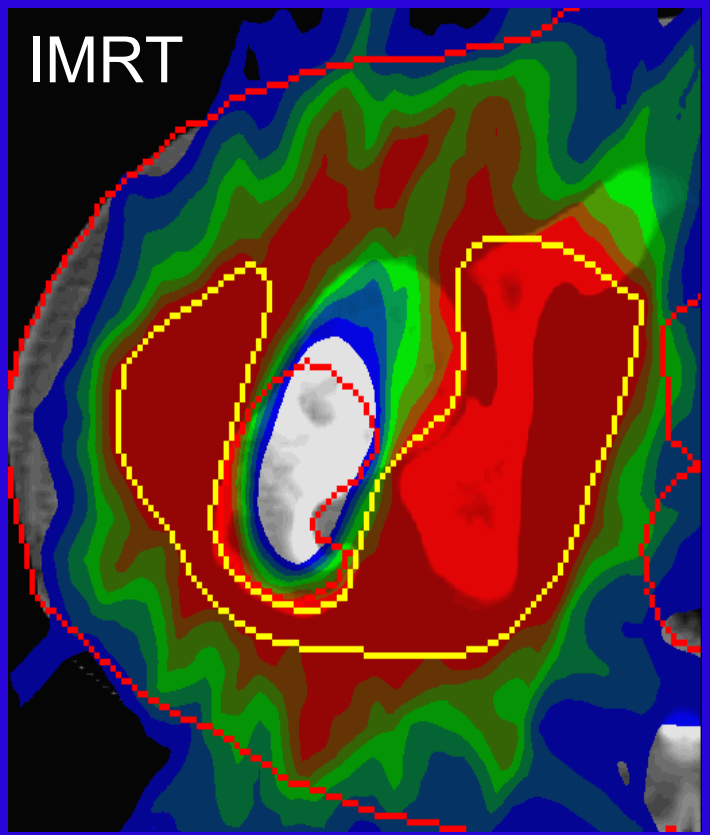
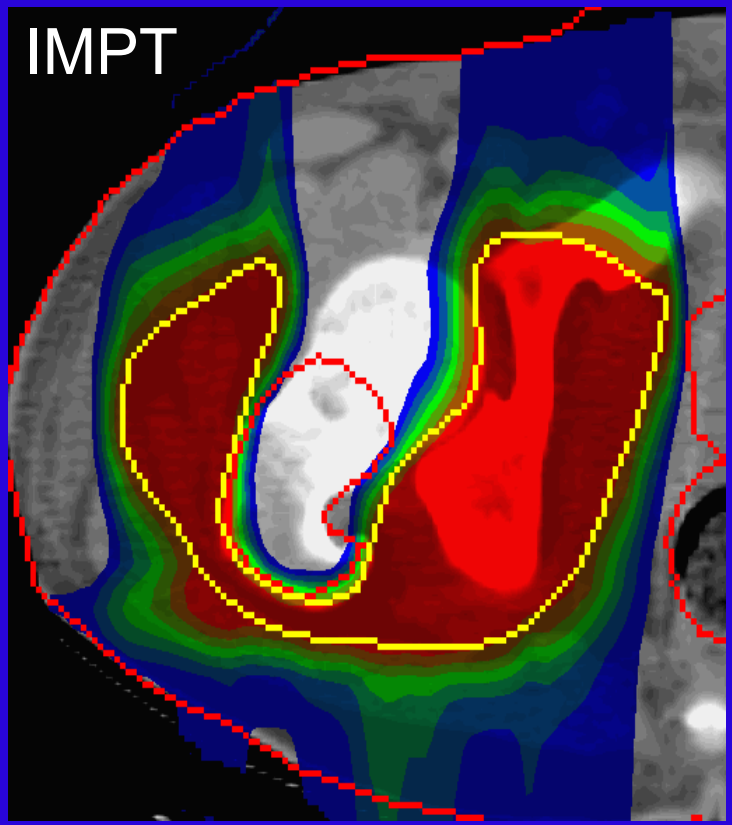
# Proton radiotherapy: an overview



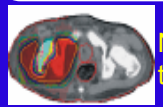




Tony Lomax

Centre for Proton Radiotherapy, Paul Scherrer Institute, Switzerland

# Overview of presentation

1. Proton therapy – basic principles
2. Treatment delivery
3. Measuring and modeling absolute dose
4. Clinical applications



# The principle of radiotherapy.

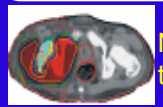
•Energy deposited by radiation (dose = J/kg or Gray) can sterilize cells through the production of free-radicals inside the cell.

•The higher the delivered dose to the whole tumour, the higher the probability of controlling it.

BUT…

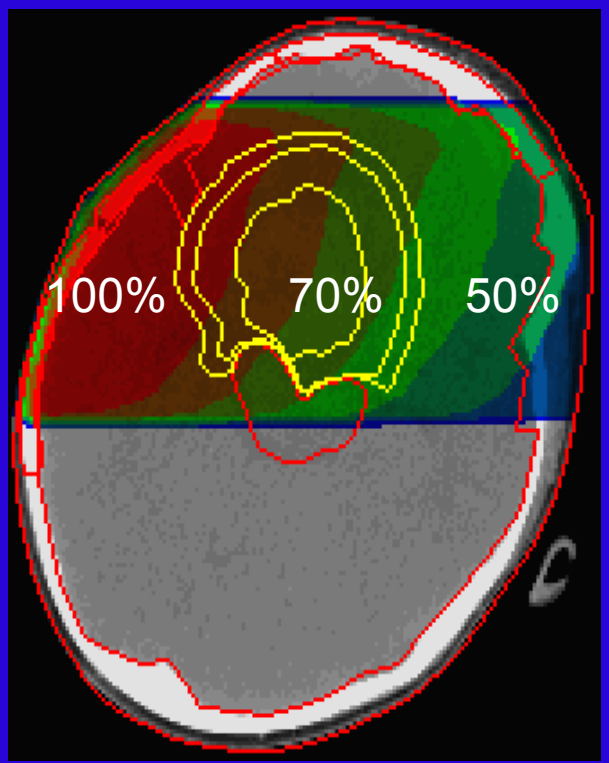
•Normal tissues will also be damaged and sterilized by irradiation in a similar way.

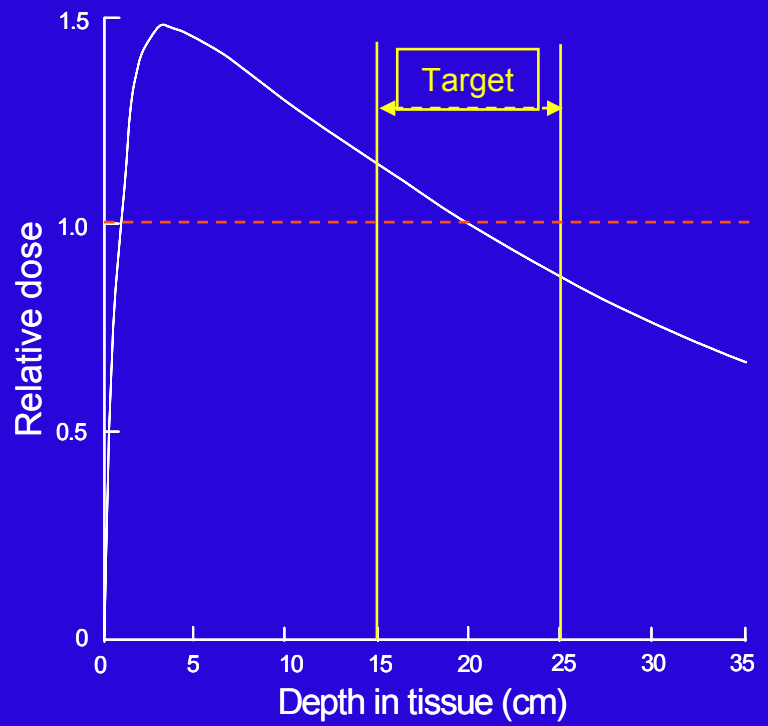
The art of radiotherapy then, is to concentrate the dose in the tumour whilst sparing the surrounding normal tissues as much as possible.



## Radiotherapy with photons and protons

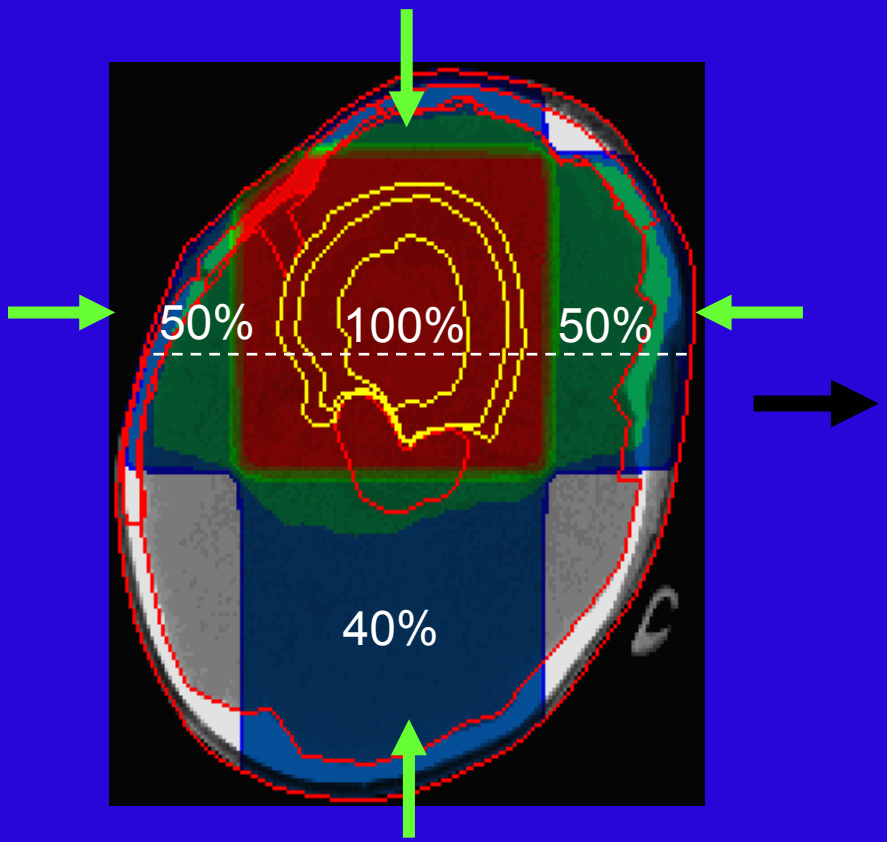
# X-ray (photon radiotherapy): A 6M(e)V photon field

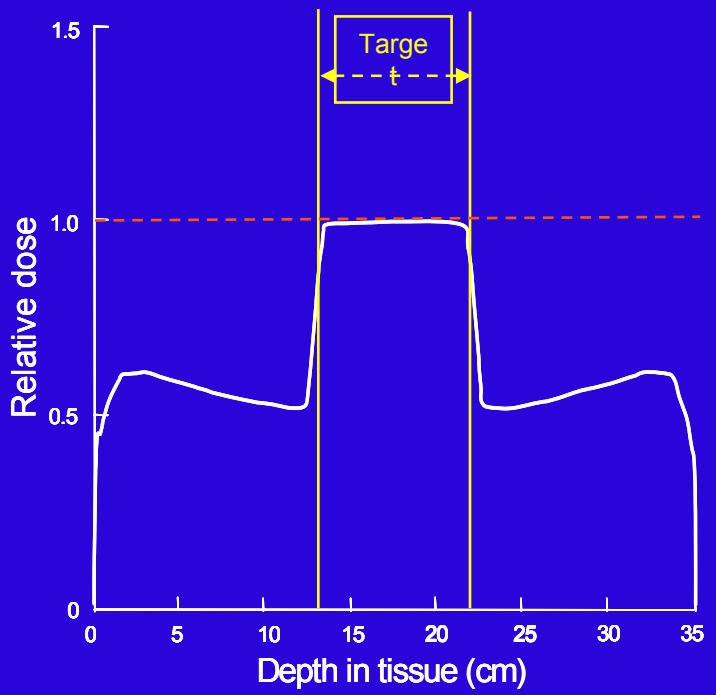


## Radiotherapy with photons and protons

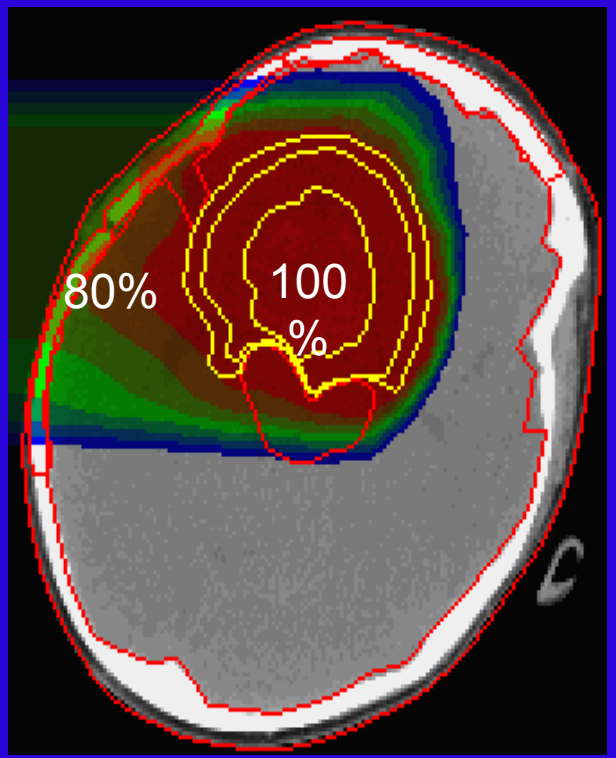
# X-ray (photon) radiotherapy: A 4-field, 6 MV photon plan

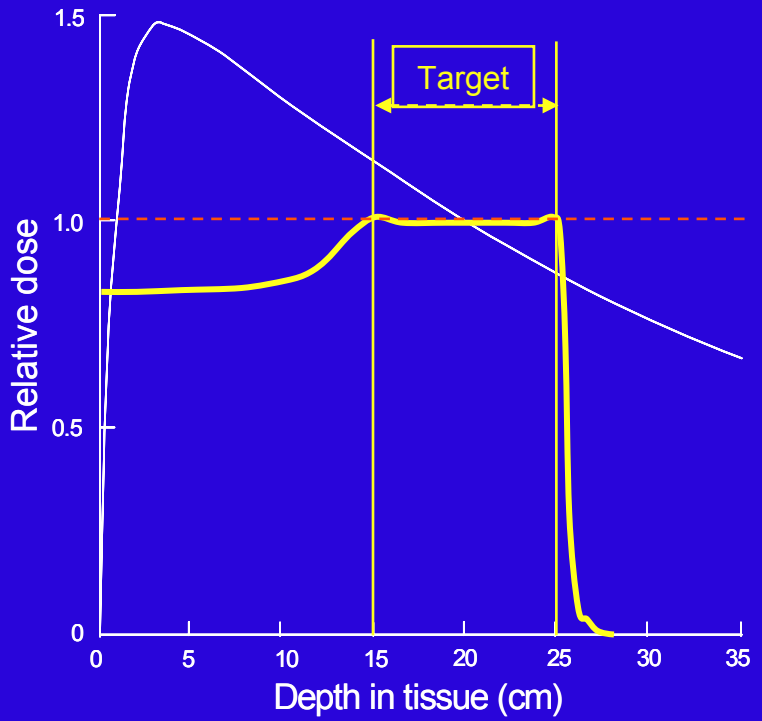


## Radiotherapy with photons and protons

# Radiotherapy with protons: A 138MeV proton field

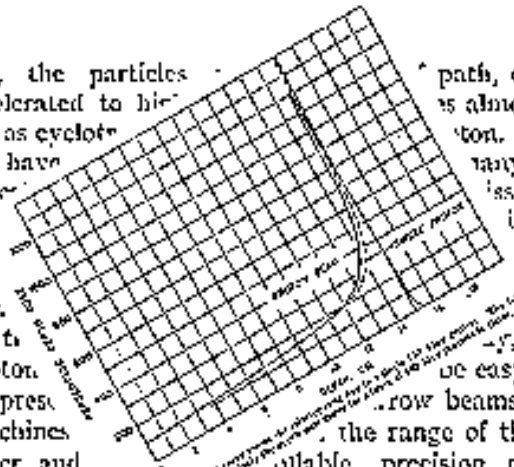


# The idea of proton therapy is NOT new

## Radiological Use of Fast Protons

ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts



Except for electrons, the particles which have been accelerated to high energies by machines such as cyclotrons, Van de Graaff generators have been directly used therapeutically. The neutrons, gamma radioactivities produced by tions of the primary pa applied to medical problem large part, been due to t penetration in tissue of proton and alpha particles from pres ators. Higher-energy machines under construction, however, and from them will in general be en enough to have a range in tissue comparable to body dimensions. It must have occurred to many people that the particles themselves now become of considerable therapeutic interest. The object of this paper is to acquaint medical and biological

path, or specific ioniza- s almost inversely with ton. Thus the specific many times less where issue at high energy meter of the path o rest.

it possible to ctly localized , with but little be easy to produce well row beams of fast protons, the range of the beam is easily ollable, precision exposure of well defined small volumes within the body will soon be feasible.

