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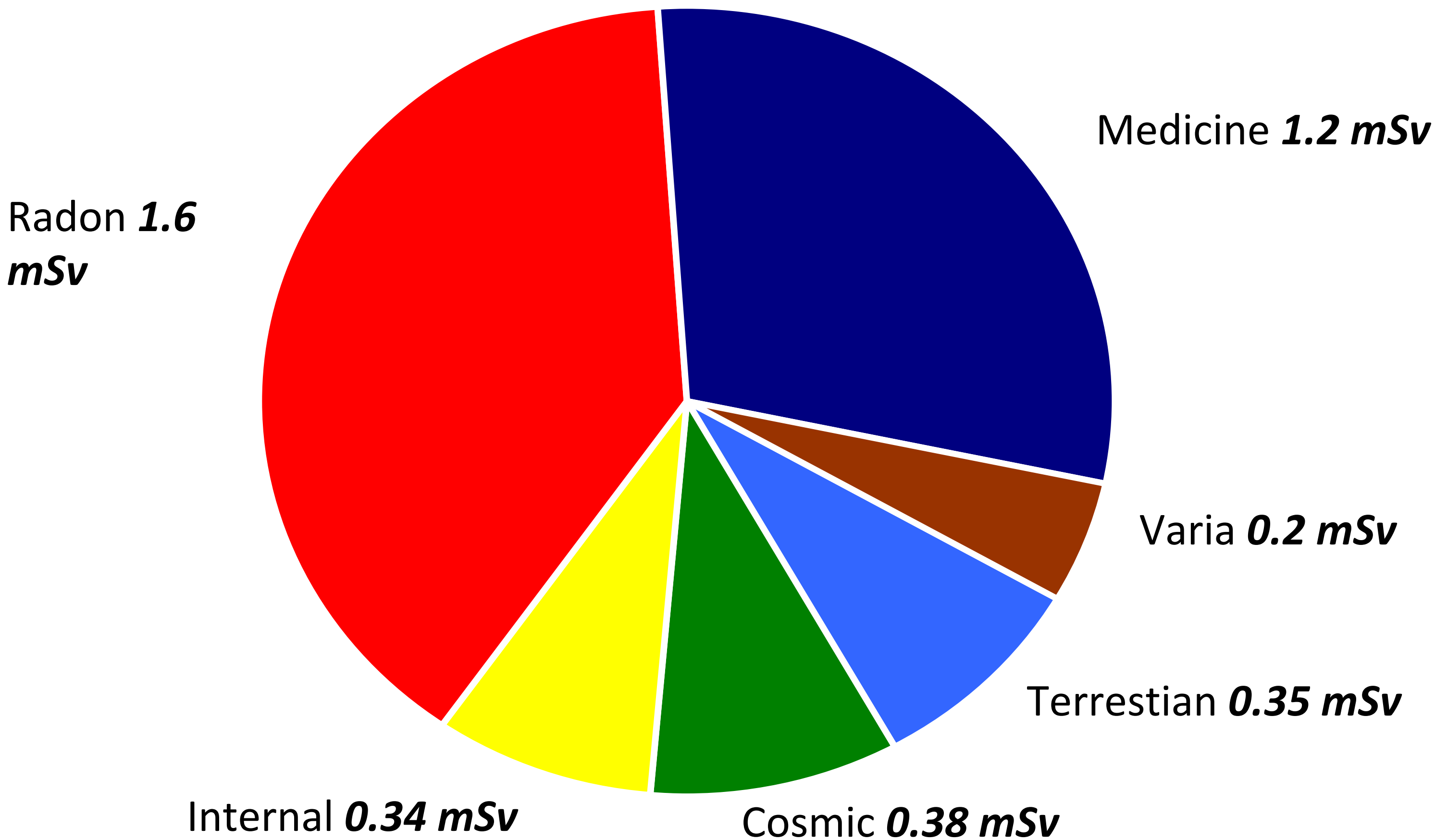
Physics of Radiation Therapy (1)

Outline

- Present epidemiological data about cancer
- Describe the general workflow of radiotherapy treatments
- Describe beam production and beam characterization

Annual dose in Switzerland

Total : ~ 4 mSv / year

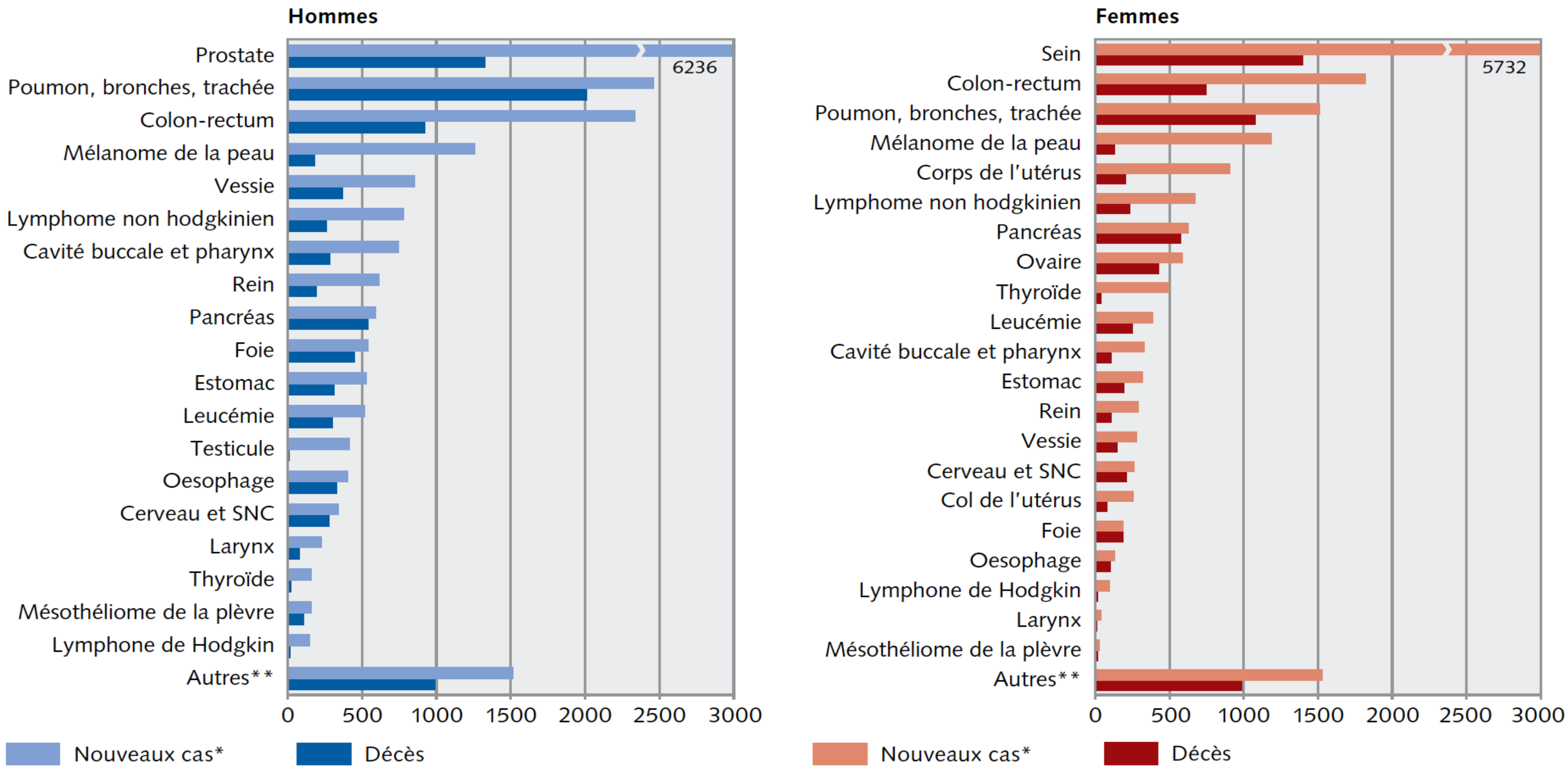


Switzerland

- 1 person on 3 to 4 will suffer from cancer
- 50 – 60 % of cancer patients will have radiation therapy
- 1 person on 6 will have radiation therapy in his/her life
- ~ 50 % will be cured with radiation therapy
- 2015 (estimate)
  - ~ 41’000 new cancers
- 35 radiation therapy centers (5 Uni)
- 71 linear acelerators or 1 / 116’000 hab.

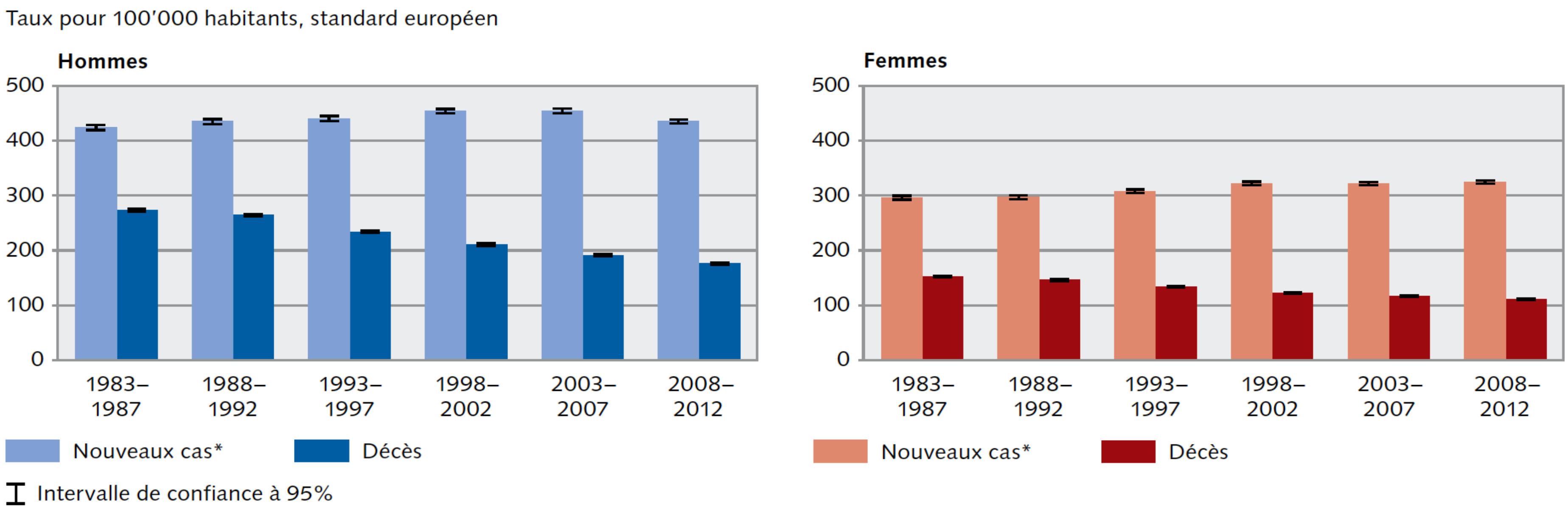
New cases

Nombre moyen par an



Le cancer en Suisse, rapport 2015, OFS

Evolution



Le cancer en Suisse, rapport 2015, OFS

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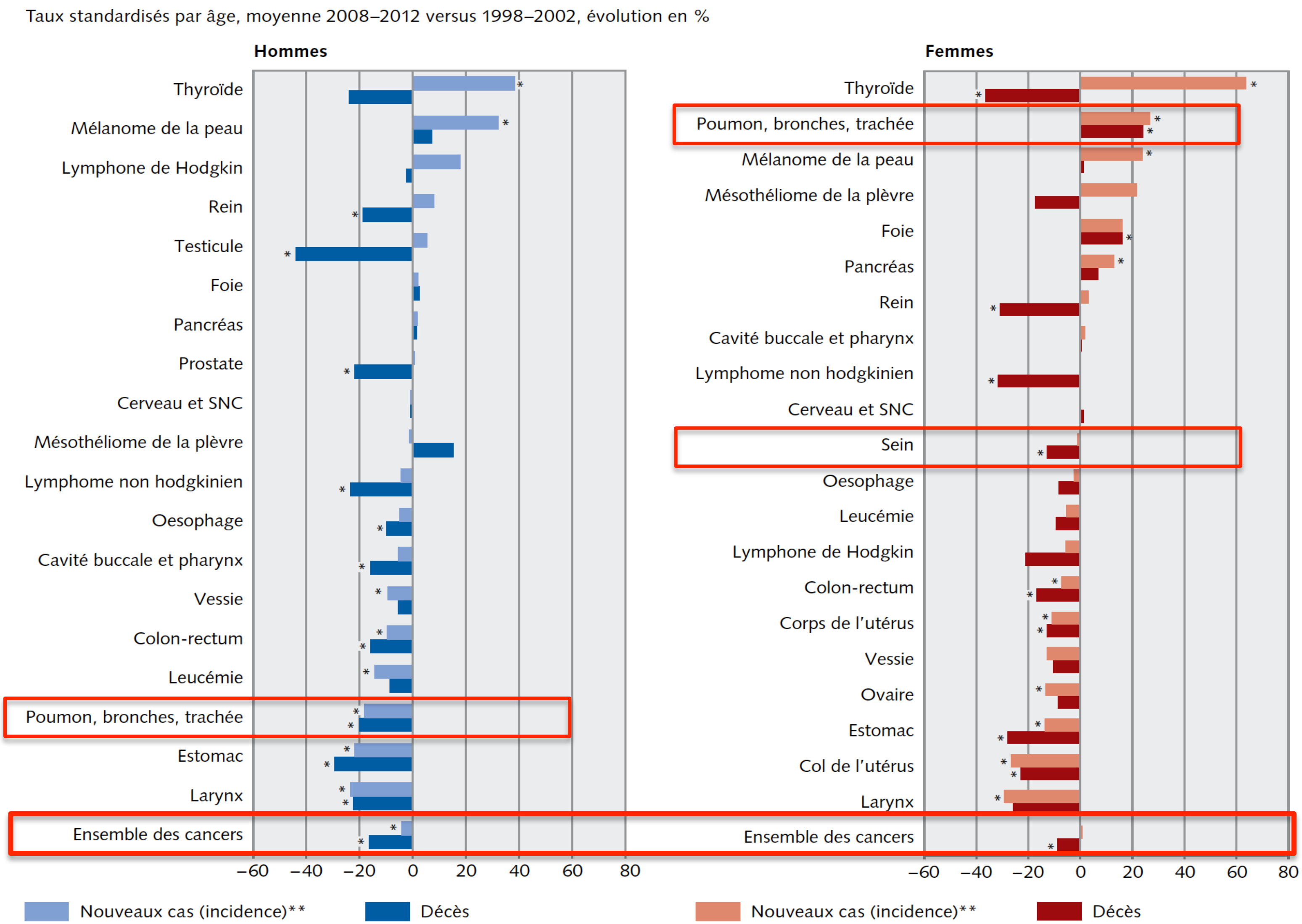
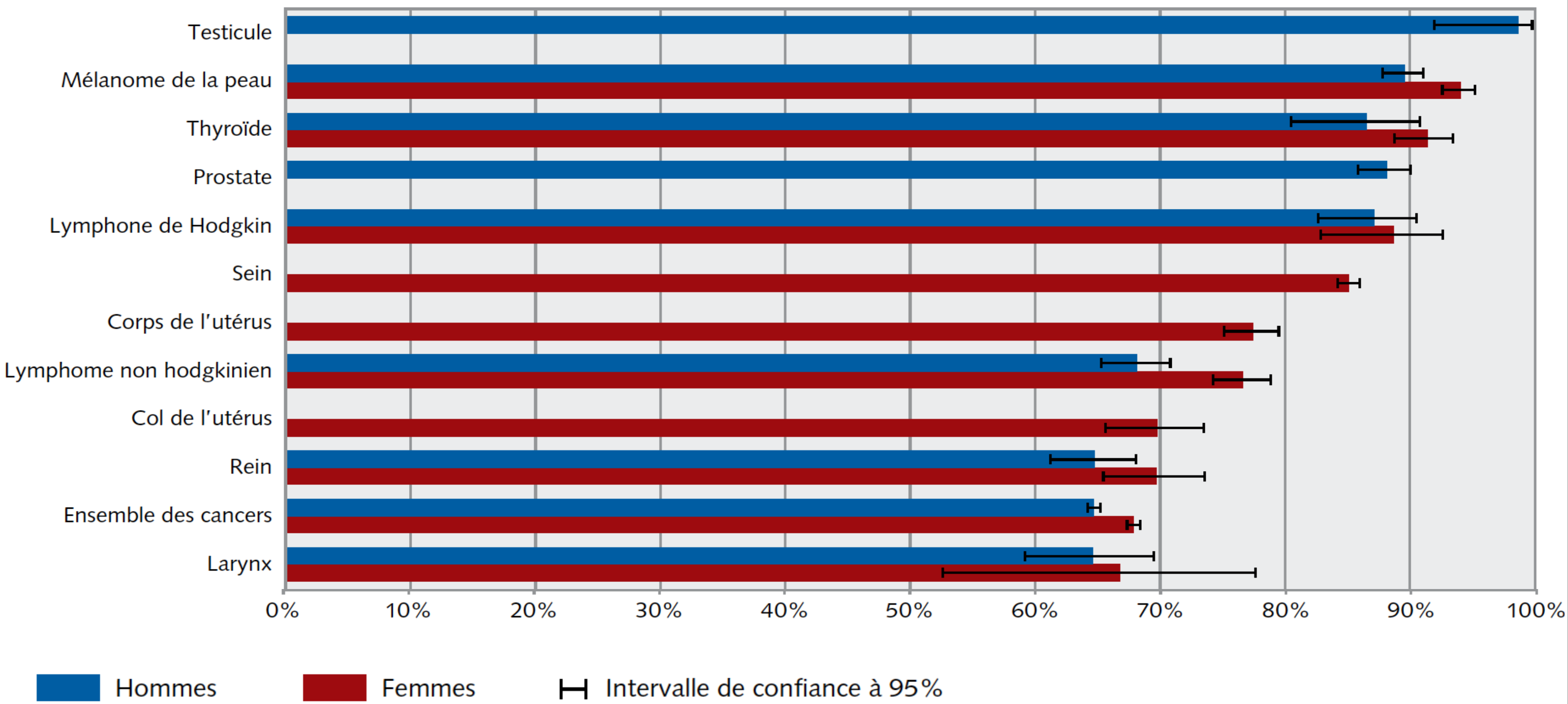


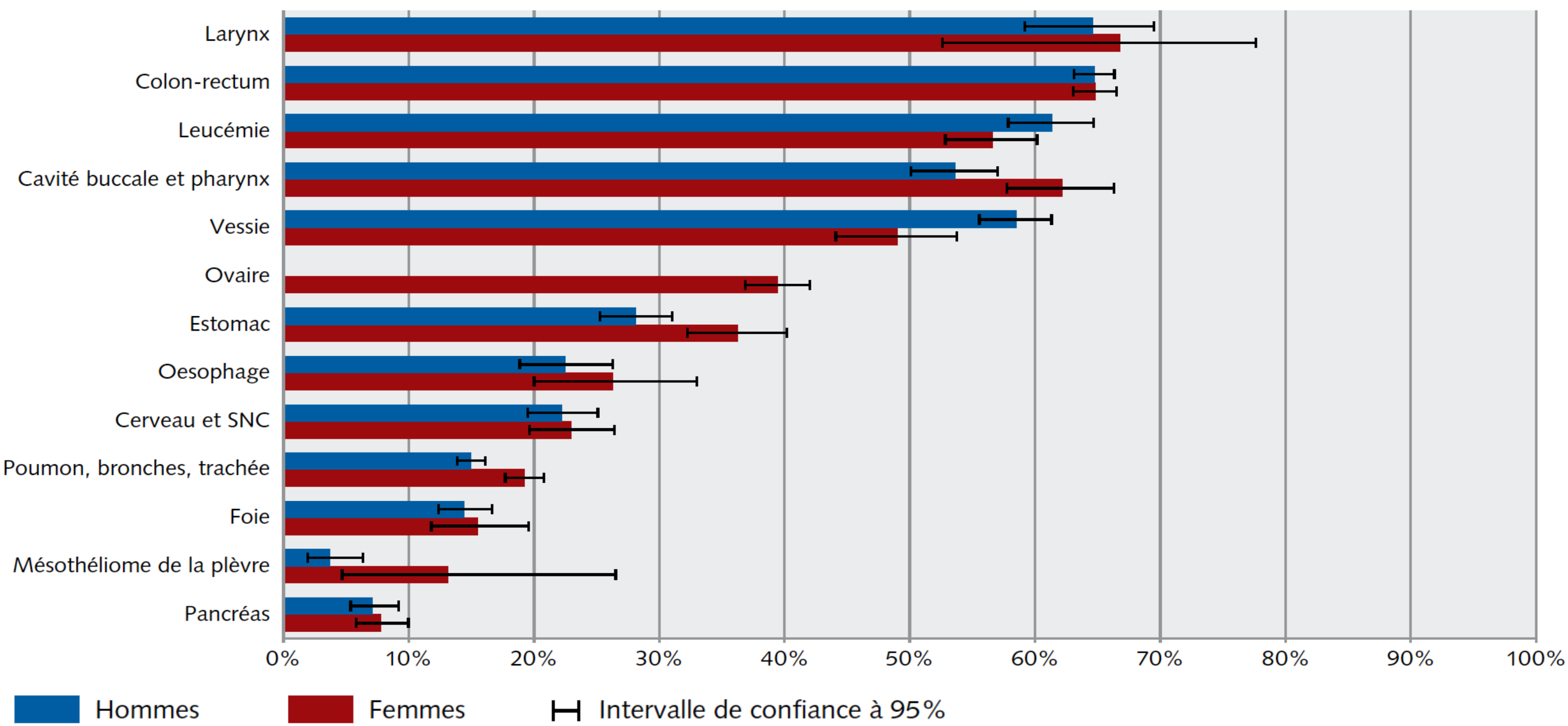
Le cancer en Suisse, rapport 2015, OFS

5 years survival



Le cancer en Suisse, rapport 2015, OFS

5 years survival



Le cancer en Suisse, rapport 2015, OFS

Risk factors

- External
  - Physics: UV, RX
  - Chemical: asbestos, benzene, tobacco, etc…
  - Biology: virus, bacteria, parasites
- Hereditary (5-10 %)
- 30 % of cancers could be avoided
  - Tobacco (world)
    - 20% of cancer mortality
    - 70% of lung cancer mortality

Absorbed dose

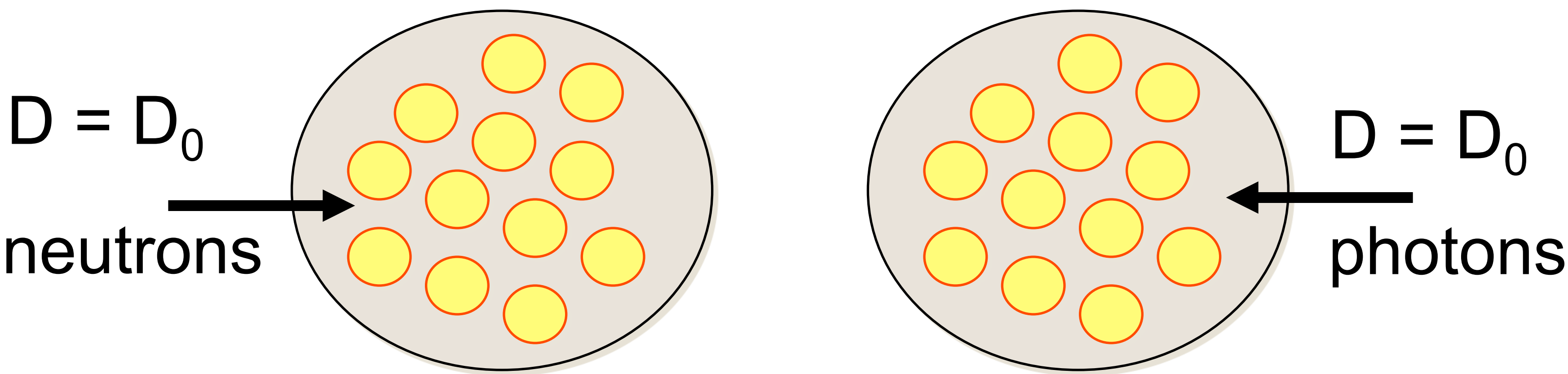
$$D = \frac{\text{Energy}}{\text{mass}} \quad [J/kg] = [Gy]$$

Main effect: heat

2 Gy in water: ~ 0.5 m°C

Absorbed dose and biological effects

- Absorbed dose is not directly linked to biological risk (or effect)



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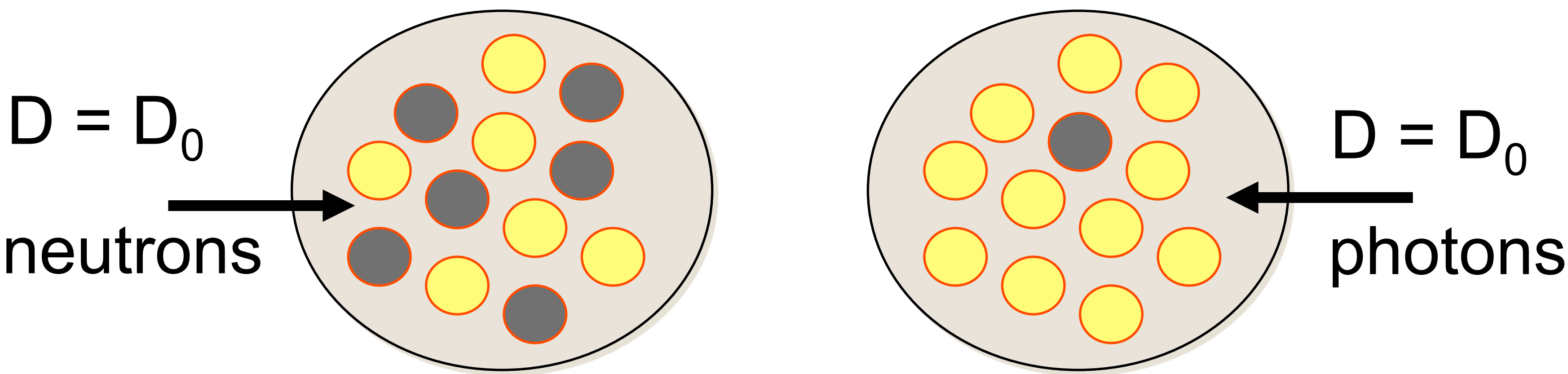
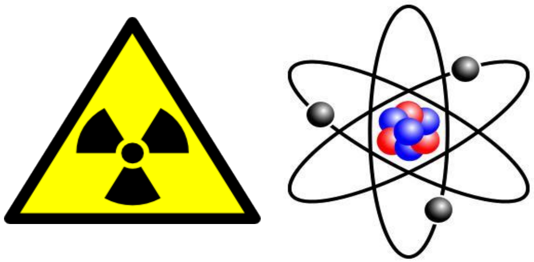


Not the same biological effect

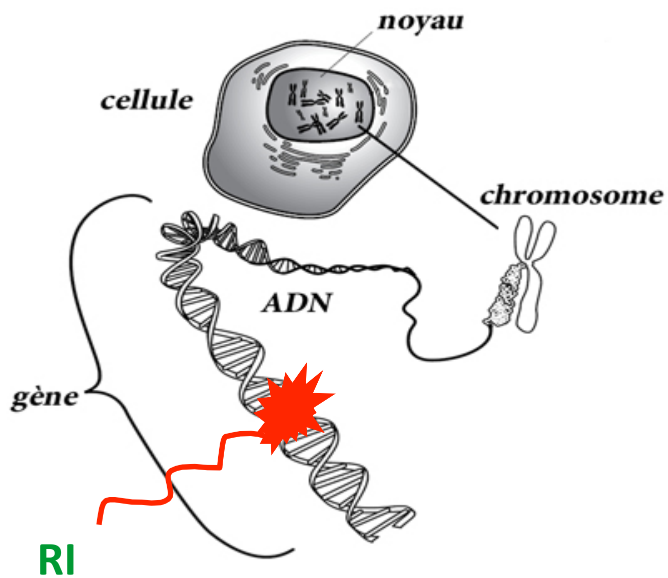
Effects of radiation

Radiations ionisantes



1. **Particules**
   - particules β
   - particules α
   - neutrons
   - protons
   - …
2. **Ondes e.m.**
   - rayons X
   - rayons γ

Lésions de l'ADN



Ionisation des atomes de la cellule (ADN)

Pas de réparation

- Mort de la cellule
- Effets **déterministes**
  - Brûlure, stérilité, mort de l'individu, …

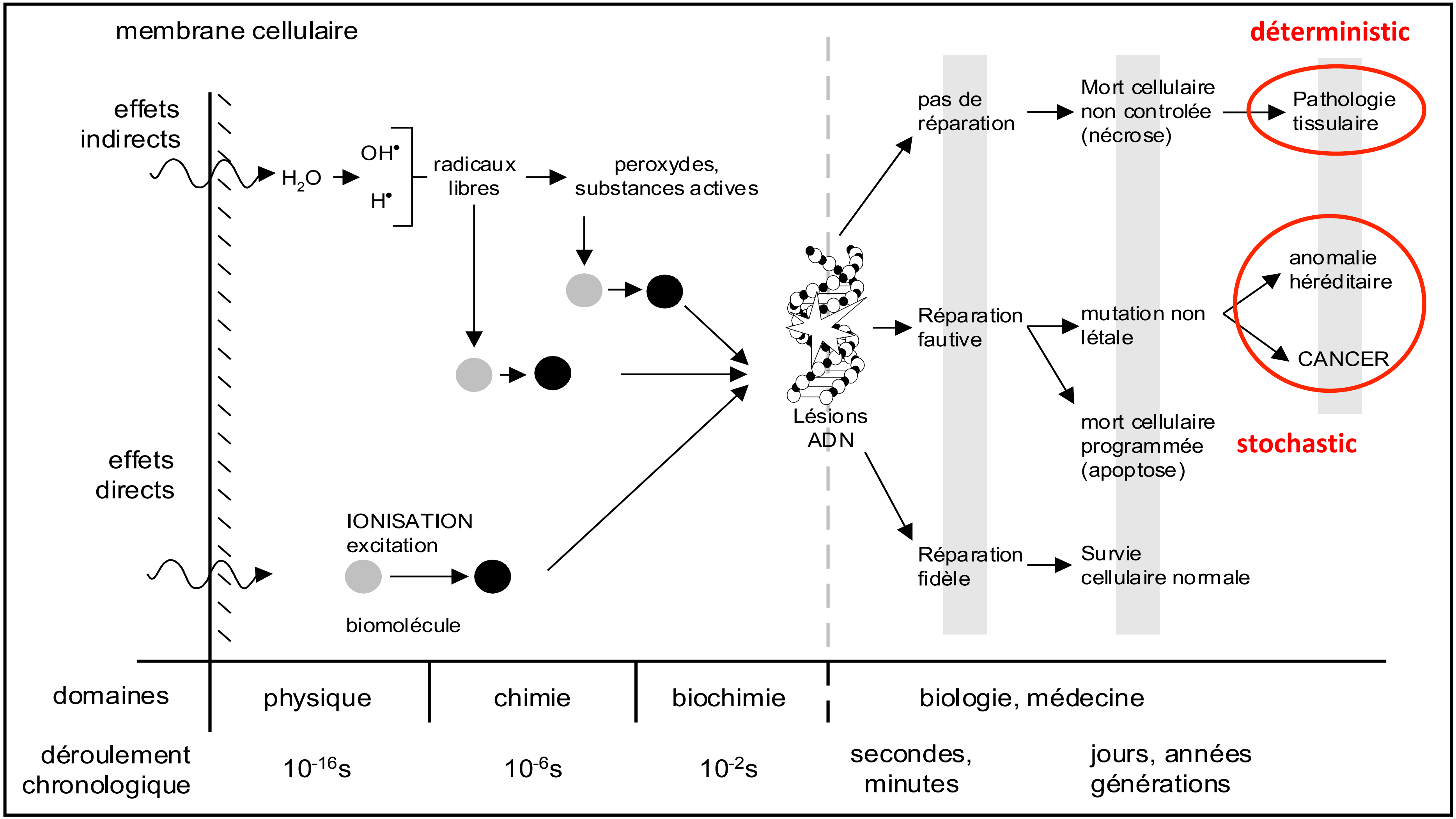
Réparation fautive

- Mutations non létales
- Effets **probabilistes**
  - CANCER
  - Anomalie héréditaire

Réparation fidèle

- Survie de la cellule
- Pas d'effet

Biological action of radiation



Cancer induction

- Epidemiological basis
  - Hiroshima & Nagazaki survivors
  - Dose level : 1 Sv
- Latency
  - Leukemia : 10 years
  - Solid tumor: 20 years

Risk factor: 5% Sv^{-1}

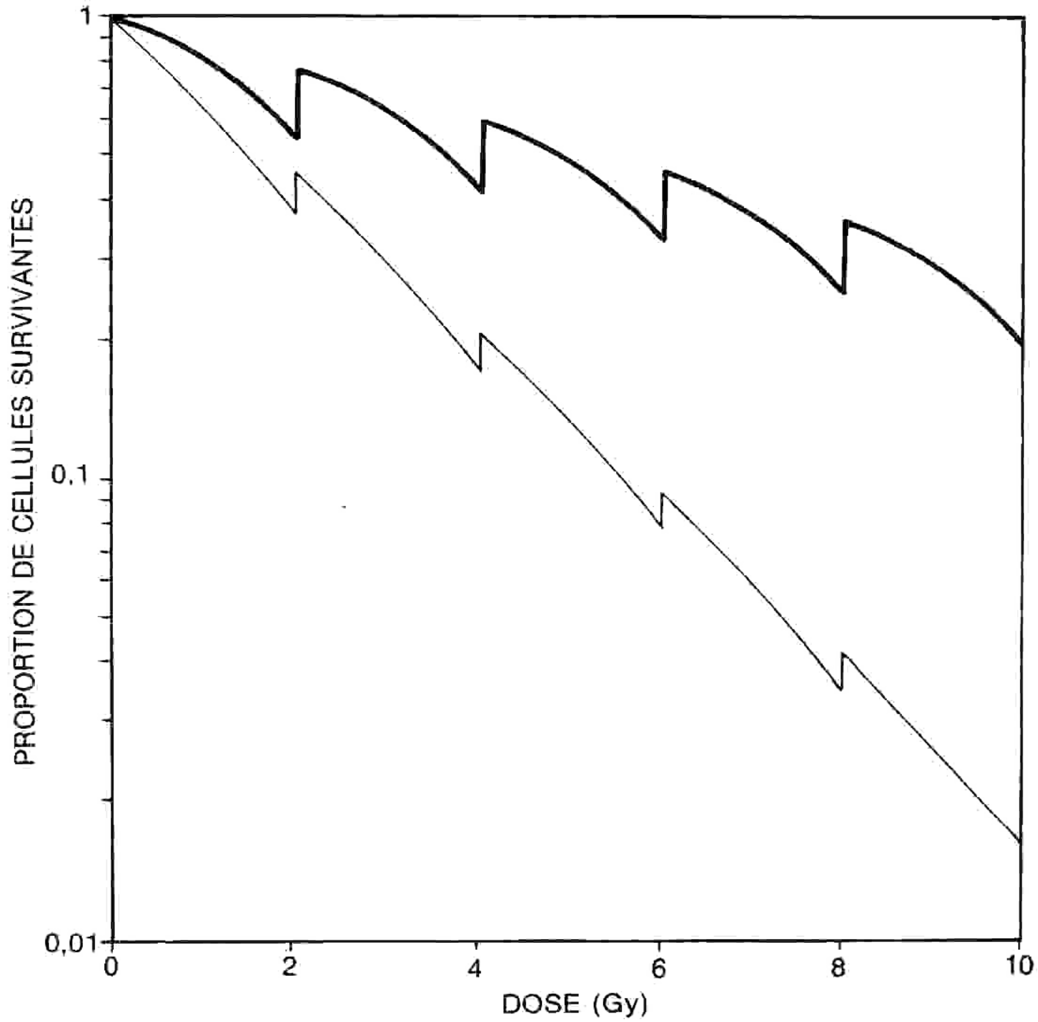
Objectives of radiation therapy

- Treatment of cancer cells
- All cells are sensitive to radiation
  - Tumoral cells (slightly) more sensitive, and
  - Weaker repair capacities
- Curative treatments
  - Permanent local control
- Palliative treatments
  - Reduction of symptoms (pain)
- Benign diseases

Fractionation

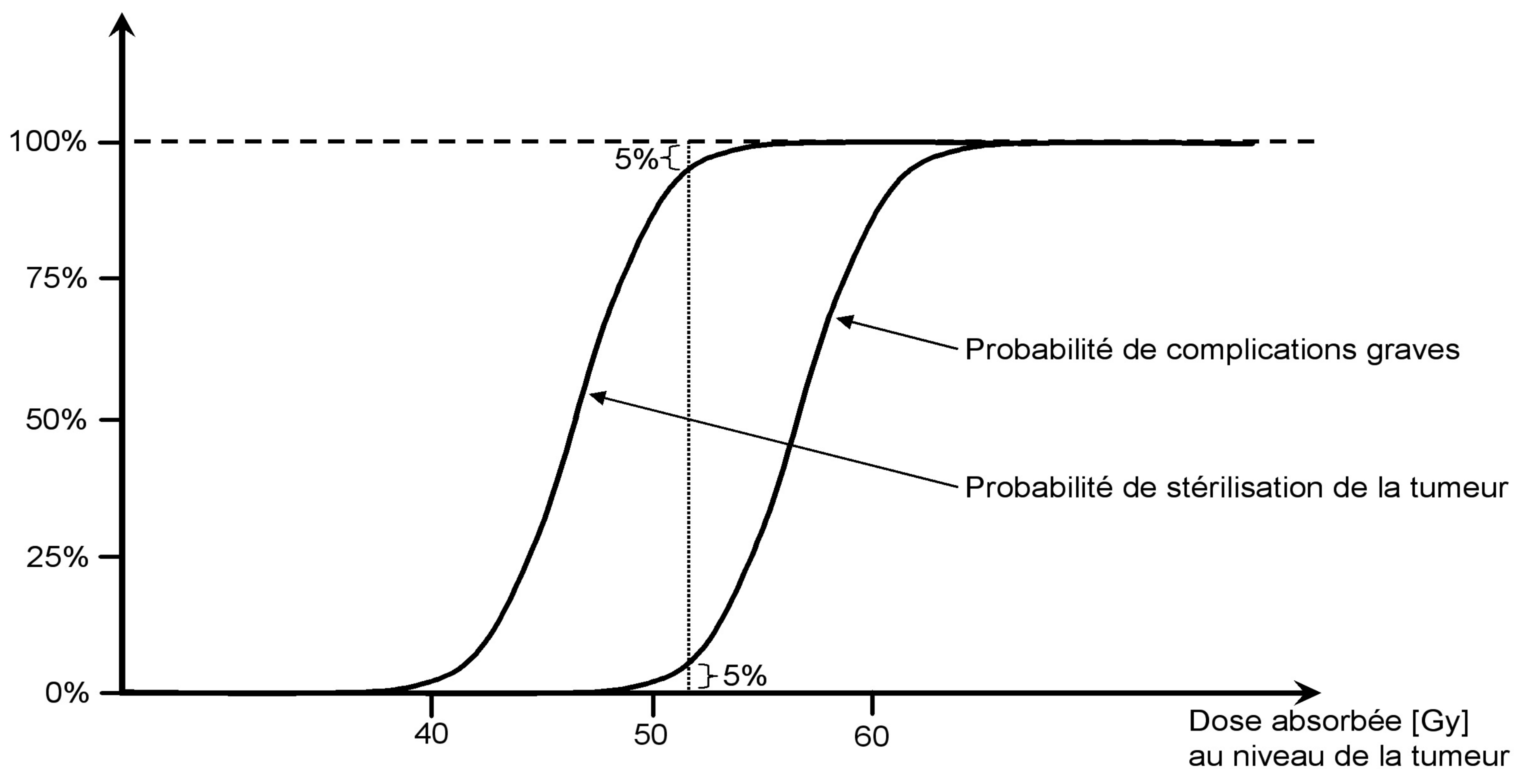
- The dose delivery is generally fractionated
  - 1 X 50 Gy ➠ death
  - 25 x 2 Gy ➠ treatment
- Healthy cell can repair (better than tumors)
- Amplification of the effect between healthy and cancer cells

