物理於醫學之運用：以游離輻射為例

(Physics in Medicine : using ionizing radiation as an example)

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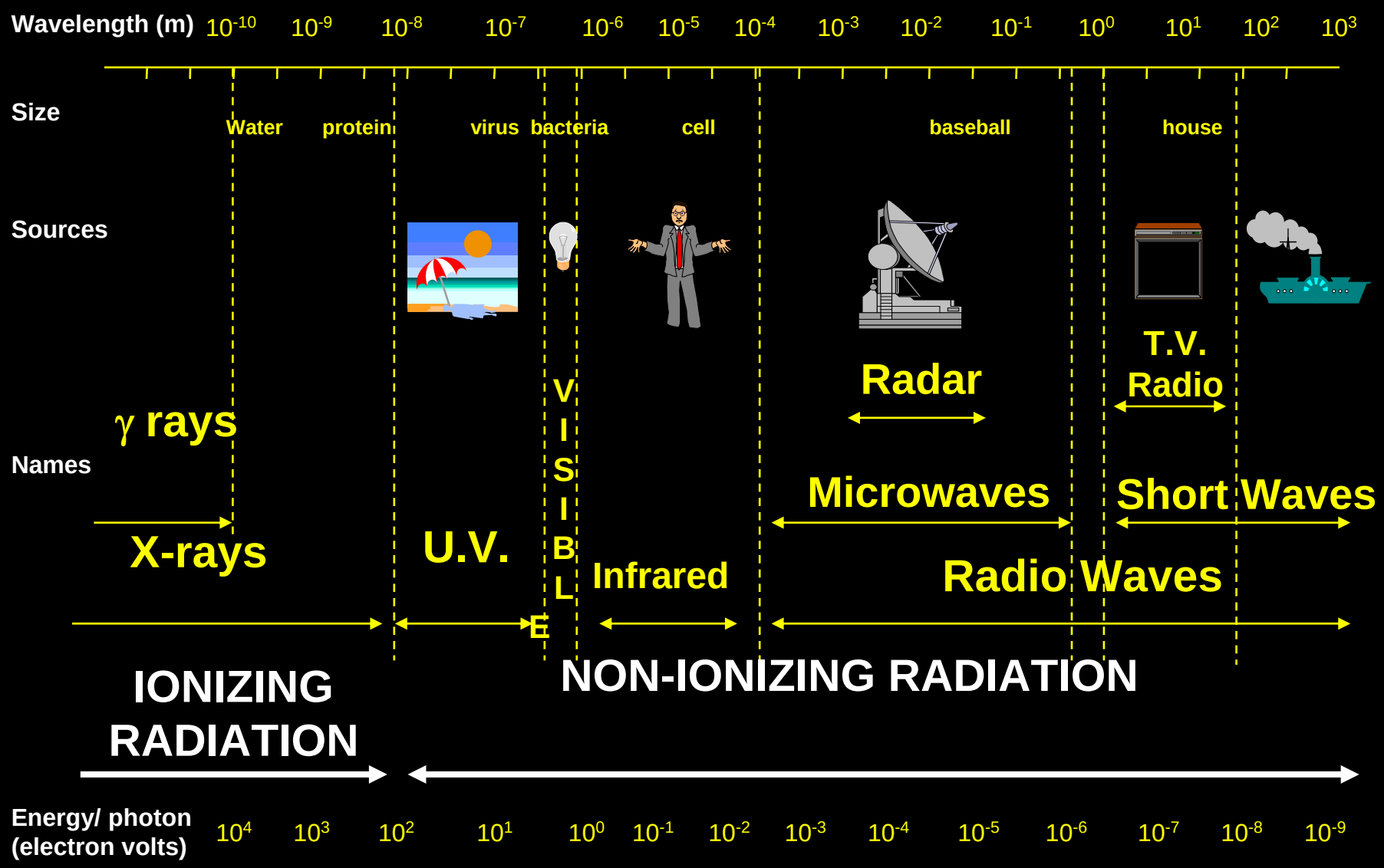
In “Physics and Life” class of NCCU

