PRESCRIBING RECORDING AND REPORTING PROTON BEAM THERAPY ICRU 78

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INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS

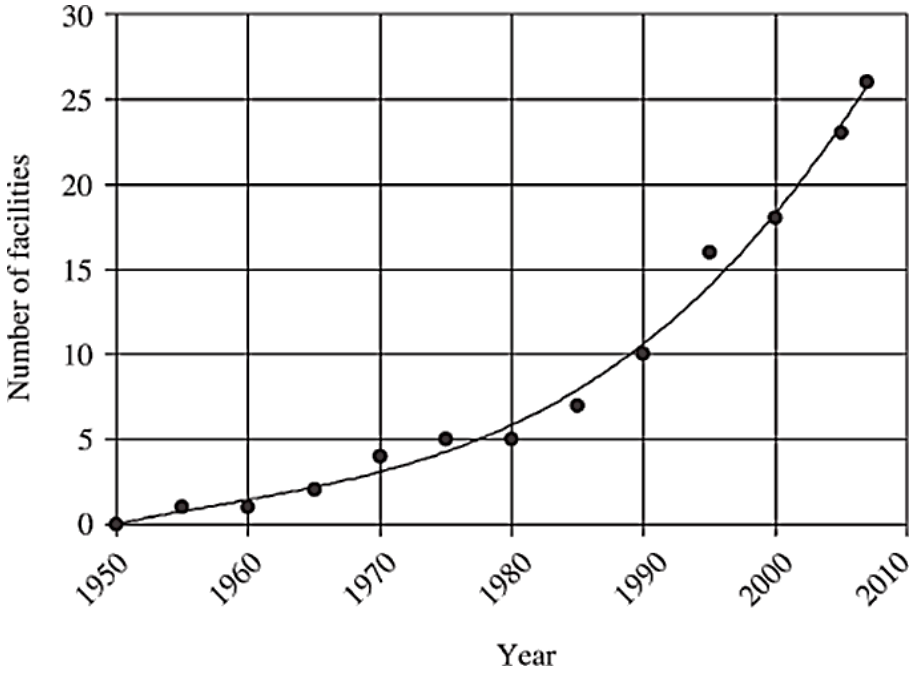
HISTORY OF PROTON THERAPY

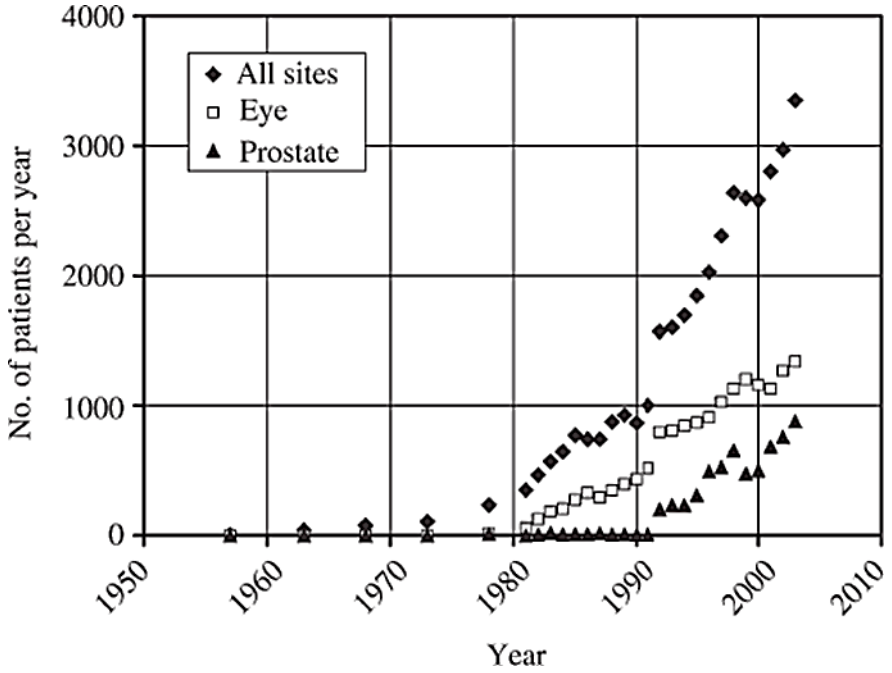
- Robert Wilson proposed the use of proton in 1946
- Irradiation of localized regions
- Significant sparing of surrounding tissues
- First biological study at University of california, Berkeley on 184 inch synchrocyclotron
- First human patient treated at University of california, Berkeley (1954)
- First patient in Europe (1957)University of Uppsala, Sweden

Dedicated Proton Therapy

- Loma Linda University medical centre
  - the first hospital based proton
  - First iso-centric gantry

No of PTC





- Five closed
  - Berkeley,CA,
  - Cambridge, MA,
  - Louvain-la-Neuve,
  - Chiba
  - Indiana University (2014)

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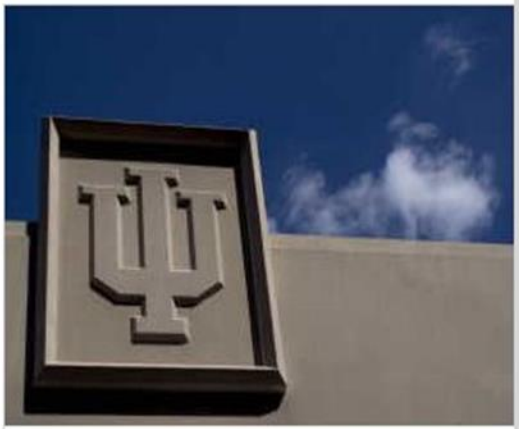
PRINT SHARE

Proton Therapy Center and Cyclotron facilities in Bloomington to close by Jan. 1, 2015

Aug. 22, 2014
FOR IMMEDIATE RELEASE

BLOOMINGTON, Ind. -- Indiana University Research and Technology Corp. and Indiana University Health announced today they have accepted the recommendation of an outside review committee to close the financially struggling IU Health Proton Therapy Center once the current roster of patients has completed treatment, which is expected to occur no later than Jan. 1, 2015.

As a result of the decision to close the cancer treatment facility, the IU Cyclotron also will close by the end of the year. The combined facility, on the northern edge of the IU Bloomington campus, employs approximately 120 people. The IU Center for Exploration of Energy and Matter, which is at the Cyclotron but not reliant on the use of the proton beam for its work, will remain open.

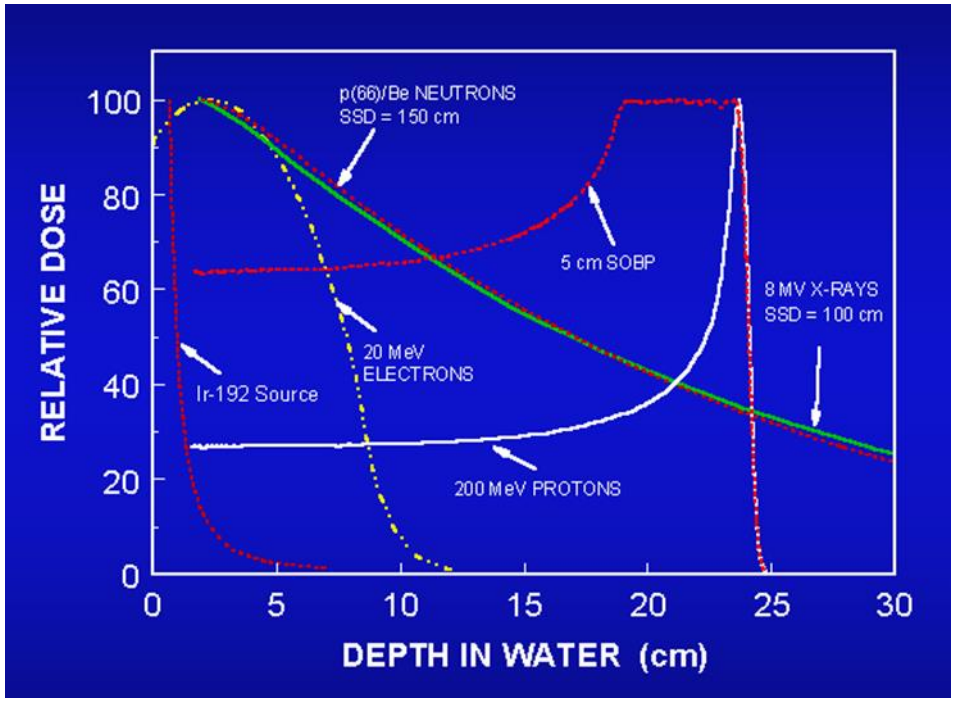


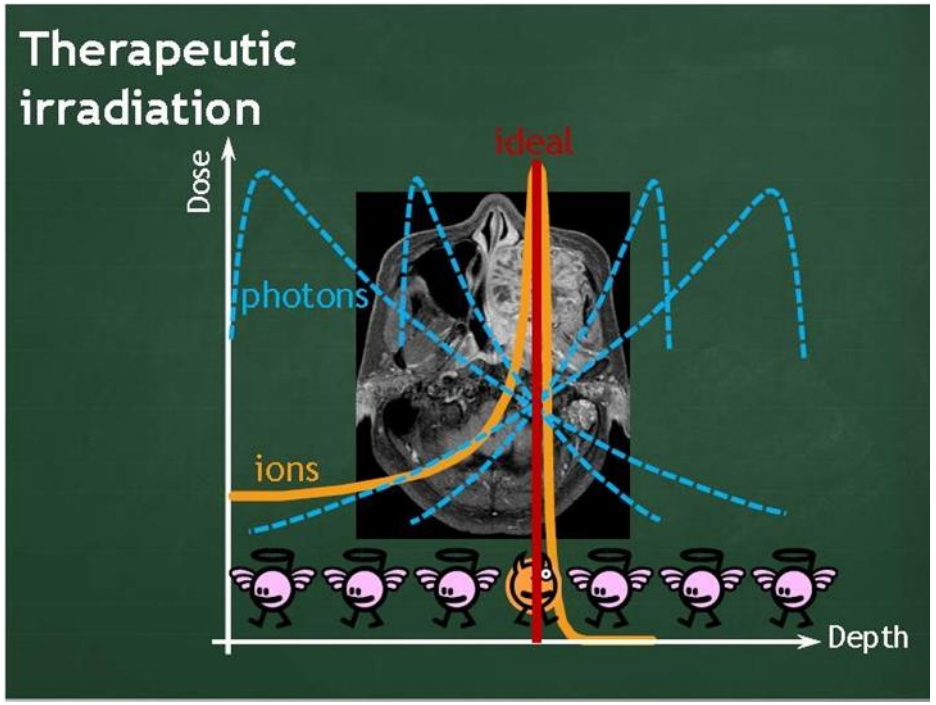
Print-Quality Photo

Media Contacts

Lack of revenue and debt incurred Out dated Technology

Proton Treatment





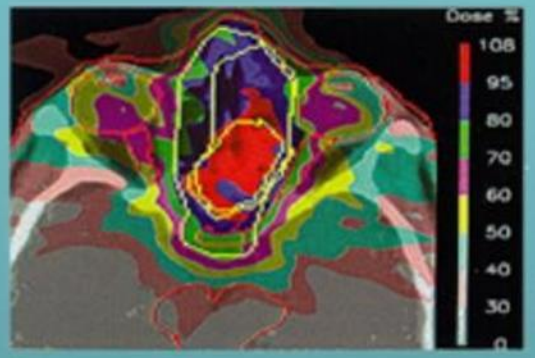
Why clinical proton beam?

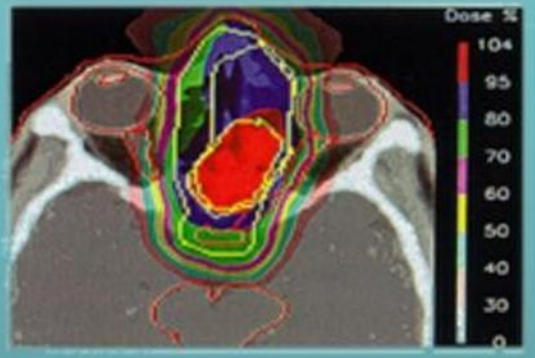
- penetration depth is *well-defined* and *adjustable*
- most energy at *end-of -range*
- protons travel in *straight lines*
- dose to *normal tissue* minimised
- no dose beyond target

PROTONS PERMIT TO DELIVER AN HIGH DOSE TO THE TUMOUR SPARING THE SOURRONDING TISSUES

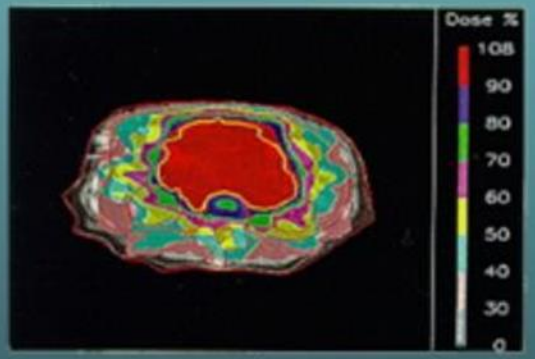
Intensity Modulateted Radiation Therapy vs PROTONS

