Safety issues related to the Synchrotron Stereotactic Radiation Therapy project at the ESRF

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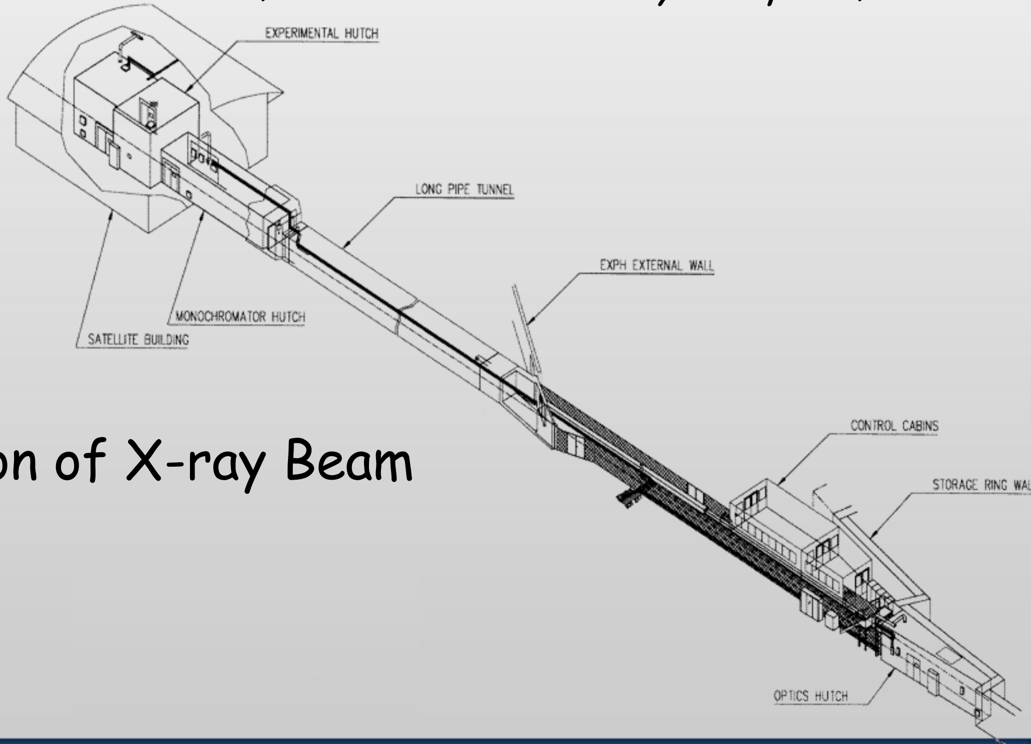


Contents

1. Introduction
2. Dosimetry and Characterisation of X-ray Beam
3. Patient Safety System
4. Planning

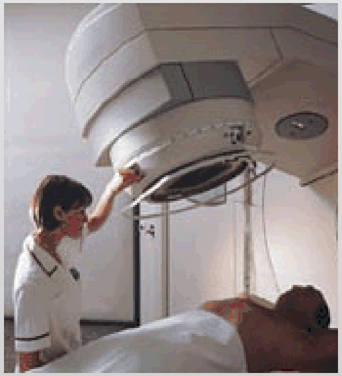
Brain Tumours

- Epidemiology :
  - 10 to 14 new cases/100.000/year
  - 65% are glioma

    High grade tumours – bad prognostic

    6 months life expectancy in 50 % of cases

- **9% of adults cancerous diseases**
- **But high social and economic impact**
- **Dramatic decrease of life quality**
- **Third cause of cancerous death in the range 15-35 years old**



Radiotherapy (MeV)
50 Gy at the tumour's location
25 fractions @ 5/week
Limited by tissue tolerance.

Stupp et al. NEJM 2005

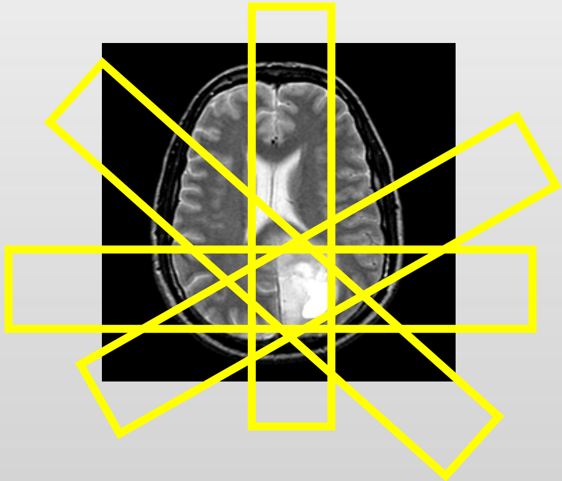
Is there another means for increasing the dose delivered to the tumour while sparing the surrounding tissue ?

CT-Therapy

- History:
  - 1980: Mello, Norman, Solberg, Iwamoto.

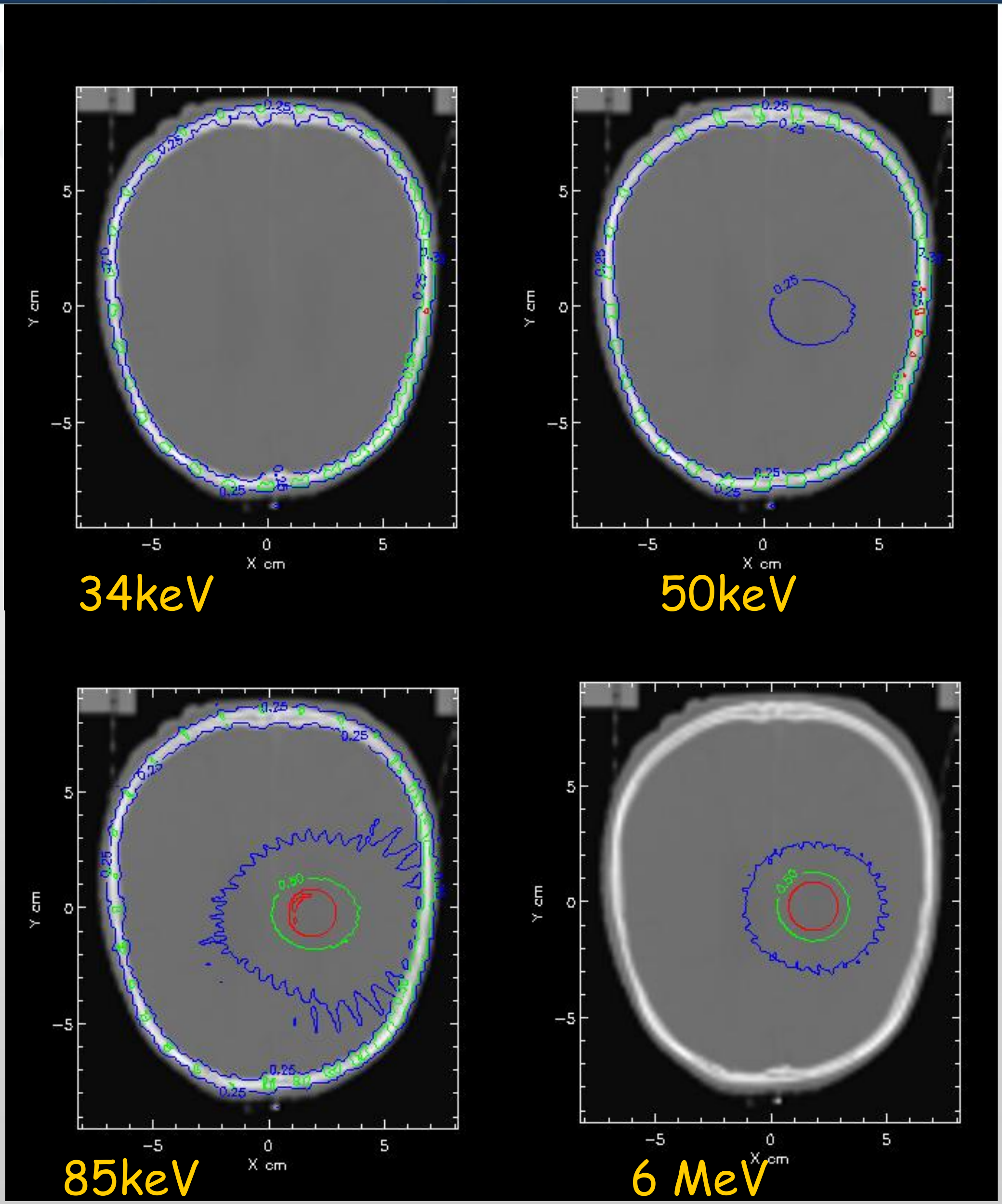
    '*Radiation dose enhancement with iodine*'.
  - 1999: First CT-Therapy with patients using a modified CT scanner.
- Principle:
  - Tumor loaded with a high Z element.

    (iodine, gadolinium, platinum, gold).
  - Beam size adjusted to the tumor dimensions.
  - Tumor positioned at the center of rotation.
  - Irradiation with kilo-Voltage X-ray beam.



without iodine

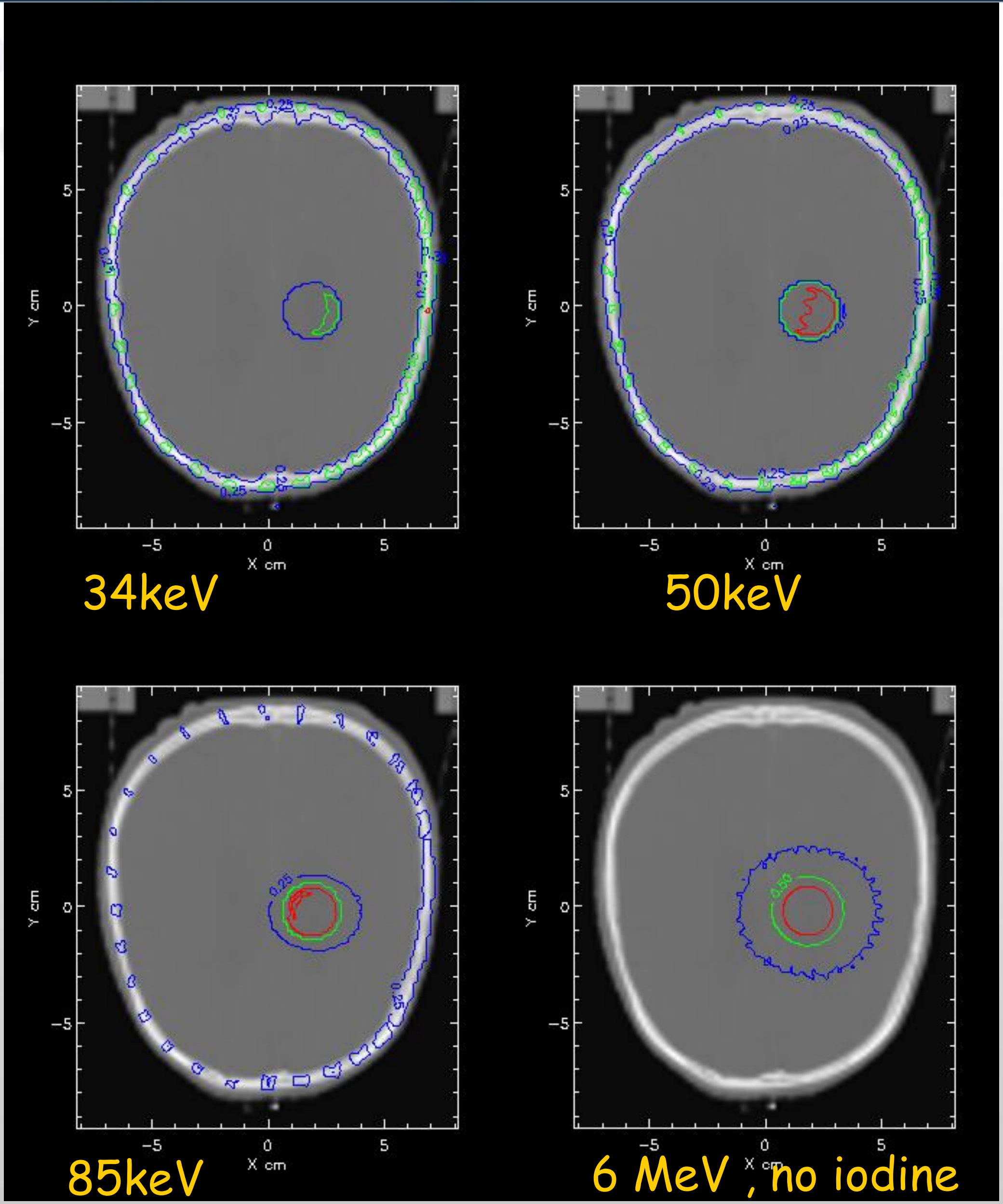
Tomo-irradiation
- beam height: 2 cm
- beam width: 2 cm