Fractionation

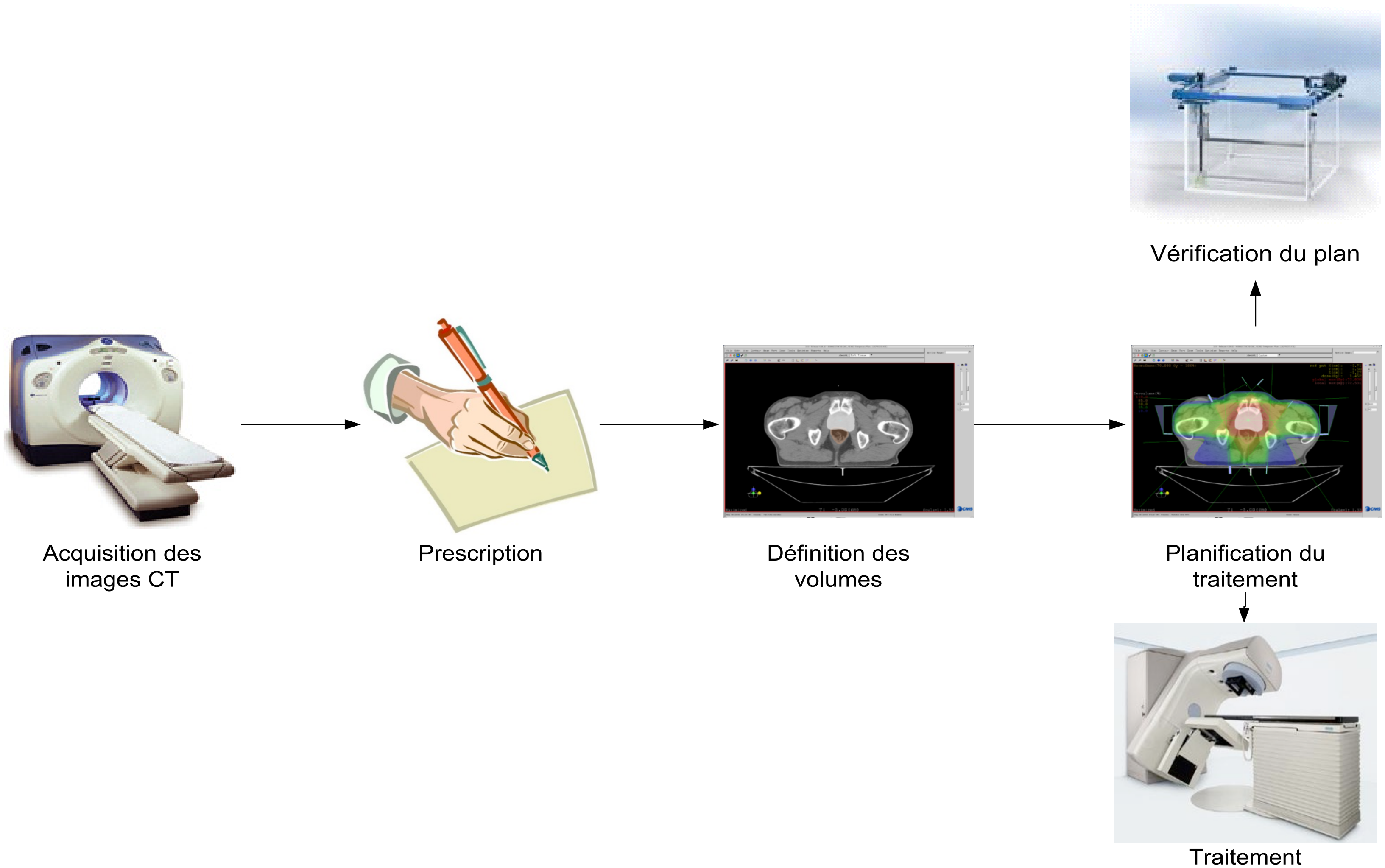


Limits of radiation therapy

- Secondary effects
- Compromise between cure and adverse effects



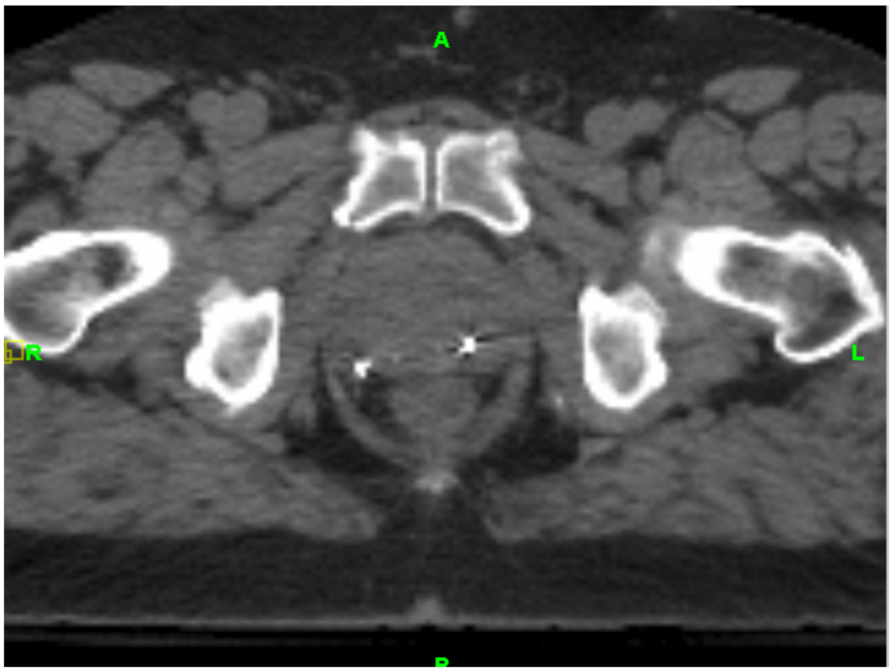
Patient workflow

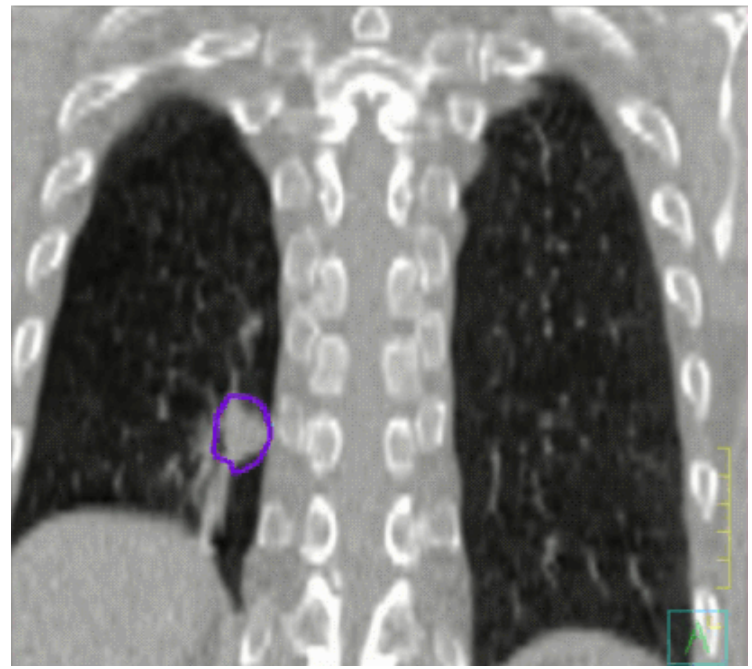


Patient workflow

Acquisition des images CT

Patient workflow





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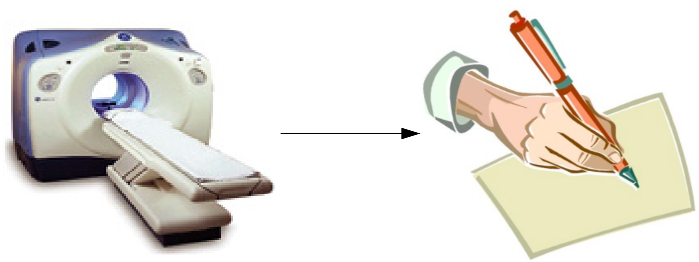


Acquisition des images CT

Prescription

Patient workflow

Acquisition des images CT

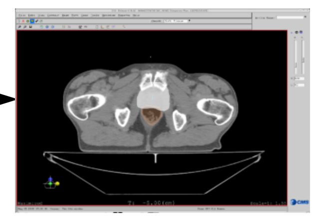
Prescription

- Absorded dose
- Representative point of the volume to be treated
- Definition of target volume

Patient workflow

Acquisition des images CT

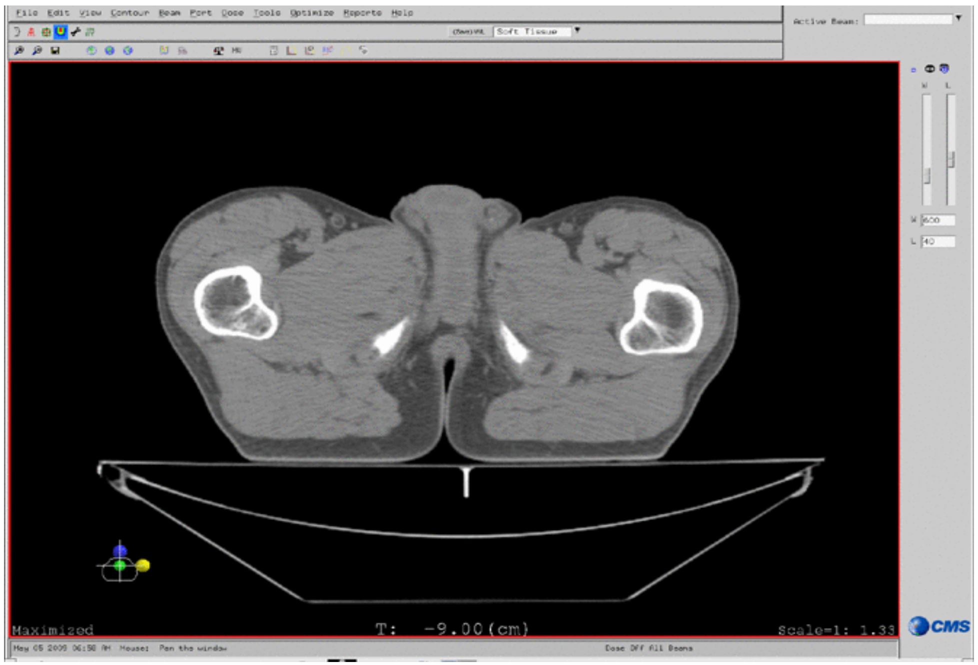
Prescription



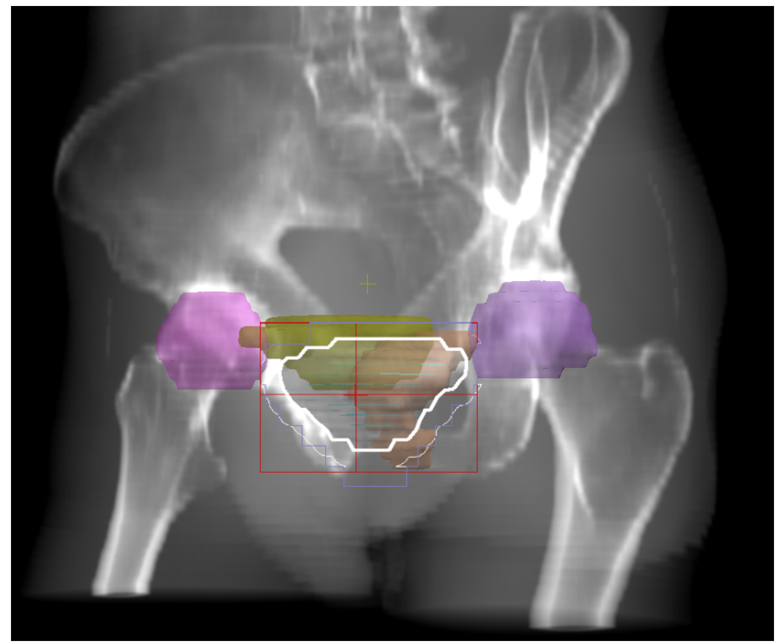
Définition des volumes

Volumes definition

- Target volume
- Organs at risk

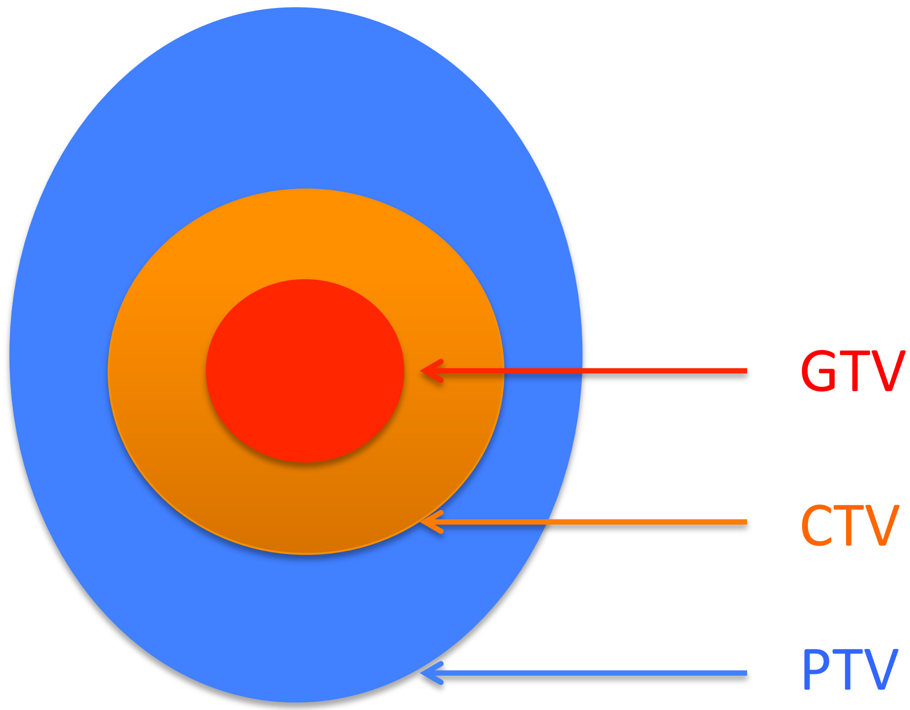


Axial view



3D view

Target volume definition

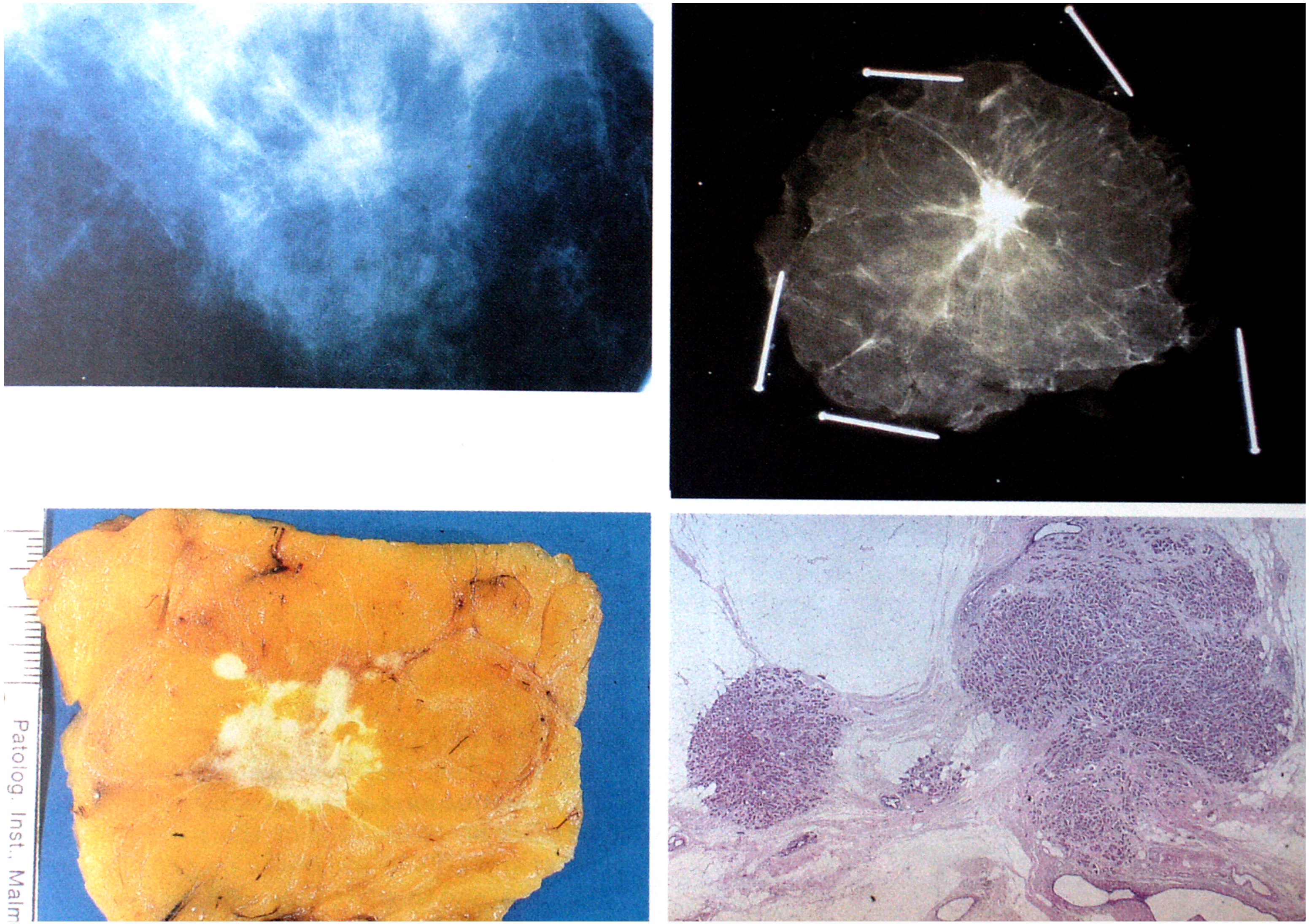


ICRU 50

Gross tumoral volume

- GTV
- **GTV is the localization and the demonstrable gross extension of the malignant growth**
- Contains
  - Primary tumor
  - Metastatic lymph nodes
  - Metastases
- May vary according to the imaging type used

Volume tumoral brut



Clinical target volume

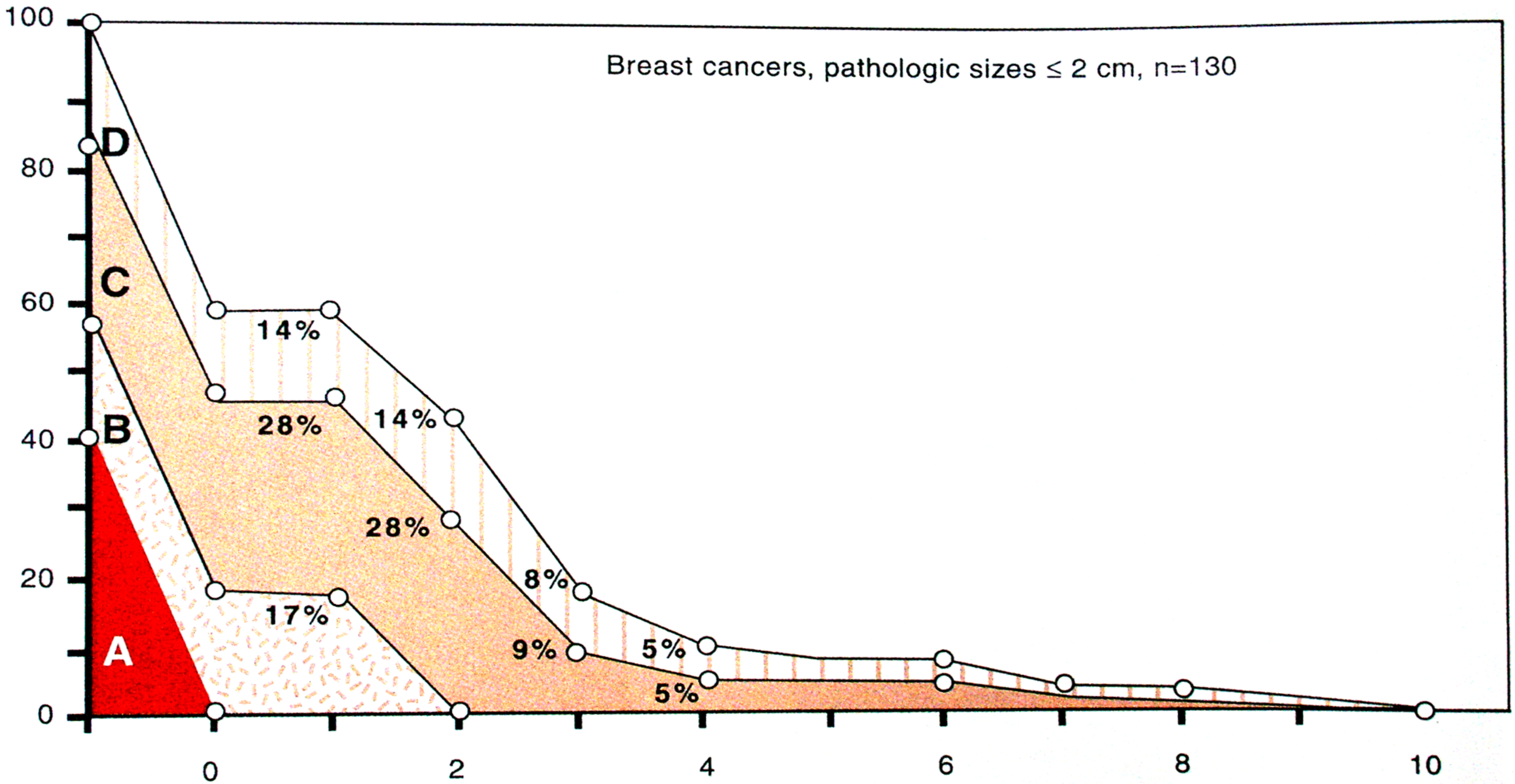
- CTV
- **The CTV is a tissue volume containing a GTV and / or infra-clinical malignant lesions that must be destroyed to achieve the objective of radical radiation therapy**
- Note that except the GTV, the CTV is mainly composed of healthy tissues

Clinical target volume

- Prescription is based on the hypothesis that there may be tumoral cells with a given probability beyond the GTV
- The estimattion of that probability is based on clinical experience and patient follow-up

Clinical target volume

Clinical target volume



Planning target volume

- PTV
- **The PTV is a geometrical concept. It is defined so that it guarantees that the CTV is adequately covered, taking all possible variations during irradiation into account**
- Note that except the CTV, the PTV contains only healthy tissues

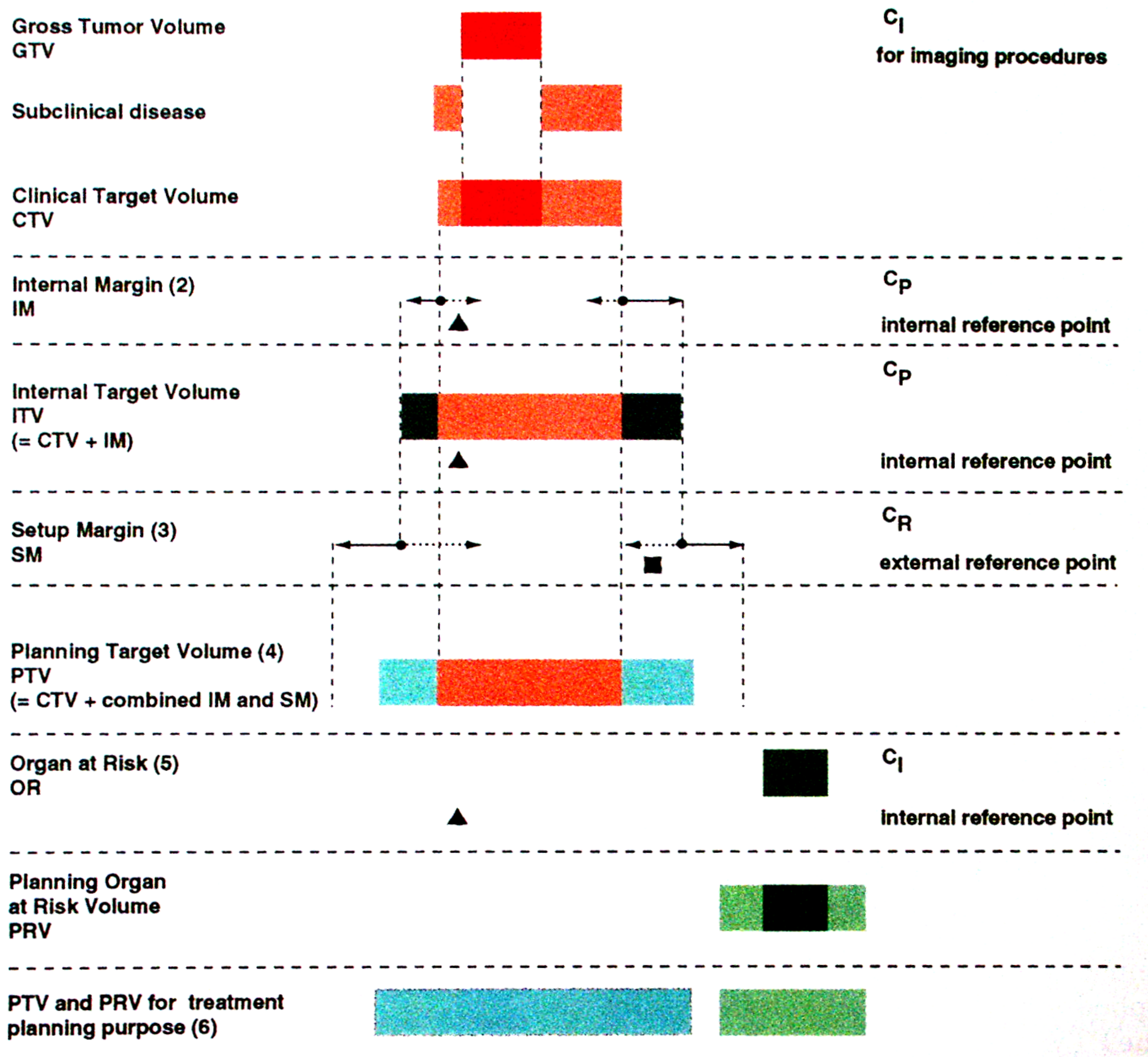
Planning target volume

- The dose distribution into the PTV is considered as representative of the dose distribution into the CTV

Planning target volume

Courtesy Dirk Verellen

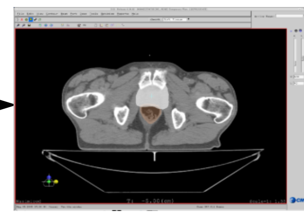
Target volume synthesis



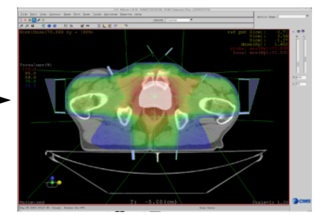
Patient workflow

Acquisition des images CT

Prescription



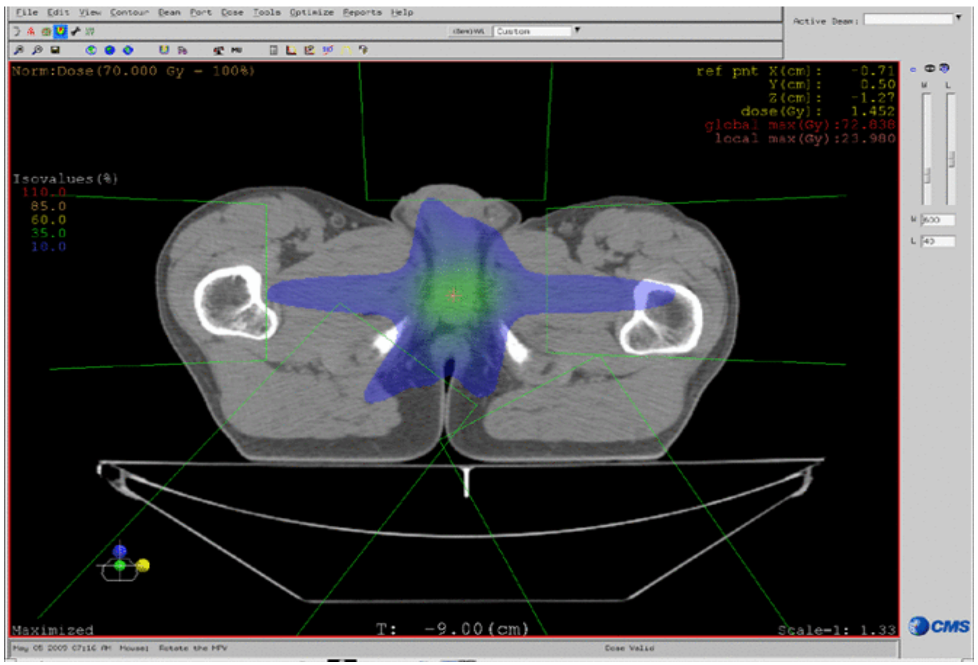
Définition des volumes



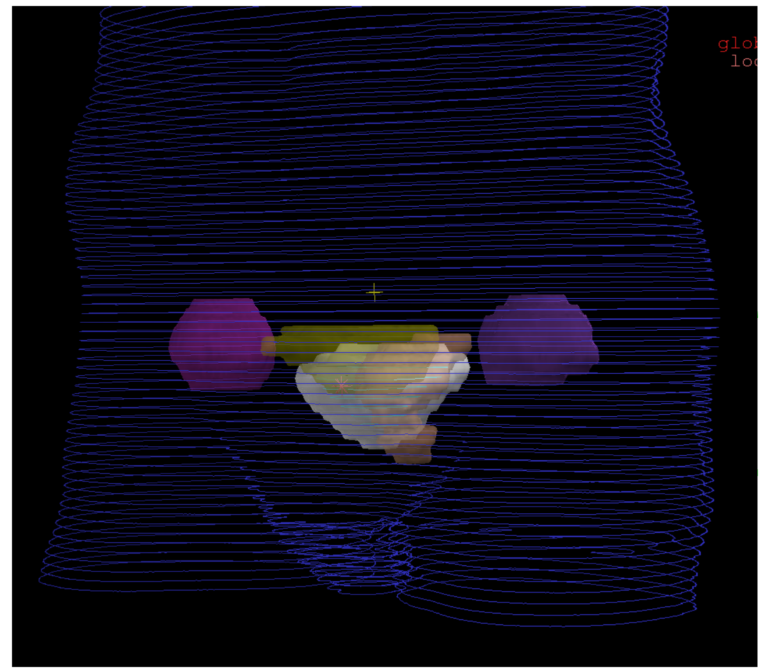
Planification du traitement

Treatment planning

- Geometrical data
- Dose distribution



Axial view

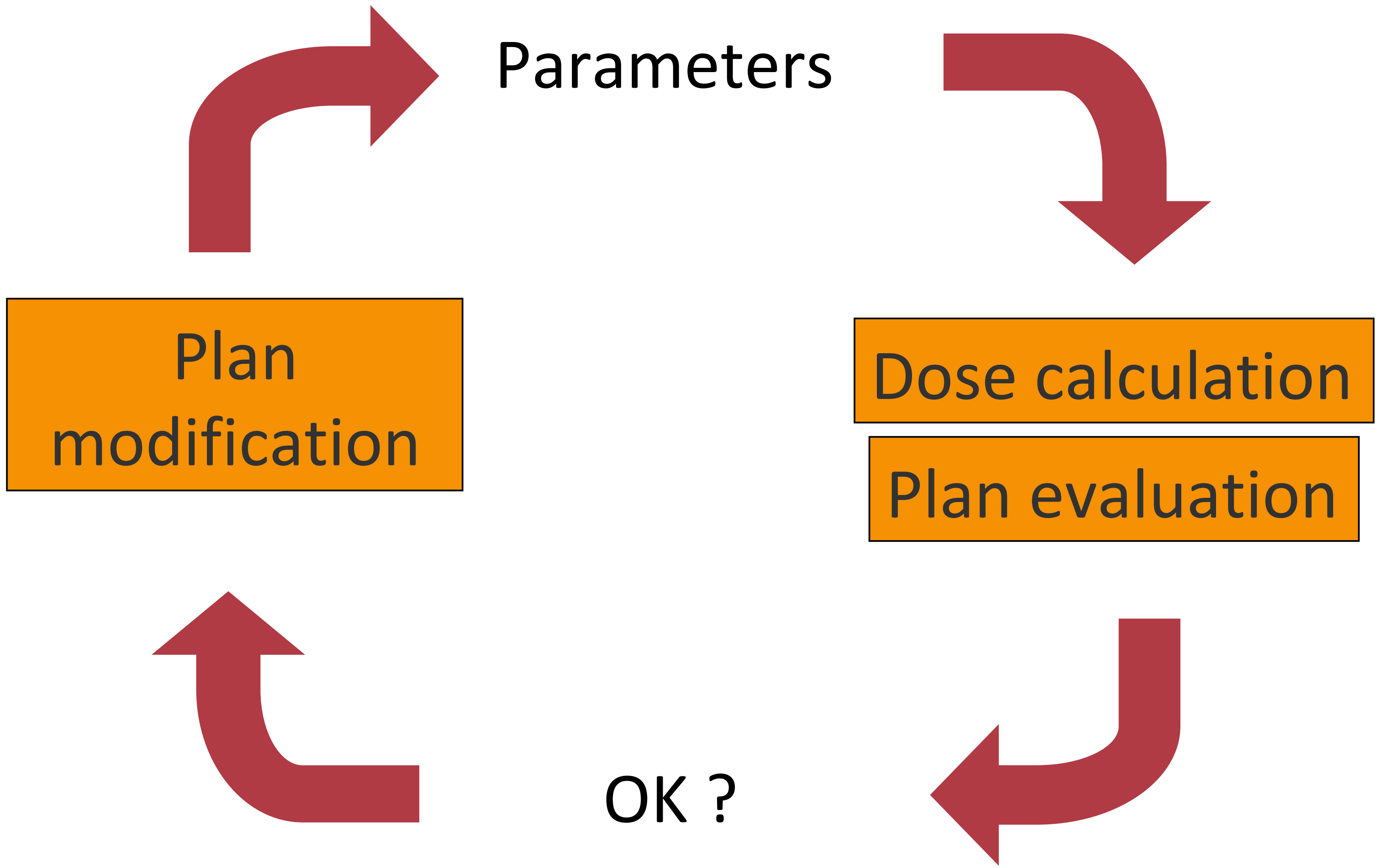


3D view

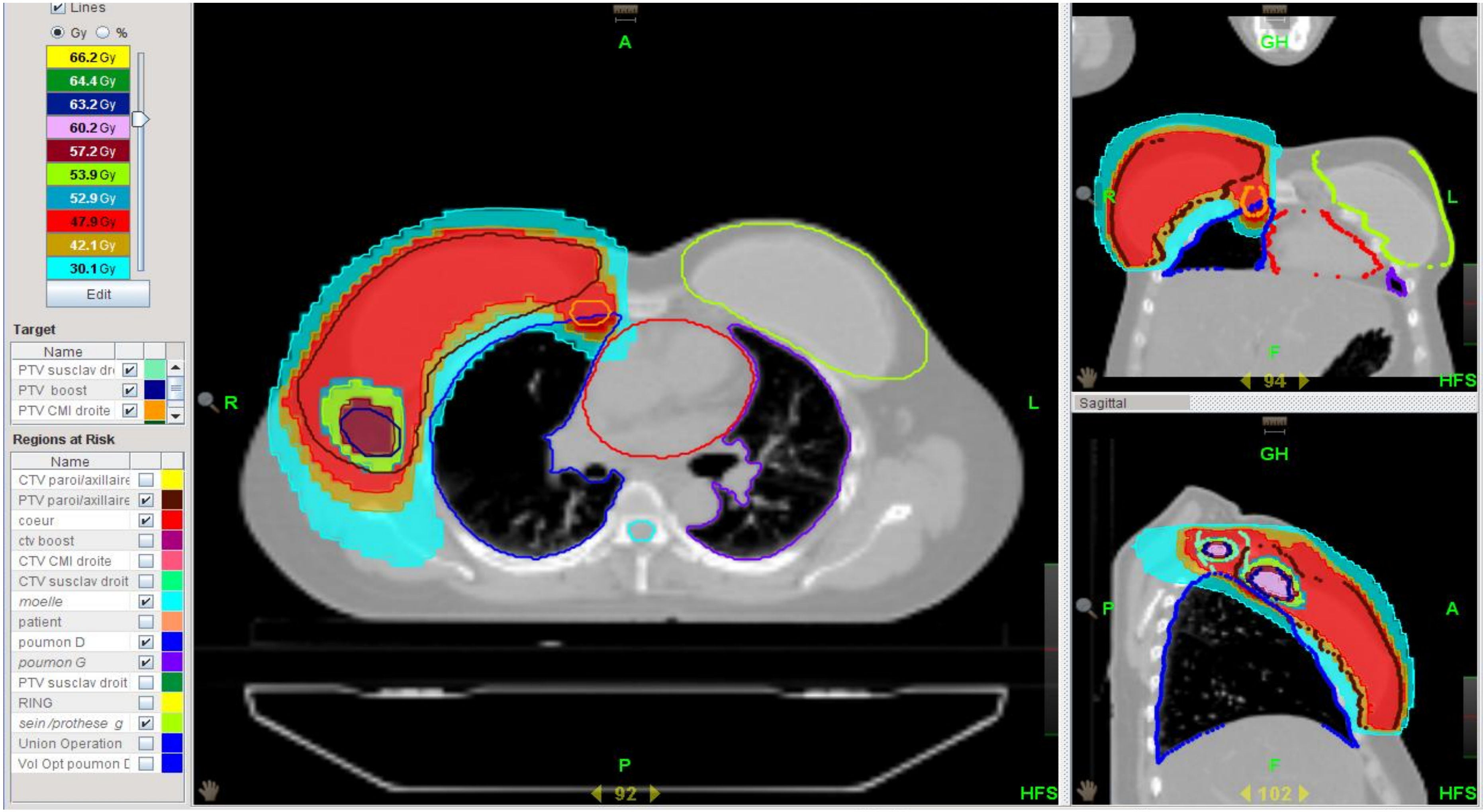
Treatment planning principles

- Definition of irradiation parameters made by physicist (or technician)
- Iterative process
- Validation by physician and physicist