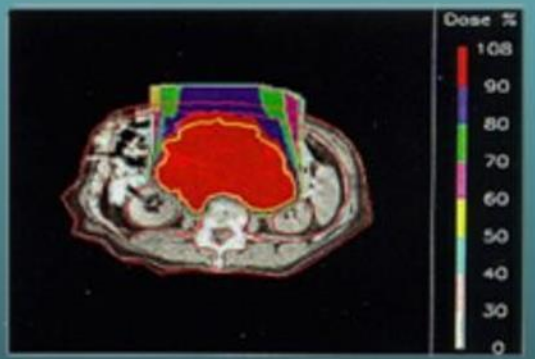
Between the eyes



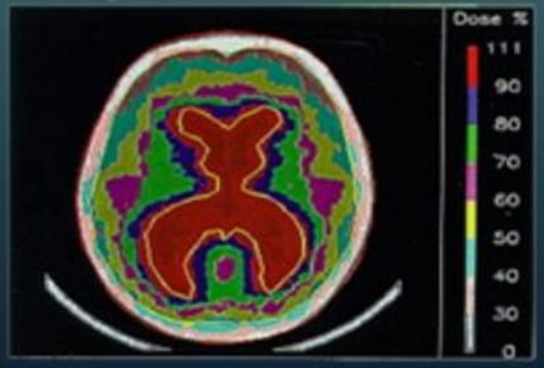


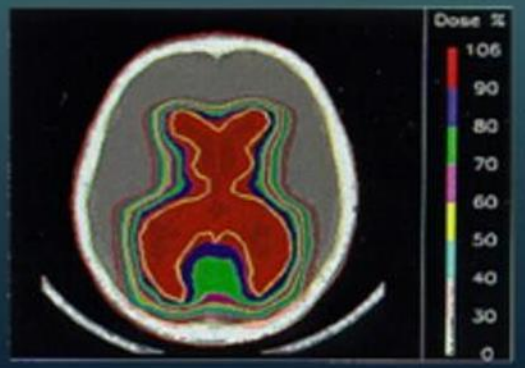
Abdomen



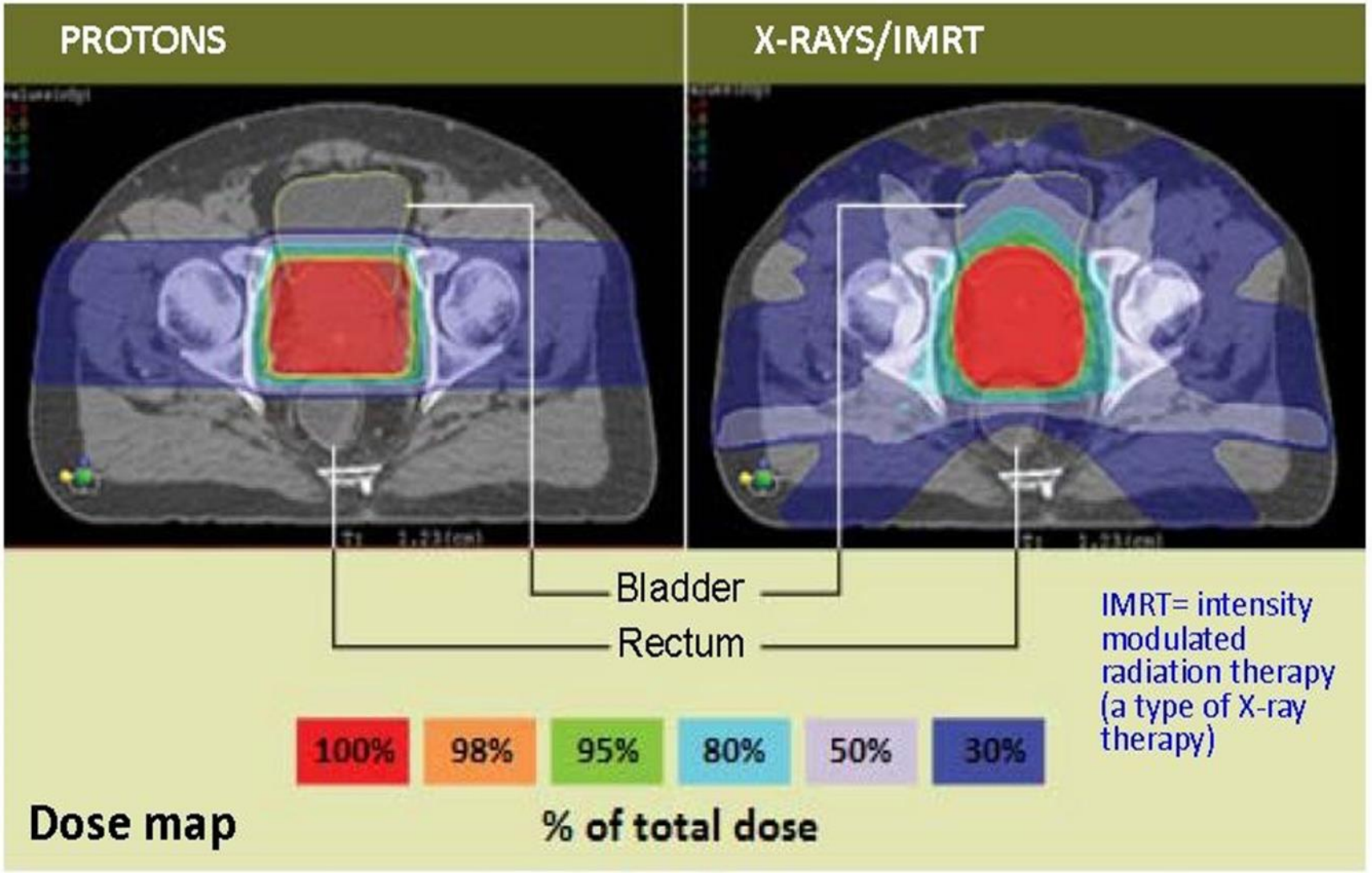


Brain





Prostate Cancer

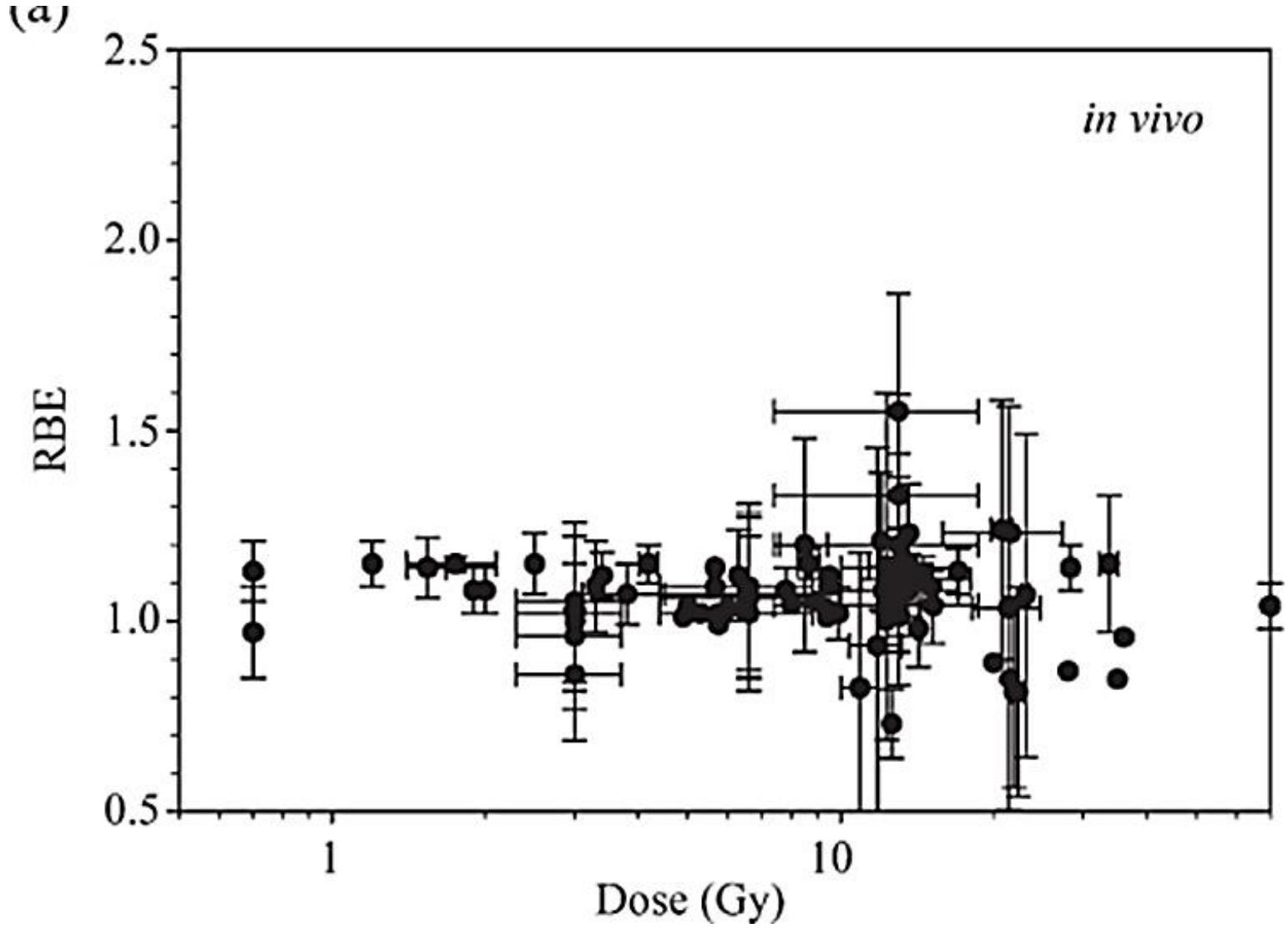


http://www.chicagoprotoncenter.com/cancers-tumors-treated/prostate-cancer

Relative Biological Effectiveness

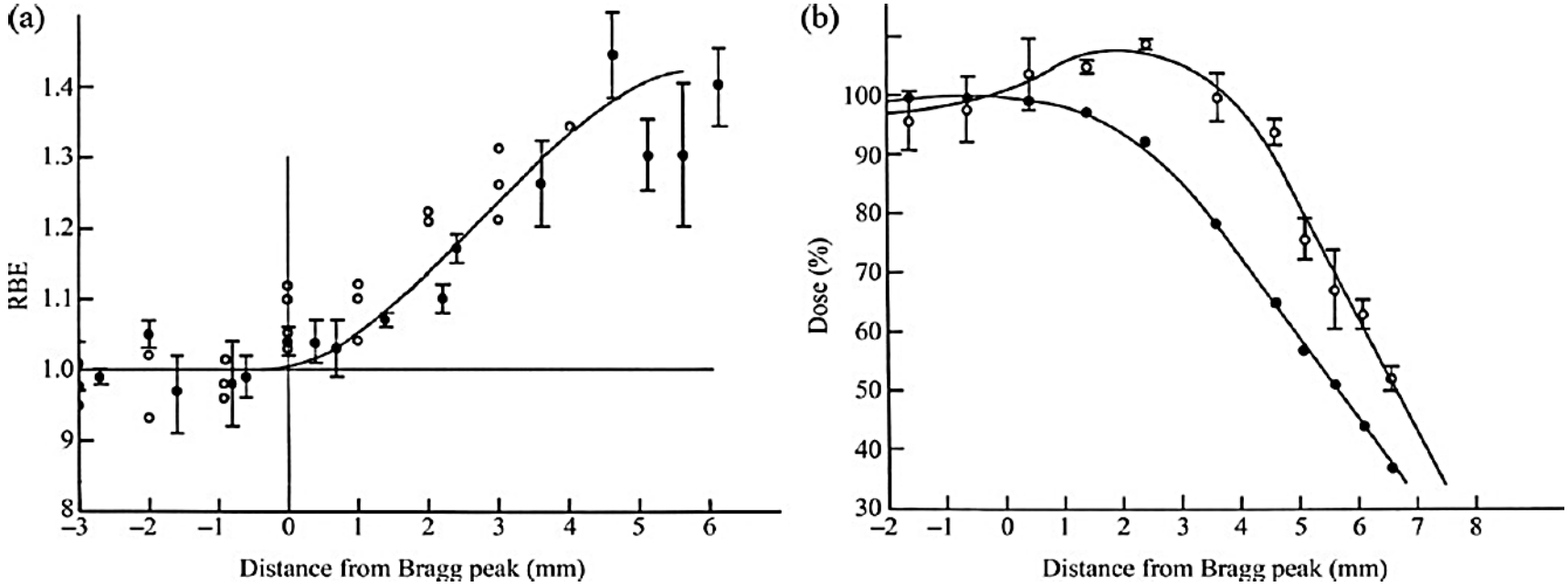
- ICRU 78 recommends 1.1 as proton RBE
- Independent of total dose, fractionation and tissue type proton energy, and position on the physical depth–dose curve up to the midpoint of the terminal Bragg peak
- fast neutrons, where RBE increases steeply as absorbed dose is decreased below 4 Gy

RADIATION BIOLOGY CONSIDERATIONS



RBE variation

- The RBE increased from 1.0–1.4 from the midpoint to 6 mm beyond the distal Bragg peak
- RBE-weighted absorbed dose is 8 percent greater than the RBE-weighted absorbed dose in the SOBP.



Bragg peak (Robertson *et al.*, 1975; reproduced with permission). (a) RBE as a function of depth normalized to the RBE at the midpoint of the distal Bragg peak contributing to the SOBP. Open circle represents RBE for unmodulated beam. Filled circle represents RBE for modulated beam. (b) Variation with depth of the absorbed dose and the RBE-weighted absorbed dose. The two curves are normalized to their values at the depth of the midpoint of the distal Bragg peak. Open circle represents RBE-weighted absorbed dose. Filled circle represents absorbed dose.

RBE variation

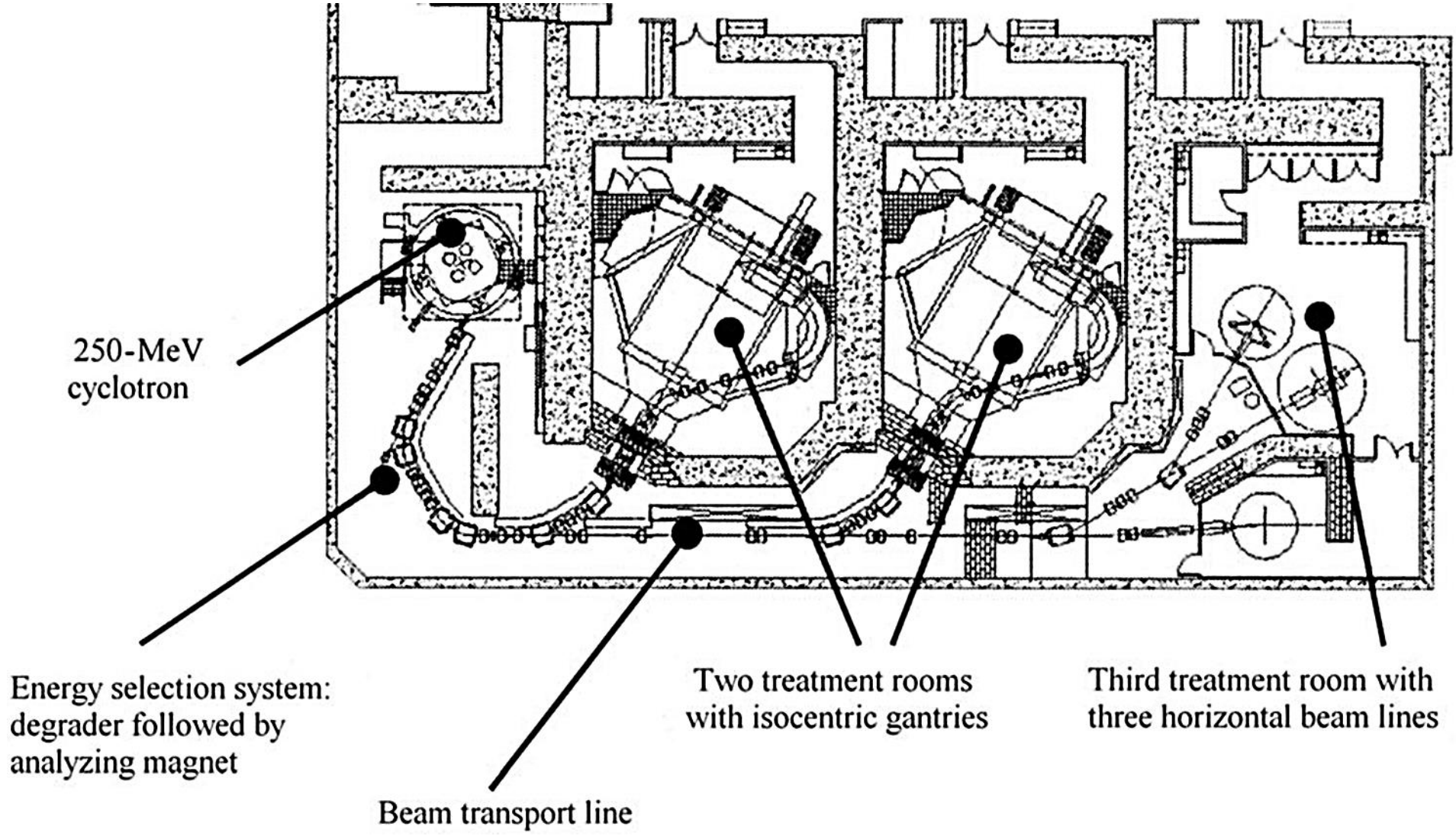
- These effects might need to be considered in treatment planning, especially for single-field treatments and when organs at risk are located at these positions.
- Absorbed dose, the ‘equivalent’ or ‘cobalt-equivalent’ dose.
- equivalent dose is already used for radiation protection purposes (ICRP, 1991)
- Commonly used symbols CGE, GyE, or Gy(E). But not recommended by SI units
- RBE-weighted absorbed dose (DRBE)

- ‘DRBE = 70 Gy (RBE)’.