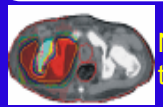
Let us examine the properties of fast protons somewhat more quantitatively. Perhaps the most important biological quantity is the specific ionization, or number of ions per centimeter of track. This

R.R. Wilson, Radiology 47(1946), 487-491

# 50 years of proton therapy..

## Nearly 50,000 patients treated in 27 centres world-wide.

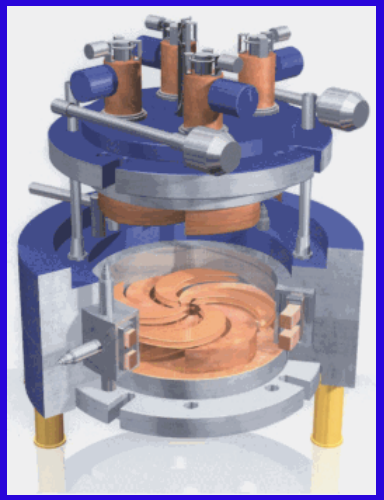
| | |
|---|---|
| Lawrence Berkeley Laboratory (USA) 1954-1992 | >2500 |
| Los Alamos (USA) 1974-1982 | >230 |
| Harvard/MGH (USA) | >11000 |
| Loma Linda (USA) | >10000 |
| Nice, Orsay (France) | >5600 |
| Dubna, Moskau, St. Petersburg (Russia) | >5200 |
| Chiba, Tsukuba, Hyogo, Kashiwa, Shizuoca (Japan) | >4900 |
| **PSI (Switzerland)** | **>4400** |
| Clatterbridge (UK) | >1300 |
| San Francisco, Bloomington (USA) | >680 |
| Berlin since 1999, Catania (Sicily) since 2000 | >680 |
| South Africa | >470 |
| Uppsala (Sweden) | >400 |
| GSI Darmstadt (Germany) | >190 |
| Wanji (China) | >30 |



# Sources of protons for therapy

Accel/Varian
250Mev
Cyclotron

3.5m
Diameter



Loma Linda
250Mev
Synchrotron

6m
Diameter

| Cyclotrons | |
|---|---|
| Relatively compact | + |
| Continuous wave | + |
| Fixed energy | - |
| Higher amount of contamination | - |

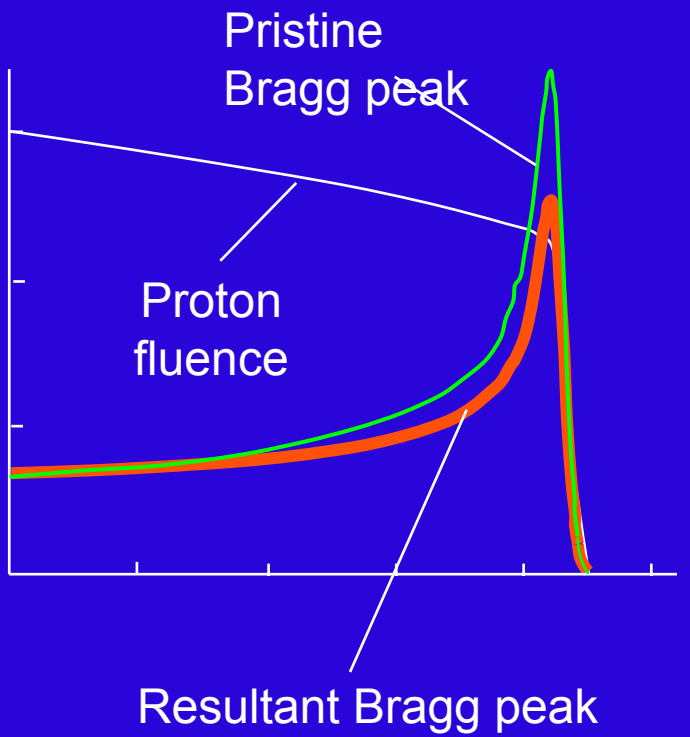
| Synchrotrons | |
|---|---|
| Somewhat larger | - |
| Pulsed | - |
| Variable energy | + |
| Less contamination | + |

# Proton interactions for radiotherapy

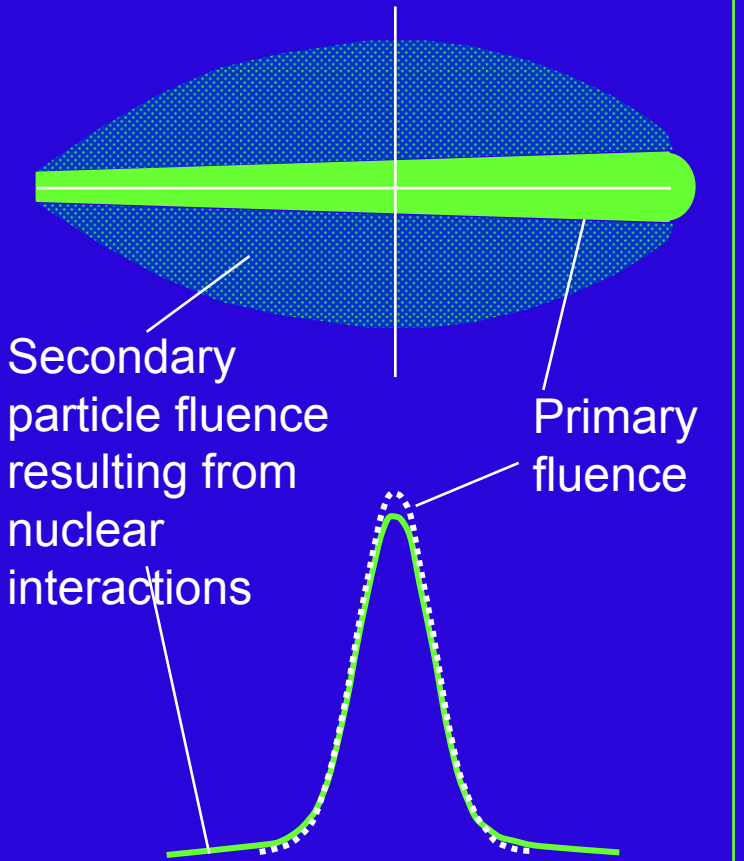
## 1. Nuclear interactions

About 20% of primary protons lost to interactions with atomic nuclei

### Effect on the depth dose curve

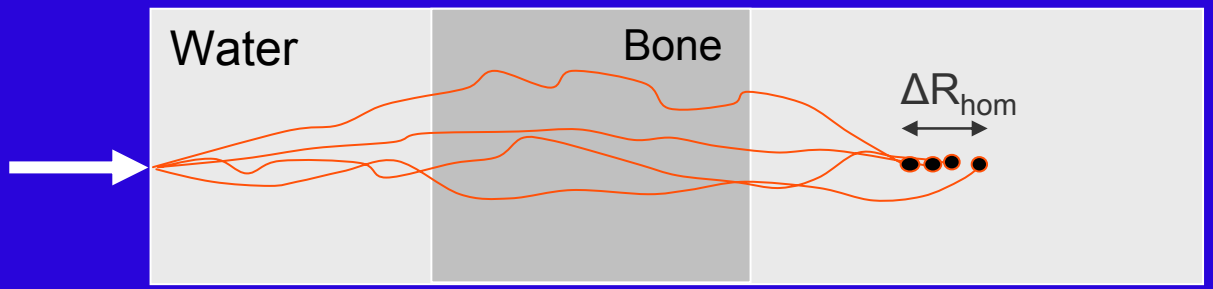


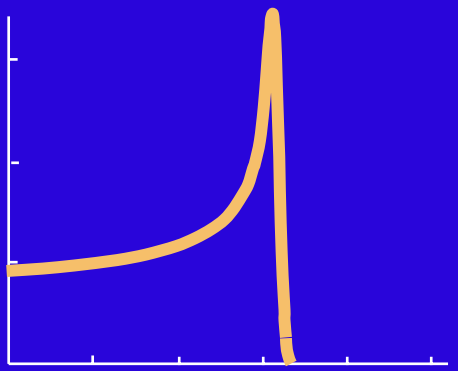

### Effect on the lateral dose distribution

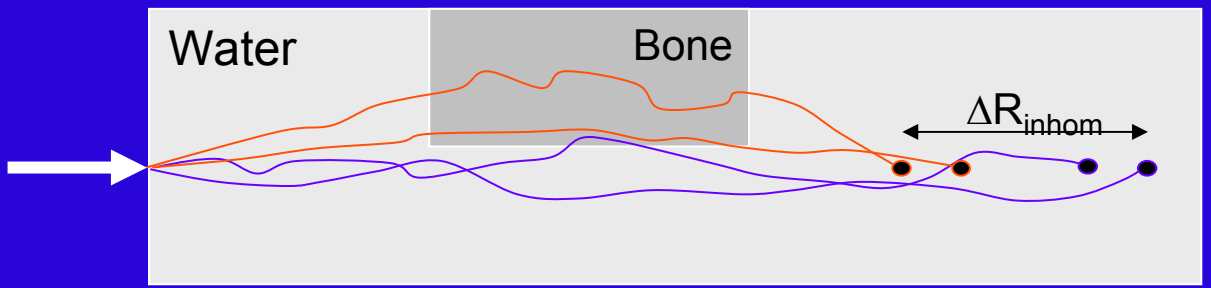


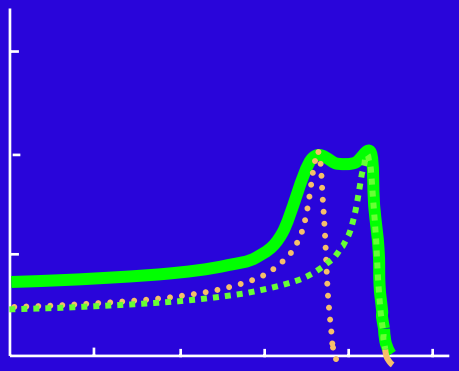
# Proton interactions for radiotherapy

## 2. Density heterogeneity effects – effect on Bragg peak shape





# Proton interactions for radiotherapy

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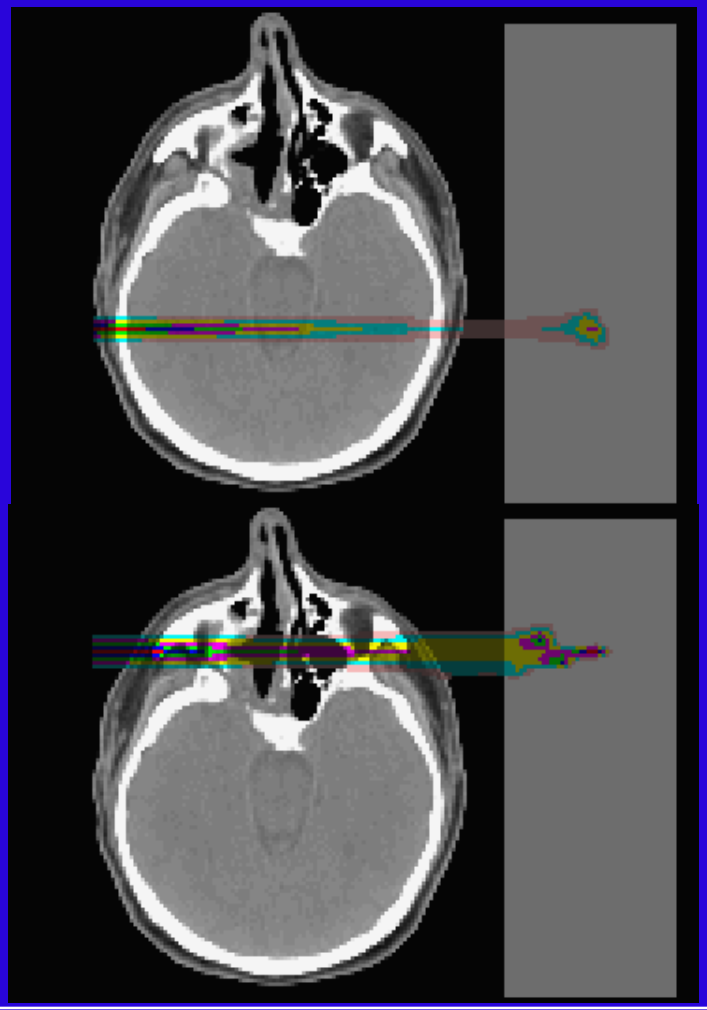
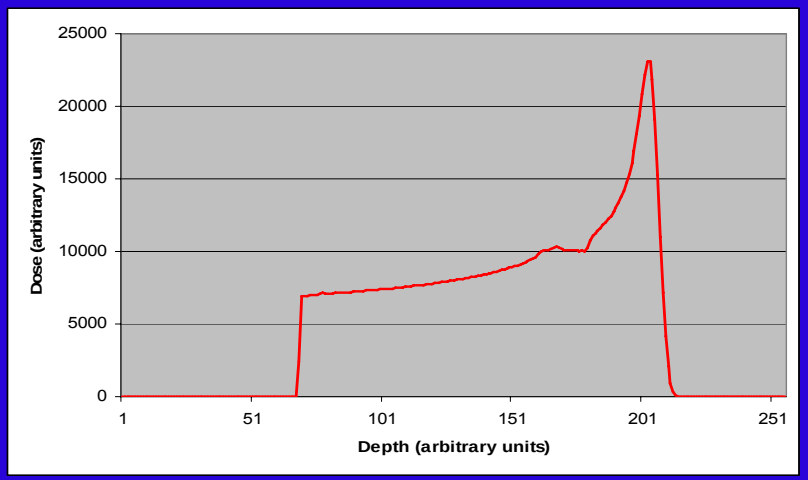
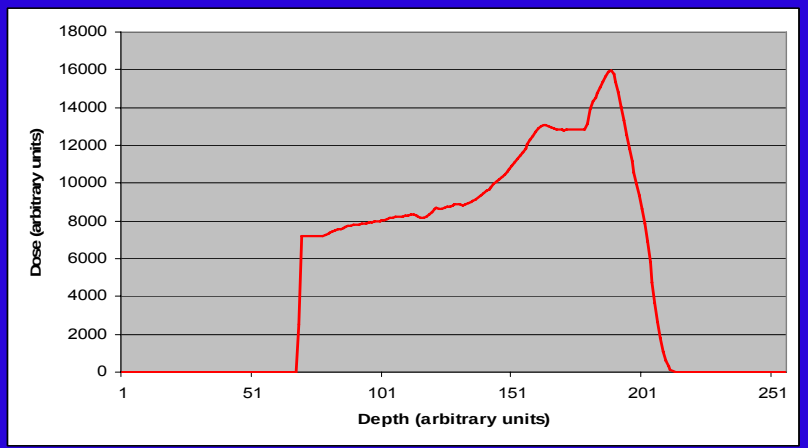
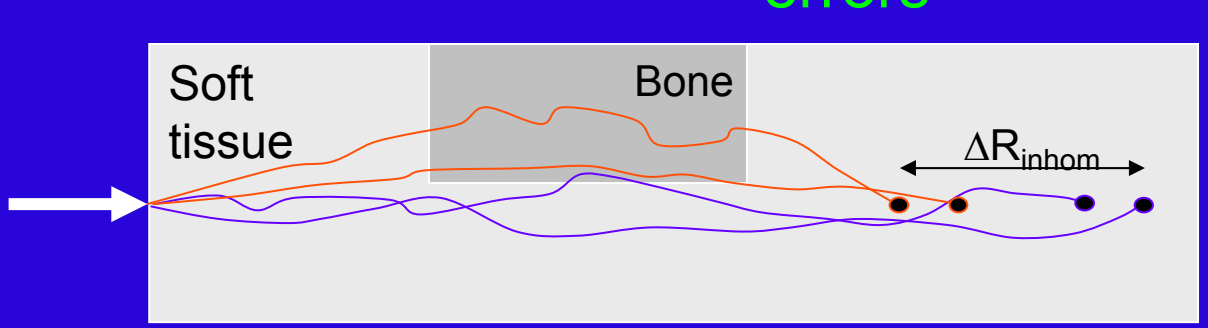