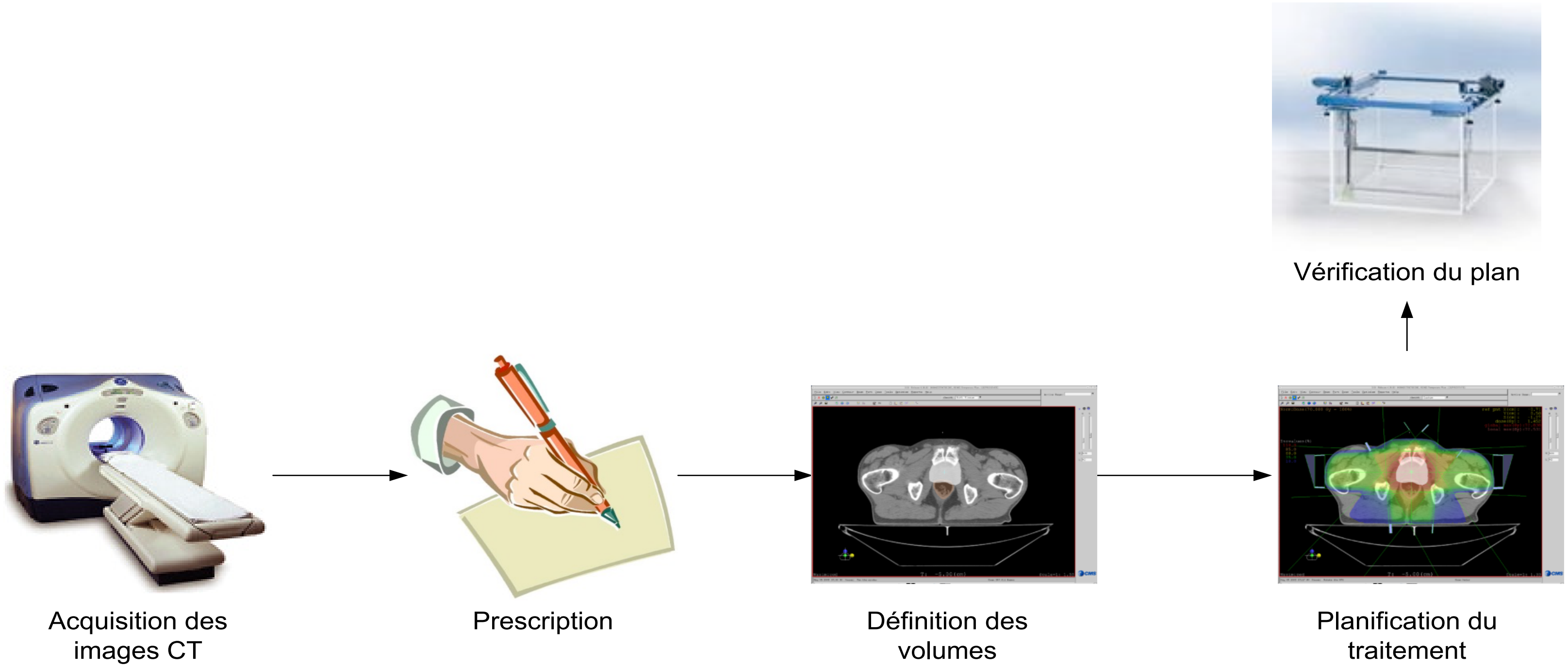
Optimisation process



Dose distribution



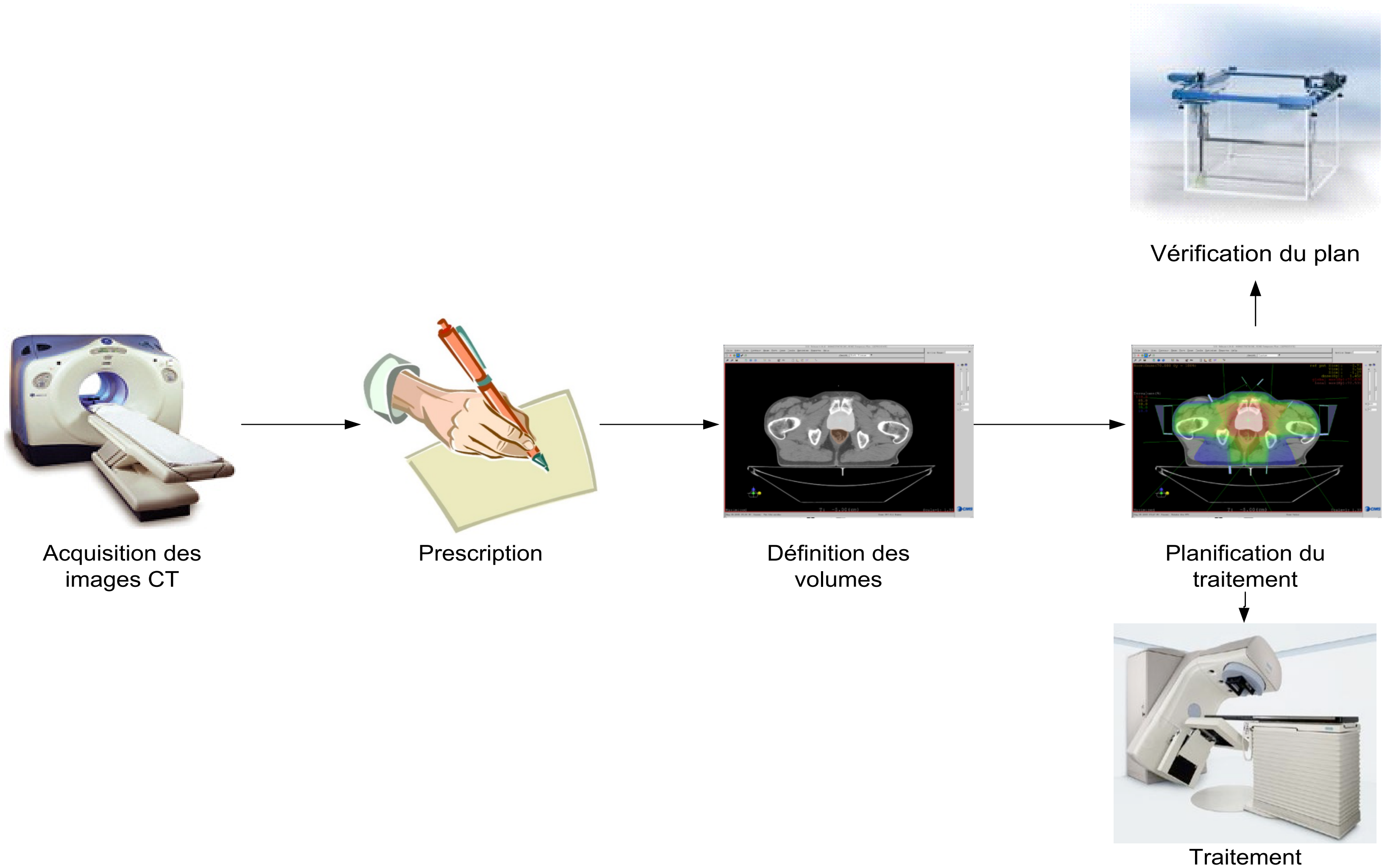
Patient workflow



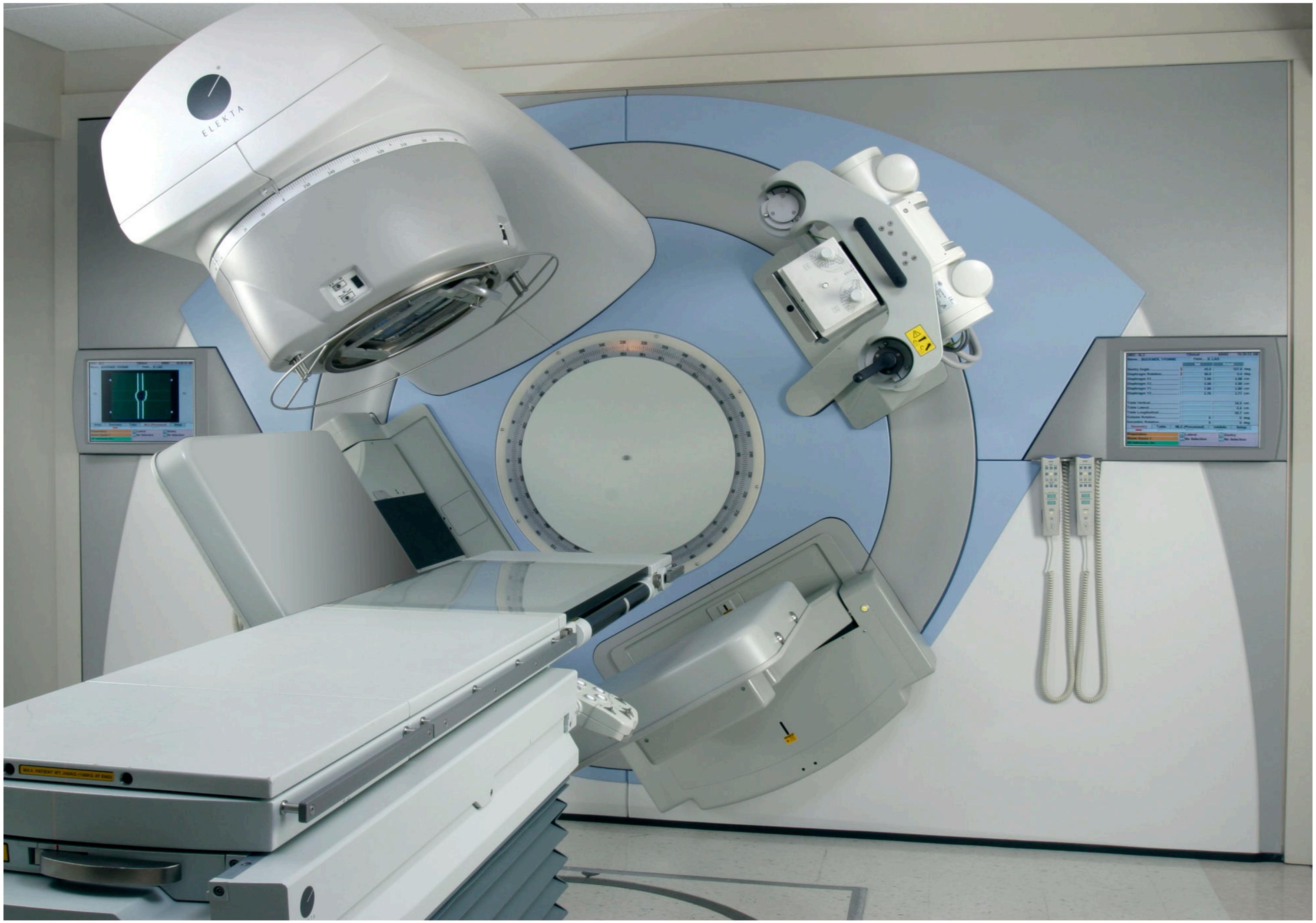
Treatment plan verification

- Prescription
  - Target coverage
  - Organs at risk tolerance
- Irradiation technique
  - Number of beams, energy, etc…
- Independent calculation or measurement of the dose / irradiation time
- Green light for treatment (medical physicist according to law)

Patient workflow



Dose delivery



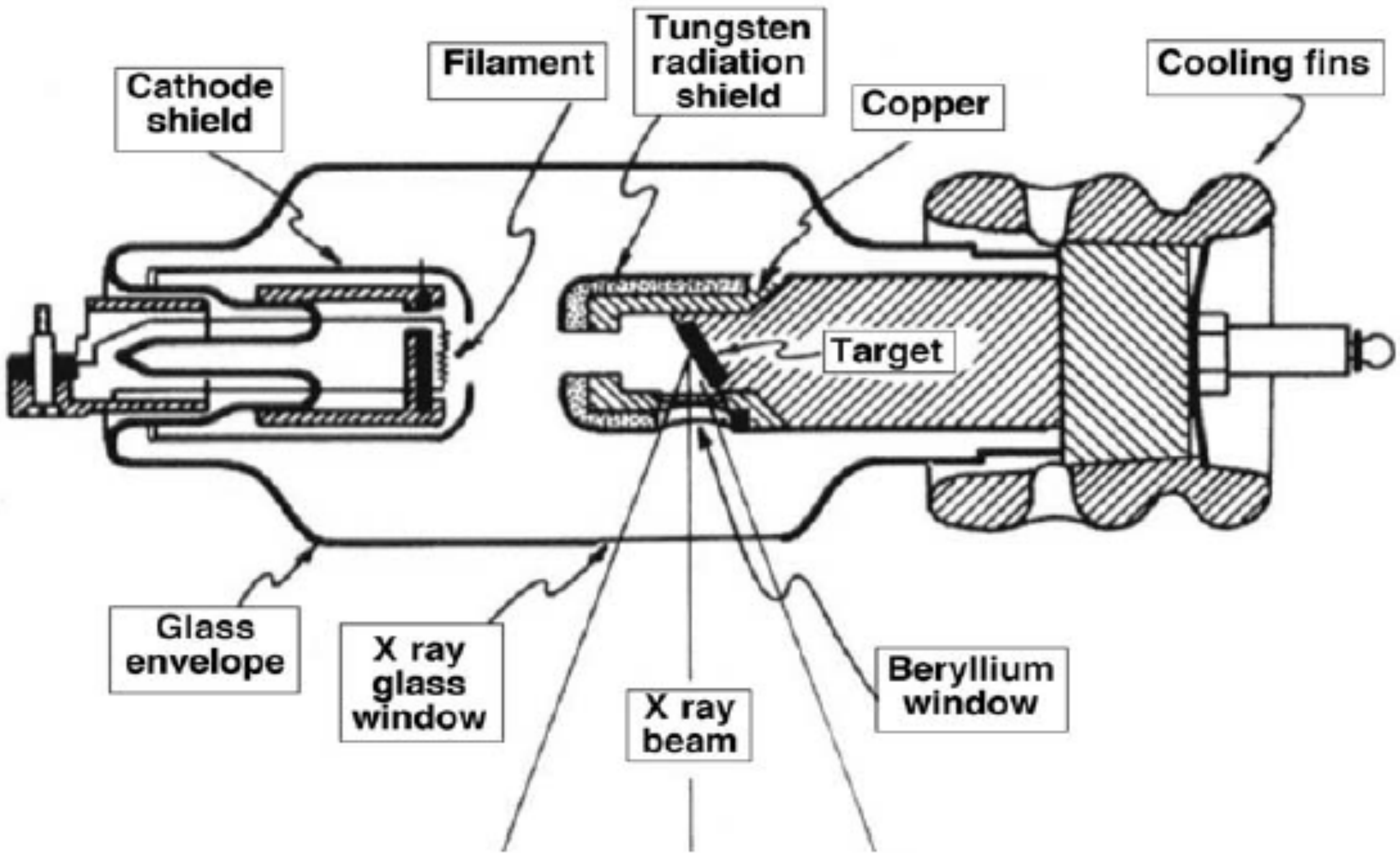
Beam production

- Introduction
- « Conventional » devices
- Cobalt 60
- Linear accelerators

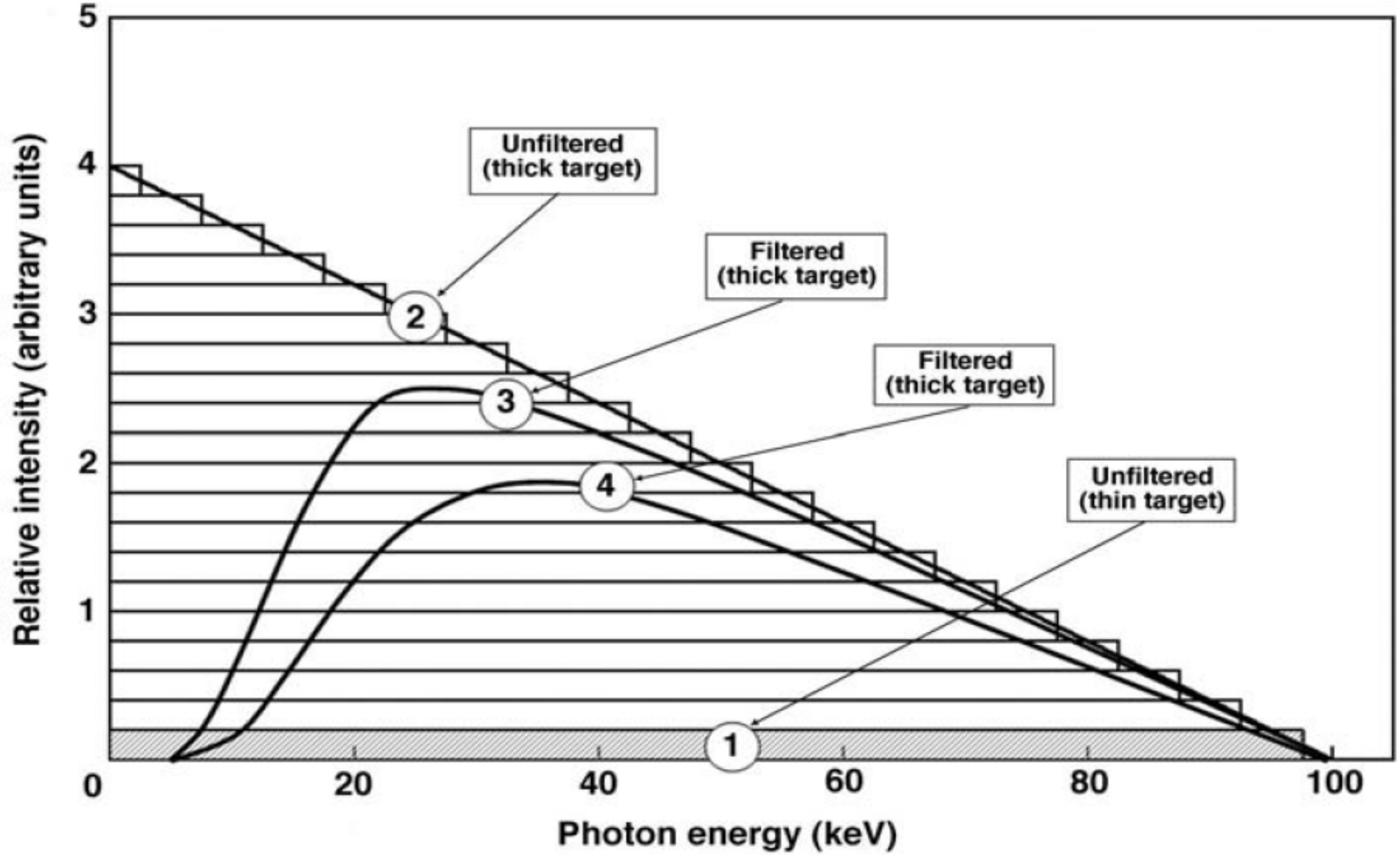
Beams used in radiation therapy

- Superficial X-rays
- Conventional X-rays
- Cobalt 60
- High energy X-rays
- High energy electrons
- High energy protons
- Heavy nuclei
- Neutrons

Conventional radiation therapy



Conventional radiation therapy



Conventional radiation therapy

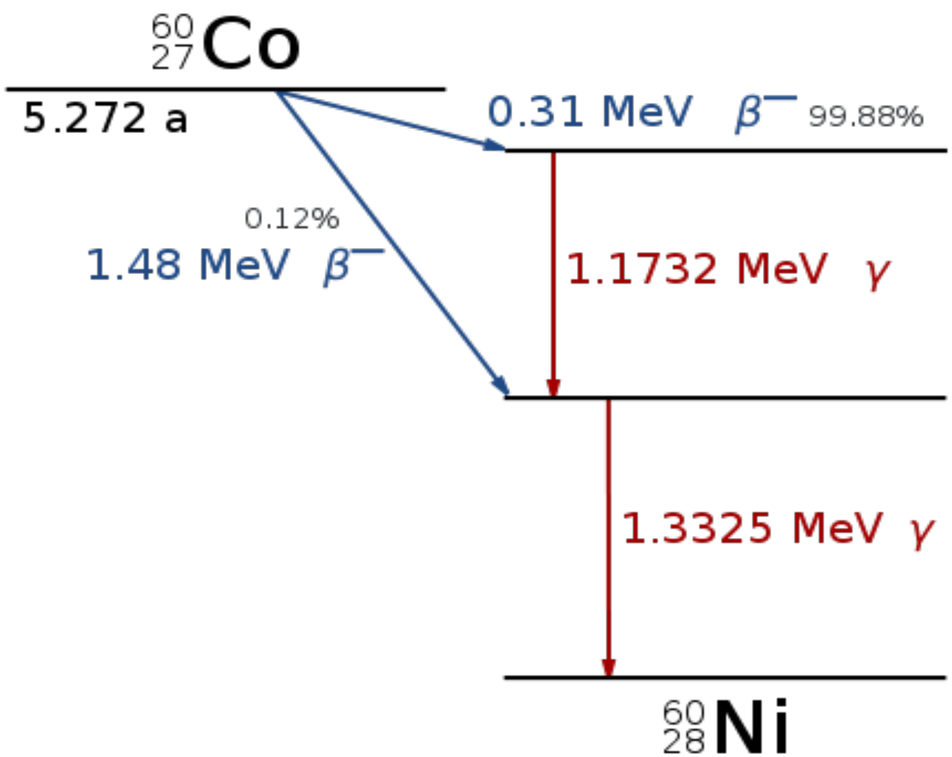
- « Traditional » X-ray tubes
- Accelerating voltage: 120 - 300 kV
- Depth of 50% : 5 - 7 cm
- Beams no more used in clinical treatments
  - But used for radiobiology

Superficial radiation therapy

- « Traditional » X-ray tubes
- Accelerating voltage: 10 - 50 kV
- Depth of 50% : 0.03 - 2 cm
- Beams used in dermatology

Cobalt 60 source

- Disintegration scheme



- Energy
  - E γ = 1.25 MeV
- T = 5.27 years
- 1 % per month
- Activity
  - 100 – 300 Tbq

Cobalt 60 source

- Production

$$^{59}_{27}\mathrm{Co} + {}^{1}_{0}\mathrm{n} \rightarrow {}^{60}_{27}\mathrm{Co} + \gamma$$

  - Radiative capture
- Size
  - 2 cm diameter
  - 2 cm heigth

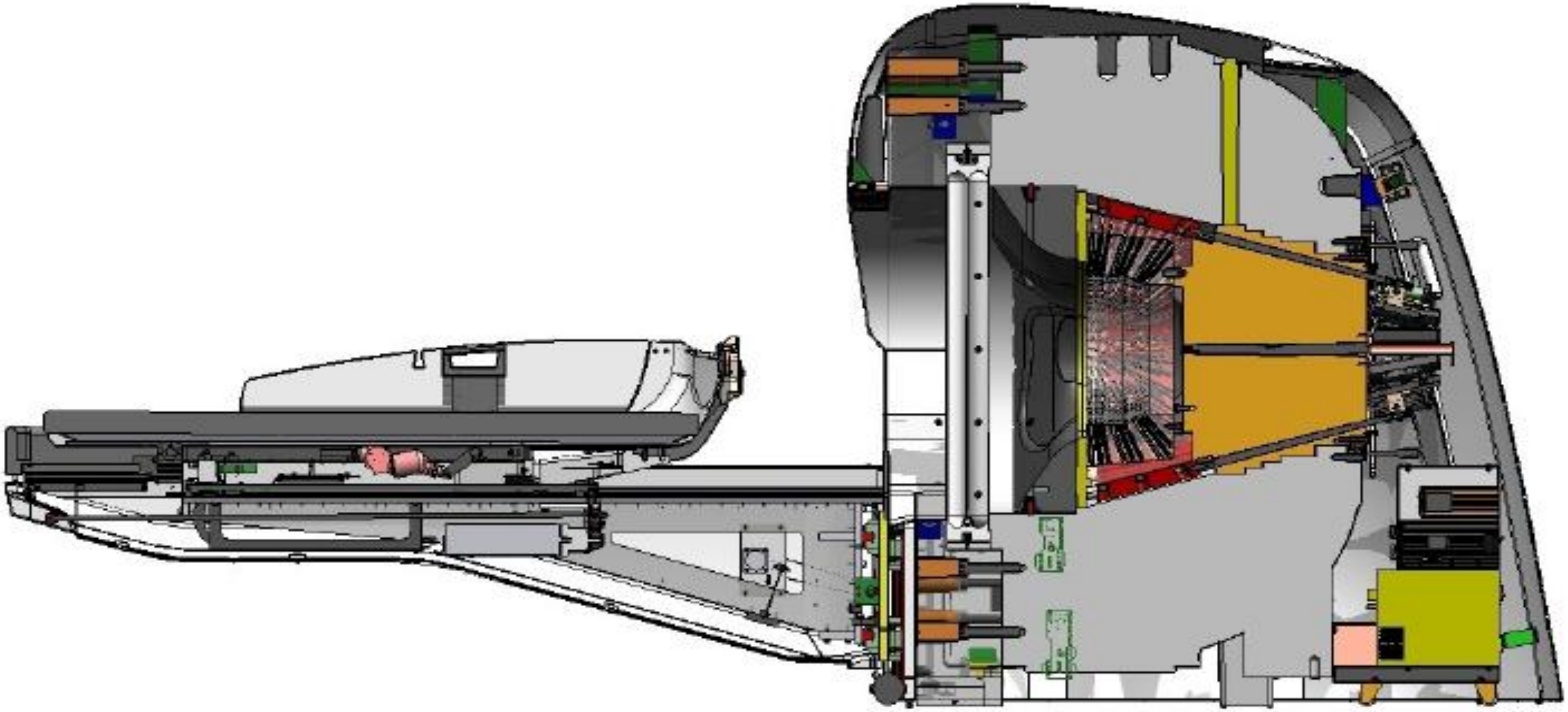
Cobalt 60 source

- Build-up zone: 5 mm
- Depth of 50% : 10 cm
- Treatment of average deep tumors
  - Head and Neck, breast, etc…
- Almost no more used
  - But in non industrialized countries

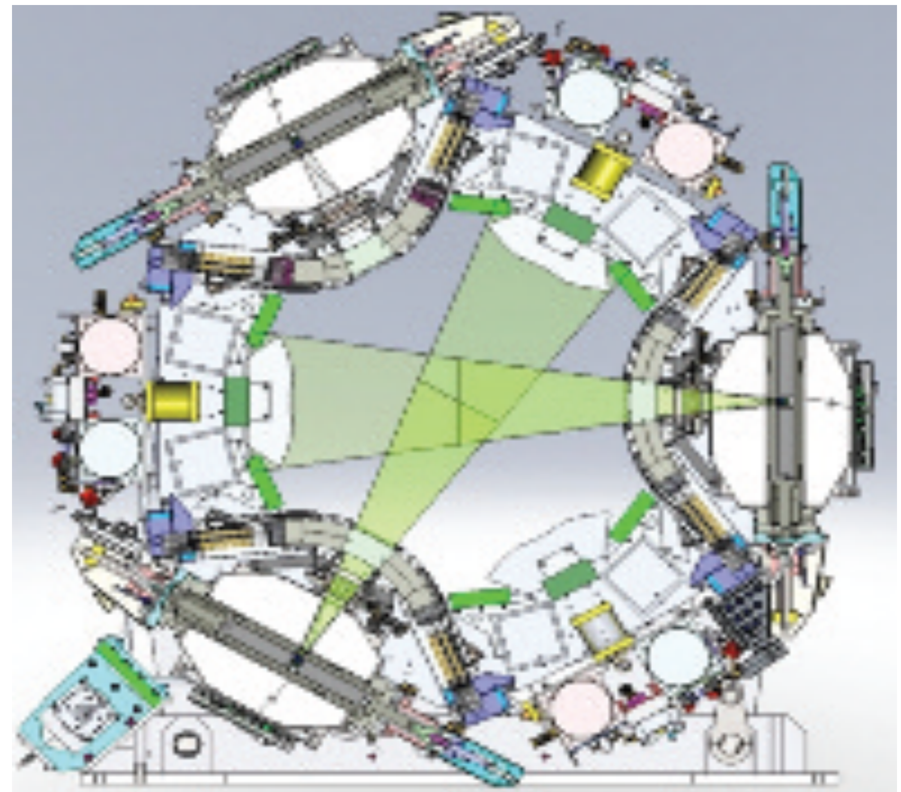
GammaKnife

- Elekta
  - Leksell Gamma Knife® Perfexion™
- 192 Co-60 sources
  - Activity: 200 TBq
- Treatment type
  - Intracranial
  - Neurosurgery

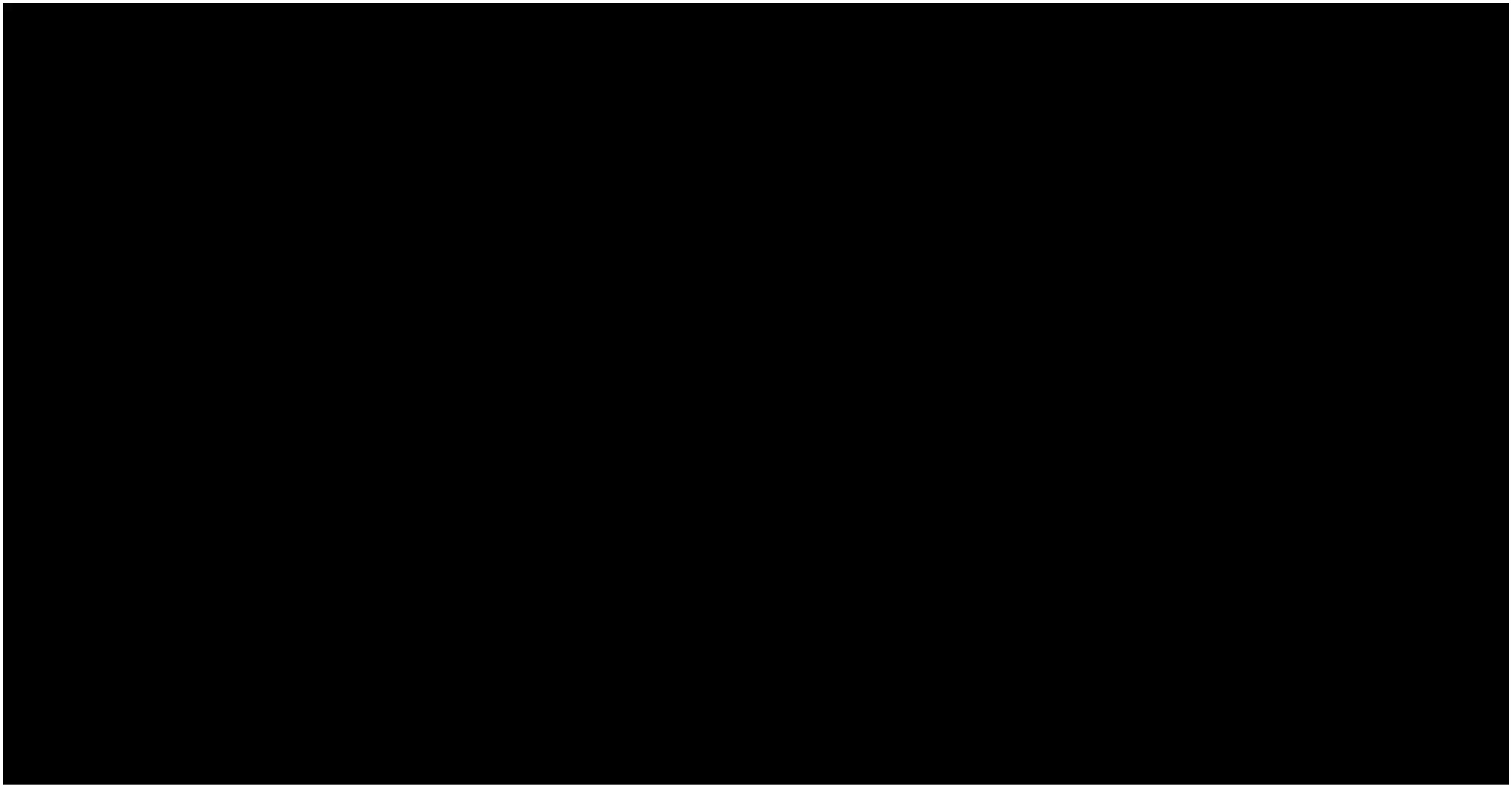
GammaKnife



ViewRay - MRIdian



ViewRay - MRIdian



Particles accelerators

- Many types
  - Nuclear physics
  - Particle physics
- Modified for medical use
- Two basic conditions to accelerate particles
  - Charged particles
  - Electric field in the direction of the particle to be accelerated path

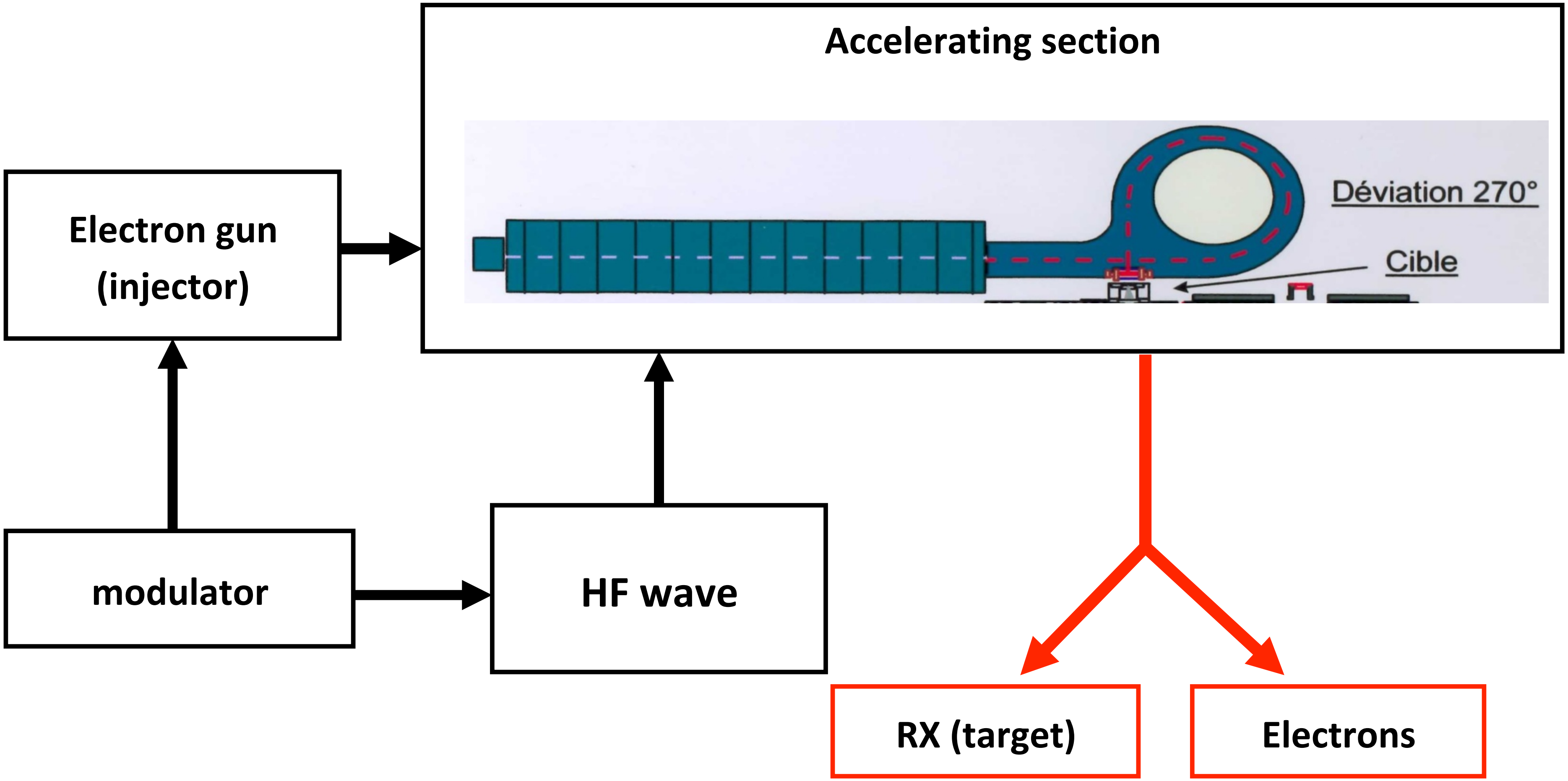
Particles accelerators

- Medical linacs are cyclic accelerators
- Energy: 4 to 25 MeV
- Microwave radiofrequency field
- Electrons linearly accelerated in a specific waveguide

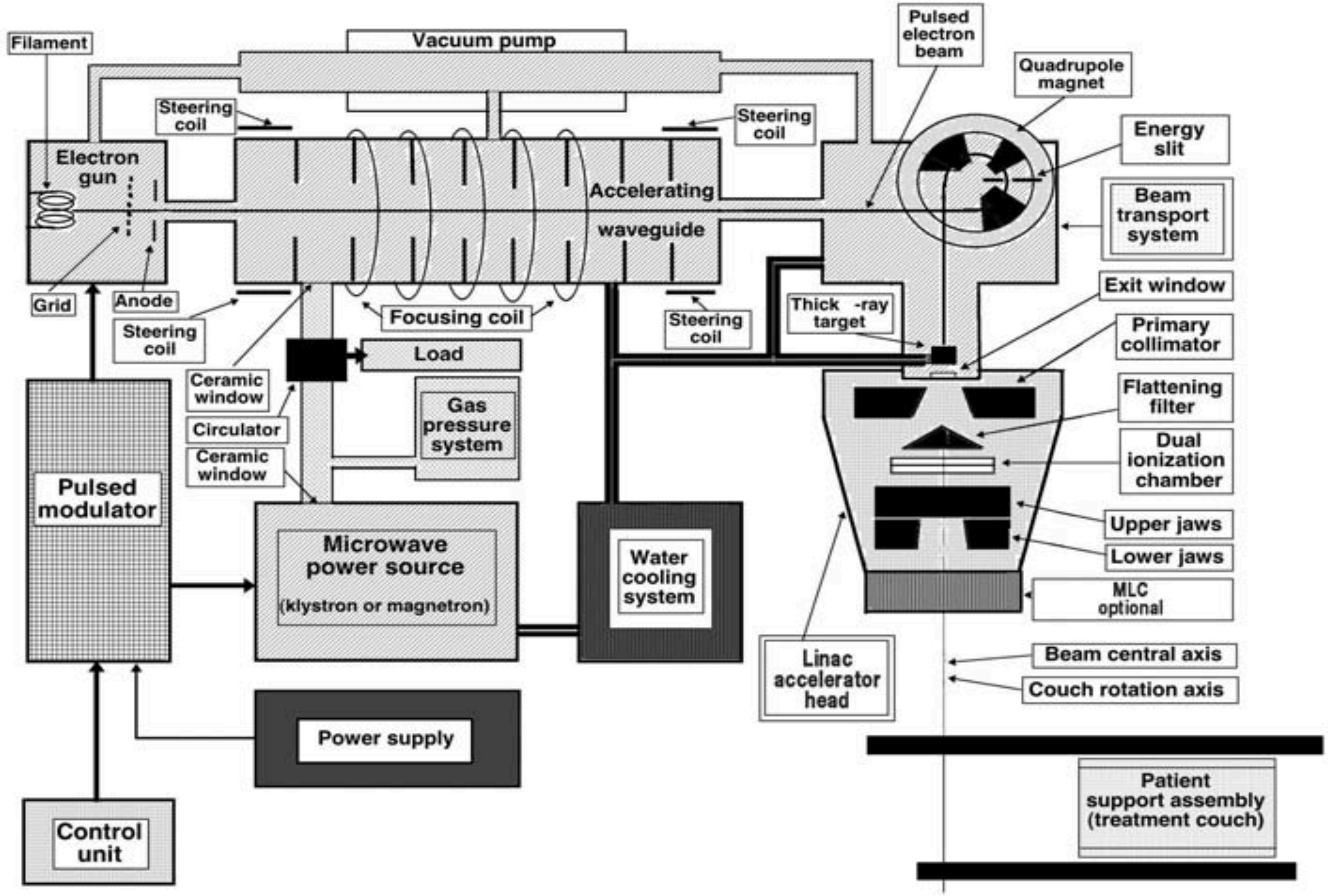
Linacs – Components

- To produce a beam we need
  - Injection system
  - Radiofrequency generator
  - Accelerating section
  - Auxiliary systems
  - Beam transport system
  - Collimation and beam control system

