STFC radiation detectors in medicine meeting, UHB

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What do we need alongside particle therapy ?

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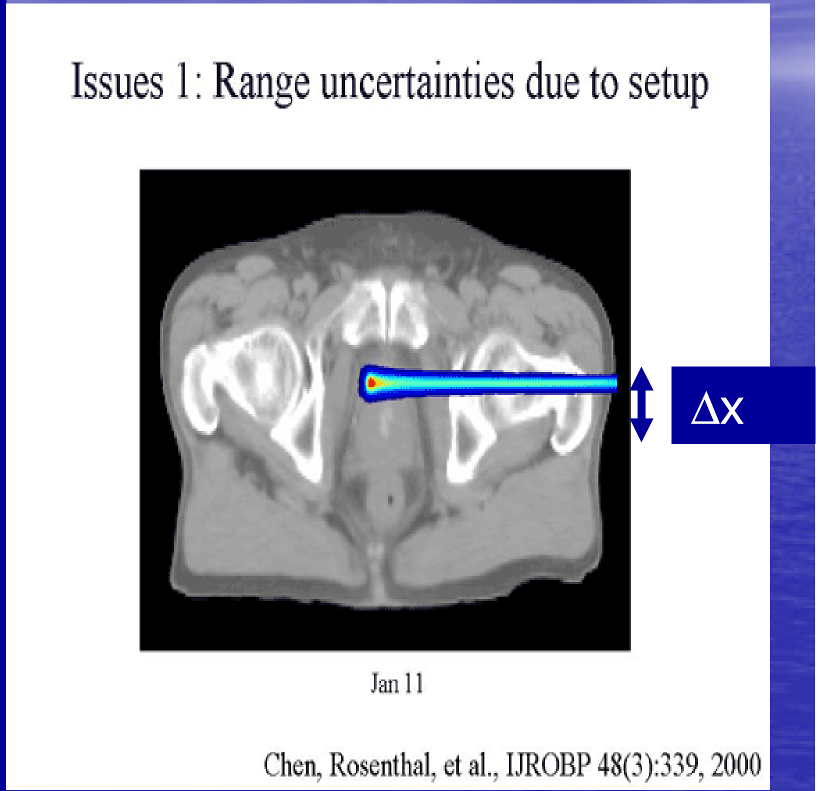
Let us reduce complacency and some prevalent attitudes

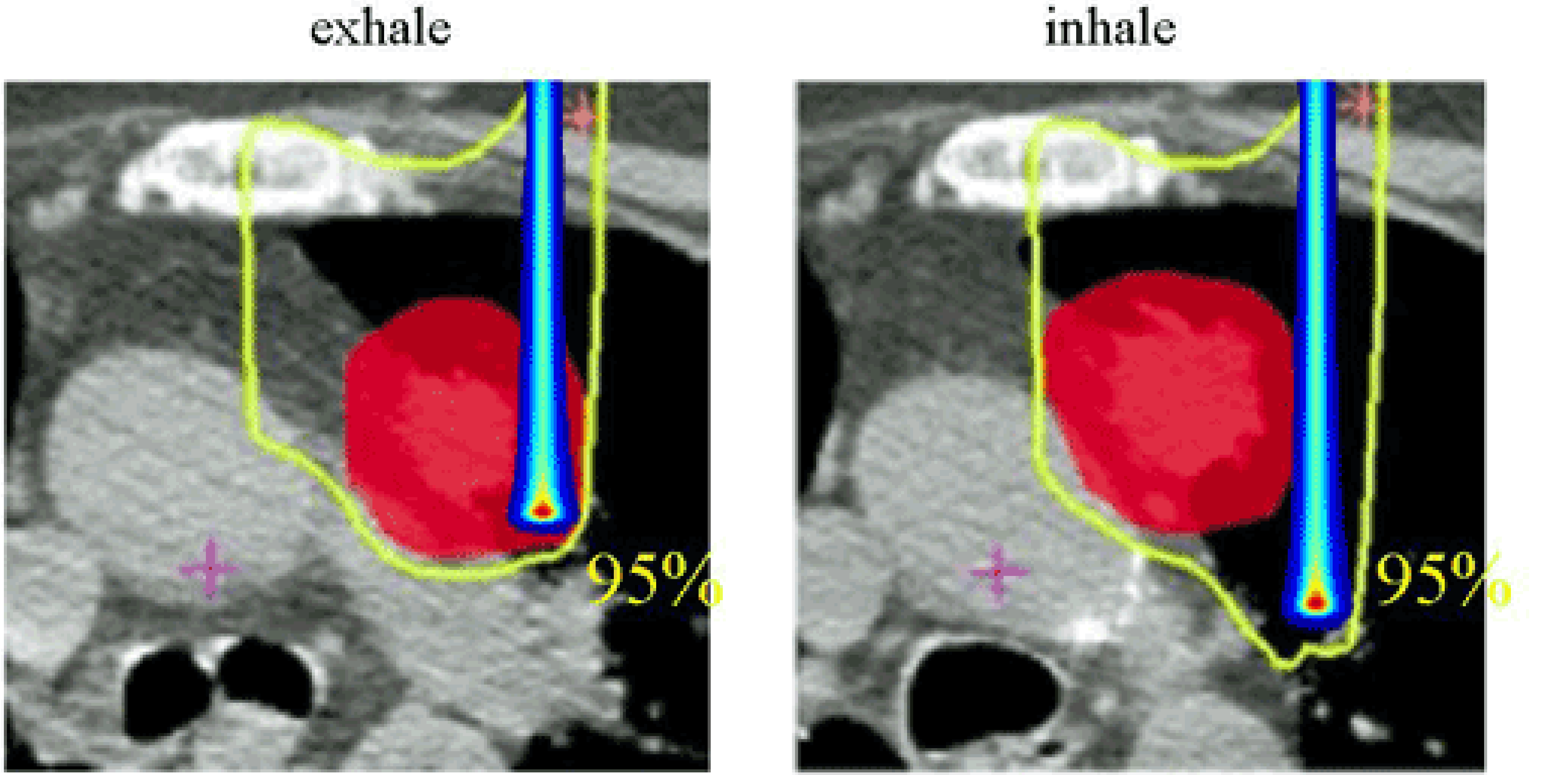
- A rose is a rose is a rose (Gertrude Stein's poem *Sacred Emily)*
- Shakespeare '**a rose by any other name would smell as sweet**'.
- Radiotherapy is the same everywhere, is highly reliable, perfected over a century……it differs in different centres and in different hands.
- Little, if any, research is necessary as it is now 'old science'.
- Nothing could be further from the truth

