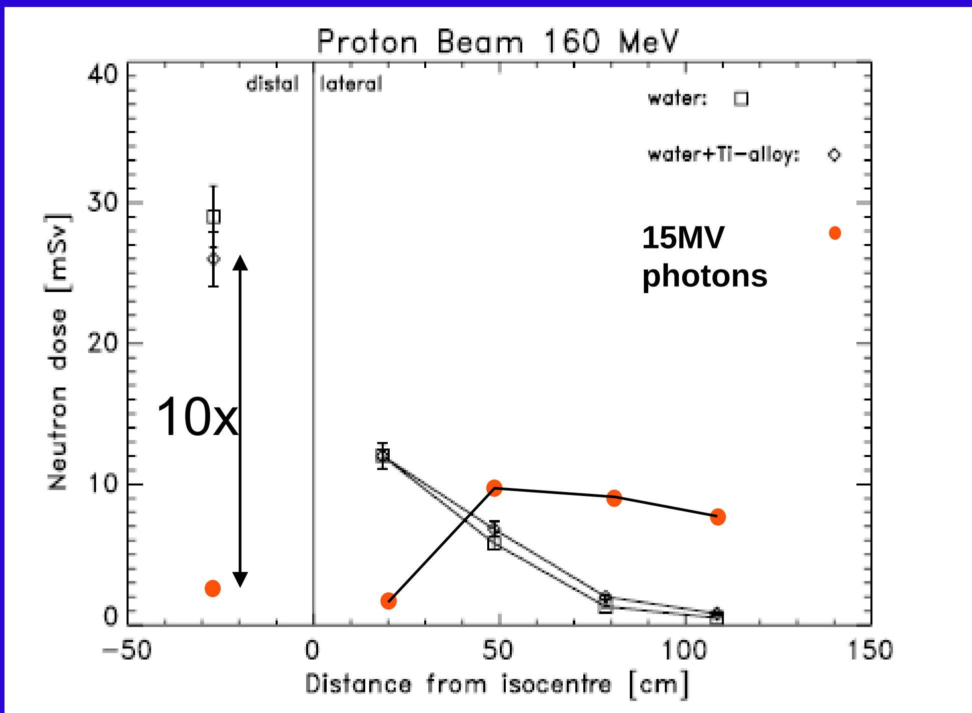
Fig. 10. The equivalent dose outside the edge of the treatment field as a fraction of the dose at the isocenter for protons with passive modulation, for a scanning proton beam, and for 6-MV X-rays, either 4-field conformal radiation therapy (CRT), or intensity-modulated radiation therapy (IMRT). The doses are rough estimates and are likely to be highly facility dependent. The passive-modulation: proton data are from Yan *et al*. (19), renormalized to a 10-cm × 10-cm field and to a neutron relative biologic effectiveness (RBE) or quality factor of 10. The pencil-beam scanning proton data are from Schneider *et al*. (18), renormalized to a 10-cm × 10-cm field and an RBE or quality factor of 10. Both proton curves were produced by Dr. Harald Paganetti, Massachusetts General Hospital and Harvard Medical School. X-ray data are 4-field CRT and IMRT. Unpublished data for a 6-MV linear accelerator were provided by Dr. C. W. Wuu, Columbia University Medical Center, New York.



Neutron dose during proton therapy: Is there a problem?

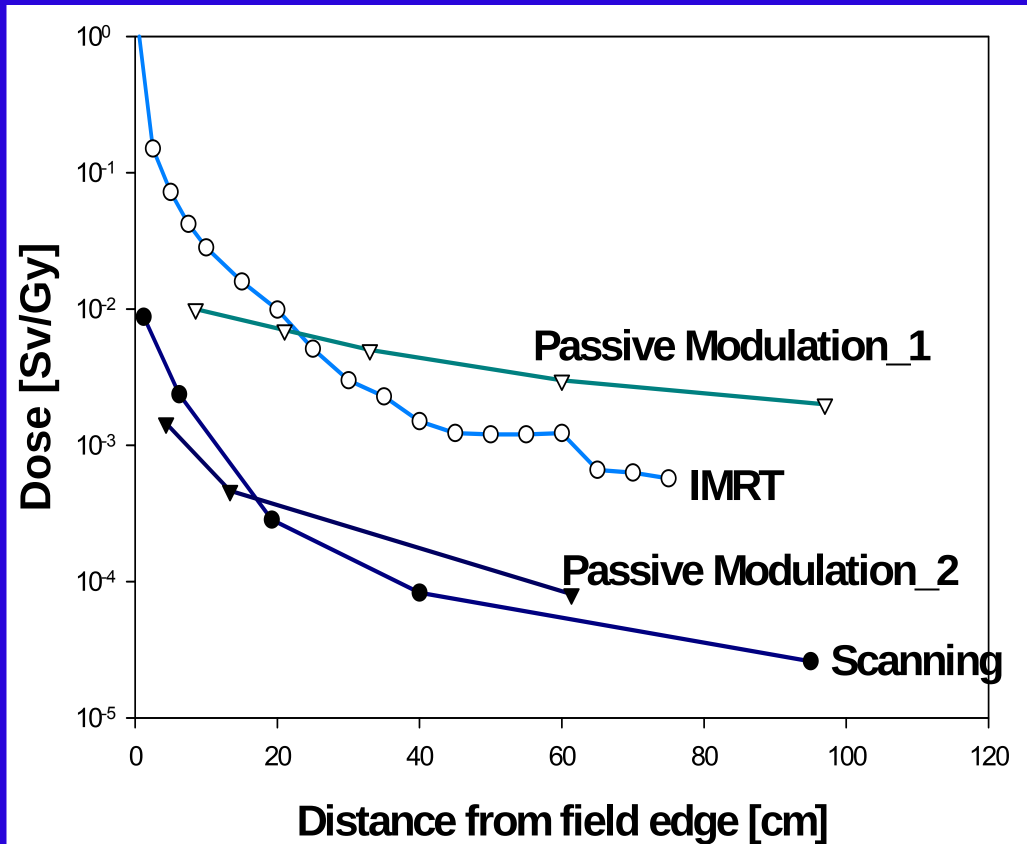
- Neutron dose equivalent from spot scanning and 15MV photons:
- Irradiation of 10 cm x 10 cm (x10cm) target to 50Gy

[Schneider U, Fiechtner A, Besserer J. Lomax A.J. Neutron dose from prosthesese materials during radiotherapy with protons and photons. Phys Med Biol 2004; 49:N119-124]



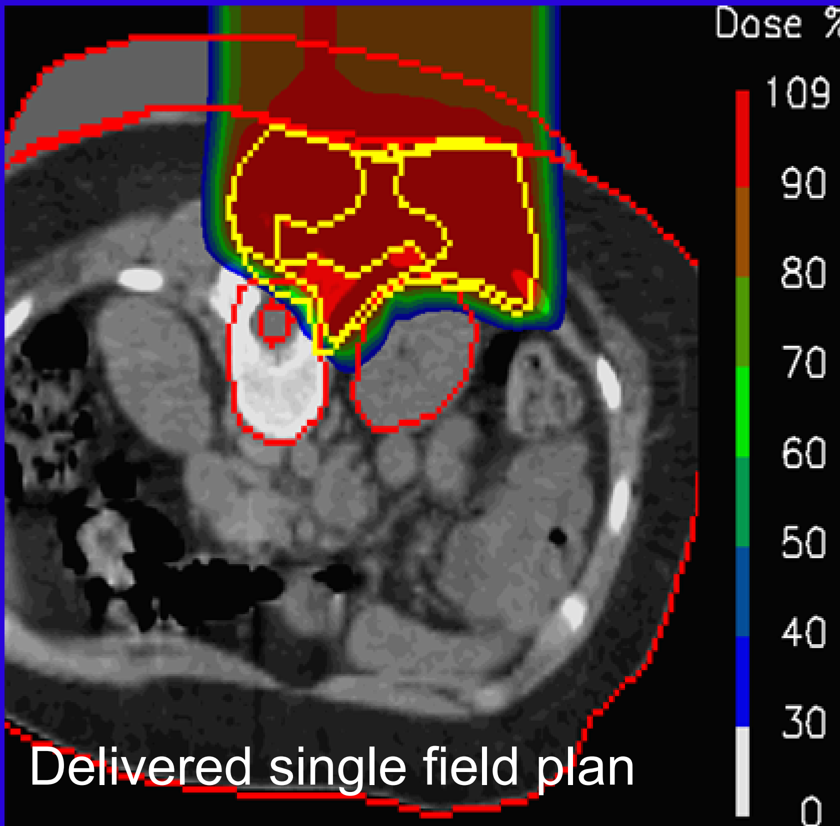
- Higher neutron dose in direction of beam
- Comparable neutron dose laterally
- Neutron dose very small compared to primary dose (~1000x smaller)

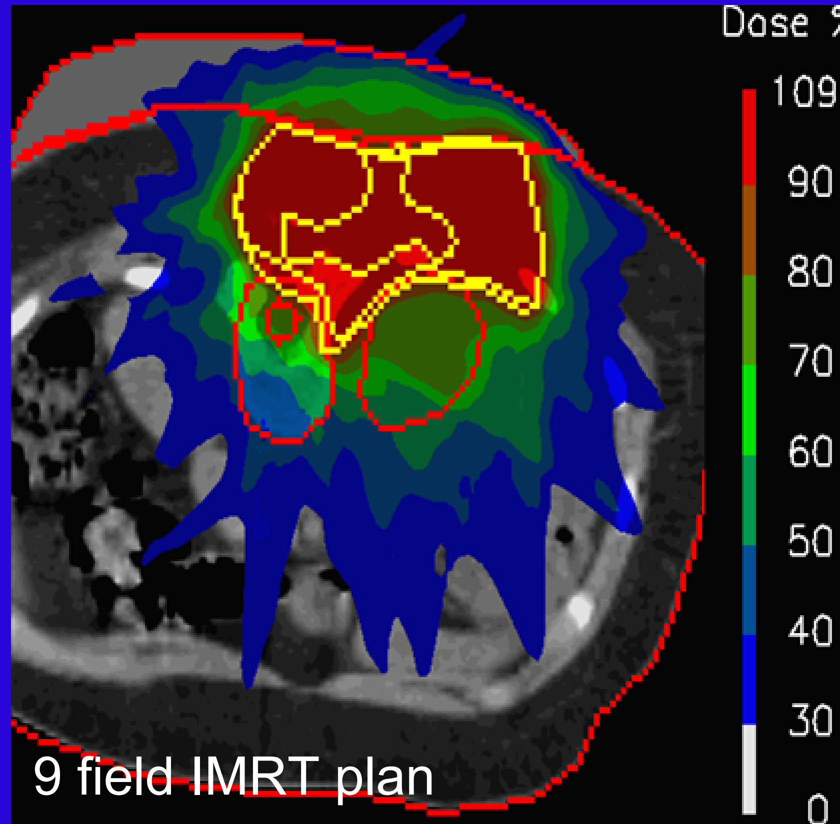
Neutron dose during proton therapy: Is there a problem?



Passive Modulation_1: Yan et al.
Passive Modulation_2: Mesoloras et al.
IMRT: Stovall et al. (3DCRT up-scaled by a factor of 3)
Scanning: Schneider et al.

Neutron dose during proton therapy: Is there a problem?

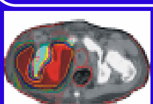




Don't forget primary dose – in this case reduced by a factor 6 for proton vs photons!

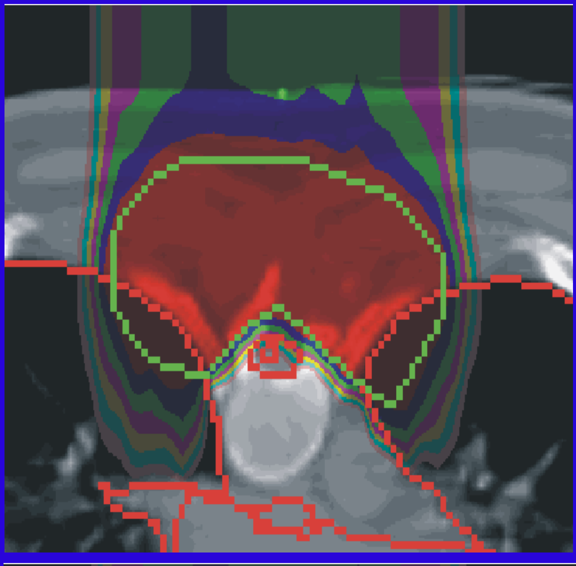
Current challenges

- The neutron problem
- Range uncertainty
- Dealing with organ motion

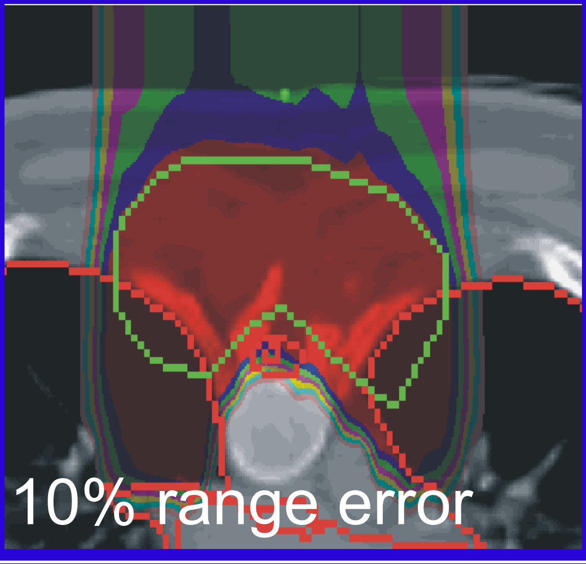


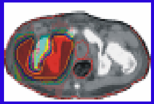
Range uncertainty

The advantage of protons is that they stop.