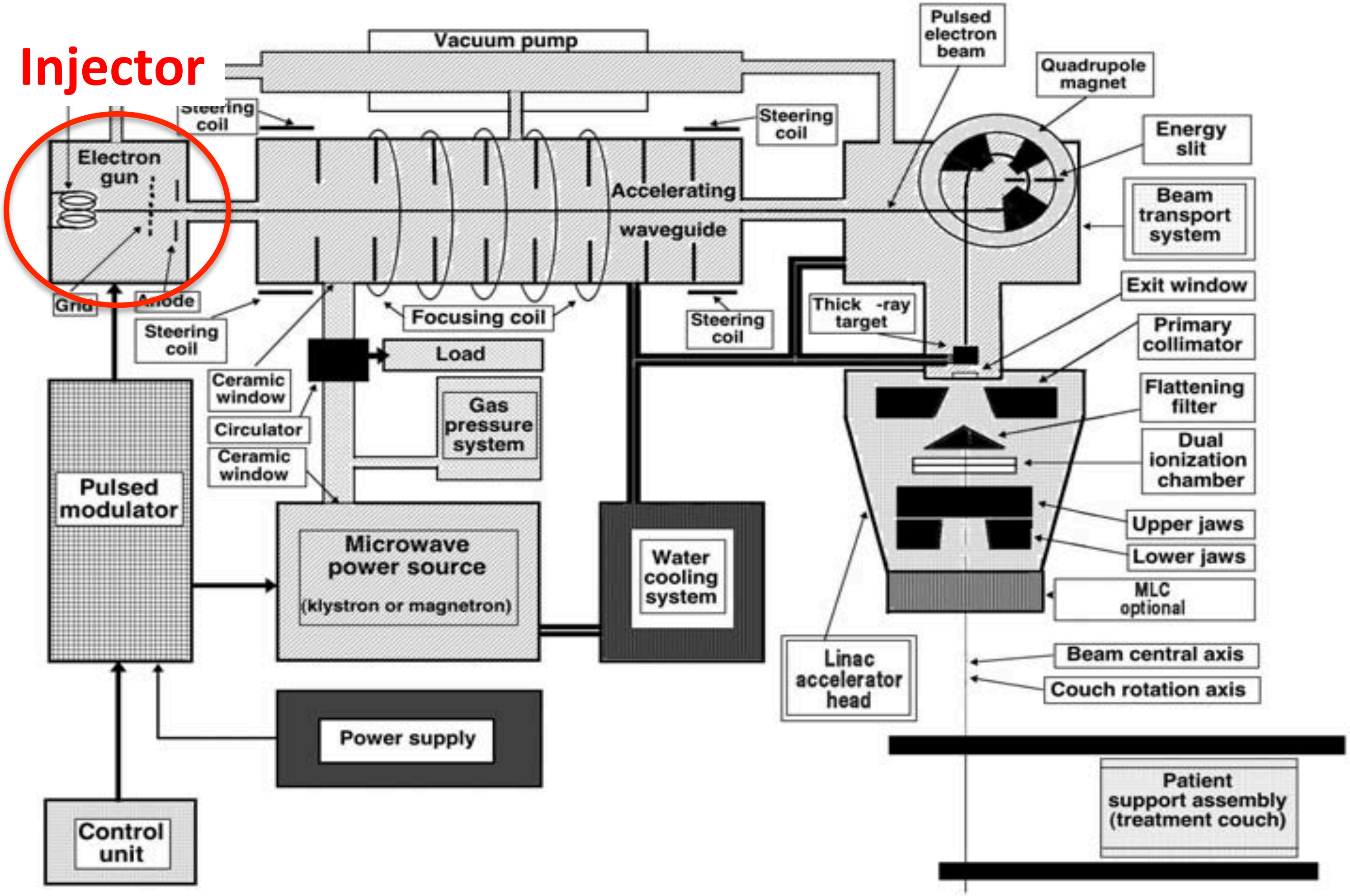
Linacs – Components



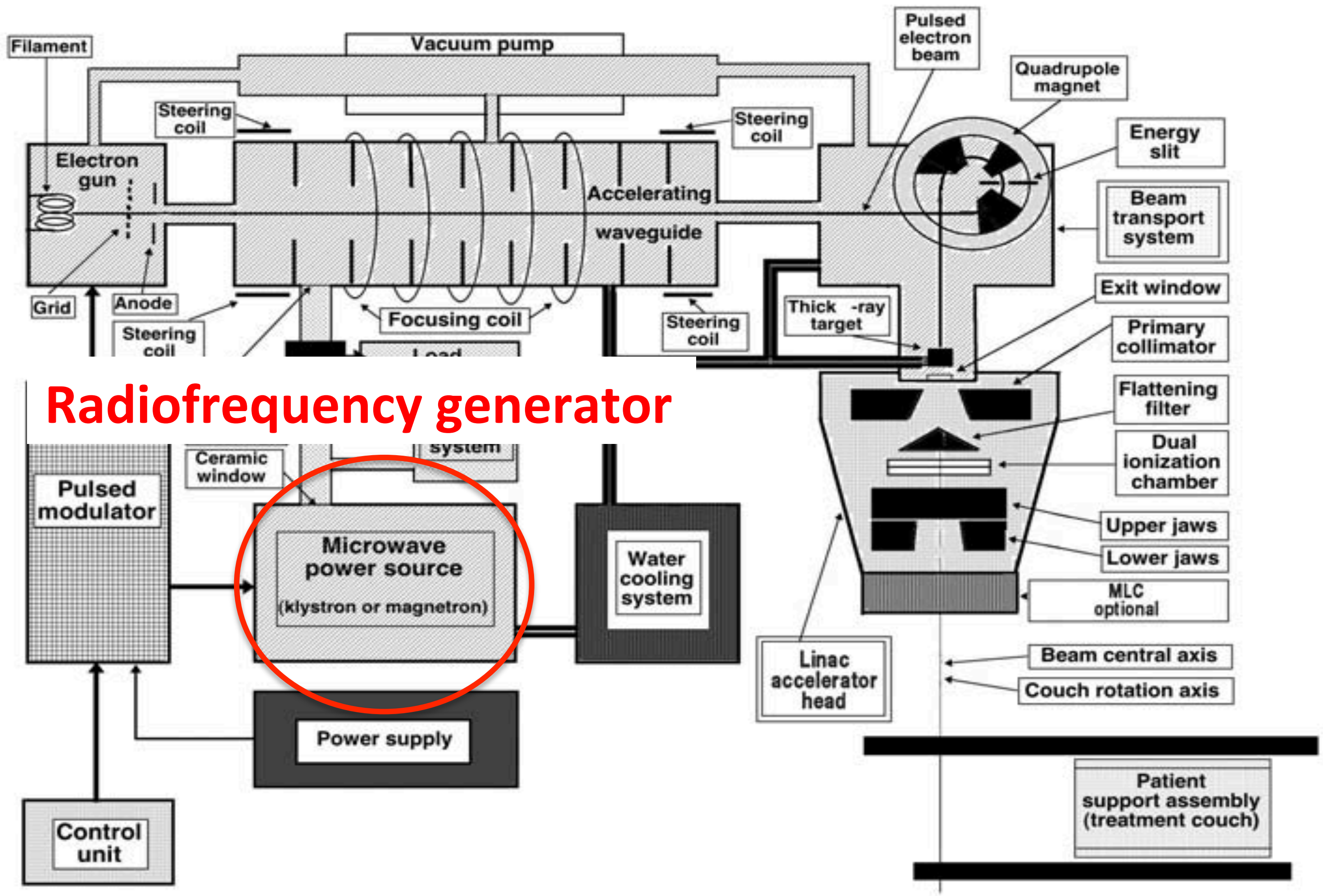
Linacs – Components



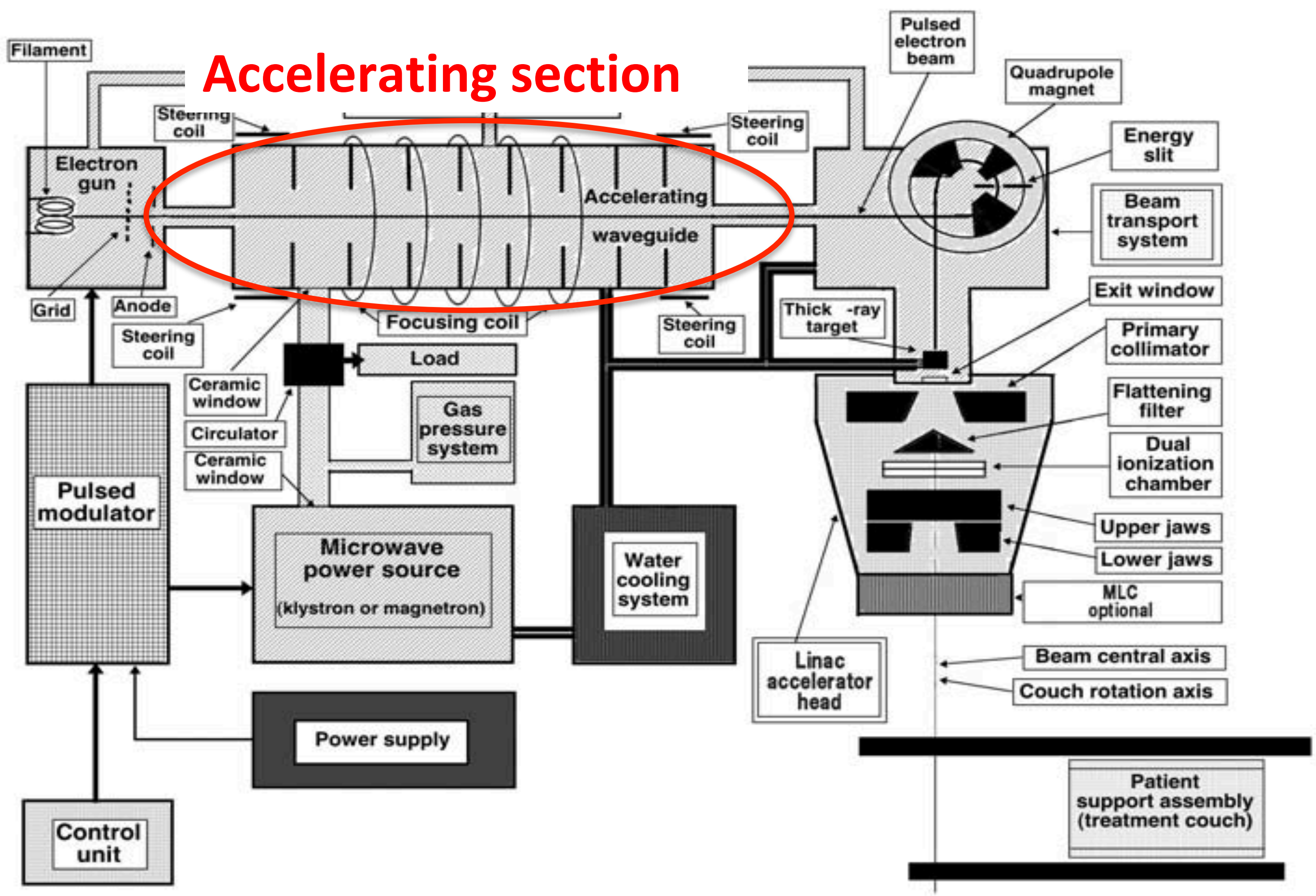
Linacs – Components



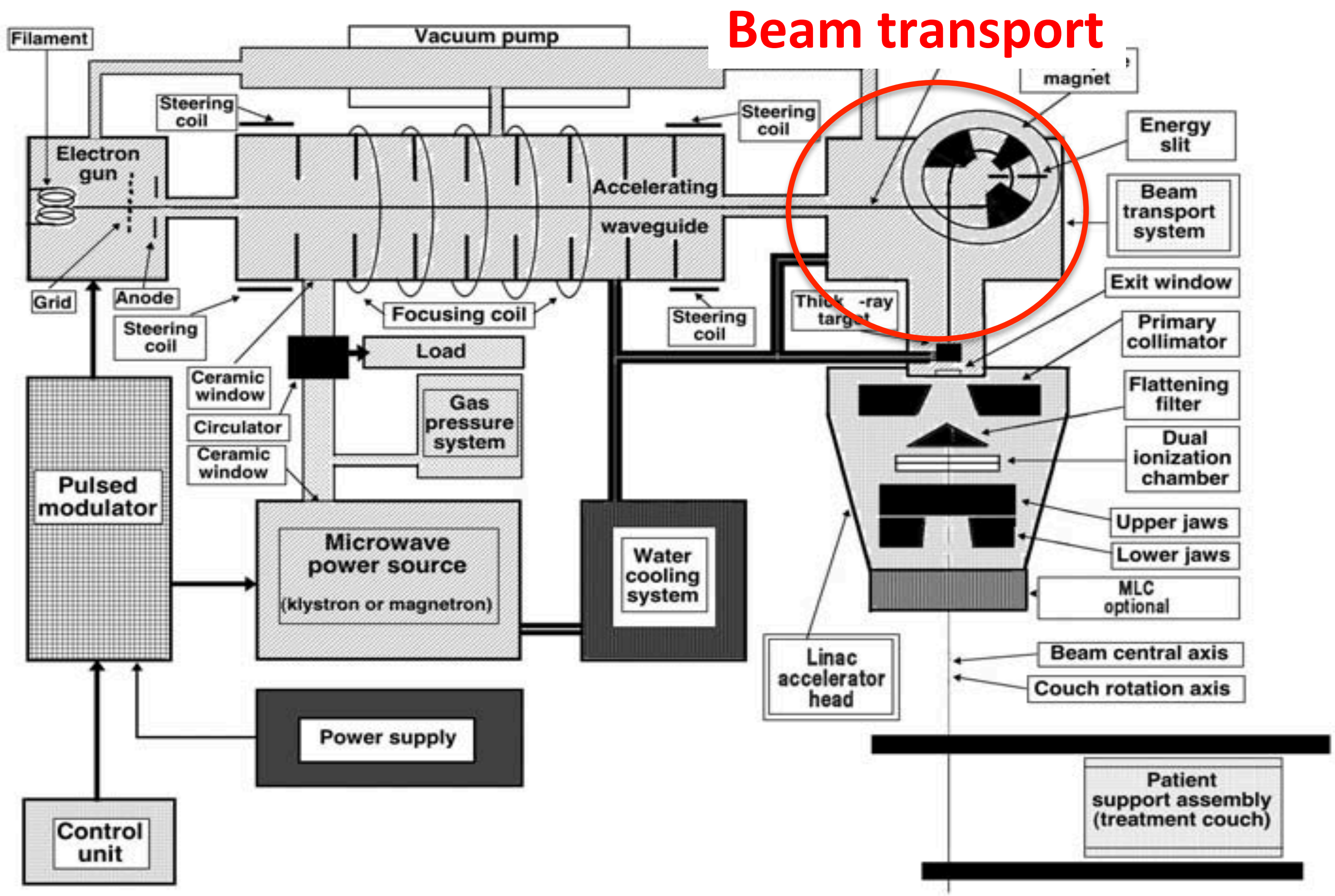
Linacs – Components



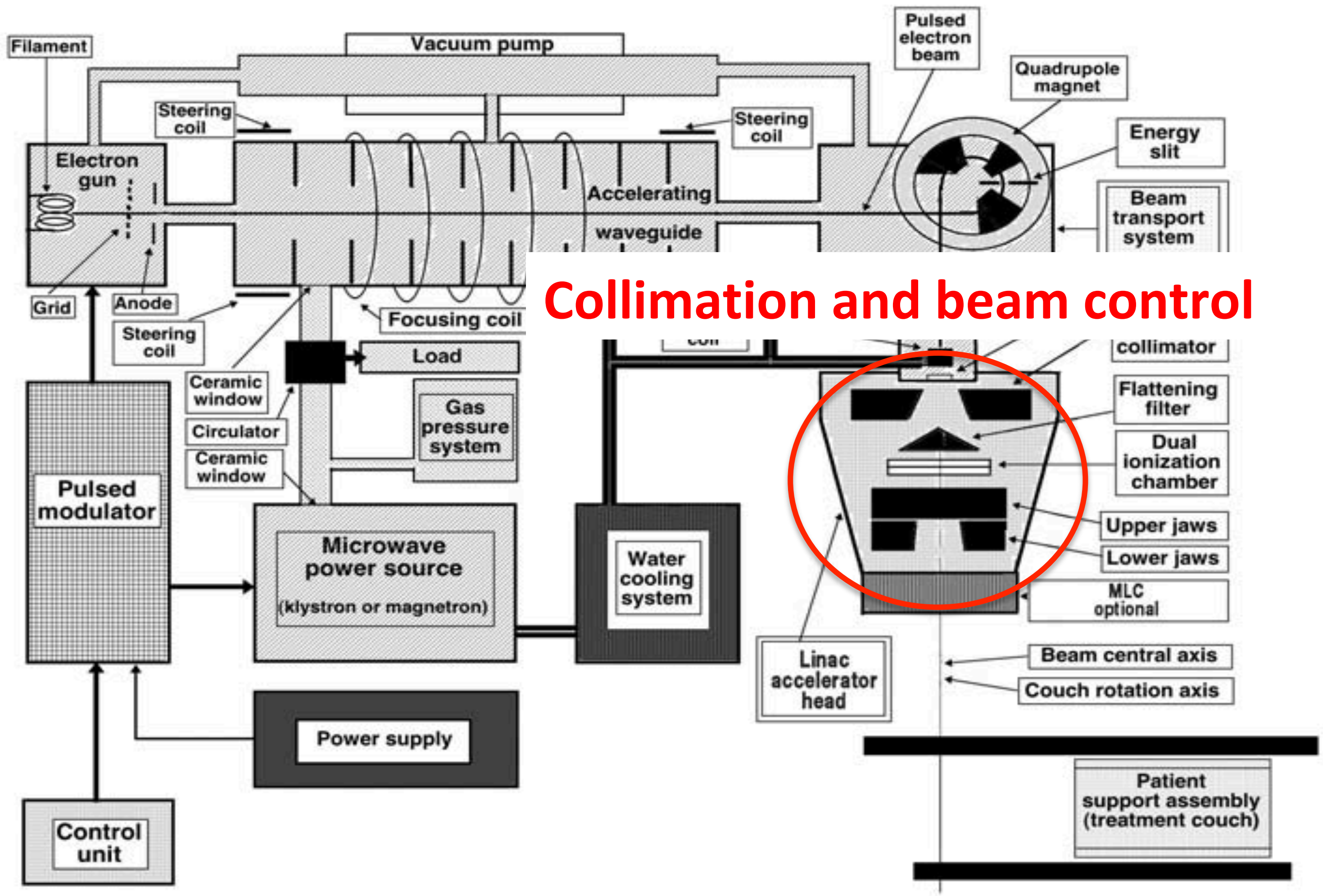
Linacs – Components



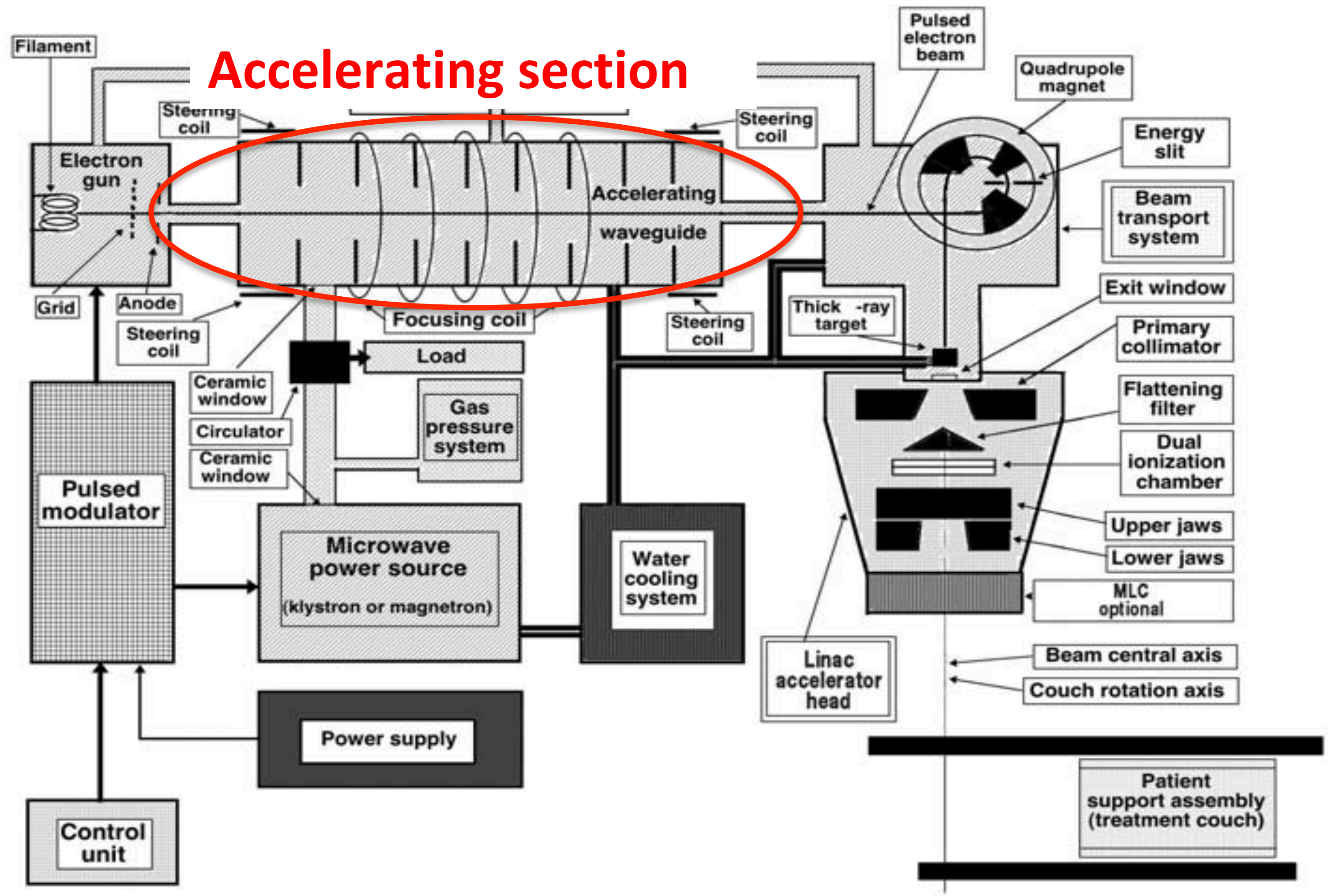
Linacs – Components



Linacs – Components



Linacs – Waveguide

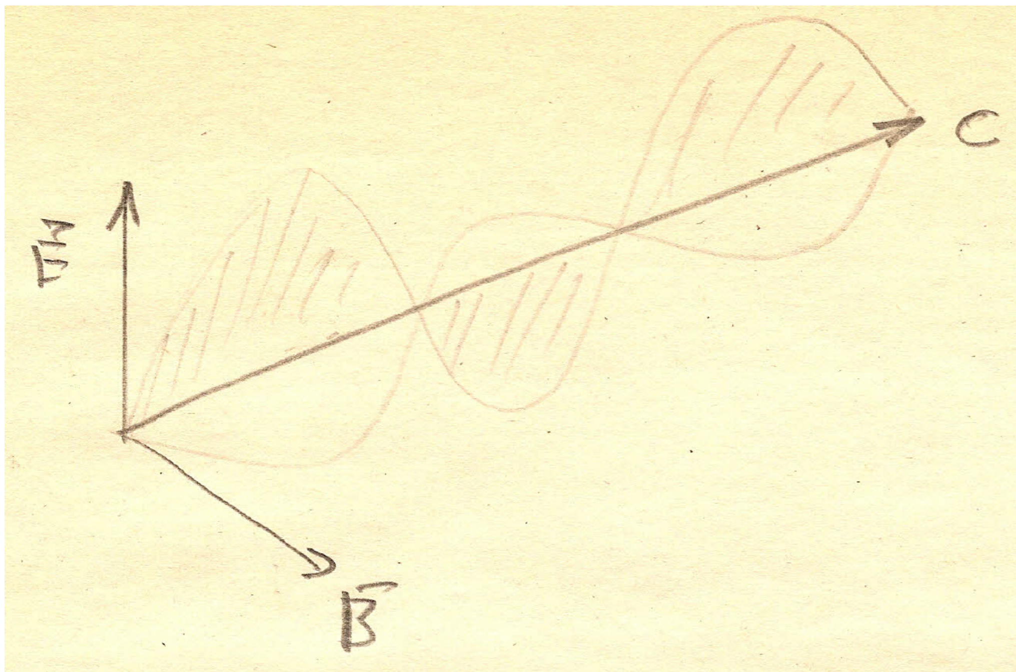


Linac – Waveguide

- Particles travel in an electric field E and in an induction magnetic field B
  - Lorentz
  $$\bar{F} = q\bar{E} + q\left(\bar{v} \times \bar{B}\right)$$
  - Work
  $$\bar{F} \cdot \bar{v} = q\bar{E} \cdot \bar{v} + q\left(\bar{v} \times \bar{B}\right) \cdot \bar{v}$$
  $$\left(\bar{v} \times \bar{B}\right) \cdot \bar{v} = 0$$
- The acceleration of charged particles is excusively due to electric field

Linac – Waveguide

- In vacuum, Electromagnetic filed propagates in the TEM mode
  - Transverse ElectroMagnetic field



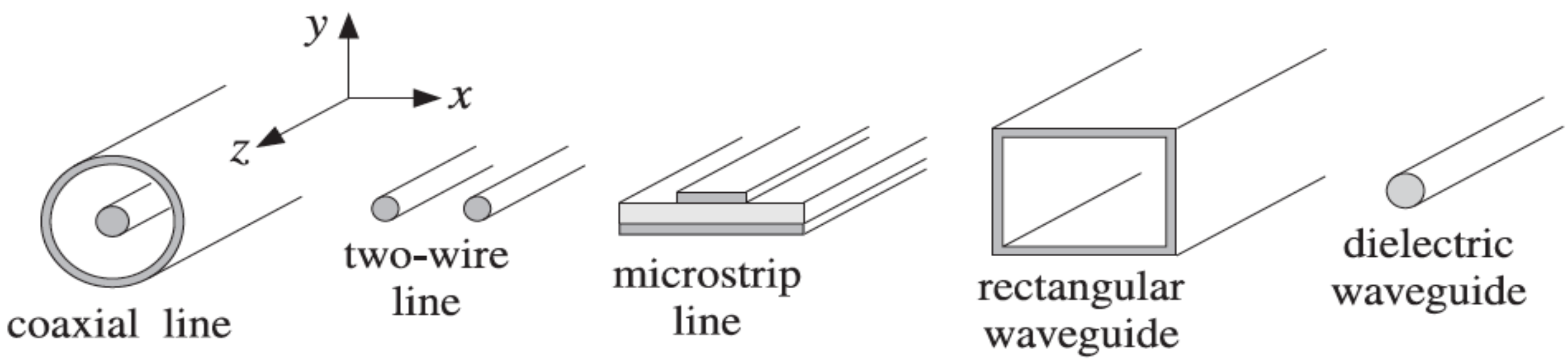
Linac – Waveguide

- For continuously accelerate electrons we need
  1. **E** // electron propagation
  2. Wave speed < c
  3. If $\mathbf{v}_{e-}$ increases, so is $\mathbf{v}_{\mathbf{E}}$
  4. Electron injection synchronized

- Solution: Waveguide

Linac – Waveguide

- Types of waveguides



- Waveguide is particular
  - There is no support for wave transport

Linac – Waveguide

- Linacs: circular waveguides
- Perfect conductor

$$\bar{n} \cdot \bar{B} = 0 \quad ; \quad \bar{n} \times \bar{E} = 0$$

- So propagation mode is
  - TM (transverse magnetic)
  - TE (transverse electric)
  - (at least one longitudinal component)

Linac – Waveguide

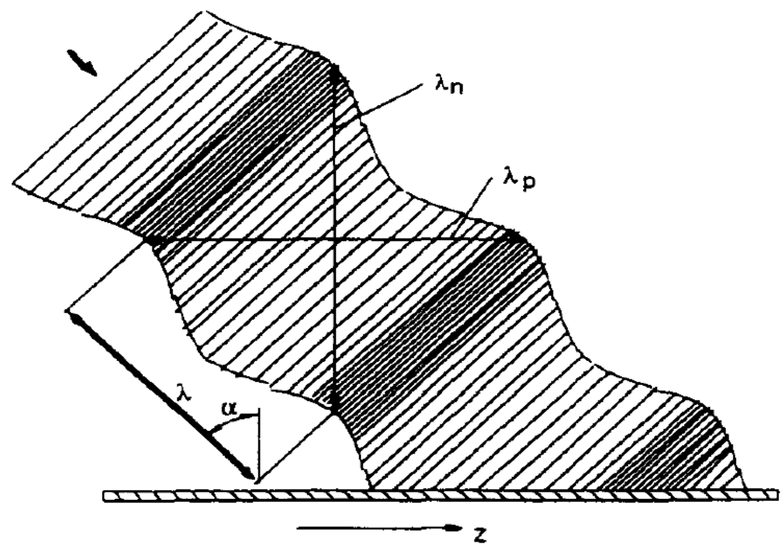
- For continuously accelerate electrons we need
  1. **E** // electron propagation ✓
  2. Wave speed < c
  3. If $\mathbf{v}_{e-}$ increases, so is $\mathbf{v}_{\mathbf{E}}$
  4. Electron injection synchronized

Linac – Waveguide

- The propagation of an « oblique » wave

$$v_{ph} = \frac{\lambda_p}{\lambda} c = \frac{c}{\sin\alpha} > c$$

$$v_g = c \sin\alpha$$

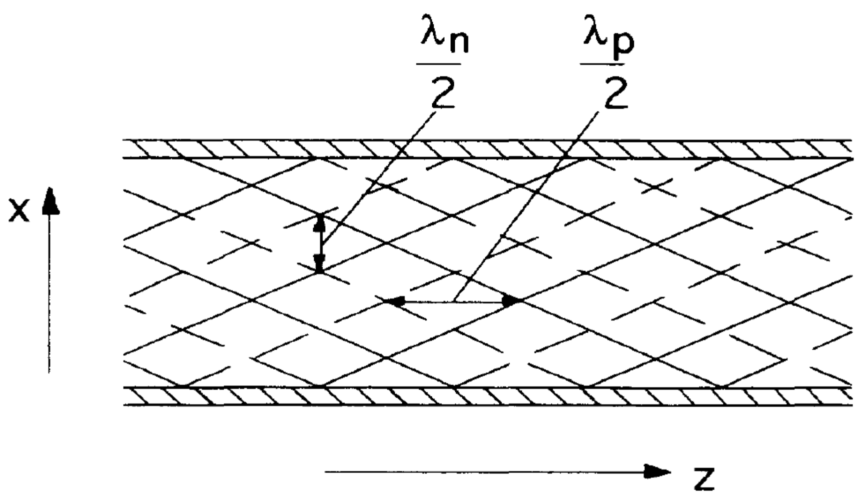


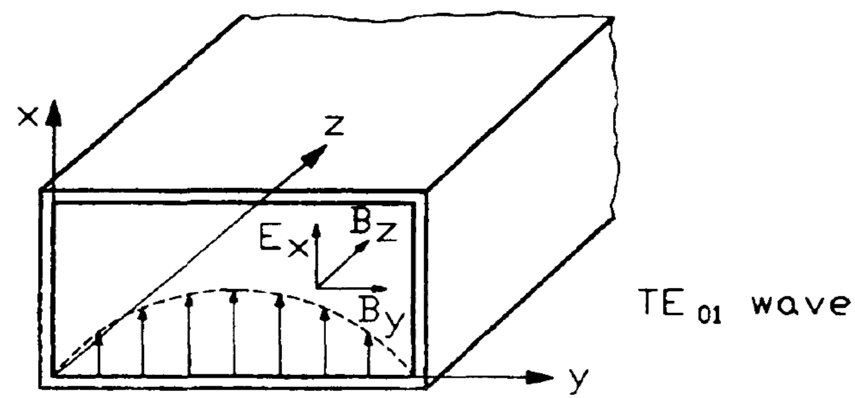
Linac – Waveguide

- In a waveguide, border condition must be satisfied for both walls

$$\bar{n} \cdot \bar{B} = 0 \quad ; \quad \bar{n} \times \bar{E} = 0$$

- α cannot be any





Linac – Waveguide

- EM wave

$$E_z(x,y,z,t) = X(x)Y(y)Z(z)T(t)$$

$$T(t) \propto e^{i\omega t}$$

$$Z(z) \propto e^{-ikz}$$

$$\Rightarrow E_z = F(x,y)e^{i(\omega t - kz)}$$

Linac – Waveguide

- In cylindrical coordinates

$$E_z = Z(z)R(r)T(t)$$

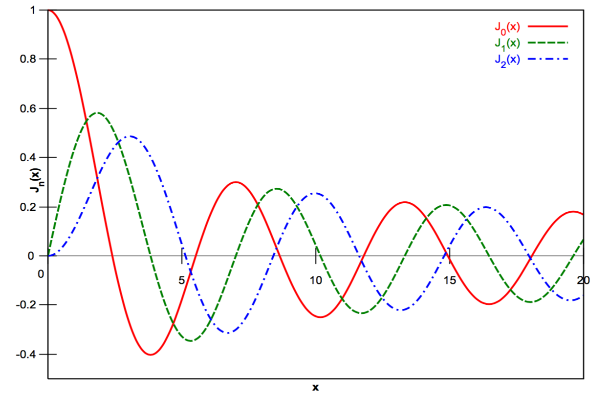
$$\frac{\partial^2 E_z}{\partial z^2} + \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial E_z}{\partial z}\right) - \frac{1}{c^2}\frac{\partial^2 E_z}{\partial t^2} = 0$$

$$\frac{\partial^2 R}{\partial r^2} + \frac{1}{r}\frac{\partial R}{\partial r} + \underbrace{\left(\frac{\omega^2}{c^2} - k^2\right)}_{K_R^2} R = 0$$

Linac – Waveguide

- The solution is a Bessel function at order 0

$$R(r) = AJ_0(K_r r)$$



- At the surface (cylinder radius a)

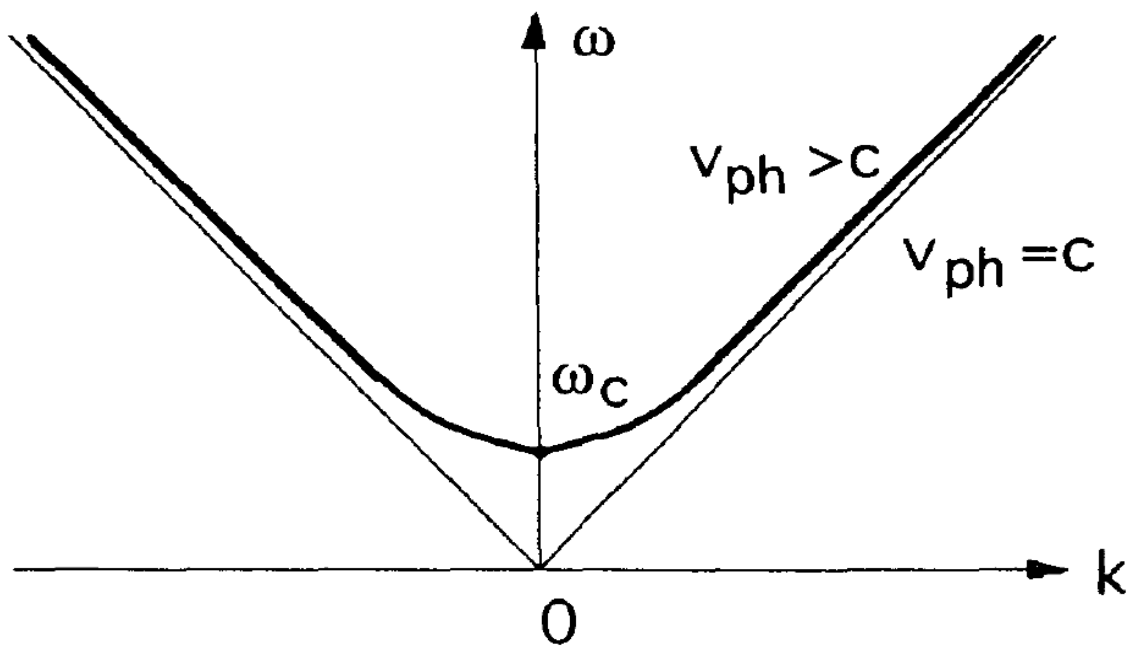
$$J_0(K_r a) = 0$$

$$\Rightarrow K_r = \frac{2.405}{a}$$

Linac – Waveguide

- Dispersion diagramme

$$\frac{\omega^2}{c^2} = K_r^2 + k^2$$



Linac – Waveguide

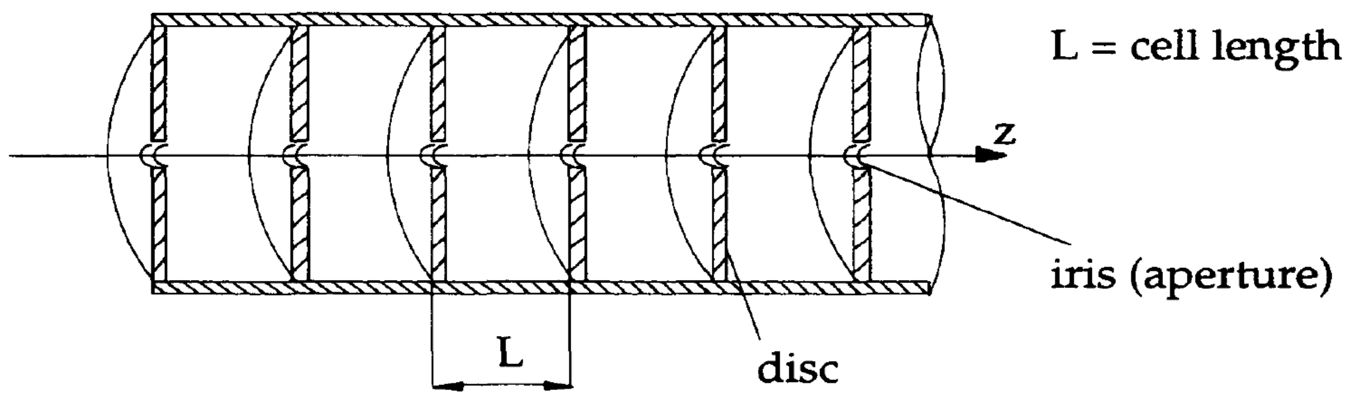
- To accelerate a particle we need

$$v_{ph} = v_p$$

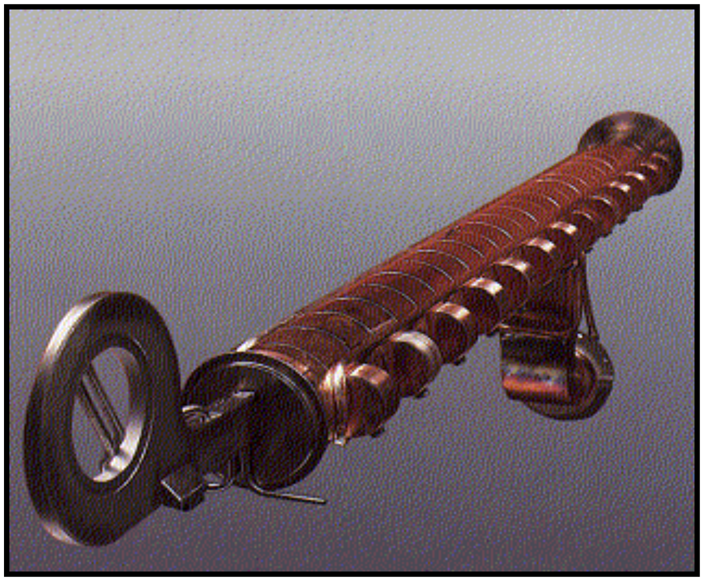
- Impossible because

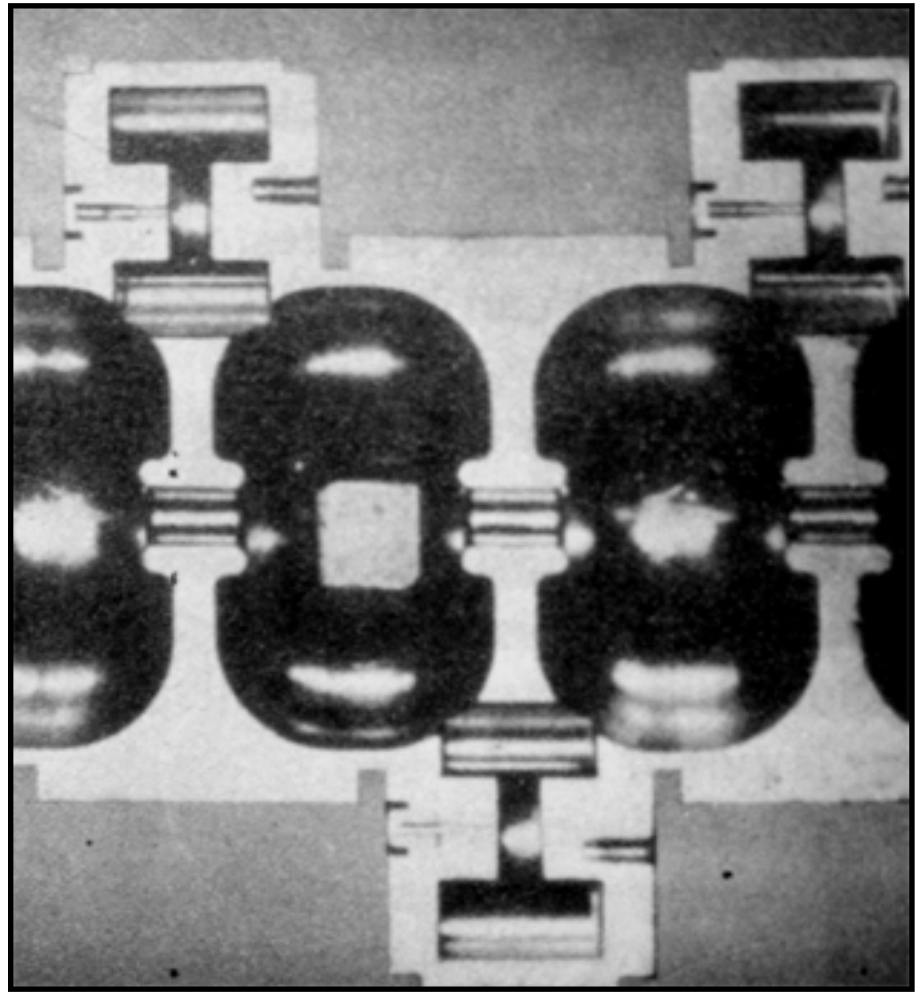
$$v_{ph} > c$$

- We slow the wave with iris



Linac – Waveguide





Linac – Waveguide

- To solve it
  - Floquet theorem
    - « In a periodical structure, for a given oscillation mode and a given frequency, the wave fuction is multiplied by a constant from one period to the other »
    - A type of fuction like: e^{-ik_0z}
  - Border conditions are too complex to satisfy only one propagation mode
  - Spectrum called harmonics space