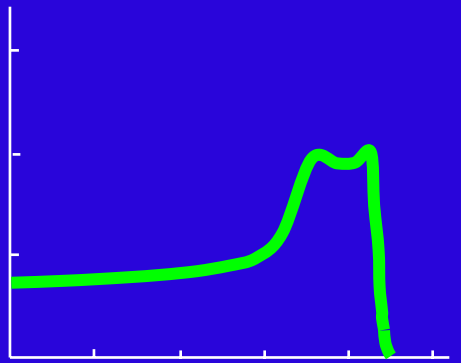


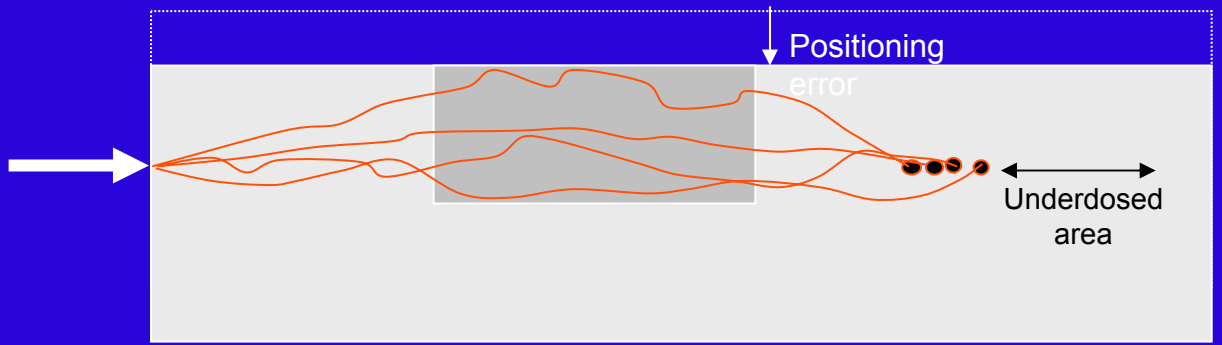



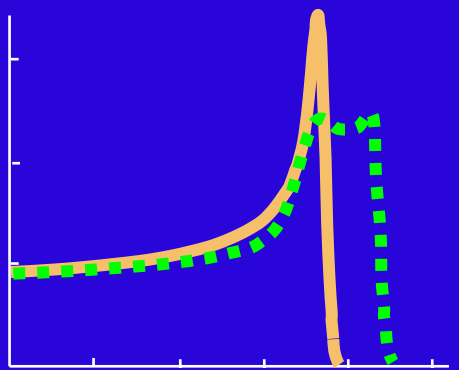
# Proton interactions for radiotherapy

## 2. Density heterogeneity effects – sensitivity to set-up errors



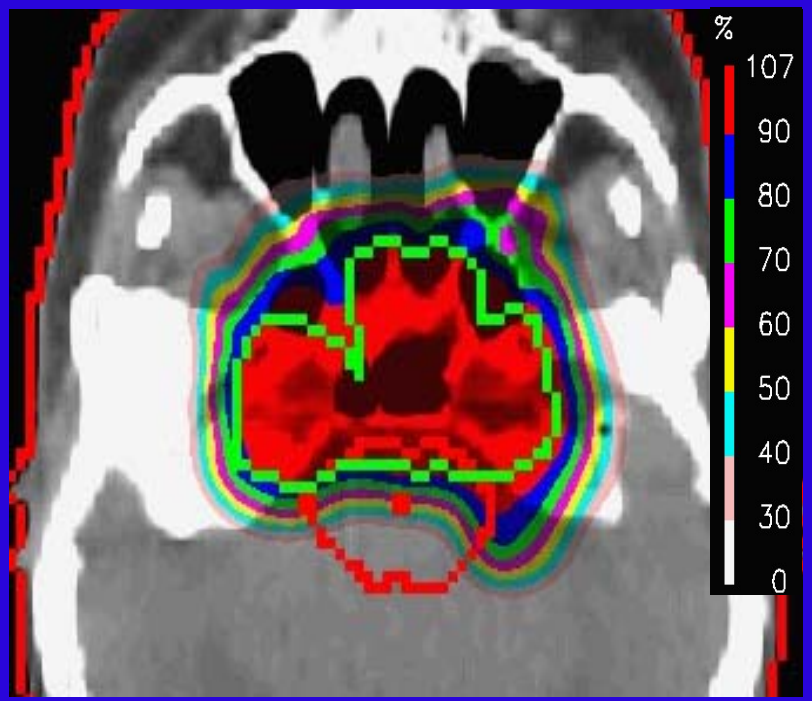





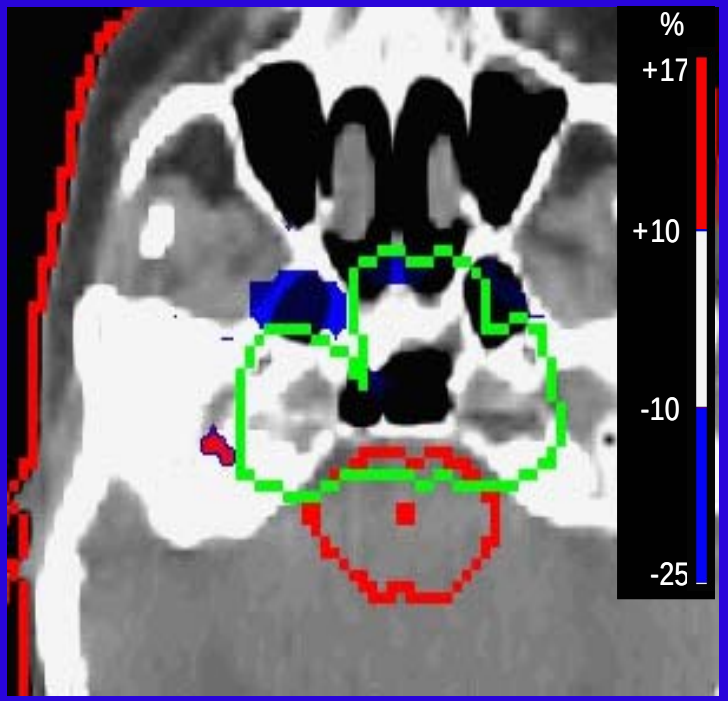



# Proton interactions for radiotherapy

## 2. Density heterogeneity effects – sensitivity to set-up errors




Nominal 3 field spot scanned proton plan



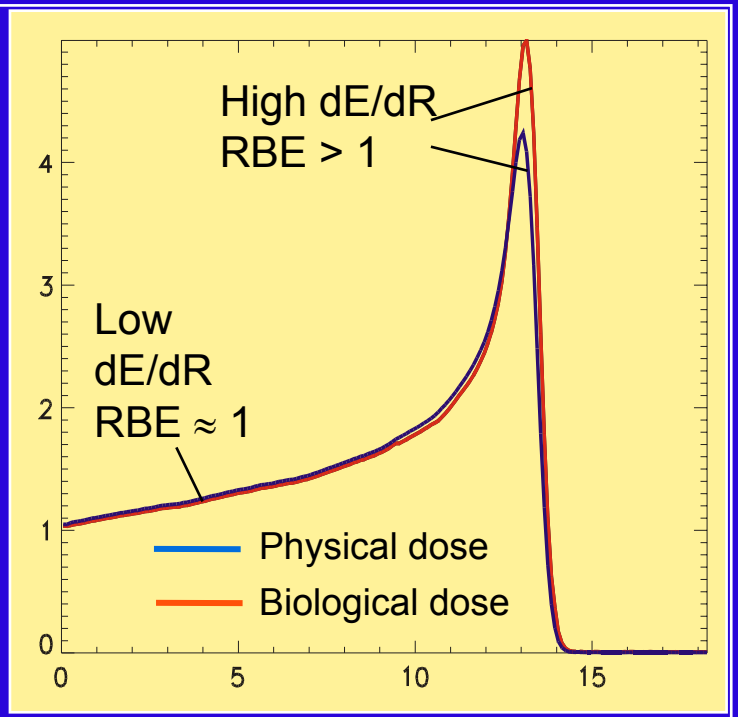

Dose differences after recalculation in repeated and translated (1-2mm) CT

Alessandra Bolsi, PSI

# Proton interactions for radiotherapy
## 3. Relative biological effectiveness (RBE)

RBE data courtesy of Harald Paganetti, Harvard

- RBE is the biological effectiveness of a radiation in damaging tissue (in comparison to $Co^{60}$)
- RBE related to Linear Energy Transfer (LET ≅ dE/dR), but is end-point, dose and tissue dependent!
- E.g. For cell inactivation of v79 chinese hamster cells with 2Gy…..




However, proton RBE considered to be globally 1.1 for all tissues and doses. There is presently no clinical evidence to indicate that this may be wrong.

# Overview of presentation

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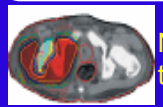
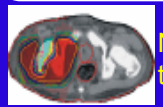
2. Treatment delivery
3. Measuring and modeling absolute dose
4. Clinical applications



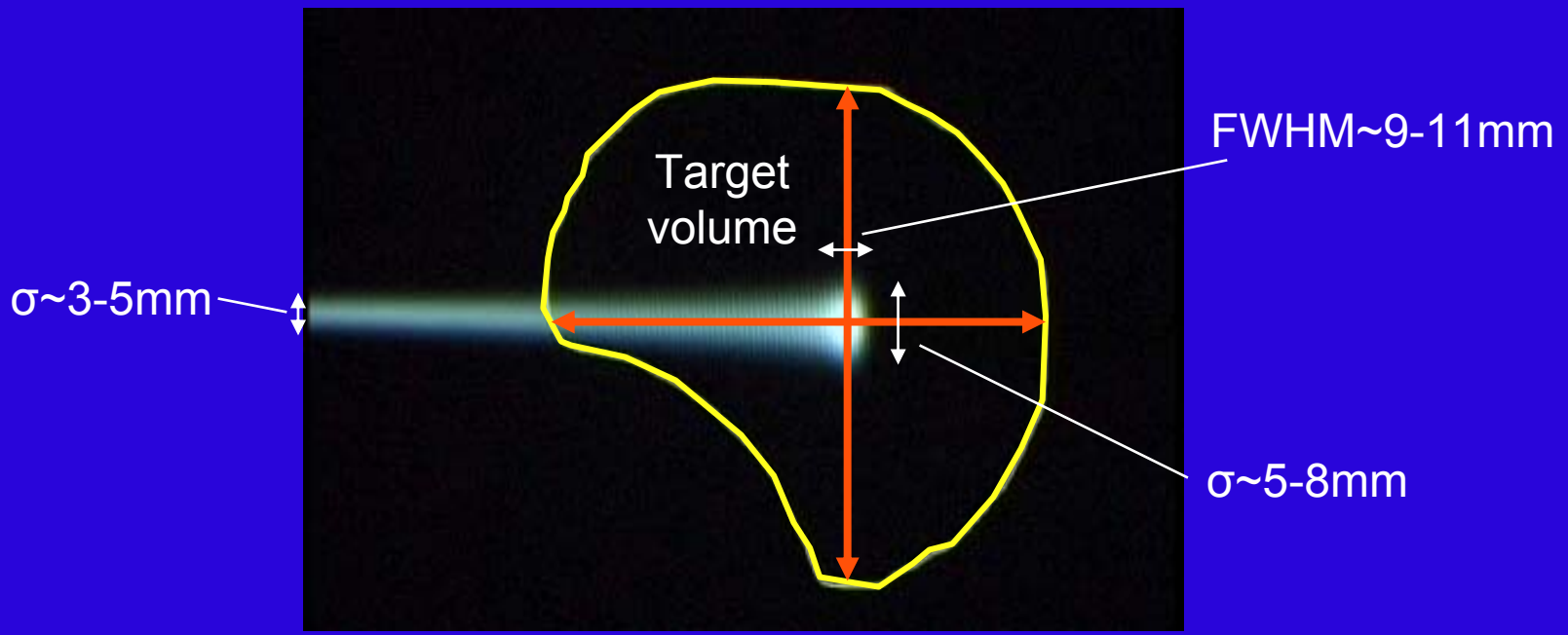
# Treatment delivery

1. Passive scattering
2. Active scanning



# The problem of lateral field size and coverage in depth

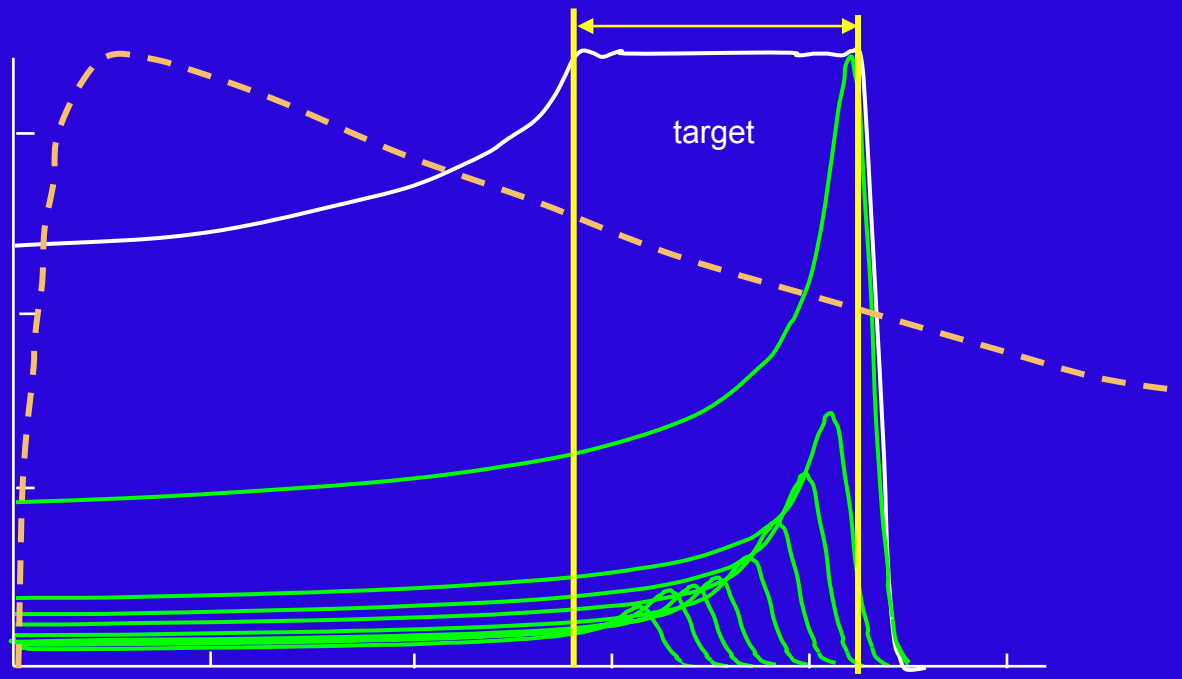
A mono-energetic proton Bragg peak is not very useful for treating anything other than the smallest tumours.




To make protons useful , we need to spread out the dose laterally and along the beam direction.

# Extending the dose in depth

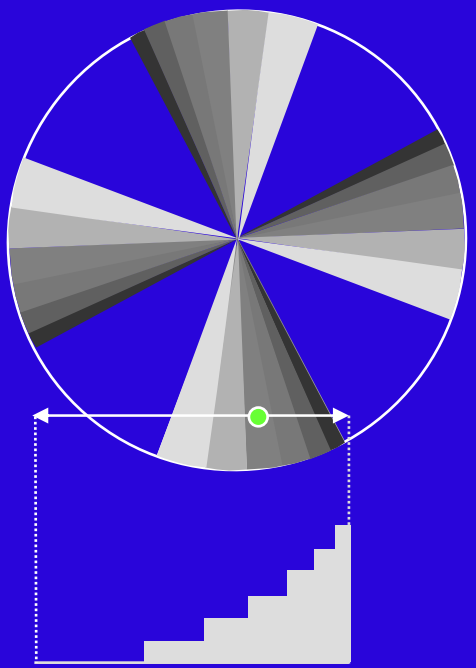
## The ‘Spread-Out-Bragg-Peak’



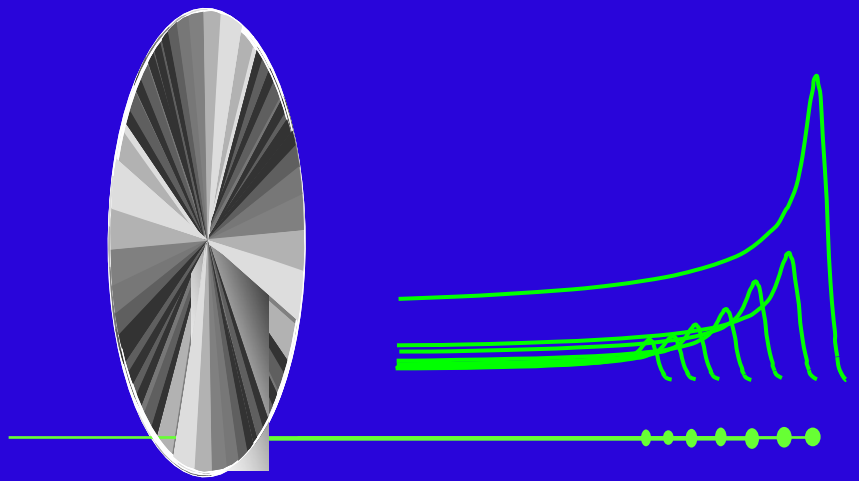
# Extending the dose in depth

## The range shifter wheel

A rotating wheel with varying thickness



The range shifter wheel in action…



RS wheel rotates continuously in beam at ~3000 rpm

# Extending the dose in depth

## The range shifter wheel

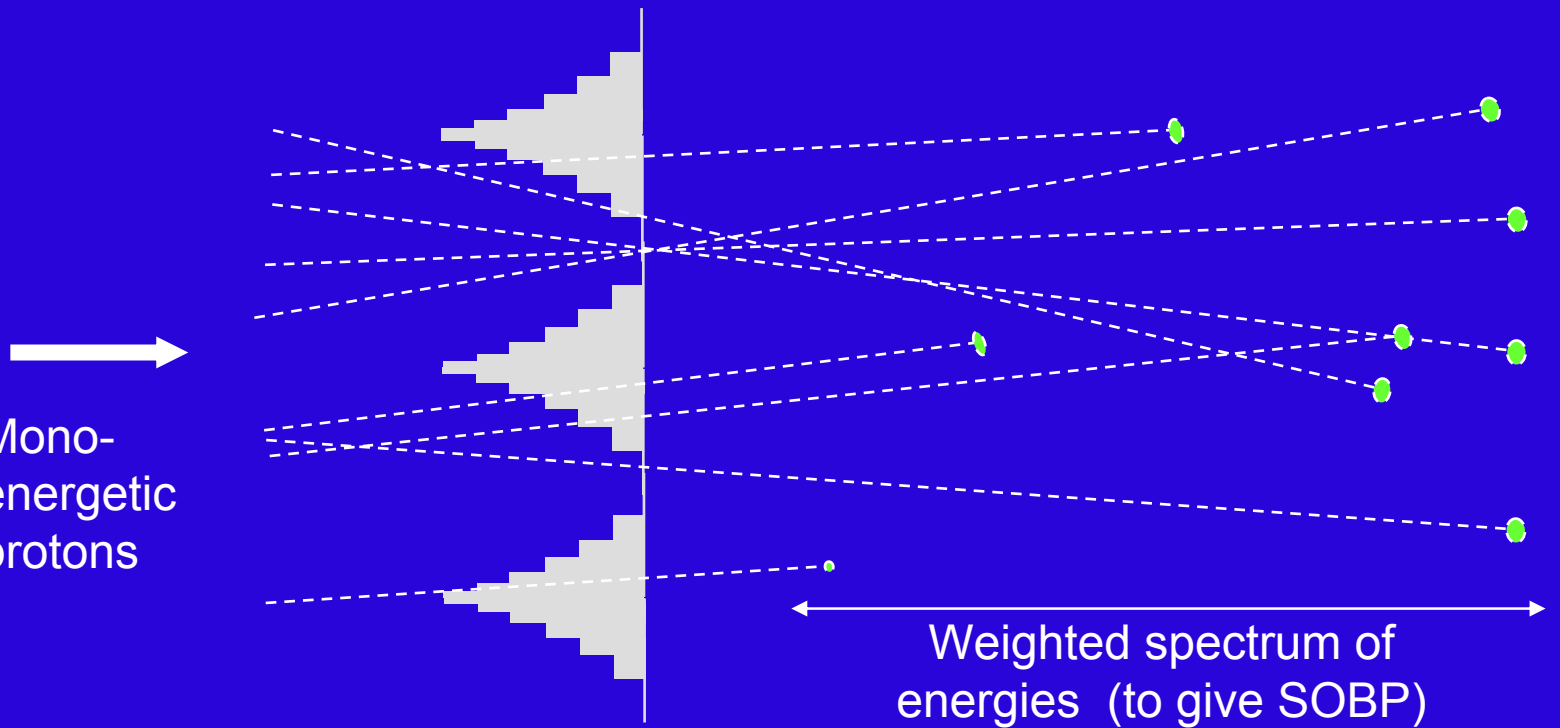

11 cm small beam range shifter wheel

Loma Linda Proton Therapy Centre

Mike Moyers, LLUMC, California

# Extending the dose in depth

## The ridge filter




Relative weighting of Bragg peaks determined by projected areas of ridge filter with different thicknesses