First we need….

- **Several beams** with good clinical ranges, 20 cm or more
- For protons, lateral scatter ↑ with depth + dose uncertainty ↑
- Better energy selection combined with high dose rates (separate features of synchrotrons and cyclotrons); dose rate and energy spread, form of treatment delivery influence detector systems.
- NS-FFAG system (BASROC/CONFORM…EPSRC grant)

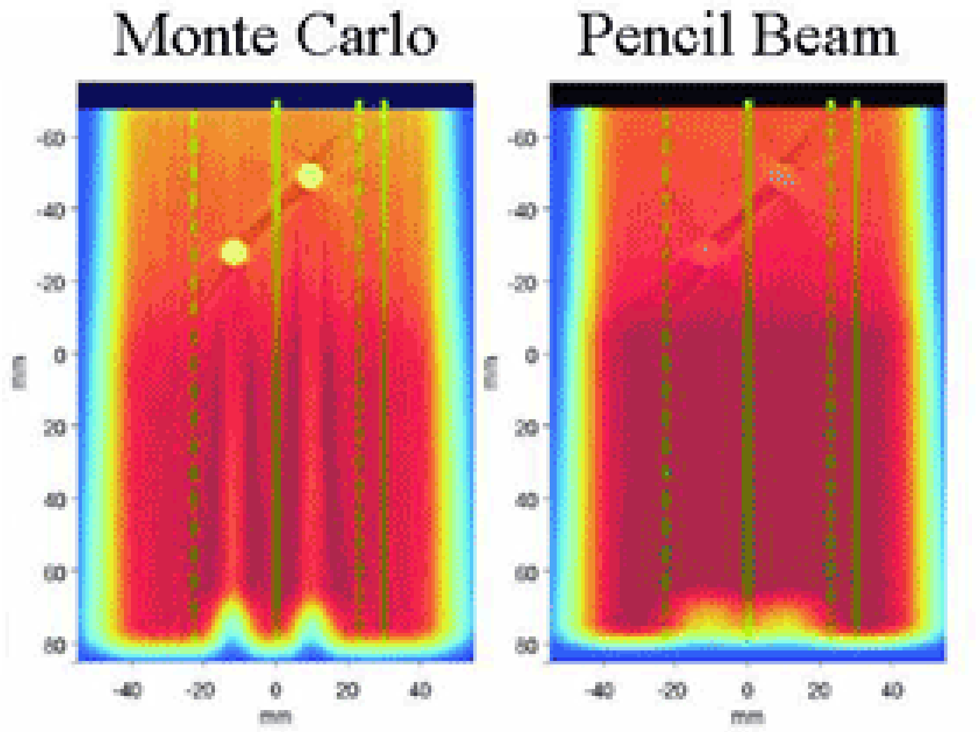


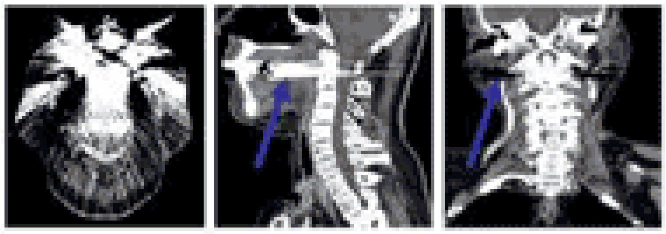
Issues 2: Range effects of breathing, 4D CT