RBE variation

RBE-weighted dose is a biologically weighted quantity designed to define doses of protons that would produce identical biological effects as doses of photons if administered under identical conditions

Proton Facility



Passive beam-delivery techniques

- Single or dual scatter
- Needs longer drift distance
- A limitation of a passive scattering system is that the compensator is designed to shape the dose distribution to the distal surface of the planning target volume
- field-shaping device and compensator should be as close to the patient's skin as possible to minimize the scattering
- range modulator is required for each energy and each spread-out Bragg peak (SOBP) length

Passive beam-delivery techniques

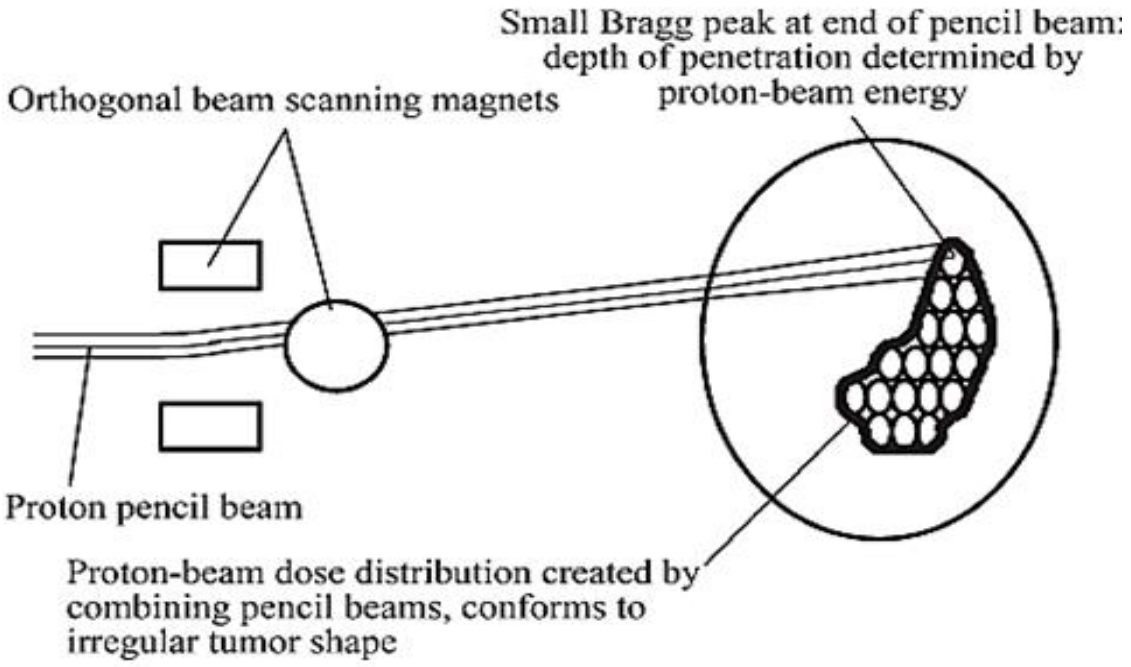
- requires a large number of modulator wheels or ridge filters
- Larger penumbra due to double-scattering system (large effective source size)

Dynamic beam-delivery techniques

- time-dependent method
- magnetically moving the beam across the target cross-section
- Discrete scanning (spot or voxel scanning)
- Beam off in transition
- Spot spacing 80% of FWHM of pencil beam profile
- Continuous scanning (raster scanning)
- Layer by layer change in energy
- Beam intensity – control system/scanning speed
- Quasi-discrete scanning
- carbon-ion, spot scan w/o beam off
- Accounts the dose between grid points

Dynamic beam-delivery techniques

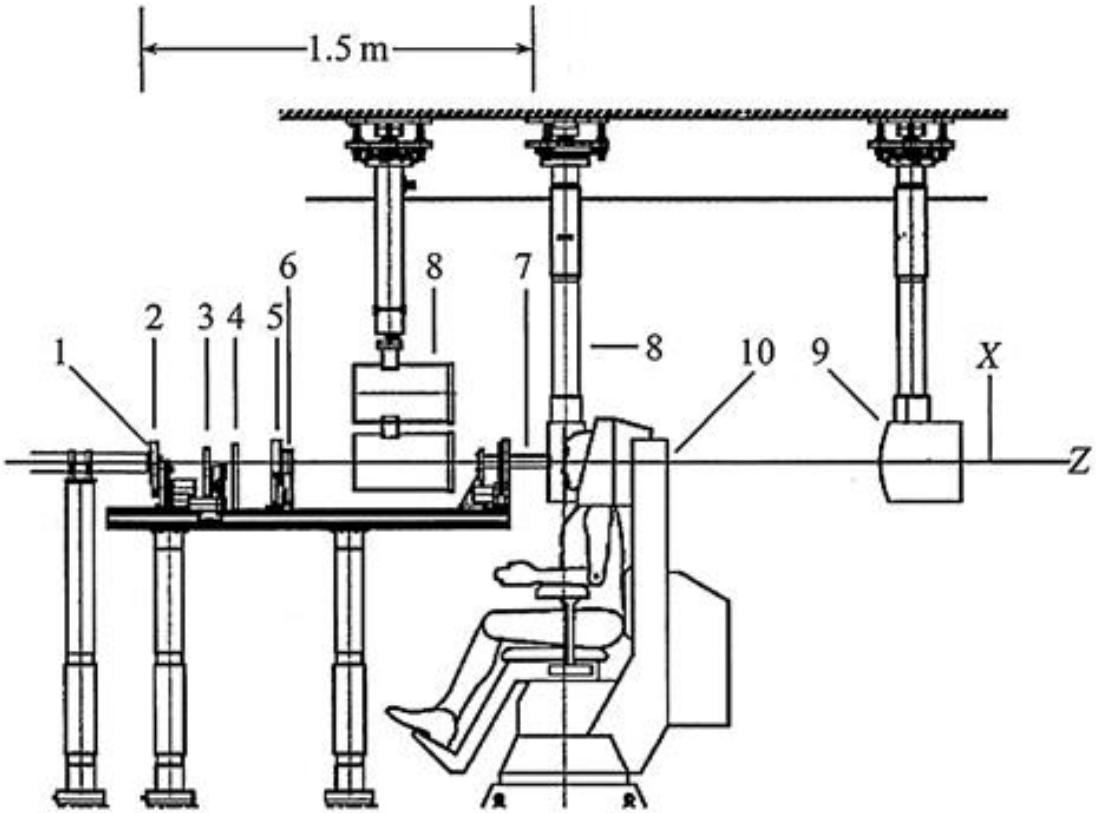
- Obviates the custom-made beam modifying devices
- Used for IMPT



Patient support and positioning

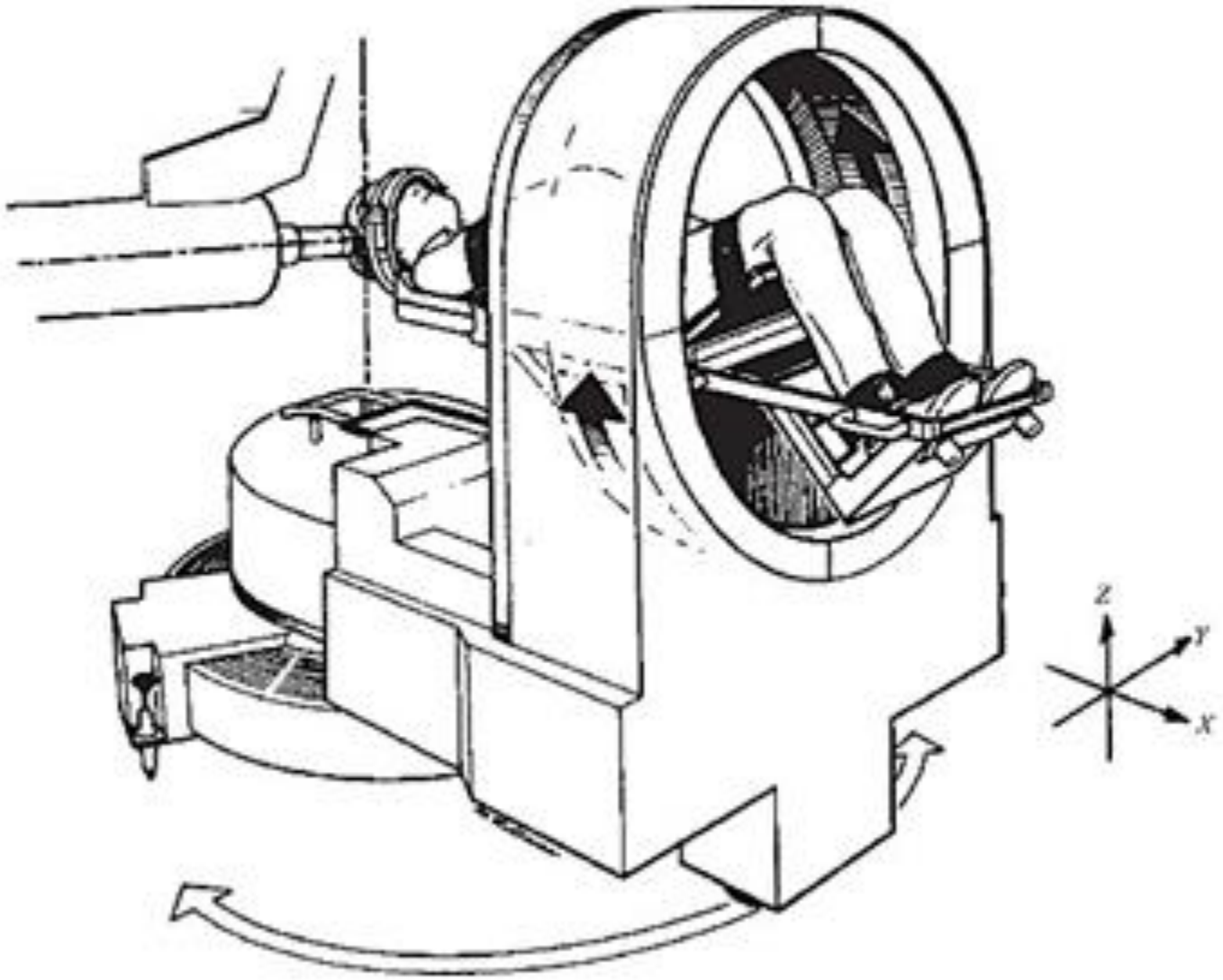
- hold the patient in a stable position during treatment
- couch or chair (robotic option – 6D)
- Orthogonal radiograph, CBCT, CT or USG
- patients pre-positioned in a positioning suite outside the tx room then transported into tx room
- increase the efficiency and patient throughput

- uveal melanomas, pituitary adenomas, brain tumors, and arteriovenous malformations



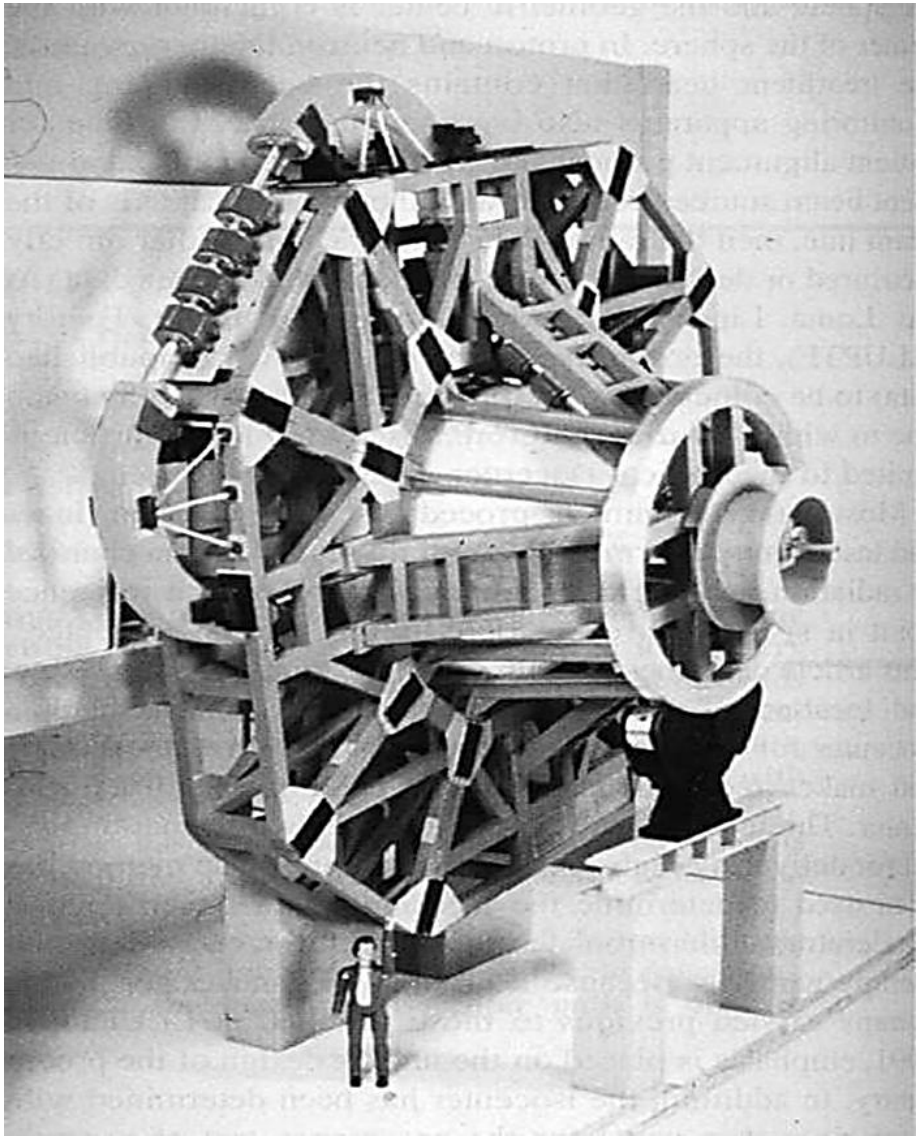
The beam enters from the left. After a 100 mm Kapton foil (1) which acts as a vacuum exit window, a computer-controlled variable range shifter (2) and a range modulator (3) are mounted close together. The beam passes a collimator (4), a segmented ionization chamber (5), And two transmission ion chambers (6). Directly in front of the patient is mounted the nozzle (7), i.e., a pipe that can hold a collimator, an aperture, a compensator, or a phantom for dosimetry experiments. An on-line x-ray imaging system (8 and 9) is mounted from the ceiling and can be removed during treatment. The patient sits in a chair with multiple degrees of freedom (10)

SRS / SRT using Proton



Gantry

- Scttering Nozzle / Scan system mounted on Gantry
- Magnet to bend the beam
- Heavy of the order of tons
- 360° or less



Accelerator

- Penetration 26–38 cm needs 200-250 MeV
- 1.8x1011 and 3.6x1011 particles per minute are required if doses of 2 Gymin-1
- Depends on Scattering or Scanning
- Linear accelerator – too long
- Cyclic accelerator
  - cyclotrons or synchrotrons

Cyclotrons

- developed by Lawrence et al. early 1930s

Synchrotron

- highly flexible in terms of energy variation
- the magnetic field and the frequency of the accelerating electric field must be increased in synchrony
- finite time required for pulsed output (~200ms cycle)
- Typical pulse repetition rate is 0.5–2 Hz.
- magnetic-field radial vectors alternate in direction between successive magnets,
- reduced size, weight, and total cost of the synchrotron
- feasible
- to use energy variation of the beam instead of range shifting

Table 3.1 Typical operating parameters of some accelerators in use in proton-therapy facilities.