Isodose lines: red = 90%, green = 50%, blue=25%

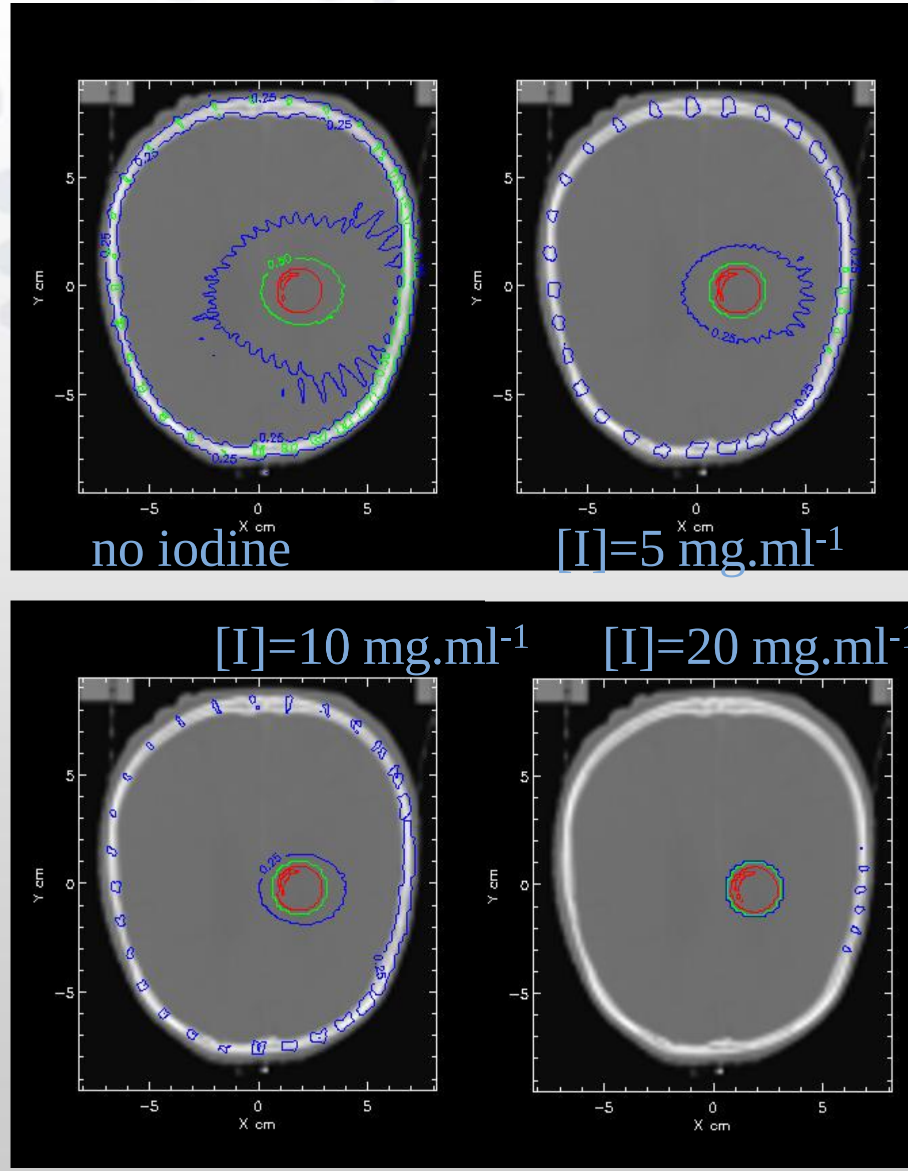
iodine 10mg/ml

Tomo-irradiation
- beam height: 2 cm
- beam width: 2 cm



Isodose lines: red = 90%, green = 50%, blue=25%

Dose distribution with increasing iodine concentration



Tomo-irradiation @ 85keV

- beam thickness: 2 cm
- beam width: 2 cm

Isodose lines: red = 90%, green = 50%, blue=25%

Boudou C, Balosso J, F. Estève, et al. Monte Carlo dosimetry for synchrotron stereotactic radiotherapy of brain tumours. *Phys Med Biol.* 2005 Oct 21;50(20):4841-51. Epub 2005 Oct 4.

SSRT clinical trials at the ESRF

Monochromatic beam

Stereotactic:

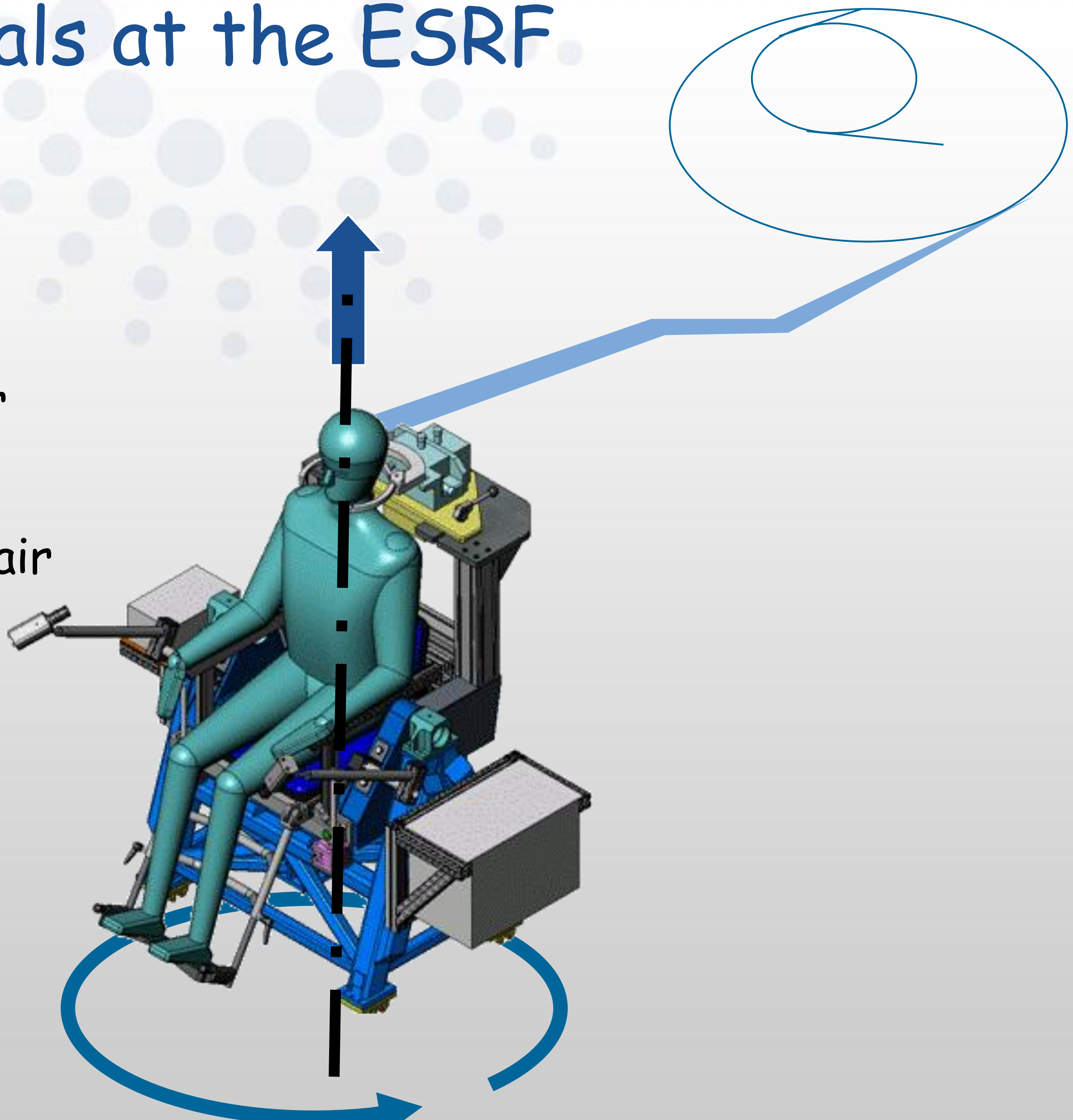
→ rotation of medical chair

Flat X-ray beam:

→ vertical movement of chair

→ Dosimetry

→ Patient safety system



SSRT clinical trials at the ESRF

Clear definition of the responsibilities of ESRF and of the hospital. ESRF is responsible for:

- the characterisation of the irradiation facility in terms of absorbed dose in water (dosimetry protocol, following international standards).
- reproducing the irradiation conditions defined by the treatment planning software.

Fundamental principle adopted by ESRF for radiation therapy projects:

Irradiation facility should be a **static** system, with no variable settings during irradiation.

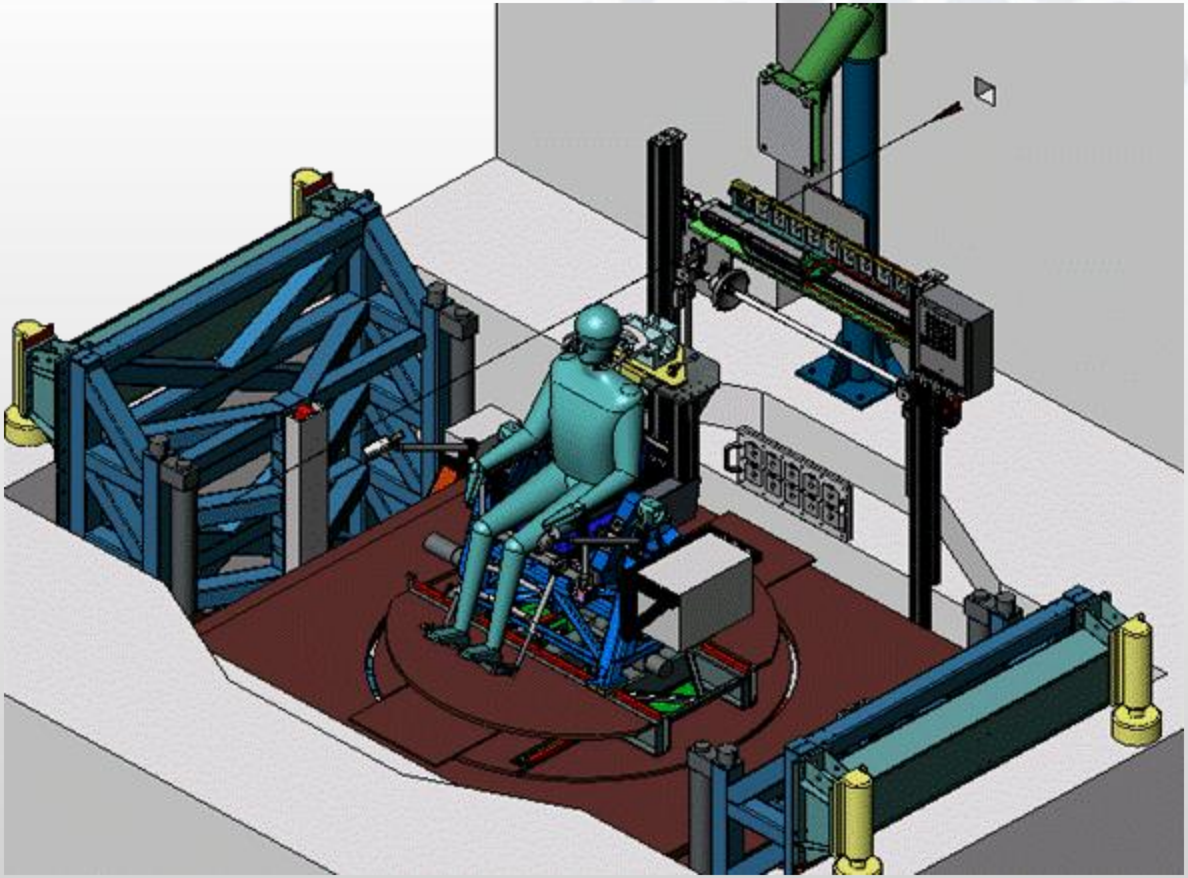
→ SSRT done for a limited number of orientations (maximum 10).

→ For each orientation, treatment planning defines the 2D beam collimation: → individual fixed collimators used for each orientation, rather than variable slit settings.

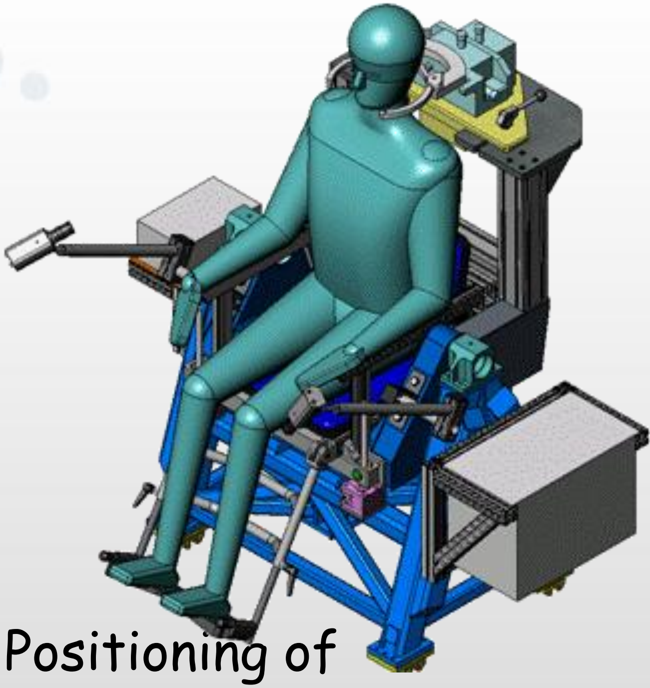
→ Coincidence" interlock on orientation angle and corresponding 2D collimator.