The disadvantage of protons is that we don't always know where…

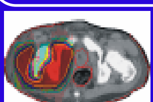




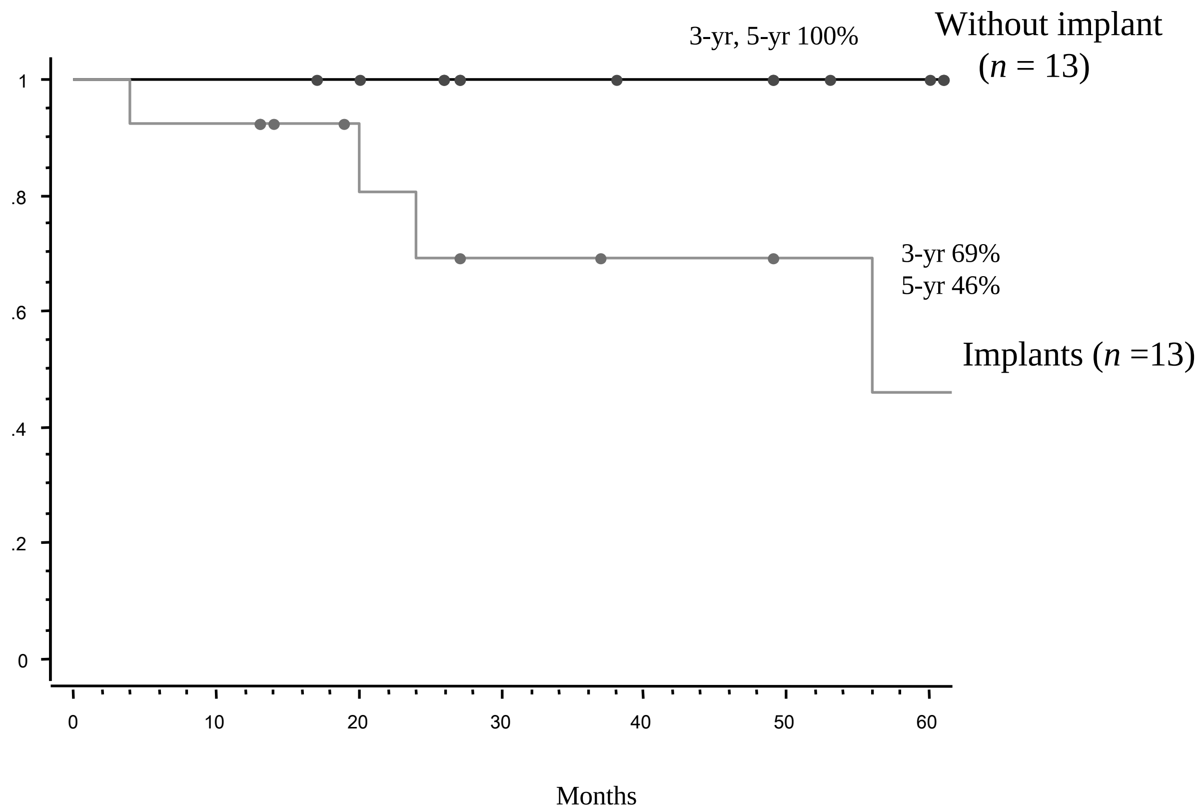
Sources of range uncertainties

- Limitations of CT data (beam hardening, noise, resolution etc) [Σ ~ 1%]
- Calibration of CT to stopping power [Σ ~ 1-2%]
- CT artifacts [Σ]

- Variations in proton beam energy [σ (~ 0.1%)]
- Variations in patient positioning [σ (~ 1-3mm)]
- Variations in patient anatomy [Σ,σ]

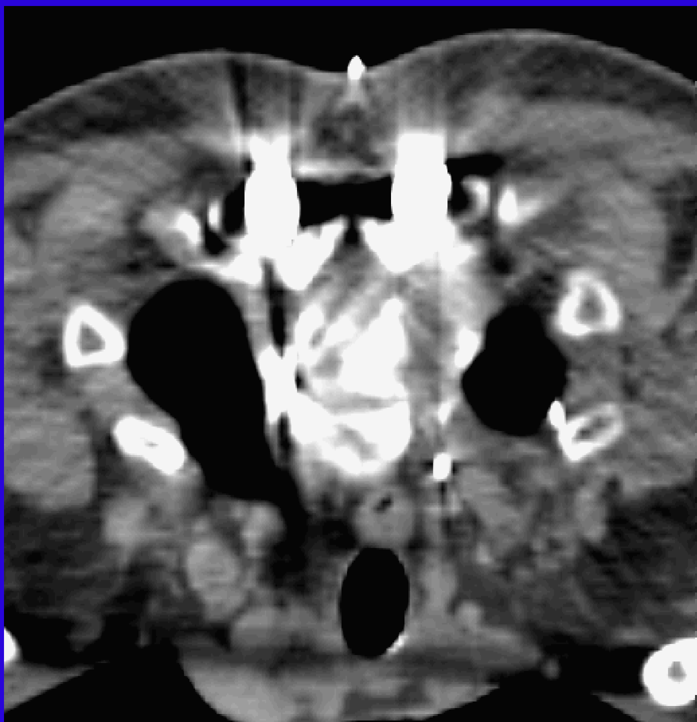


The problem of CT artifacts



Rutz et al (PSI), To be submitted to IJROBP

The problem of CT artifacts



- More advanced initial tumour at diagnosis?
- Problems in defining CTV?
- Problems in dose calculation?
- Problems in range calculations?

Rutz et al (PSI), To be submitted to IJROBP

Variations in patient anatomy

Patient set-up inaccuracies

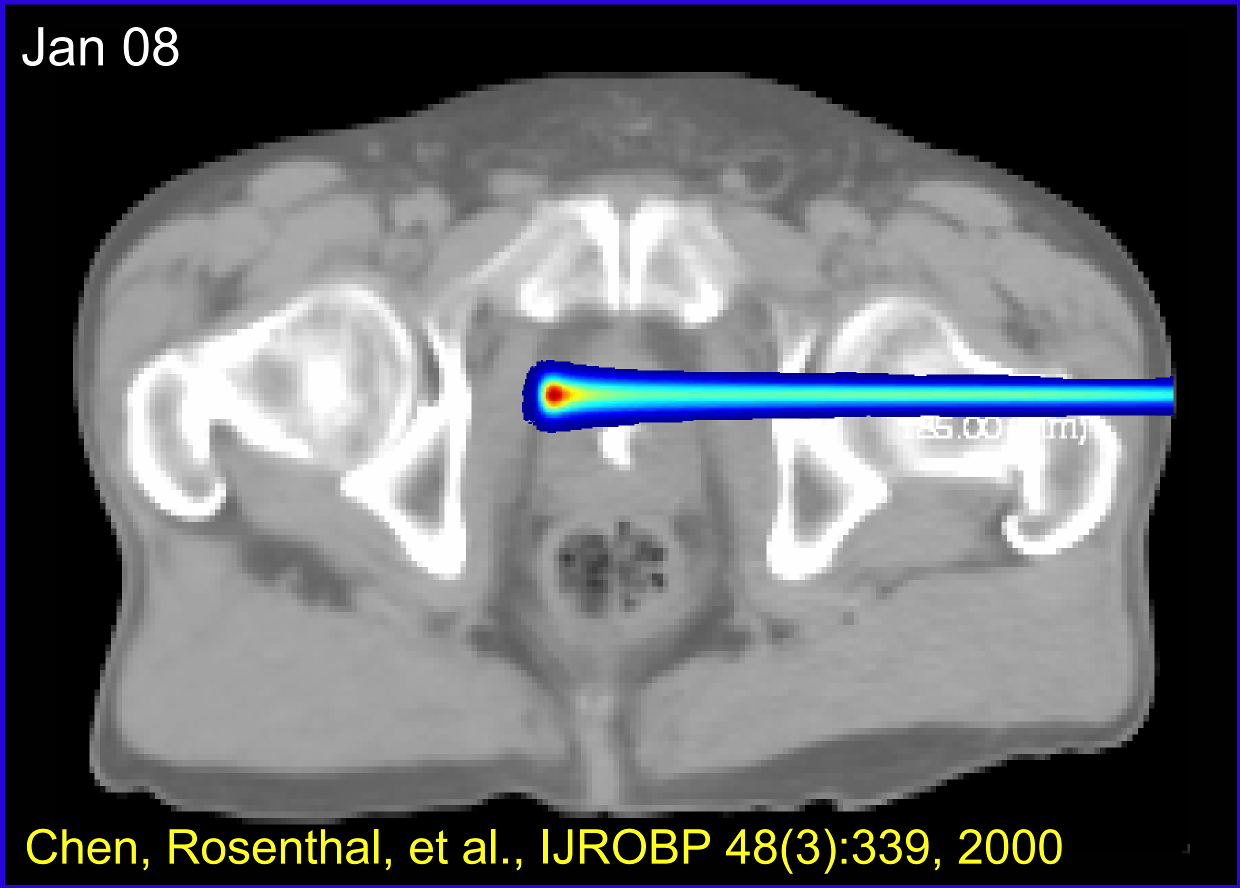


Image courtesy of Thomas Bortfeld, MGH, Boston

Variations in patient anatomy

Patient set-up inaccuracies

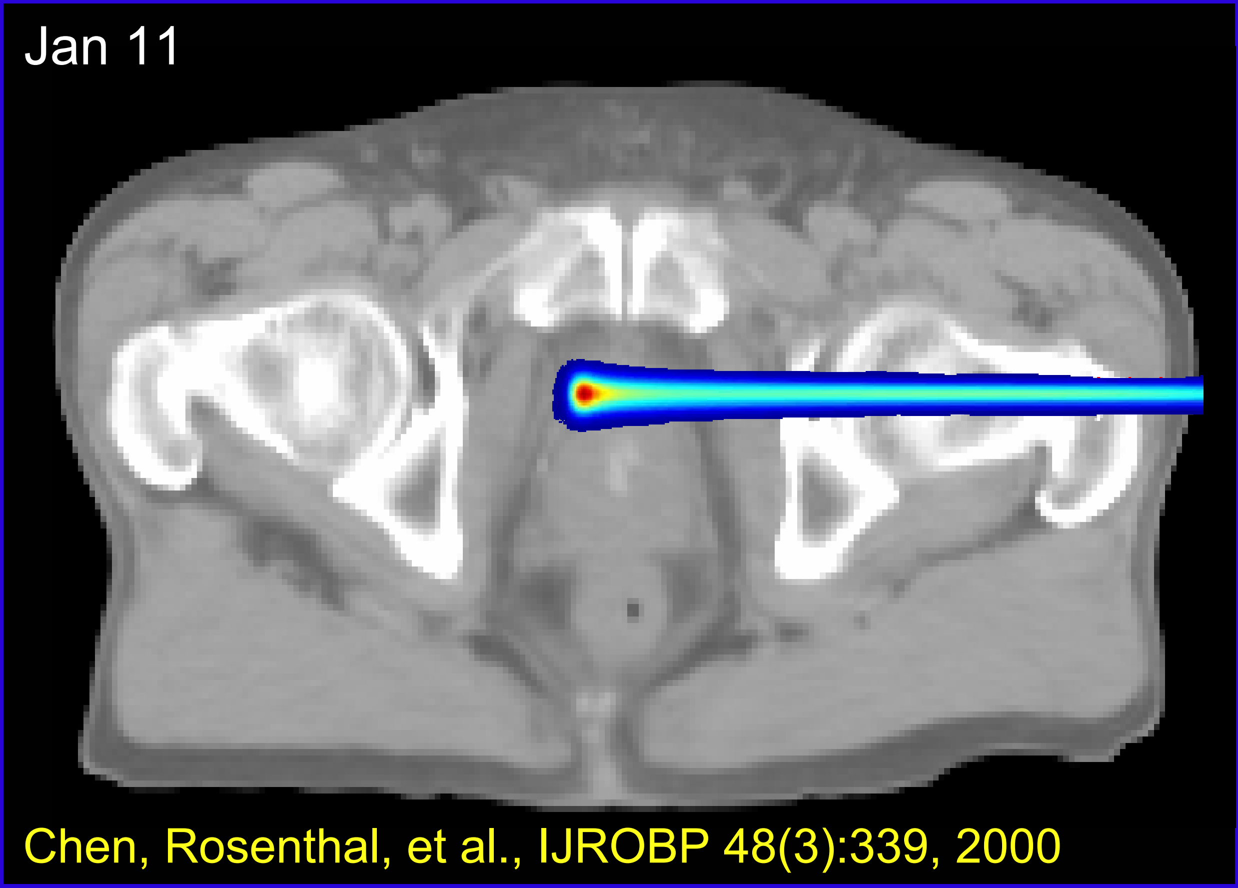
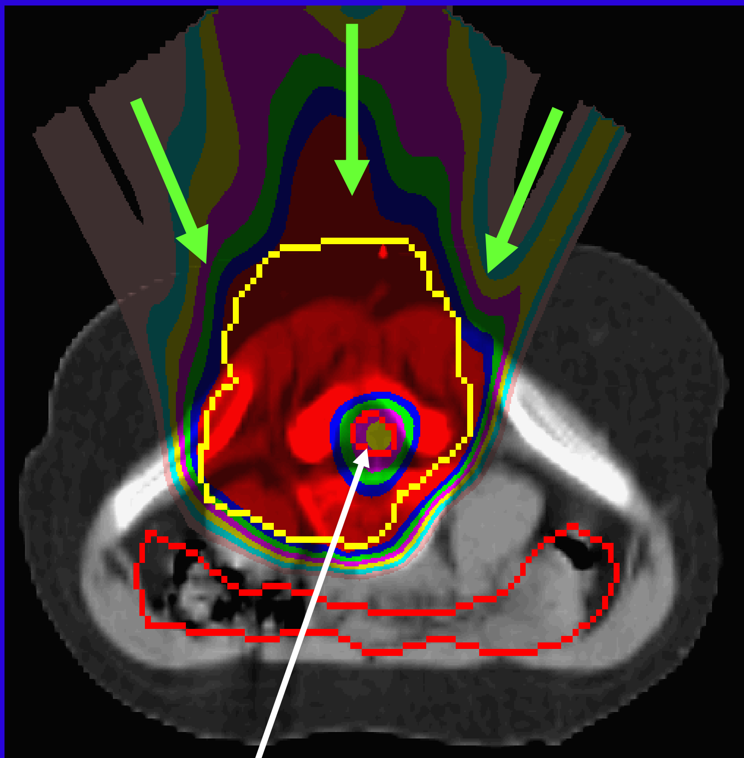


Image courtesy of Thomas Bortfeld, MGH, Boston

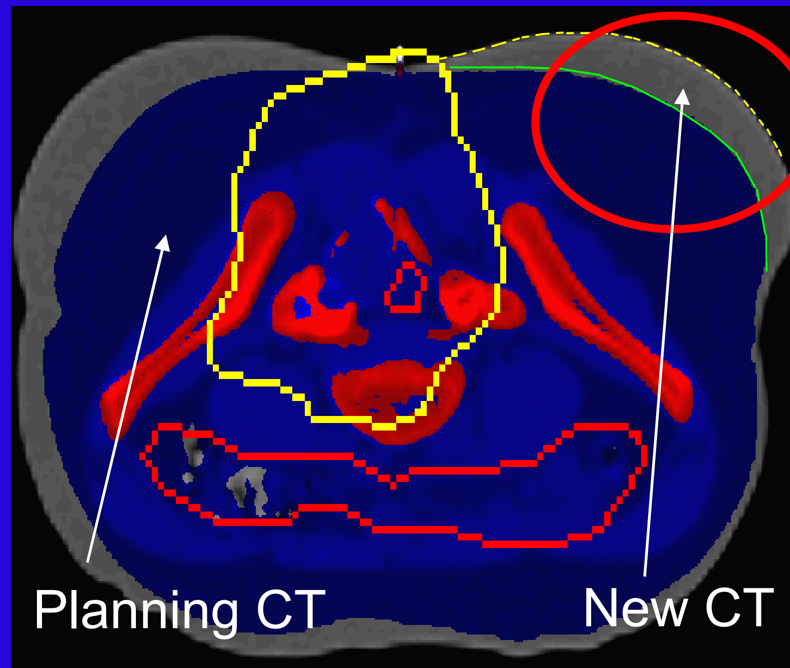
Variations in patient anatomy

3 field IMPT plan to an 8 year old boy



Note, sparing of spinal cord in middle of PTV

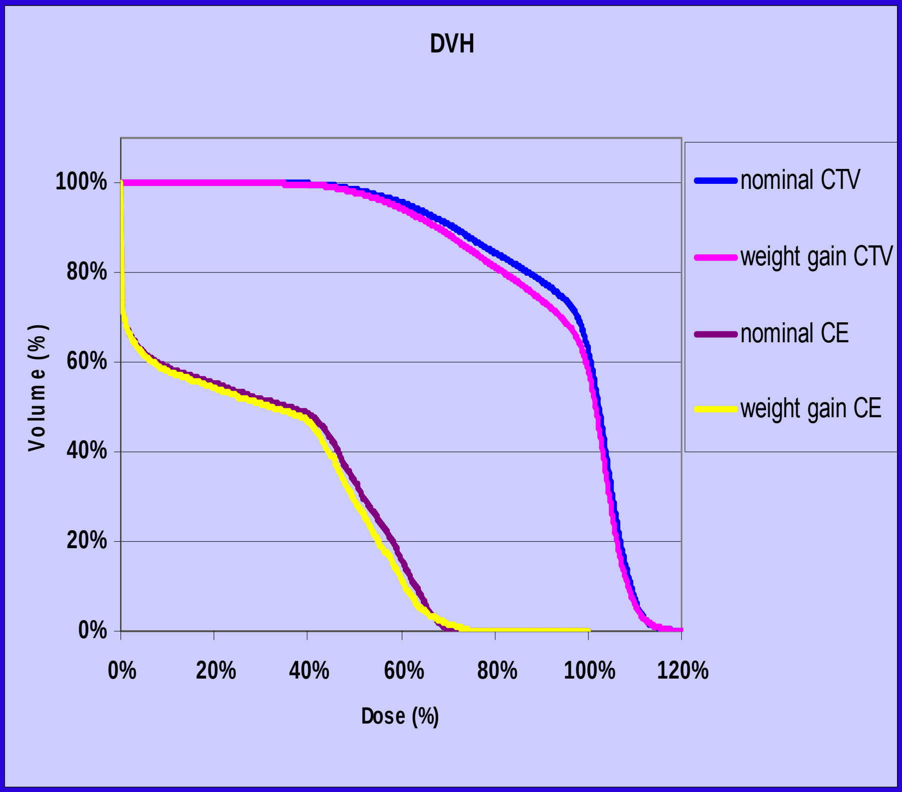
During treatment, 1.5kg weight gain was observed