Linac – Waveguide

- One gets

$$E_z(r,z,t) = F(r,z)e^{i(\omega t - k_0 z)}$$

$$F(r,z+L) = F(r,z)$$

$$F(r,z) = \sum_n a_n(r)e^{i(2\pi n/L)z}$$

- To be put into wave equation
- We can then find a solution where $v_{ph} < c$

Linac – Waveguide

- For continuously accelerate electrons we need
  1. **E** // electron propagation ✓
  2. Wave speed < c ✓
  3. If $\mathbf{v}_{e-}$ increases, so is $\mathbf{v}_{\mathbf{E}}$
  4. Electron injection synchronized

Linac – Waveguide

- Electron speed
  - 40 keV : ~ 0.4 c
  - 1 MeV: 0.941 c
  - 10 MeV: 0.999 c
- First cavities are a bit smaller
- Then, speed is « constant » and the electron only gain energy

Linac – Waveguide

- For continuously accelerate electrons we need
  1. **E** // electron propagation ✓
  2. Wave speed < c ✓
  3. If $\mathbf{v}_{e-}$ increases, so is $\mathbf{v}_{E}$ ✓
  4. Electron injection synchronized

Linac – Waveguide

- Electrons are injected at the wave propagation speed
  - ~ 0.4 c (40 keV)
- Electrons cannot be injected in a pulsed manner at 3 GHz
  - Continuous injection
  - E different -> creation of bunches

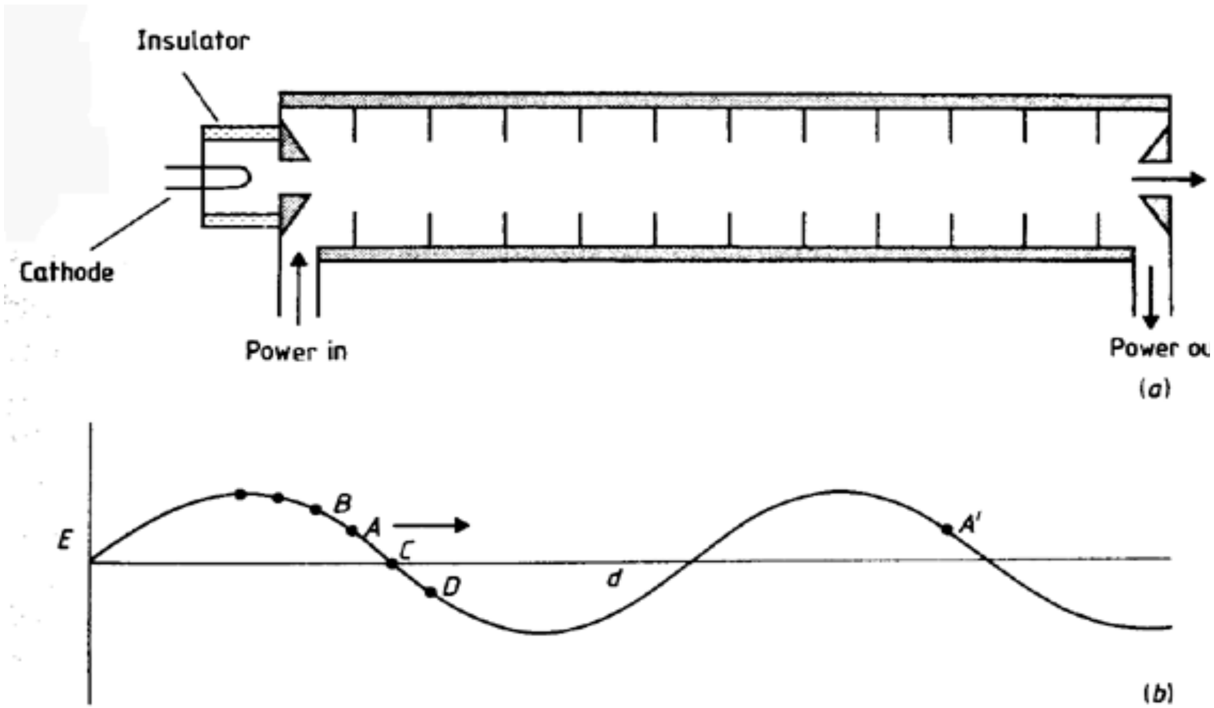
Linac – Waveguide

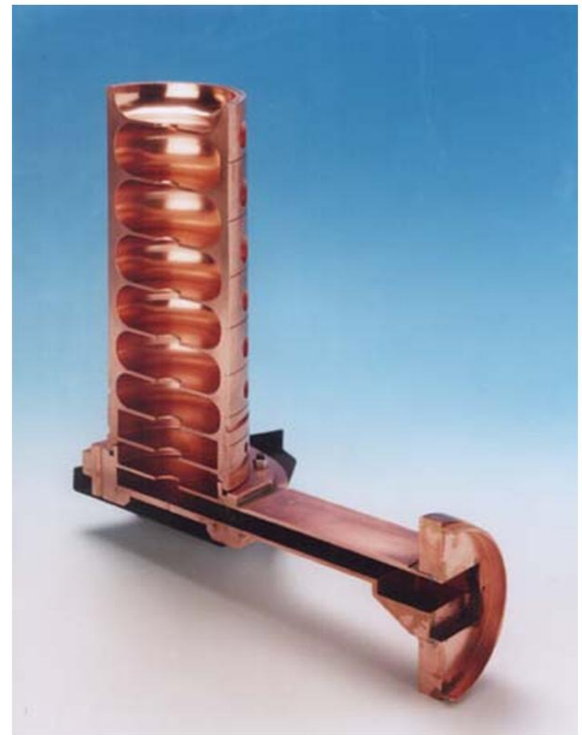
- For continuously accelerate electrons we need
  1. **E** // electron propagation ✓
  2. Wave speed < c ✓
  3. If $\mathbf{v}_{e-}$ increases, so is $\mathbf{v}_{E}$ ✓
  4. Electron injection synchronized ✓

Linac – Types

- Travelling wave accelerator
- Stationary wave accelerator
  – Creation of « knots and bellies » in the cavities
- No specific rule for the choice

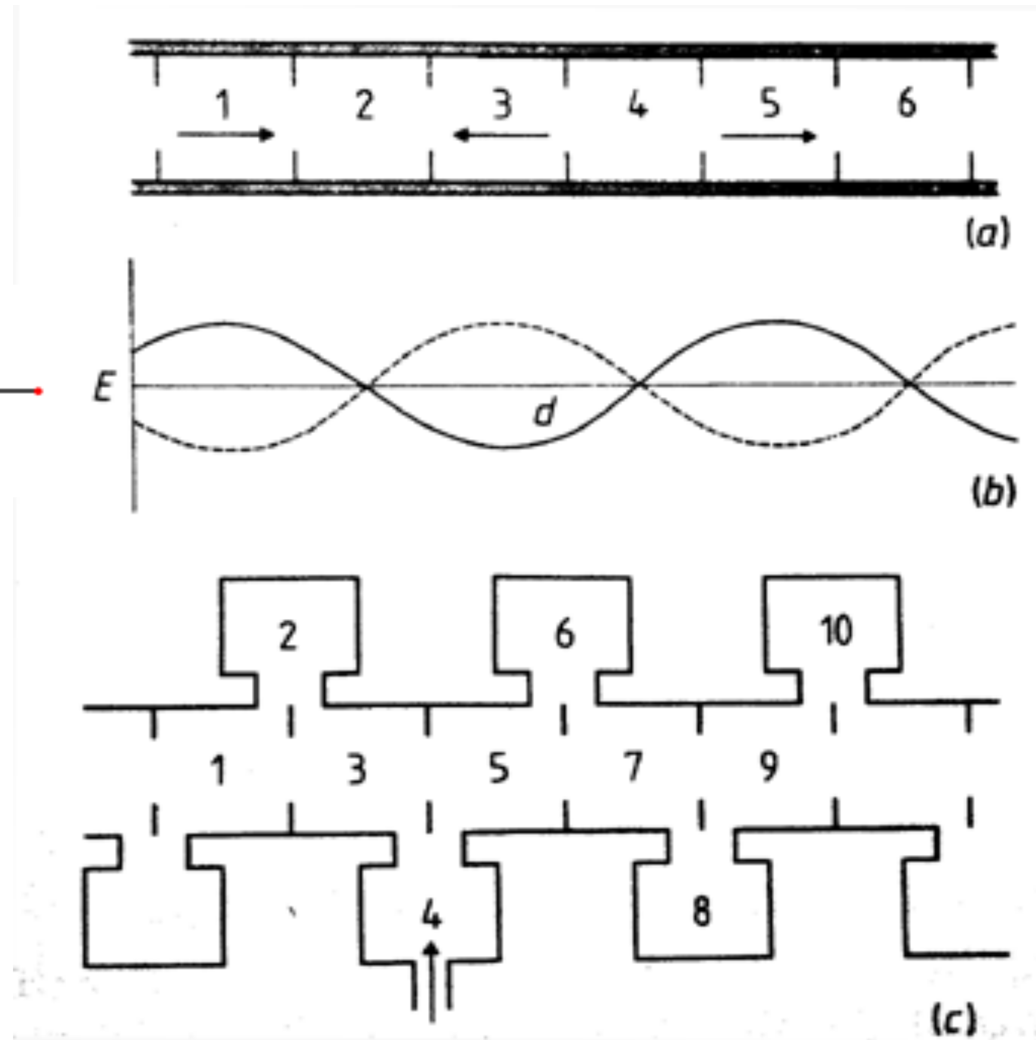
Travelling wave accelerator



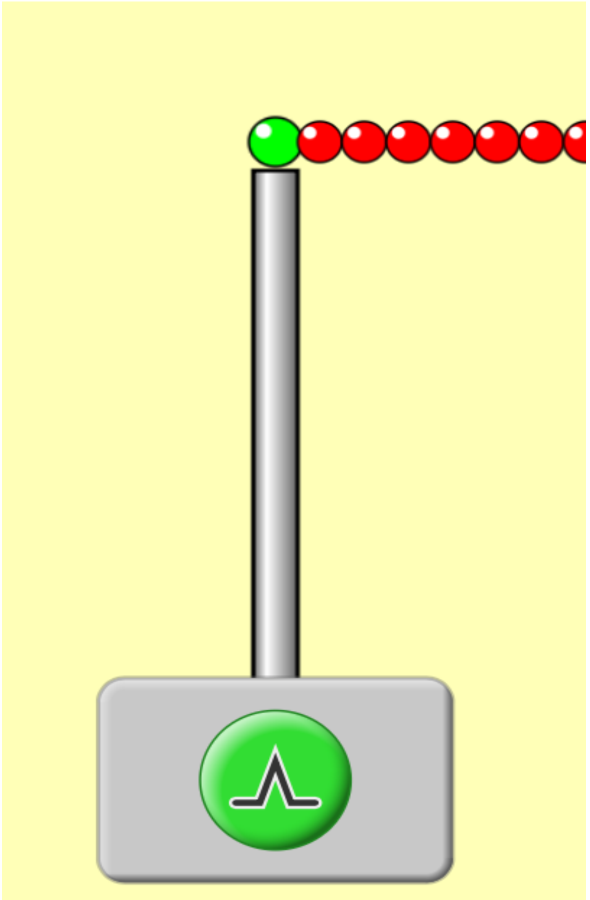


CHUV

Stationary wave accelerator

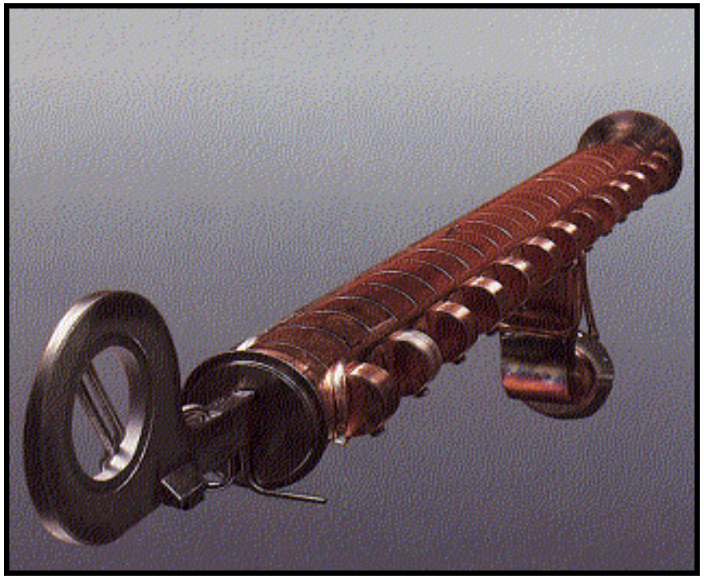


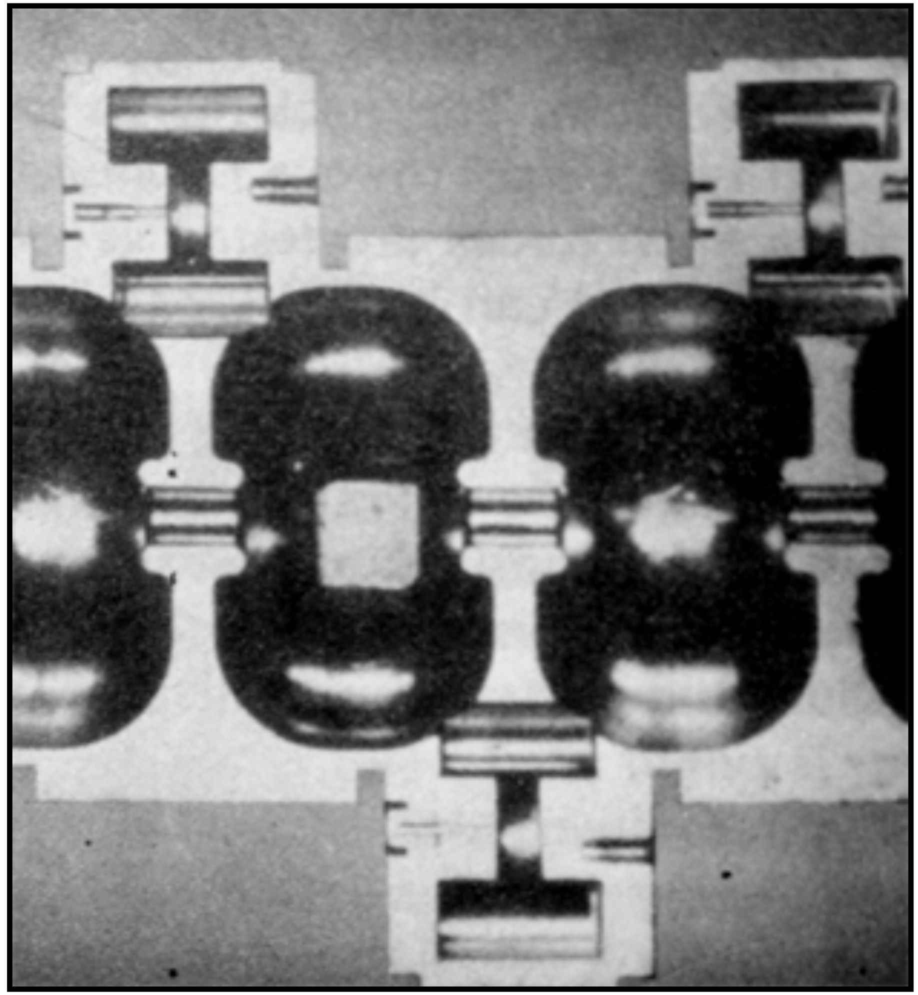
Stationary wave accelerator



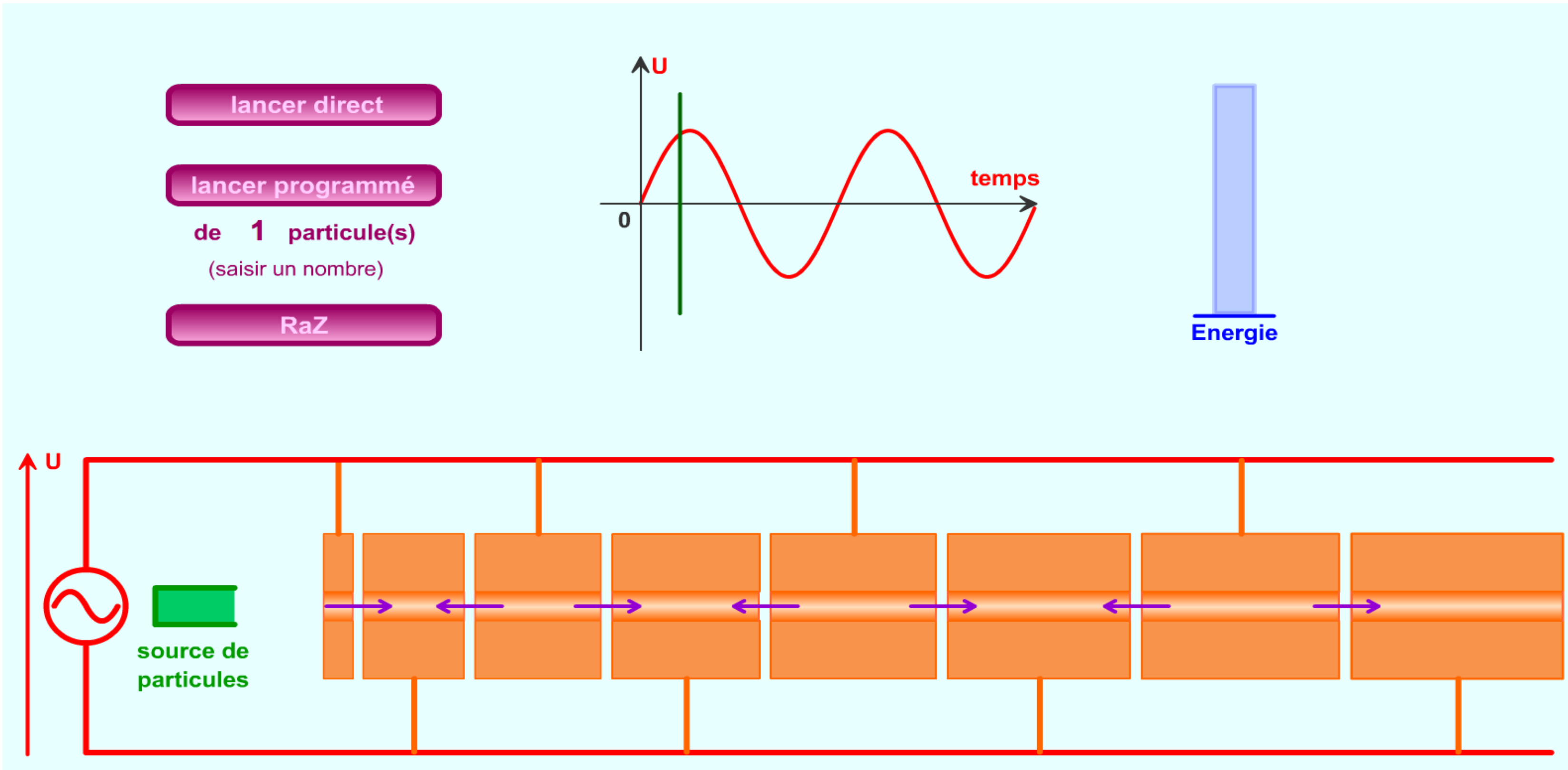
Phet.colorado.edu

Stationary wave accelerator



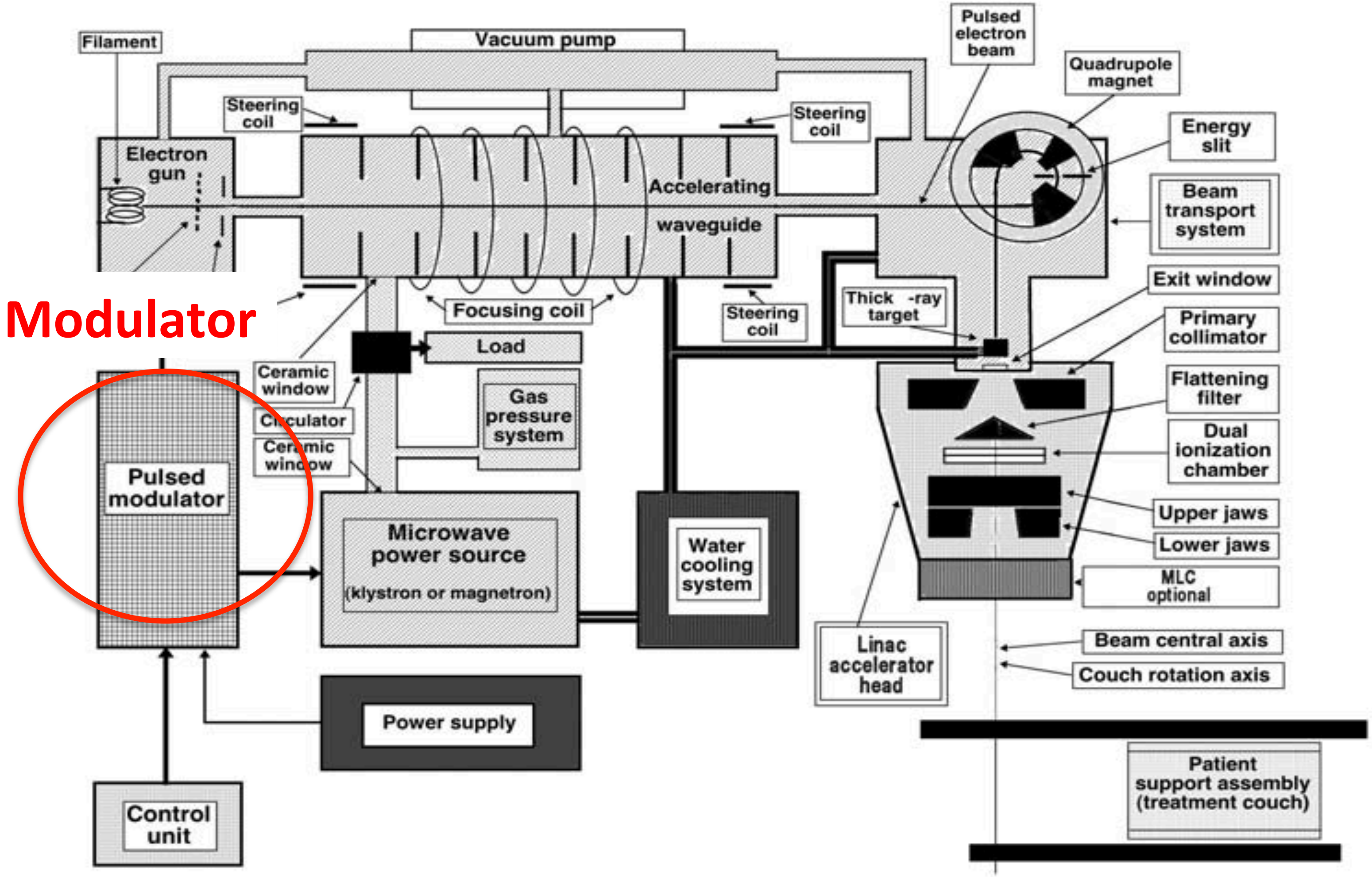


Stationary wave accelerator



www.sciences.univ-nantes.fr

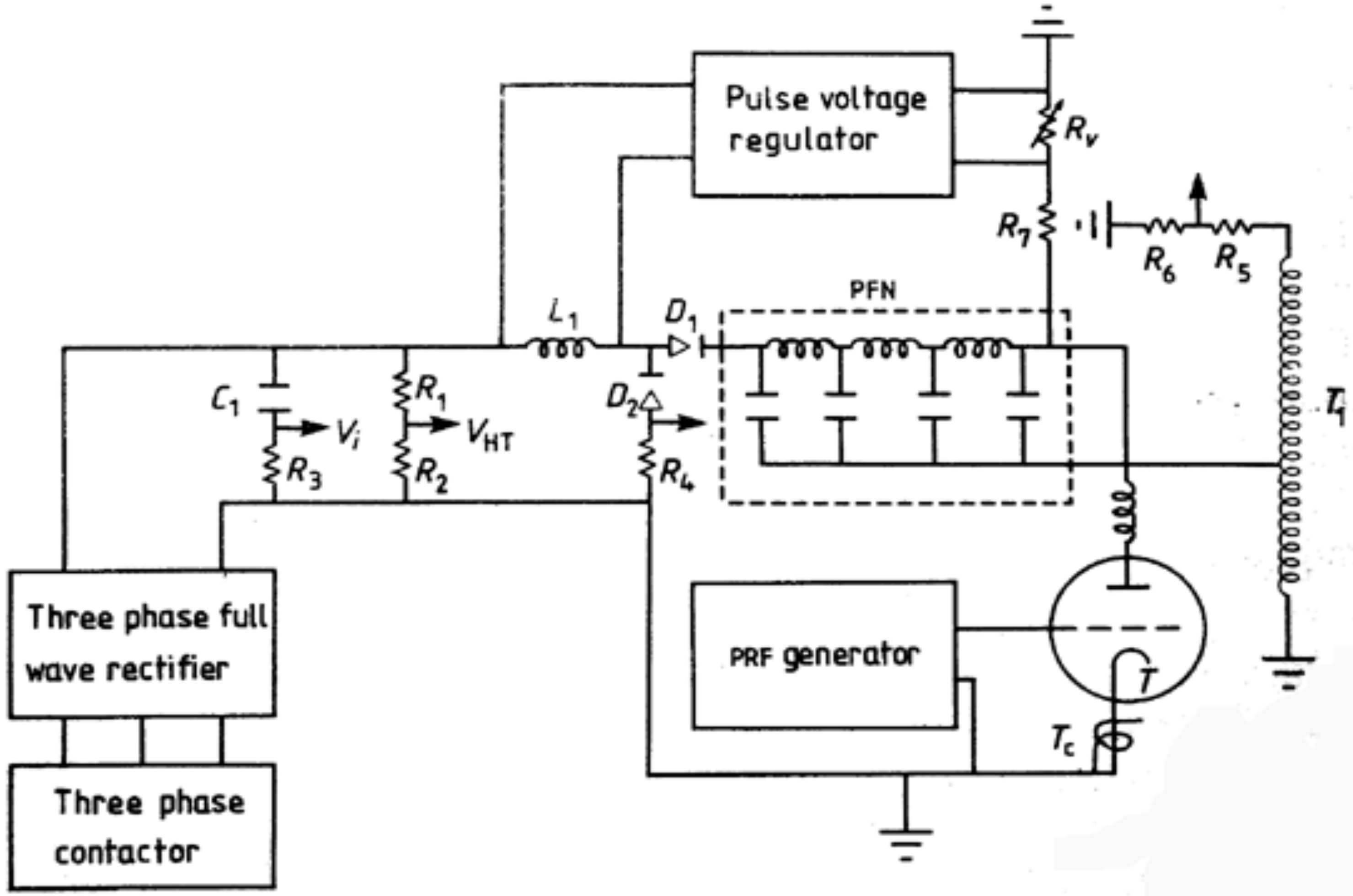
Linacs – Modulator



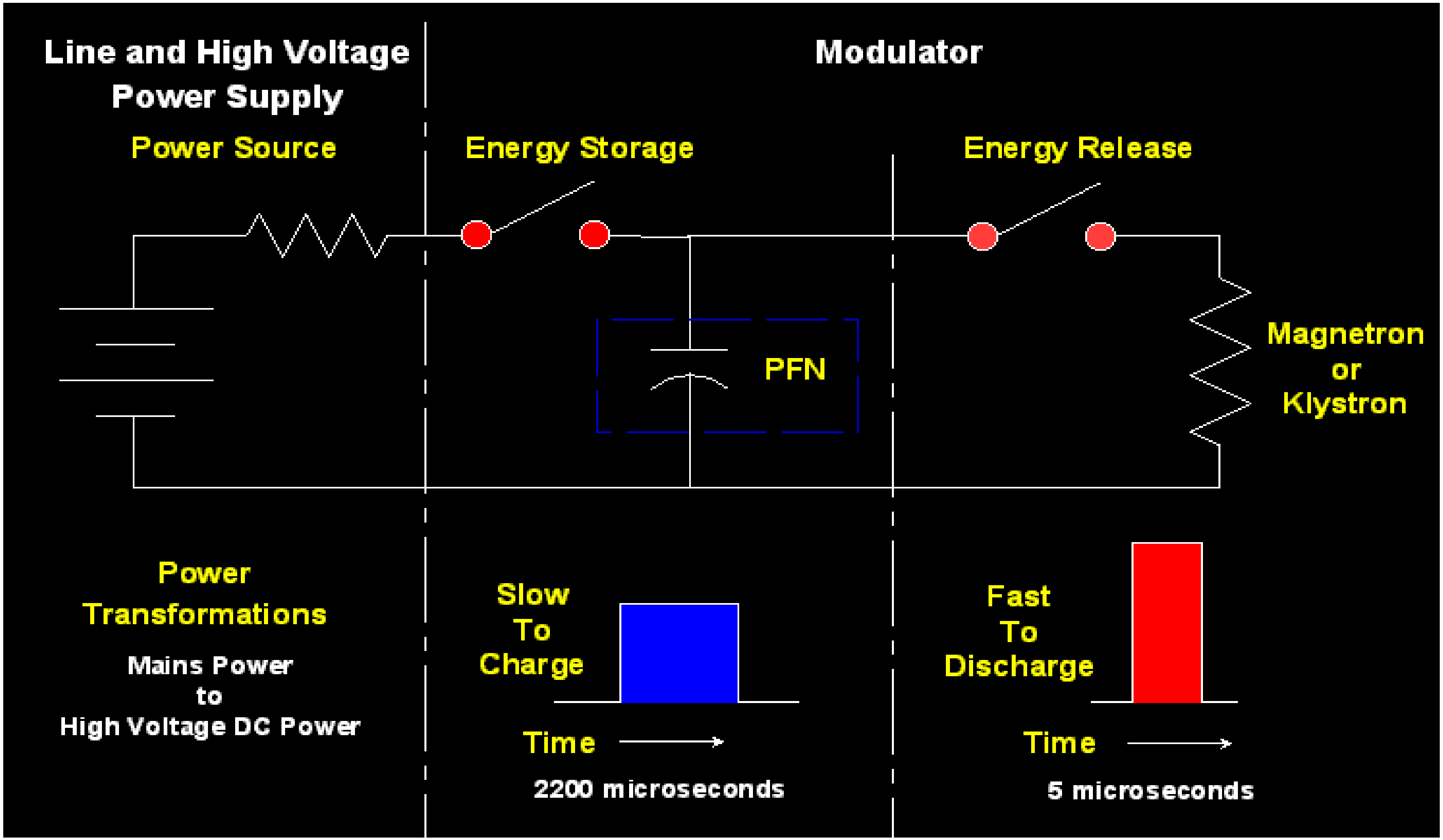
Linacs – Modulator

- Produces high-voltage for microwave generator
  - PFN (pulse forming network)
    - Produces pulsed high-voltage
    - Capacities in series
  - PRF (pulse repetition frequency)
    - Controls the repetition frequency
  - Thyratron
    - Ultra-fast switch
    - Elekta Synergy, 1200 A during 3.2 μs