→ All motors inhibited (wiggler, slits, monochromators , …).

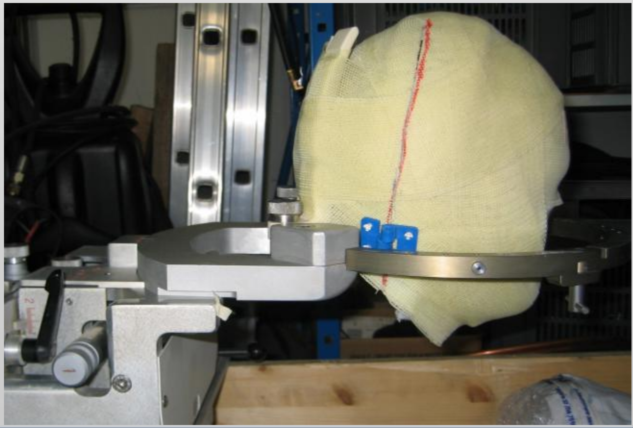
SSRT clinical trials at the ESRF



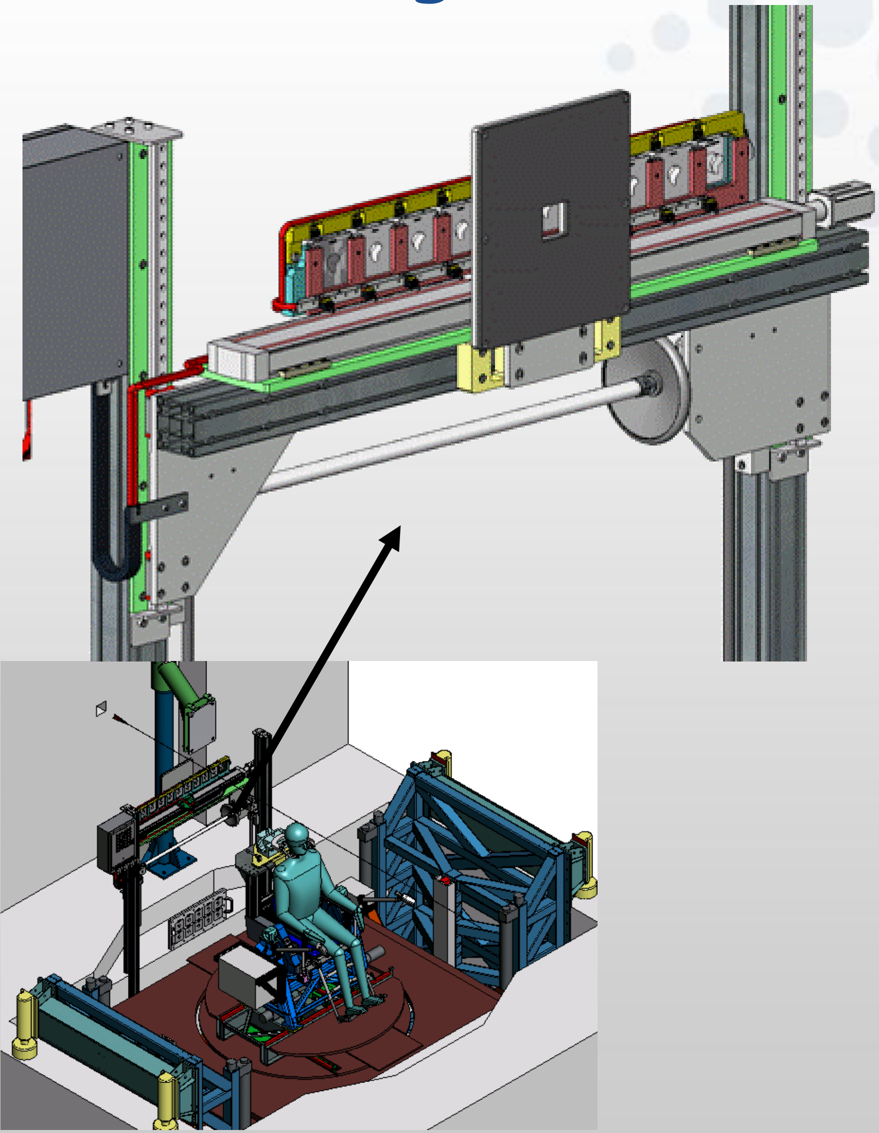
Final configuration

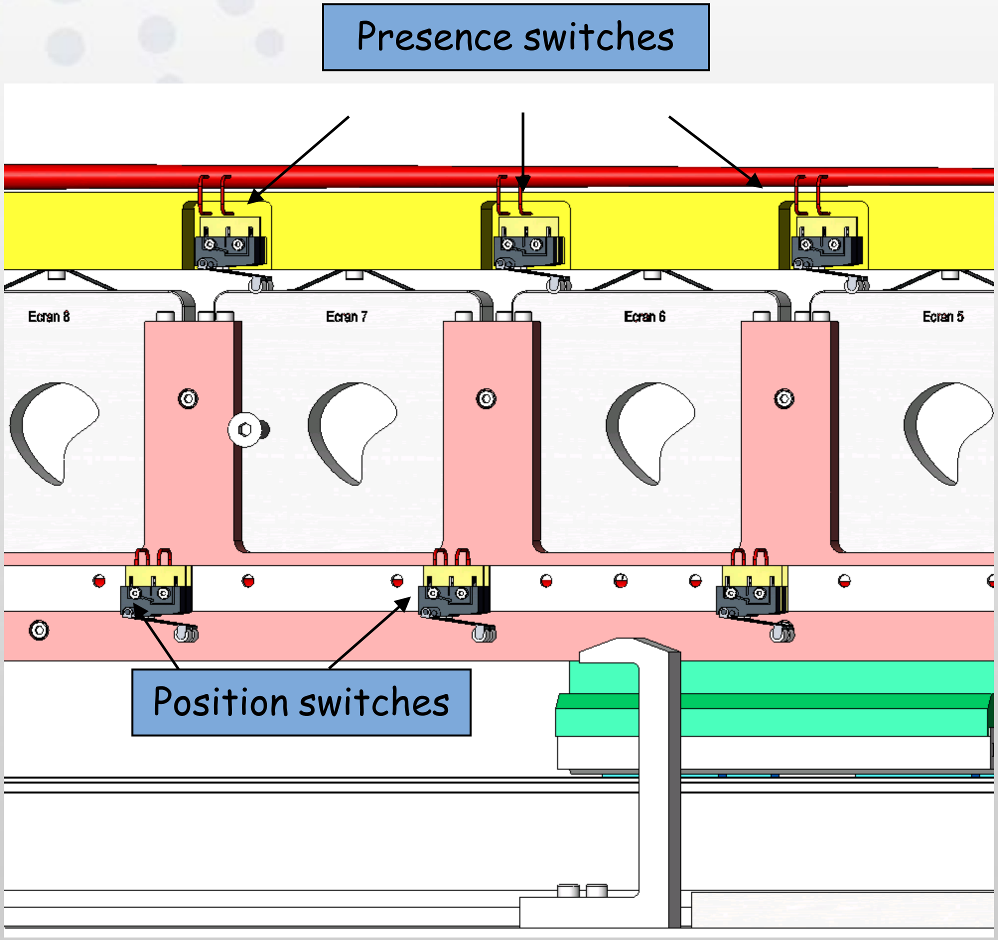


Positioning of patient's head



Positioning of 2D collimators





Fabrication of 2D collimators

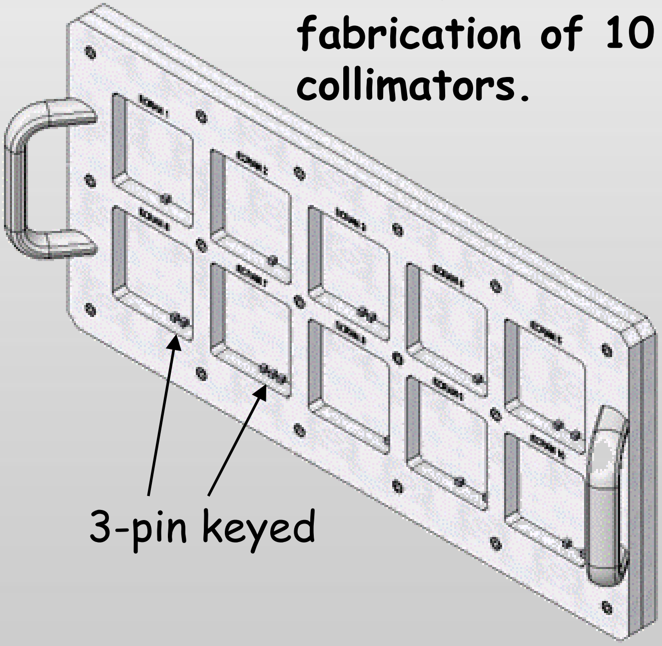
<u>CERROBEND or MCP 69</u>

Bi 49.4%; Pb 30.9%; Sn 12.1%; Cd 7.6%

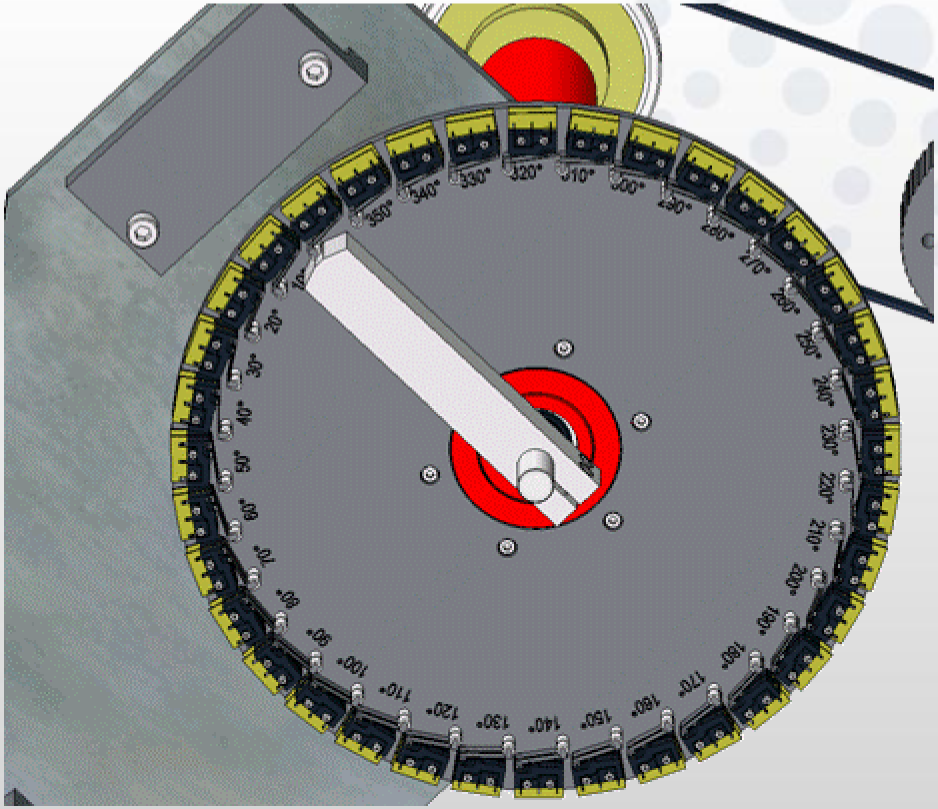
Melting point: 69°C

Density 9.7 g/cm^3

Mould for the fabrication of 10 collimators.