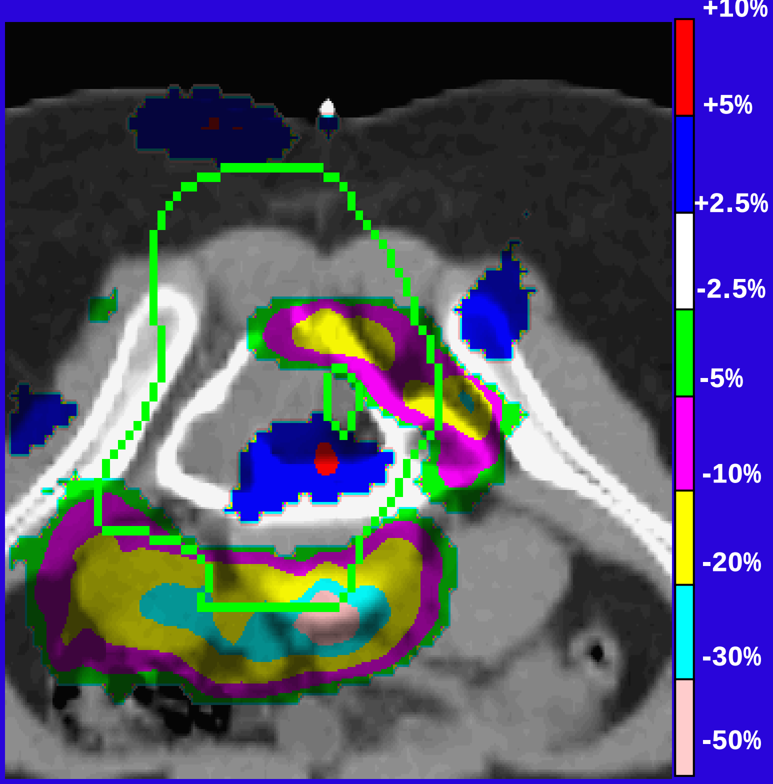
Max range differences:
SC 0.8cm
CTV 1.5cm

Francesca Albertini and Alessandra Bolsi (PSI)

Variations in patient anatomy



Dose differences

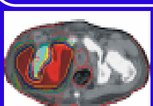


Differences between nominal and 'weight gain' CT's

Francesca Albertini and Alessandra Bolsi (PSI)

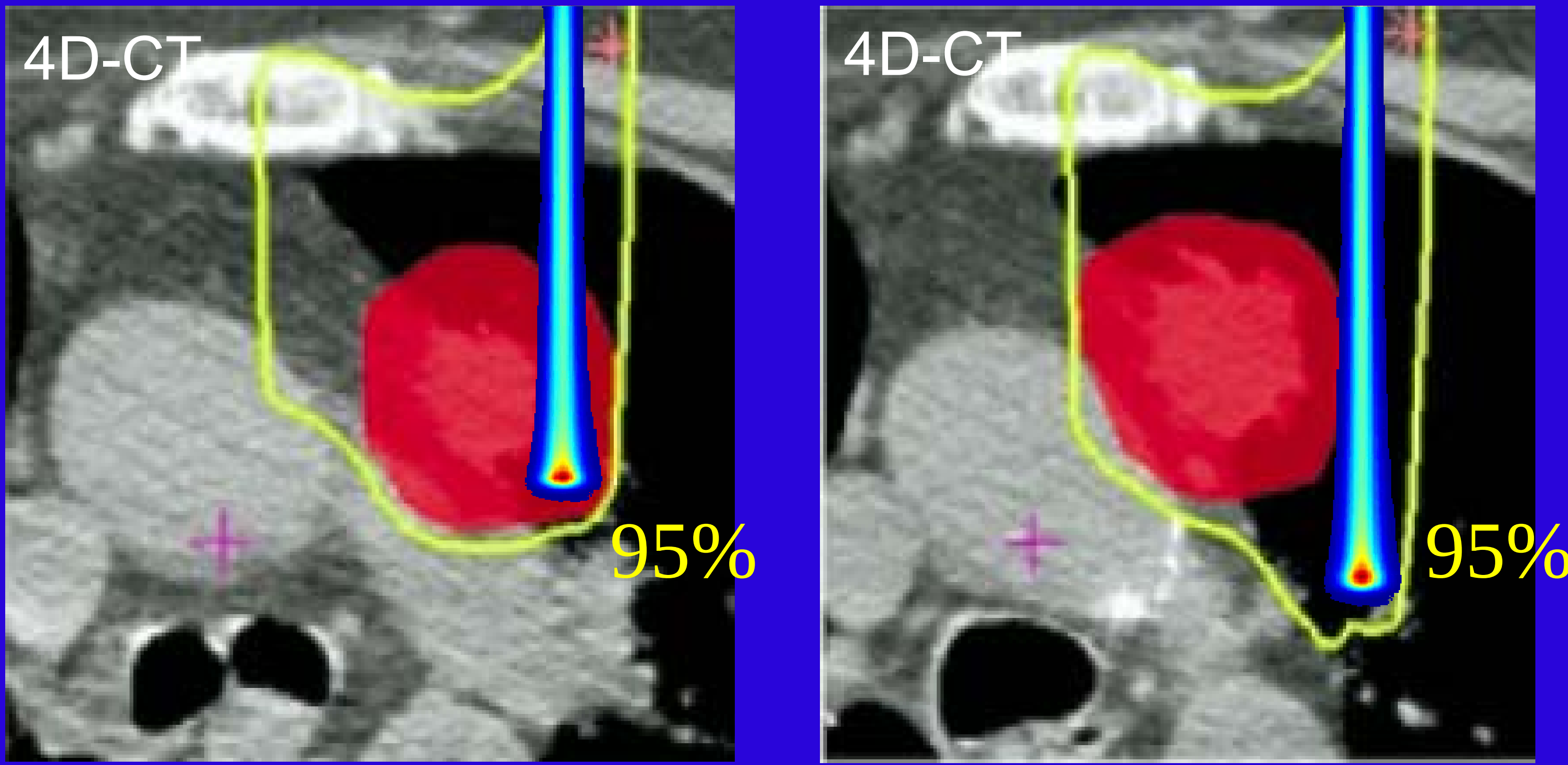
Current challenges

- The neutron problem
- Range uncertainty
- Dealing with organ motion



Organ motion and range uncertainty

exhale inhale

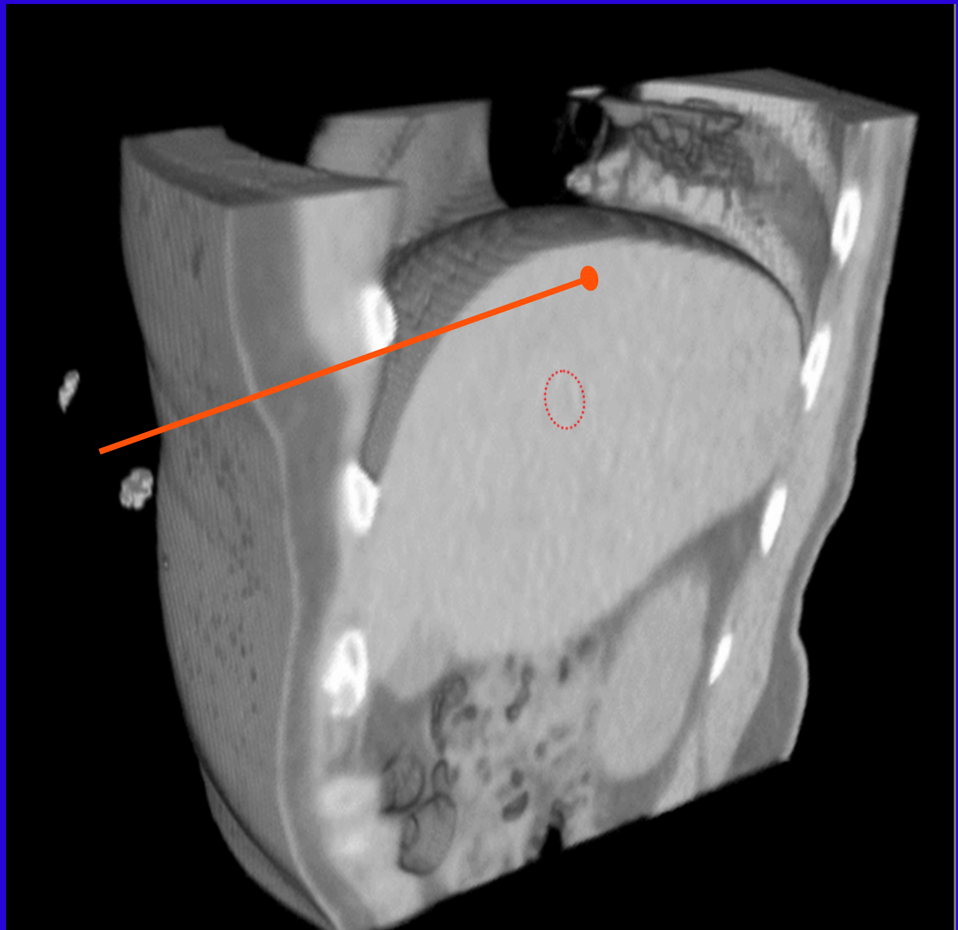


Engelsman et al., IJROBP 64(5):1589-1595, 2006

Images courtesy of Thomas Bortfeld, MGH, Boston

Organ motion and the ‘interplay’ effect

A scanned beam in a static patient…

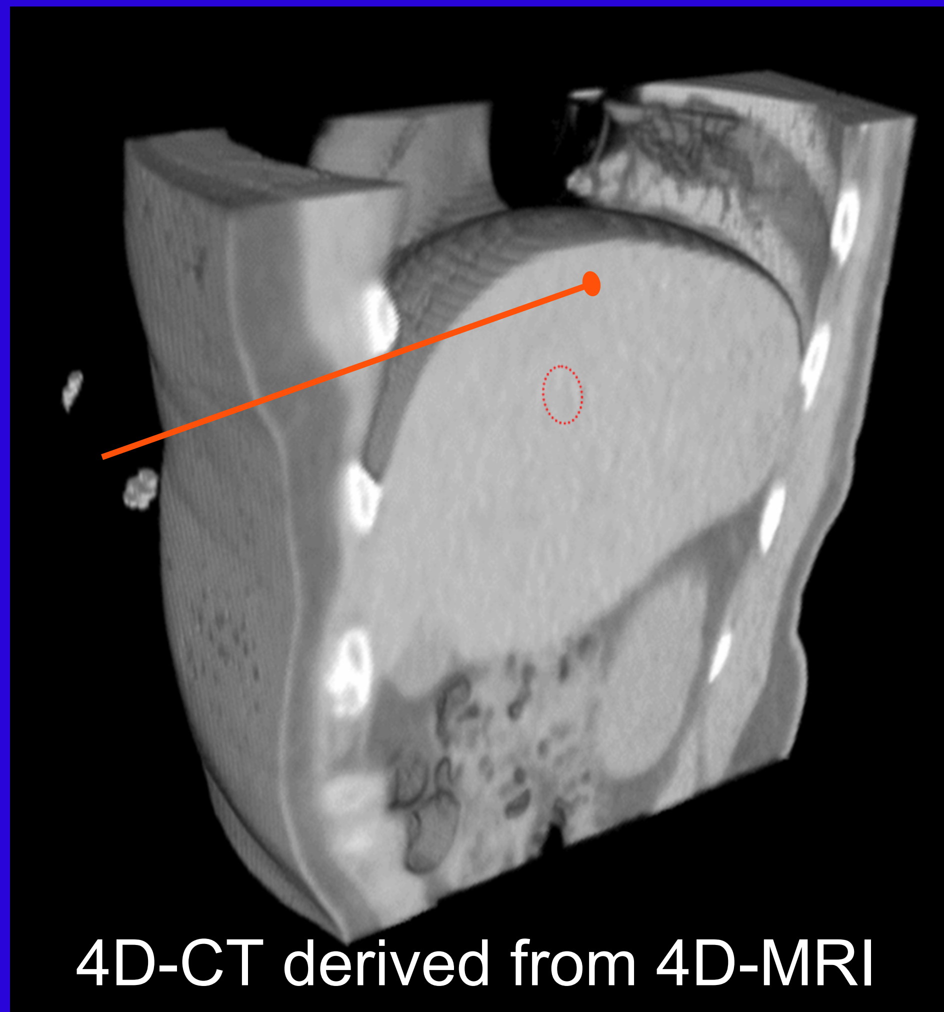


4D-CT derived from 4D-MRI

Martin von Siebenthal, Phillipe Cattin, Gabor Szekely, Tony Lomax, ETH, Zurich and PSI, Villigen

Organ motion and the 'interplay' effect

…but real patients move.