Parameter	Cyclotrons		Synchrotrons	
	MGH	PSI	LLUMC	PMRC
Magnet ring or magnet max. diameter (m)	4.34	3.198	6.71	7.00–7.82
Magnet weight (tons) or number of magnets in ring	165 tons	90 tons	8 magnets	6 magnets
Energy at extraction (MeV)	230	250	70 to 260	70 to 250
Beam current (nA) or particles per pulse (ppp)	300 nA	500 nA	3.4×10^{10} ppp	7.5×10^{10} ppp
Pulse repetition rate (s)	CW	CW	2.2 s cycle	2 s to 7 s spill length 0.2 s to 0.5 s between spills
Extraction system	Electrostatic deflection 70 kV	Electrostatic deflection	Lambertson magnet	RFDE
RF cavity frequency (MHz)	106.1	74	0.974 to 9.713	1.5 to 2.0
Field strength (T) Hill	2.9	≈3.6		
Valley maximum	0.9	≈2.0	1.52	1.814
Average power consumption (kW)	446	350	350	?
Ion source or injector type	Cold cathode	Cold Cathode	2 MeV RFQ	7 MeV linac
RF voltage (kV)	130 peak	100 peak	0.3	1.3

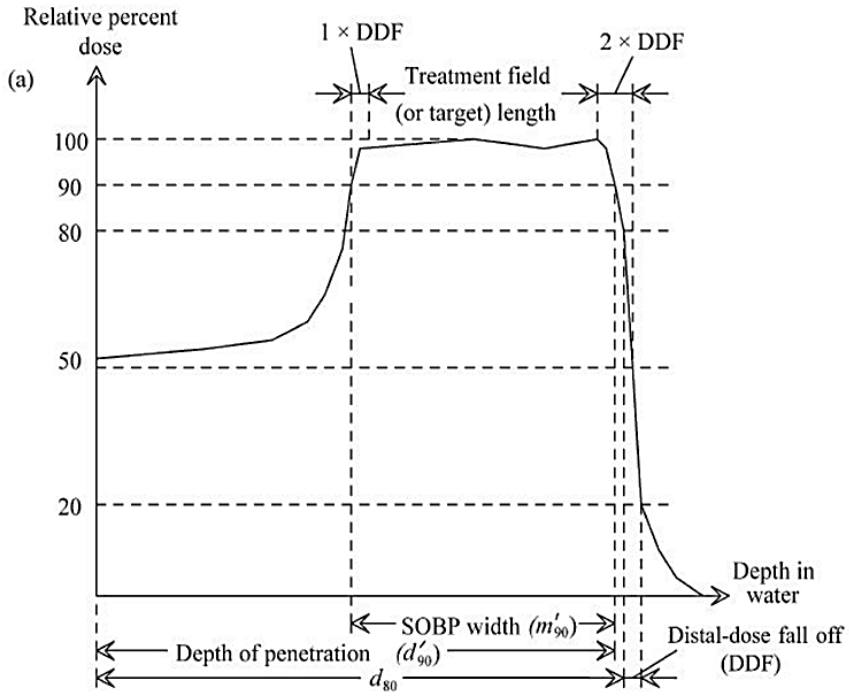
MGH, Massachusetts General Hospital, Boston, MA, USA; PSI, Paul Scherrer Institute, Villigen, Switzerland; LLUMC, Loma Linda University Medical Center, Loma Linda, CA, USA; PMRC, Proton Medical Research Center, Tsukuba, Japan; CW, continuous wave.

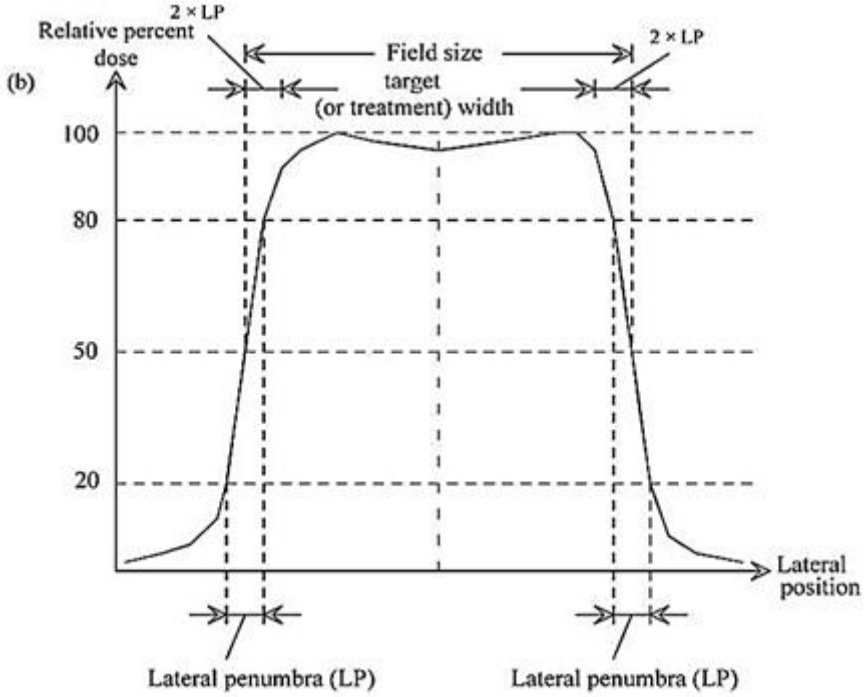
Beam parameters – Passive Scatter

- Profile of the SOBP
- Lateral profile
- Beam width, penetration
- Flatness & symmetry
- Lateral penumbra and distal dose fall-off
- Depth of penetration (d’90)
  - Distal 90% Dmax
- Distal-dose fall off (DDF)
  - 80% - 20% Dmax
- SOBP length (m’90)
  - Distance between distal and proximal 90% of Dmax

Beam parameters – Passive Scatter

- Lateral penumbra (LP)
  - 80% - 20% width in the lateral profile
- Field size
  - distance (in mm) between the 50% in lateral profile





Beam parameters – Passive Scatter

- Target (or treatment) length & Width
- Lateral flatness $$F_{\mathrm{lp}} - \left(\frac{d_{\mathrm{lp\,max}} - d_{\mathrm{lp\,min}}}{d_{\mathrm{lp\,max}} + d_{\mathrm{lp\,min}}}\right) \times 100,$$
- Lateral symmetry $$S_{\mathrm{lp}} - \left(\frac{D_1 - D_2}{D_1 + D_2}\right) \times 100,$$ (D1 & D2 integral dose on each half of profile)

Beam parameters – Dynamic Scan

- Passive scan parameters not appropriate
- Integrated dose distribution by superimposing a large number of individual pencil beams.
- TPS requires depth dose curves and lateral profiles of finite pencil beams
- multi-channel or integrating detector is required

Dosimetry

- Absolute dose determination:
  - Calorimetry (cumbersome)
    - extremely small temperature differences
  - Faraday cups (not accurate/recommended)
  - Carbon activation (complicated)
  - ionization chambers
    - cheap, robust, easy to use, and require little ancillary equipment
- Water medium – Tissue equivalent
- Discuss ICRU 59 (1998) & TRS 398 (2000)

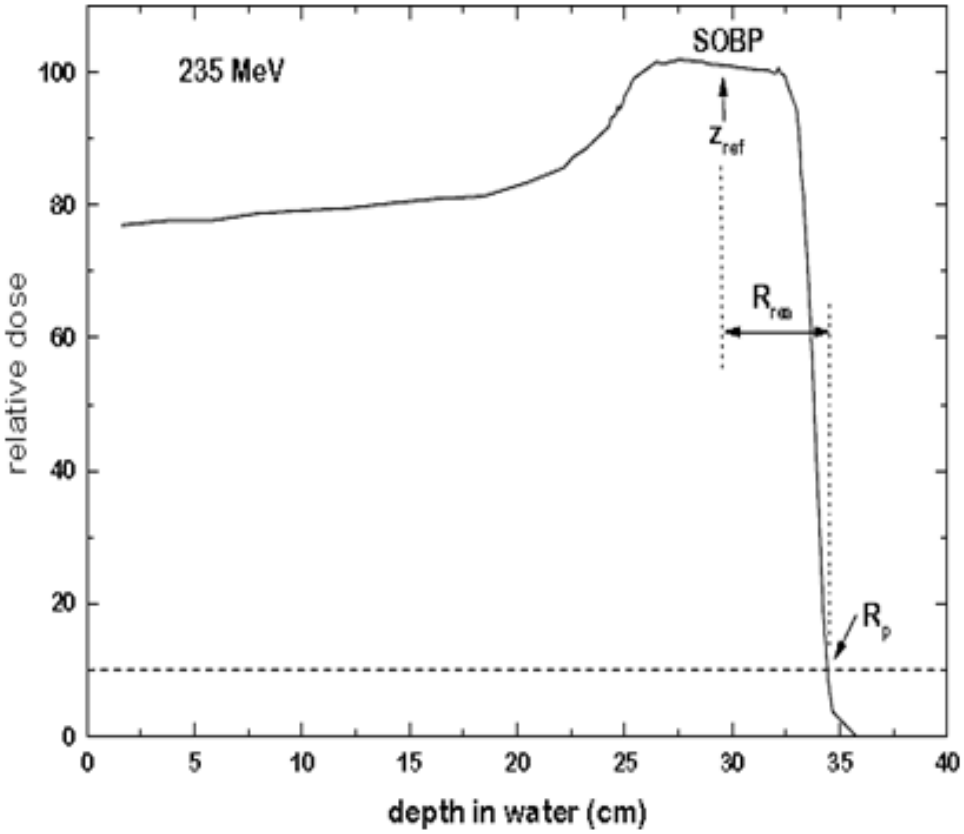
Dosimetry

- TRS 398
  - 60Co (refernece beam, with correction)
  - Uniform standard in dosimetry
  - Comparing clinical results
- ionization chamber (Cylinderical/PP)
  - Water → chamber wall → air
  - Difference in Stopping Power

$$\frac{D_{medium}}{D_{cavity}} = \frac{S_{col,medium}}{S_{col,cavity}}$$

beam quality index

- Residual range, Rres
- *Rres = Rp – z*
- Rp is the practical range (the depth at which the absorbed dose beyond the Bragg peak or SOBP falls to 10% of its maximum value)
- *z is the depth of measurement*



Reference Condition BQI

TABLE 10.I. REFERENCE CONDITIONS FOR THE DETERMINATIONOF PROTON BEAM QUALITY (R_{res})

Influence quantity	Reference value or reference characteristics
Phantom material	water
Chamber type	cylindrical and plane-parallel
Reference point of chamber	for plane-parallel chambers, on the inner surface of the window at its centre. For cylindrical chambers, on the central axis at the centre of the cavity volume
Position of reference point of chamber	for plane-parallel and cylindrical chambers, at the point of interest
SSD	clinical treatment distance
Field size at the phantom surface	10 cm x 10 cm For small field applications (i.e. eye treatments), 10 cm x 10 cm or the largest field clinically available

TABLE 10.III. CALCULATED VALUES OF k_Q FOR PROTON BEAMS, FOR VARIOUS CYLINDRICAL AND PLANE-PARALLEL IONIZATION CHAMBERS AS A FUNCTION OF BEAM QUALITY R_{res}

Ionization chamber type [a]	Beam quality R_{res} (g cm^{-2})															
	0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	7.5	10	15	20	30
Cylindrical chambers																
Capintec PR-05P mini	-	1.046	1.045	1.044	1.044	1.044	1.043	1.043	1.043	1.043	1.043	1.043	1.043	1.043	1.042	1.042
Capintec PR-05 mini	-	1.046	1.045	1.044	1.044	1.044	1.043	1.043	1.043	1.043	1.043	1.043	1.043	1.043	1.042	1.042
Capintec PR-06C/G Farmer	-	1.038	1.037	1.036	1.036	1.036	1.036	1.035	1.035	1.035	1.035	1.035	1.035	1.035	1.034	1.034
Exradin A2 Spokas	-	1.057	1.055	1.054	1.054	1.054	1.054	1.054	1.054	1.054	1.054	1.053	1.053	1.053	1.053	1.052
Exradin T2 Spokas	-	1.020	1.018	1.018	1.018	1.017	1.017	1.017	1.017	1.017	1.017	1.017	1.017	1.016	1.016	1.016
Exradin A1 mini Shonka	-	1.045	1.043	1.043	1.042	1.042	1.042	1.042	1.042	1.042	1.042	1.042	1.042	1.041	1.041	1.041
Exradin T1 mini Shonka	-	1.009	1.007	1.007	1.006	1.006	1.006	1.006	1.006	1.006	1.006	1.005	1.005	1.005	1.005	1.004
Exradin A12 Farmer	-	1.043	1.042	1.041	1.041	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.040	1.039	1.039
Far West Tech IC-18	-	1.007	1.006	1.005	1.005	1.005	1.004	1.004	1.004	1.004	1.004	1.004	1.004	1.003	1.003	1.003
FZH TK 01	-	1.032	1.031	1.030	1.030	1.030	1.030	1.029	1.029	1.029	1.029	1.029	1.029	1.029	1.028	1.028
Nuclear Assoc 30-750	-	1.037	1.035	1.034	1.034	1.034	1.034	1.034	1.034	1.033	1.033	1.033	1.033	1.033	1.033	1.032
Nuclear Assoc 30-749	-	1.041	1.039	1.039	1.038	1.038	1.038	1.038	1.038	1.038	1.038	1.037	1.037	1.037	1.037	1.036
Nuclear Assoc 30-744	-	1.041	1.039	1.039	1.038	1.038	1.038	1.038	1.038	1.038	1.038	1.037	1.037	1.037	1.037	1.036
Nuclear Assoc 30-716	-	1.041	1.039	1.039	1.038	1.038	1.038	1.038	1.038	1.038	1.038	1.037	1.037	1.037	1.037	1.036
Nuclear Assoc 30-753 Farmer shortened	-	1.041	1.040	1.039	1.039	1.038	1.038	1.038	1.038	1.038	1.038	1.038	1.038	1.037	1.037	1.037
Nuclear Assoc 30-751 Farmer	-	1.037	1.036	1.035	1.035	1.035	1.035	1.034	1.034	1.034	1.034	1.034	1.034	1.034	1.033	1.033
Nuclear Assoc 30-752 Farmer	-	1.044	1.042	1.041	1.041	1.041	1.041	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.039
NE 2515	-	1.033	1.032	1.031	1.031	1.031	1.031	1.030	1.030	1.030	1.030	1.030	1.030	1.030	1.029	1.029
NE 2515/3	-	1.043	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.040	1.039	1.039	1.039	1.039	1.038
NE 2577	-	1.043	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.040	1.039	1.039	1.039	1.039	1.038
NE 2505 Farmer	-	1.033	1.032	1.031	1.031	1.031	1.031	1.030	1.030	1.030	1.030	1.030	1.030	1.030	1.029	1.029
NE 2505/A Farmer	-	1.021	1.019	1.019	1.018	1.018	1.018	1.018	1.018	1.018	1.018	1.018	1.017	1.017	1.017	1.016
NE 2505/3, 3A Farmer	-	1.043	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.040	1.039	1.039	1.039	1.039	1.038
NE 2505/3, 3B Farmer	-	1.025	1.023	1.023	1.022	1.022	1.022	1.022	1.022	1.022	1.022	1.021	1.021	1.021	1.021	1.020
NE 2571 Farmer	-	1.043	1.041	1.041	1.040	1.040	1.040	1.040	1.040	1.040	1.040	1.039	1.039	1.039	1.039	1.038
NE 2581 Farmer	-	1.020	1.018	1.017	1.017	1.017	1.017	1.017	1.017	1.016	1.016	1.016	1.016	1.016	1.016	1.015
NE 2561 / 2611 Sec Std	-	1.040	1.038	1.038	1.037	1.037	1.037	1.037	1.037	1.037	1.037	1.037	1.036	1.036	1.036	1.036
PTW23323 micro	-	1.027	1.025	1.025	1.025	1.024	1.024	1.024	1.024	1.024	1.024	1.024	1.024	1.023	1.023	1.023
PTW23331 rigid	-	1.037	1.035	1.034	1.034	1.034	1.034	1.034	1.033	1.033	1.033	1.033	1.033	1.033	1.033	1.032
PTW23332 rigid	-	1.031	1.029	1.028	1.028	1.028	1.028	1.028	1.027	1.027	1.027	1.027	1.027	1.027	1.027	1.026
PTW23333	-	1.033	1.031	1.031	1.030	1.030	1.030	1.030	1.030	1.030	1.030	1.029	1.029	1.029	1.029	1.028
PTW30001/30010 Farmer	-	1.033	1.031	1.031	1.030	1.030	1.030	1.030	1.030	1.030	1.030	1.029	1.029	1.029	1.029	1.028