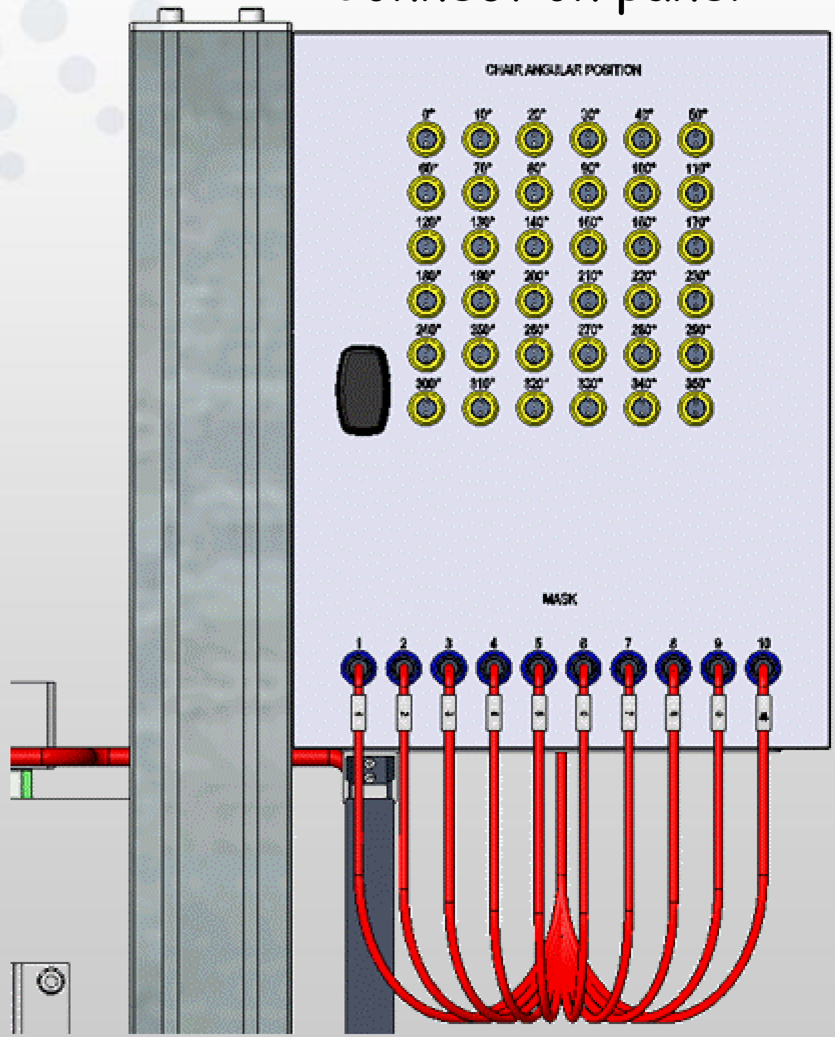


Angular positioning of medical chair



Rotation arm
(fixed to the rotation axis of the chair;
located below the chair)

Connection panel



Dosimetry and characterisation of the beam

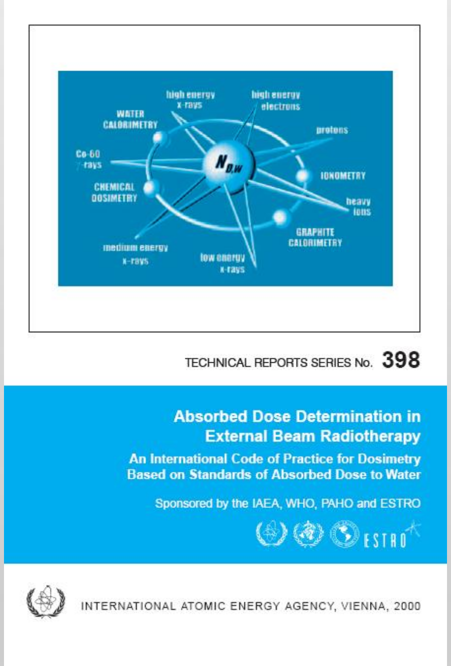
Dosimetry and characterisation of the X-ray beam and absorbed dose determination based on IAEA International Code of Practice no. 398 for dosimetry based on standards of absorbed dose to water:

1.3 Types of radiation and range of beam qualities

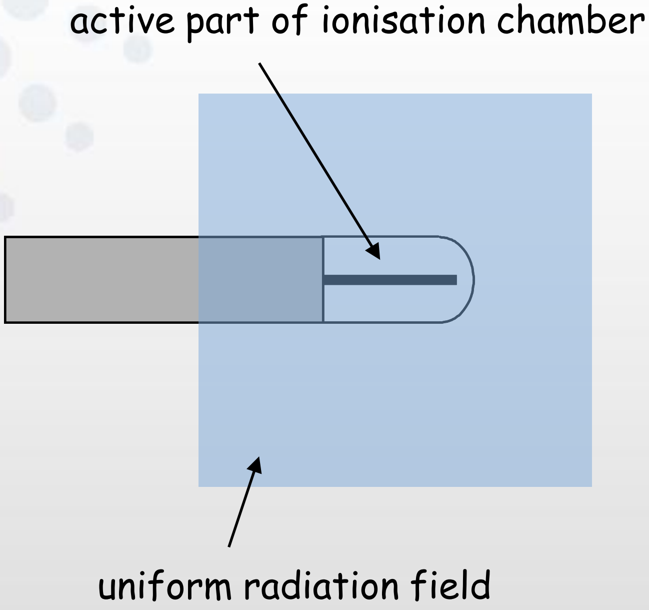
(b) Medium energy X rays with generating potentials above 80 kV and HVL of 2 mm Al.

80 keV X-rays:

$$\frac{\ln(2)}{\mu_{photo\ electric} + \mu_{compton}} = 1.4\ cm\ Al$$



Dosimetry and characterisation of the beam

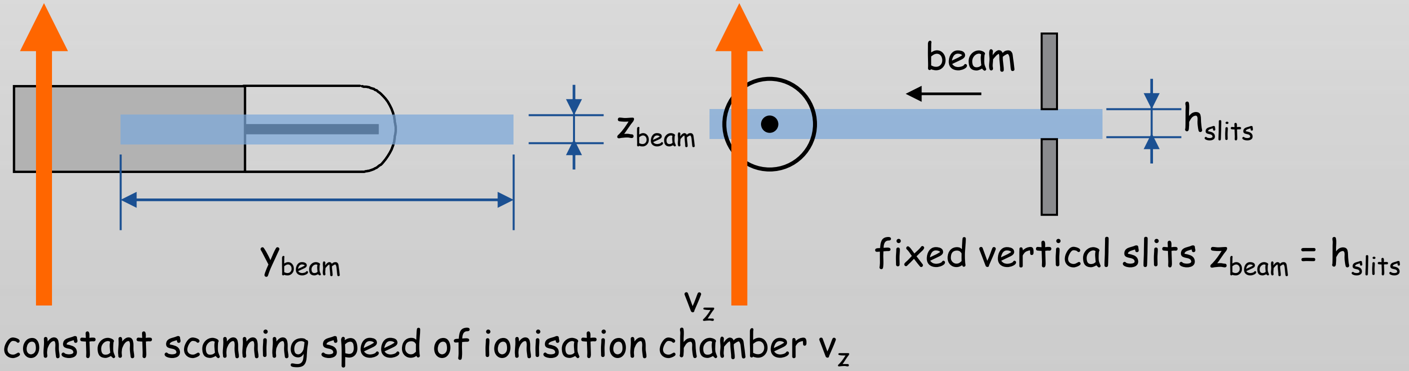


Calibration of ionisation chambers:

Uniform broad radiation fields, with transverse dimensions much larger than the corresponding dimensions of the ionization chamber.

Use of ionisation chamber in a flat beam:

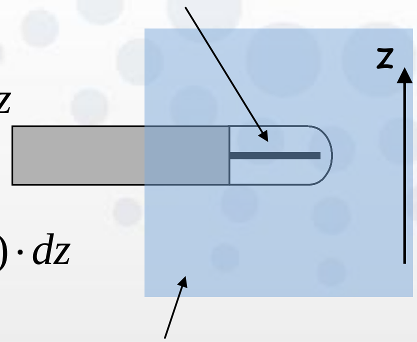
Can we still use the broad beam calibration factors of the ionisation chamber?

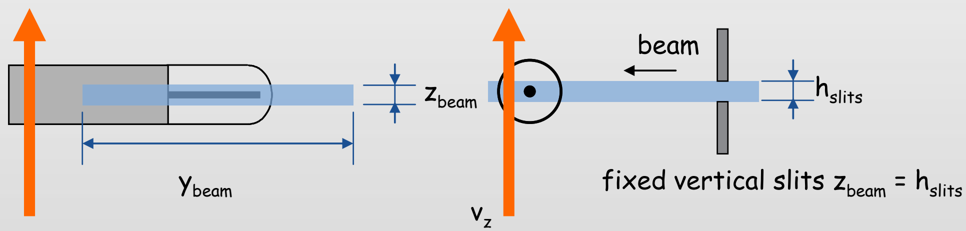


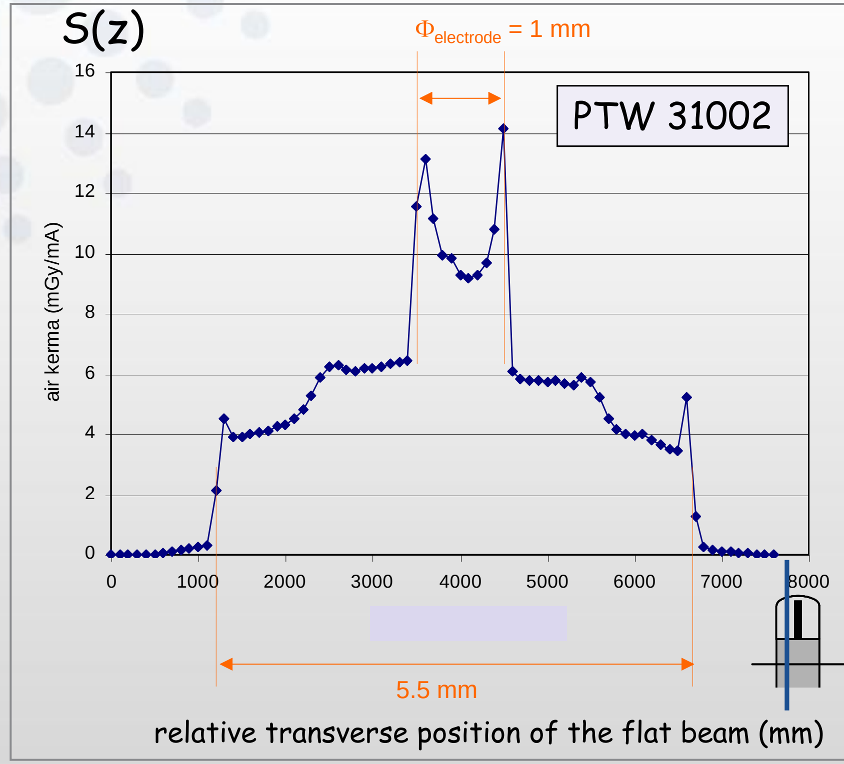
Dosimetry and characterisation of the beam

$$\dot{D}_{calibration} \propto \dot{D}_{beam} \times \int_{active\ volume} S(z)\cdot dz$$

$$\dot{D}_{calibration} = C \times \dot{D}_{beam} \times \int_{active\ volume} S(z)\cdot dz$$







$$D_{measured} = C \times \dot{D}_{beam} \times \int_{\Delta z = z_{beam}} S(z)\cdot dz$$

$$D_{measured} = C \times \int_{active\ volume} \left(S(z) \times \int_{\Delta t = z_{beam}/v_z} \dot{D}_{beam}\cdot dt \right) \cdot dz$$

$$D_{measured} = C \times \dot{D}_{beam} \times \frac{z_{beam}}{v_z} \times \int_{active\ volume} S(z)\cdot dz$$

$$\dot{D}_{calibration} = D_{measured} \times \frac{v_z}{z_{beam}}$$

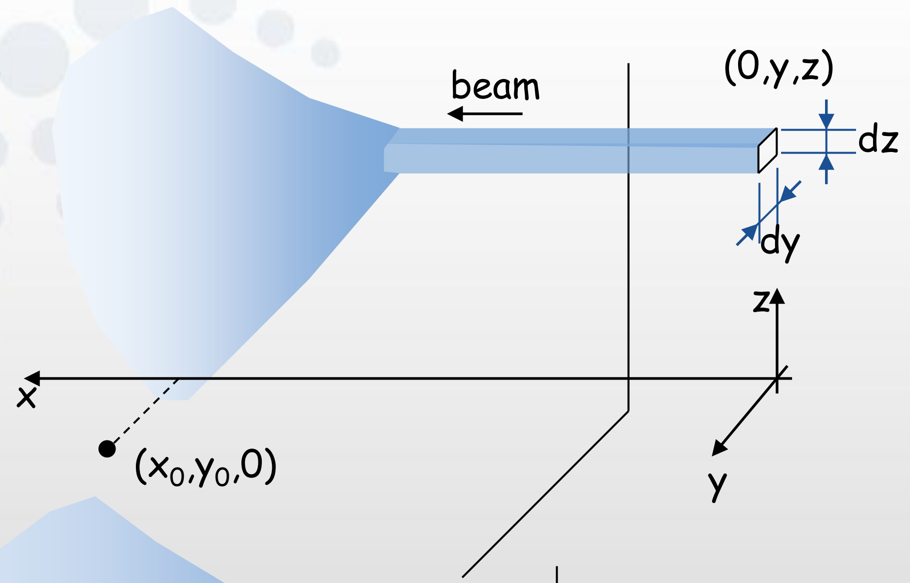
Dosimetry and characterisation of the beam

Pencil-type beam

F_0: uniform differential fluence at $x = 0$ (photons/cm^2/s)

T_{pencil}: appropriate conversion factor (Gy·cm^2)

$$\dot{D}(x_0, y_0, 0) = F_0 \times T_{pencil}(x_0, y_0; y, z) \cdot dy \cdot dz$$