# Extending the dose in depth

## The ridge filter

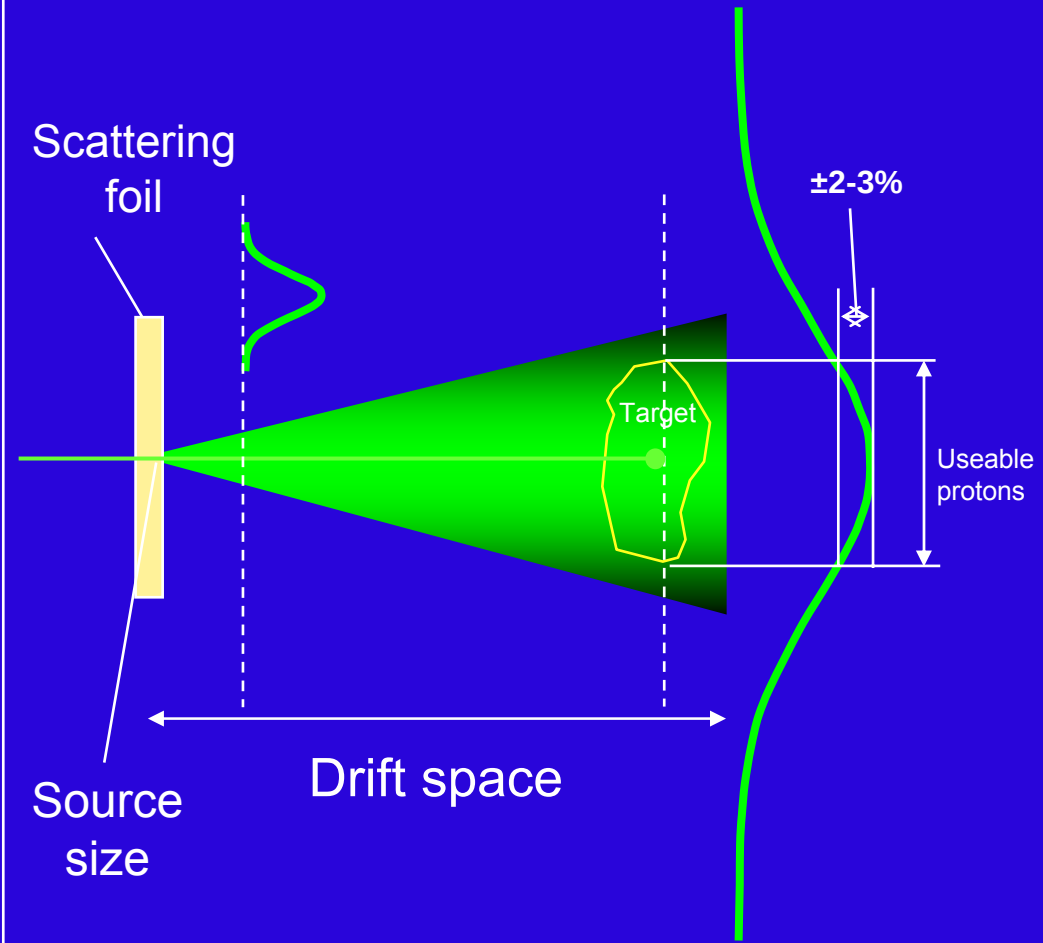

Ridge filters

Kashiwa, Japan

Mike Moyers, LLUMC, California

# Extending the dose laterally

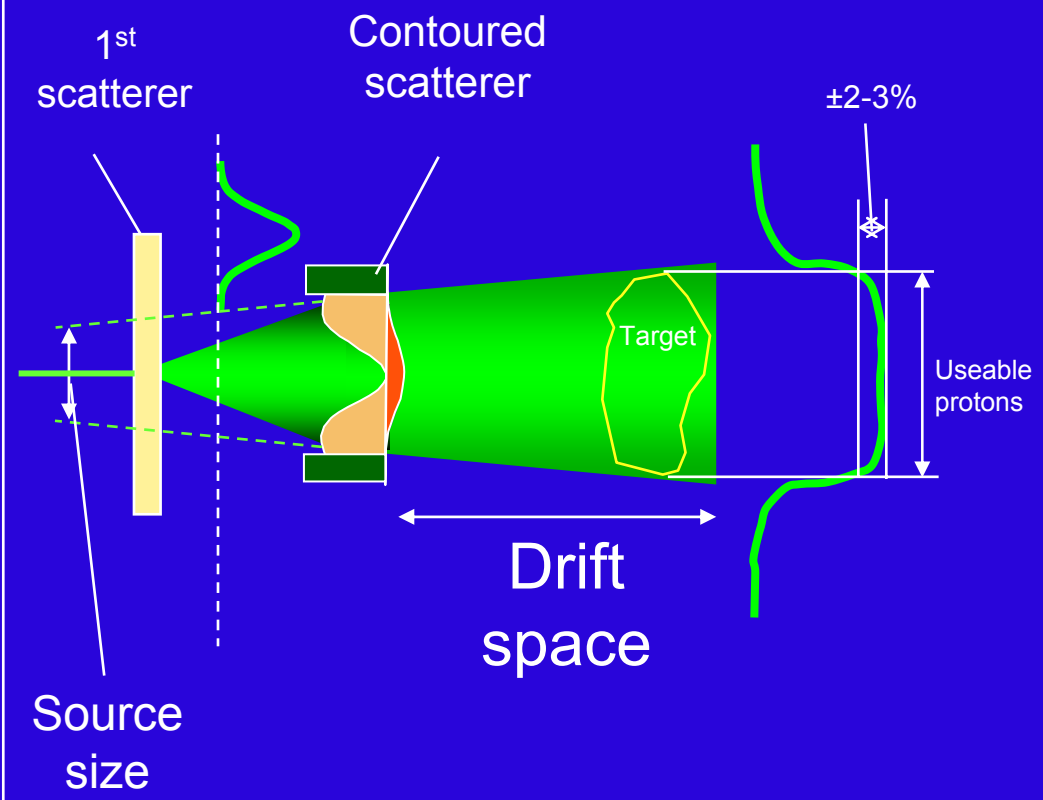
## Single scattering




- Beam broadened in Gaussian form by insertion of scattering foil
- Drift space to patient required for beam to broaden to desired field size (typically 20cm)
- 'Flat' dose achieved by working in top (flattest) part of Gaussian
- Very poor efficiency (very few protons contribute dose to target)
- Good penumbra after collimation (source size similar to initial beam size)

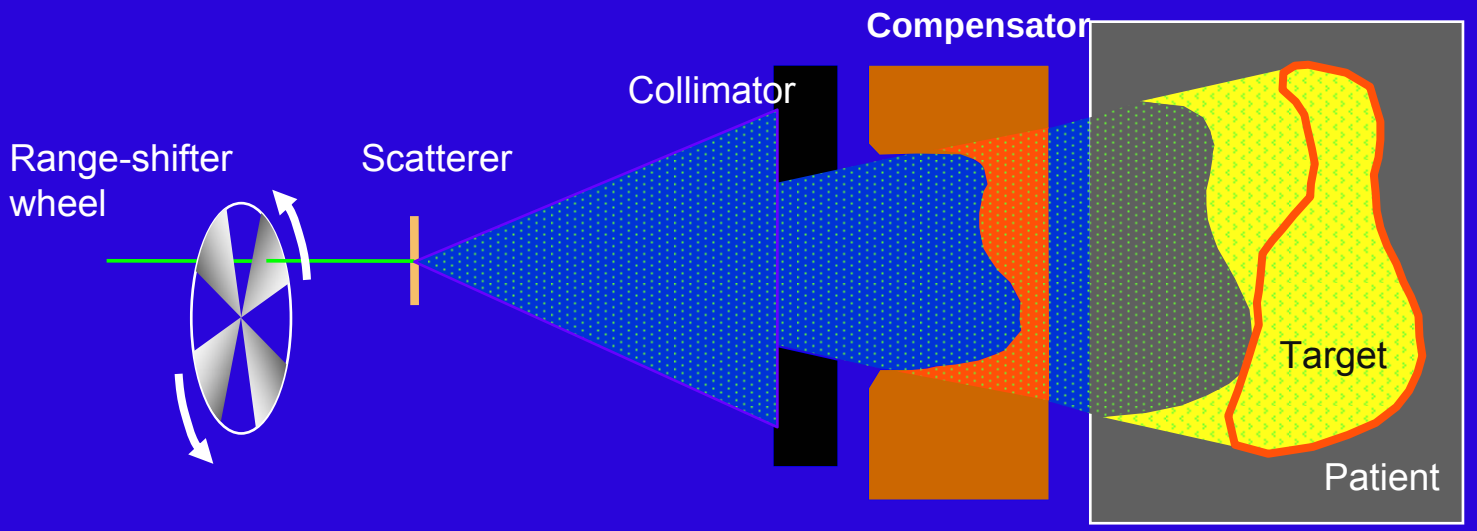
# Extending the dose laterally

## Double scattering



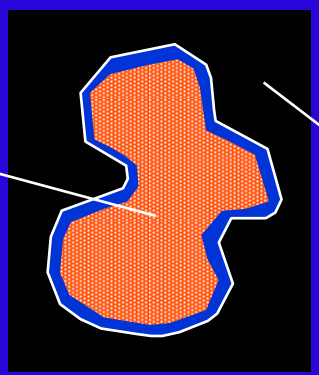

- Second, composite and contoured scatterer, flattens beam
- For similar drift space, larger field sizes are possible (to 40cm)
- Better homogeneity of dose across field
- Much better efficiency (many more protons contribute dose to target)
- However, worse penumbra due to large virtual source size

# Passive scattering in practice




## The collimator

2D Projection of target along beam direction

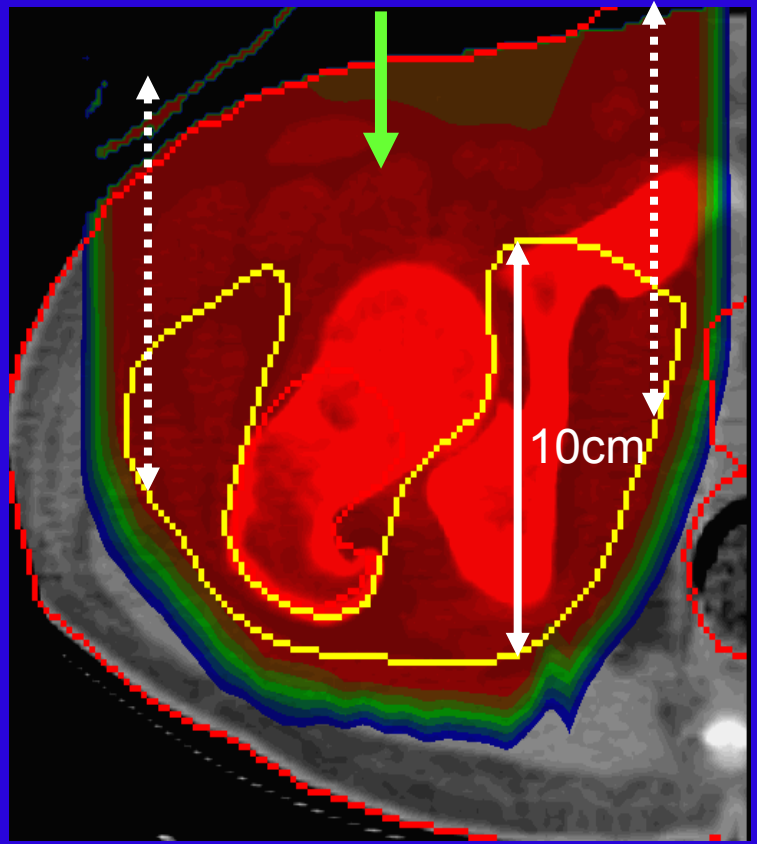


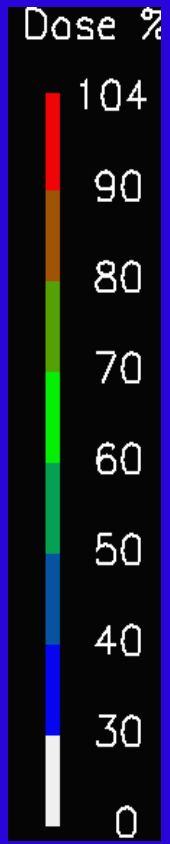
Field specific aperture (collimator) matching projected shape of target

- Each delivered field (incident direction of irradiation) requires specific collimator and compensator
- As range shifter is up-stream of scatterer(s), extent of SOBP is fixed across field

# Passive scattering in practice

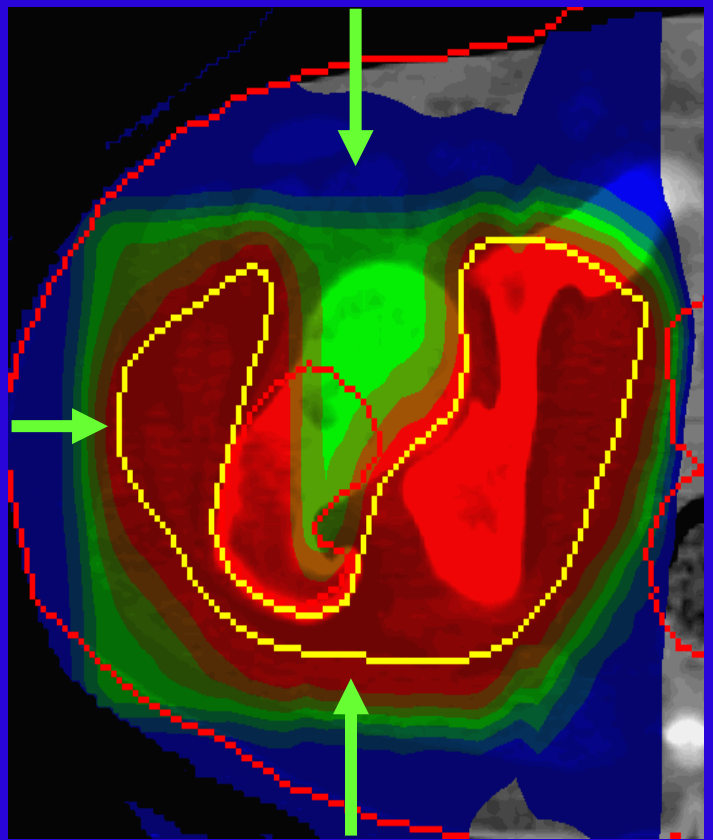
## Single passively scattered field




Fixed extent SOBP leads to poor sparing of normal tissue proximal to target

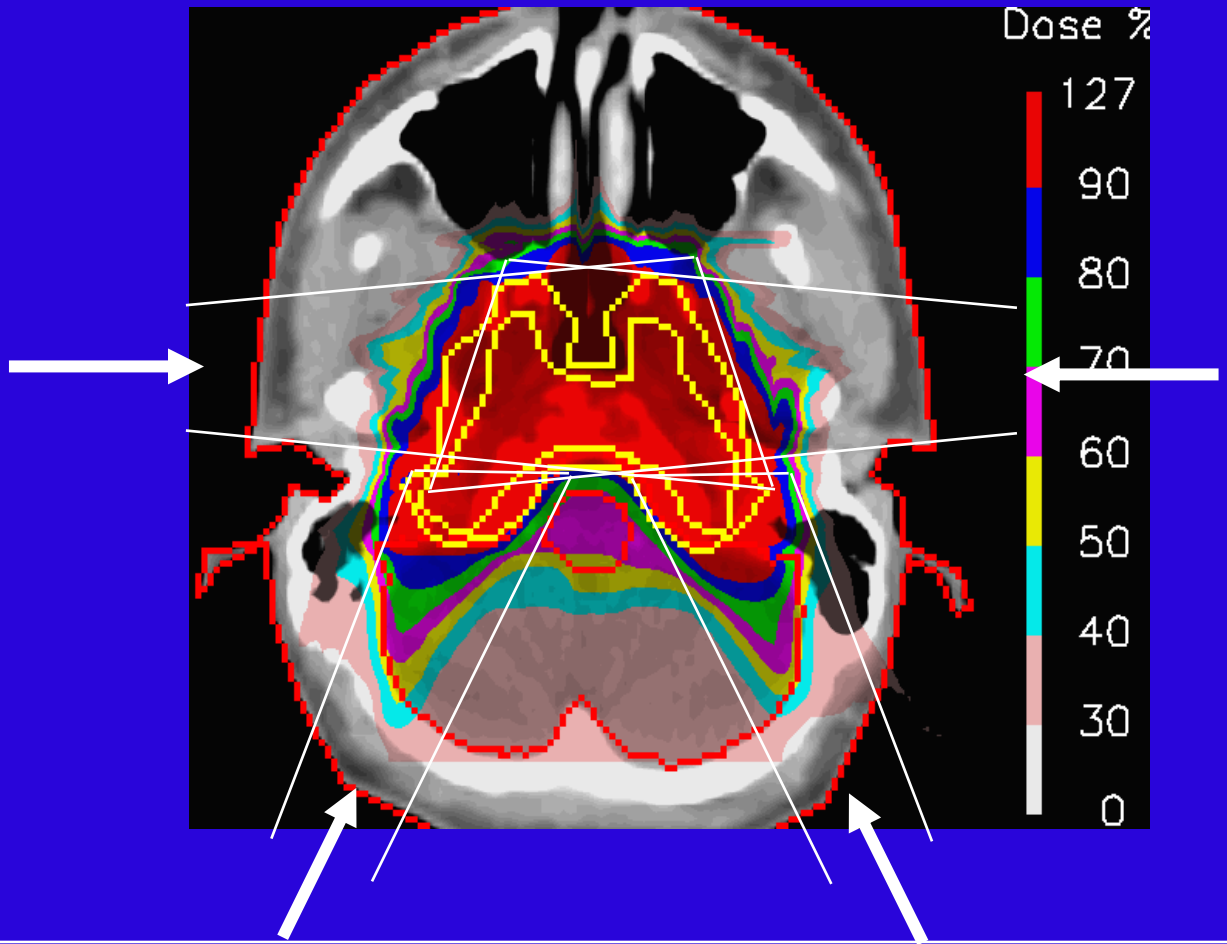
## Three passively scattered fields



Conformation of dose can be improved through the use of multiple fields

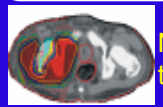
# Passive scattering in practice

Field patching – Matching distal and lateral field edges to improve sparing of neighbouring organs. E.g….

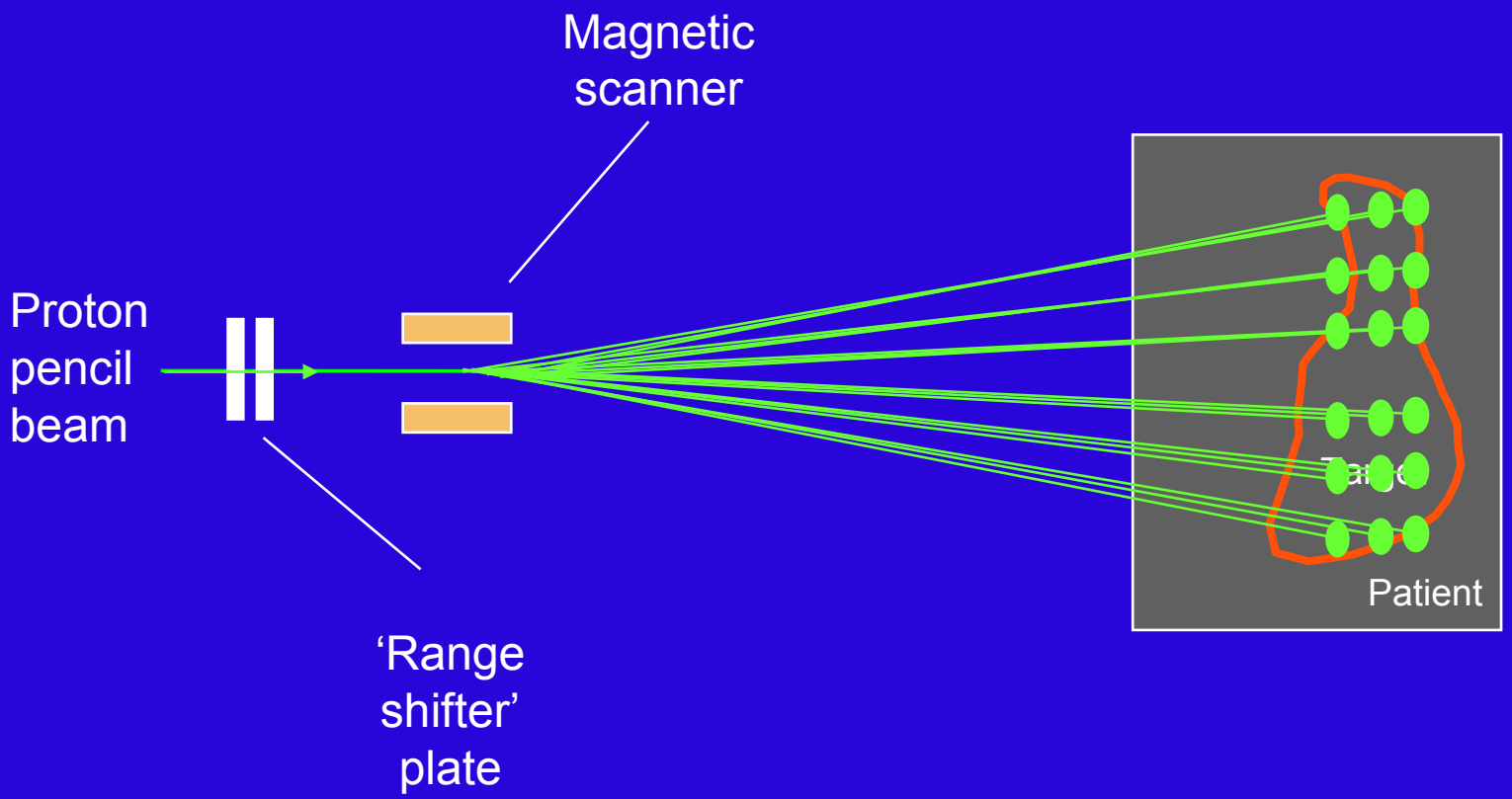


# Treatment delivery

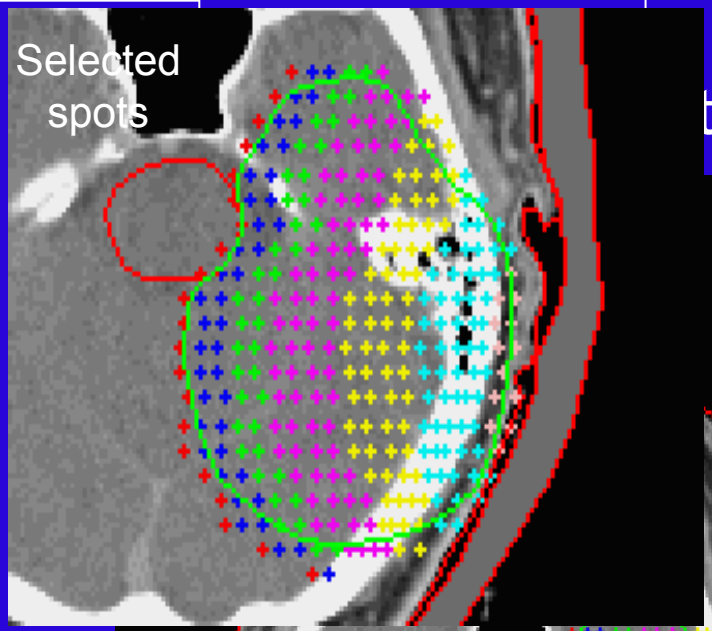
1. Passive scattering
2. Active scanning