- Absorbed dose to water ($D_{w,,Q_0}$) at the
- reference depth, zref, in water for a reference calibration beam of quality Q0 and **in the absence of the chamber** is given by

$$D_{w,Q_0} = M_{Q_0} N_{D,w,Q_0}$$

- The absorbed dose to water at the reference depth zref in water, in a proton beam of quality Q and in the absence of the chamber

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0}$$

TABLE 10.II. REFERENCE CONDITIONS FOR THE DETERMINATION OF ABSORBED DOSE IN PROTON BEAMS

Influence quantity	Reference value or reference characteristics
Phantom material	water
Chamber type	for $R_{res} \geq 0.5$ g cm^{-2}, cylindrical and plane-parallel. for $R_{res} < 0.5$ g cm^{-2}, plane-parallel.
Measurement depth z_{ref}	middle of the SOBP [a]
Reference point of chamber	for plane-parallel chambers, on the inner surface of the window at its centre. For cylindrical chambers, on the central axis at the centre of the cavity volume
Position of reference point of chamber	for plane-parallel and cylindrical chambers, at the measurement depth z_{ref}.
SSD	clinical treatment distance
Field size at the phantom surface	10 cm x 10 cm, or that used for normalization of the output factors whichever is larger. For small field applications (i.e. eye treatments), 10 cm x 10 cm or the largest field clinically available

10.8. Worksheet

Determination of the absorbed dose to water in a proton beam

User: _____ Date: _____

1. Radiation treatment unit and reference conditions for $D_{w,Q}$ determination

Proton therapy unit: _____ Nominal energy: _____ MeV

Nominal dose rate: _____ MU min^{-1} Practical range, R_p: _____ g cm^{-2}

Reference phantom: water Width of the SOBP: _____ g cm^{-2}

Reference field size: _____ cm x cm Reference SSD: _____ cm

Reference depth, z_{ref} : _____ g cm^{-2} Beam quality, $Q(R_{res})$: _____ g cm^{-2}

2. Ionization chamber and electrometer

Ionization chamber model: _____ Serial no.: _____ Type: ☐ cyl ☐ pp

Chamber wall / window material: _____ thickness: _____ g cm^{-2}

Waterproof sleeve / cover material: _____ thickness: _____ g cm^{-2}

Phantom window material: _____ thickness: _____ g cm^{-2}

Absorbed-dose-to-water calibration factor $N_{D,w}$ = _____ ☐ Gy nC^{-1} ☐ Gy rdg^{-1}

Reference conditions for calibration P_o: _____ kPa T_o: _____ °C Rel. humidity: _____%

Polarizing potential V_1: _____ V Calibration polarity: ☐ +ve ☐ –ve ☐ corrected for polarity effect

User polarity: ☐ +ve ☐ –ve

Calibration laboratory: _____ Date: _____

Electrometer model: _____ Serial no.: _____

Calibrated separately from chamber: ☐ yes ☐ no Range setting: _____

If yes Calibration laboratory: _____ Date: _____

3. Dosimeter reading[a] and correction for influence quantities

Uncorrected dosimeter reading at V_1 and user polarity: _____ ☐ nC ☐ rdg

Corresponding accelerator monitor units: _____ MU

Ratio of dosimeter reading and monitor units: M_1 = _____ ☐ nC MU^{-1} ☐ rdg MU^{-1}

(i) Pressure P: _____ kPa Temperature T: _____ °C Rel. humidity (if known): _____%

$$k_{TP} = \frac{(273.2 + T)}{(273.2 + T_o)} \frac{P_o}{P} = \_\_\_\_\_$$

(ii) Electrometer calibration factor[b] k_{elec}: ☐ nC rdg^{-1} ☐ dimensionless k_{elec} = _____

(iii) Polarity correction [c] rdg at $+V_1$: M_+ = _____ rdg at $-V_1$: M_- = _____

$$k_{pol} = \frac{|M_+| + |M_-|}{2M} = \_\_\_\_\_$$

Worksheet – TRS 398

(iv) Recombination correction (two-voltage method)

Polarizing voltages: V_1 (normal) = _____V V_2 (reduced)= _____V

Readings[d] at each V: M_1= _____ M_2= _____

Voltage ratio V_1 / V_2 = _____ Ratio of readings M_1 / M_2 = _____

Use Table 4.VII for a beam of type: ☐ pulsed ☐ pulsed-scanned

a_0 = _____ a_1 = _____ a_2 = _____

$$k_s = a_0 + a_1\left(\frac{M_1}{M_2}\right) + a_2\left(\frac{M_1}{M_2}\right)^2 = \_\_\_\_\_ \quad \text{e,f}$$

Corrected dosimeter reading at the voltage V_1:

$$M_Q = M_1 k_{TP} k_{elec} k_{pol} k_s = \_\_\_\_\_ \ \square\ \text{nC MU}^{-1} \ \square\ \text{rdg MU}^{-1}$$

4. Absorbed dose to water at the reference depth, z_{ref}

Beam quality correction factor for user quality Q: k_Q= _____

taken from ☐ Table 10.III ☐ Other, specify: _____

Absorbed-dose calibration of monitor at z_{ref}:

$$D_{w,Q}(z_{ref}) = M_Q N_{D,w} k_Q = \_\_\_\_\_ \text{ Gy MU}^{-1}$$

Uncertainty - Dosimetry

TABLE 10.IV. ESTIMATED RELATIVE STANDARD UNCERTAINTY [a] OF $D_{w,Q}$ AT THE REFERENCE DEPTH IN WATER AND FOR A CLINICAL PROTON BEAM, BASED ON A CHAMBER CALIBRATION IN ^{60}Co GAMMA RADIATION

Physical quantity or procedure	Relative standard uncertainty (%)	
User chamber type:	cylindrical	plane-parallel
Step 1: Standards Laboratory	*SSDL* [b]	*SSDL* [b]
$N_{D,w}$ calibration of secondary standard at PSDL	0.5	0.5
Long term stability of secondary standard	0.1	0.1
$N_{D,w}$ calibration of the user dosimeter at the standards laboratory	0.4	0.4
Combined uncertainty in Step 1	*0.6*	*0.6*
Step 2: User proton beam		
Long-term stability of user dosimeter	0.3	0.4
Establishment of reference conditions	0.4	0.4
Dosimeter reading M_Q relative to beam monitor	0.6	0.6
Correction for influence quantities k_i	0.4	0.5
Beam quality correction, k_Q	1.7	2.0
Combined uncertainty in Step 2	*1.9*	*2.2*
Combined standard uncertainty in $D_{w,Q}$ (Steps 1 + 2)	**2.0**	**2.3**

TRS 398 Vs ICRU 59

- TRS 398
  - Includes secondary electron transport and nuclear interactions
  - Water to air stopping-power ratios includes chamber perturbation factors
  - Graphite-to-air-stopping power ratio (swall,air stopping- power ratios) is 0.8 percent higher than ICRU 59 (uses monte carlo calculated data)
- Overall relative uncertainties in proton-absorbed dose determinations are 2.6 percent (ICRU 59) and 2.0 percent (TRS 398)

TRS 398 Vs ICRU 59

Table 4.14. Comparison of ICRU 59 (ICRU, 1998) dosimetry protocol and TRS 398 (IAEA, 2000) dosimetry code of practice for clinical proton beams.

Feature/quantity	ICRU 59 (ICRU, 1998)	TRS 398 (IAEA, 2000)
Ionization chamber	Cylindrical	Cylindrical and plane-parallel ($R_{res} > 0.5$ g cm^{-2}) Plane-parallel ($R_{res} < 0.5$ g cm^{-2})
Wall material	Graphite or A-150 plastic	Graphite for cylindrical chambers
Gas filling	Ambient air	Ambient air
Chamber volume	>0.5 cm^3 for beams >5 cm diameter ~0.1 cm^3 for beams <5 cm diameter	–
Water proof sleeve	–	<1 mm thick PMMA
Dose specification	Water	Water
Calibration beam	^{60}Co	^{60}Co
Calibration coefficient	Primarily N_K, also N_X, $N_{D,w}$	$N_{D,w}$ only
Beam quality	Residual range (to distal 10 % level)	Residual range (to distal 10 % level)
Phantom material	Water (or other materials which match electron density of water)	Water
Reference point for measurement	Middle of SOBP	Middle of SOBP Depth of 3 g cm^{-2} for plateau irradiations
Field size	–	10 × 10 cm^2
SSD	–	Clinical treatment distance
Stopping powers	ICRU (ICRU, 1993a)	PETRA (Medin and Andreo, 1997b)
$(w_{air}/e)_p$ (J C^{-1})	34.8 ± 0.7 (ambient air)	34.23 ± 0.13 (dry air)
$(w_{air}/e)_{^{60}Co}$ (J C^{-1})	33.77 ± 0.05 (ambient air)	33.97 ± 0.07 (dry air)
$(s_{w,air})_{^{60}Co}$	1.134	1.133
Chamber perturbation factors	No	Yes
Relative uncertainty in absorbed dose (1σ)	2.6 % (Jones, 2001d)	2.0 % (cylindrical chambers) 2.3 % (plane-parallel chambers)

Dosimetry

- A 10x10x10 cm3 water volume irradiated to a homogeneous dose of 1 Gy. Rest as usual TRS 398
- The main differences in the dosimetry of passive and active systems are in beam monitoring and relative dosimetry

Table 4.15. Proton dosimetry comparisons with ionization chambers. The relative maximum measured dose differences are given in the last column.

Reference	Protocol	Number of chambers	Beam energy (MeV)	Max. difference (%)
Kacperek *et al.* (1991)	ECHED	8	60	4.5
Jones *et al.* (1992)	ECHED	7	60–80	2.5
Jones *et al.* (1994a)	ECHED	7	200	1.8
Schreuder *et al.* (1994)	AAPM/ECHED	7	135–185	1.4
Medin *et al.* (1995)	TRS 277	7	170	1.5
Jones (1996)	ECHED	6	58–168	2.3
Palmans *et al.* (1996)	ECHED	10	85	1.2
Vatnitsky *et al.* (1996b)	AAPM/ECHED	23	100–250	5.8
Hiraoka *et al.* (1997)	-	5	70	0.8
Cuttone *et al.* (1999)	ECHED	3	28–62	2.1
Vatnitsky *et al.* (1999b)	ICRU 59	11	155	2.9
Nohtomi *et al.* (2001)	ICRU 59	5	250	1.5
Palmans *et al.* (2001)	TRS 398	17	75	1.5
Fukumura *et al.* (2002)	TRS 398	8	150	0.9
Kacperek *et al.* (2002)	ICRU 59	10	63	3.2
Vatnitsky *et al.* (2002)	ICRU 59/TRS 398	6	100–155	3.1

AAPM, AAPM (1986); ECHED, Vynckier *et al.* (1991; 1994); TRS 277, IAEA (1997a); ICRU 59, ICRU (1998); TRS 398, IAEA (2000).

Beam Monitoring

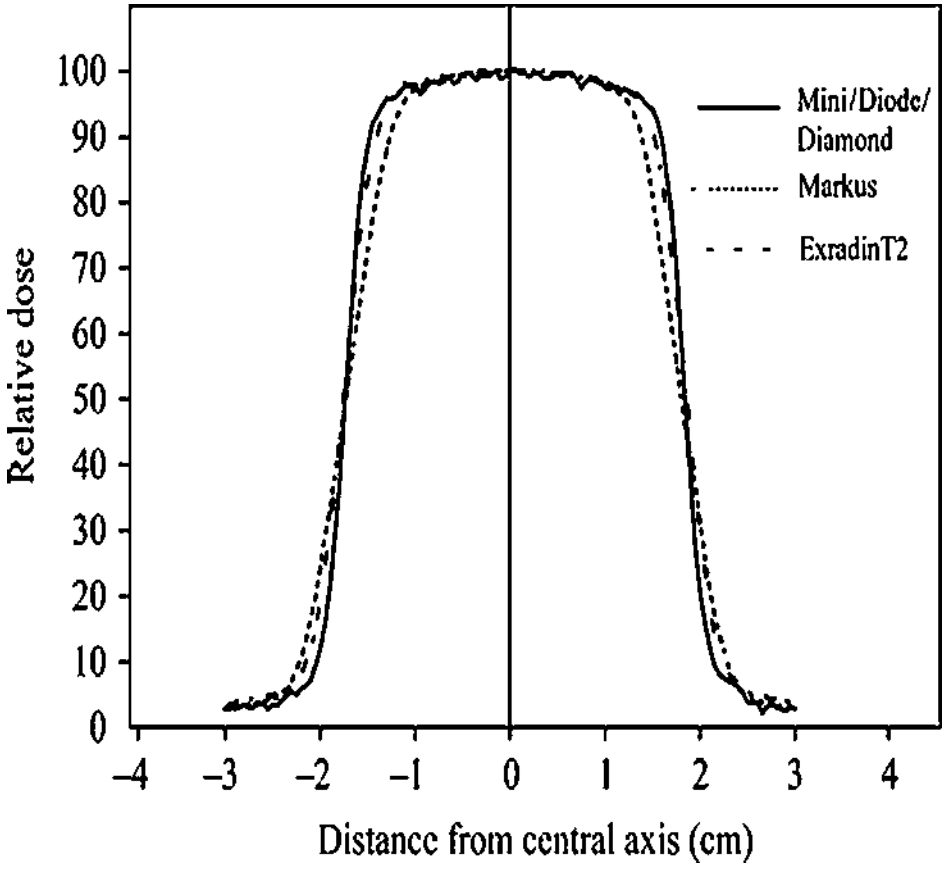
- Two independent dose monitors on daily basis recommended
- Beam profile (center, flatness, symmetry)
- Range/Energy measurement
  - Synchrotron:
    - beam position and intensity monitors in the synchrotron are used to calculate proton velocity. Inhibits delivery for ±MeV
  - Cyclotron:
    - Bending magnet field strength. Incorrect beam energy will be bent to wrong angle – abort the treatment

RELATIVE DOSIMETRY

- Absolute dosimetry – Reference condition
- Relative dosimetry – non-reference condition
  - Detector calibration not required
  - Daily QA, Commissioning & TPS data
  - O/p factors for individualized patient portal
  - Detector
    - sensitivity, energy independence, response linearity, and spatial resolution
    - ionization chambers, silicon diodes, radiographic films, diamond detectors, gels, scintillators, thermo luminescence dosimeters (TLDs), and radio chromic films

RELATIVE DOSIMETRY

- 3.5 cm field width
- Smaller Active Volume (than field size)
- ionization chambers is a compromise between the sensitive volume and spatial resolution



Stopping power

- Stopping power is defined as the average energy loss of a particle per unit path length, measured for example in keV/µm
- LET i.e. "the average energy locally imparted to the medium by a charged particle of specific energy traversing a certain distance

Stopping power

Charged particle gradually loses its energy mostly through vast interactions with electrons and nuclei.

- stopping power
  - Collision stopping power (with electrons) (S_{col})
  - Radiative stopping power (Bremsstrahlung) (S_{rad})
  - energy loss dE in a unit length dx
  - Unit: MeV/m, keV/μm, eV/nm, etc...