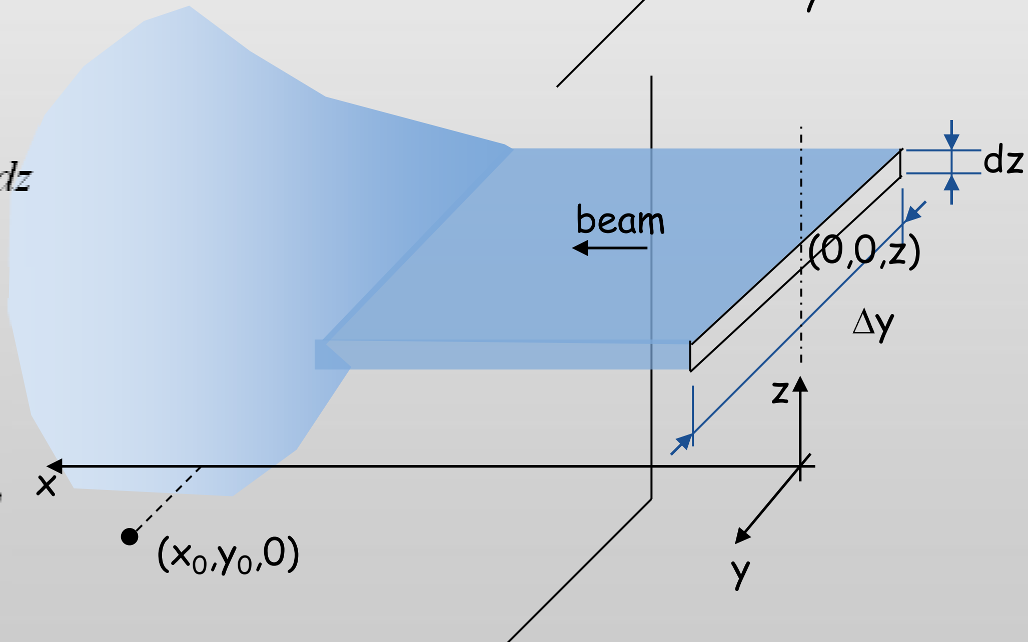


Uniform broad beam

$$\dot{D}_{broad}(x_0, y_0, 0) = F_0 \times \iint_{\Delta y, \Delta z} T_{pencil}(x_0, y_0; y, z) \cdot dy \cdot dz$$

$$\dot{D}_{broad}(x_0, y_0, 0) = F_0 \times \int_{\Delta z} T_{flat\ \Delta y}(x_0, y_0, z) \cdot dz$$

$$T_{flat\ \Delta y}(x_0, y_0, z) \cdot dz = dz \times \int_{\Delta y} T_{pencil}(x_0, y_0; y, z) \cdot dy$$



Dosimetry and characterisation of the beam

Scanning object + phantom through beam at constant speed v_z

$$\dot{D}(x_0, y_0, 0, t) = F_0 \times T_{flat\ \Delta y}(x_0, y_0, z(t)) \times z_{beam}.$$

$$D(x_0, y_0, 0) = \int_{\Delta t} \dot{D}(x_0, y_0, 0, t) \cdot dt,$$

$$z(t) = z_0 + v_z \cdot t$$

$$dz = v_z \cdot dt$$

$$D(x_0, y_0, 0) = \frac{z_{beam}}{v_z} \times F_0 \times \int_{\Delta z} T_{flat\ \Delta y}(x_0, y_0, z) \cdot dz$$

$$D(x_0, y_0, 0) = \frac{z_{beam}}{v_z} \times \dot{D}_{broad}(x_0, y_0, 0)$$

Duality between broad beam dose rate and integrated dose from vertical scan through flat beam.

Broad beam field size:

- Horizontal: slits → Δy
- Vertical: height of scan → Δz

Absorbed dose under reference conditions:

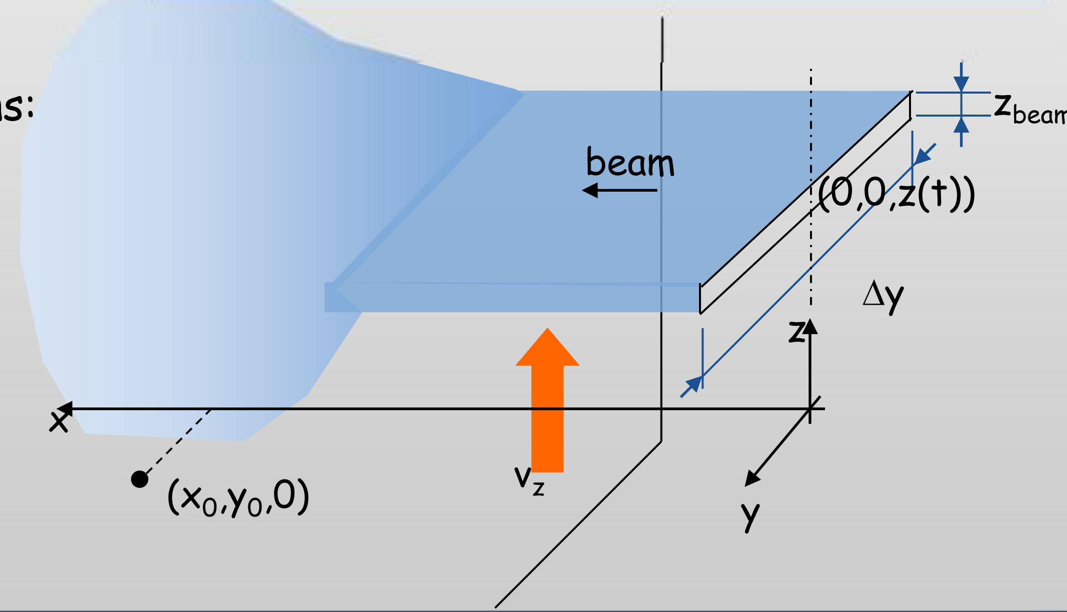
- x_0 → IAEA: $z_{ref} = 2\ g/cm^2$
- $y_0 = 0$

Central axis depth dose:

- Different values of x_0
- $y_0 = 0$

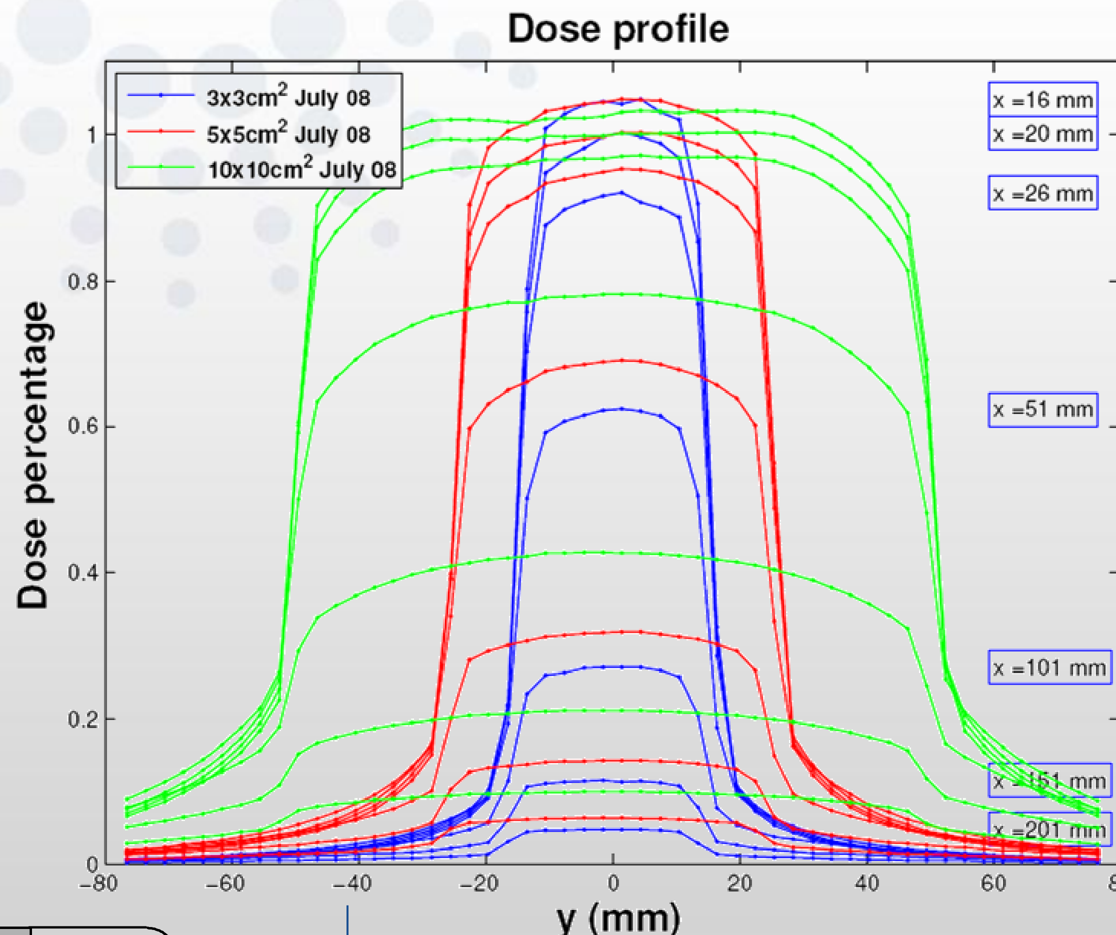
Horizontal dose profiles:

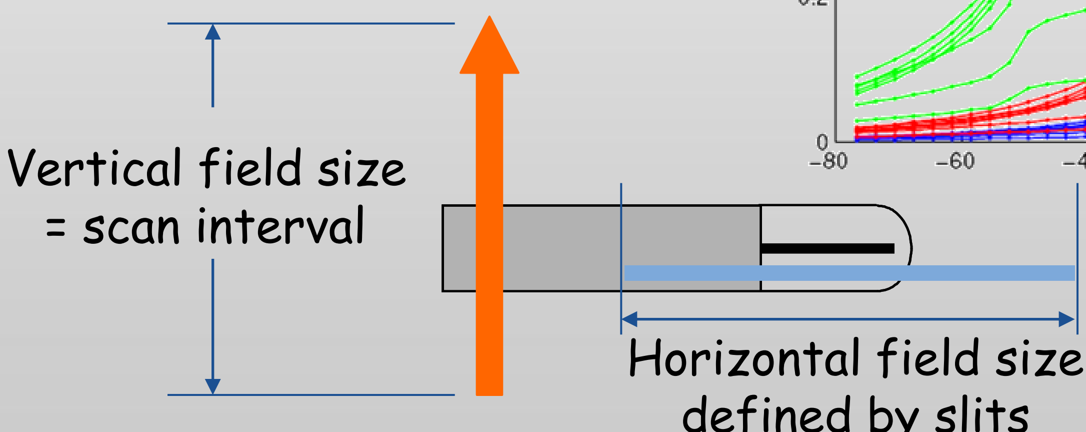
- $x_0 = 0$
- Different values of y_0



Dosimetry and characterisation of the beam

Example:
horizontal dose profiles, measured in water phantom, for different depths and for different field sizes.

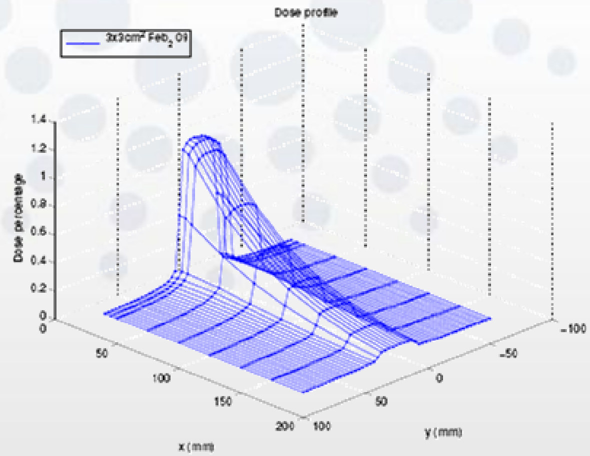


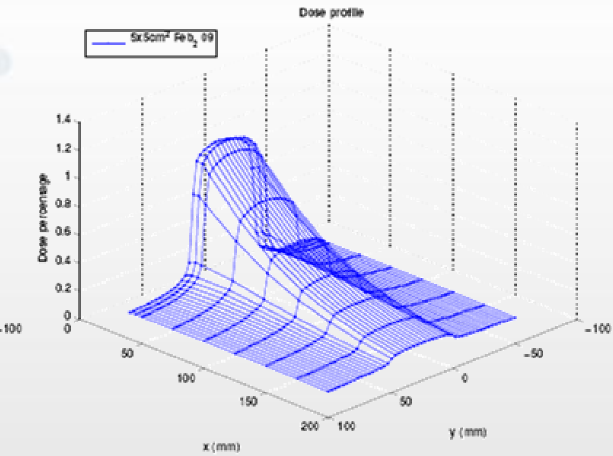


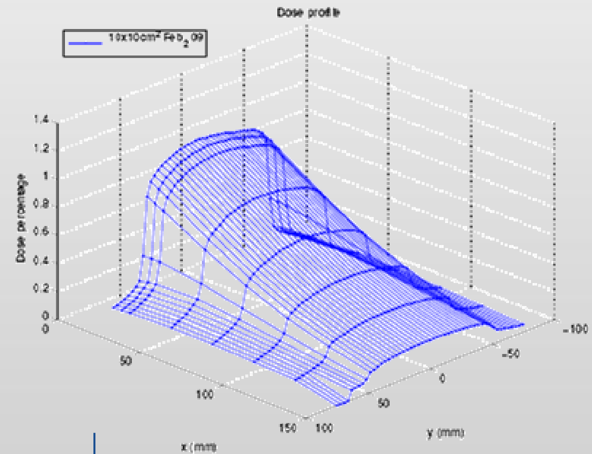
ionisation chamber:
PTW semiflex 31002

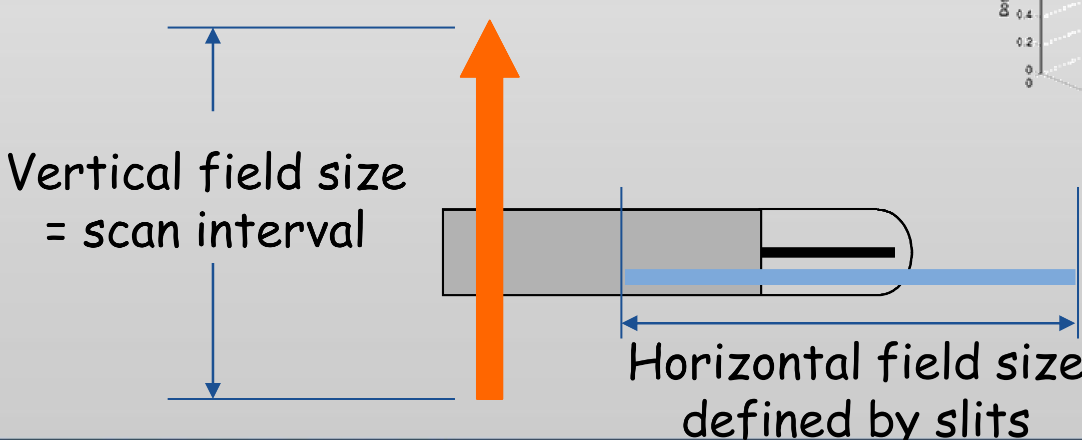
Dosimetry and characterisation of the beam

Example:
horizontal dose profiles, measured in water phantom, for different depths and for different field sizes.