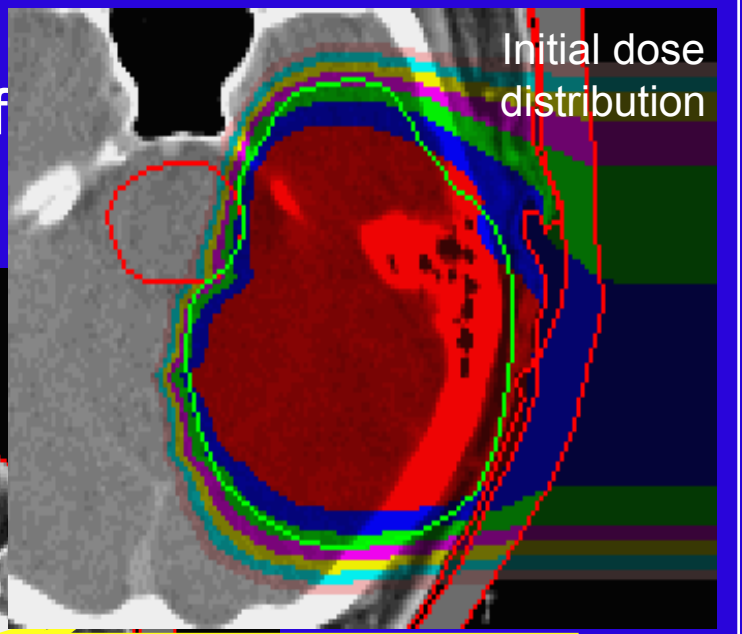
# Active scanning

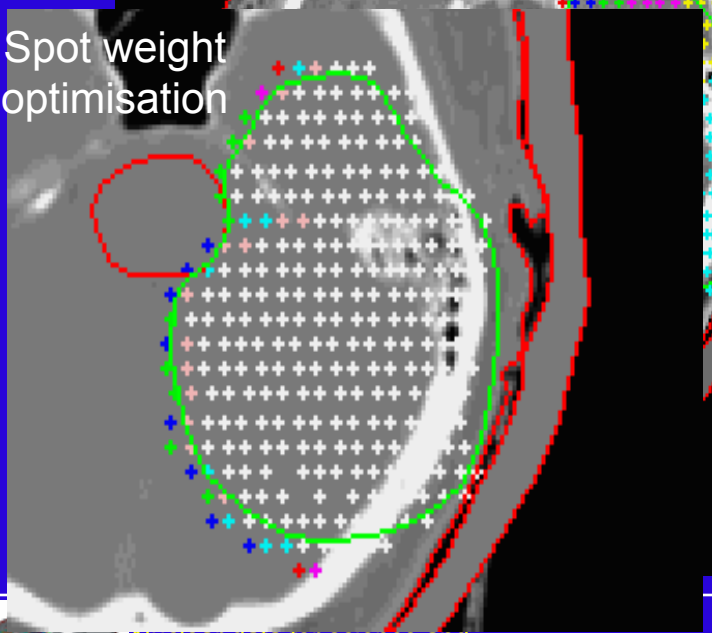


# Treatment delivery – active scanning



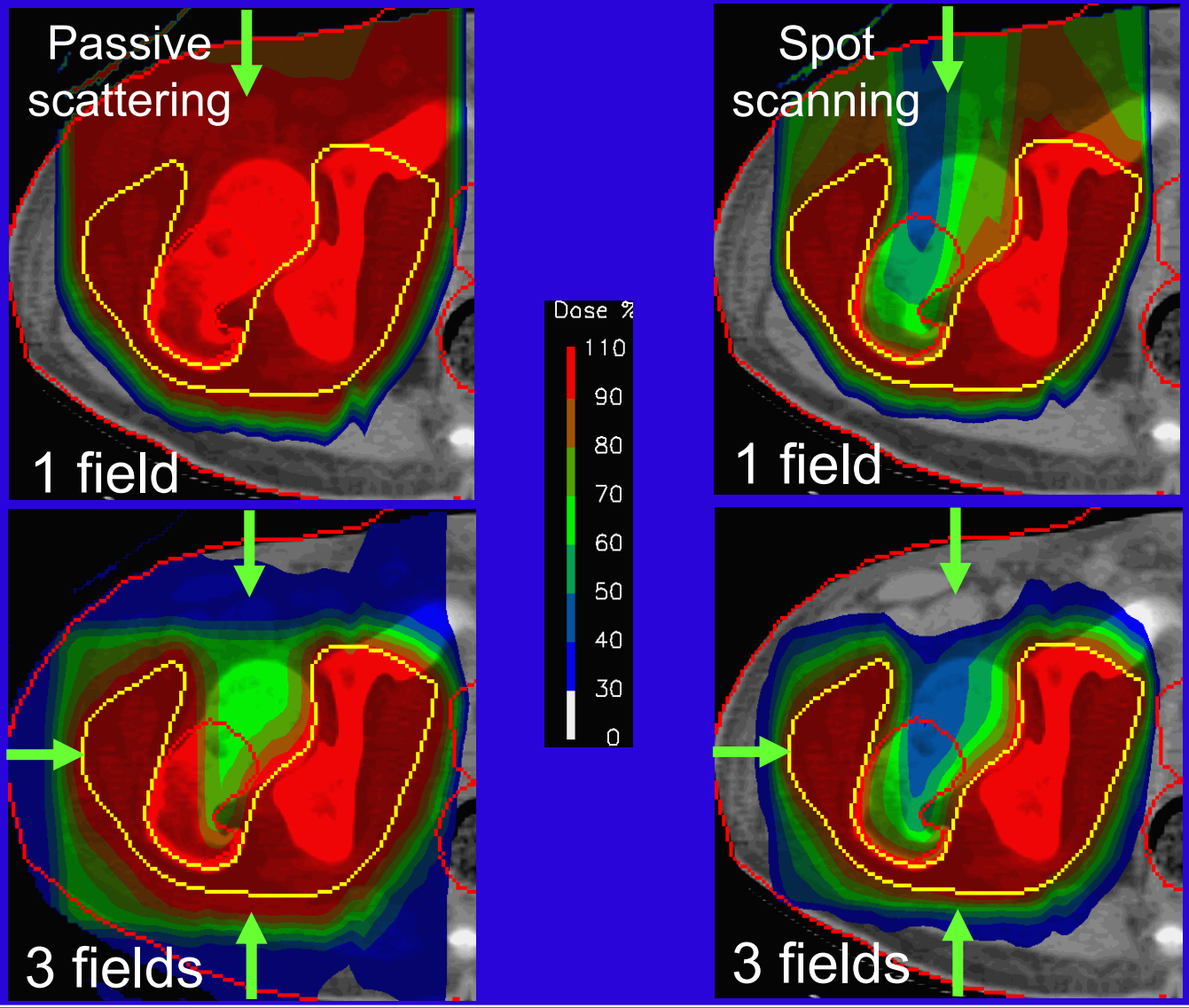

Dose calculation



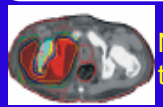

Dose Calculation

# Passive scattering and active scanning compared

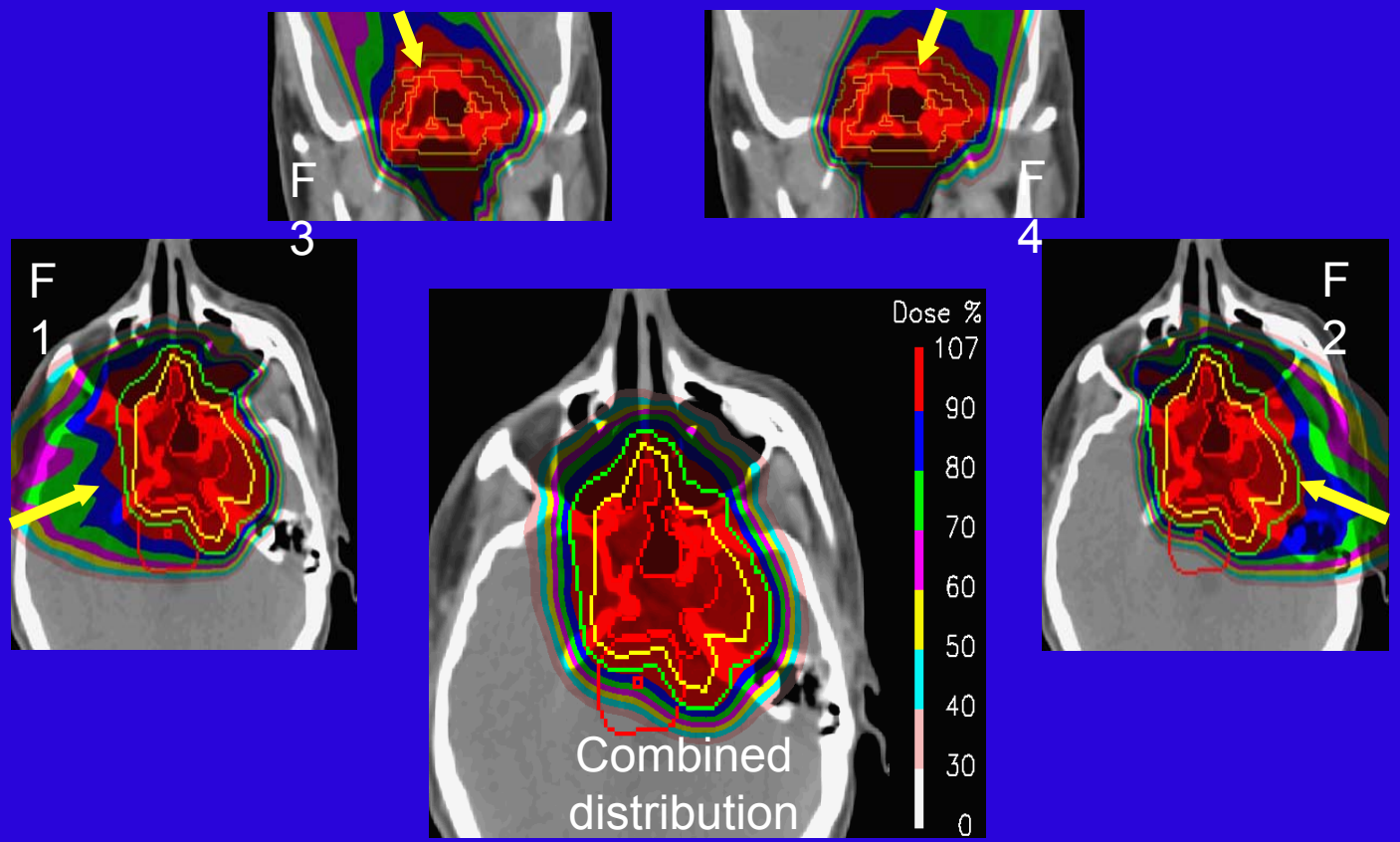


# Passive and scanning delivery compared.

| Passive | | Scanning | |
|---|---|---|---|
| Mature technology | + | New technology | - |
| Insensitive to organ motions | + | Very sensitive to organ motions | - |
| Relatively inflexible | - | Very flexible | + |
| Field specific hardware required | - | No field specific hardware required | + |
| Large gantries required | - | Smaller gantries | + |
| Integral dose | - | Integral dose | + |

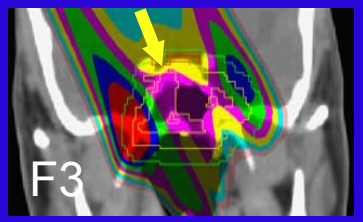


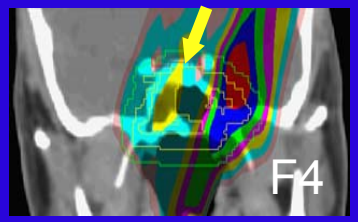
# A spot scanned plan consists of the addition of one or more individually optimised fields.

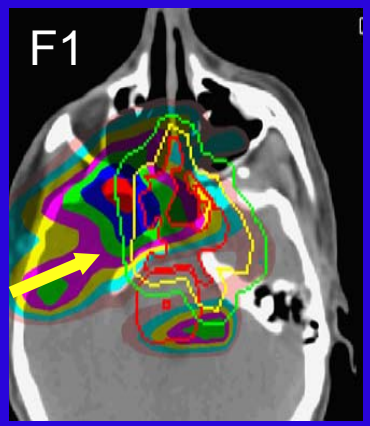


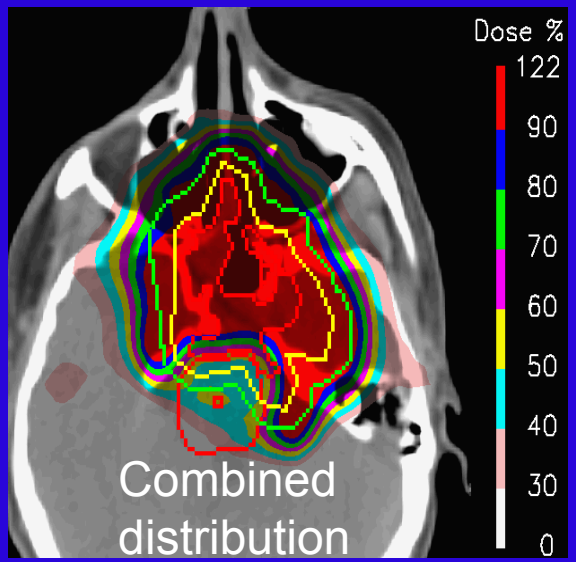

Note, each individual field is homogenous across the target volume

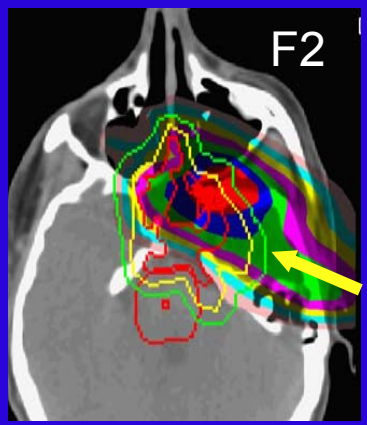
# However, this doesn't have to be the case. We can also optimise all Bragg peaks from all fields simultaneously. E.g..