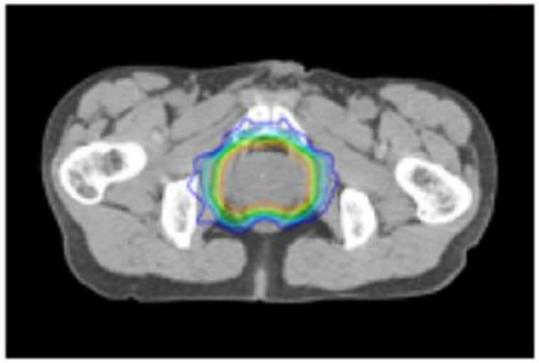
$$S = S_{col} + S_{rad}$$

Importance of patient setup

Photon vs Proton

Effect of setup error on dose distribution

IMRT 7Field +3deg

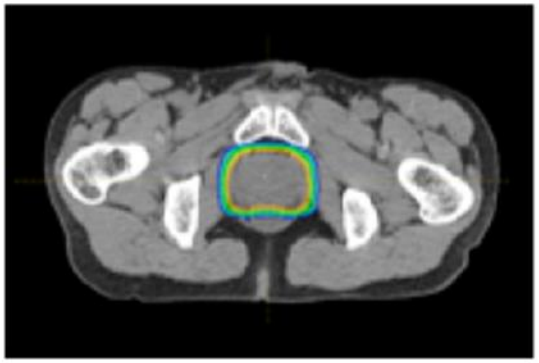


PTV

D95=70.2Gy -> 70.2Gy

Dmin=63.6Gy -> 63.0Gy

Proton 2Field +3deg



PTV

D95=70.2GyE -> 69.3GyE

Dmin=65.2GyE -> 61.8GyE

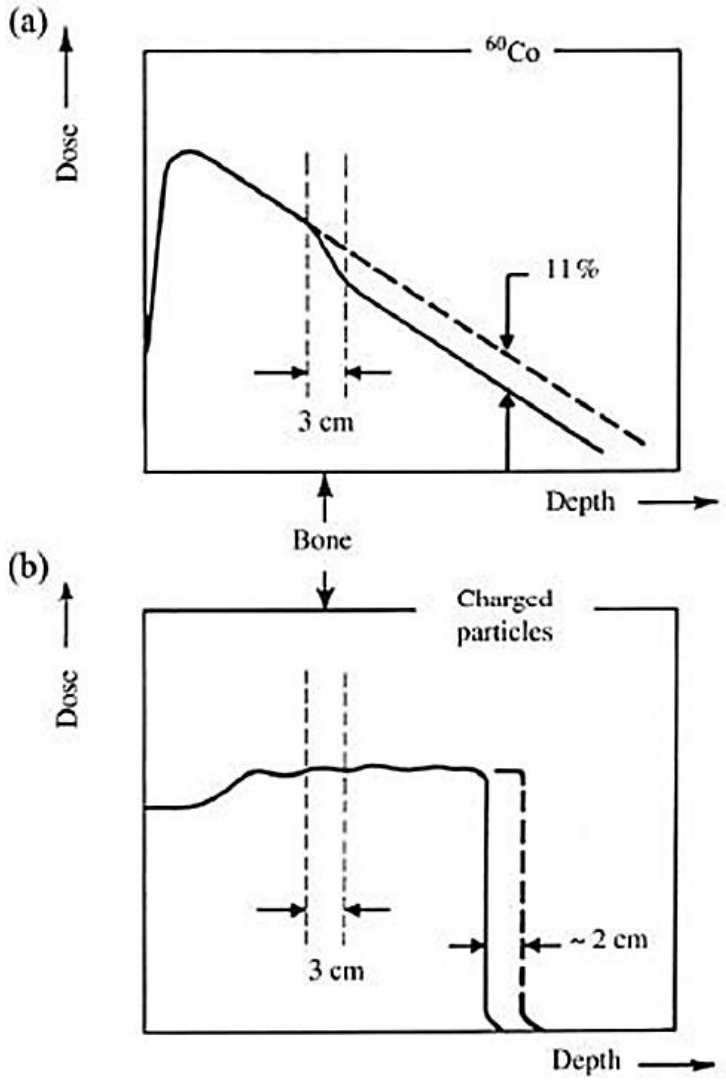
Volume Definitions

- Gross tumor volume (GTV) (ICRU 62)
  - the gross palpable, visible, or clinically demonstrable location and extent of the malignant (or otherwise) growth
- Clinical target volume (CTV) (ICRU 62)
  - is a tissue vol ume that contains a demonstrable GTV and / or subclinical malignant disease that must be eliminated. This volume must be treated adequately in order to achieve the aim of radical therapy.
- The traditional concept of PTV with setup uncertainty based expansion of the CTV is not applicable to proton therapy.
- account both motion and range uncertainties

PTV

- Lateral margins and the margins in depth (relative to the proximal and distal tumor surfaces) solve different problems
- Numerically different
- in principle, need a separate PTV with different margins laterally and along the direction of each beam.
- Alternatively determine beam parameters using CTV rather than PTV
- PTV needed for reporting and recording purpose
- PTV be defined relative to the CTV on the basis of lateral uncertainties alone (with adjustment in beam for range uncertainties)

Effect of High density material



- 3cm bone in beam path
- ^{60}Co
  - Intensity/dose reduced (11%)
  - Still penetrates deeply
- Proton
  - Penetration reduced
  - Dose in the Hdregion unaffected

Margin for proton therapy

ASTRO Model Policies

PROTON BEAM THERAPY (PBT)

In X-ray therapy, to account for uncertainties in the planning and delivery processes, a final margin is then added to create a Planning Target Volume (PTV). Analogous to the approach used in X-ray therapy, a lateral target expansion guards against under-dosing the target in the presence of daily setup variation and/or organ and patient motion. With PBT, however, the target expansion in the beam direction must also ensure coverage for uncertainties in the range of the proton beam which may not perfectly match the radiologic depth of the target. The expansion in the beam direction may be different from the lateral expansion. Because the lateral and range expansions may differ for each beam, there is no longer a single PTV that is sufficient for a multi-field proton plan. Rather than prescribing a uniform dose to a PTV, in PBT the plan should be designed to cover the CTV in the presence of expected uncertainties.

https://www.astro.org/uploadedFiles/_MAIN_SITE/Daily_Practice/Reimbursement/Model_Policies/Content_Pieces/ASTROPBTModelPolicy.pdf

Radiation quality

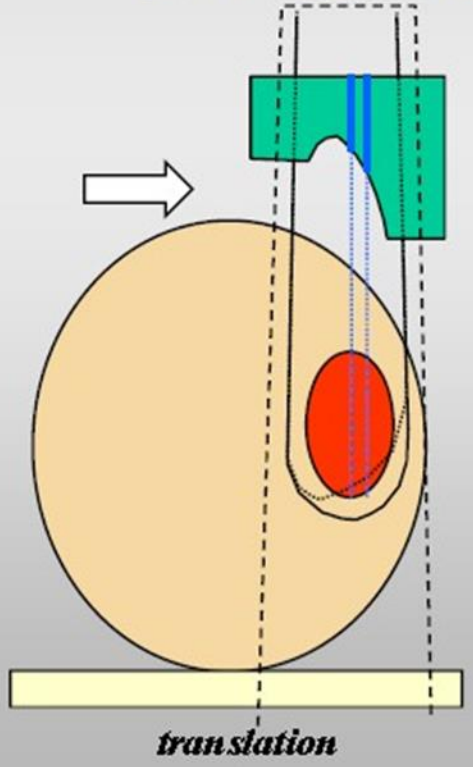
- Affect the distal fall-off , the lateral penumbra, and low dose outside the field at large off-axis distances
- Passive Sactter – Neutron originated from Nozzle
- + Patient (nuclei interaction)
- Dynamic Scan – only Patient (nuclei interaction)
- Theoretically increased risk of radiation-induced secondary cancer
- Limited clinical experience/Evidence

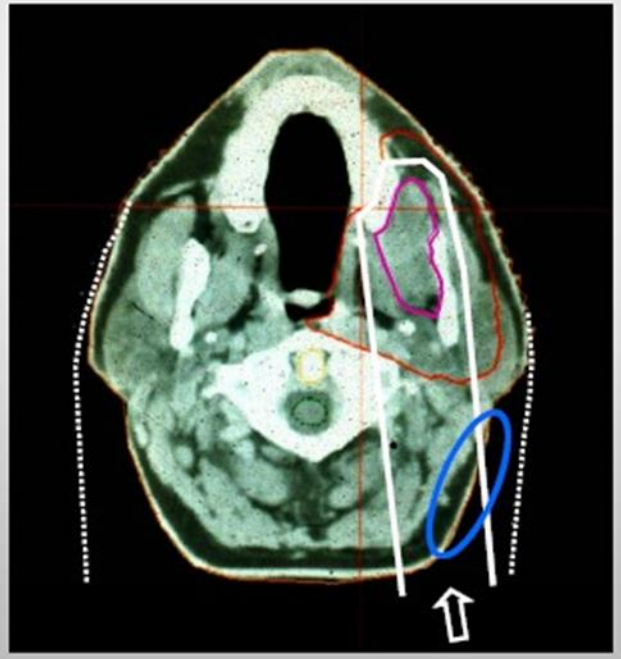
• Scattered beams	Generally designed to produce a near-uniform dose distribution within the target volume for each beam
• Scanned beams (continuous or discrete)	Can either produce a near-uniform dose distribution or, more usually, a highly non-uniform dose distribution within the target volume for each beam—and are thus suitable for use in intensity-modulated proton therapy (IMPT)
• Wobbled beams (a special case of beam scanning, using relatively wide finite pencil beams)	Generally producing a near-uniform dose within the target volume for each beam

- Selection of beam directions
- concerned about entrance dose.
- Avoid beam directions that pass through complex or high-Z heterogeneities
- maximum separation between the PTV and distal critical OAR
- Avoid superficial or shallow sensitive structures. (due to lack of skin sparing)

BEAM DIRECTION NEAR–TANGENT TO A SKIN:TISSUE INTERFACE

- **The greatest inhomogeneity is that which exists at the interface between the patient and the surrounding air**
- **if the beam direction is near–tangent to a skin:tissue interface, the dose distribution can be very sensitive to patient motion or misalignment**



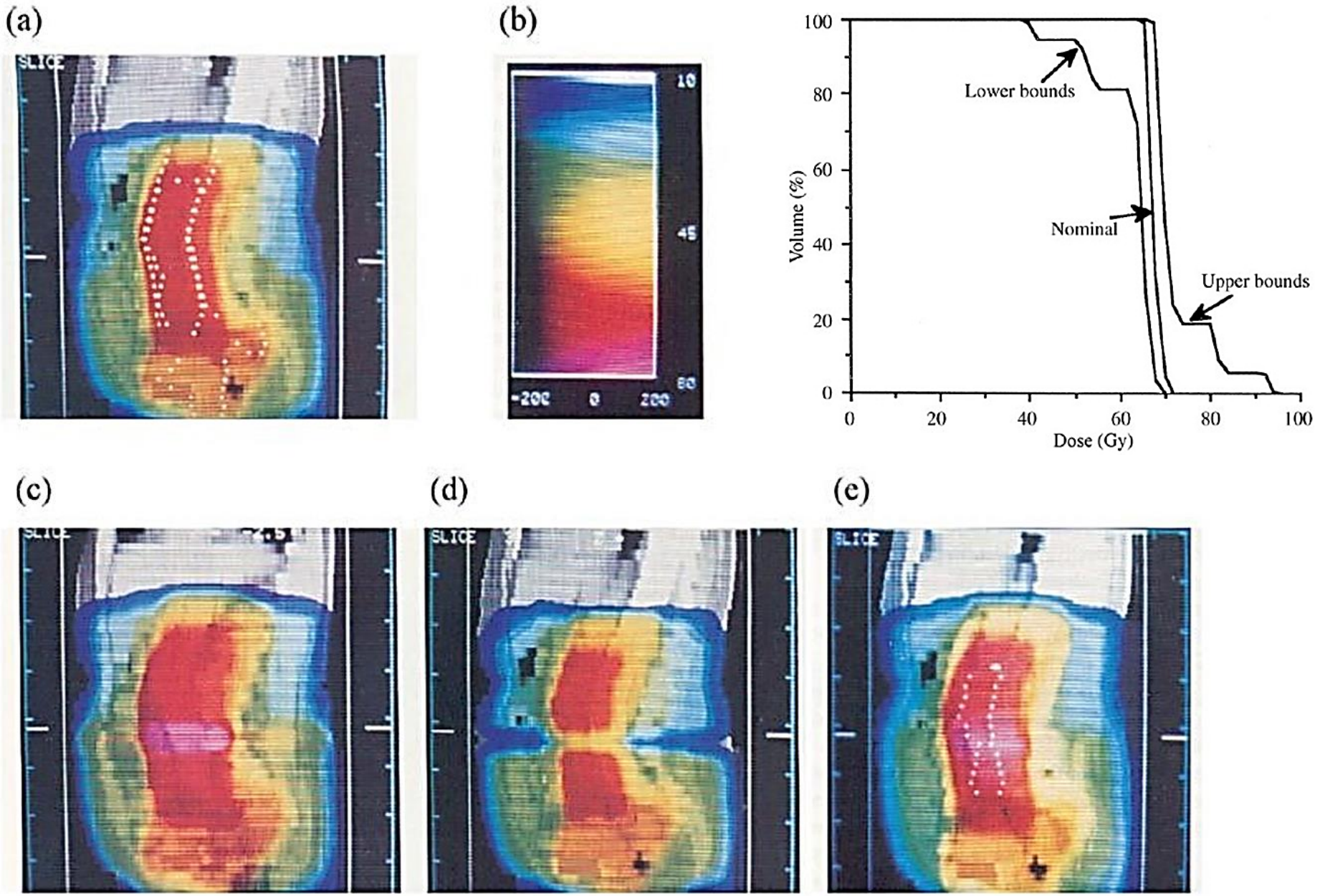


UNCERTAINTY IN DELIVERED DOSE

- Radiation therapy is inherently probabilistic.
- Most of the parameter involved in RT associated with uncertailty.
  - Eg: immobilization and localization
  - physiologic motions, effects of heterogeneities, and imperfections in the techniques to compensate for them
  - algorithms used to estimate dose

UNCERTAINTY IN DELIVERED DOSE

- uncertainty in the dose at selected points in three-dimensions within the patient
- uncertainties in quantities such as D98%, D50%, EUD, TCP, and NTCP
- confidence level (CL) must be specified
- a photon dose distribution is relatively robust in the face of uncertainties.