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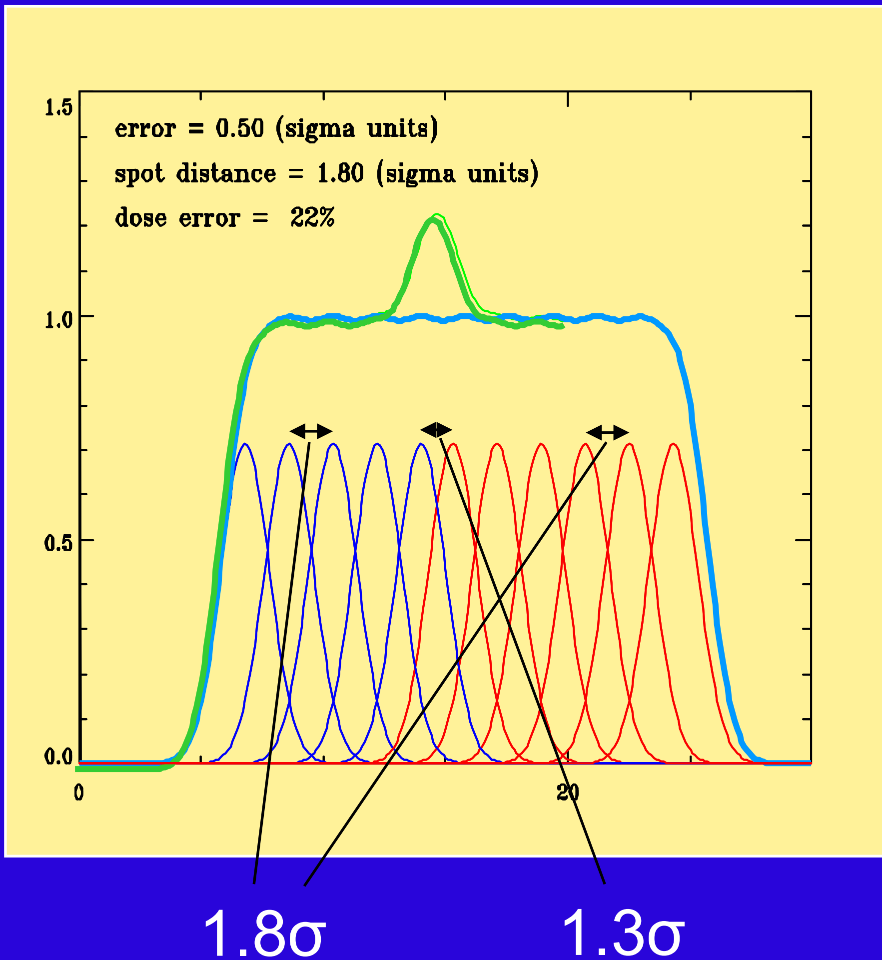


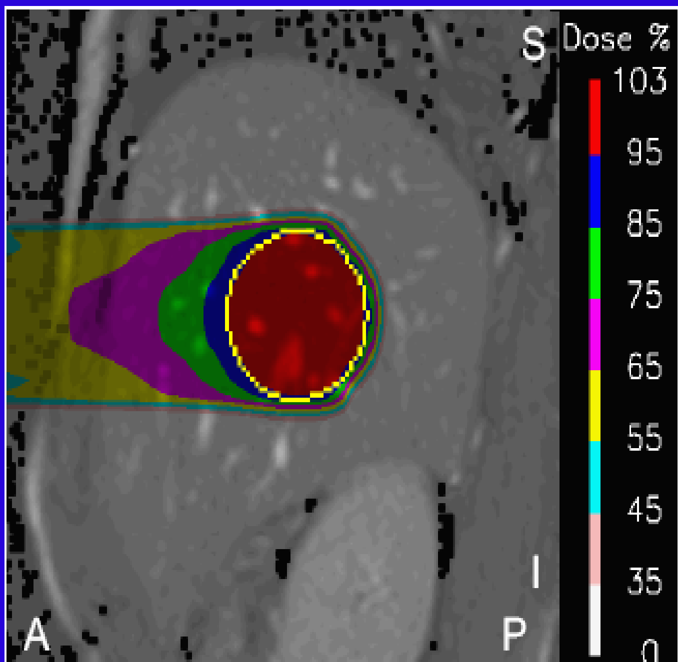
Assume σ = 0.5cm

For this example, dose errors of ~20% can result from motion (positioning) errors of 2.5mm

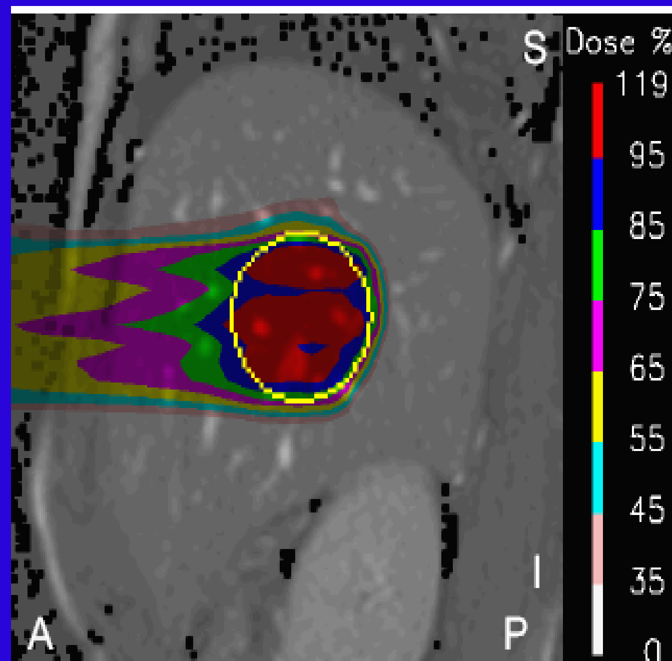
Phillips et al., PMB, 37:223-234,1992

Organ motion and the 'interplay' effect

Nominal (static) dose



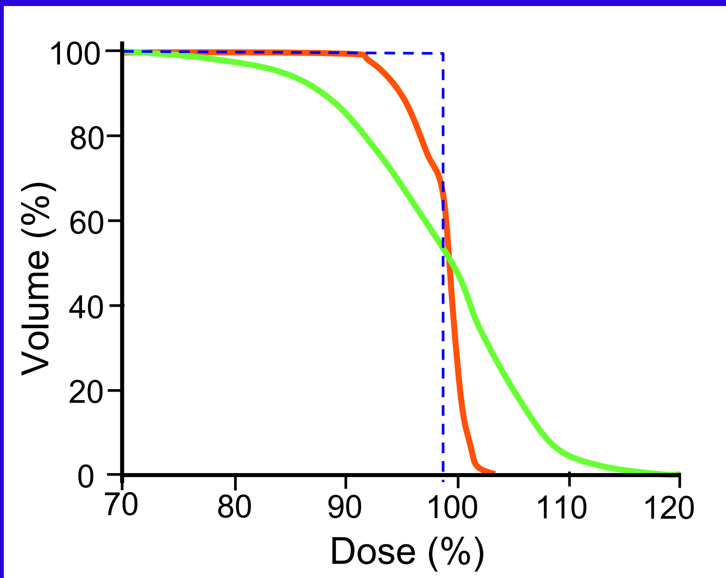
Calculated with 'real' motion from 4D-MRI of volunteer



Organ motion and the 'interplay' effect

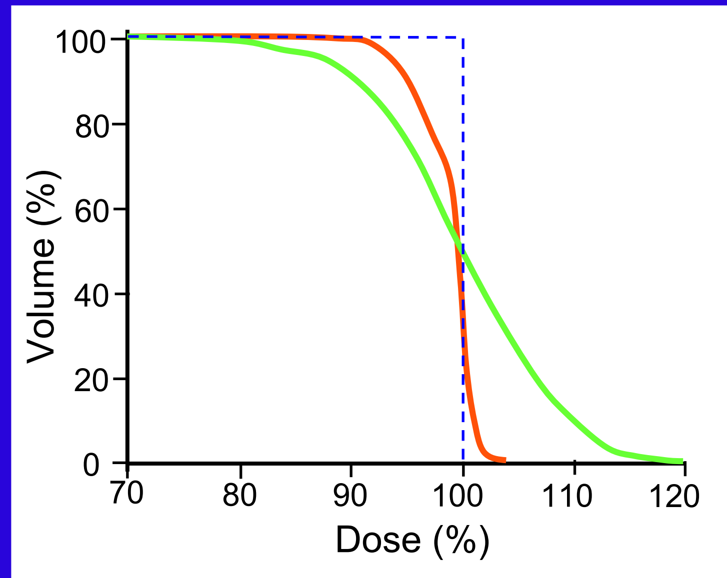
Motion patient 1

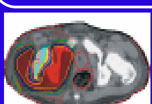
Amplitude ~ 11mm



Motion patient 2

Amplitude ~ 8mm





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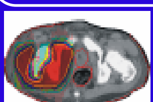
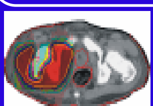
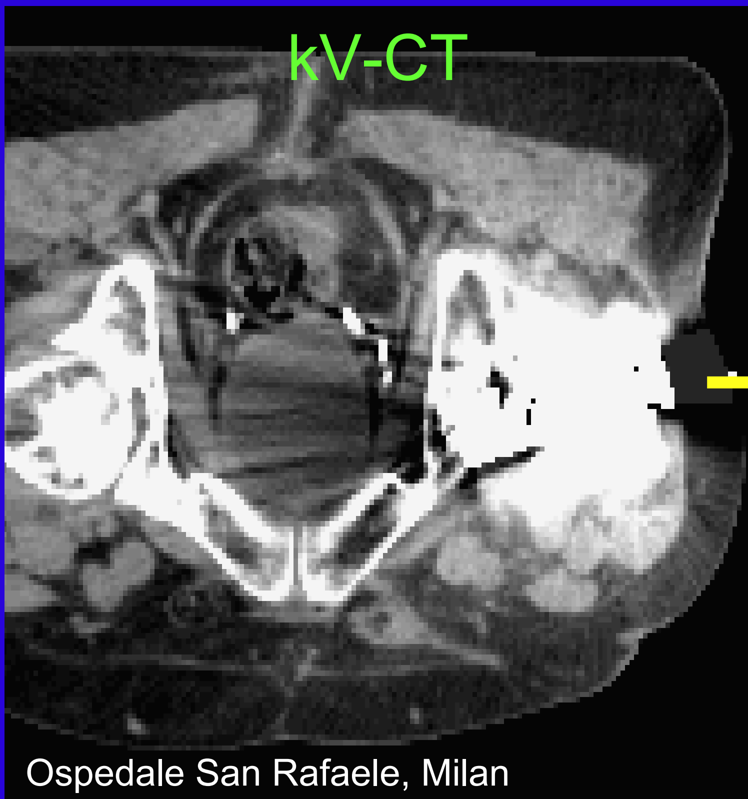


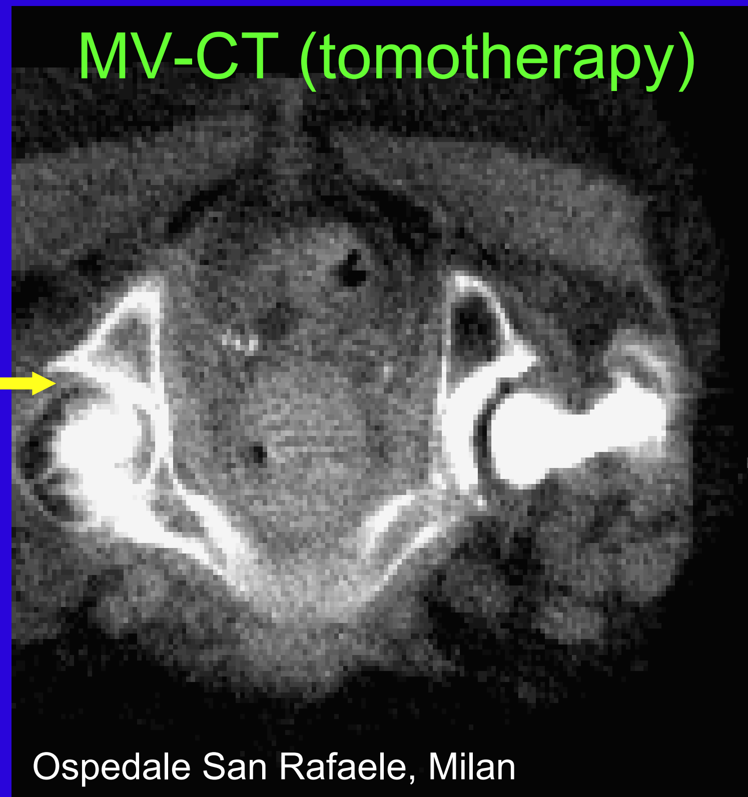
Potential solutions to …

- …range uncertainty
- …the organ motion problem



Mega-Voltage CT for artifact free imaging



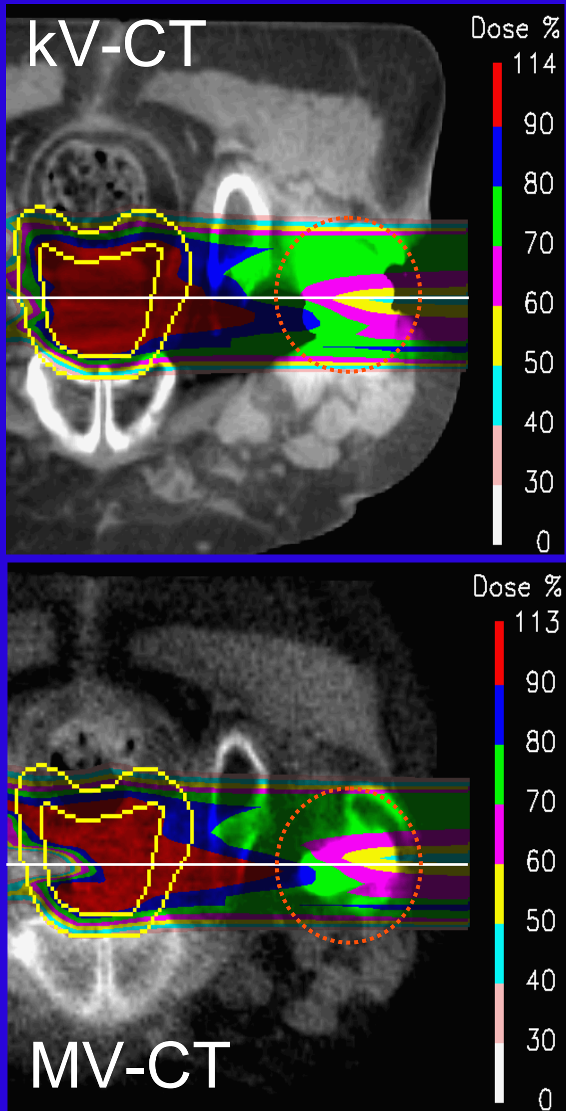


Accuracy of range calculation due to reconstruction artifacts?