上課內容

- 游離輻射之定義及生物作用
- 游離輻射之歷史
- 游離輻射之醫學應用
- 腫瘤放射治療之簡介
- 先進之放射治療設備

游離輻射之定義及生物作用

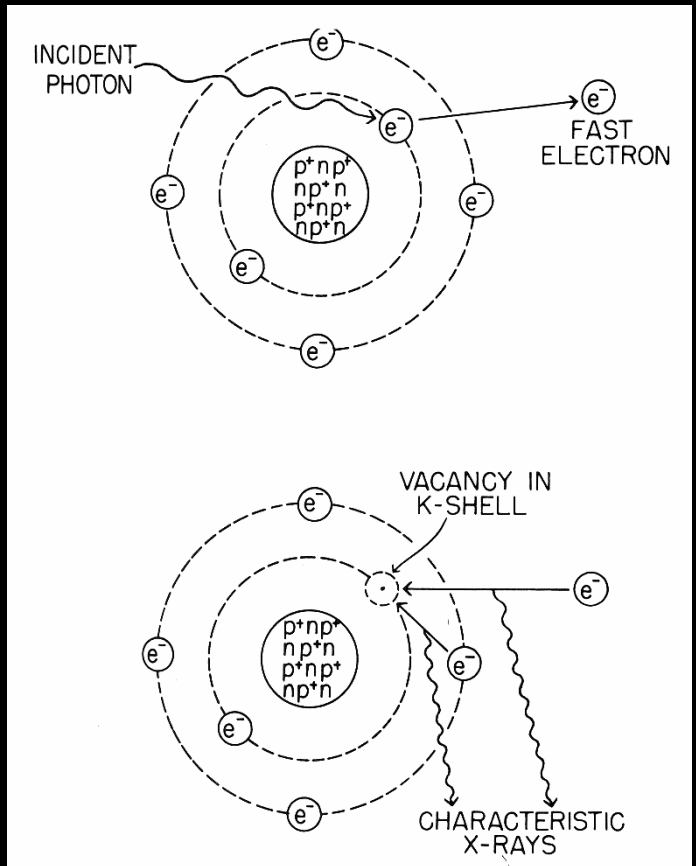
電磁波


Wavelength (m)
10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3}
Size
Water
protein
virus
bacteria
cell
baseball
house
Sources
Names
γ rays
X-rays
U.V.
VISIBLE
Infrared
Radar
Microwaves
T.V.
Radio
Short Waves
Radio Waves
IONIZING RADIATION
NON-IONIZING RADIATION
Energy/ photon (electron volts)
10^{4} 10^{3} 10^{2} 10^{1} 10^{0} 10^{-1} 10^{-2} 10^{-3} 10^{-4} 10^{-5} 10^{-6} 10^{-7} 10^{-8} 10^{-9}

輻射種類 (Type of radiation)

定義：

- 游離 (ionization):
  - 將核子核外電子完全彈出軌道外
  - 每一游離電子約需33 eV/per.
- 激發 (Excitation):



游離輻射特性

- 電磁波 (Electromagnetic radiation)

Velocity = c: 3 x 10^{10} cm/s,

$\lambda\nu$=c ((λ: wavelength, ν: frequency)