(a)
(b)
(c)
(d)
(e)
SLICE
10
45
80
-200
0
200
100
80
60
40
20
0
Volume (%)
Lower bounds
Nominal
Upper bounds
0
20
40
60
80
100
Dose (Gy)

UNCERTAINTY IN DELIVERED DOSE

- Worst case hybrid dose distribution for 5mm shift
- Cold spot in PTV & hotspot in OAR

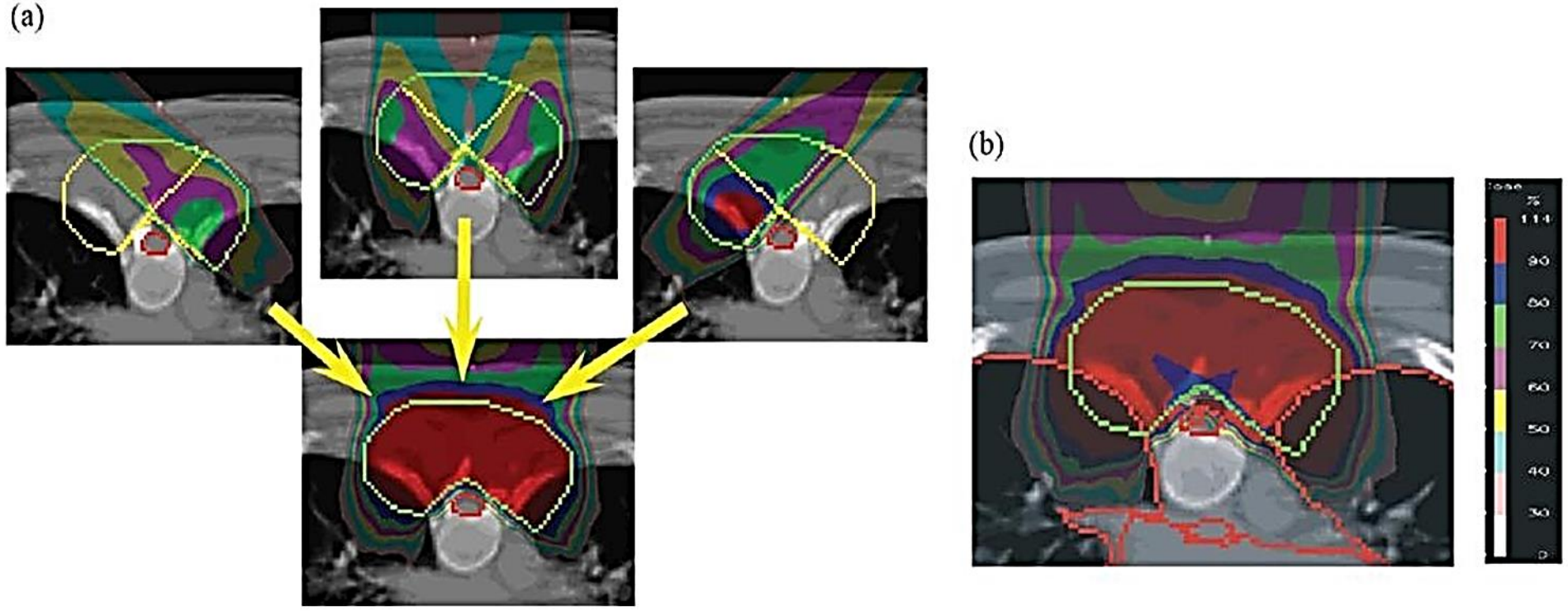
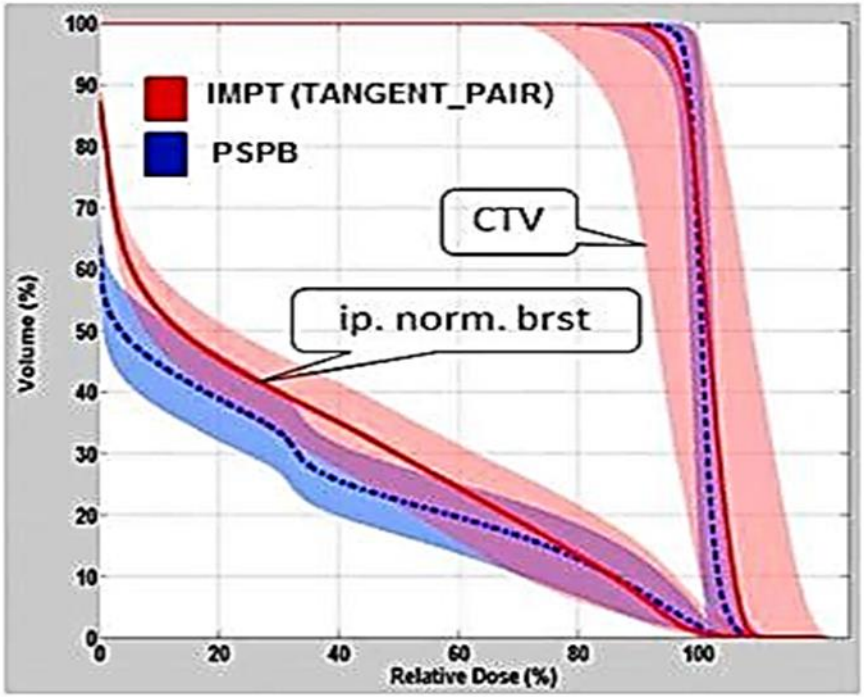
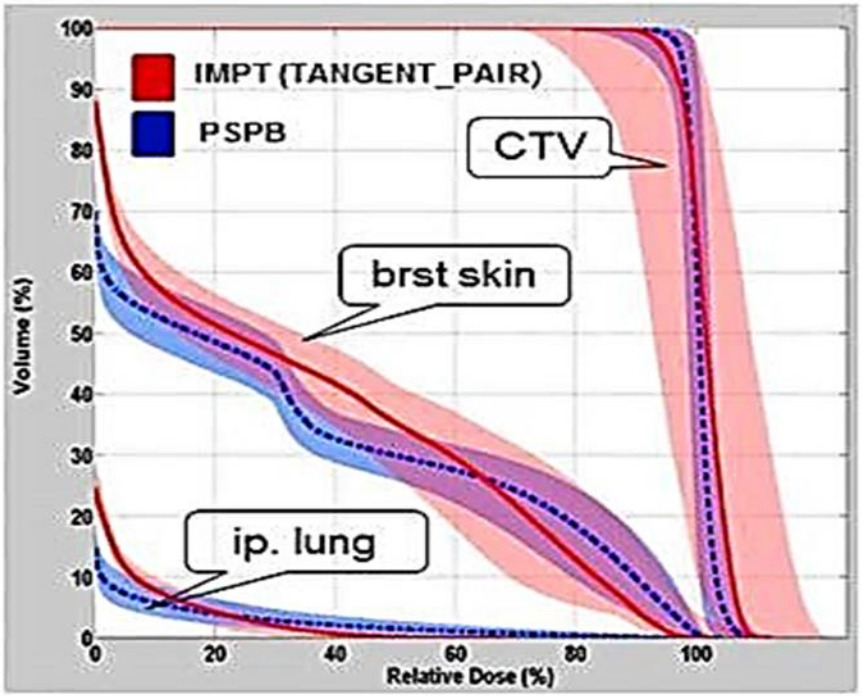


Figure 8.2. (a) The individual beams of a three-beam IMPT plan for a thoracic chordoma, with the nominal combined dose distribution at the bottom. (b) The 'worst case' distribution resulting from 5 mm shifts along each major axis of the patient. The worst-case distribution is calculated at each point by taking the minimum dose of these shifted doses within the CTV and the maximum dose

UNCERTAINTY IN DELIVERED DOSE

- DVH uncertainty band





- find the plan which on average has the best score when averaging over all sources of uncertainty

QUALITY ASSURANCE

- Safe Tx and Minimal exposure
- QA depends on equipment and delivery tech
- preclinical testing are physics and dosimetry acceptance checks
- Establish benchmark (baseline values)
  - depth doses, off-axis profiles, field size factors, penumbra sizes, and beam ranges

QUALITY ASSURANCE

Table 9.1. Quality-assurance procedures for passive beam-delivery systems.

Daily checks

- Aperture alignment; room lasers, interlocks; communication; patient-positioning system
- Depth–dose and lateral profiles (range, entrance dose, uniformity of range modulation and Bragg-peak width, flatness, symmetry)
- Dose monitor calibration, check of MU value under standard condition
- Individual patient treatment calibration and range checks

Weekly checks

- Patient-positioning and imaging systems
- Beam-line apparatus
- Respiratory-gating equipment
- Dose delivered to randomly selected patients (comparison of planned dose distributions to those measured in a water phantom)

Annual or scheduled inspection checks

- x-ray patient positioning and alignment systems
- CT Hounsfield number calibration
- Comprehensive tests of therapy equipment
  - monitor chambers, timers, beam-delivery termination and control interlocks, stray radiation exposure to patients, gantry isocenter, depth–dose and lateral profiles, baseline data for daily QA checks

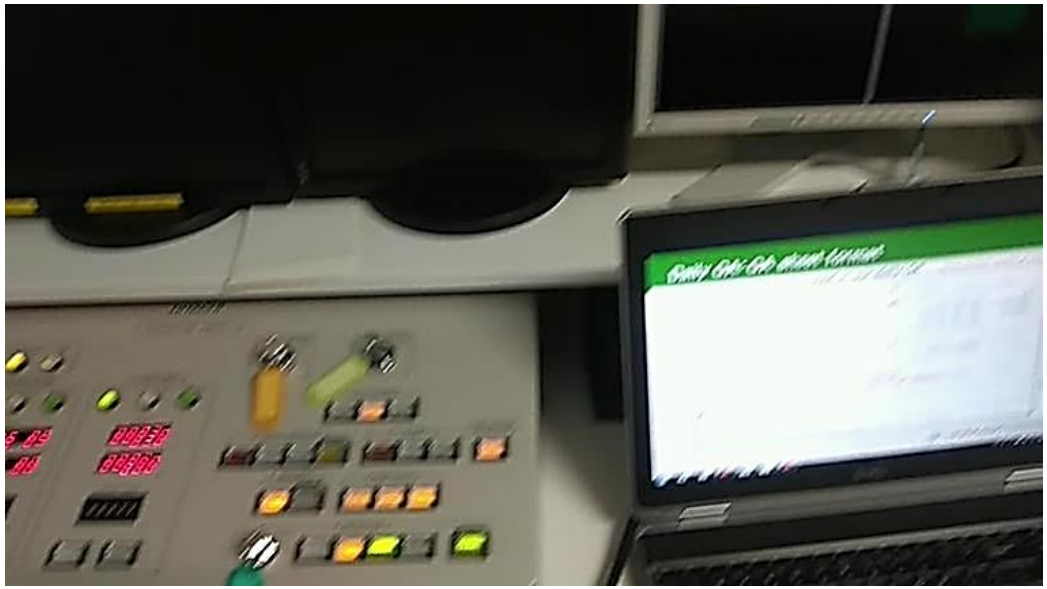
QUALITY ASSURANCE

- coincidence of the proton-beam isocenter and the patient setup-laser positions (phosphor imaging plate)
- Monitor chamber response Vs Gantry angle (rotating ganrty)
- periodic QA of stereo photogrammetric positioning systems and x-ray imaging systems
- mechanical accuracy of the couch (robotic)

Table 9.2. Additional quality-assurance procedures for scanning beam-delivery systems.

Daily checks
• Dose rate and monitor ratios for the pencil beam • Performance of the beam-position monitors • Depth–dose curve of a pencil beam in a water phantom • Calibration of the primary dose monitor
Weekly checks
• Qualitative three-dimensional check of the outline and range of the dose distribution for one patient's irradiation field in a water phantom
Half-yearly checks
• Calibration of the primary dose monitor and the phase space of the beam tunes
Annual or scheduled inspection checks
• Check of the beam characteristics o calibration of the whole dosimetry system, performance of the scanning system in terms of dose linearity and dose-rate dependence

Daily check – Scanning beam



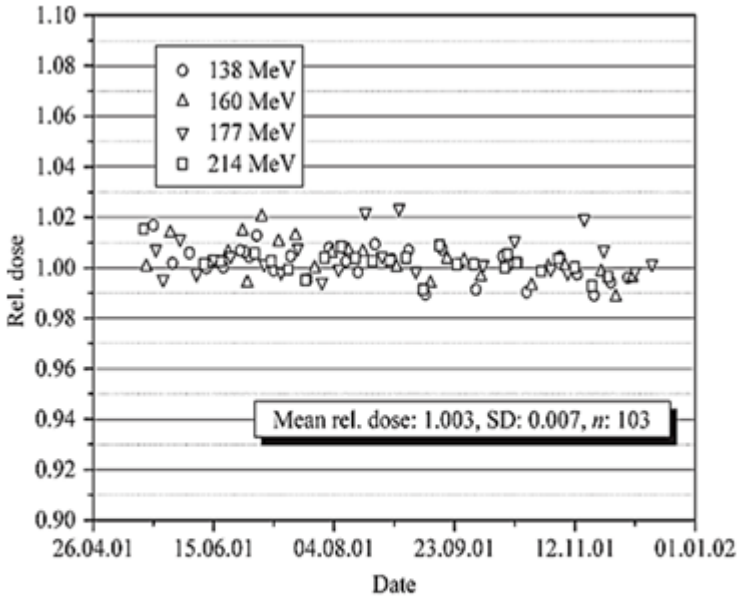
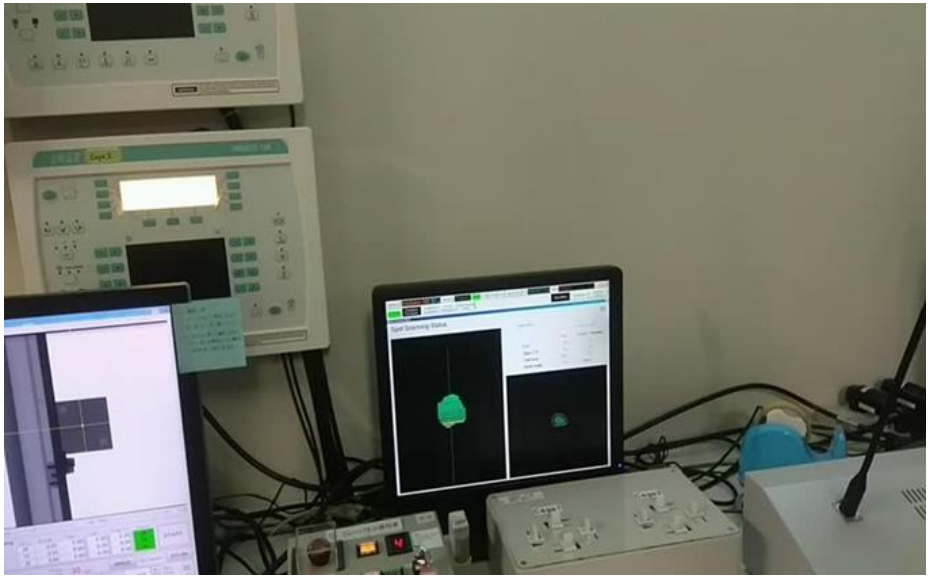


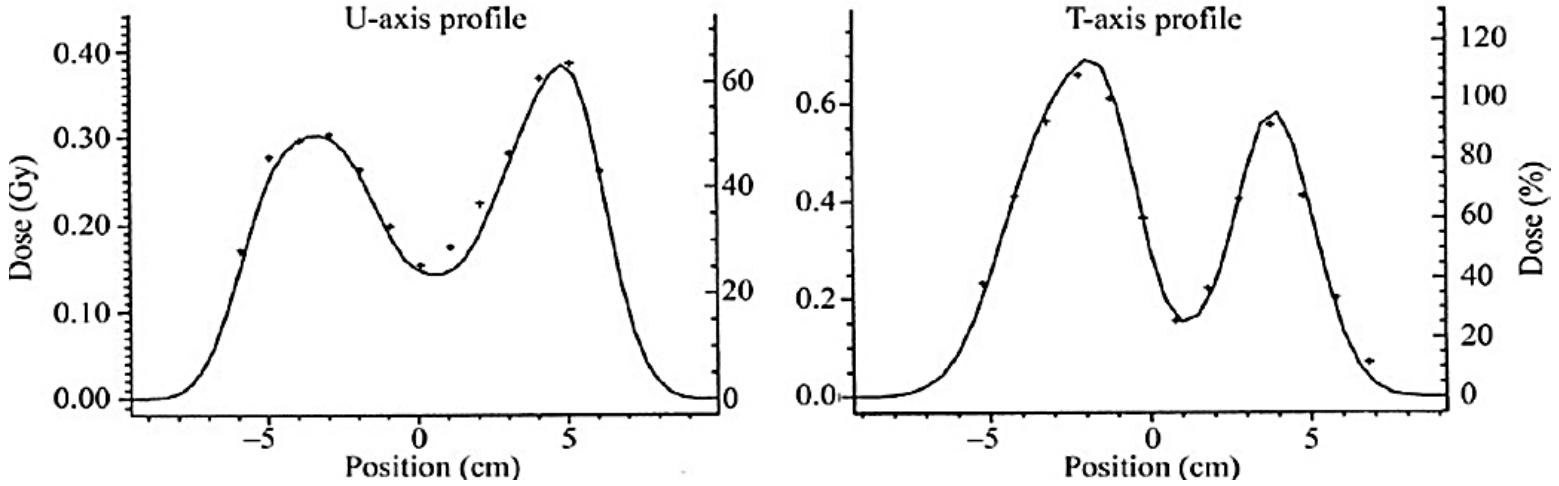
Figure 9.2. Dose measured daily in the center of a reference volume in a scanning beam (n is the number of data points) (Coray *et al.*, 2002; reproduced with permission).