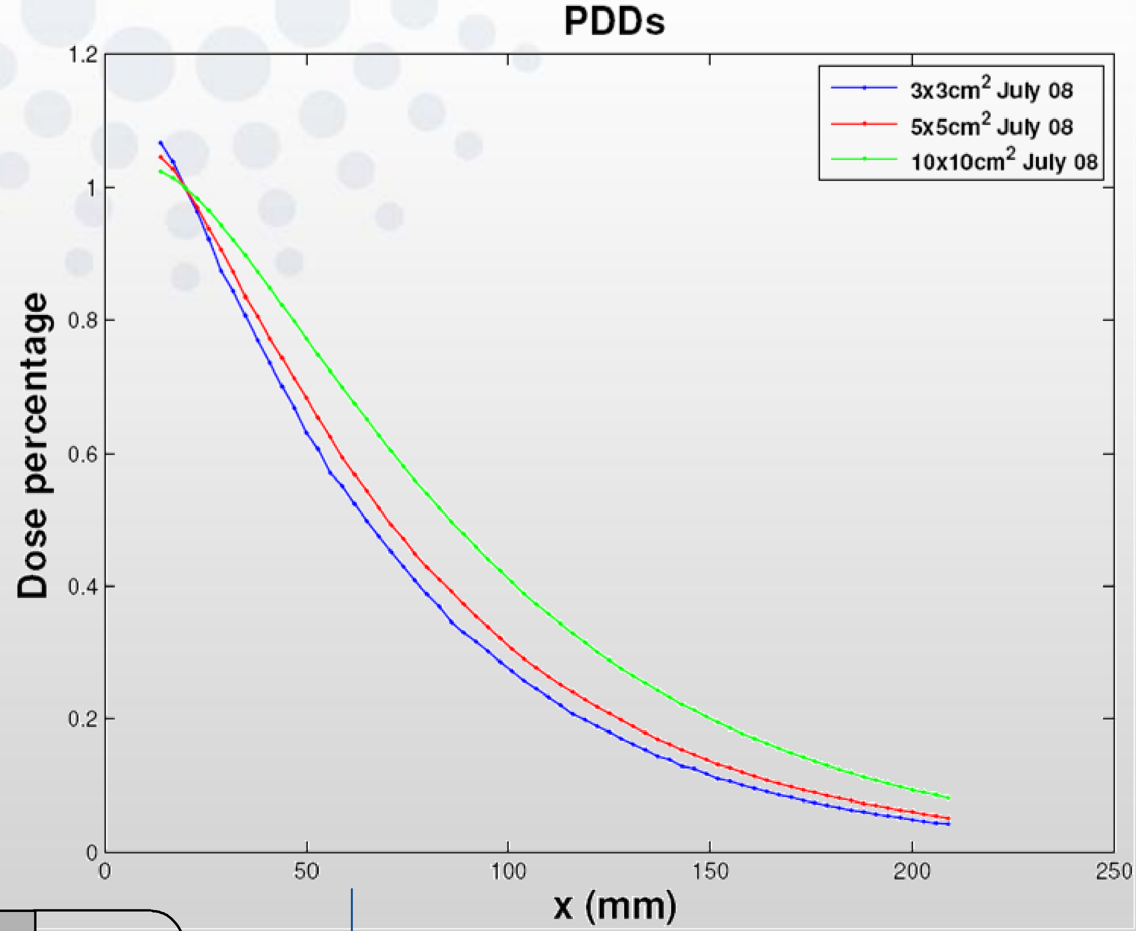


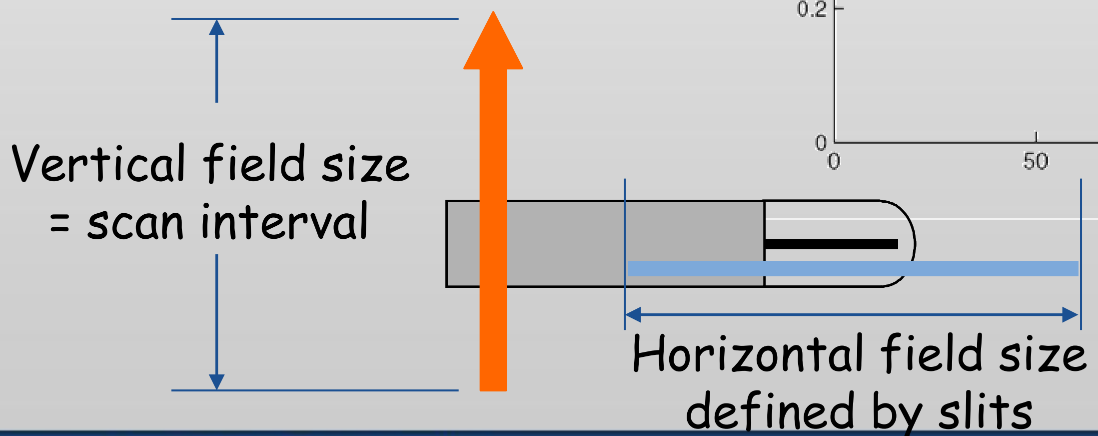


ionisation chamber:
PTW semiflex 31002

Dosimetry and characterisation of the beam

Example:
percentage depth profiles measured in water phantom.



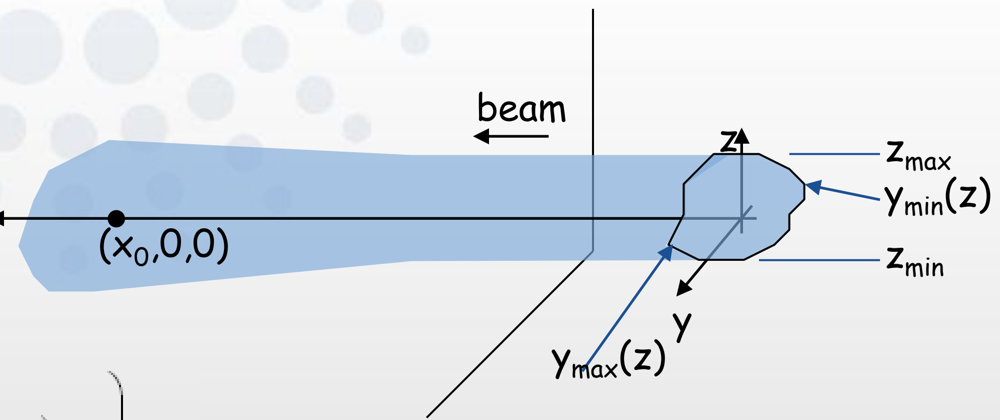


ionisation chamber:
PTW semiflex 31002

Dosimetry and characterisation of the beam

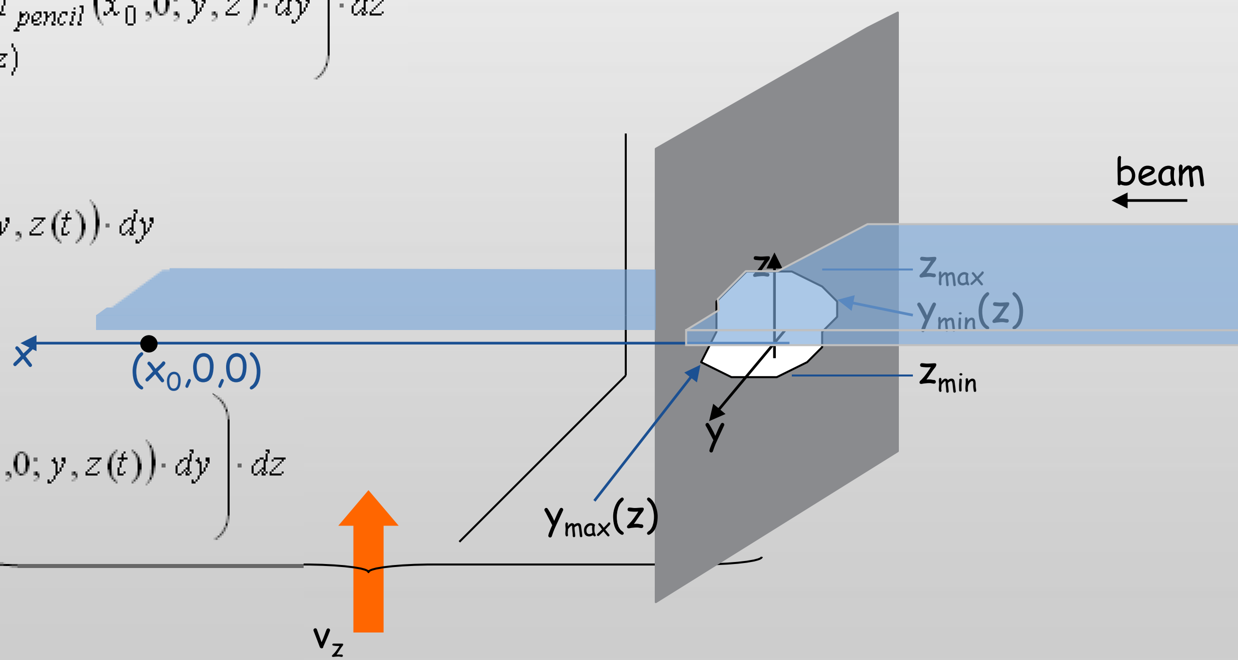
<u>Treatment planning software</u>

For each orientation:
- 2D beam profile
- Dose to tumour
  → Corresponding absorbed dose in water at reference depth



$$\dot{D}_{2D\,beam}(x_0,0,0) = F_0 \times \int_{z_{min}}^{z_{max}} \left(\int_{y_{min}(z)}^{y_{max}(z)} T_{pencil}(x_0,0;y,z)\cdot dy \right)\cdot dz$$