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

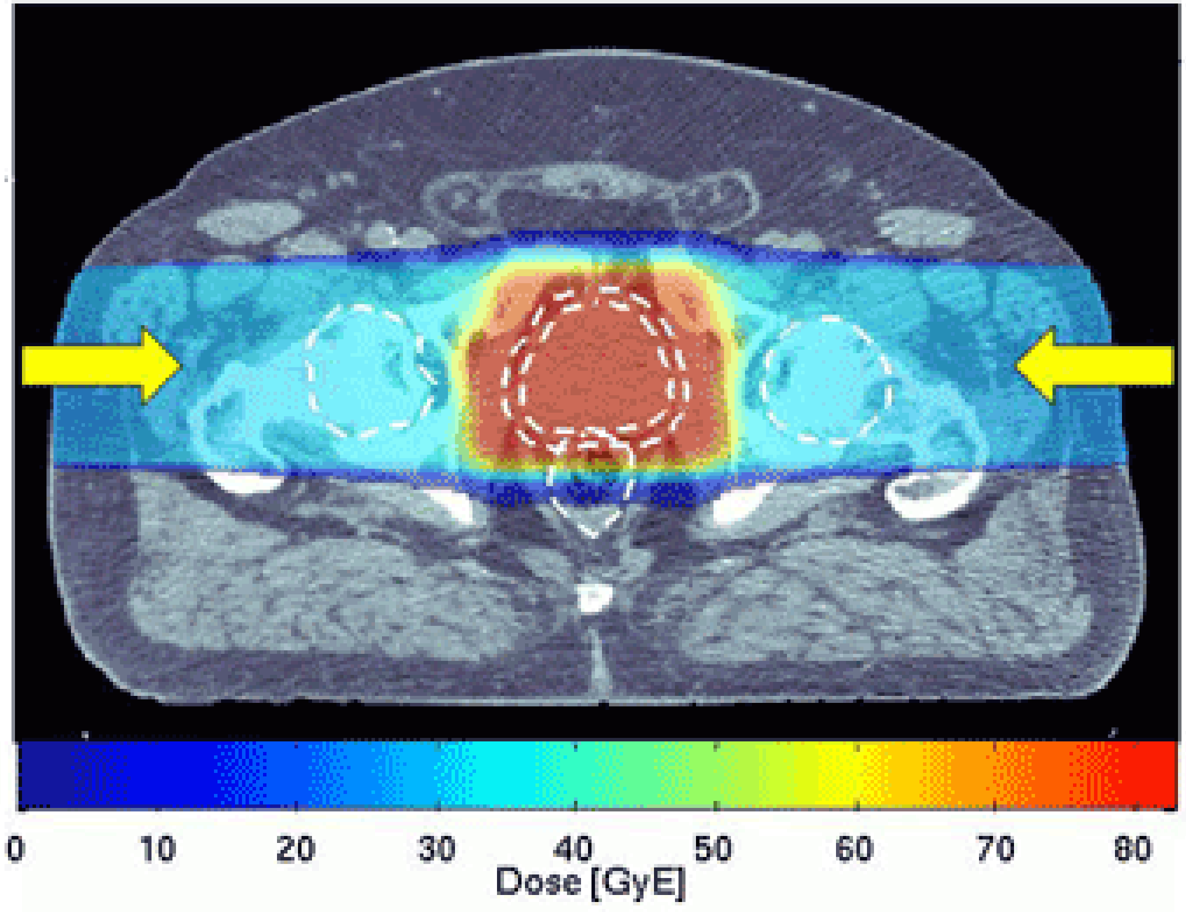
Issues 4: Range uncertainties due to metallic implants and CT artifacts