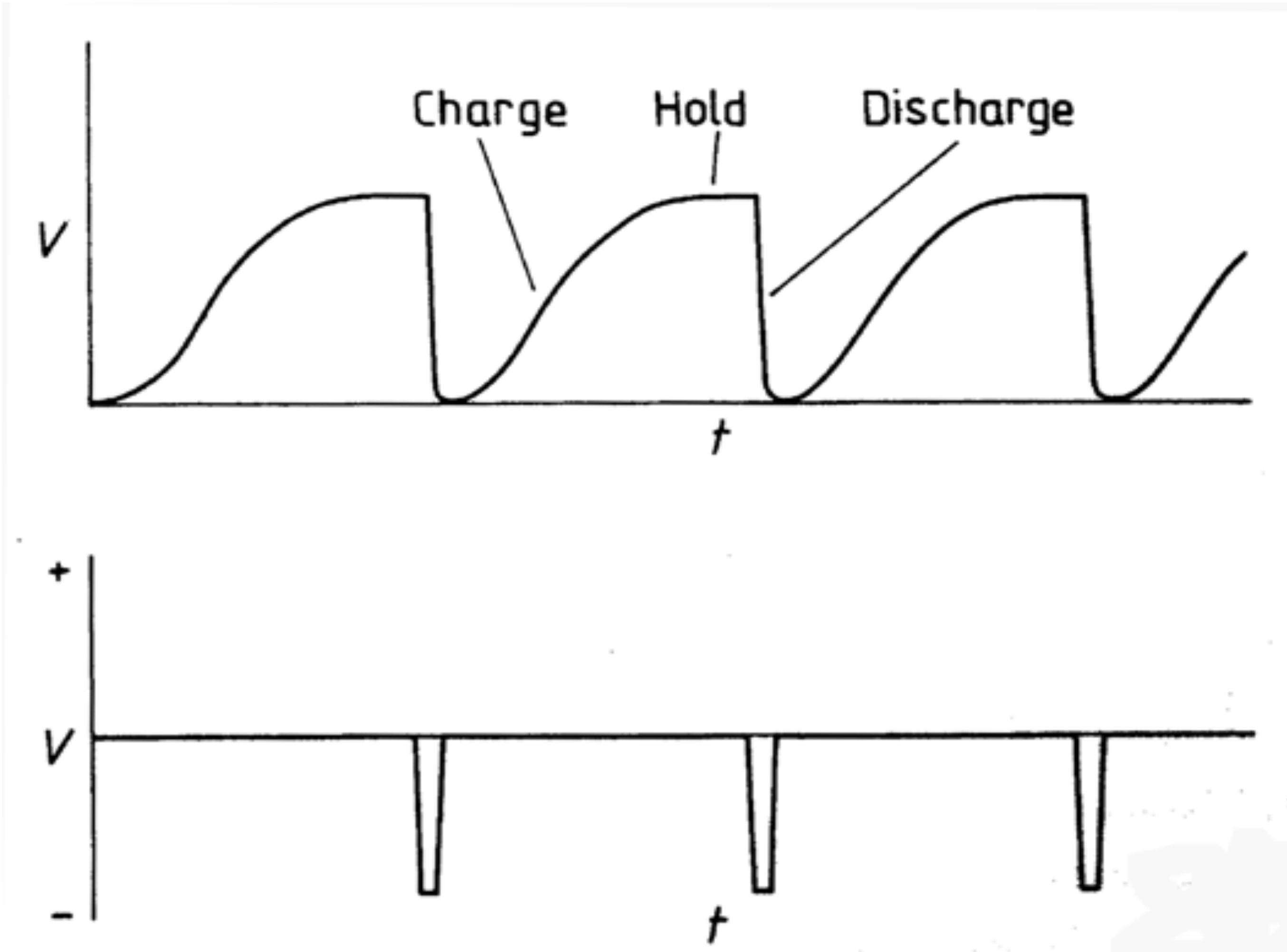
Linacs – Modulator



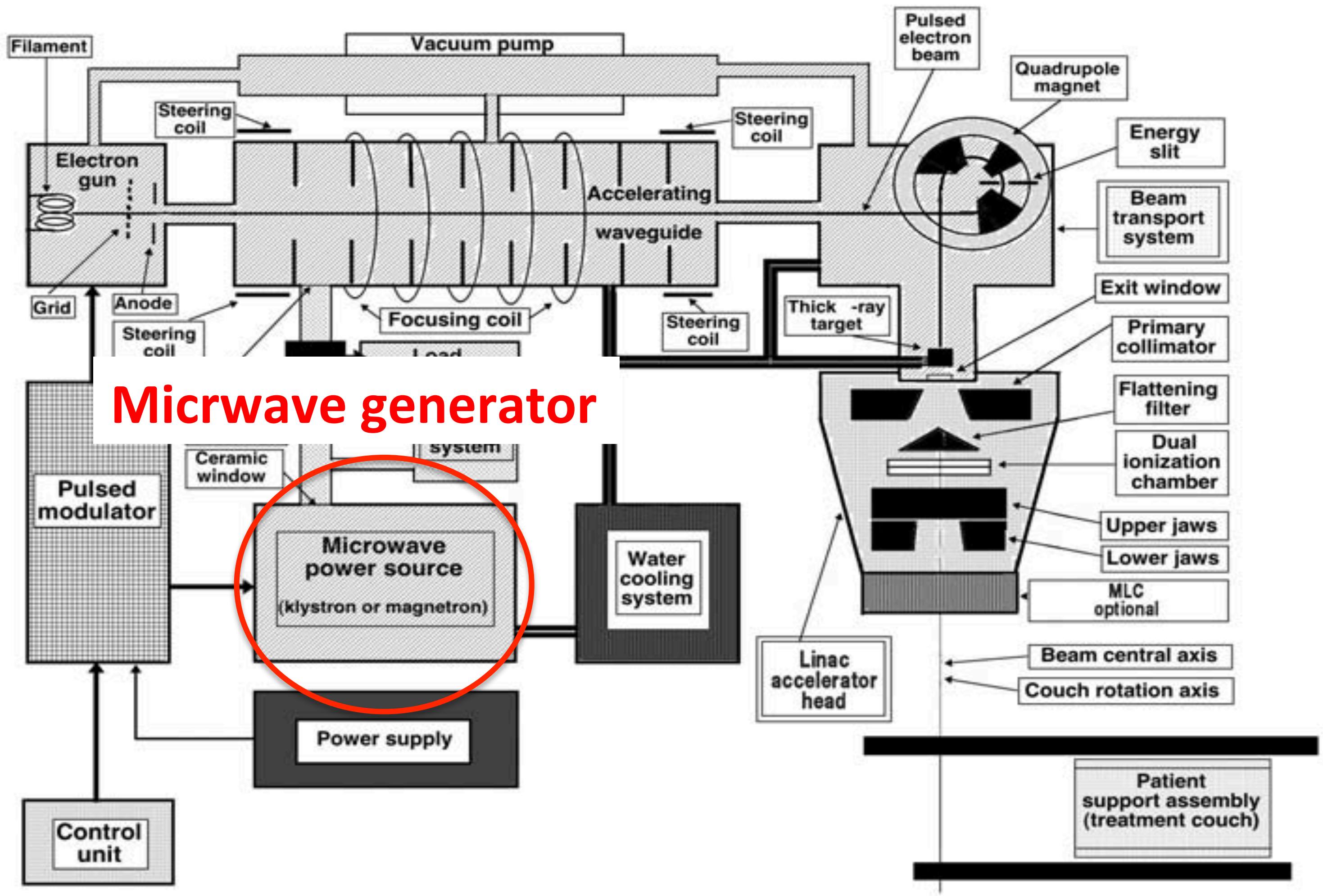
Linacs – Modulator



Linacs – Modulator



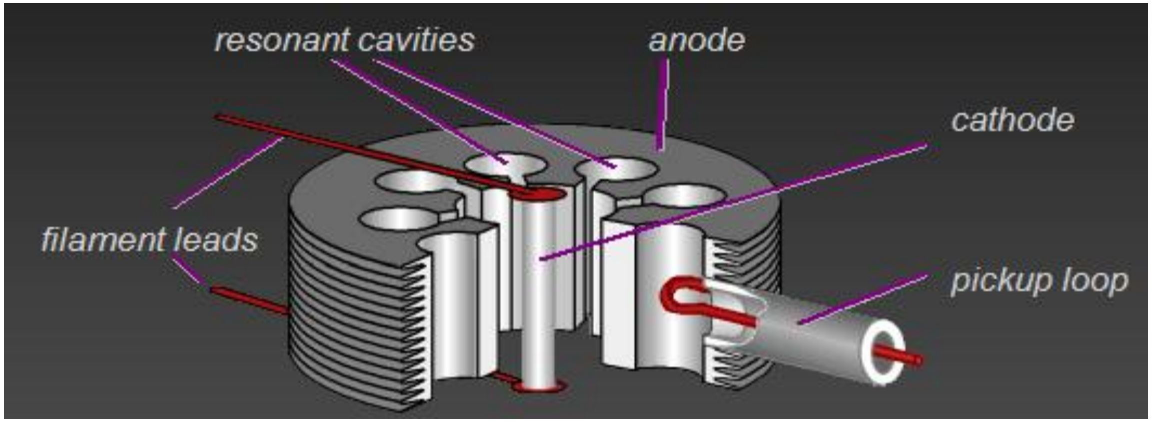
Linacs – Microwave generator

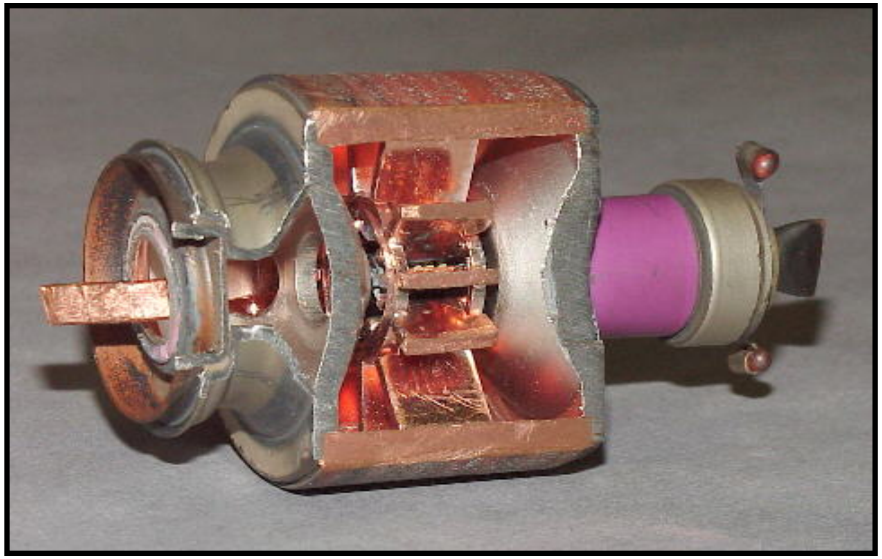


Linacs – Microwave generator

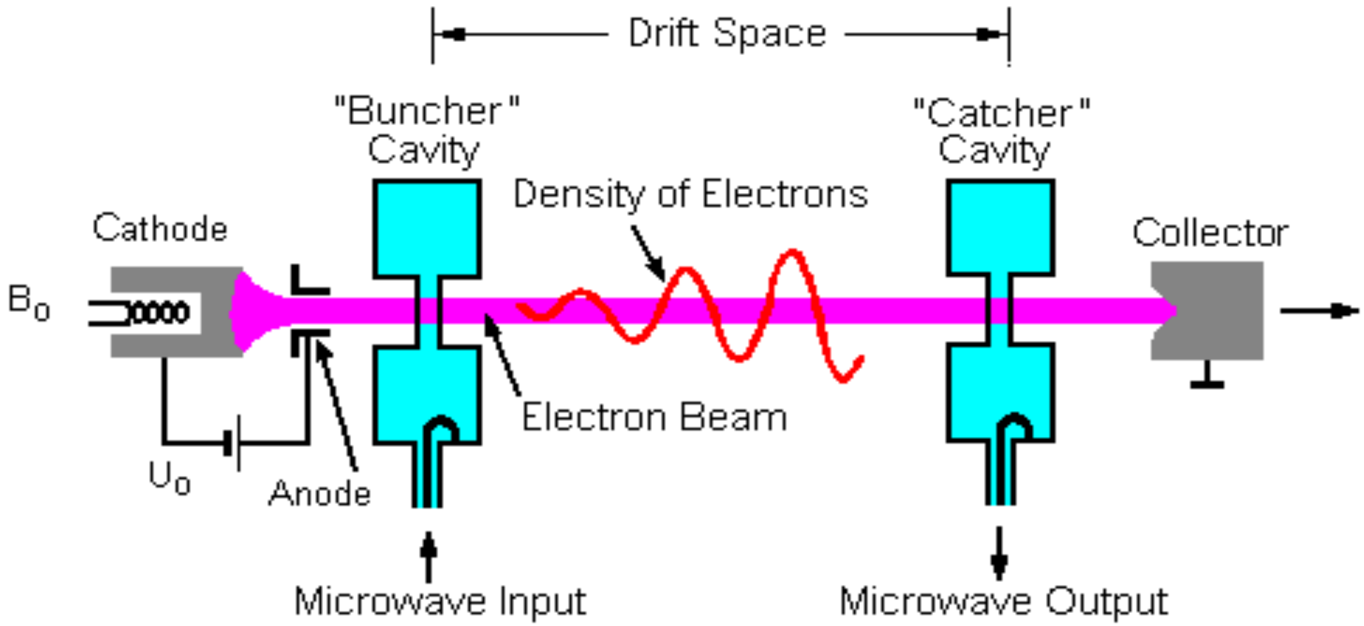
- Electrons produce EM field in resonant cavities
  - 3 GHz micrwaves
- In "S" band (3 GHz)
  - Some MW impulsions in some μs
    - 5 MW for Elekta Synergy during 3.2 μs

Magnetron


resonant cavities
anode
cathode
filament leads
pickup loop

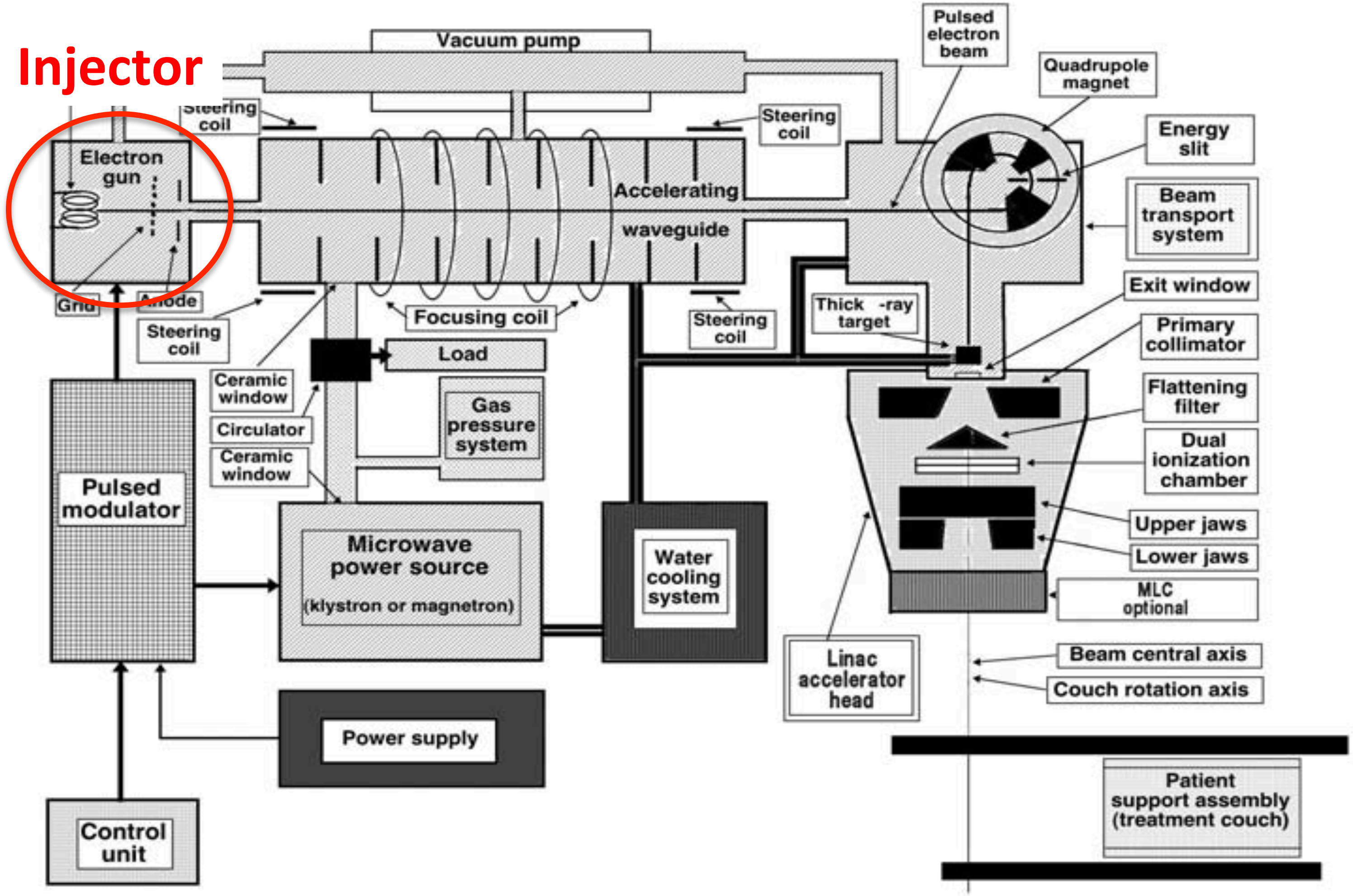


Klystron



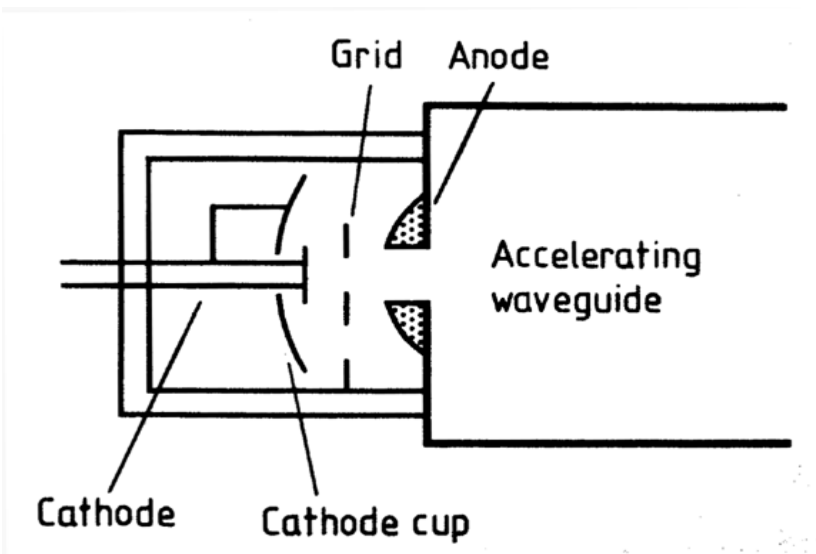
Drift Space
"Buncher" Cavity
"Catcher" Cavity
Density of Electrons
Cathode
Collector
B_0
Electron Beam
U_0
Anode
Microwave Input
Microwave Output

Linacs – Injector



Linacs – Injector

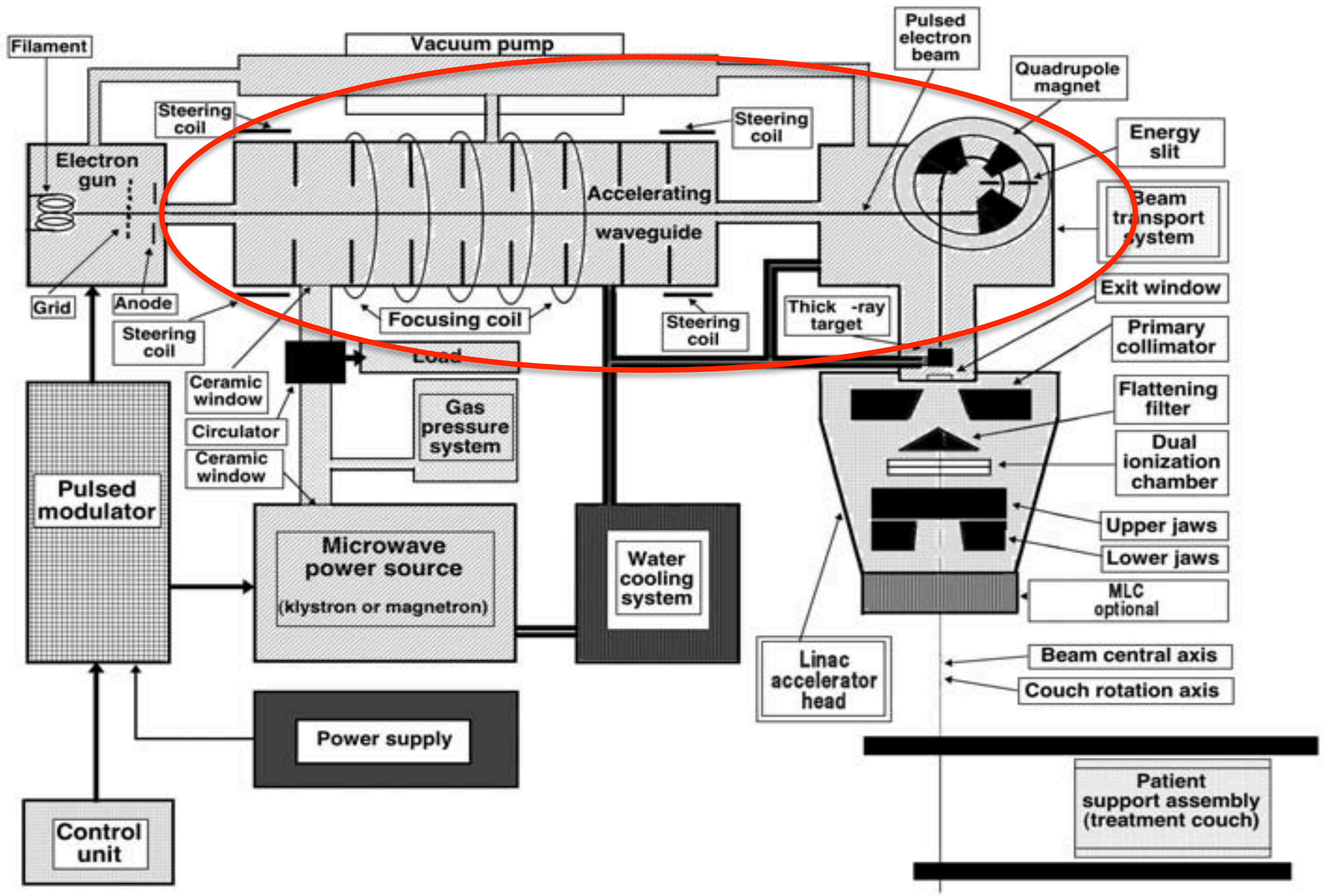
- System of triode
  - Cathod: electron production
  - Anode: electron acceleration
  - Grid: switch



Auxiliary systems

- Cooling
  - Air, water, oil
  - Modulator and magnetron: oil
  - Waveguide and head: water
  - Other: air
  - Multiple exchanges
  - Strict control of the temperature
- Vacuum
  - Ionic pumps (24h/24h)
  - 10^{-6} mbar

Linac – Beam transport

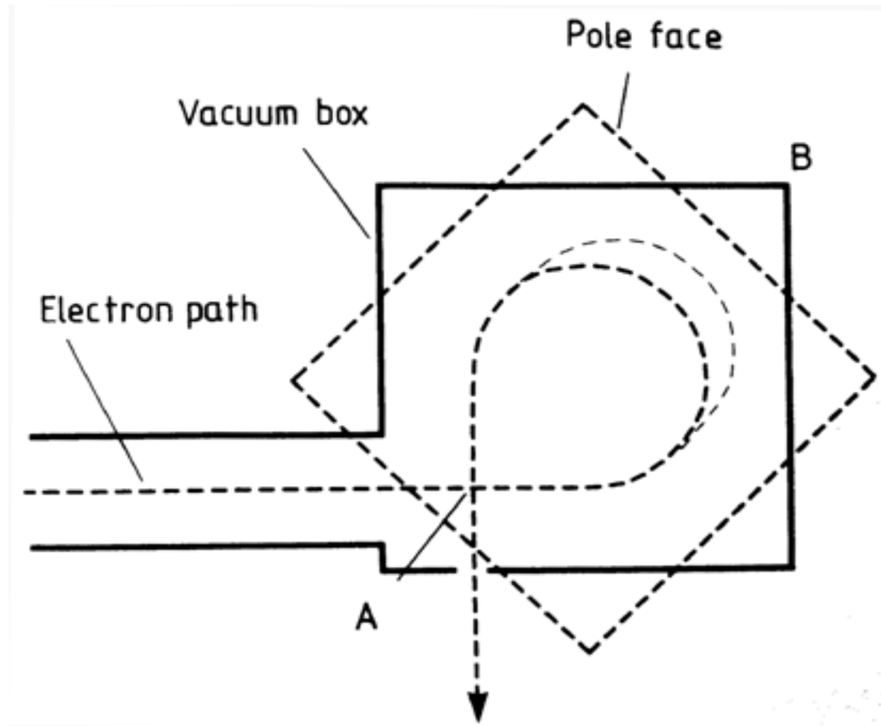


Linac – Beam transport

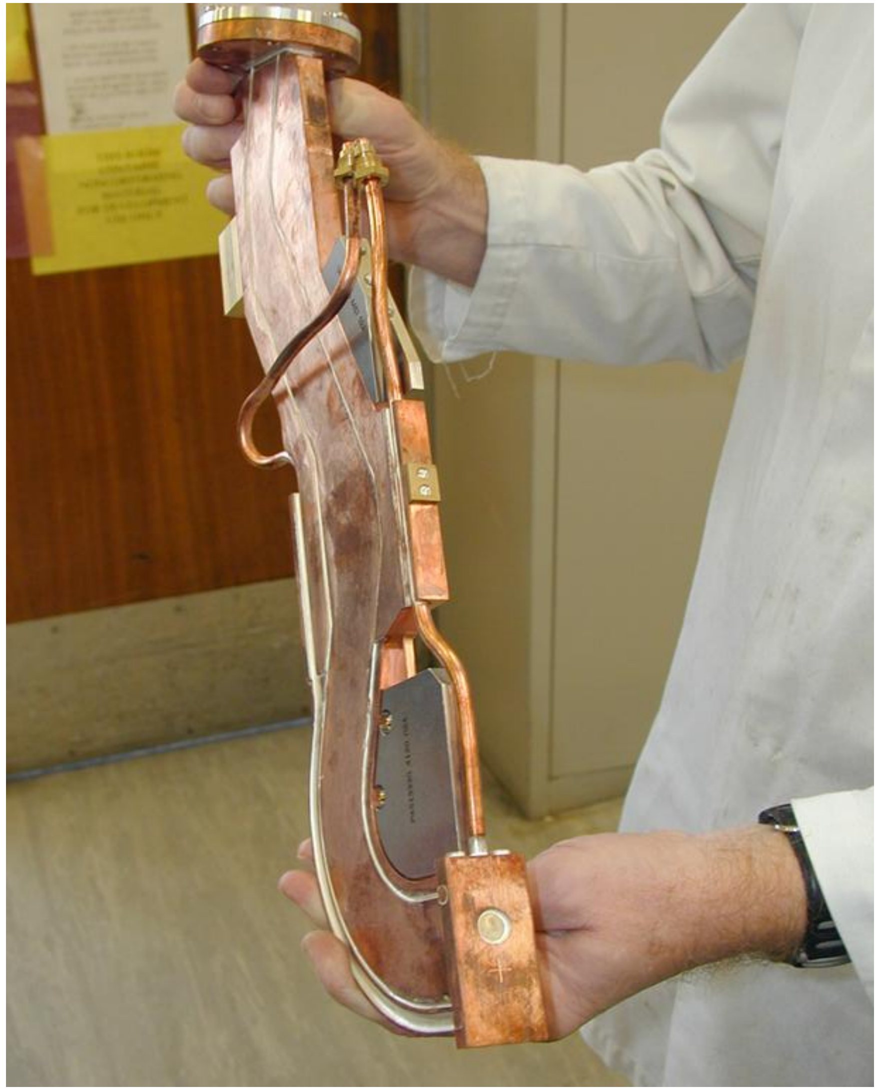
- Used to transport the electron beam from the accelerating structure to
  - The target for X-ray production
  - The output window for e^- production
- Composed of
  - Bending magnet(s)
  - Directional coils
  - Focusing coils

Bending magnet

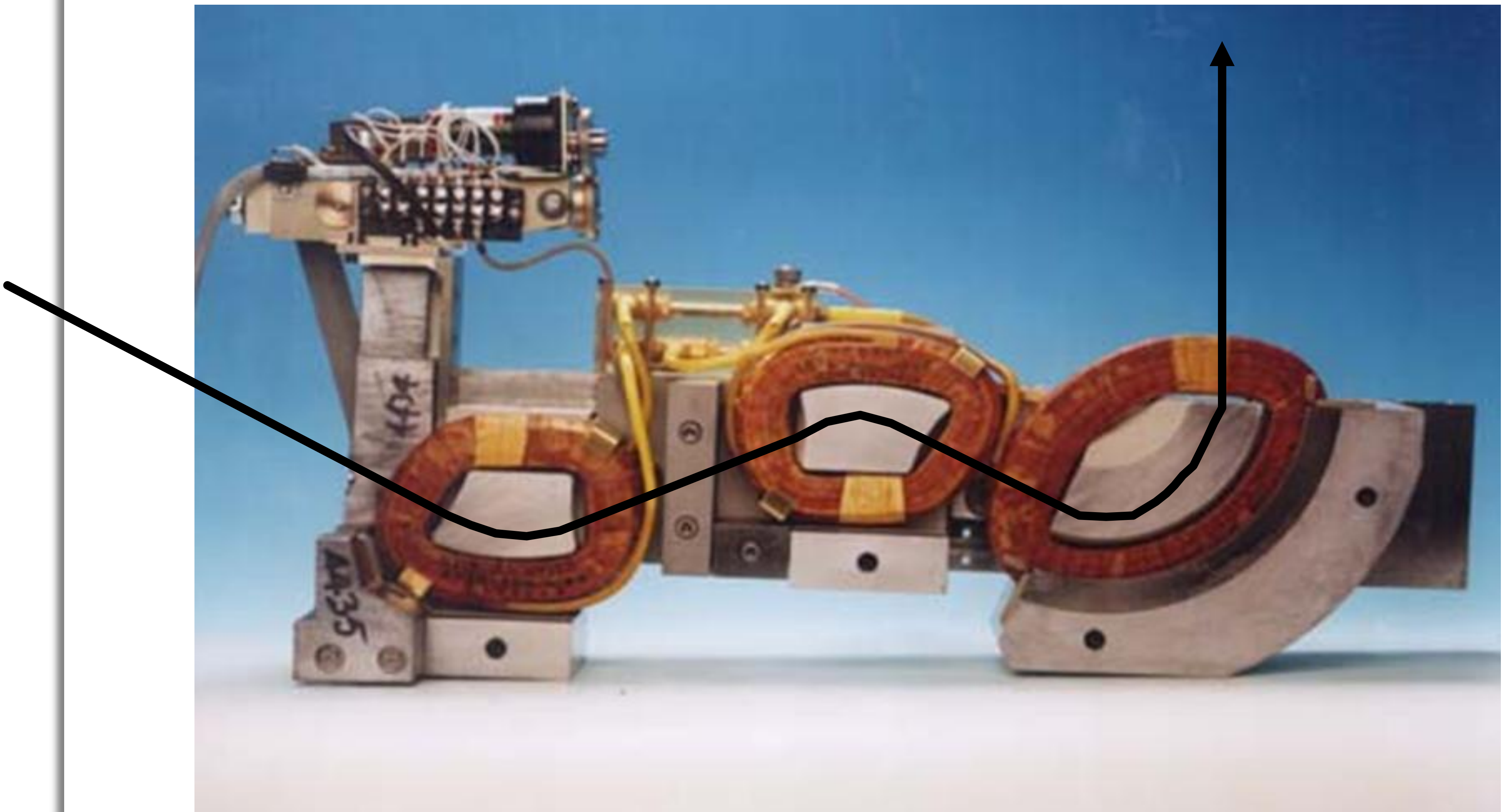
- Lorentz : $\vec{F} = q\vec{E} + q\left(\vec{v} \times \vec{B}\right)$
- Gives the correct trajectory to electrons
- Electron energy selection