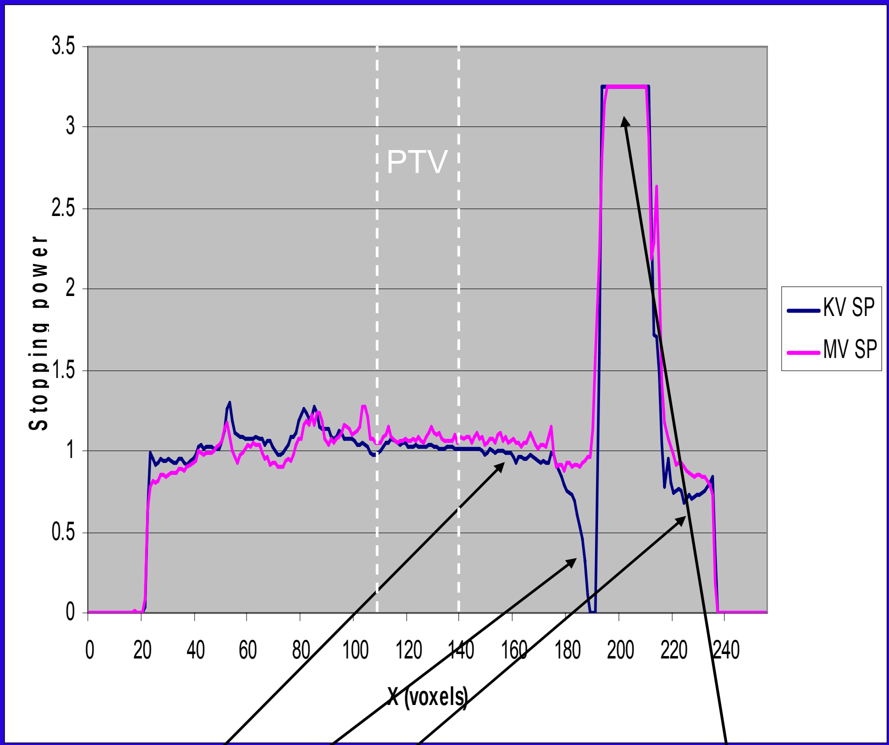
No artifacts and linear relationship CT units to proton stopping power

Francesca Albertini (PSI)

Mega-Voltage CT for artifact free imaging



Stopping power profiles



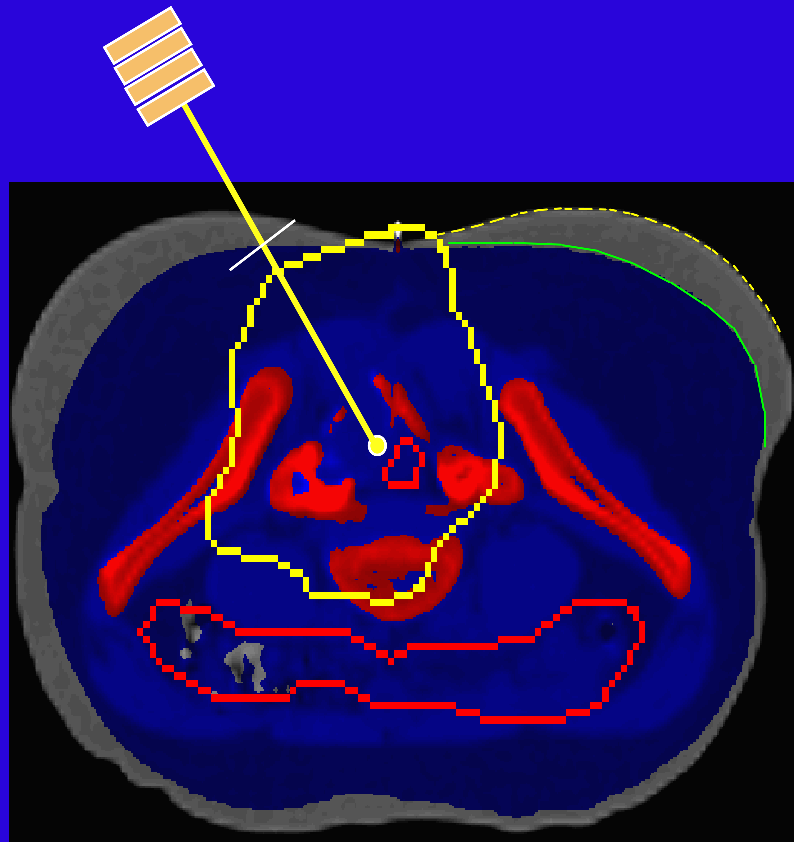
kV-CT artifacts

Prosthesis

Francesca Albertini (PSI)

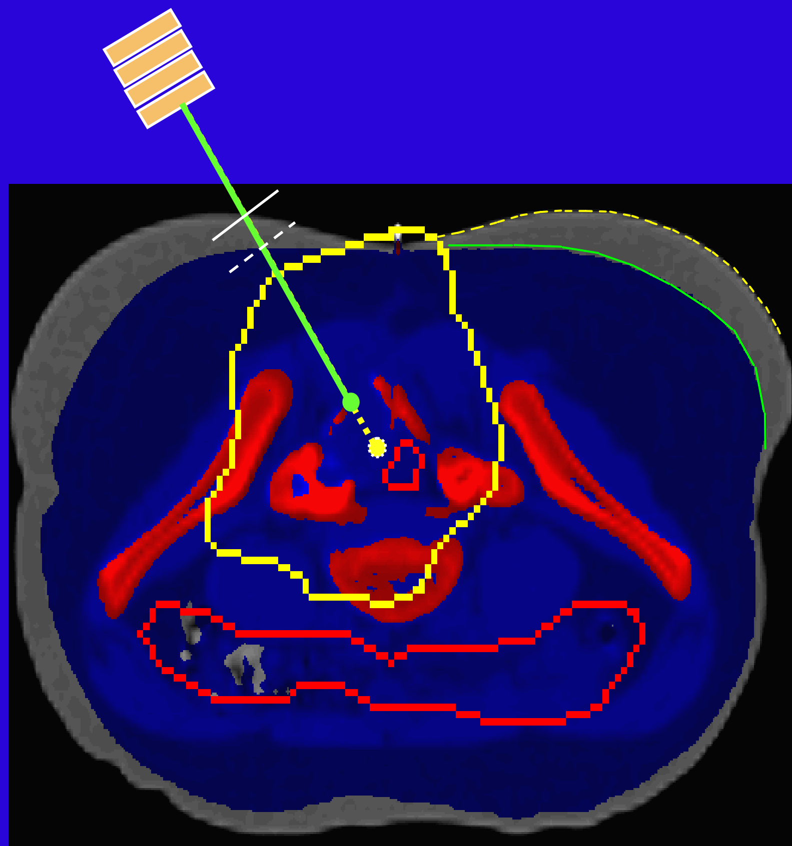
Range adapted proton therapy

Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range



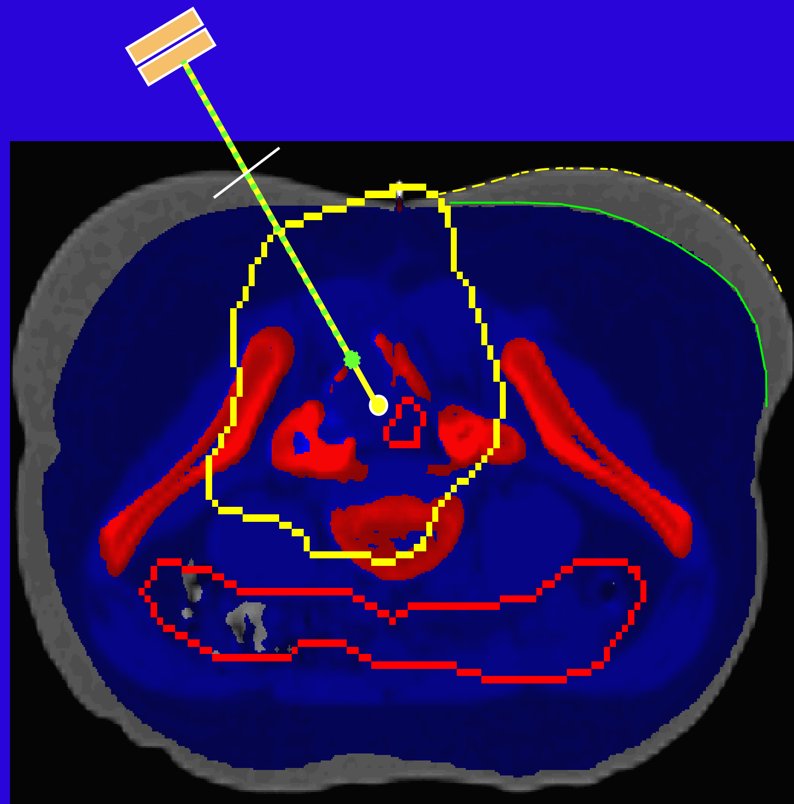
Range adapted proton therapy

Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range

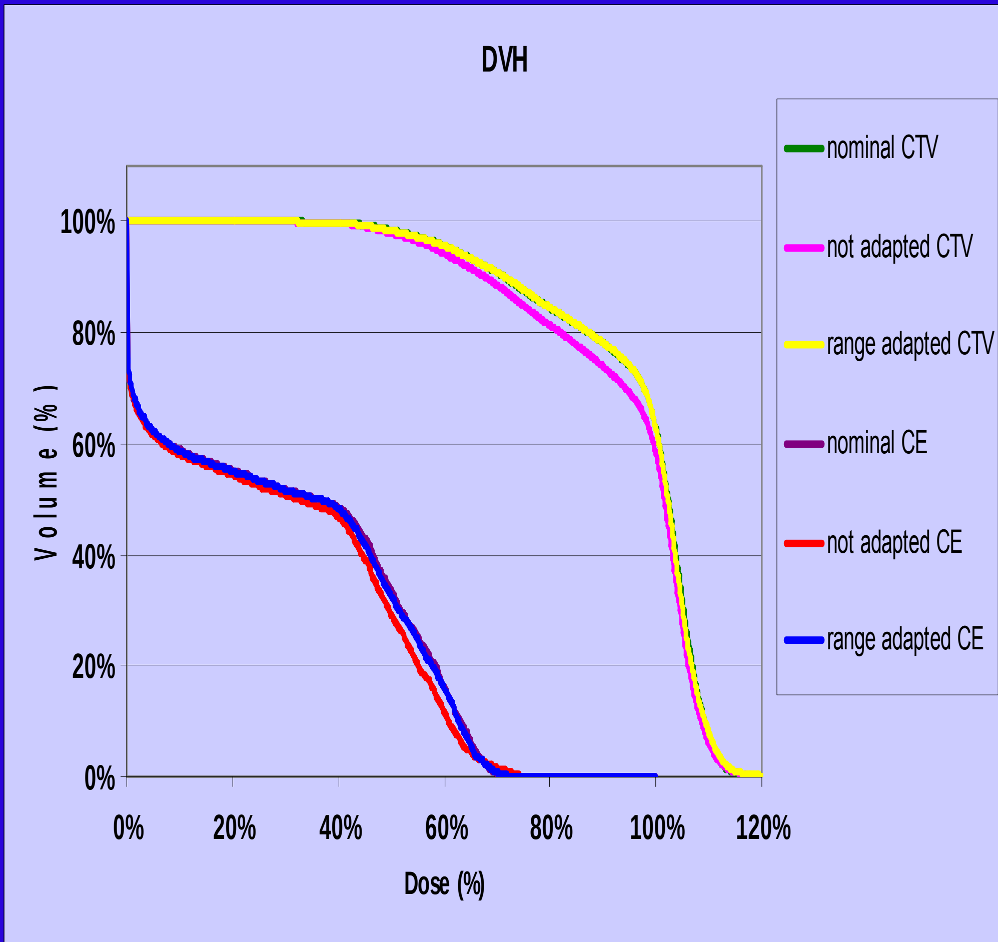


Range adapted proton therapy

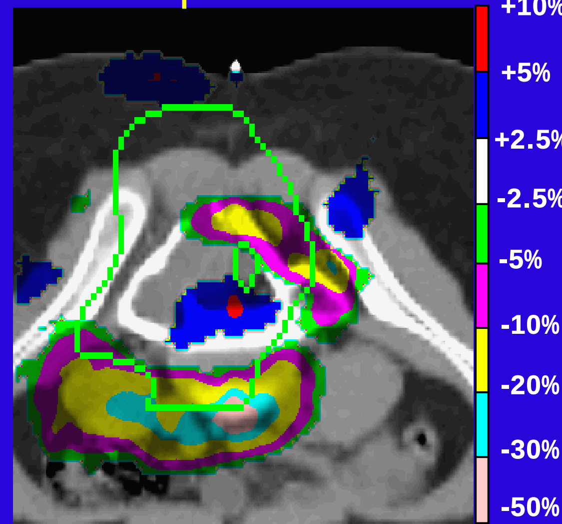
Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range