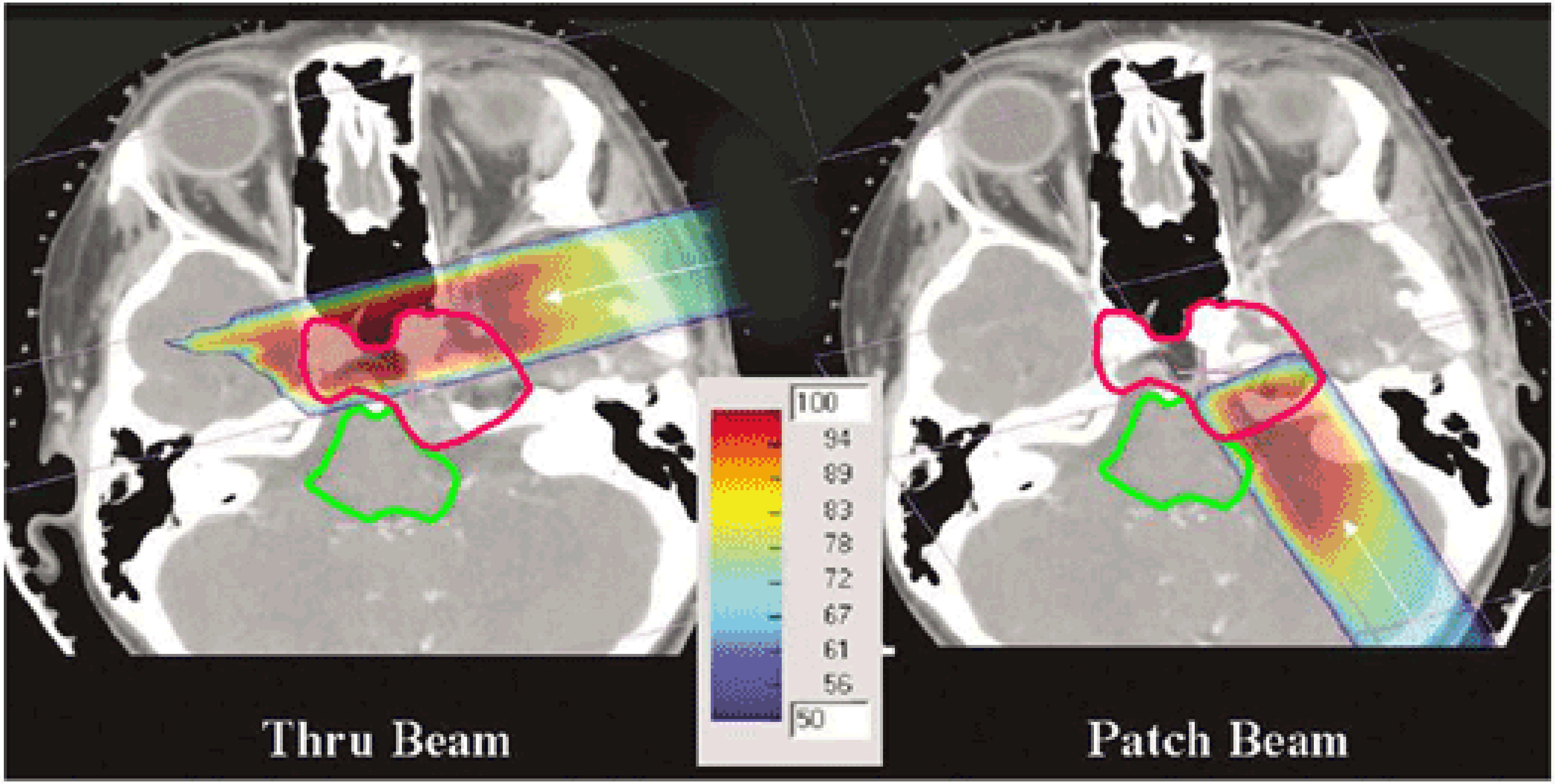


And several competing algorithms

Accounting for range uncertainties by "overshooting" **…using opposed fields**



Accounting for range uncertainties by "field patching"



J. Adams and M. Bussiere

MASSACHUSETTS GENERAL HOSPITAL
RADIATION ONCOLOGY

Physical uncertainties in particle therapy

- Variation in particle ranges for a given energy spectrum……precise positions of Bragg peak
- Effects of temperature, pressure, tissue in-homogeneities,
- Differences in treatment planning systems using pencil beams and Moliere scattering only
- secondary electron equilibrium at tissue and metallic artefact interfaces and multiple small air cavities
- Need: excellent high spatial resolution detectors specifically for particle therapy

What needs to be measured?

- Particle counts
- Energies
- LET along beams
- Dose
- Spatial distribution

ENVISION project grant (EU FP7 funded)

….the UK roles (Vojnovic, Hill, Jones) are:

- To determine accuracy and reproducibility of Bragg peak positions using physical and virtual phantoms
- To determine clinical significance of above
- Starts February 2010 with a 'kick-off' meeting at CERN

Lineal Energy [Y] (measurable using a Rossi Counter device) is closely related to LET

LET = x/L where x is energy, L is track length
Y=x/Lav,
where Lav is average path length across the chamber and is proportional to pulse size which reflects the absorbed dose.