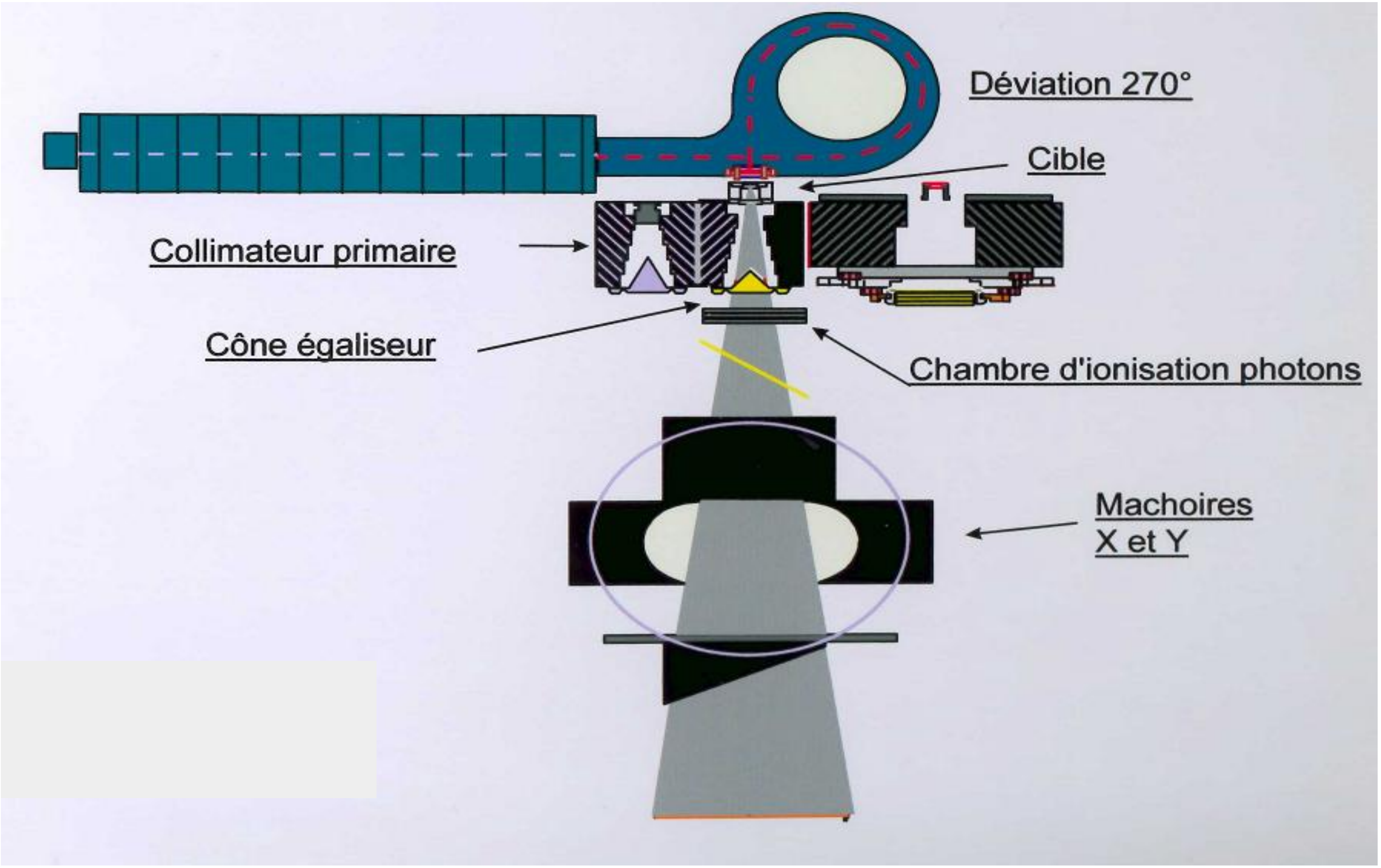
Bending magnet



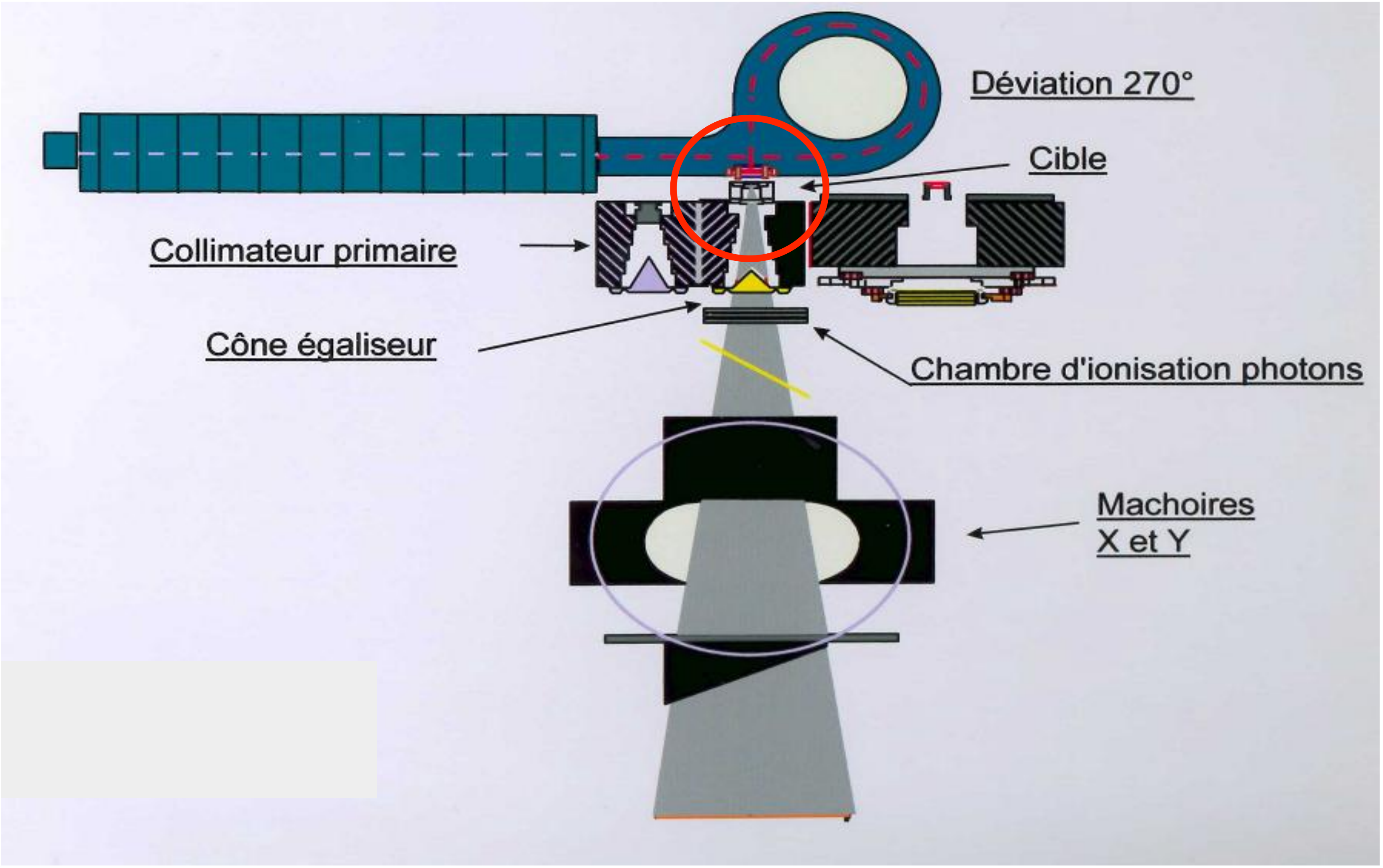
Bending magnet



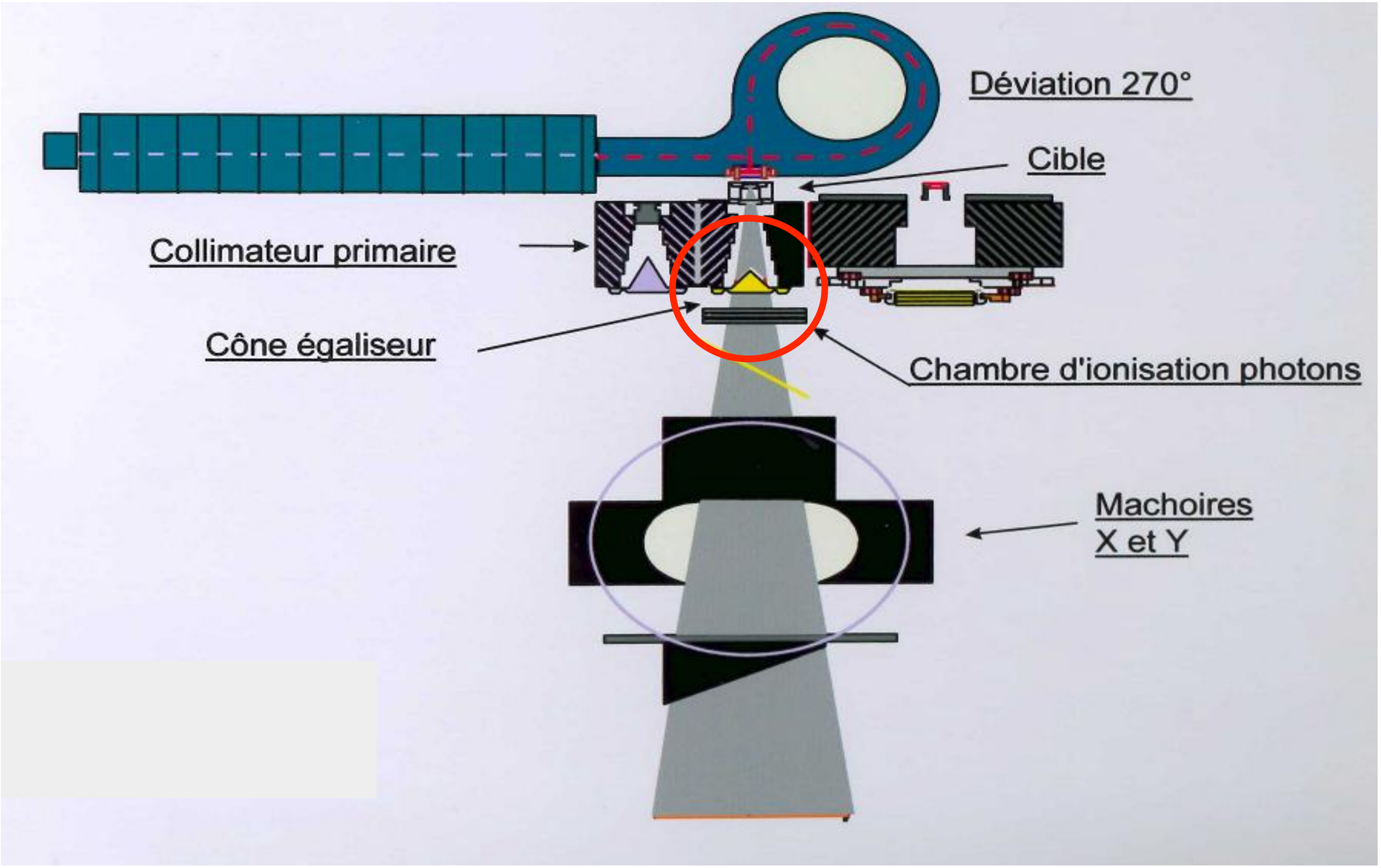
Head components - Photons



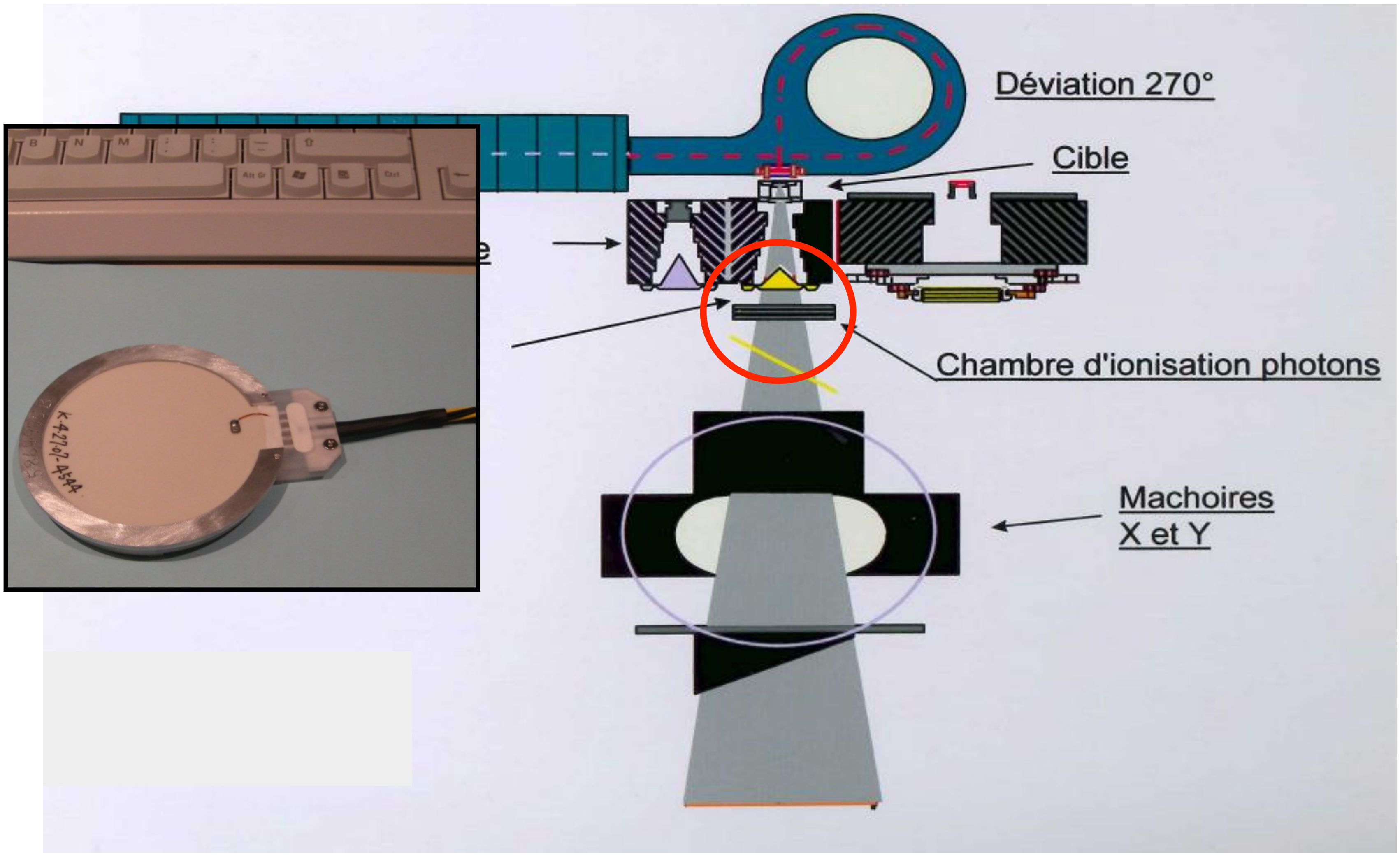
Head component - Target



Head component – Flattening cone



Transmission ion chamber



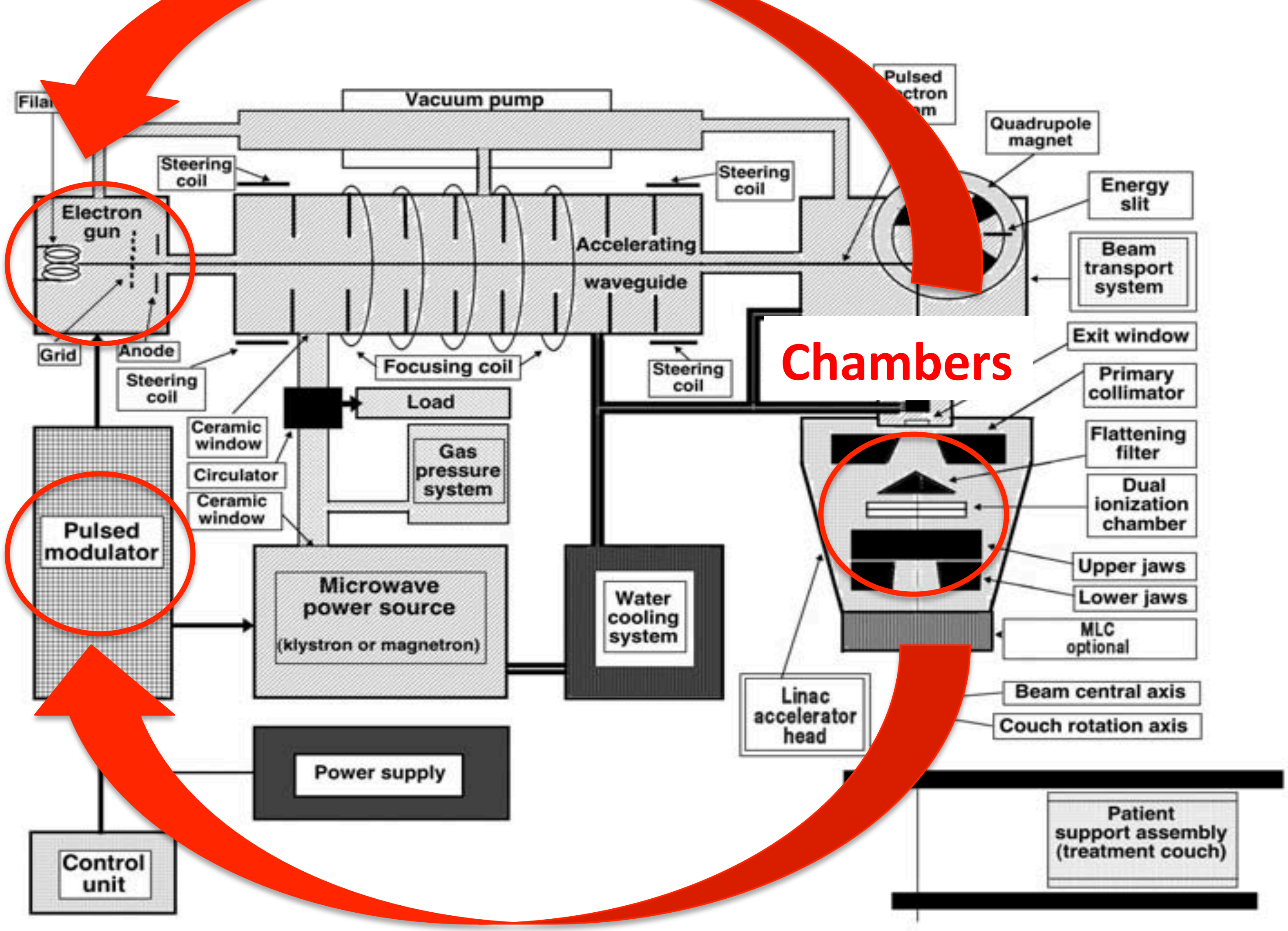
Transmission ion chamber

- Key element for safety
  - Dose rate control
- Controlled by two independent chambers placed after the exit window
  - Both chambers must measure the same signal
  - Check the adequate beam stop

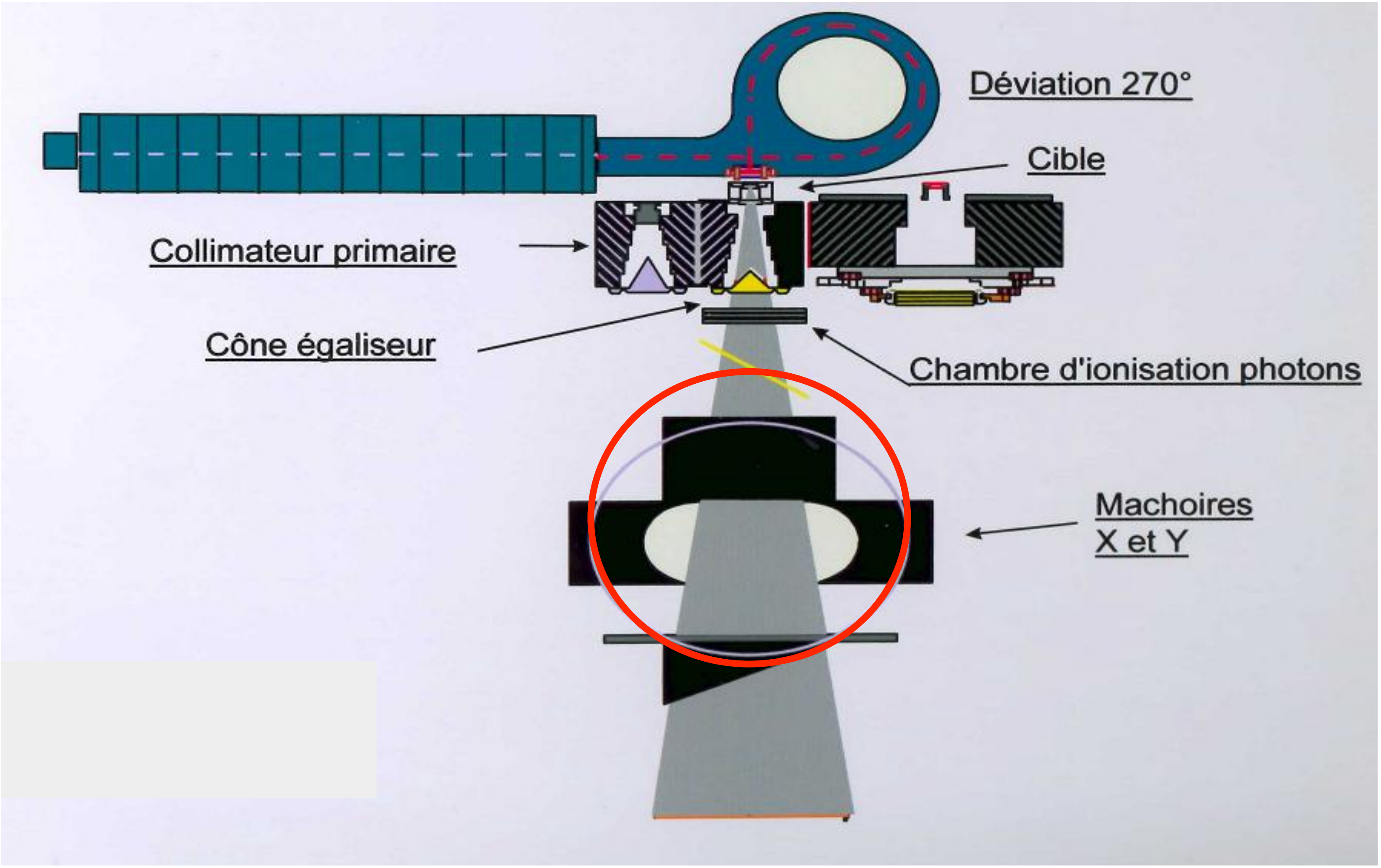
Transmission ion chamber

- Retro-control system to control the dose rate
  - Tuning of
    - PFN
    - Injection current
    - Field frequency

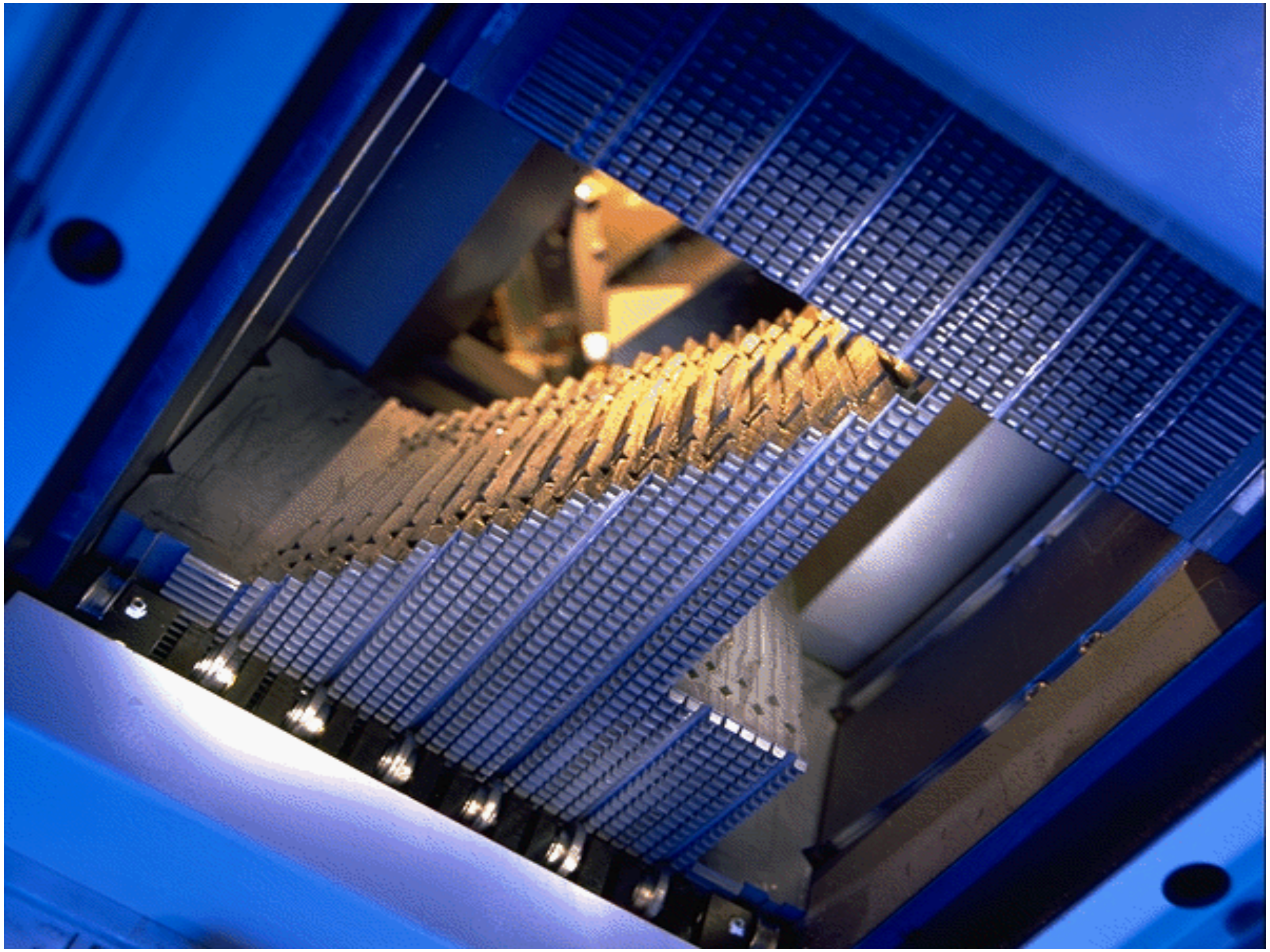
Transmission ion chamber



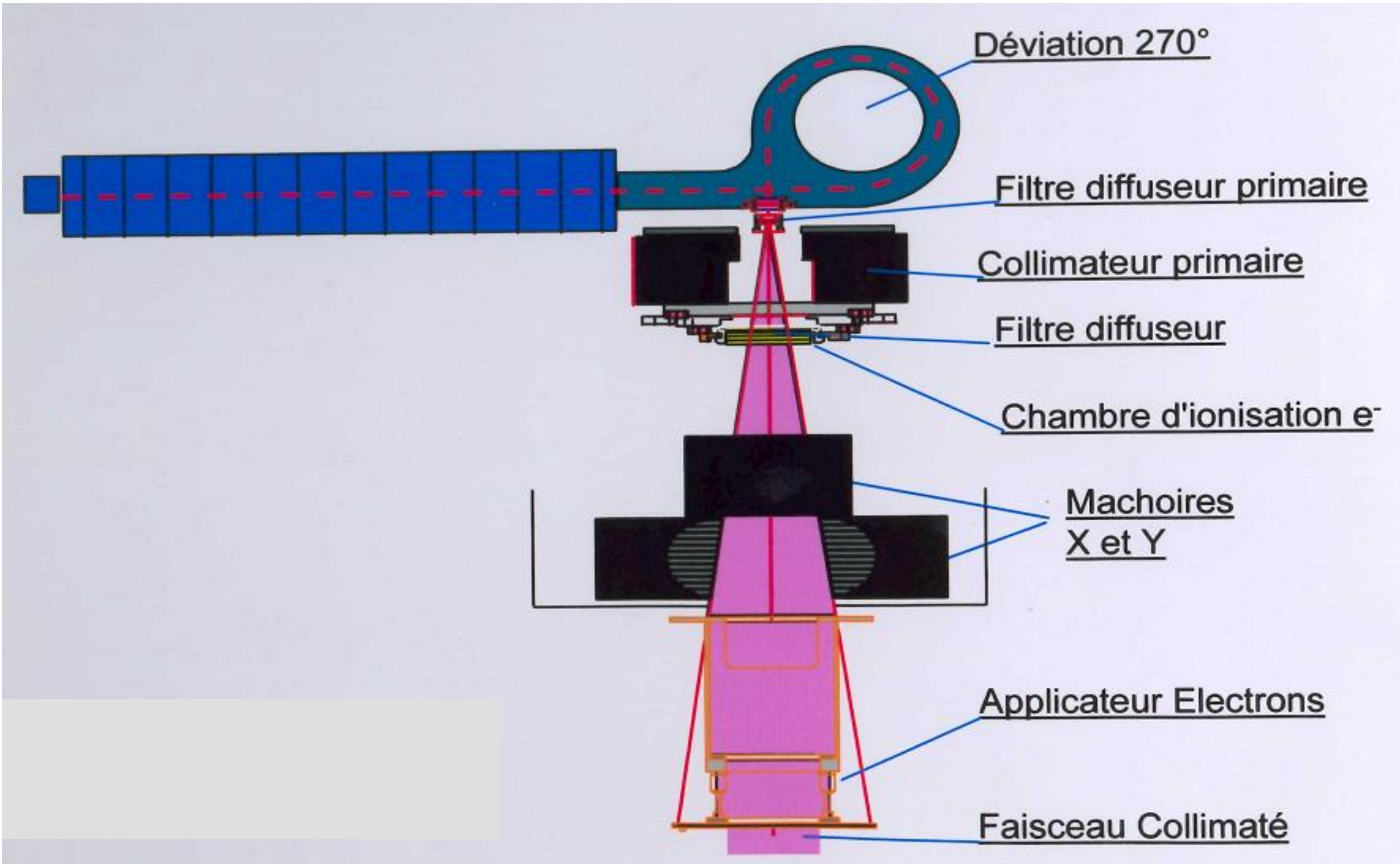
Multileaf collimator (MLC)



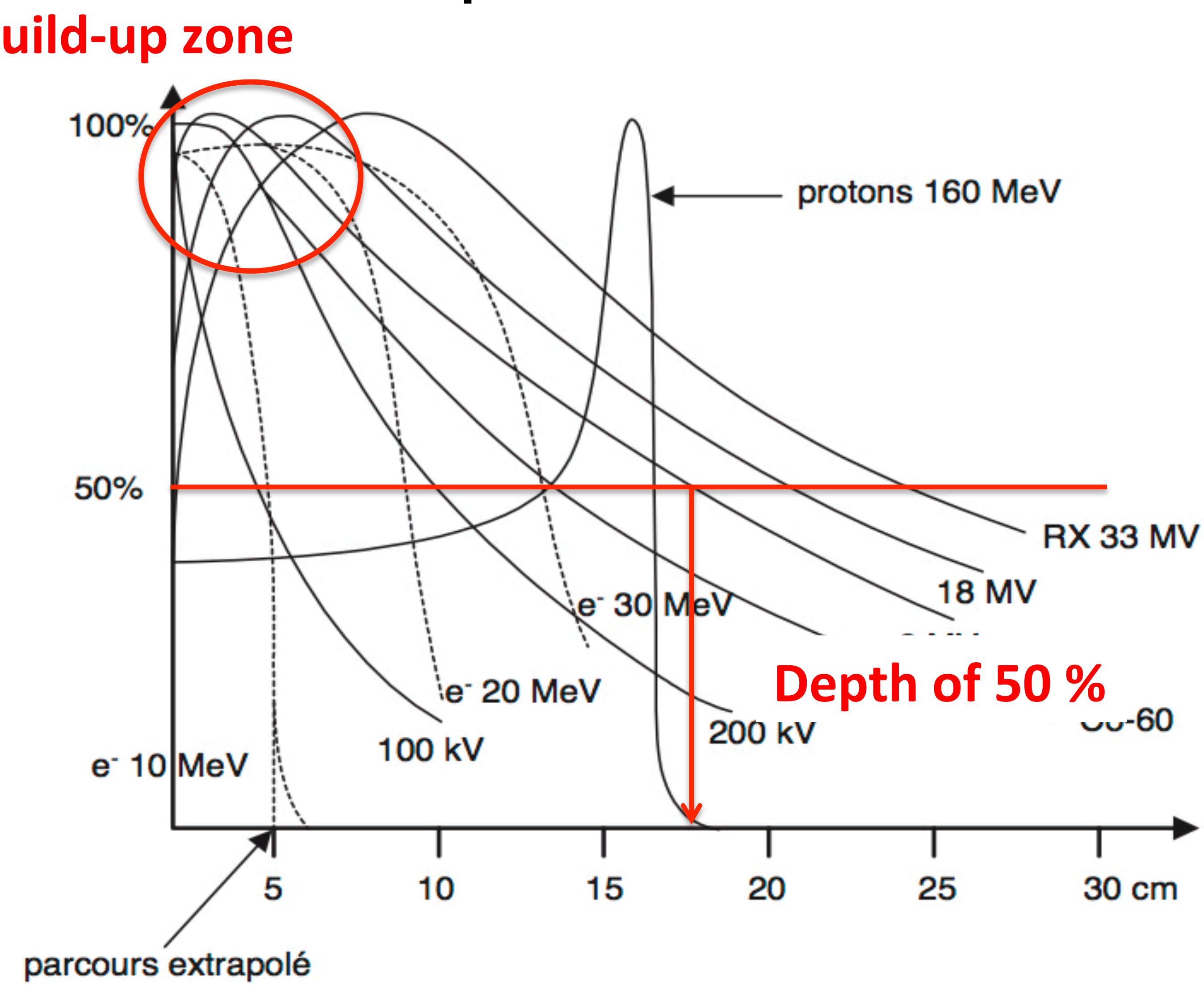
MLC



Head components - Electrons



Types of dose deposition into matter



High-energy X-rays

- Linear accelerator
- Energy : 4 - 25 MeV
- Build-up zone: somecm
- Depth of 50 % : 10 - 15 cm
- Important exit dose
- Treament of most tumor sites

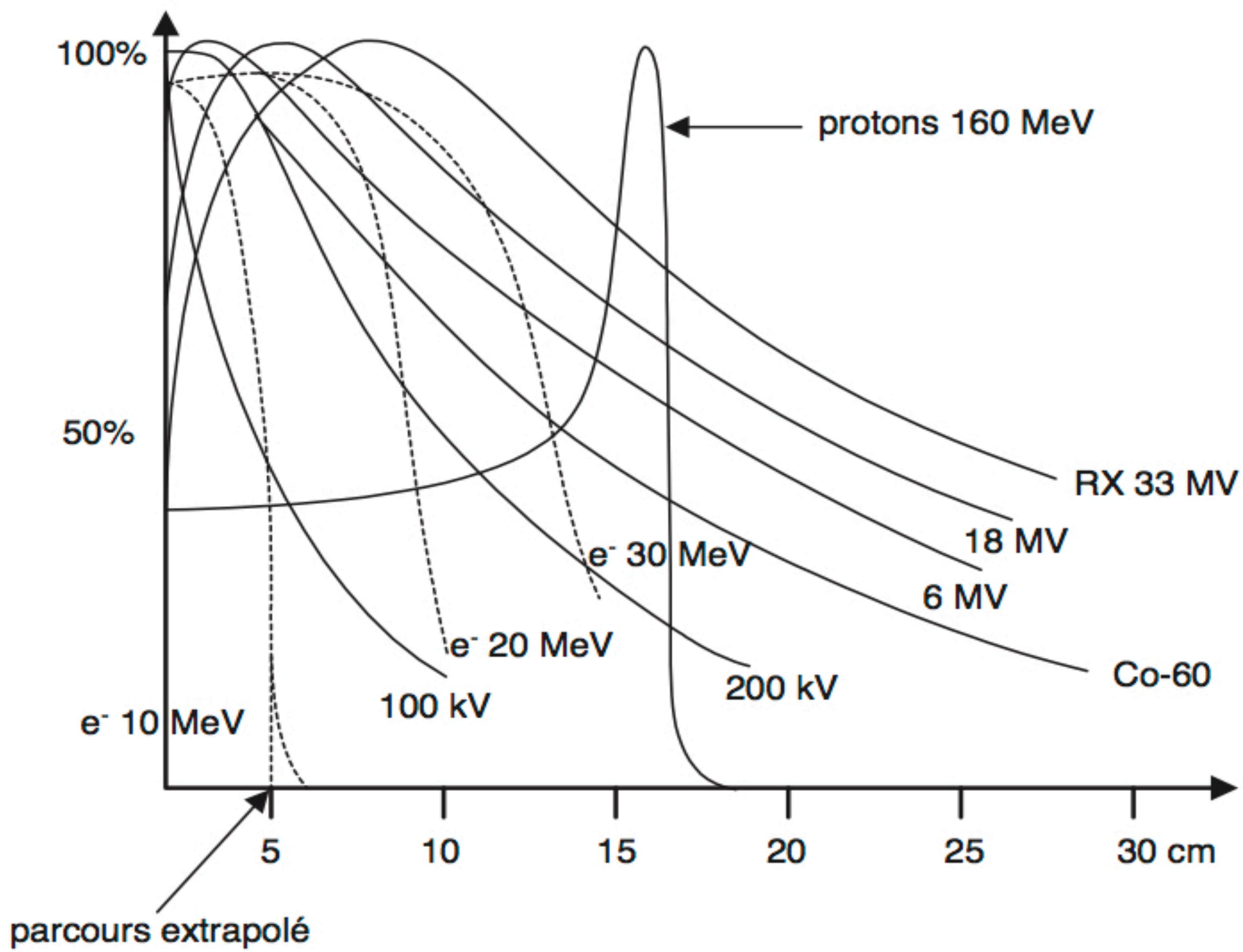
High-energy electrons

- Linear accelerators
- Energy : 3 - 25 MeV
- Important dose decrease into matter
- Extrapolated path: R(cm) ~ E(MeV)/2
- Treatment of superficial tumors
- When an organ at risk is behind the target volume

High-energy protons

- Cyclotron or synchro-cyclotron
- Energy : 50 - 500 MeV
- Bragg peak

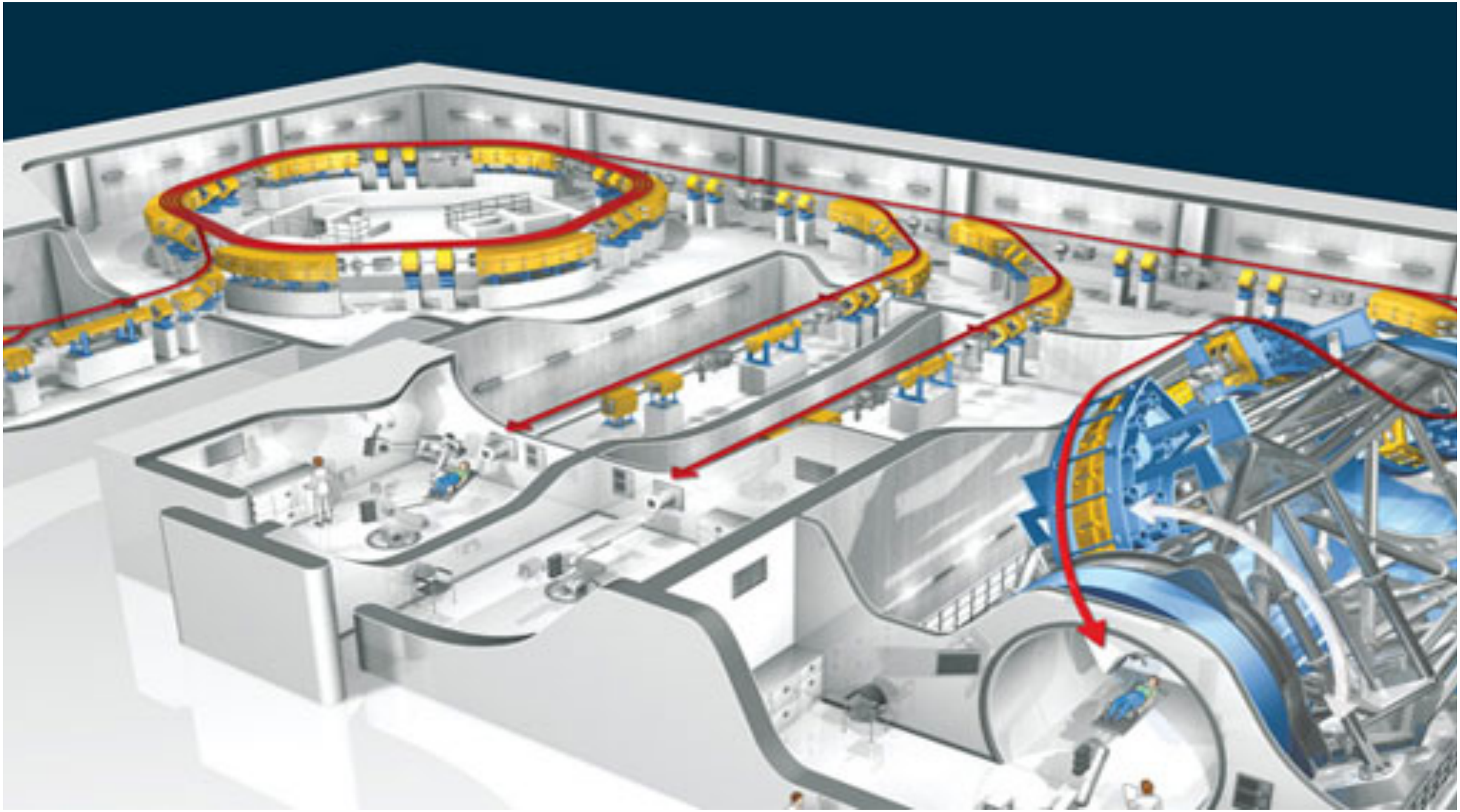
Types of dose deposition into matter



Heavy nuclei

- Hélium, Carbon, Oxygen, etc… beams
- Interesting because of high LET

Heavy nuclei



Heidelberg facility, http://www.symmetrymagazine.org/article/august-2010/accelerators-for-americas-future

Beam characterisation

- Introduction
- Dosimetric parameters of X-ray beams
- Measurement means
- Examples

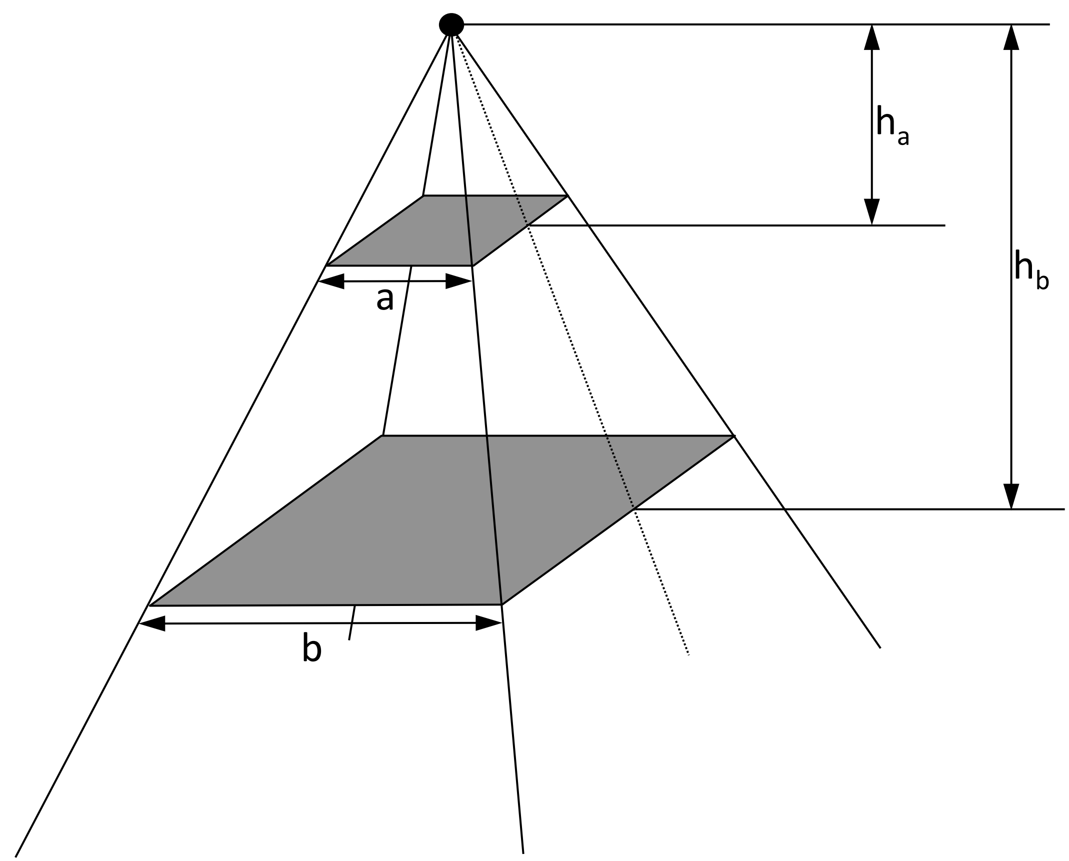
Inverse square law

- External radiaiton therapy
  - Punctual source
  - Divergent beam
- N total constant
  - No interaction in air

$$\frac{a}{b} = \frac{h_a}{h_b}$$

$$N_{tot} = \phi_A \cdot A = \phi_B \cdot B$$

$$\frac{\phi_A}{\phi_B} = \frac{B}{A} = \frac{b^2}{a^2} = \frac{h_b^2}{h_a^2}$$



Photon penetration into matter

- In vacuum
  - Inverse square law
- In matter
  - Absorption
  - Diffusion
- These three effects make the dose deposition into matter a complex process

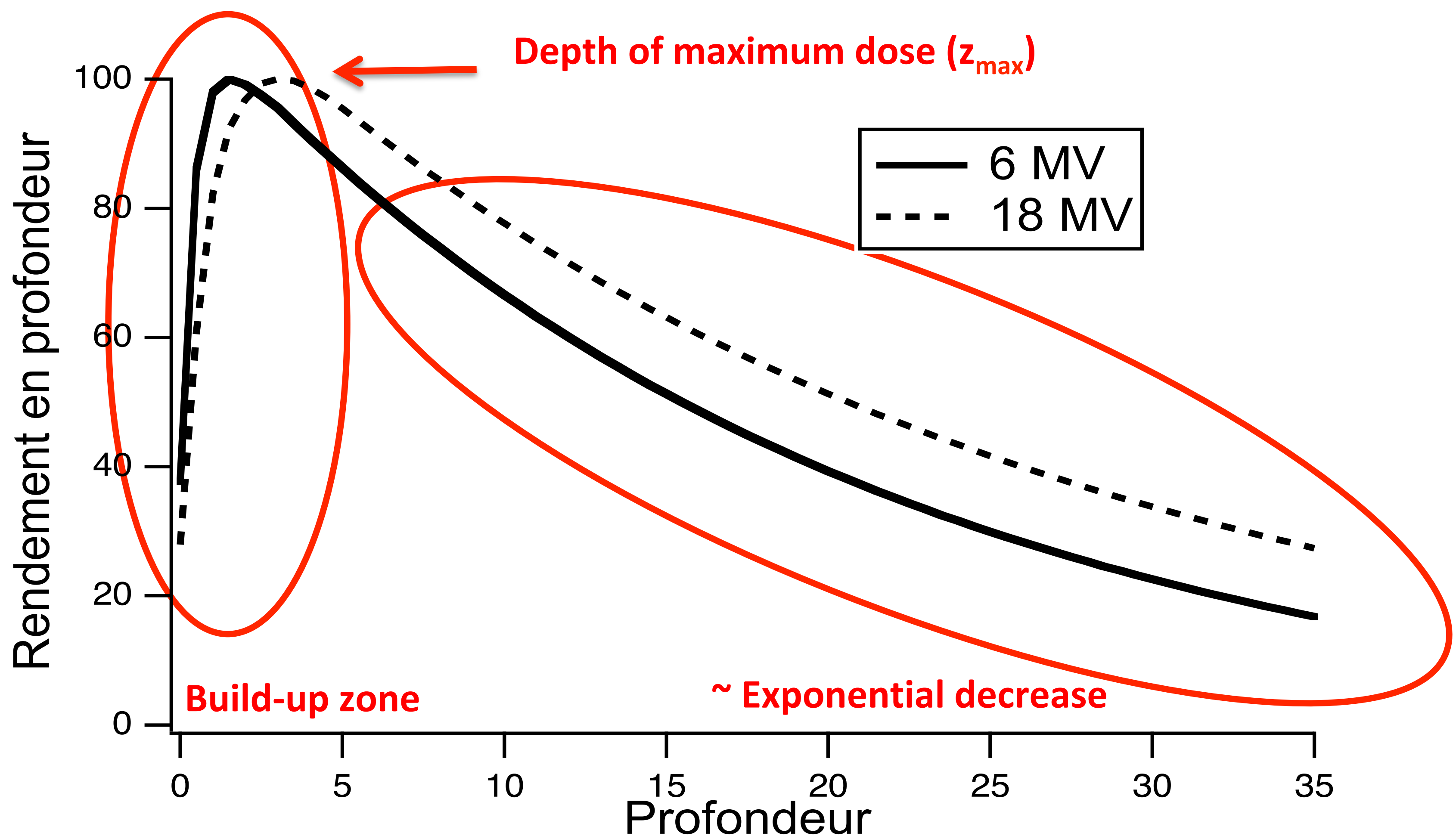
Patient dose

- The quality of a patient treatment depends on the precise determination of the dose
  - In the target volume
  - In healthy tissues
- A point dose in a patient is determined
  - From a point dose called reference point
  - With dosimetric parameters that « propagate the dose from the reference point

Patient dose

- Dosimetric parameters are determined
  - By measurements with detectors
  - In water equivalent phantoms
- Reference dose is determined in water and is metrologically traceable

Patient dose



Build-up zone

- Before a certain depth near the surface
  - Missing secondary electrons due to absence of interacting material before surface dose
- After a certain depth near the surface
  - The number of electrons entering a small volume is the same as the one exiting that volume
  - Electronic equilibrium