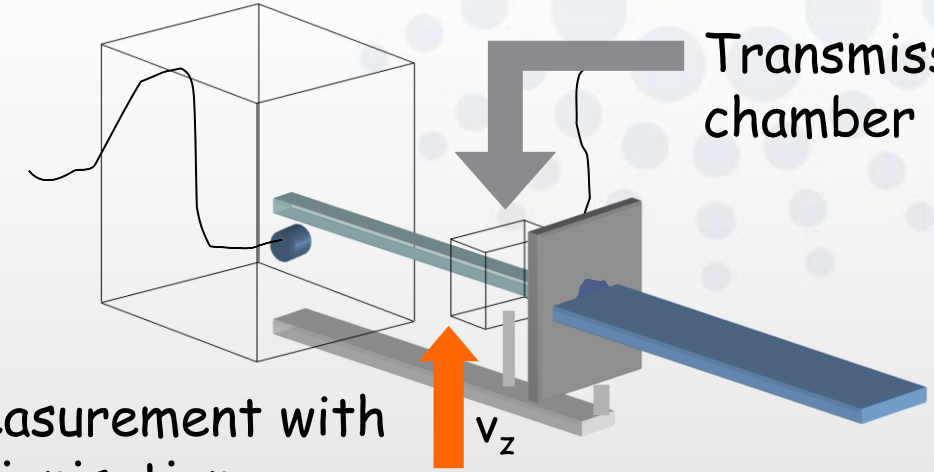
$$\dot{D}(x_0,0,0,t) = F_0 \times z_{beam} \times \int_{y_{max}(z)}^{y_{max}(z)} T_{pencil}(x_0,0;y,z(t))\cdot dy$$



$$D(x_0,0,0) = F_0 \times \frac{z_{beam}}{v_z} \times \int_{z_{min}}^{z_{max}} \left(\int_{y_{max}(z)}^{y_{max}(z)} T_{pencil}(x_0,0;y,z(t))\cdot dy \right)\cdot dz$$

$$D(x_0,0,0) = \frac{z_{beam}}{v_z} \times \dot{D}_{2D\,beam}(x_0,0,0)$$

Dosimetry and characterisation of the beam

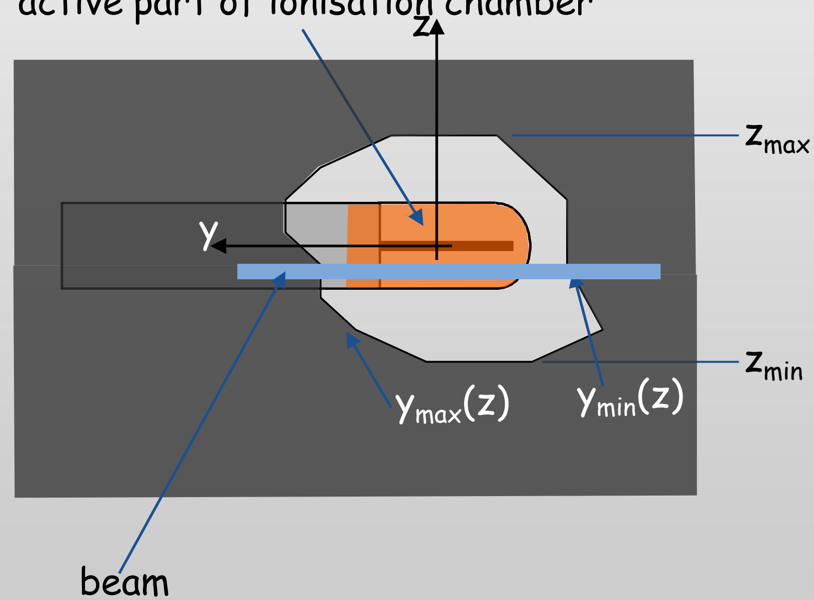


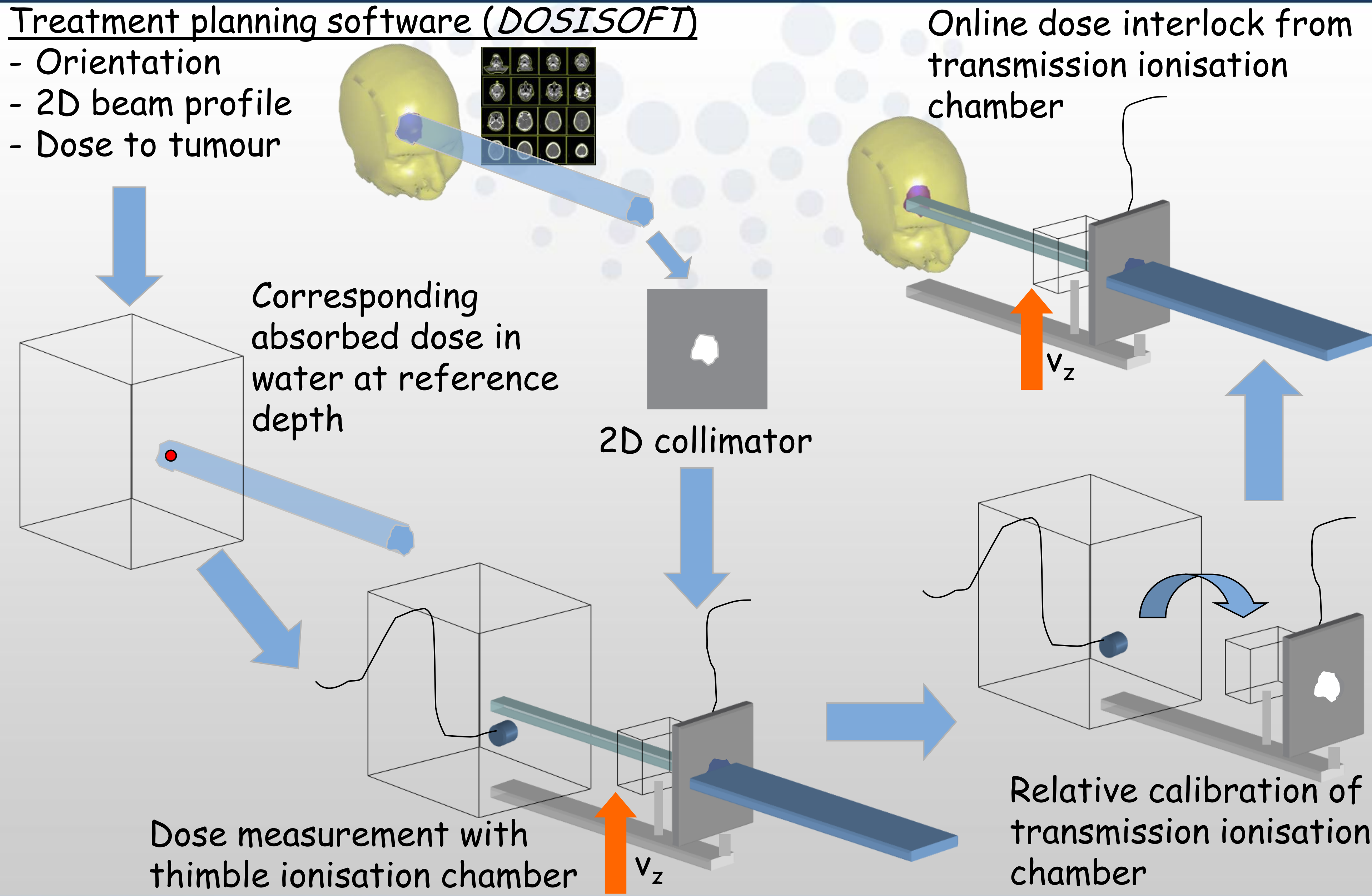
Transmission ionisation chamber

Dose measurement with thimble ionisation chamber

$$D(x_0,0,0)=\frac{z_{beam}}{v_z}\times \dot{D}_{2D\,beam}(x_0,0,0)$$

Interlock on integrated dose
→independent on z_{beam} and v_z.




Treatment planning software (*DOSISOFT*)
- Orientation
- 2D beam profile
- Dose to tumour
Online dose interlock from transmission ionisation chamber
Corresponding absorbed dose in water at reference depth
2D collimator
v_z
Dose measurement with thimble ionisation chamber
v_z
Relative calibration of transmission ionisation chamber

Patient Safety System

The patient safety system is based on the patient safety system that was developed for the angiography clinical trials, which was approved by the French authorities:

- Redundant, relay based system, based on standard ESRF personnel safety systems;
- Use of fast relays for critical interlocks;
- Direct interlock to storage ring RF transmitters.

The existing system has been modified to take into account:

- The different irradiation orientations;
- The individual 2D collimator for each orientation;
- More precise integrated dose interlock:
  - Precision measurement of the vertical chair position;
  - Precision measurement of the vertical chair speed.

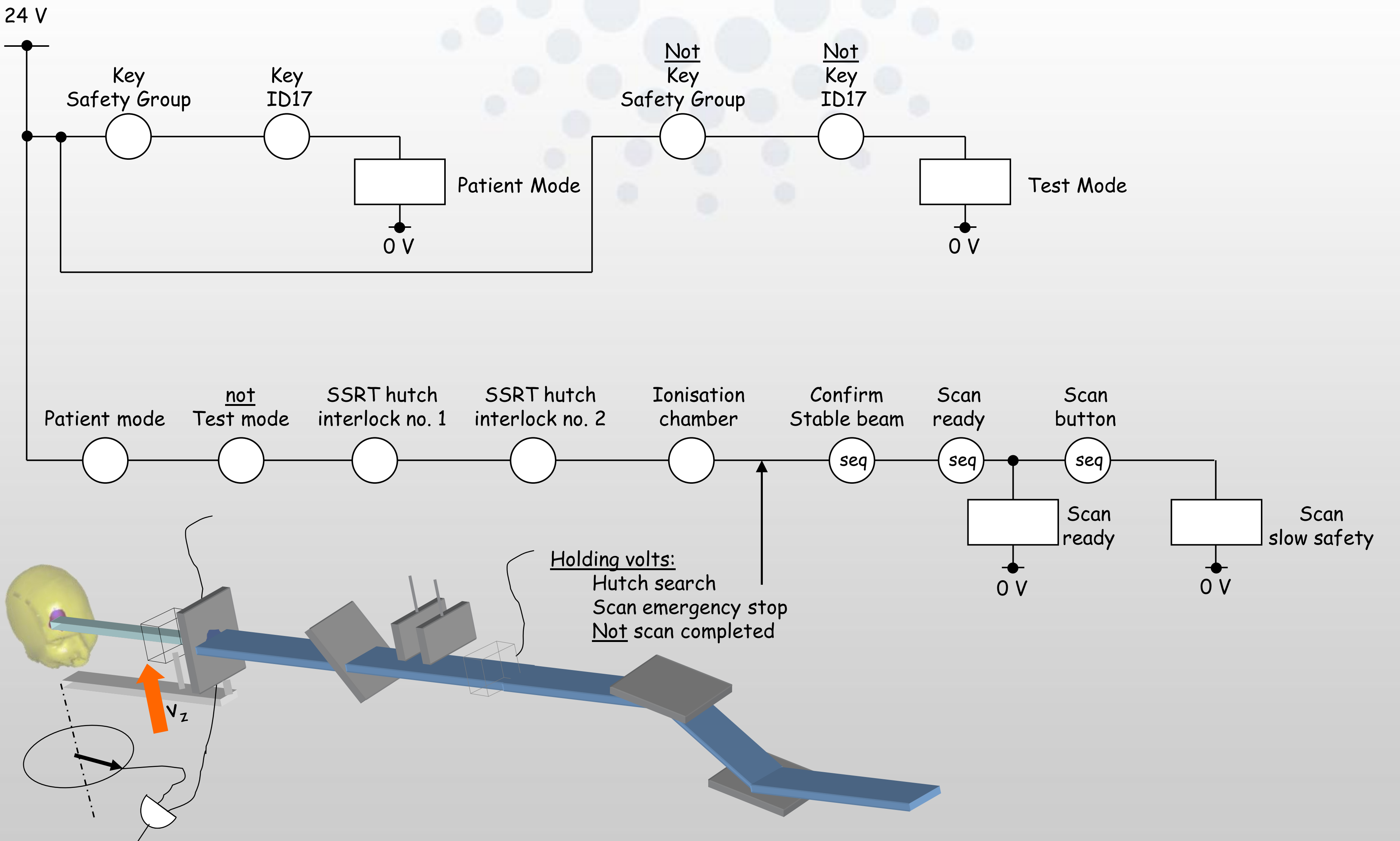
Patient Safety System

The only part of the patient safety system managed by software:

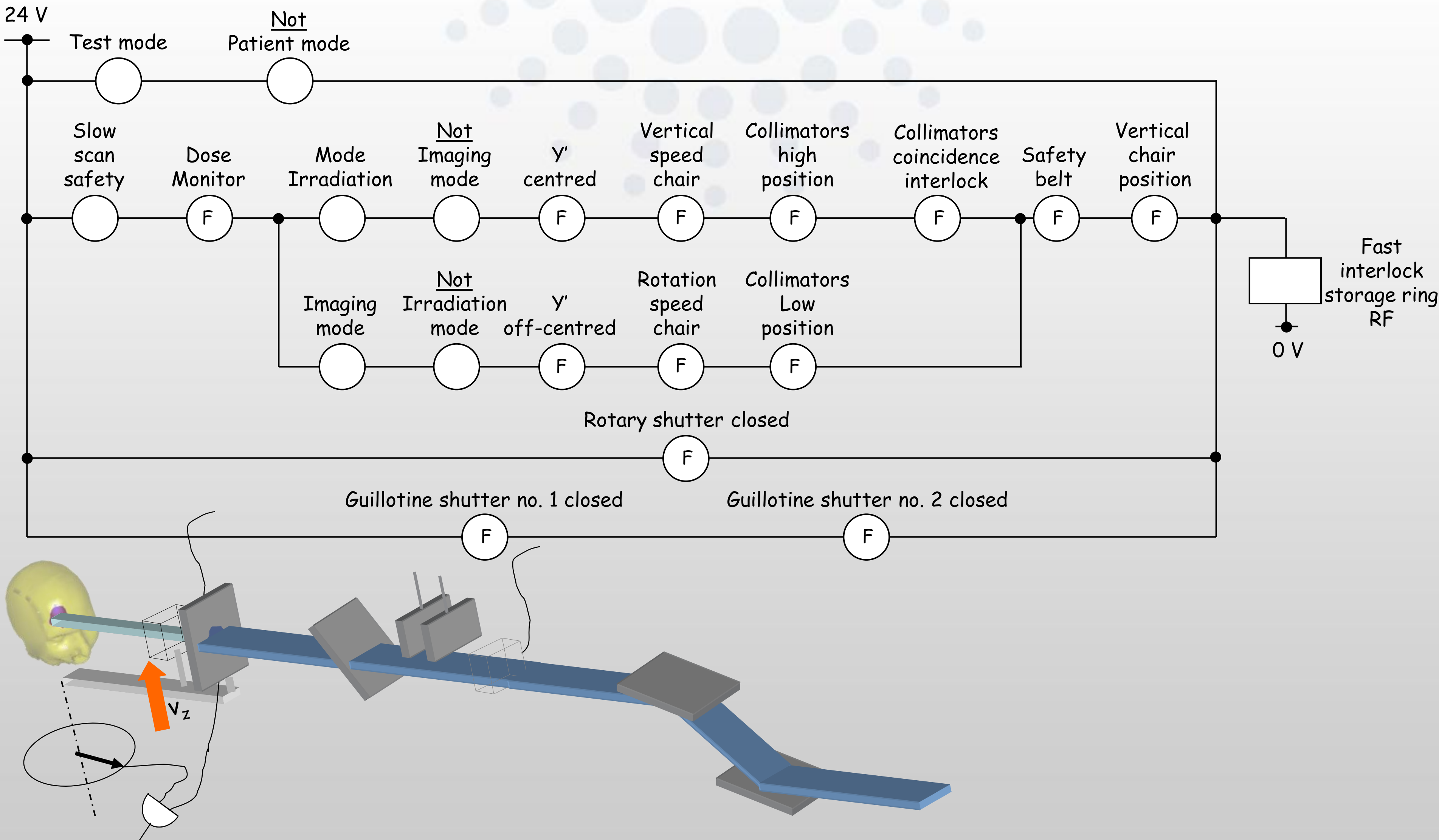
The integrated dose, predefined for each orientation, is obtained by adjusting the vertical speed of the chair, as a function of the exact intensity of the stored electron beam.