TPS QA

- TG 53 & IAEA TRS 430 are applicable
- CT Hounsfeld units to proton stopping powers (Not coverd in TG53 & TRS 430)
- consistency of the CT Hounsfield
- Verify “apertures/compensators/bolus” calculation
- no patient-specific devices (scanning beam)
- proton radiography
- Real-time PET imaging considered a potential tool for QA in proton therapy



PRESCRIBING, RECORDING, AND REPORTING PROTON-BEAM THERAPY

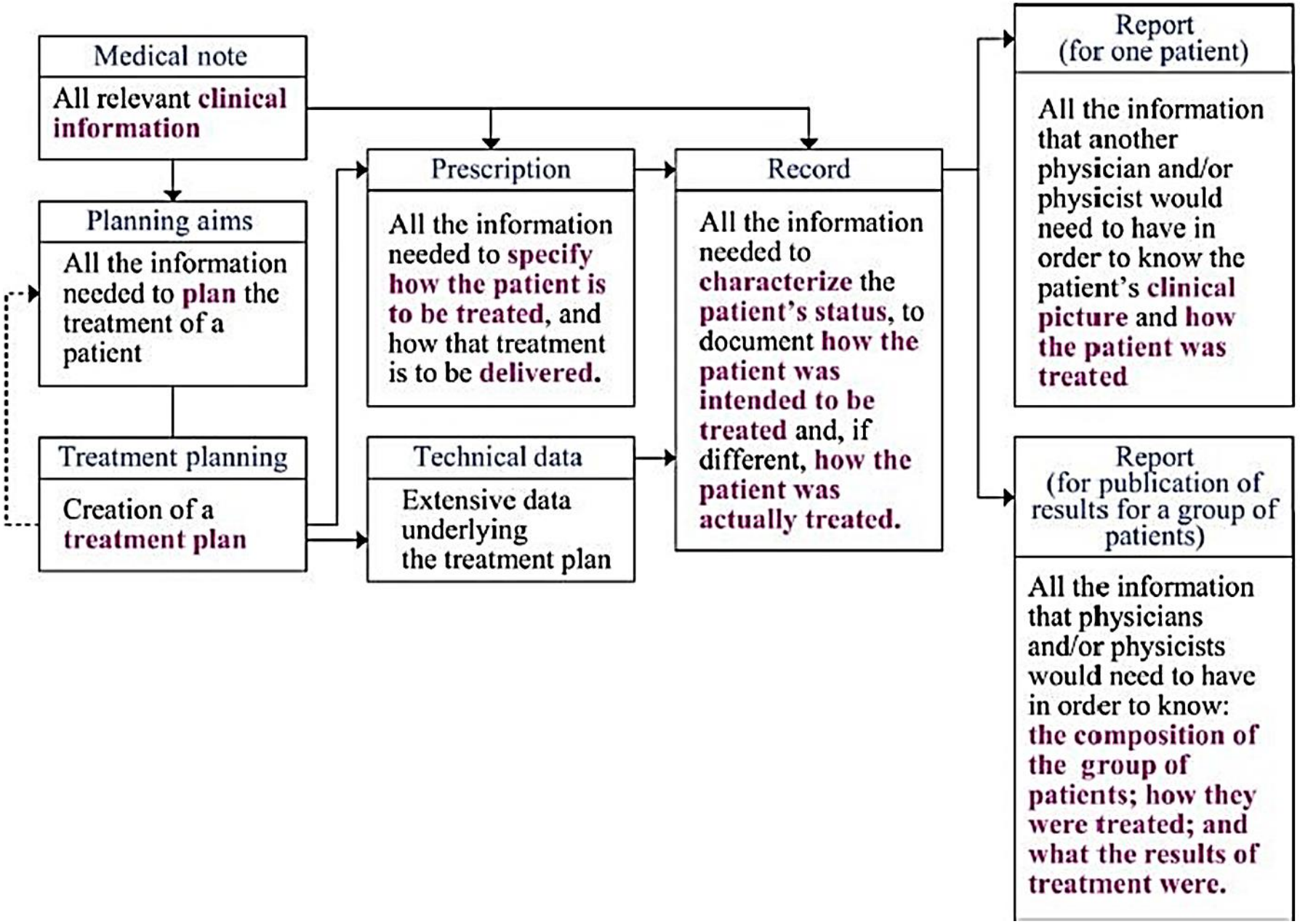


QA for respiratory synchronized Treatment

- Benchmarks for periodic QA
  1. differences between observed respiration signal and actual organ movement;
  2. phase uncertainty at CT scanning for treatment planning to make reference images;
  3. setting of the threshold level of the extent of the movement;
  4. movement of organ during allowed period for irradiation.

PRESCRIBING, RECORDING, AND REPORTING TREATMENT

1. Initial medical note	History of present illness, co-morbidities, physical examination, findings on imaging and pathological studies, and general management strategy.
2. Planning aims	All the information needed to plan the treatment of the patient.
3. Treatment planning	The process of simulating a number of delivery strategies for a radiation treatment and choosing the best one to use for treatment
4. Treatment prescription	Instructions for treatment delivery to achieve the planned dose distribution and authorization of the technical details to deliver the treatment plan
5. Technical data	Data required for treatment delivery according to the treatment plan (with the prescription, treatment plan, doses and technical data approved and fixed).
6. Record of the treatment	Storage of all data relevant to the patient's treatment.
7. Report(s) of the treatment	For example, completion note, report to the referring and other physician(s), publications.


Medical note
All relevant clinical information
Planning aims
All the information needed to plan the treatment of a patient
Treatment planning
Creation of a treatment plan
Prescription
All the information needed to specify how the patient is to be treated, and how that treatment is to be delivered.
Technical data
Extensive data underlying the treatment plan
Record
All the information needed to characterize the patient's status, to document how the patient was intended to be treated and, if different, how the patient was actually treated.
Report (for one patient)
All the information that another physician and/or physicist would need to have in order to know the patient's clinical picture and how the patient was treated
Report (for publication of results for a group of patients)
All the information that physicians and/or physicists would need to have in order to know: the composition of the group of patients; how they were treated; and what the results of treatment were.

Planning Aims

- radiation oncologist gives these aims to the planner
- Planning aims be part of the archived records
- any compromises between initial and final aims with reasons
- Doses should be specified as RBE-weighted absorbed doses [in Gy (RBE)]
- Normal tissue
  - Dose volume, Serial-like/Parallel-like / NTCP
- which plan would best achieve the planning aims

Prescription

- Delineations of GTV, CTV, PTV, OAR, RVR, etc
- Approved plan with dose distribution
- Prescribed D_{RBE}, dose–volume constraints
  - ICRU ref dose, $D_{98\%}$, $D^{2\%}$, VD (volume receiving ≥Rx)
- Normal-tissue constraints (Dose/Dose volume)
- Fractionation scheme (no of #, Inter# interval, OTT)
- Medical aspects that affect how the treatment is to be performed
- Technical data required to perform the treatment

Technical Data

- Physician's approval covers both the treatment plan, and the **technical aspects** required to implement
- The reality is that the **Radiation Oncologist accepts** the calculations and statements of physicists and engineers
- The responsibility for the existence and correctness of these data lies in the hands of the physicist
  - Physicist should formally approve these technical data that should be included in the treatment record

Data required for

- Planning aims
- Prescription
- Tx record

Table 10.1. Summary of the data required in each of the three areas 'planning aims', 'prescription', and 'treatment record'. Required items are identified by colored table cells. Items specific to, or that contain information concerning, proton-beam therapy are, in addition, crosshatched.

	Planning aims	Prescription	Treatment record	Note
Patient data				
Identifying information	■	■	■	*note 1*
Demographics			■	*note 2*
Contact information			■	*note 3*
Patient's responsible physician			■	
Patient's responsible physicist			■	
Disease data				
Tumor characteristics			■	*note 4*
History			■	*note 5*
Treatment intent			■	*note 6*
Volumes of interest				
Target volumes (GTV, CTV, and PTV)	■	■	■	
Organs at risk (OAR) and any PRVs	■	■	■	
Prescription (for the entire course of therapy)				*note 7*
Number of treatment segments	■	■	■	*note 8*
For all segments combined				
For target volume (usually PTV)				
Prescription dose	■	■	■	*note 9*
Goal dose	■	■	■	*note 10*
Margins	■	■	■	*note 11*
Fractionation scheme	■	■	■	*note 12*
For each organ at risk (OAR)				
Dose/dose–volume constraints, if any	■	■	■	*note 13*

note 1 For example, patient name, identifying code, and photograph (if any).

note 2 For example, age, sex, and race.

note 3 For example, patient's address, person to contact, and referring physician.

Table 10.1. Continued

For each segment (if more than one)				
Modality				*note 14*
Target volume goal dose for segment				*note 15*
OAR constraints for segment (if any)				*note 16*
Treatment technique (*e.g.*, IMRT or uniform)				*note 17*
Beam arrangements				*note 18*
Immobilization technique				*note 19*
Patient position (*e.g.*, prone, supine, seated)				

Overall plan/beam arrangements

For the plan used for each segment:				
List of beams				
Beam weights				
For each beam in the plan				
Modality				
Maximum energy or penetration (protons)				
Beam direction relative to patient				

Dose information for overall plan *note 20*

For the overall course and, if desired, for each segment separately				
Target volume dose/dose–volume statistics				*note 21*
OAR (PRV) dose/dose–volume statistics				*note 22*
Two-dimensional dose distributions in selected planes				*note 23*
DVHs for selected VOIs				*note 24*

Plan deviations (if any)

Explanation of, and remedial actions, if any				*note 25*

Technical data

Table 10.2. List of some technical data that should be recorded. Items that are specific to or concerning, proton-beam therapy are shaded.

Patient data

Three-two-dimensional data for imaging studies (*e.g.*, three-dimensional array of Hounsfield numbers for CT)
Delineation data of all VOIs, SOIs, and POIs

For each treatment segment

Segment name and/or identifying information
Segment dose
Plan identification

For each plan: non-dosimetric information

Plan name and/or identifying information
The list of beams used in the plan
The weight of each beam
List of SOIs, if any
List of POIs, if any

For each plan: dosimetric information

Three-dimensional dose distribution for the plan (three-dimensional array of values)
Selected two-dimensional dose sections (two-dimensional array of values)
Dose-volume (or dose-surface) histograms for each VOI (two-dimensional array of values)
Doses received by any SOIs (two-dimensional array of values)
Doses received by any POIs

For each beam

Beam name and/or identifying information
Modality: protons(energy), photons(energy), electrons(energy)
The equipment configuration used for the beam (gantry angle, couch settings, *etc.*)
Beam weights and monitor units

For scattered beams
The settings of the collimator (if any)
The angle of rotation of the nozzle or snout
The name, and ID and quantitative description of the aperture or the multi-leaf collimator (MLC) (if any)
The name, and ID and quantitative description of the compensator (if any)
The name, and ID and quantitative description of other beam modifying devices (if any)
The distance from the collimator or compensator to the patient's skin surface
Extent in depth of SOBP and depth of beam penetration
For wobbled beams, in addition to data for scattered beams
Wobbled beam characteristics (spot size, wobbling pattern, *etc.*)
For scanned beams
Scan sequence(s) (*e.g.*, Cartesian grid or contour-following, grid spacing(s)
Pencil-beam characteristics (shape, FWHM at isocenter in air, *etc.*)
Intensity and energy or penetration at each scan dwell-point

History of treatments

Record of dose(s) delivered per fraction
Full record of delivered treatments if record and verify system used

Patient-specific quality assurance

Before treatments begin
Methods used
Results obtained
During treatments
Methods used
Results obtained

Equipment identification

Make, type, and version number of therapy equipment used
Make, type, and version number of treatment-planning system(s) used

ADDITIONAL ASPECTS

- Therapy equipment
  - type of accelerator (cyclotron or synchrotron)
  - delivery equipment (gantry or fixed beam)
  - beam-shaping configuration (Scan/Scatter/Collimator/Compensator) - grid pattern, pencil width, dwell times, and repainting Spec.
  - motion tracking, if applicable.
  - Uniform intensity / IMPT
  - Additional equipment (if proton + proton)
- Heterogeneities
  - affect proton range and dose homogeneity
  - Margins (depth & Lateral)

RECORDING PROTON-BEAM THERAPY

- Comprehensive treatment record
  - Tx intention & actual treatment
  - demographic data, tumor status, the prescription, underlying technical data and follow up
- Retained least as long as the law prescribes
- 3D dose distribution (if scan pattern)

REPORTING THE TREATMENT OF A SINGLE PATIENT

- Uniform
  - useful exchange of clinical information between centres
  - reduces the risks of confusion.
- Mostly proton radiation therapy should be reported at level 3 (ICRU)
- Initial medical note
- Completion note
  - summary of the overall treatment plan
  - D_{RBE} to the PTV, CTV, and GTV ($D_{98\%}$, $D_{2\%}$)
  - D_{RBE} to OAR
  - patient's status upon Tx completion and plans for future follow-up.
  - Used as summary report to referring physics

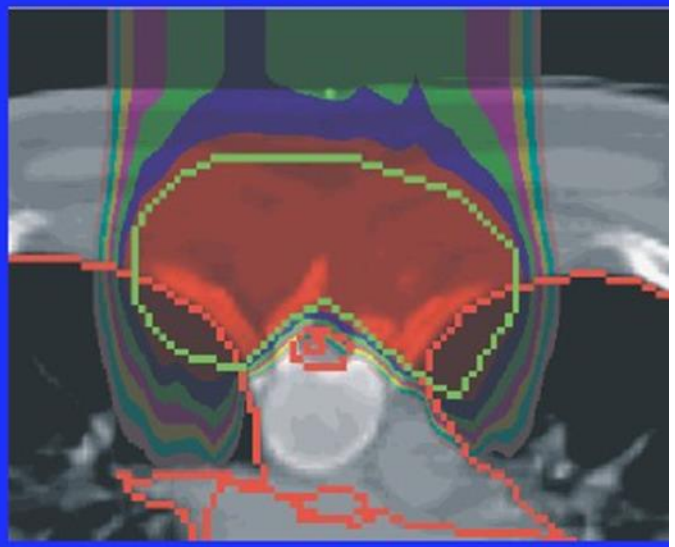
REPORTING PROTON-BEAM THERAPY FOR A SERIES OF PATIENTS

- Reporting the results of proton-beam therapy is very similar to ICRU Reports 50, 62, and 71
- ICRU 50 - Prescribing, Recording and reporting photon beam therapy (1993)
- ICRU 62 - Prescribing, Recording and reporting photon beam therapy (Supplement to ICRU50) (1999)
- ICRU 71 – Prescribing, Recording and reporting Electron beam therapy (2004)
- **ICRU 83 – Prescribing, Recording and reporting photon beam Intensity Modulated Radiation therapy (2010)**

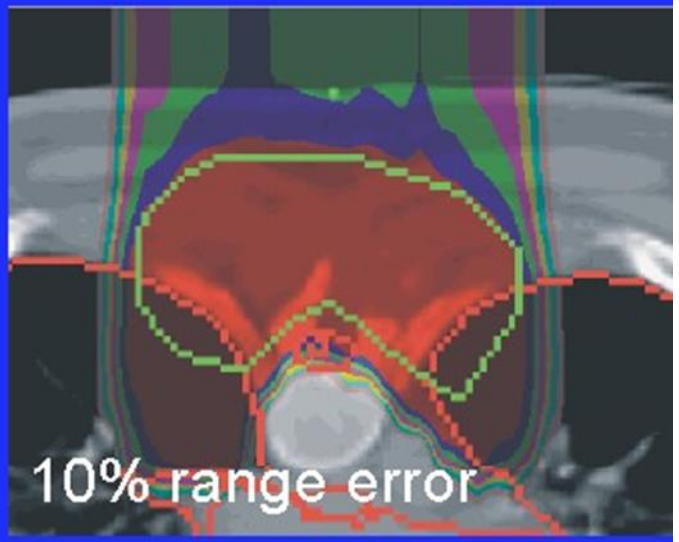
Dealing with uncertainties – range uncertainties.

PAUL SCHERRER

The advantage of protons is that they stop.



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



Summary

- In depth understanding of new treatment delivery technique
- Standard dosimetry protocol needed for Comparing clinical / dosimetric results from different institutes
- The RBE-weighted dose is better suited for proton therapy
- ICRU 78 standardize techniques and procedures and to harmonize the clinical descriptions of proton treatments with those of other modalities

Thank you