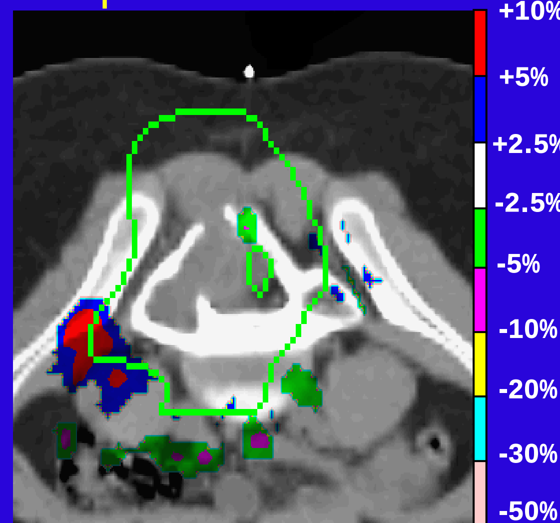
Range adapted proton therapy



not adapted-nominal

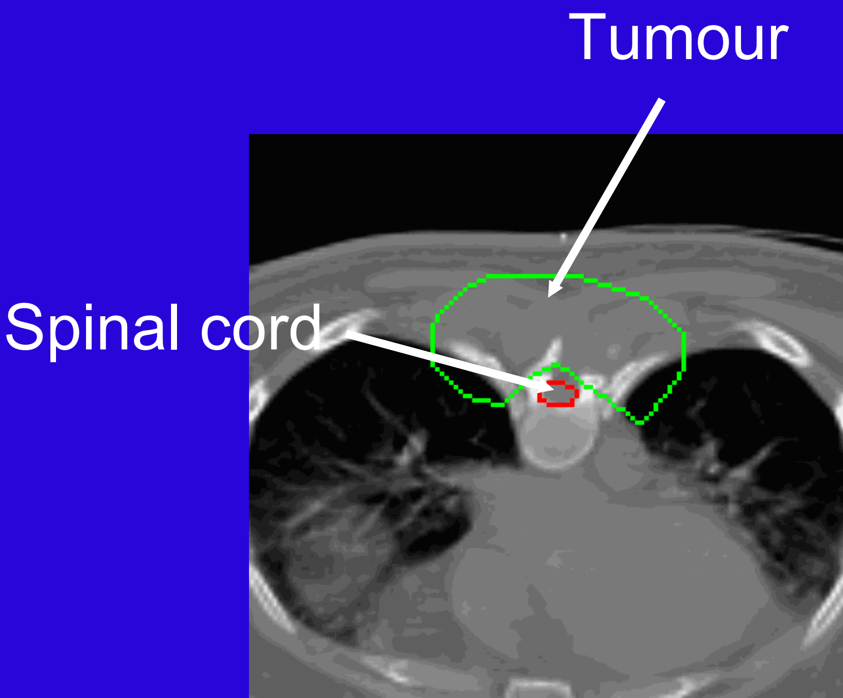


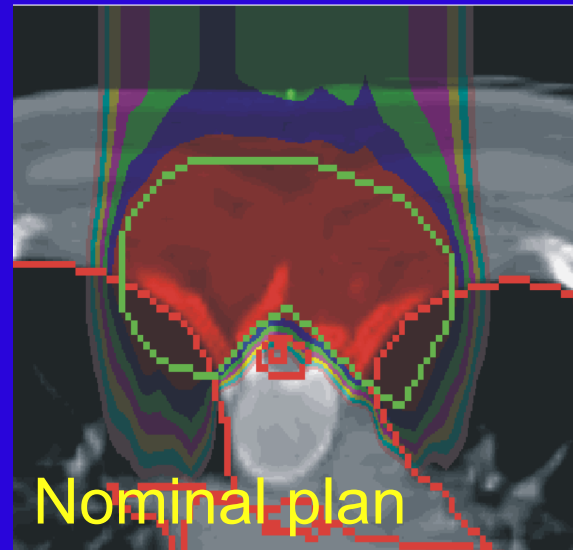
adapted -nominal

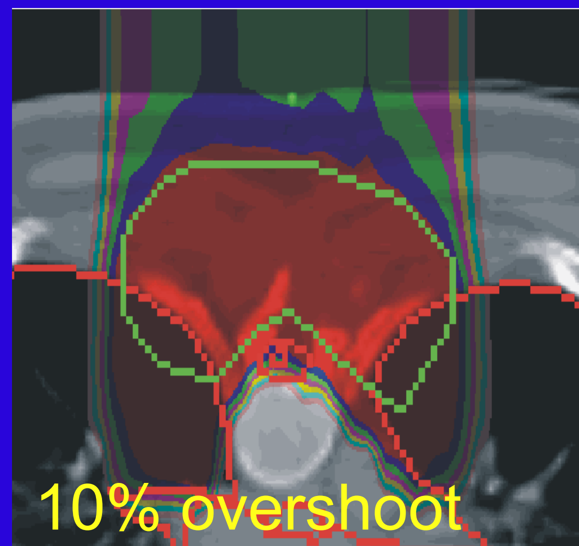


Robust planning techniques

Example paraspinal case

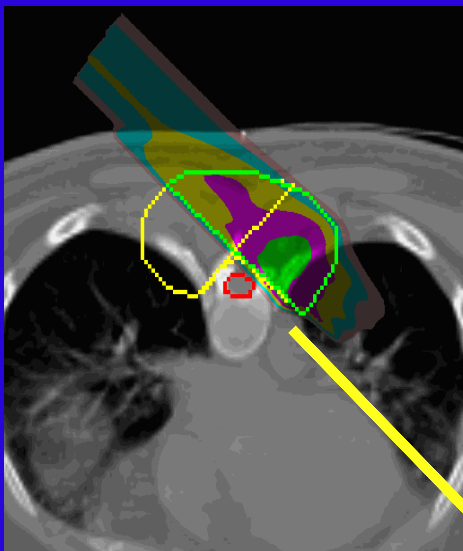


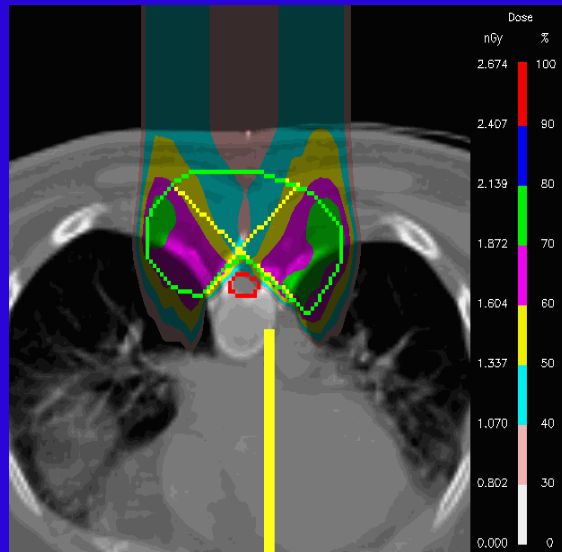


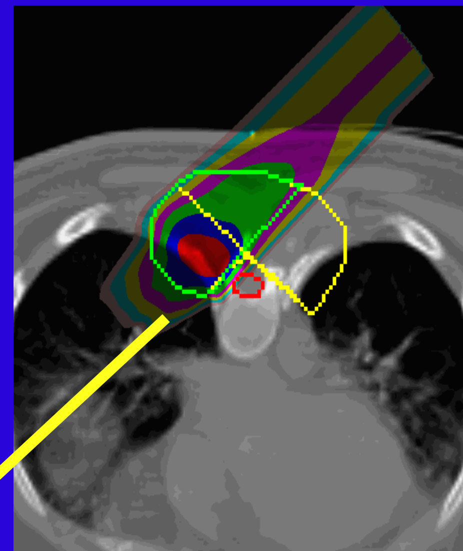


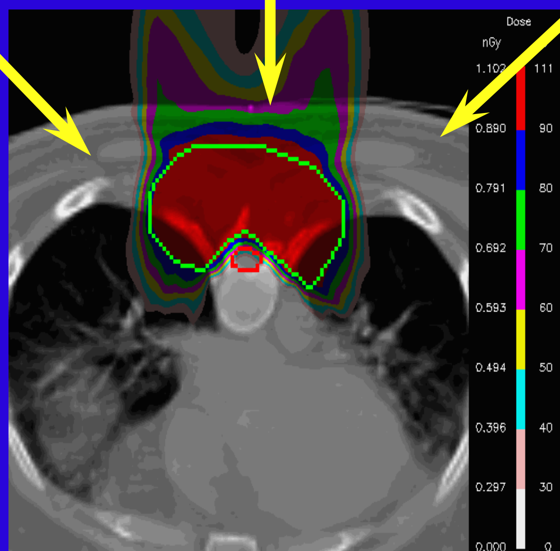
Lomax et al.:Med. Phys. 28(3): 317-324, 2001

Robust planning techniques





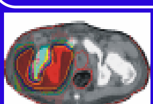




3 patched, intensity modulated fields....

...give a homogenous dose without the use of fields that abut distally against the spinal cord

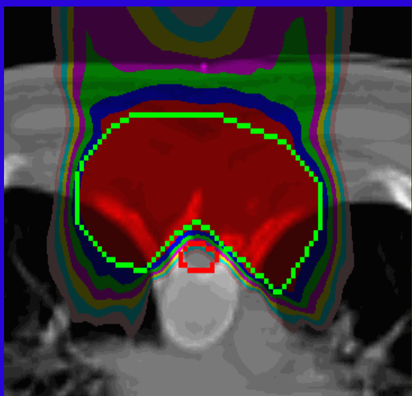
Lomax et al.:Med. Phys. 28(3): 317-324, 2001



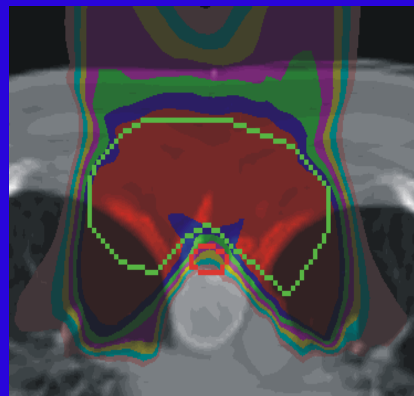
Robust planning techniques

Nominal plans | 10% overshoot plans

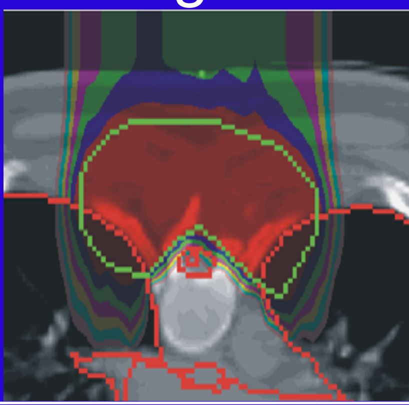
IMPT



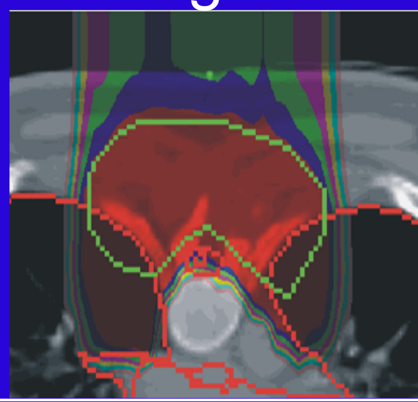
IMPT



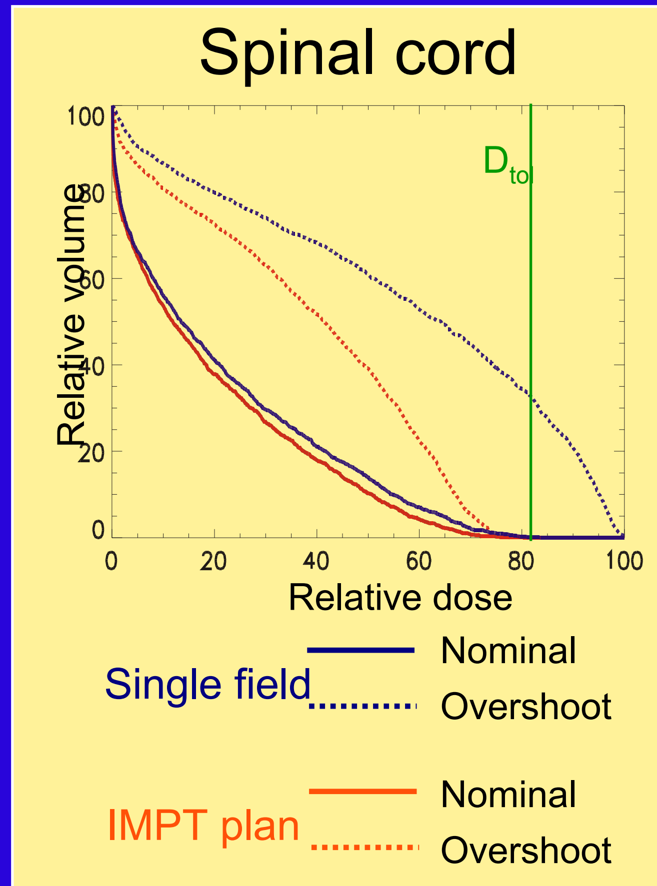
Single field



Single field



DVH analysis



Robust planning techniques

Incorporate range uncertainty into optimisation function using gaussian probability functions for range uncertainty

E.g.

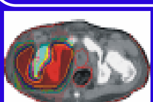
$$\underset{\boldsymbol{w}}{\text{minimize}} \quad \langle E(\boldsymbol{w})\rangle := \int \sum_{i \in PAT} \alpha_i \left[D_i(\boldsymbol{w}, \bar{\boldsymbol{\rho}} + \boldsymbol{\sigma\delta}) - D_i^{pres}\right]^2 P(\boldsymbol{\delta}) d\boldsymbol{\delta}$$

subject to

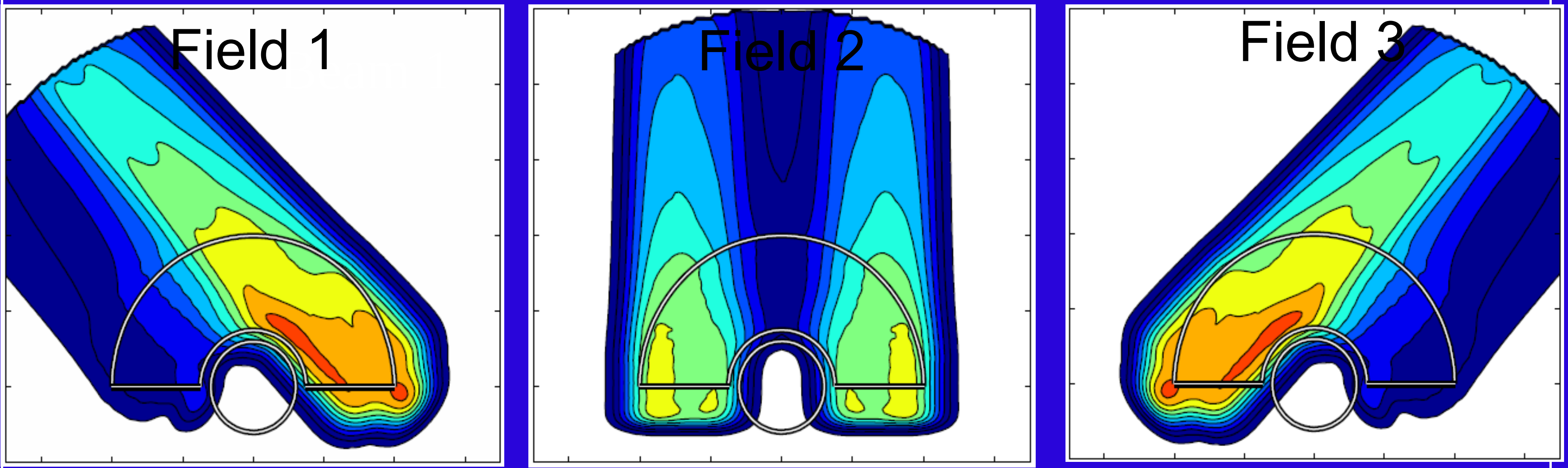
$$w_j \geq 0 \quad (\forall j \in PB)$$

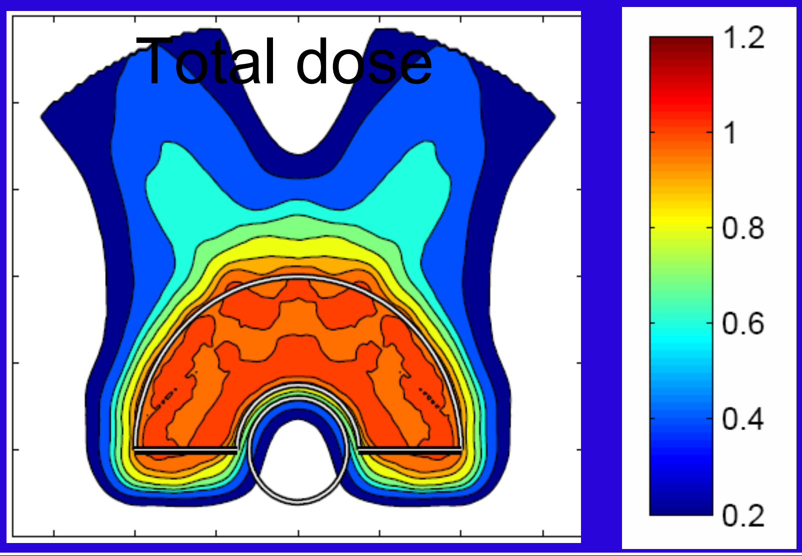
Where $\overline{\rho} + \sigma\delta$ assigns an uncertainty to the range of each pencil beam in the optimisation