- Beam intensity read prior to start of irradiation:
  - → Vertical speed of chair calculated and limits set;
  - → Limits set for transmission ionisation chambers.
- "Confirm stable beam" in the patient safety system freezes these limits.
- If irradiation not started within 1 minute, irradiation is aborted.

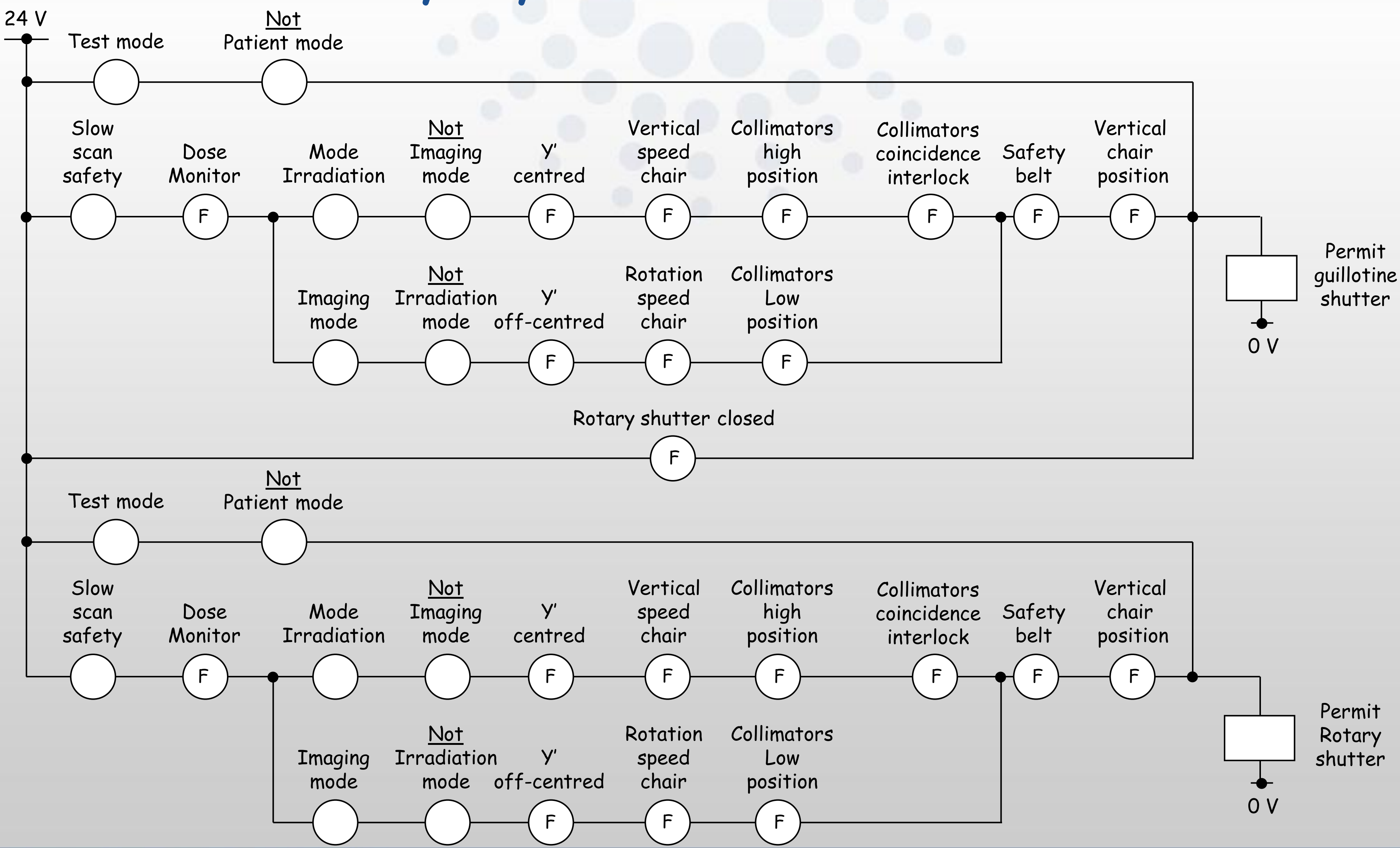
Patient Safety System



Patient Safety System

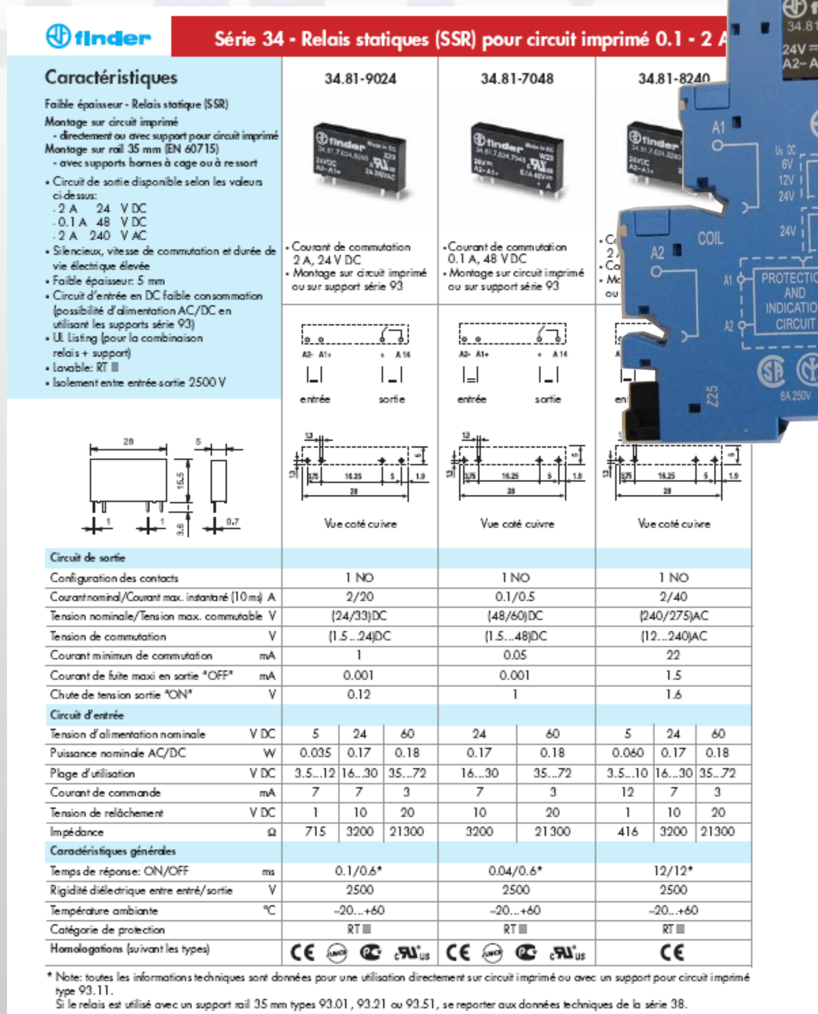


Patient Safety System



Patient Safety system

Central cubicle of SSRT patient safety system during initial testing



finder

Série 34 - Relais statiques (SSR) pour circuit imprimé 0.1 - 2 A

Caractéristiques

Faible épaisseur - Relais statique (SSR)
Montage sur circuit imprimé
- directement ou avec support pour circuit imprimé
Montage sur rail 35 mm (EN 60715)
- avec supports bornes à cage ou à ressort

- Circuit de sortie disponible selon les valeurs ci-dessus:
  - 2 A 24 V DC
  - 0.1 A 48 V DC
  - 2 A 240 V AC
- Silencieux, vitesse de commutation et durée de vie électrique élevée
- Faible épaisseur: 5 mm
- Circuit d'entrée en DC faible consommation (possibilité d'alimentation AC/DC en utilisant les supports série 93)
- UL Listing (pour la combinaison relais + support)
- Lavable: RT III
- Isolement entre entrée-sortie 2500 V

34.81-9024
- Courant de commutation 2 A, 24 V DC
- Montage sur circuit imprimé ou sur support série 93

34.81-7048
- Courant de commutation 0.1 A, 48 V DC
- Montage sur circuit imprimé ou sur support série 93

34.81-8240
- C[illegible] 2 [illegible]
- Co[illegible]
- Mo[illegible] ou [illegible]

entrée — sortie

Vue coté cuivre

	34.81-9024			34.81-7048		34.81-8240		
Circuit de sortie								
Configuration des contacts	1 NO			1 NO		1 NO		
Courant nominal/Courant max. instantané (10 ms) A	2/20			0.1/0.5		2/40		
Tension nominale/Tension max. commutable V	(24/33)DC			(48/60)DC		(240/275)AC		
Tension de commutation V	(1.5...24)DC			(1.5...48)DC		(12...240)AC		
Courant minimun de commutation mA	1			0.05		22		
Courant de fuite maxi en sortie "OFF" mA	0.001			0.001		1.5		
Chute de tension sortie "ON" V	0.12			1		1.6		
Circuit d'entrée								
Tension d'alimentation nominale V DC	5	24	60	24	60	5	24	60
Puissance nominale AC/DC W	0.035	0.17	0.18	0.17	0.18	0.060	0.17	0.18
Plage d'utilisation V DC	3.5...12	16...30	35...72	16...30	35...72	3.5...10	16...30	35...72
Courant de commande mA	7	7	3	7	3	12	7	3
Tension de relâchement V DC	1	10	20	10	20	1	10	20
Impédance Ω	715	3200	21300	3200	21300	416	3200	21300
Caractéristiques générales								
Temps de réponse: ON/OFF ms	0.1/0.6*			0.04/0.6*		12/12*		
Rigidité diélectrique entre entré/sortie V	2500			2500		2500		
Température ambiante °C	-20...+60			-20...+60		-20...+60		
Catégorie de protection	RT III			RT III		RT III		
Homologations (suivant les types)	CE			CE		CE		

* Note: toutes les informations techniques sont données pour une utilisation directement sur circuit imprimé ou avec un support pour circuit imprimé type 93.11.
Si le relais est utilisé avec un support rail 35 mm types 93.01, 93.21 ou 93.51, se reporter aux données techniques de la série 38.

Fast relays

Evaluation of the radiological risk

Energy of X-rays : around 80 keV, quasi-monochromatic spectrum.

Measured dose rate: **2.6 mGy/s/mA**.

→ Dose rate at 200 mA : **520 mGy/s**.
→ Dose rate at 300 mA : **780 mGy/s**.

Reaction time in case of problem (e.g. sudden stop of chair): **5 ms**.

- 5 ms : already achieved during angiography clinical trials;
- Development on safety systems foreseen to reduce this reaction time down to 2 ms.

5 ms:
520 mGy/s → **2.6 mGy** over-dose on max. surface of 30 x 1 mm^2.
780 mGy/s → **3.9 mGy** over-dose on max. surface of 30 x 1 mm^2.

Annual limit for equivalent dose to skin for the public : 50 mSv
→ 5 ms delay : accidental dose <1/10 annual limit.

For comparison:
Dose rate during angiography clinical trials : 12.5 Gy/s (at 200 mA).

Planning

Approval of medical protocol by ethical committee

- Submission June 2009
- Approval expected before summer 2009

Approval from French Nuclear Authorities

- Simultaneous submission to
  - ASN (*Autorité de Sûreté Nucléaire*)
  - AFSSAPS (*Agence Française de Sécurité Sanitaire des Produits de Santé*)
- First contacts in 2008 (ASN) and 2009 (AFSSAPS)
- Submission August 2009
- Approval expected end 2009

Treatment planning software

- Commissioning from July 2009 onwards

Patient Safety System

- Installation August 2009

People involved

Medical Investigators

- Pr Jacques BALOSSO, *oncology radiotherapy*
- Pr Jean François LE BAS, *radiology*
- Pr François ESTEVE, *biophysics*
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Technical and Scientific support staff

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