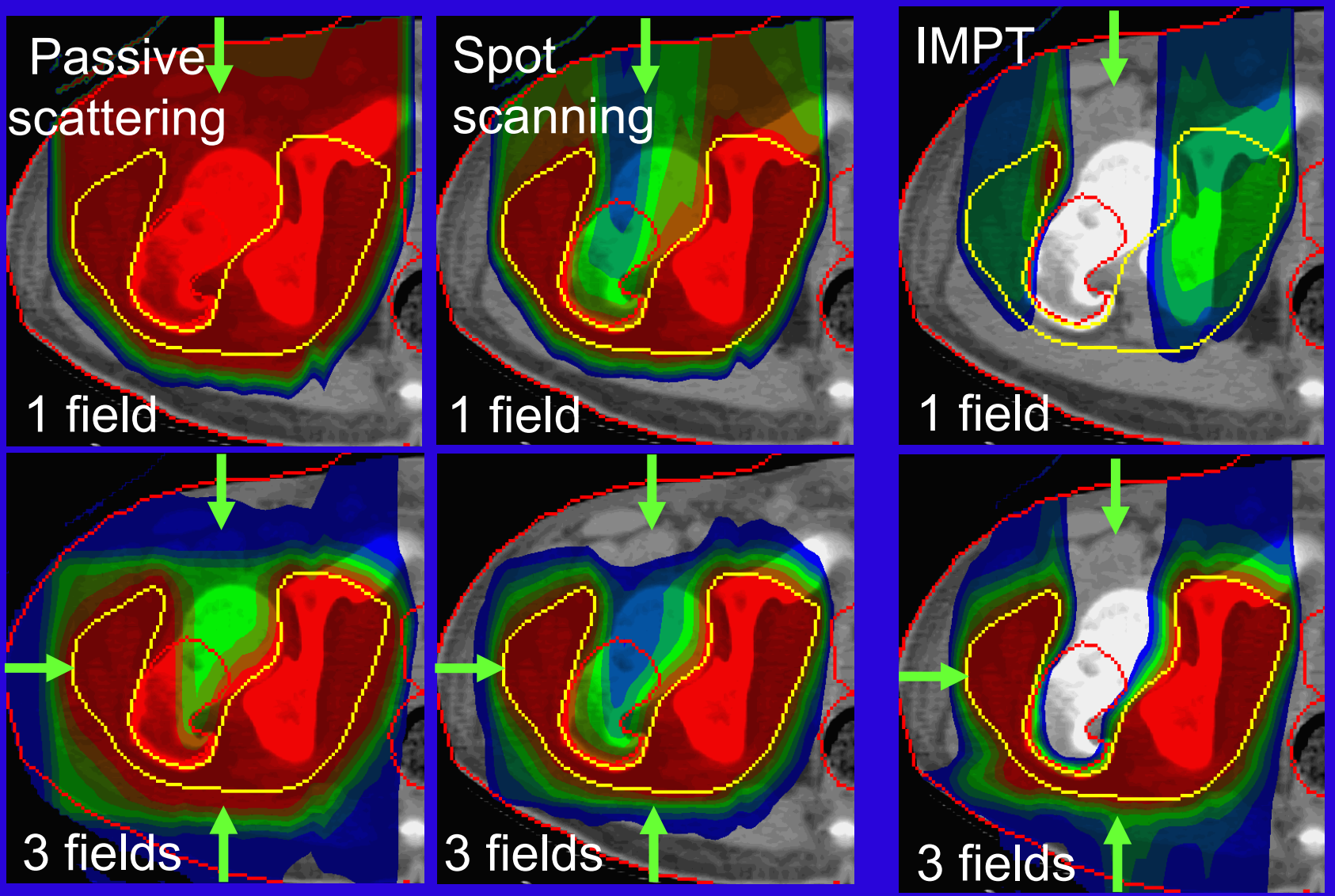



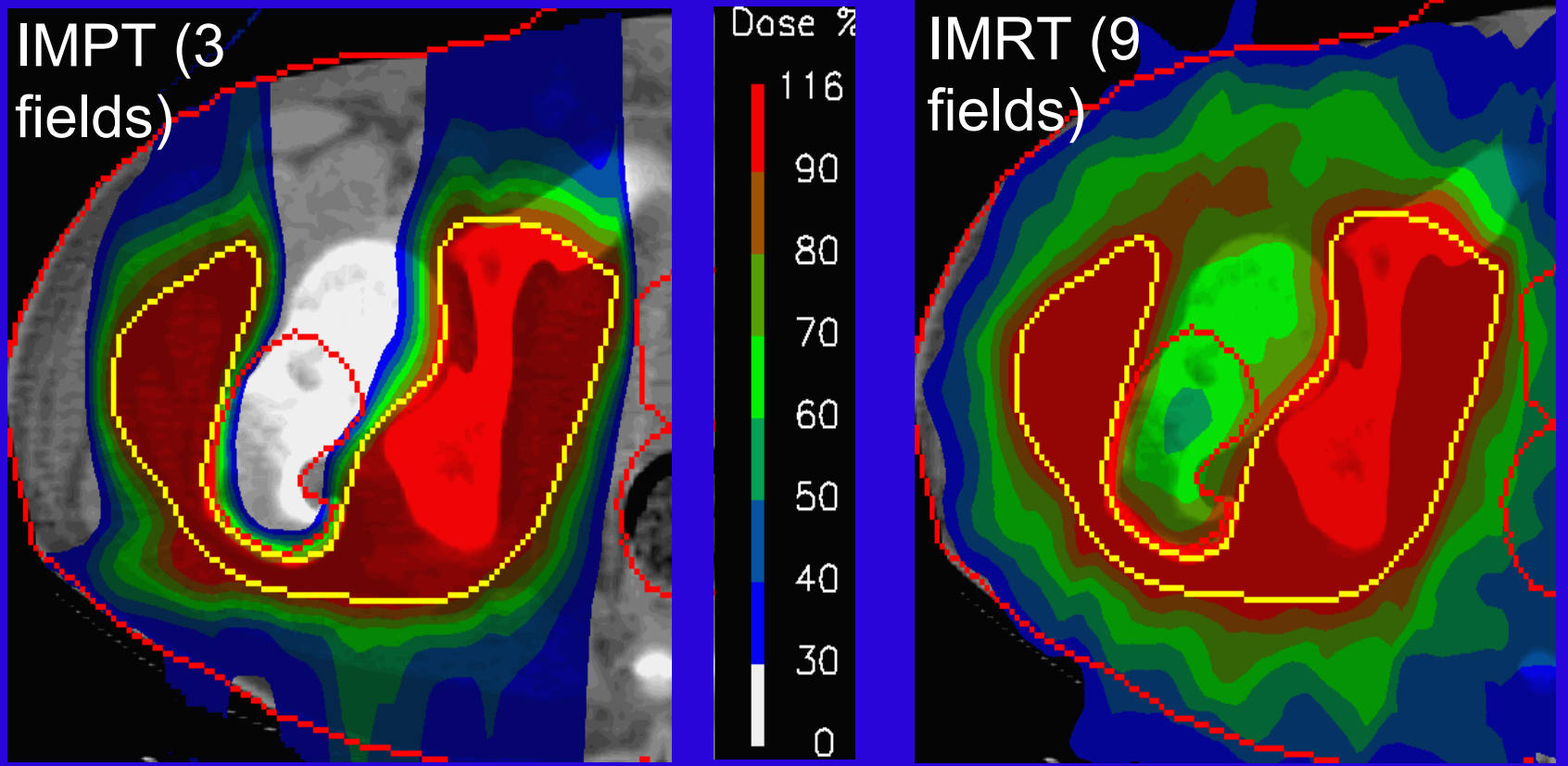

This technique is called 'Intensity Modulated Proton Therapy' (IMPT)

# The three ‘orders’ of proton therapy compared



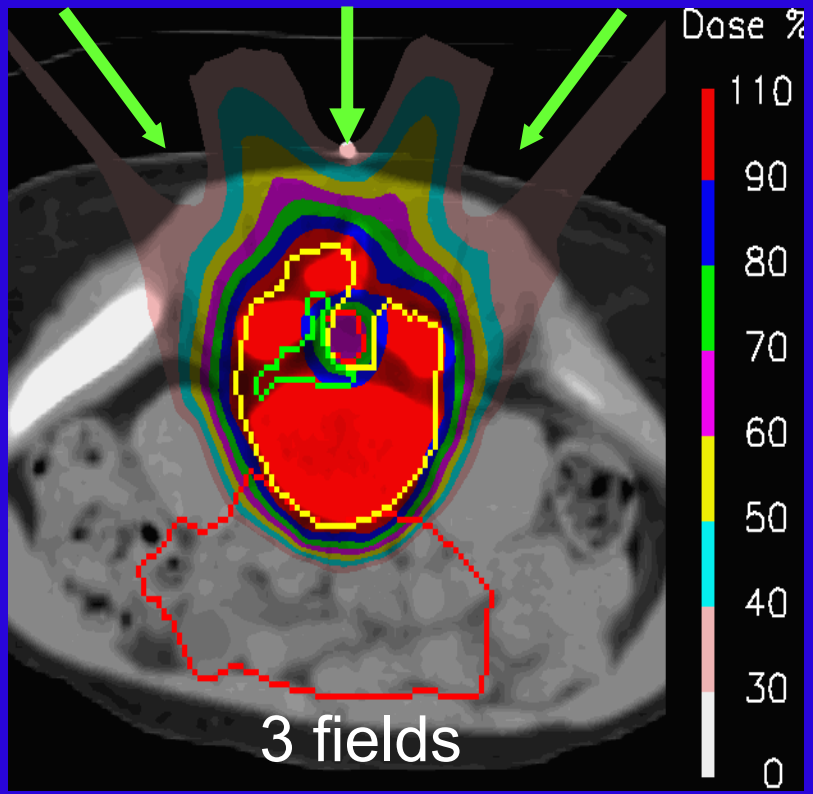
# Intensity Modulated Proton Therapy: The potential

## E.g. Ewings Sarcoma (evaluation only)

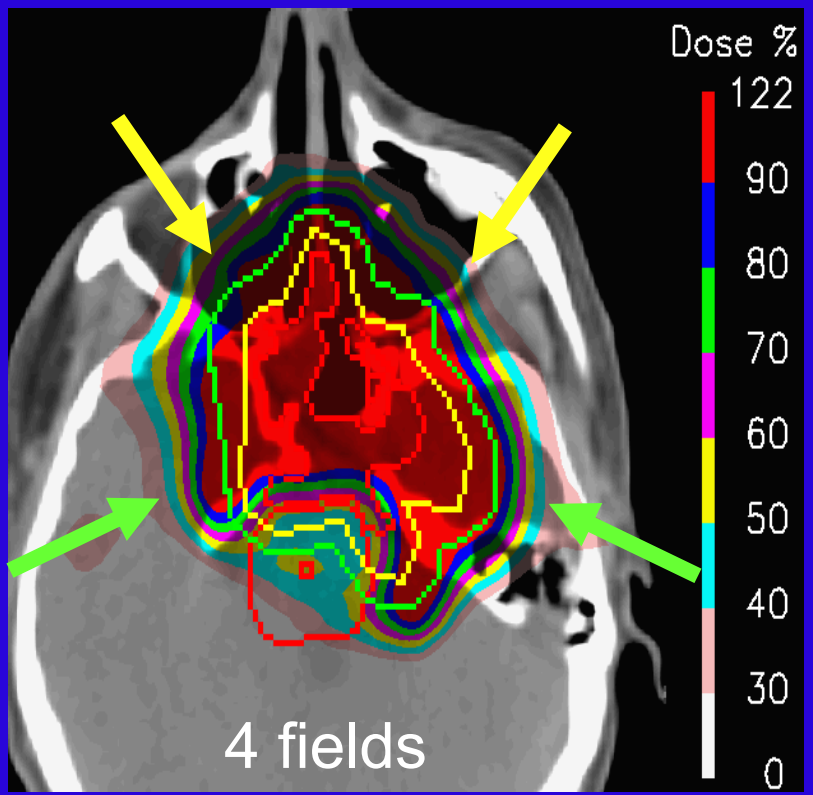


# Two examples of clinical IMPT plans delivered at PSI

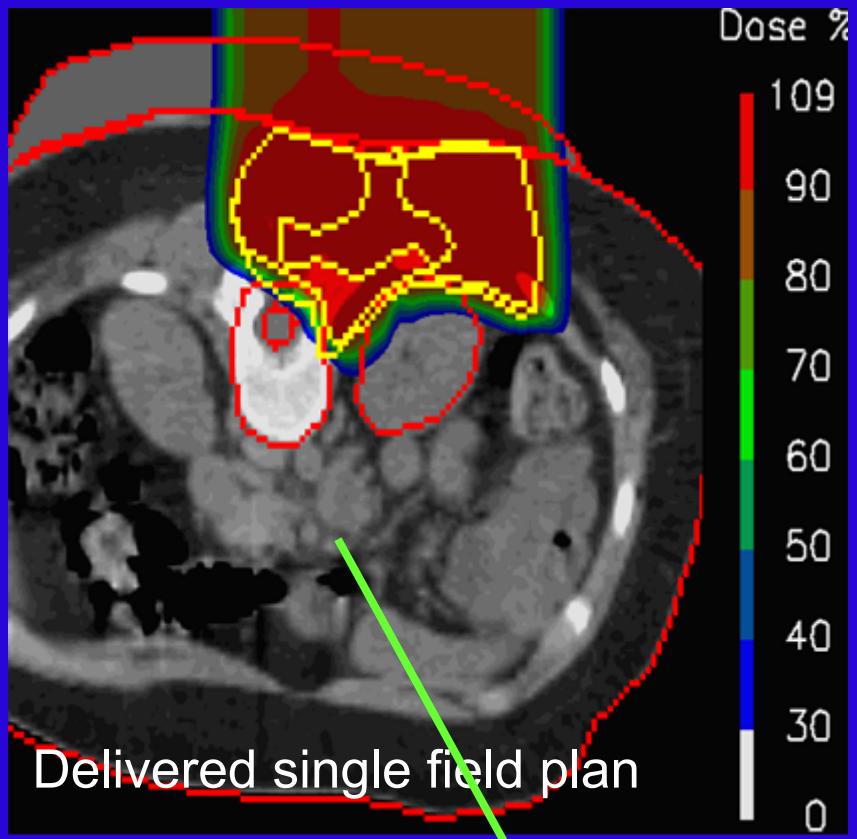
Sacral chordoma,
10 year old girl

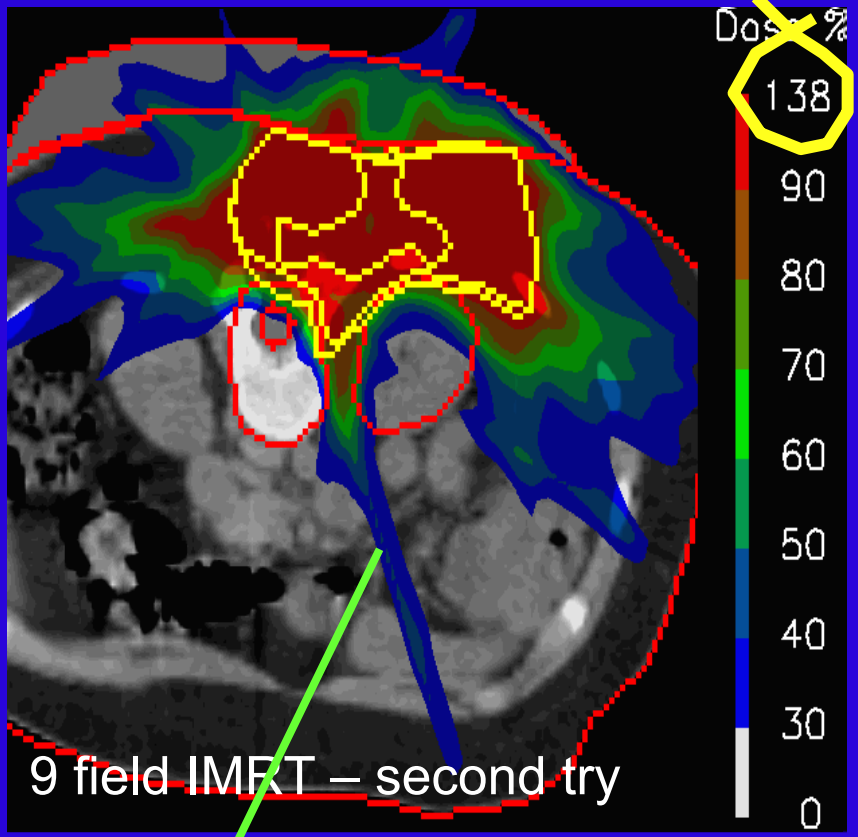



Skull-base chordoma



# A clinical example - Desmoid tumor (12 year old boy)

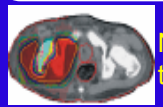



Factor 6 lower integral dose for protons

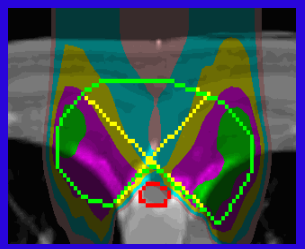
# Overview of presentation

1. Proton therapy – basic principles
2. Treatment delivery
3. Measuring and modeling absolute dose
4. Clinical applications



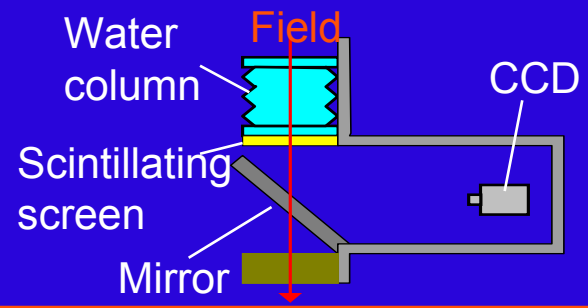
# 2D relative dosimetry for an IMPT field

2D CCD dosimetry of posterior field



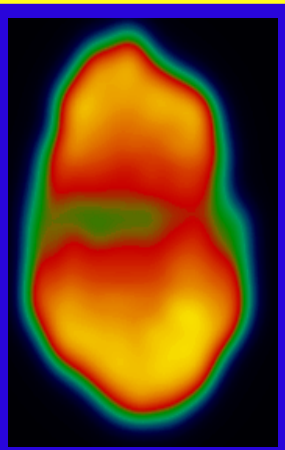
The CCD dosimetry system

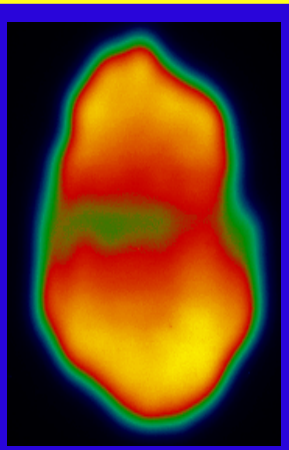
(M Schippers, S Boon, KVI)




D(w) = 4.3cm

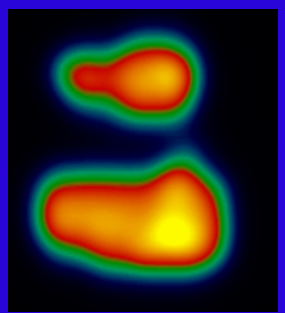
D(w) = 7.8cm

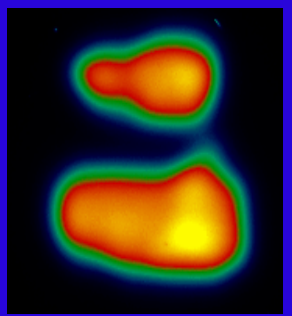


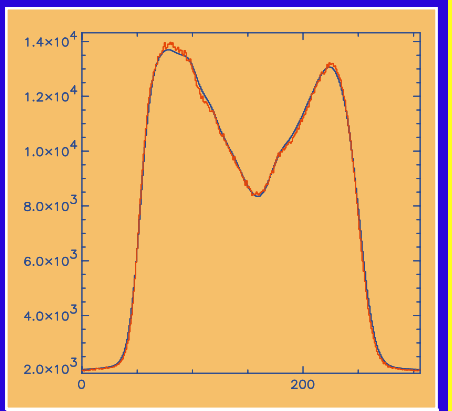


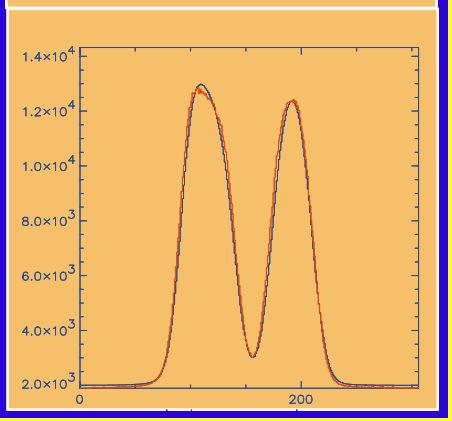
Calculation

Measurement



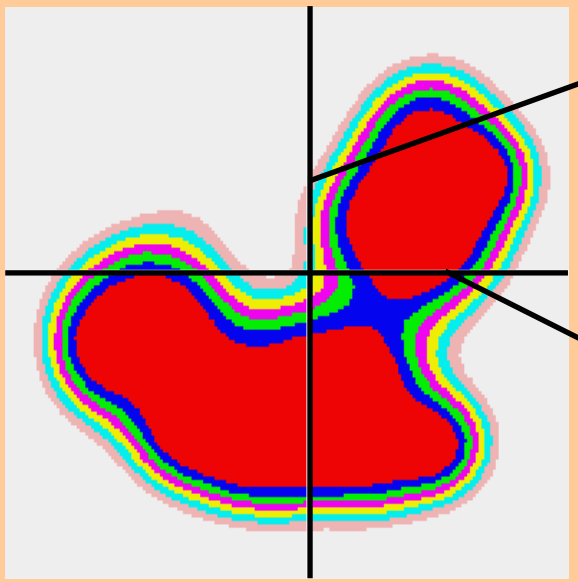


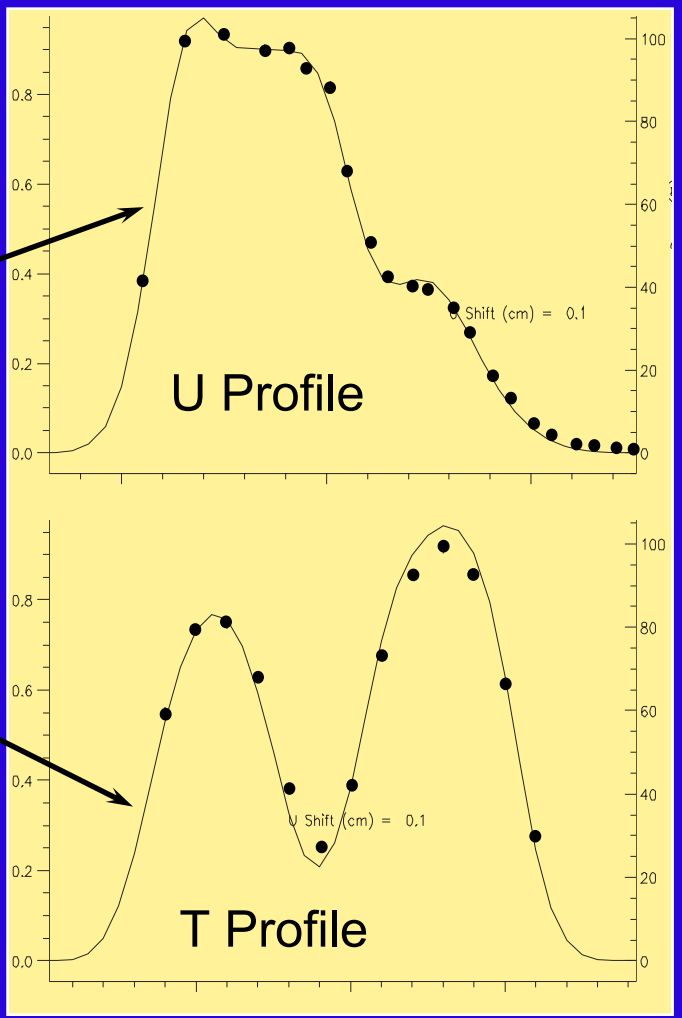


# Ionisation chamber measurements (absolute dose).

Calculated dose in water
(orthogonal to beam direction)