At present Y within patient can be estimated by calculation

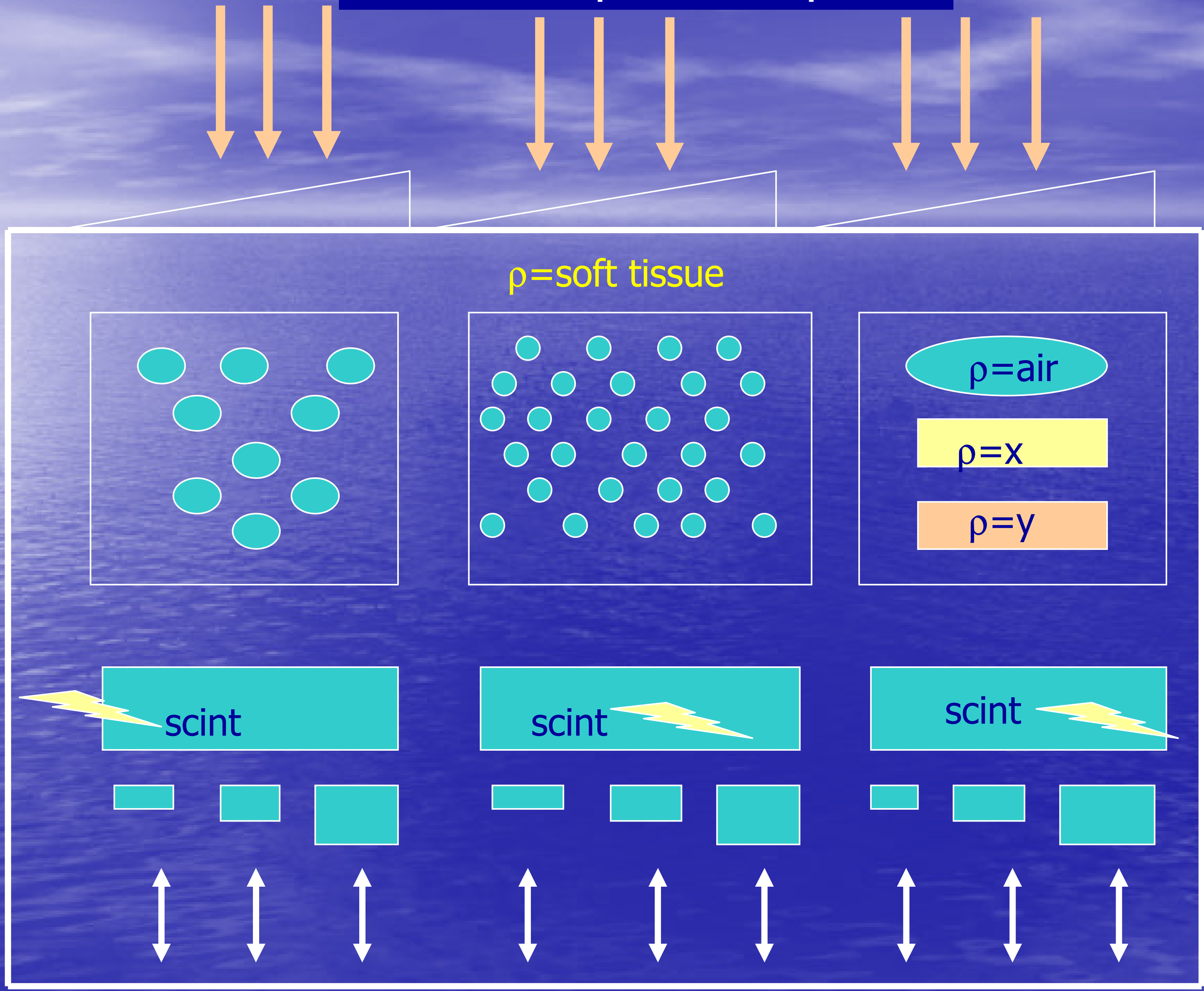
Three phantoms

(1) PHYSICAL
Dosemeters and inhomogeneities

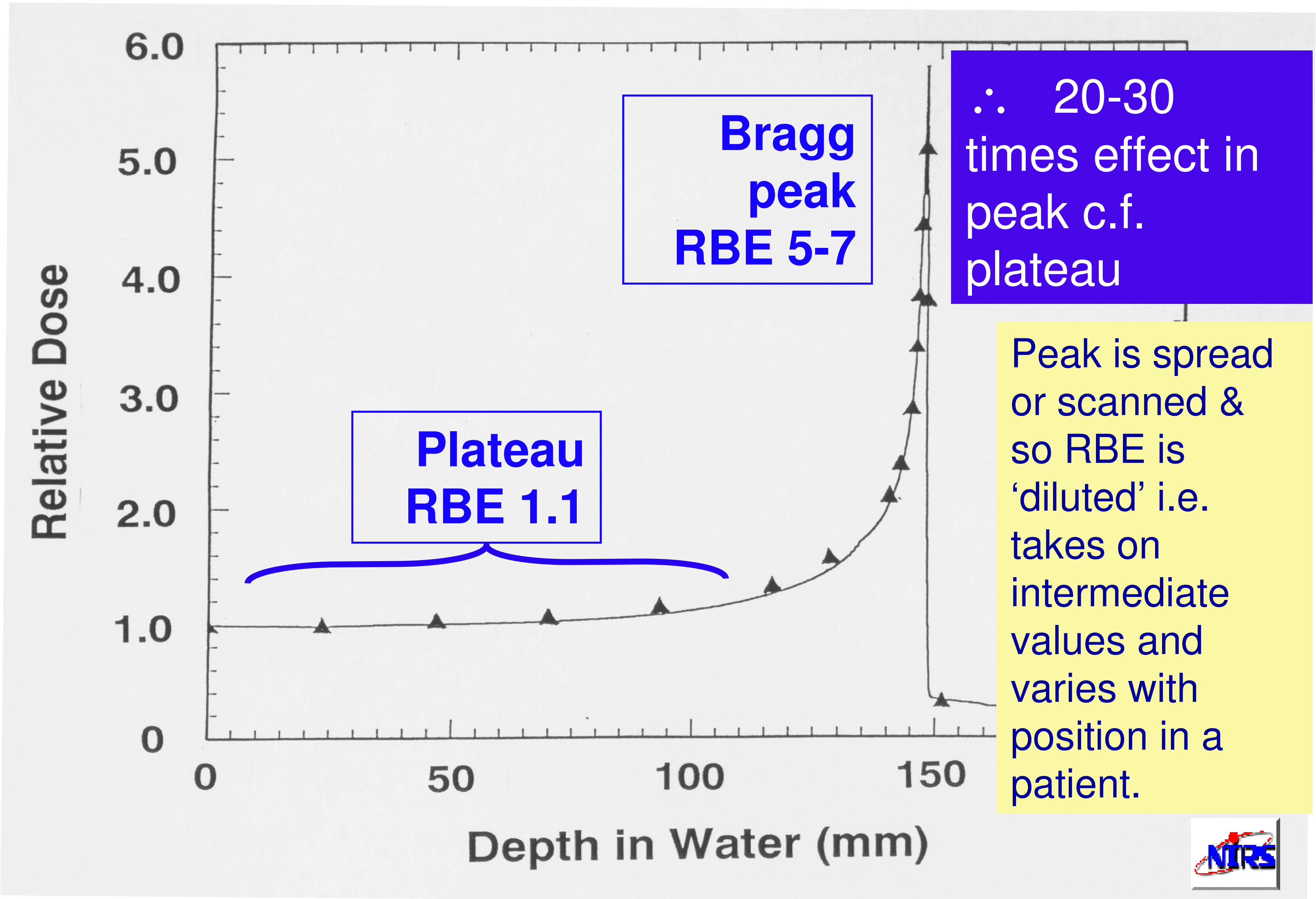
(2) VIRTUAL
MC simulation of 1

(3) BIOLOGICAL
Replica of 1 with Embedded cell compartments

Schematic phantom plan



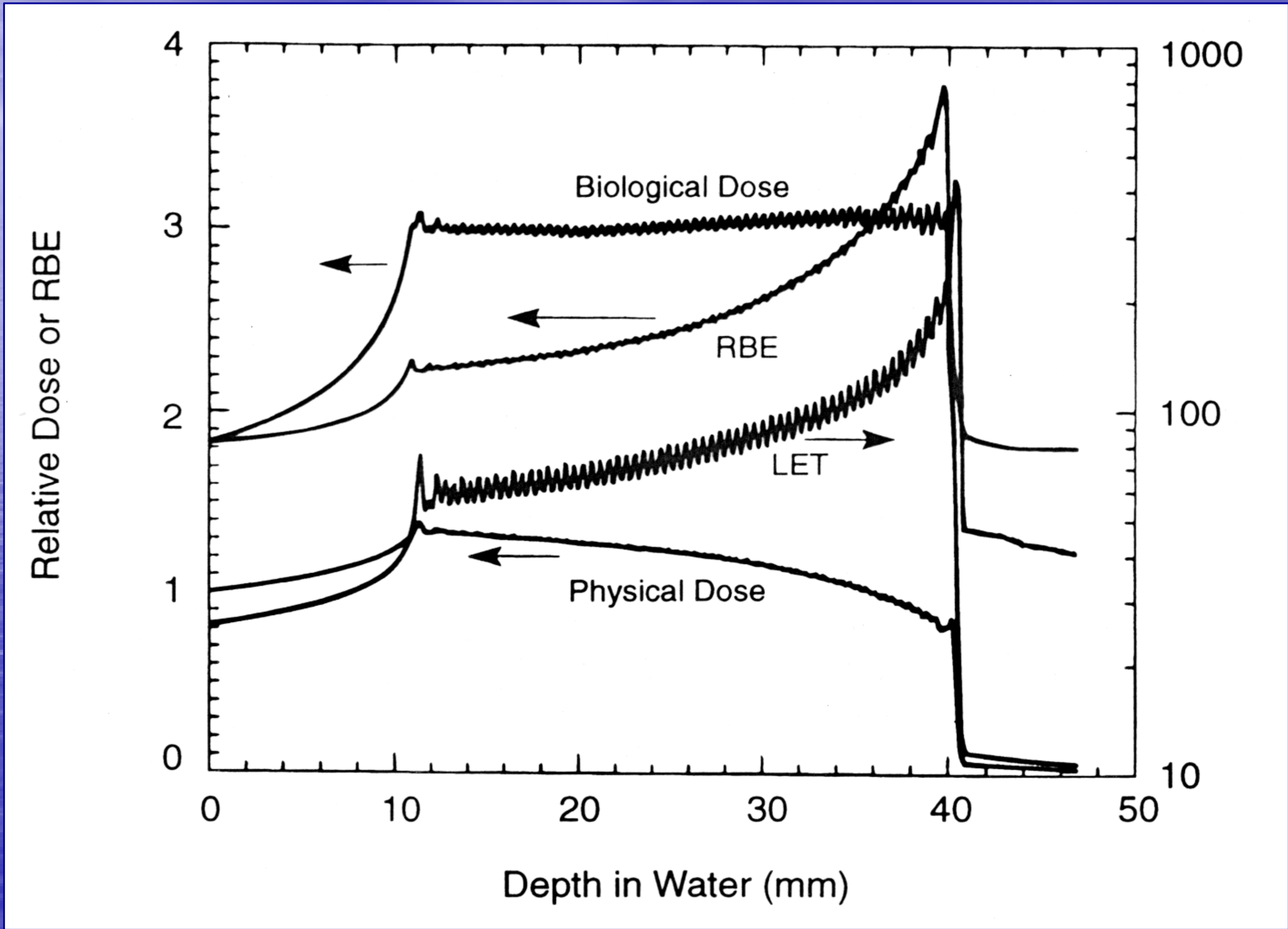
Carbon Ion Beam Profile



∴ 20-30 times effect in peak c.f. plateau

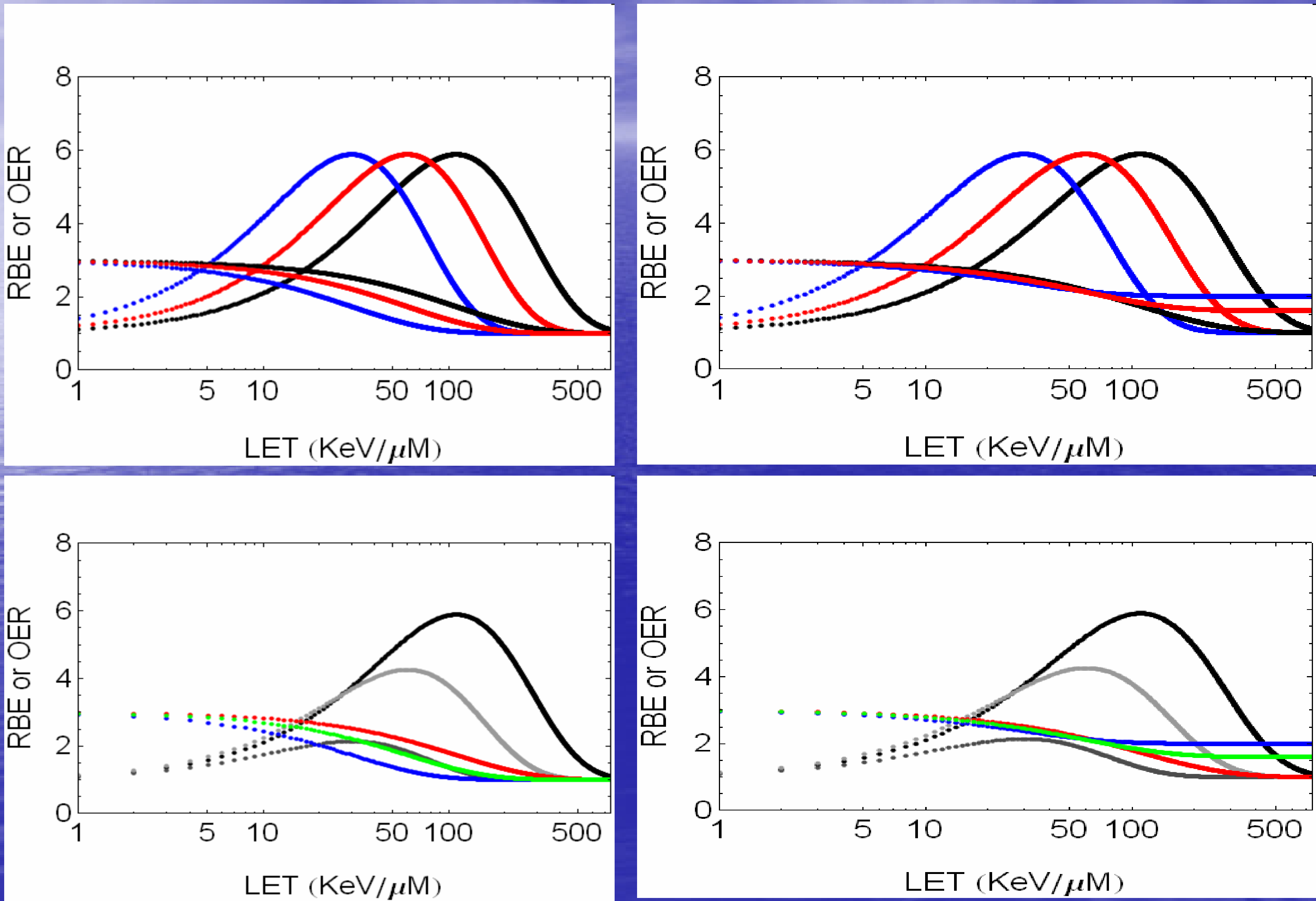
Peak is spread or scanned & so RBE is ‘diluted’ i.e. takes on intermediate values and varies with position in a patient.

Radiobiological complexity of ions
SOBP



T. Kanai et al, *Rad Res*, 147:78-85, 1997 (HIMAC, NIRS, Chiba, Japan)

LET, RBE and OER……some hypotheses



Practical Example – for single fraction

For Co-Eq Gy of 28 Gy single fraction: Using a fixed RBE of 3 we obtain high LET dose of 28/3 = 9.33 Gy