Unkelbach et al, PMB, 52;2755-2773, 2007



Robust planning techniques



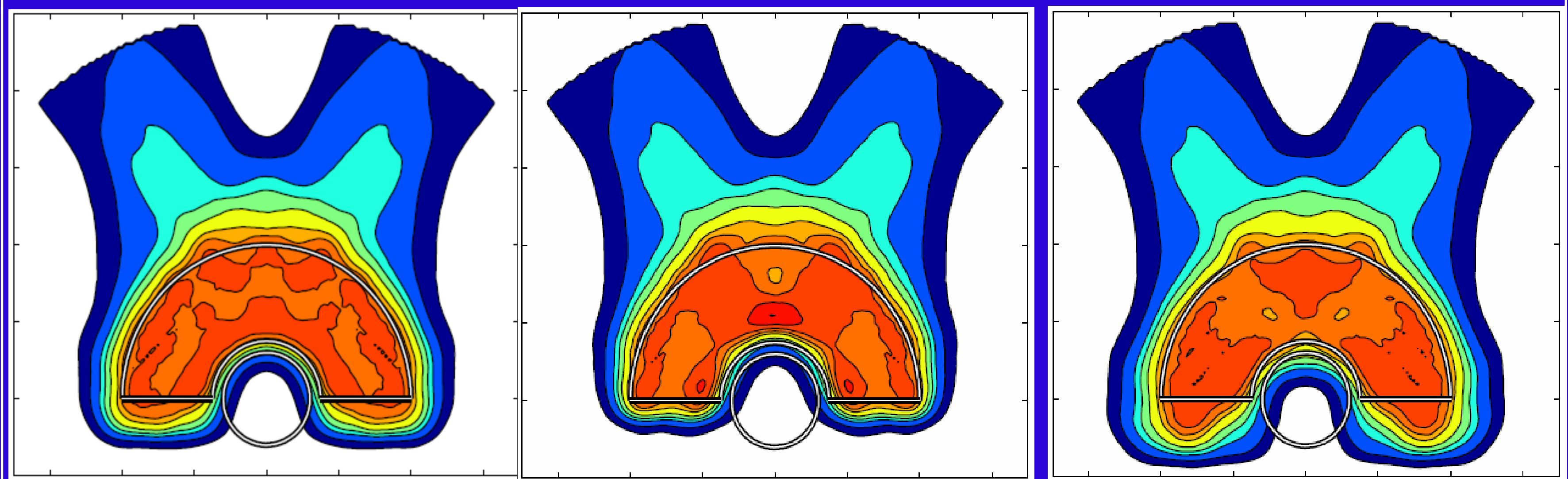


Optimised fields using 'robust' optimisation

Unkelbach et al, PMB, 52;2755-2773, 2007

Robust planning techniques

Effect of 5mm range uncertainty on robustly optimised plan

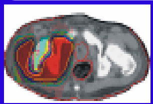


nominal range | 5 mm undershoot | 5 mm overshoot

Unkelbach et al, PMB, 52;2755-2773, 2007

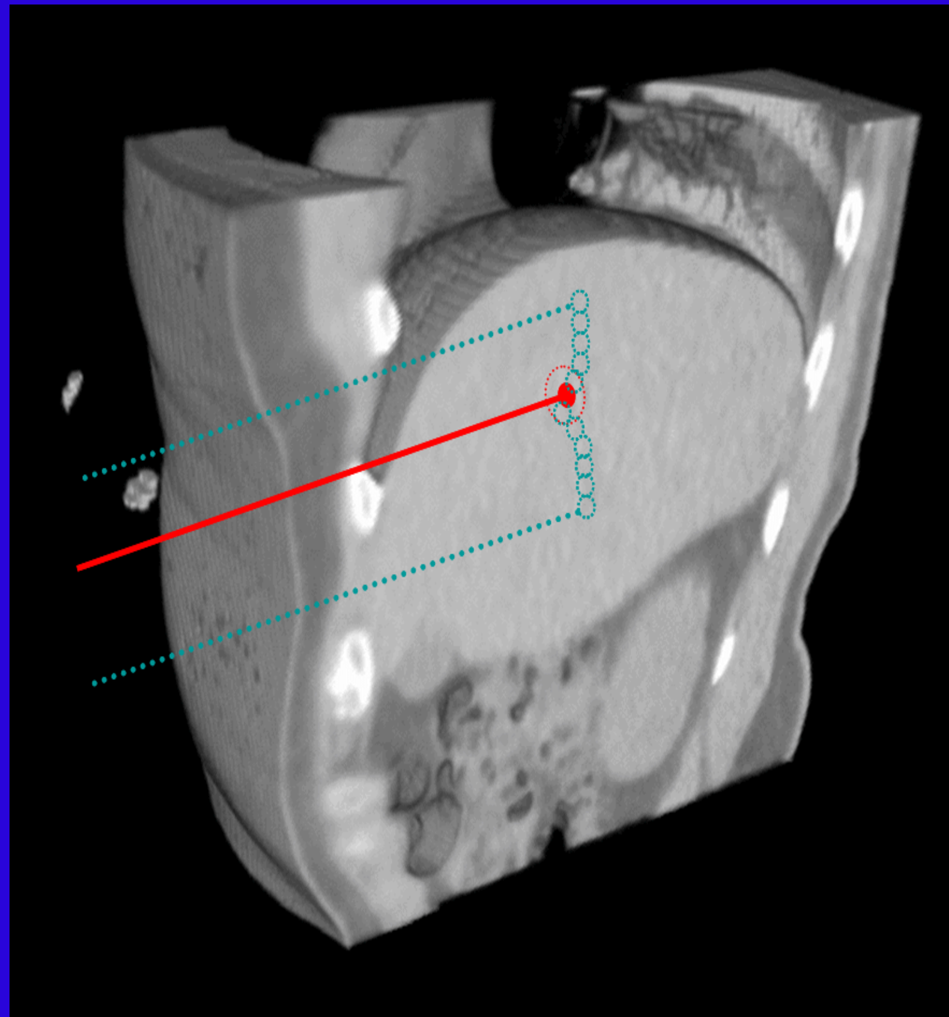
Potential solutions to …

- …range uncertainty
- …the organ motion problem



Tumour tracking

Track motion of tumour using scanning system based on some anatomical/physiological signal



+ Most conformal

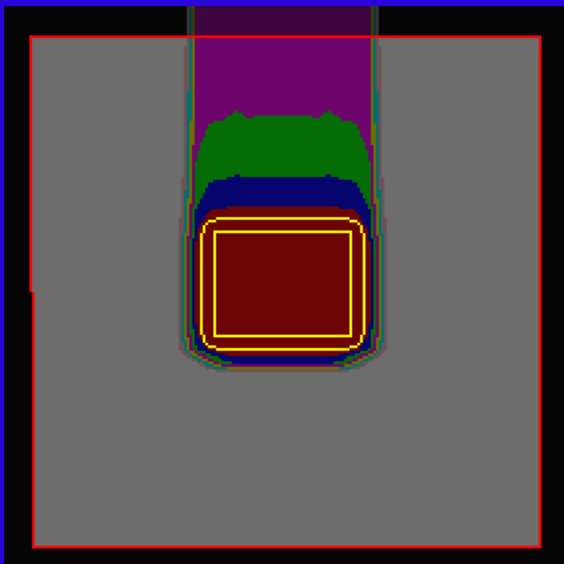
+ Most efficient

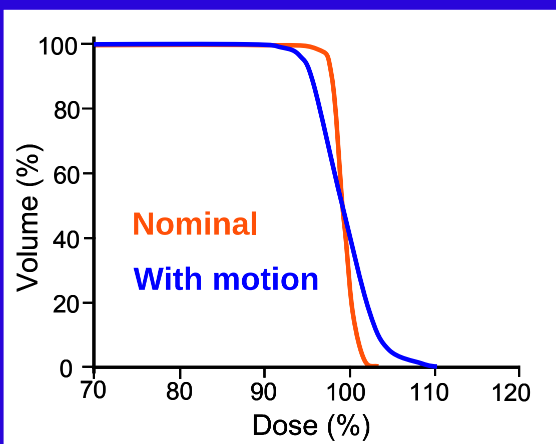
- Very complex!

- Difficult QA

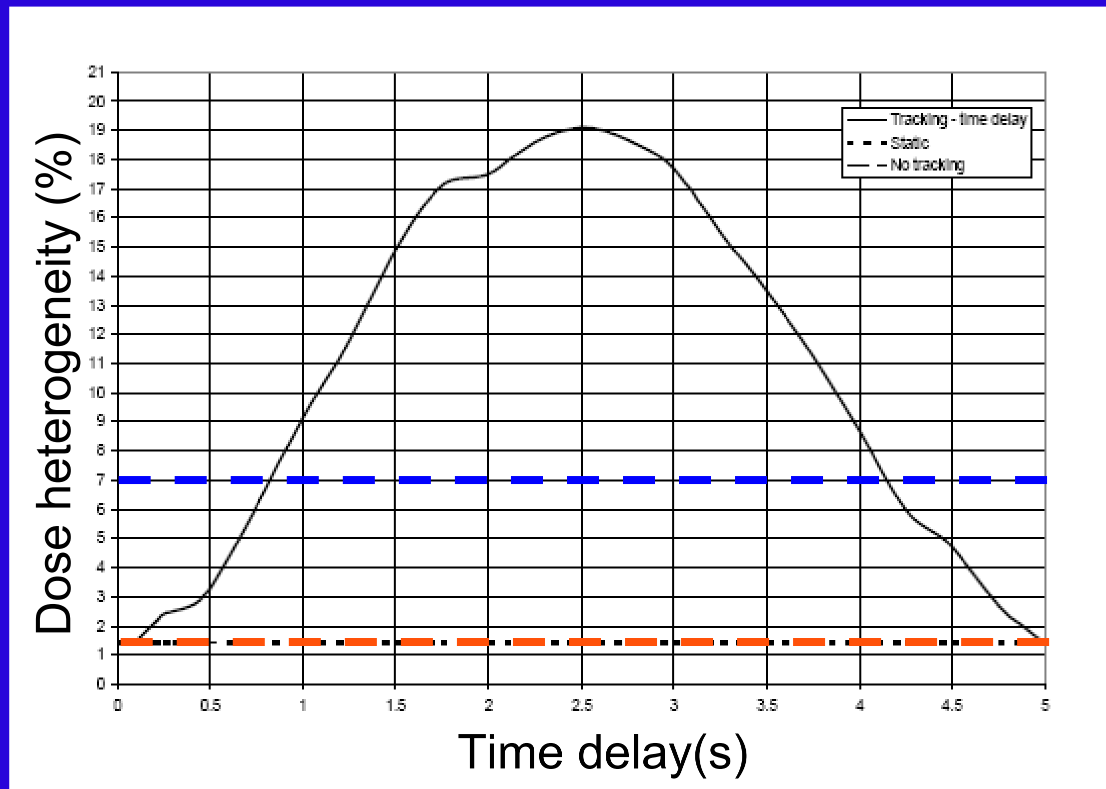
- Reliability of tracking signal?

Tumour tracking





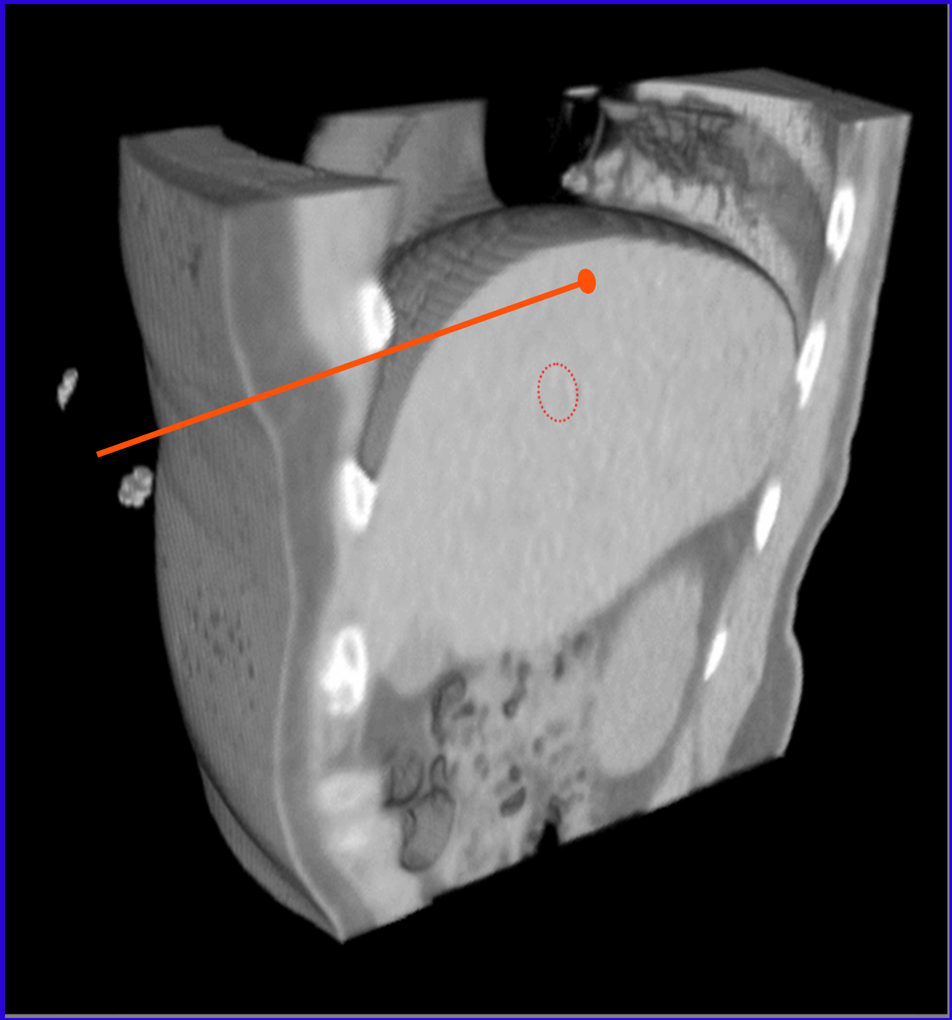
Dose heterogeneity as function of tracking delay



Steven van de Water, PSI

Rescanning

Repaint scanned beam many times such that statistics dictate coverage and homogeneity of dose in target (c.f. fractionation)