Depth of maximum dose

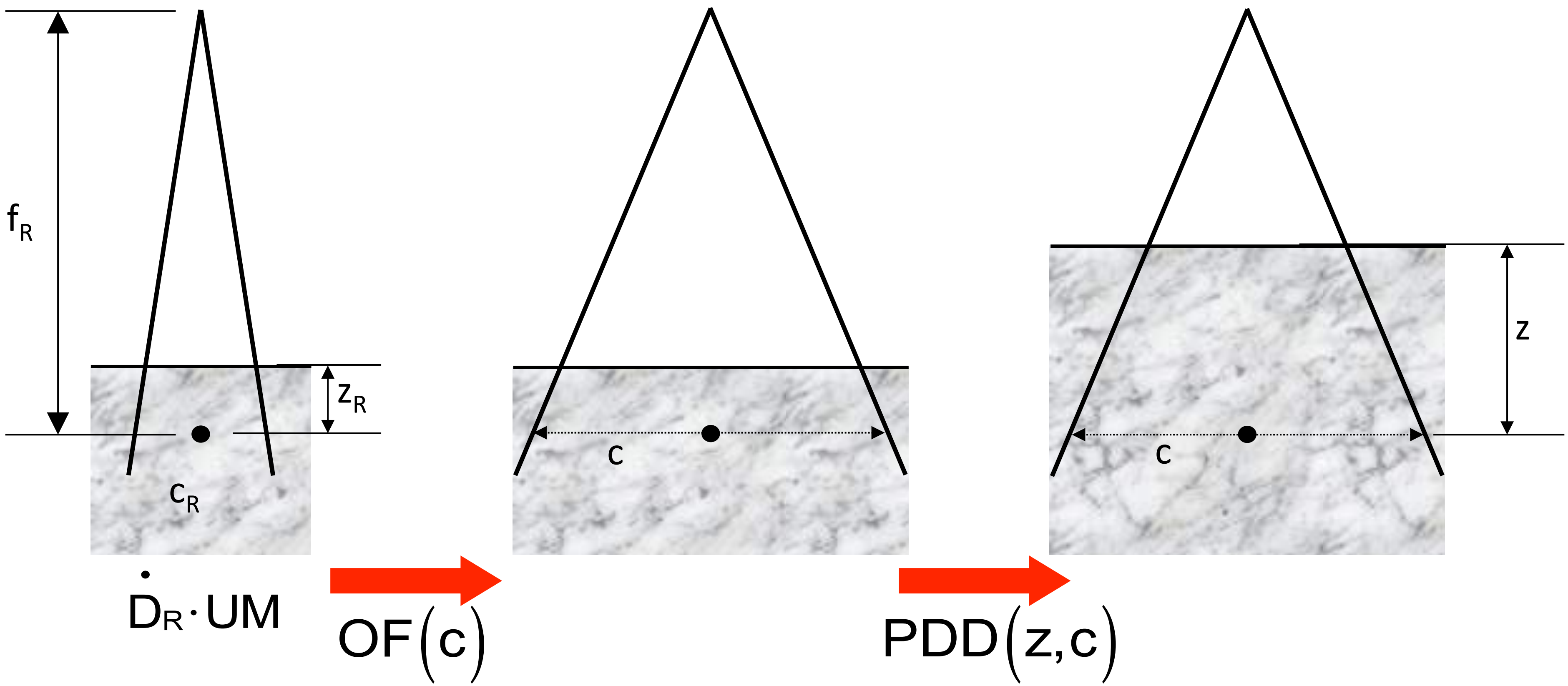
- Mainly depend on the beam energy
- Z_{max} increases with beam energy
  - Co-60: ~ 0.5 cm
  - 6 MV: ~ 1.5 cm
  - 18 MV: ~ 3 cm
- Clinical advantage
  - Sparing skin

Dosimetric parameters

- Reference conditions
  - Isocentric
  - Fixed source-skin distance
- Parameters

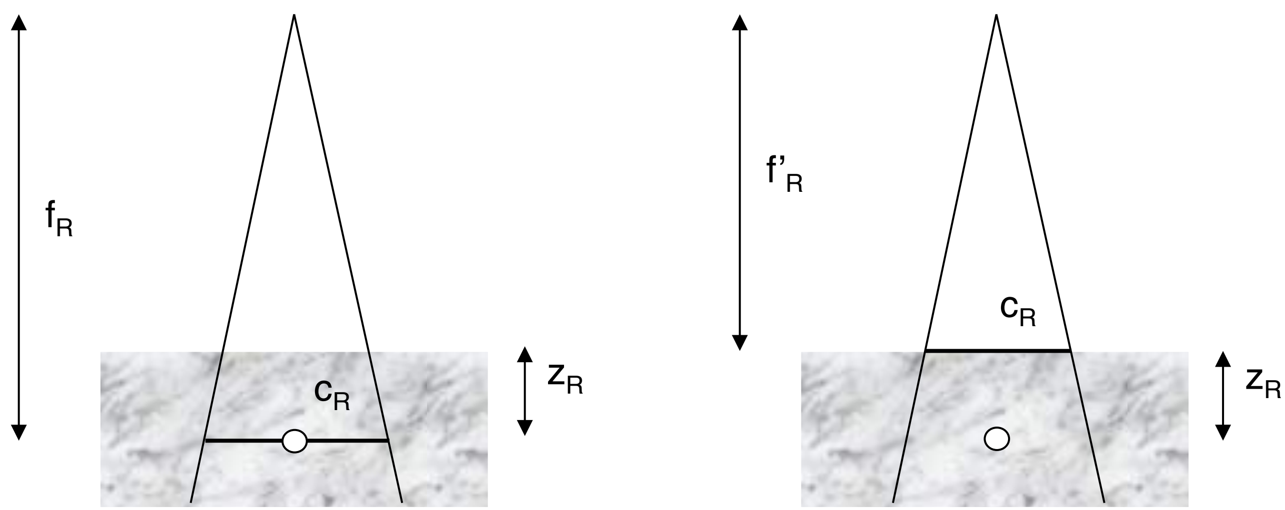
– Measure depth	z
– Field size	A
– Source-skin distance	DSP (SSD)
– Source-axis distance	DSA (SAD)
– Photon energy	E

General concept for dose calculation



Reference conditions

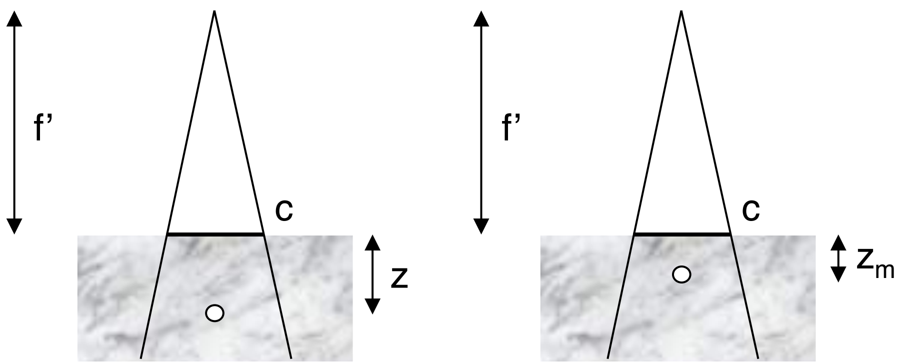
- Isocentric condition
  - The measurement point for basic quantities is isocenter (f_R)
  - Depth of reference point is z_R=10 cm
  - Field size at isocenter is c_R=10x10 cm^2



a) condition isocentrique

b) condition à DSP fixe

Depth dose rate or percent depth dose

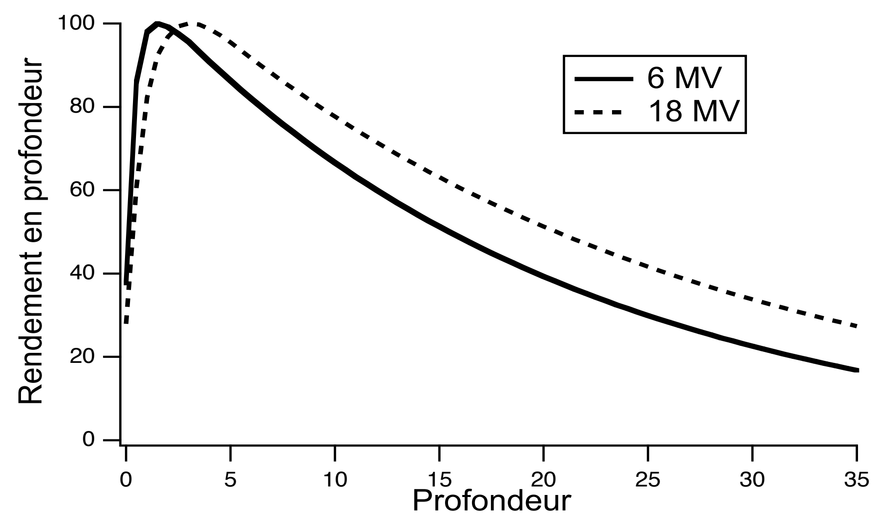


a) numérateur b) dénominateur

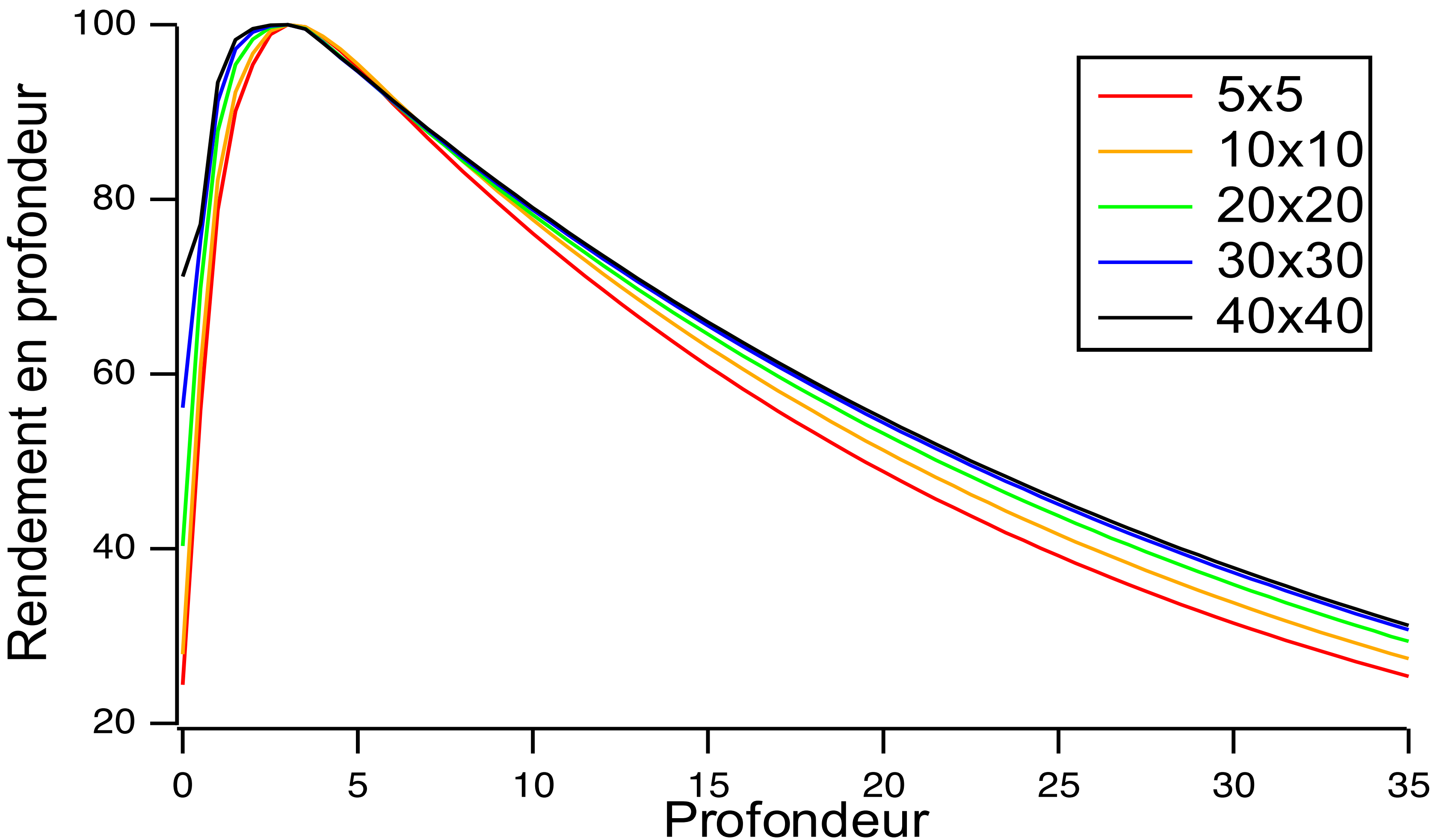
- Dose on beam axis
- Depends on
  - Depth
  - Field size
  - SSD

$$RP(z,s,f') = \frac{D'(z,s,f')}{D'(z_m,s,f')} \cdot 100$$

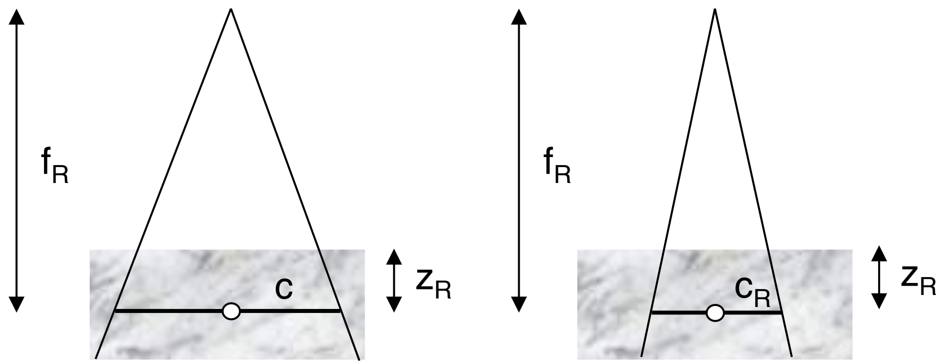
$$RP_R(z,s,f') = \frac{D'(z,s,f')}{D'(z_R,s,f')} \cdot 100$$



Depth dose rate or percent depth dose



Output factor



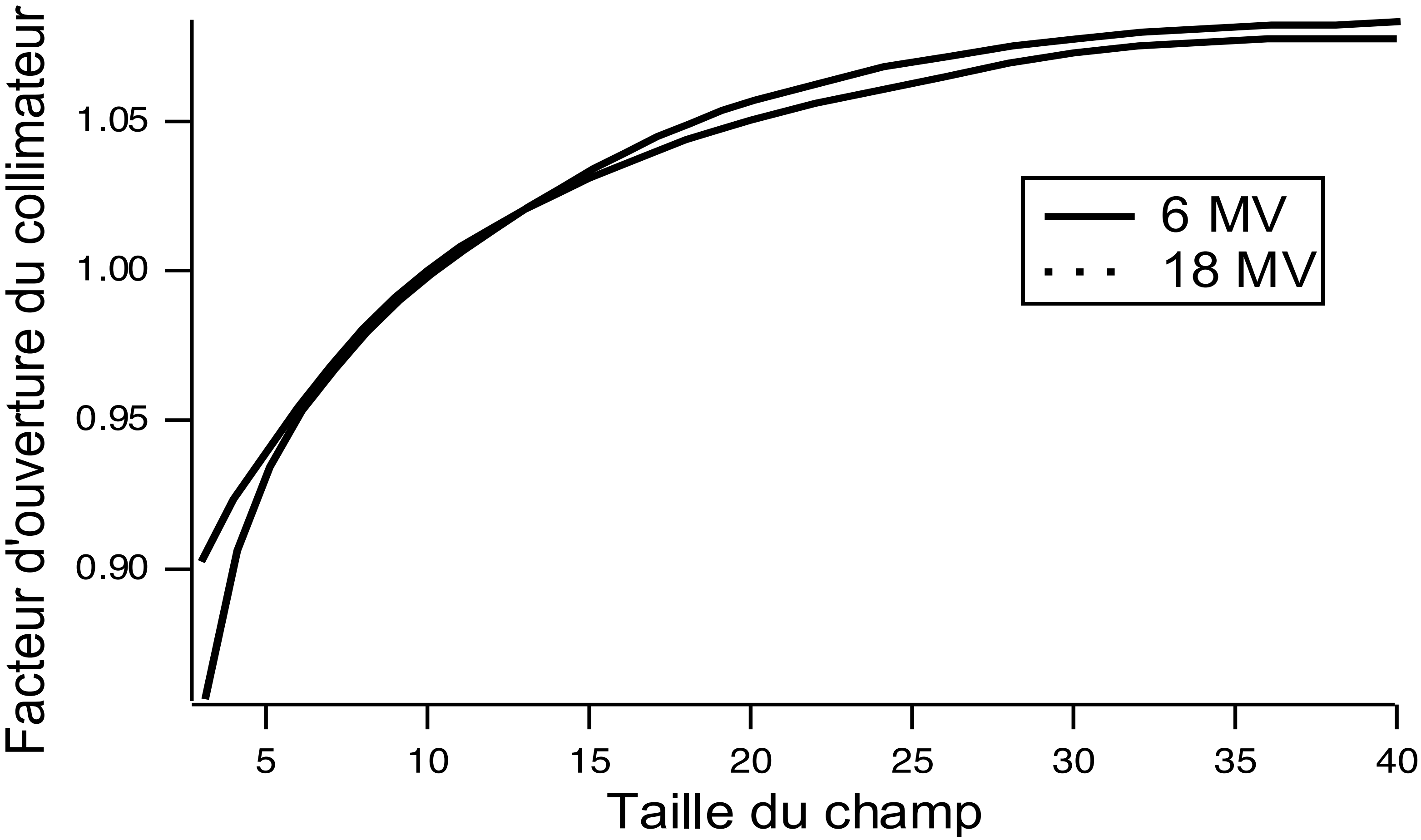
a) numérateur b) dénominateur

$$FOC_R(c) = \frac{D(z_R, c)}{D(z_R, c_R)}$$

- Normalized to 10x10 cm^2 beam
- Depend on
  - Field size
  - Energy

$$FOC_R(20x20) = \frac{D(20x20)}{D(10x10)}$$

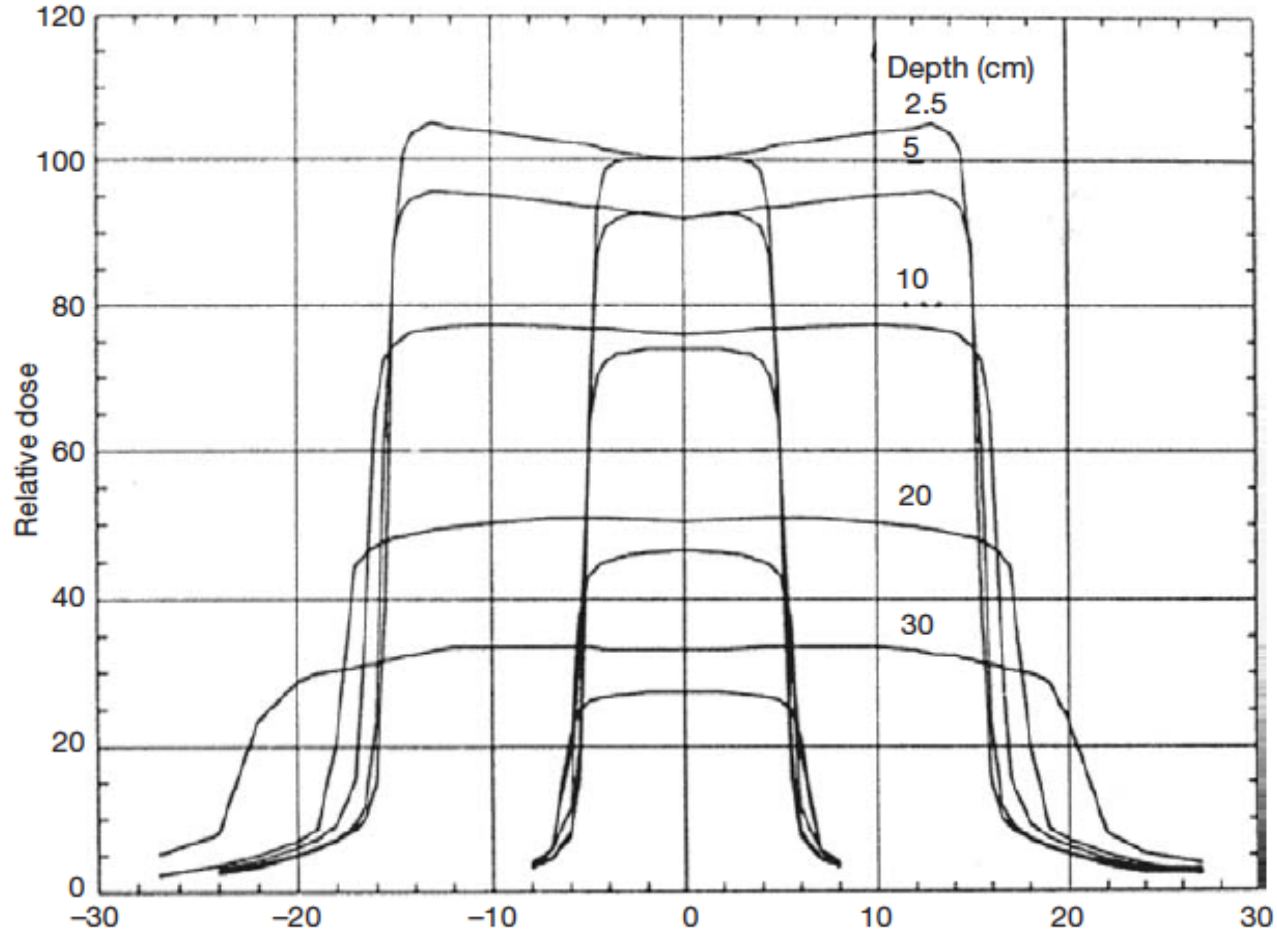
Output factor



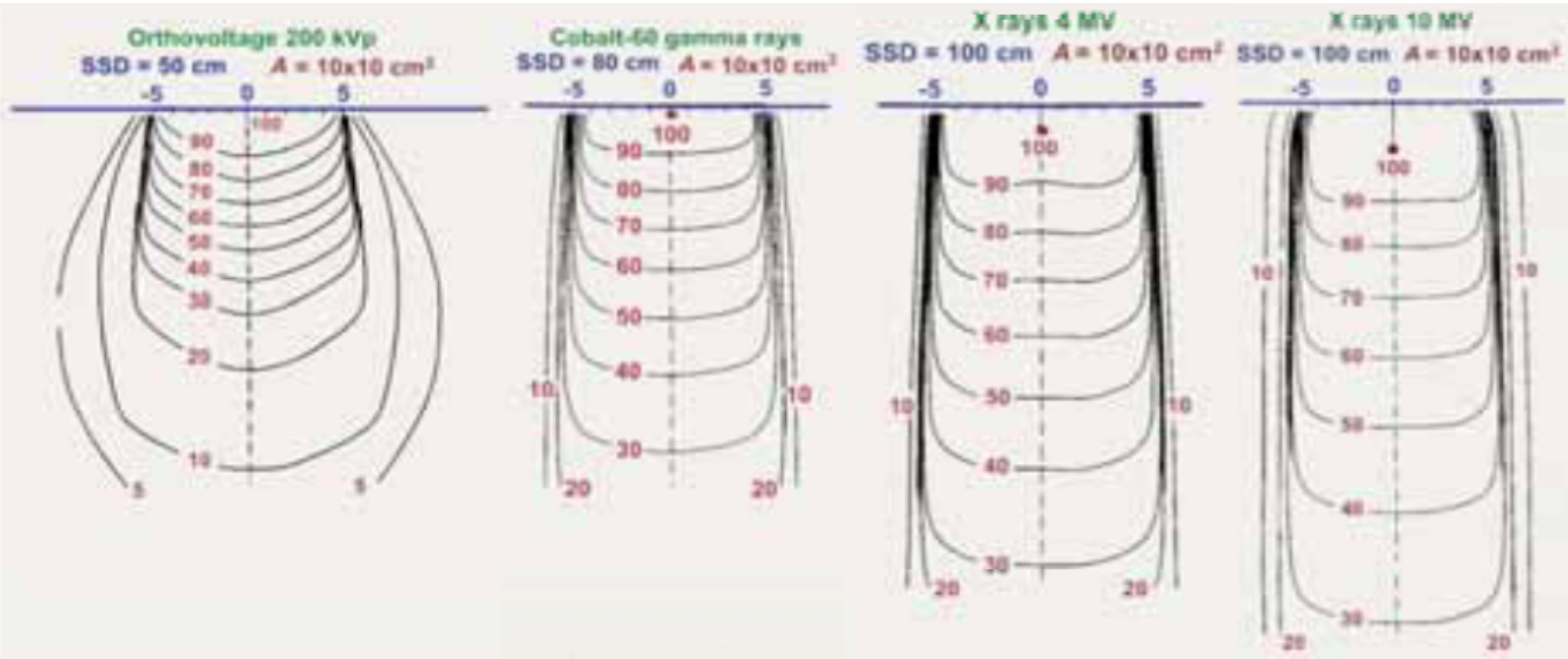
Off-axis ratio or profiles

- A beam profile is composed of
  - Central region: flat region from the axis to 1-1.5 cm of the beam border
  - Penumbra: border of the beam region with a strong dose gradient
  - Umbra (off beam): off beam region where there is still dose due to transmission through collimator and to scatter

Off-axis ratio or profiles



Isodoses in a water phantom

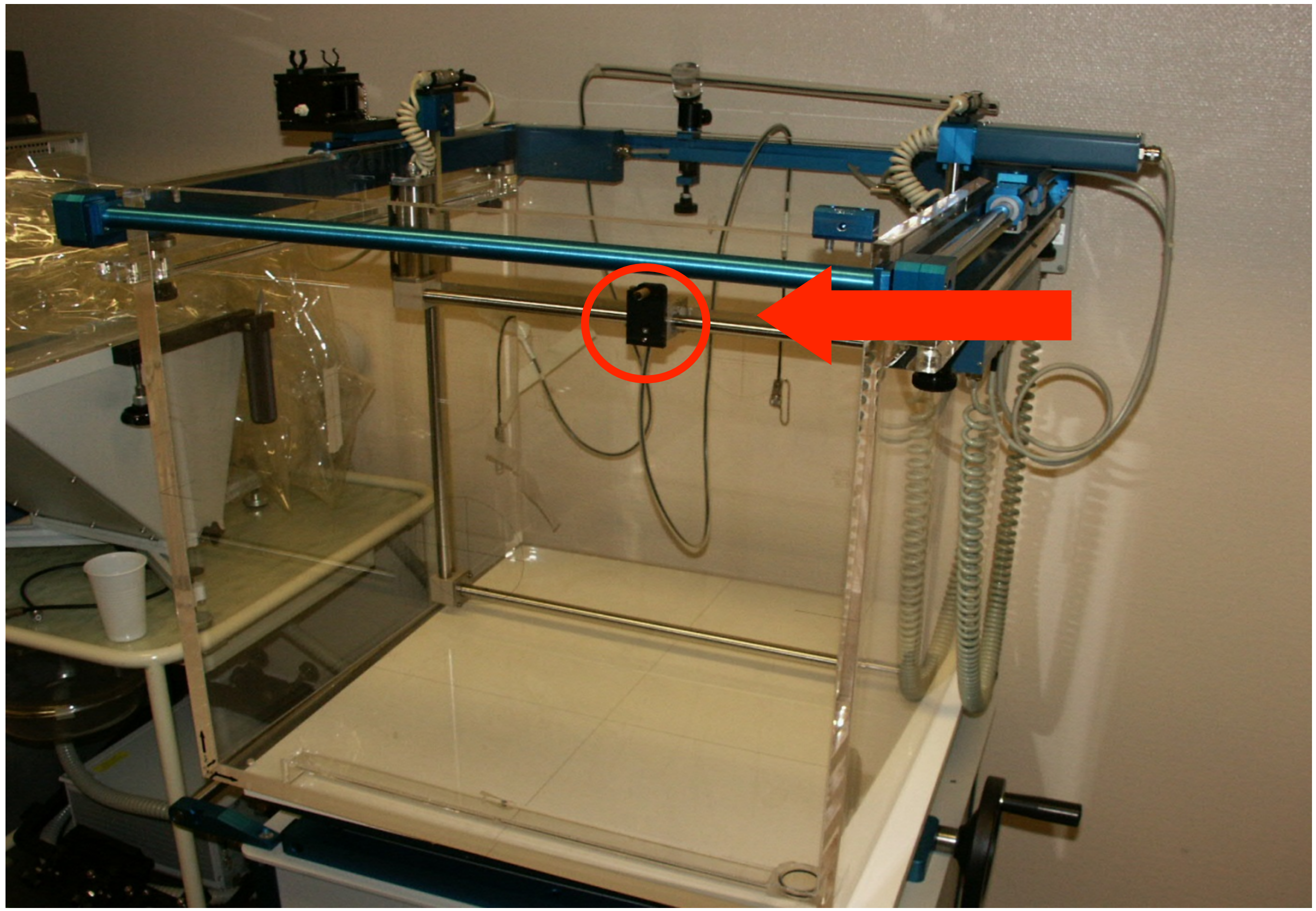


Measurement means

- Water tank
  - Large volume
  - Three-axis motorization
  - Computer controlled movements correlated with dose measurements

Measurement means

- Water tank

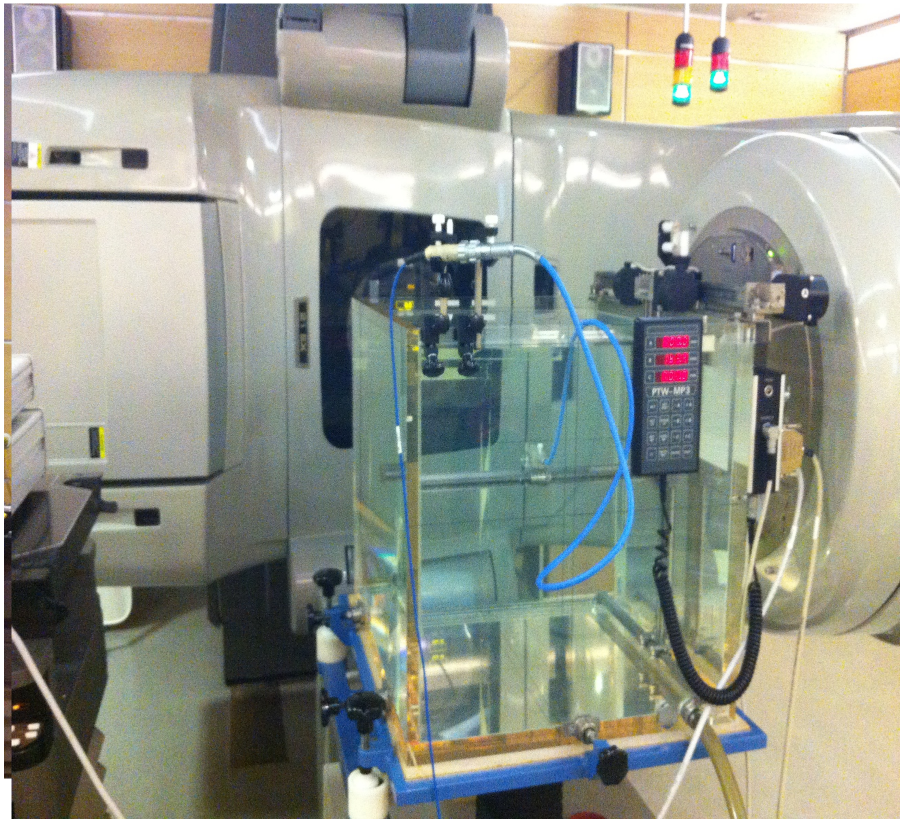


Measurement means

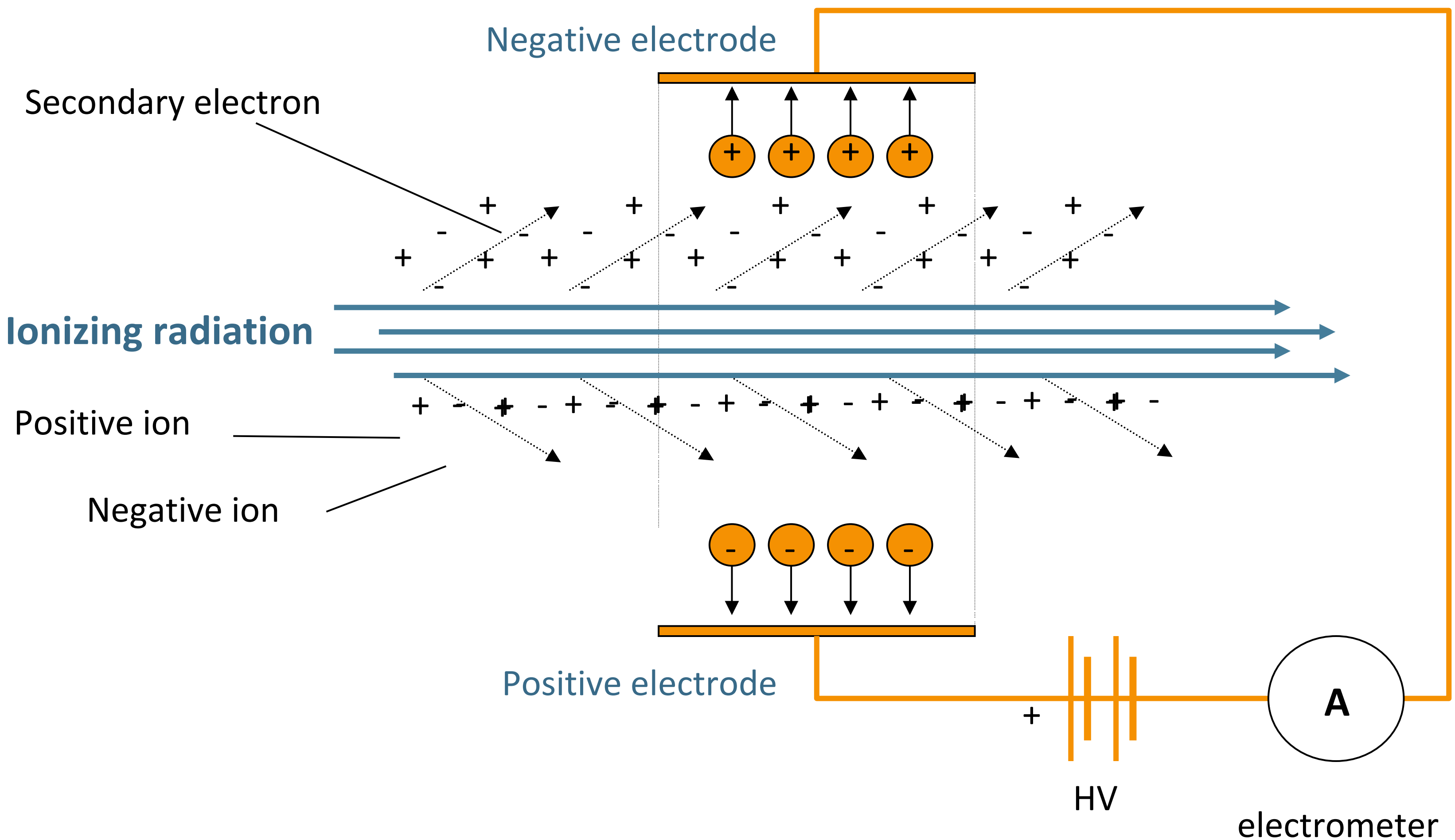
- Ionization chamber
- Diodes
- Films
- 2D and 3D detectors

- Solid water

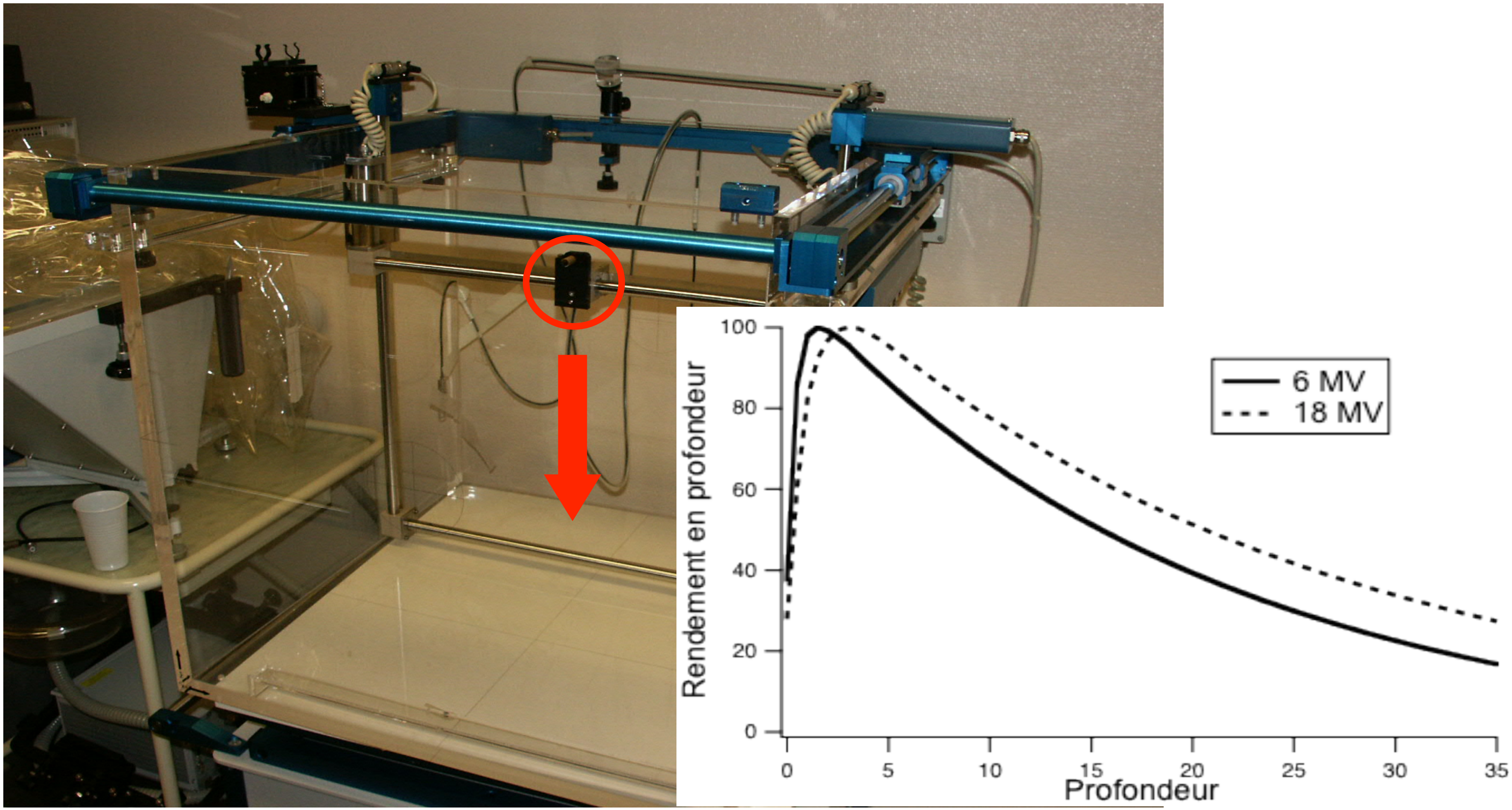
Dosimetric means



Ion chamber


Negative electrode
Secondary electron
Ionizing radiation
Positive ion
Negative ion
Positive electrode
+
HV
A
electrometer

Measurement means



Hand dose calculation - Principle

- Precise measurement of reference dose
  - Metrology with a secondary standard
    - Once a year
    - Calibration of beam monitoring (trnasmission chambers)
- Calculation of dose at any point with dosimetric parameters
  - PPD
  - Output factor
  - Profiles

Hand dose calculation

$$D(z,c) = \dot{D}_R \cdot UM \cdot FOC(c) \cdot RTP(z,c)$$