The high LET BED, (RBE_{MAX} = 7, RBE_{MIN} = 1.3) is then given by: $D(RBE_{max}+RBE_{min}{}^{2}.d/(\alpha/\beta)_{L})$

$= 9.33(7+(1.3^{2}\times 9.33)/10) = 80\ Gy_{10}$;

The equivalent cobalt dose is given by the solution for d in 80 = d(1+d/10), → d=23.7 Gy.
This is significantly different: the 28 Gy Co Eq Gy worked out using a fixed RBE of 3 is estimated to be equivalent to only 23.7 Gy
Similarly, 34 Co Gy Eq is estimated to be 27.2 Gy

Two very different processes…X-rays and CPT

X-ray errors: ΔPhysical dose $\rightarrow$ Δ BED; correct for the change in BED as follows

- solve iso-effect equations for various classes of tissues (with different α/β values) and tumour.
- obtain compromise BED (tumour and normal tissues) and re-calculate compensatory physical doses for delivery.
- for errors occurring late in treatment course additional time may elapse……needing another loop for calculating altered tumour BED

References Jones B and Dale RG. Radiobiological compensation of treatment errors in radiotherapy. British J Radiology, 81, 323-326, 2008.

Dale RG, Hendry JH, Jones B, Deehan C et al. Practical methods for compensating for missed treatment days in radiotherapy, with particular reference to head & neck schedules. Clinical Oncology, 14, 382-393, 2002.

CPT errors

1. ΔPhysical dose → Δ LET → Δ RBE → Δ BED

2. solve isoeffect equations for various classes of tissues (for different α/β values, RBEmax and RBEmin), obtain 'compromise' BED

3. re-calculate compensatory physical doses for delivery

4. for errors occurring late in treatment course additional time may elapse……needing another loop for calculating altered tumour BED

Reference: Jones B, Crabe-Fernandez A, Dale RG. Calculation of high-LET radiotherapy dose required for compensation of overall treatment time extensions. Brit J Radiol 79, 254-257, 2006