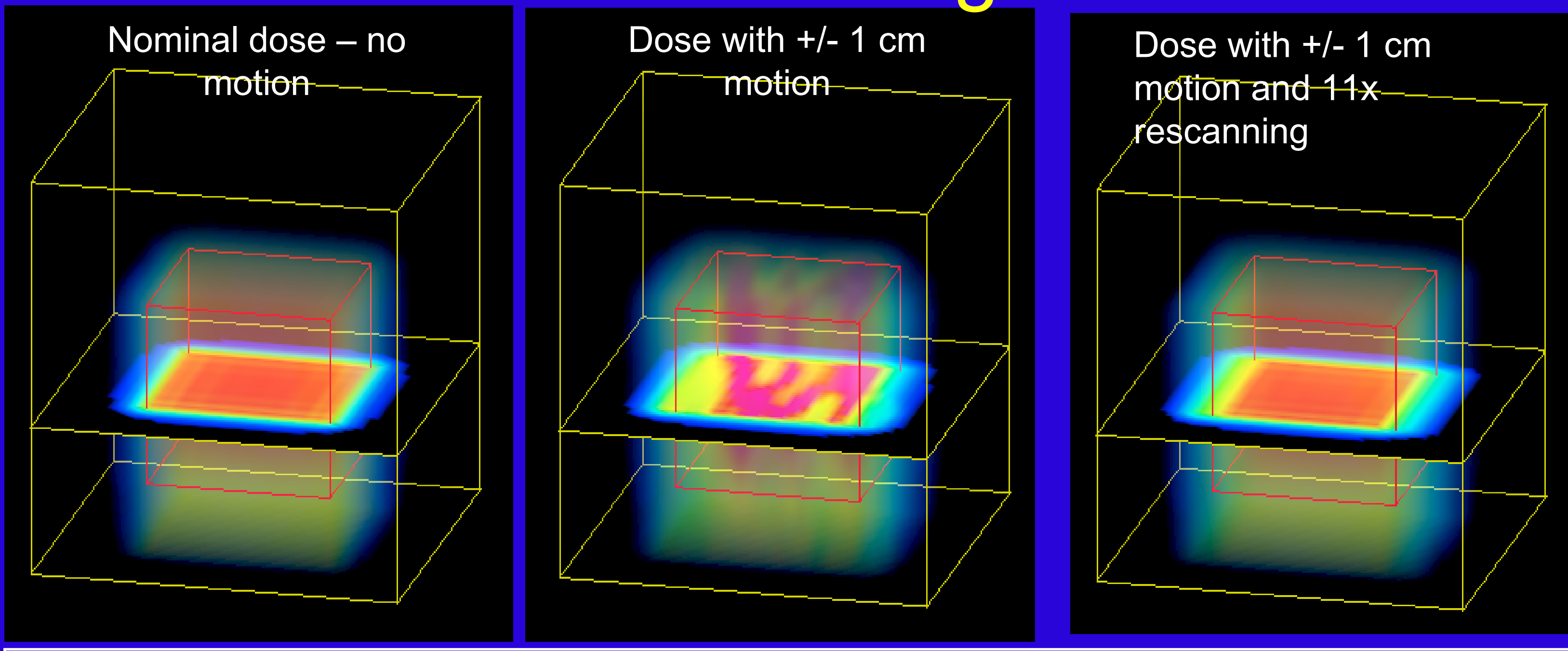
+ Simple method

+ Robust

- Fast scanning required

- Not very conformal

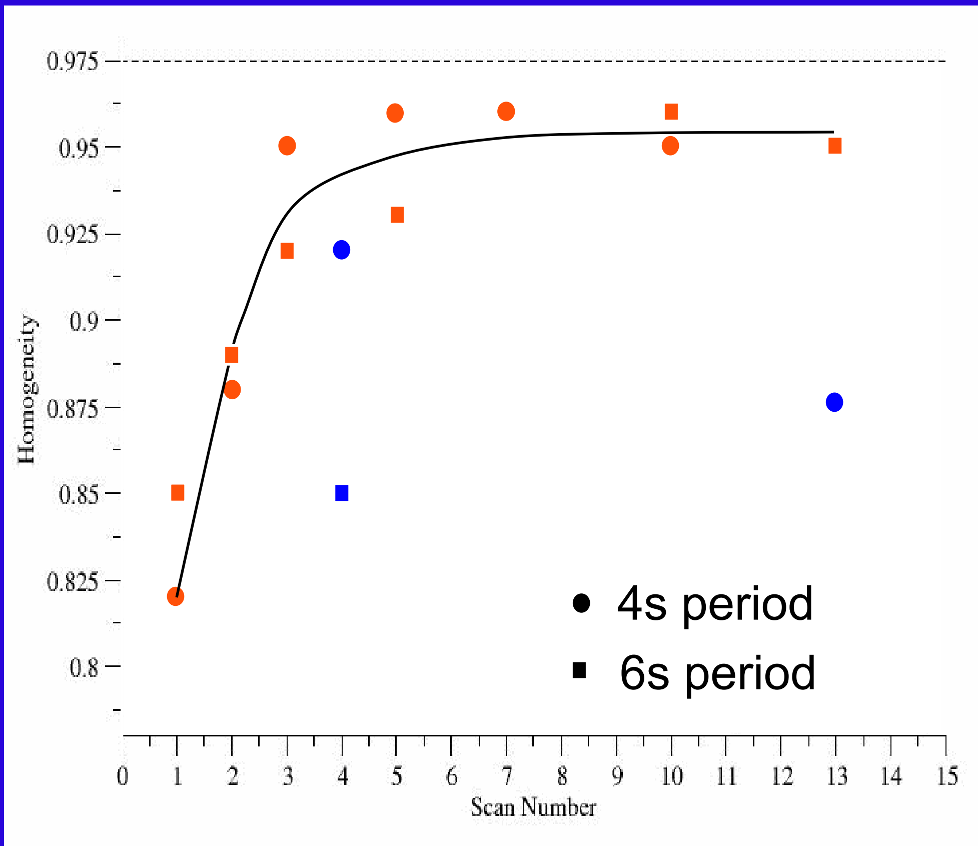
Rescanning



Applying the total prescribed dose in *n* steps (each spot is applied n times rather than once) provides a better homogeneity.
The error is statistically decreased by $\sqrt{n}$

Rescanning

Analysis of Cos^4 motion with 1cm peak-to-peak amplitude



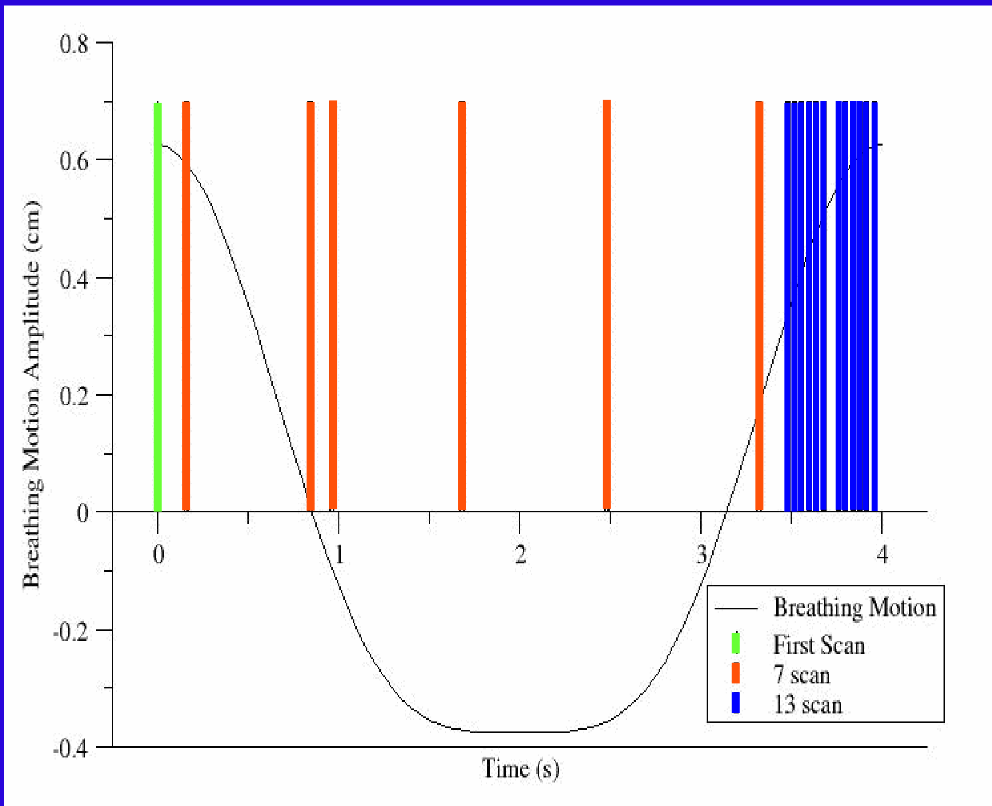
- Cylindrical target volume
- Re-scanned different times to same total dose
- Scan times calculated for realistic beam intensities and dead times between spots
- Analysis carried out for different periods of motion

Not always improving homogeneity with number of re-scans!

Marco Schwarz, Trento

Rescanning

The 'synchronicity' effect



- Very preliminary results
- A 'real' effect for perfectly regular breathing?
- Could well be less of an issue when breathing is more irregular
- For regular breathing, could be avoided by selecting the re-scanning period to avoid effect or varying period scan-to-scan
- Probably not a big issue in reality?

Marco Schwarz, Trento

Gating

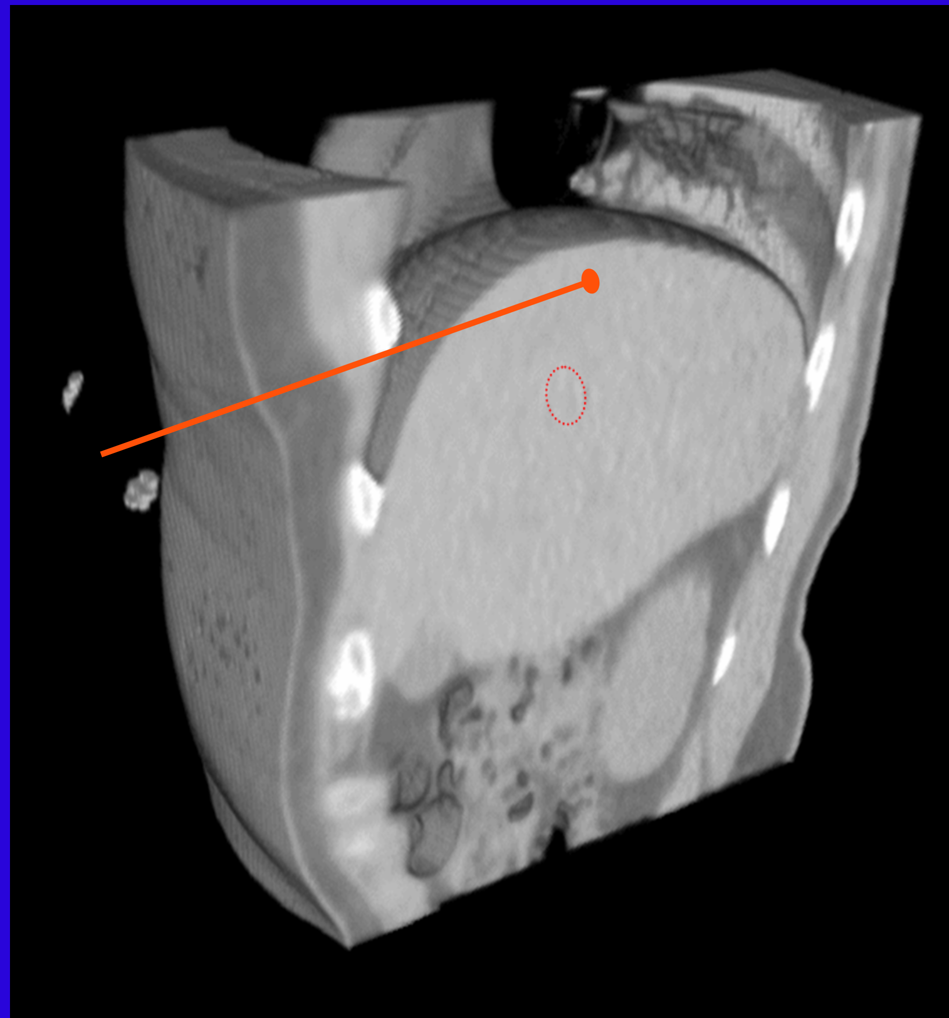
Reduce magnitude of motion by gating delivery to small window of motion cycle

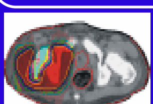
+ Simple method

- Reliability of gating signal?

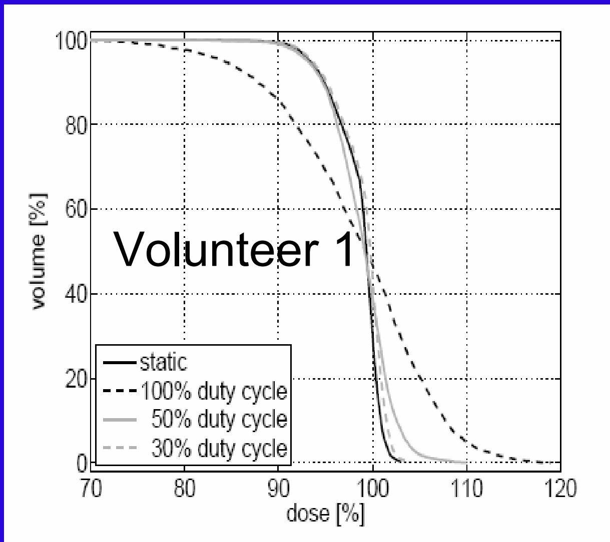
- Inter/intra fraction variability of motion?

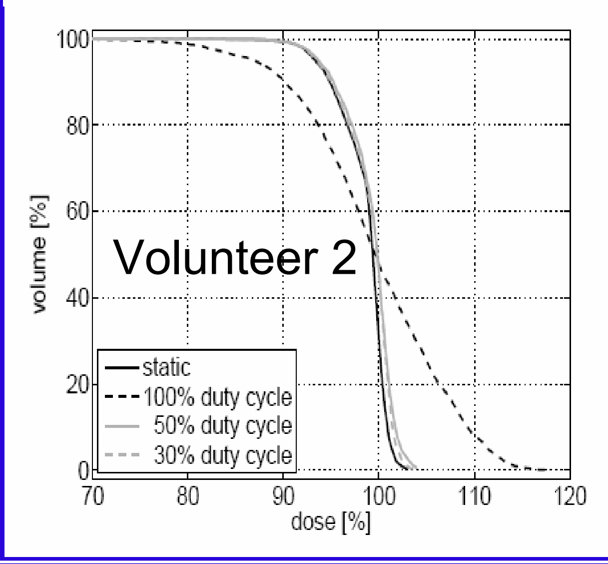
- Residual motion?



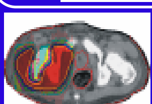


Gating



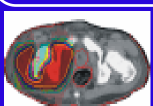


- 4D dose calculation applied to cylindrical target in presence of 'real' motion (4D-MRI of volunteers) in liver
- Calculations performed for static, 100, 50 and 30% duty cycles
- Gating signal taken from diaphragm wall motion ('ideal' gating)
- Irregularities in breathing and amplitude over duration of treatment taken into account
- Results for two volunteers
  1. T_{av} = 4.7s, A_{av} = 10.9mm
  2. T_{av} = 7.1s, A_{av} = 8.3mm



Summary.

- Proton therapy is fast moving from the research institute to the hospital
- Due to the adoption of proton therapy in a number of ‘flag-ship’ institutes in the USA, they will certainly have a higher profile in the next few years.
- Scanning and IMPT will play an ever increasing role in proton therapy, with most manufactuers offering or developing such systems
- However, proton therapy brings challenges in dosimetry, delivery accuracy and organ motion management
- There’s lot’s of interesting science still to be done….!



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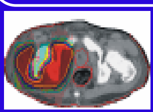

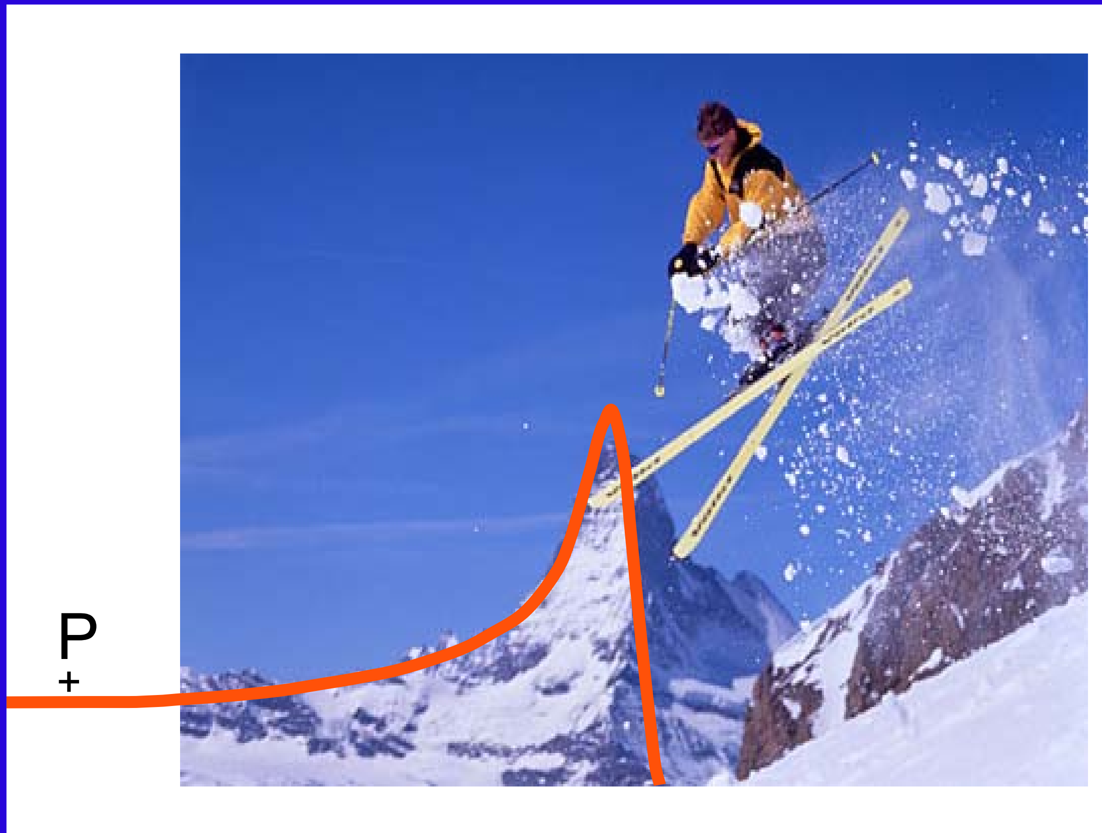

Thanks for your attention…