# Calculating 'Monitor Units' for spot scanning

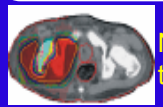
Faraday cup measurement → Protons per Monitor unit

## Treatment planning:

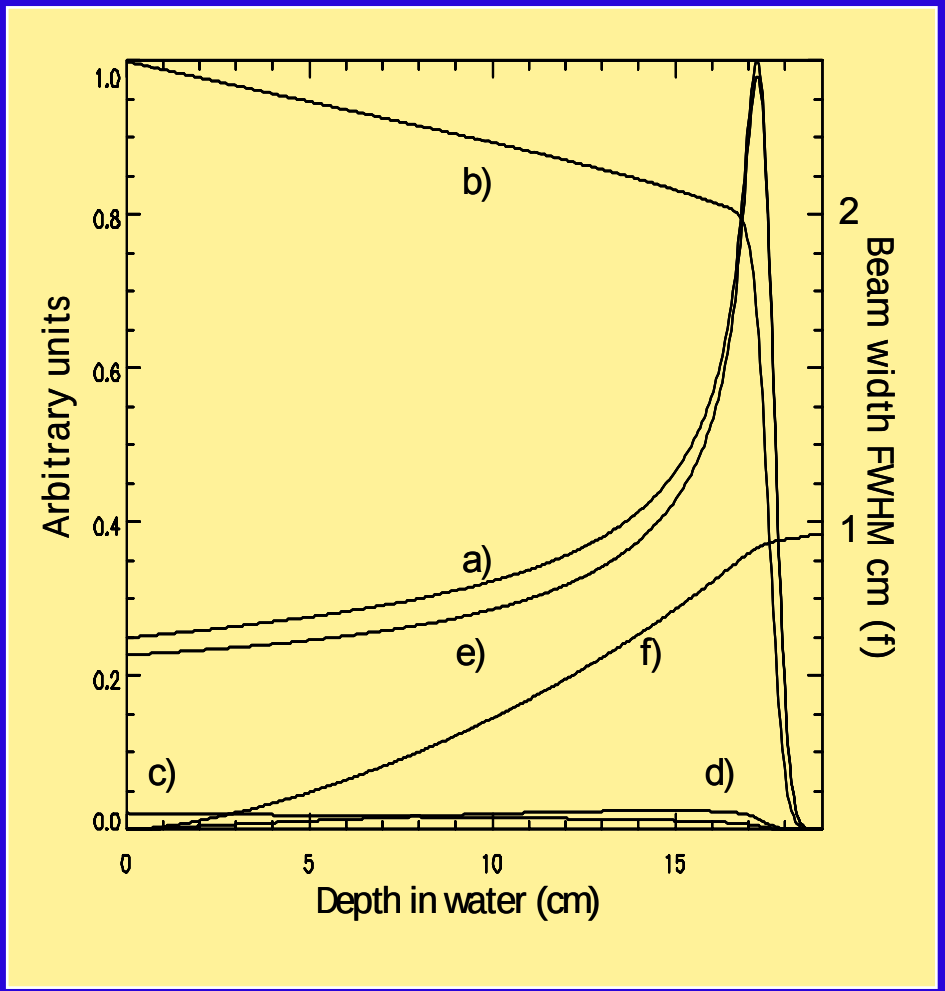
- Dose calculation based on depth dose curve derived directly from Bethe-Bloch formulation[1,2]
- Beam flux attenuation (0,H cross-sections)[1,2]
- Nuclear interaction effects[2]

Dose calculation in homogenous phantom (10x10x10cm box) → Thimble chamber measurements

[1]Scheib S. Diss. ETH Zürich Nr.10451
[2]Pedroni E. et al Phys Med Biol. 2005 Feb 7;50:541-61



# Modeling nuclear interaction effects




Scheib 1993 (PhD thesis)

Kinetic energy from NI deposited in following way:

33% at point of interaction

33% Distributed linearly to end of range (triangle approximation)

33% Lost (photons/neutrons)

a) Deposited dose

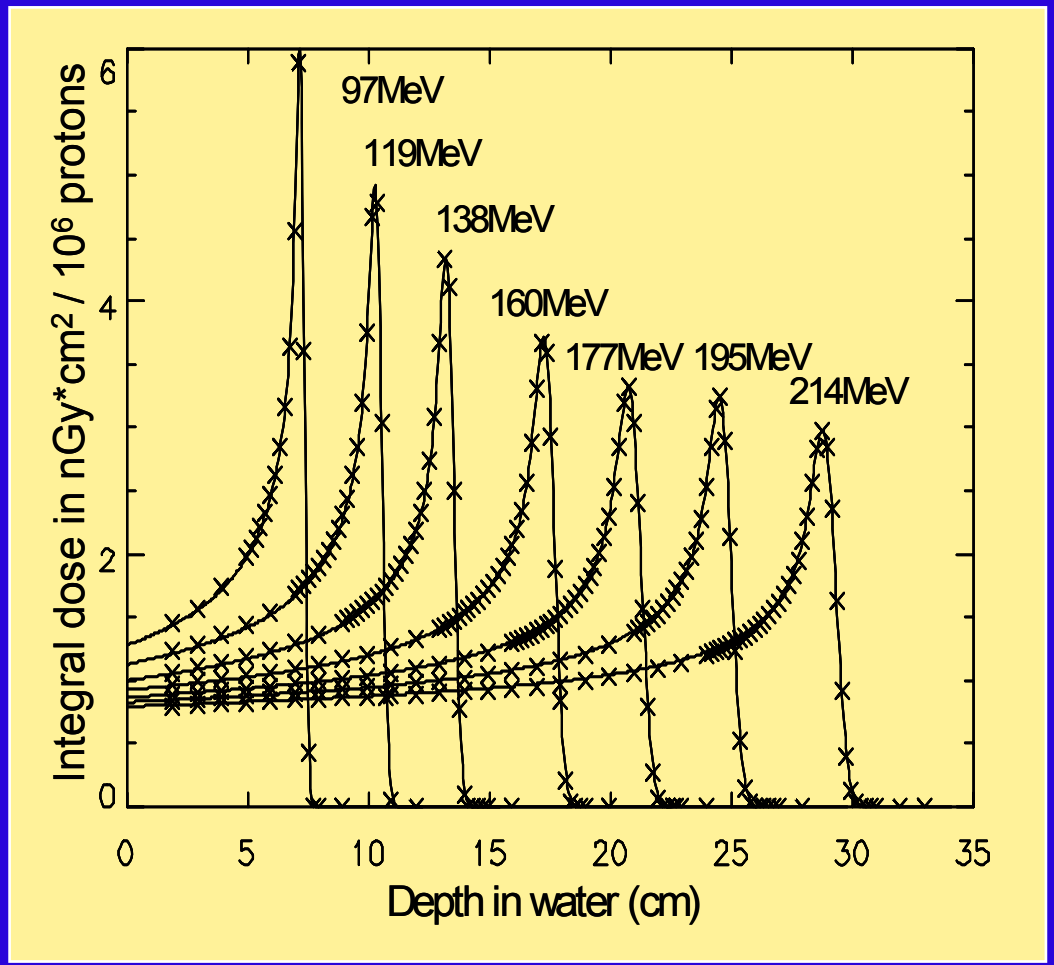
b) Proton fluence

c) Local deposited dose as result of NI

d) Dose deposited by 'long range' secondaries

e) Dose from primary protons

# Modeling nuclear interaction effects




Comparison to measurements

Scheib 1993 (PhD thesis)

# Modeling nuclear interaction effects

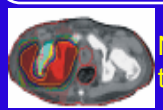
## Absolute dosimetry and MU calculations at PSI

| Energy | Protons /MU | Dose accuracy from model |
|---|---|---|
| 138 MeV | 6555 | -0.1% |
| 160 MeV | 7333 | -0.1% |
| 177 MeV | 7921 | -2.2% |

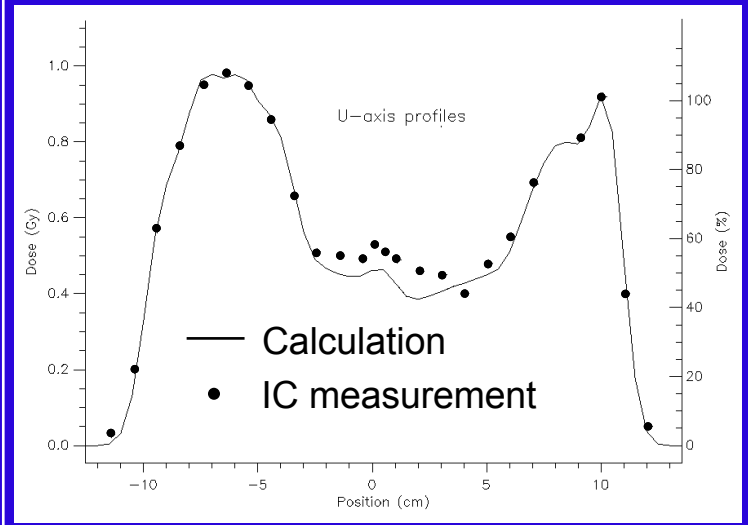
Dose measured in centre of 10x10x10cm uniform dose field

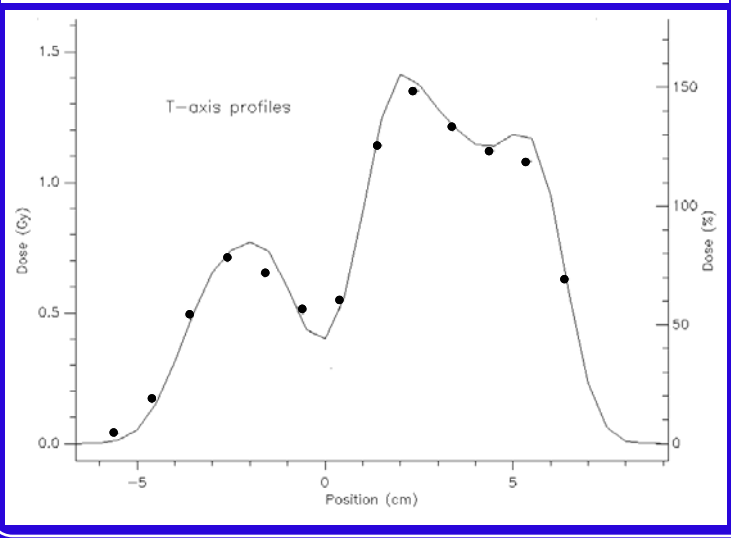
1 MU ~ 7000 Protons ~ 1fC (proton charge)

Shixiong Lin, PSI



# Modeling nuclear interaction effects

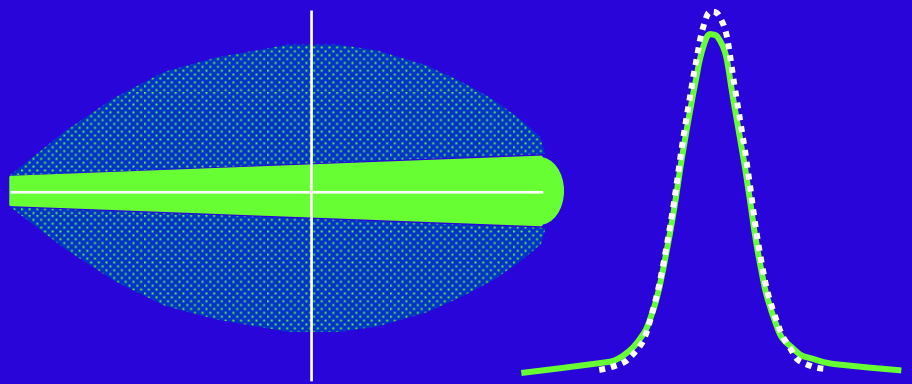



## In clinical practice

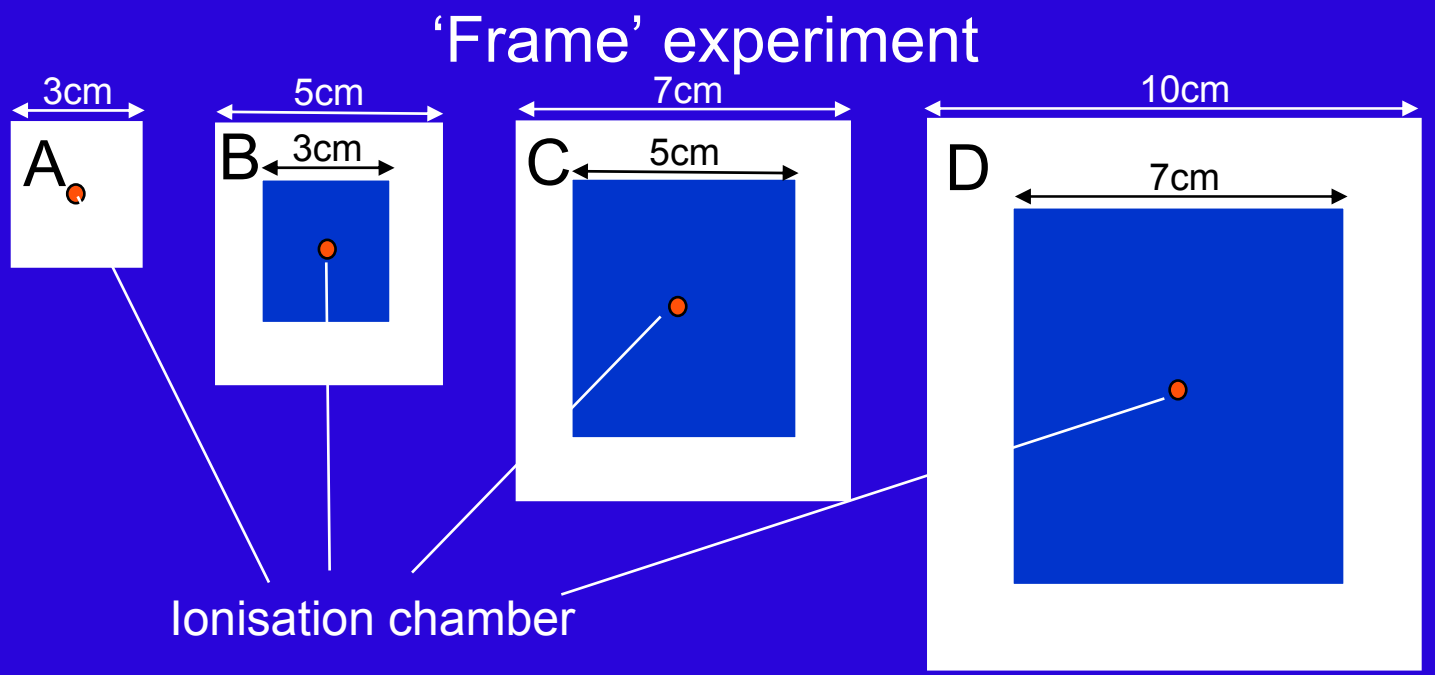
Based on field specific IC measurements, measured dose varies 1-9% c.f. calculation in complex fields (IMPT)

Problem of lateral distribution of secondary particles?