Biological Effective Doses for High LET schedules

$$E = N(\alpha_H d_H + \beta_H {d_H}^2)$$

$$BED = \frac{E}{\alpha_L} = n\left(\frac{\alpha_H d_H}{\alpha_L} + \frac{\beta_H {d_H}^2}{\alpha_L}\right)$$

$$RBE_{MAX} = \frac{\alpha_H}{\alpha_L};$$

$$RBE_{MIN} = \sqrt{\frac{\beta_H}{\beta_L}},$$

$$\therefore RBE_{MIN}{}^2 . \beta_L = \beta_H$$

Thence

$$BED = nd_H\left(RBE\max + \frac{RBE\min^2 d_H}{(\alpha/\beta)_L}\right)$$

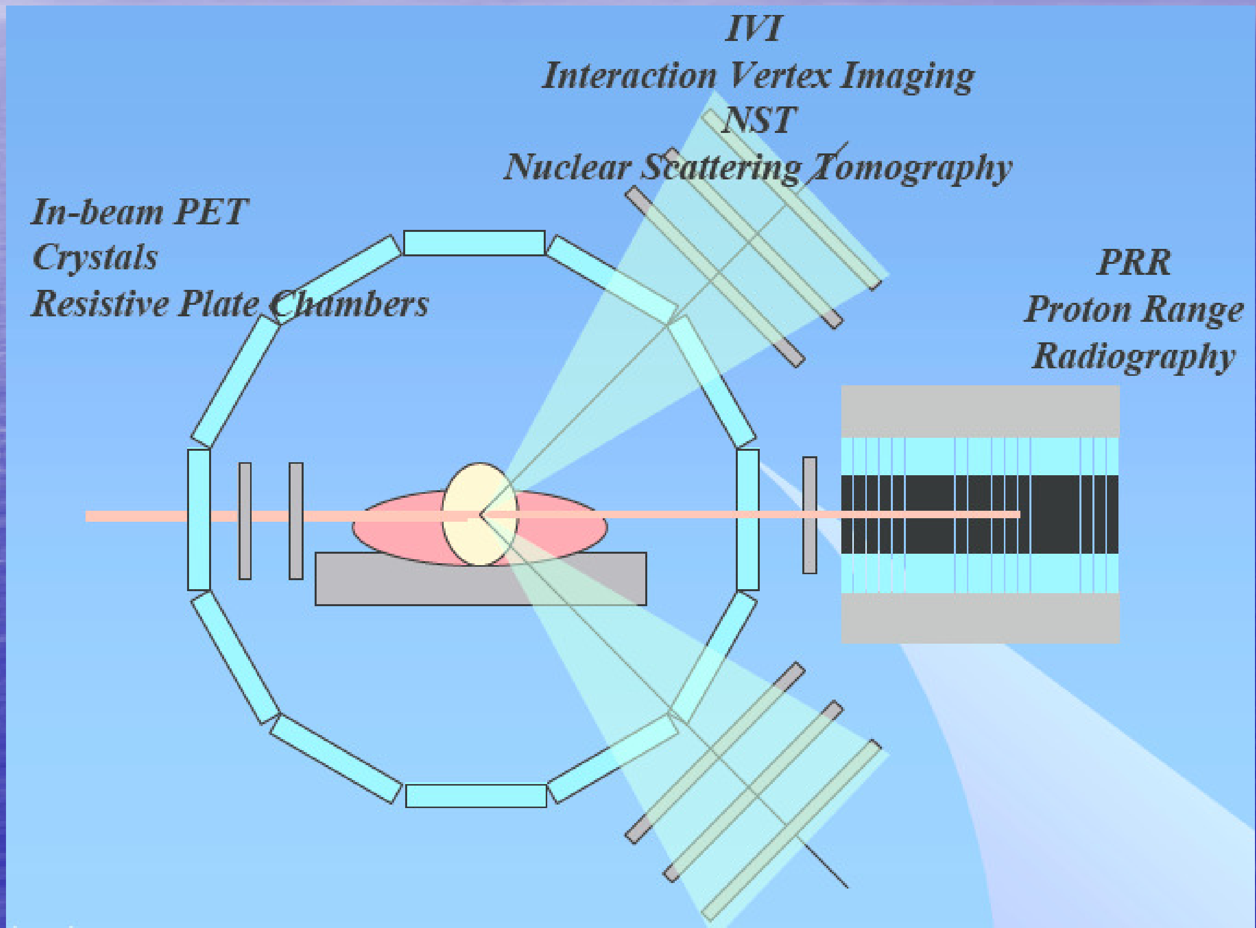
$$BED = nd_H\left(RBE\max + \frac{RBE\min^2 d_H}{(\alpha/\beta)_L}\right) - K_L(T - T_K)$$

- **the low LET α/β ratio is used**
- **RBEs act as multipliers**
- **RBE values will be between RBEmax and RBEmin depending on the precise dose per fraction**
- **K_L is daily low LET BED required to compensate for repopulation ≅K_H/RBE_{max}**

Accounting for mixed radiation fields as when Bragg peak position changes

- Radiation effects in biology are non-linear
- Different qualities of radiations, as occur in high LET beams, produce further non-linear interactions
- EPSRC grant …. Birmingham/Oxford looking at these mixed field LET interactions to better inform modelling

The detectors of AQUA (for CNAO and later A.D.A.M.)



Some other wishes….

- Proton radiography…feasible in parts of the body where 230 MV protons pass through….brain, head, neck, limbs, chest wall and in most locations if acceleration to a higher energy possible e.g. protons to ~ 300 MeV.
- Wide range of time resolution for different techniques
- Rapid MC 3-D dose computing for 'adaptive' treatments following immediate pre-treatment imaging
- Detectors for better beam characterisation and real-time monitoring with feedback for actual treatments