# Modeling nuclear interaction effects

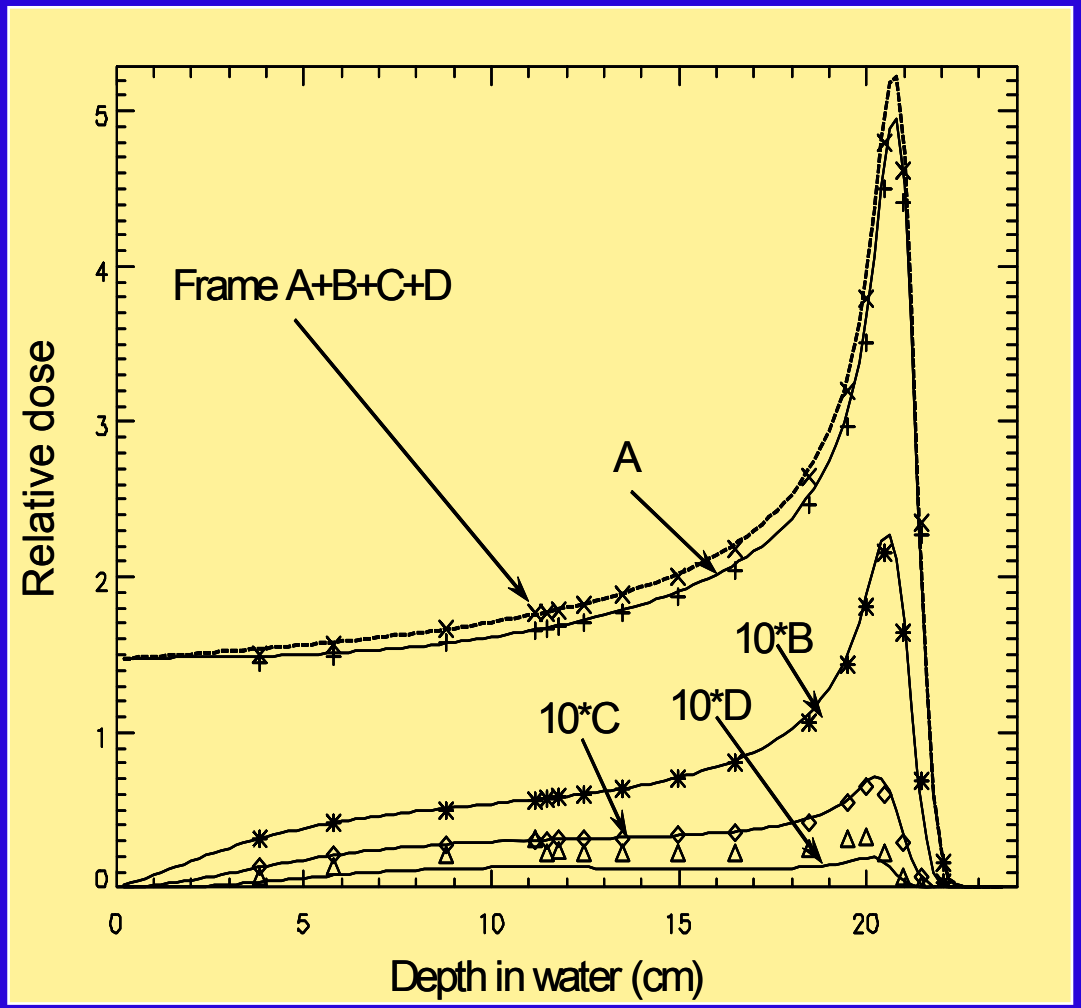
## Experimental determination of lateral contribution of secondary particles (protons)




## Measure dose at centre of various frame sizes (A-D)

Pedroni et al, PMB, 50 (2005) 541-561

# Modeling nuclear interaction effects



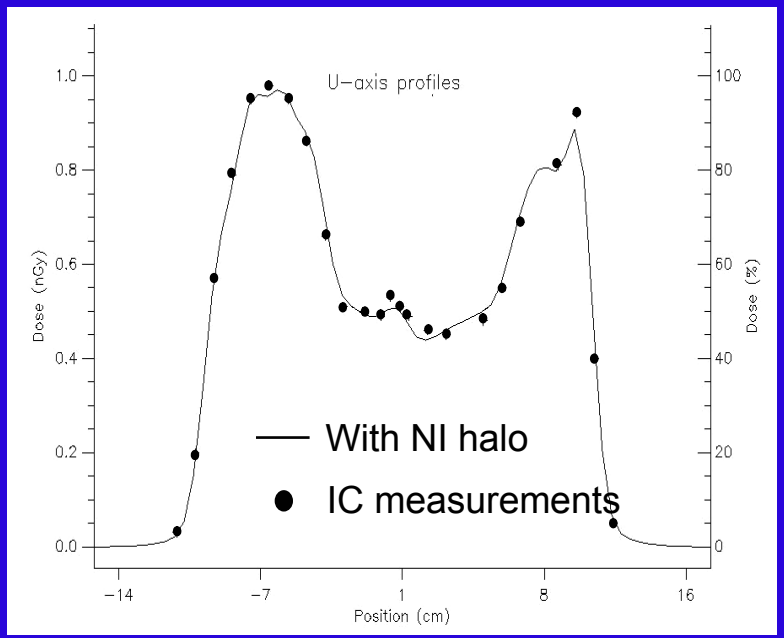

Depth dose distributions for frames (177 MeV)

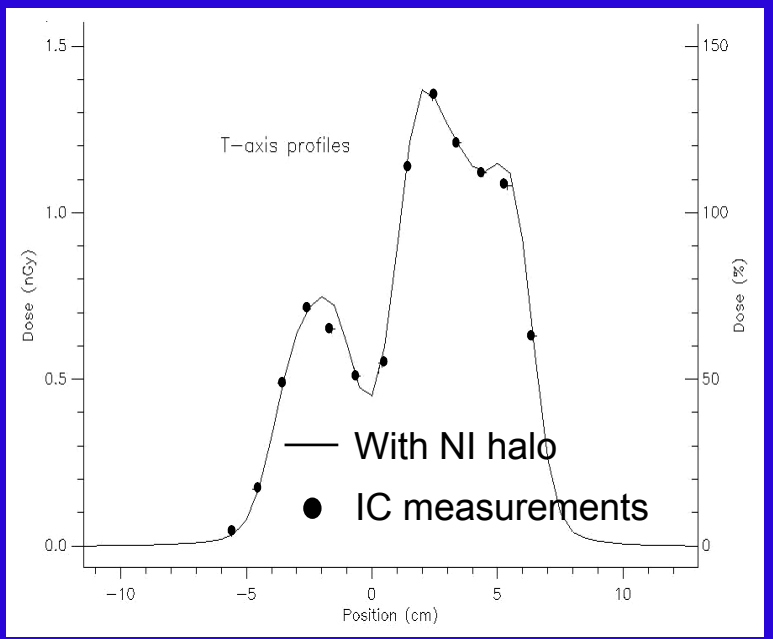
From these distributions, possible to derive analytical model (gaussian approximation) for lateral distribution of secondary particles

Pedroni et al, PMB, 50 (2005) 541-561

# Modeling nuclear interaction effects

## IC Measurements compared to extended (gaussian) dose model including lateral distribution of secondary particles




Bolsi et al , SASRO, 2005

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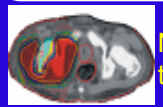
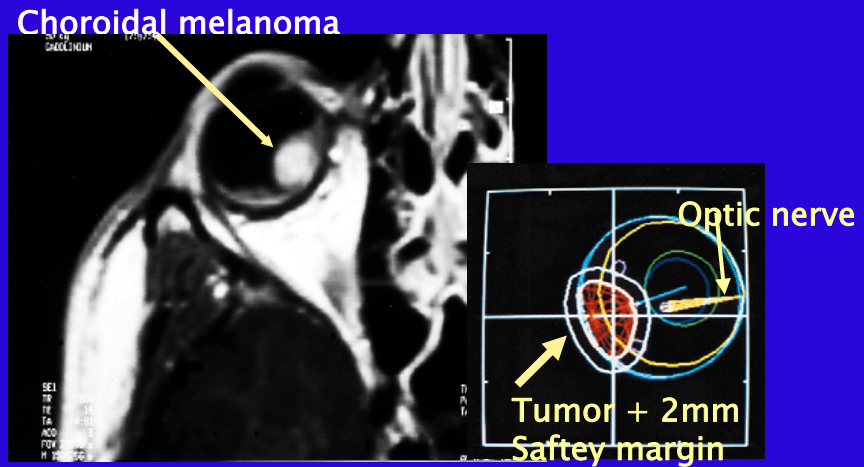
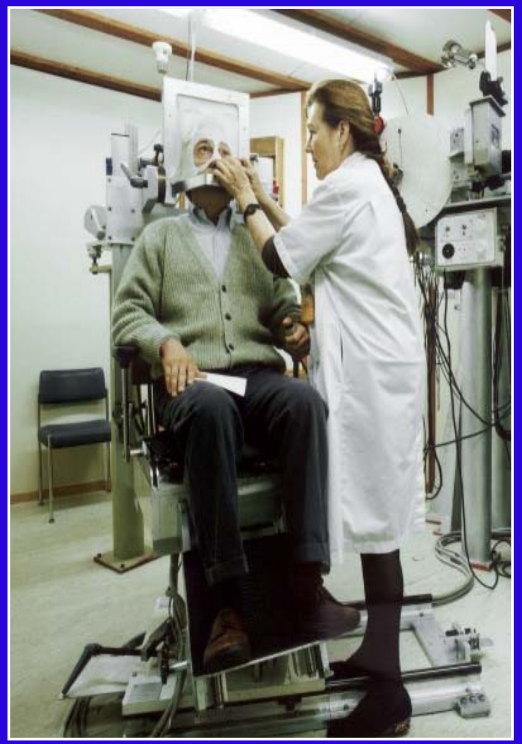


# Proton therapy of uveal melanomas at PSI



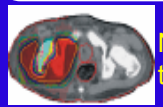

**Cooperation with Prof. Zografos**
**Eye infirmary,**
**University of Lausanne**

# Clinical results at PSI for uveal melanomas

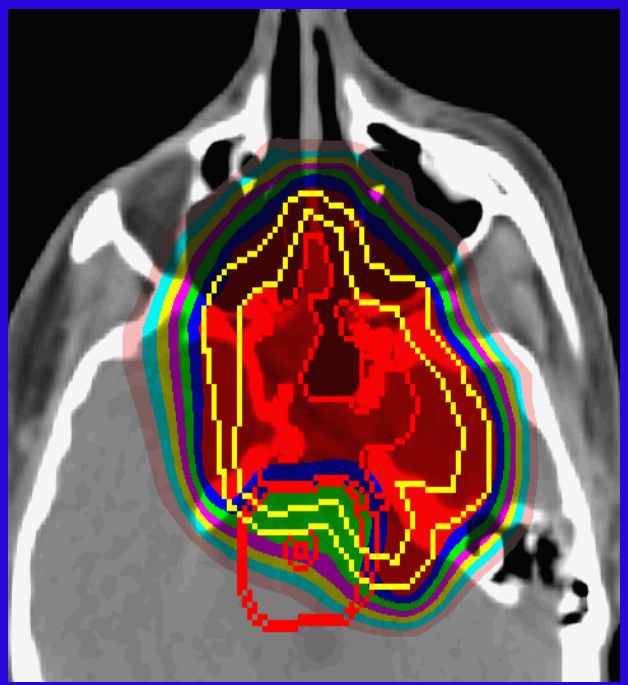
## Since 1984 >4200 patients treated at PSI

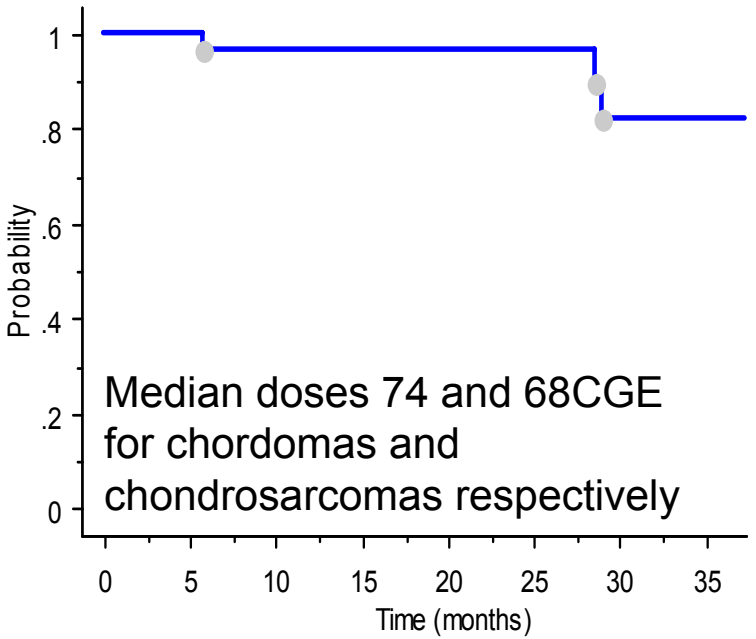
- Local tumour control
  98% over all patients
  (best for small tumours
  worse for large tumours)

- Retention of irradiated eye after 10 years
  100% for small tumours
  90% for large tumours



# Chordomas and chondrosarcomas of the base of skull: PSI results





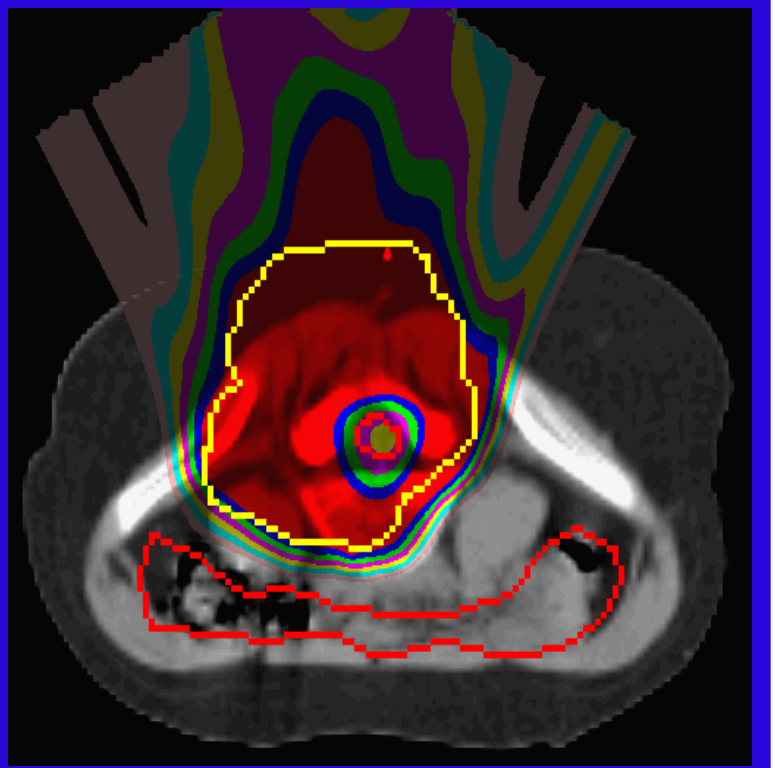

Complication free survival chordomas/chondrosarcomas
(n=29, median follow-up 29 months)

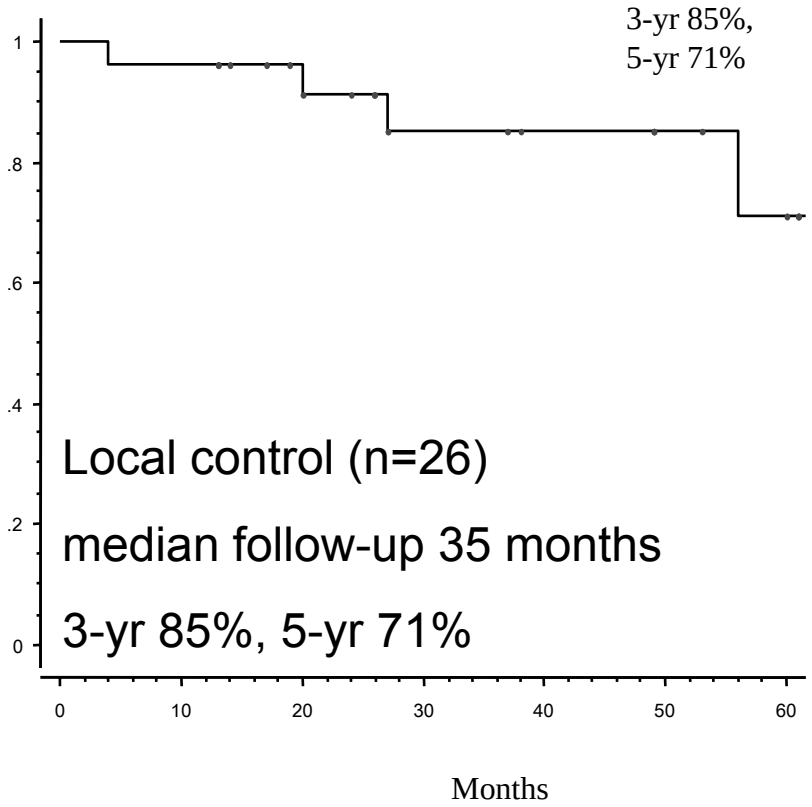
Weber et al, Int. J. Radiat. Oncol. Biol. Phys, 63, 2005

# Comparison of reported results for chordomas of the base of skull

| | | n | Radiation | Mean dose | LC 3-yr | LC 5-yr | LC 10-yr |
|---|---|---|---|---|---|---|---|
| Castro, 1994 | | 53 | Helium, Neon | 65 | | 63 | |
| Terahara, 1999 | | 115 | PT, RT | 69 | | 59 | 44 |
| Hug, 1999 | | 58 | PT, RT | 71 | 67 | 59 | |
| Noel, 2003 | | 67 | PT, RT | 67 | 71 | | |
| Schulz-Ertner, 2003 | | 67 | Carbon, RT | 60* | 87 | | |
| Igaki, 2004 | | 13 | PT, RT | 72 | 67 | 46 | |
| Weber, 2005 | | 18 | PT | 74 | 87 | | |
| | | | | | | | |

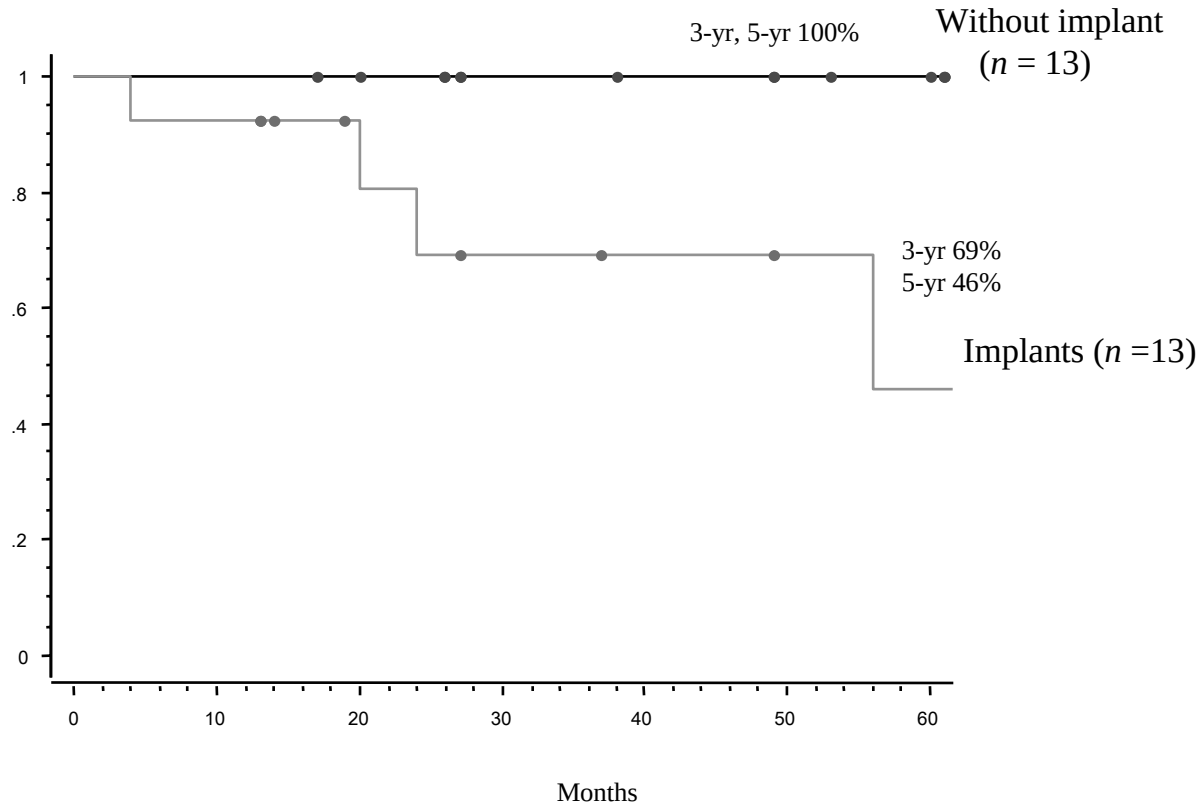
# Chordomas and chondrosarcomas of the spinal axis






Rutz et al, To be published

# Chordomas and chondrosarcomas of the spinal axis




Rutz et al, To be published

# Summary.

- Protons have been used clinically for almost 50 years with more than 50000 patients treated
- Proton delivery is still predominantly based on passive scattering
- However, next generation of commercial proton facilities will be ‘scannning’ and IMPT capable.
- For scanning, absolute dosimetry can be accurately predicted from basic physics principles, but effects of secondary particle distributions also need to be modeled, particularly in complex fields
- There are many other challenges for proton therapy c.f. conventional RT! See next lecture.