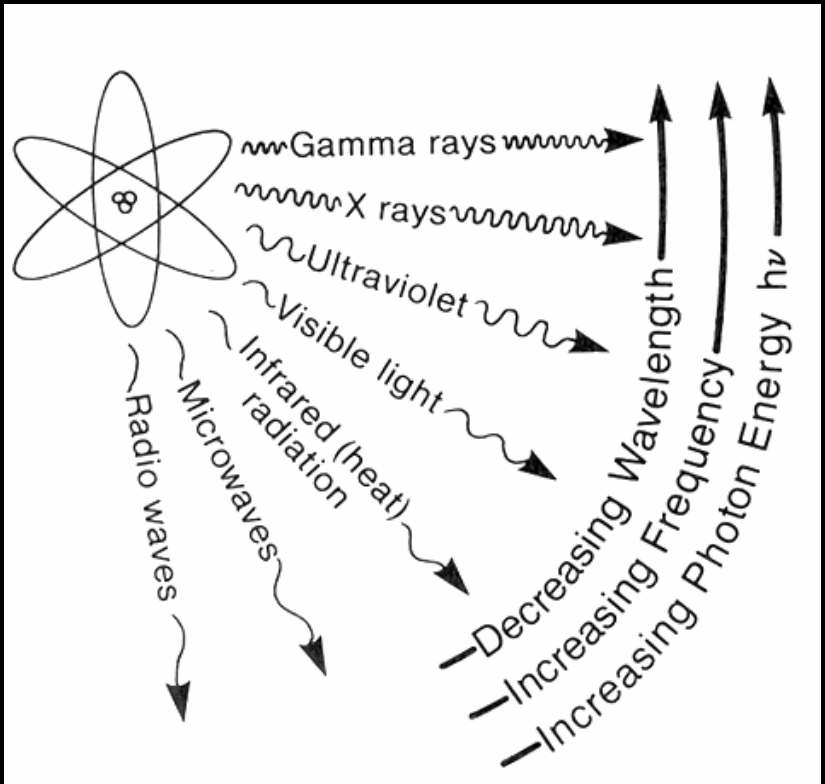
- Photons: “packets” of energy

E = hv (E= energy, h = Planck’s constant, v= frequency)

$$\lambda(\text{Å}) = \frac{12.4}{E(\text{keV})}$$

keV= 1.6 x 10^{-9} ergs

A=10^{-8} cm



X-射束與伽碼射束 (Gamma-ray)

- X-射線 (X-ray): 核外發生
  - Accelerating of electron to hit the target, energy loss by the form of x-ray.
  - Diagnostic and therapeutic X-ray
- 伽馬線（γ-ray）:核內發生
  - Decay of isotope
  - Co-60, Cs-137 ……

Definition of radiation dose

Unit:

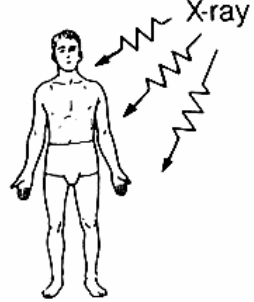
1 Gy = 1 J/Kg, (4 Gy = 4 J/kg)

1 calorie = 4.18 J, (1 J=0.24 calorie)

increase 1°C => 1 Kcalorie/1 Kg

1 Gy = 1 J/Kg = 0.0002 ^{o}C

Total-Body Irradiation



Mass = 70 kg
LD/50/60 = 4 Gy
Energy absorbed =

$$70 \times 4 = 280 \text{ joules} = \frac{280}{4.18} = 67 \text{ calories}$$

X-ray

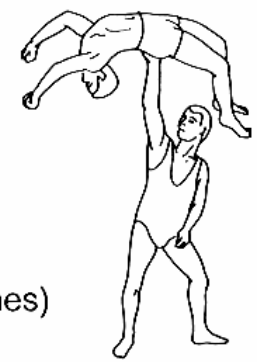
A

Drinking Hot Coffee

Excess temperature (°C) = 60° − 37° = 23°
Volume of coffee consumed to equal the energy in the LD/50/60 = $\frac{67}{23}$ = 3 mL = 1 sip

B

Mechanical Energy: Lifting a Person



Mass = 70 kg
Height lifted to equal the energy in the

$$\text{LD/50/60} = \frac{280}{70 \times 0.0981} = 0.4 \text{ m (16 inches)}$$

C

LD/50/60: 在60天內引起一半照射生物死亡所需的劑量。在人類為4格雷。(LD: Lethal dose)

游離輻射:

- 能量被身體吸收。
- 與非游離輻射相比，其生物效應不在於吸收能量的總量，而在於其吸收能量的總量的品質。

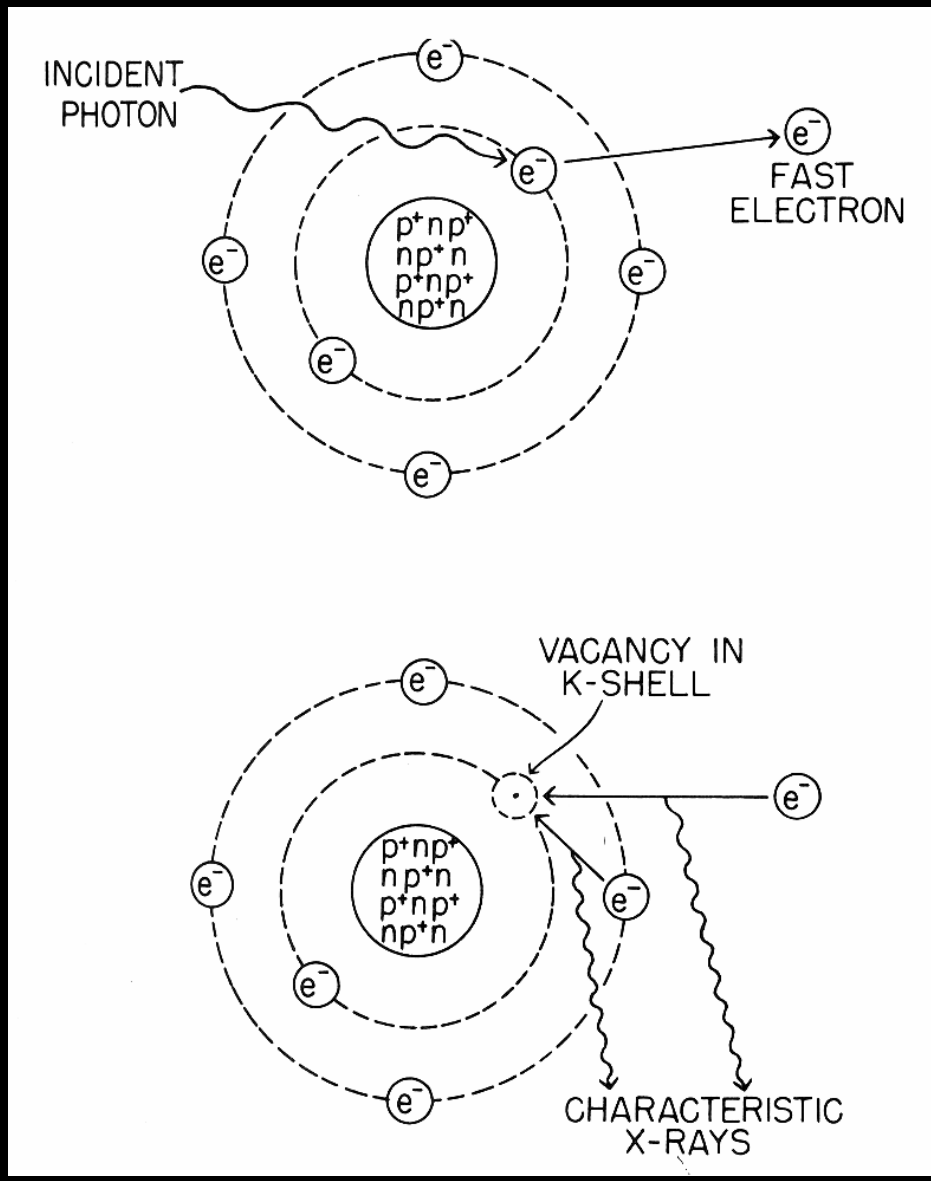
X-射束的吸收

品質的關鍵：游離”

1. 光電效應 (Photoelectric process):

lower energy range

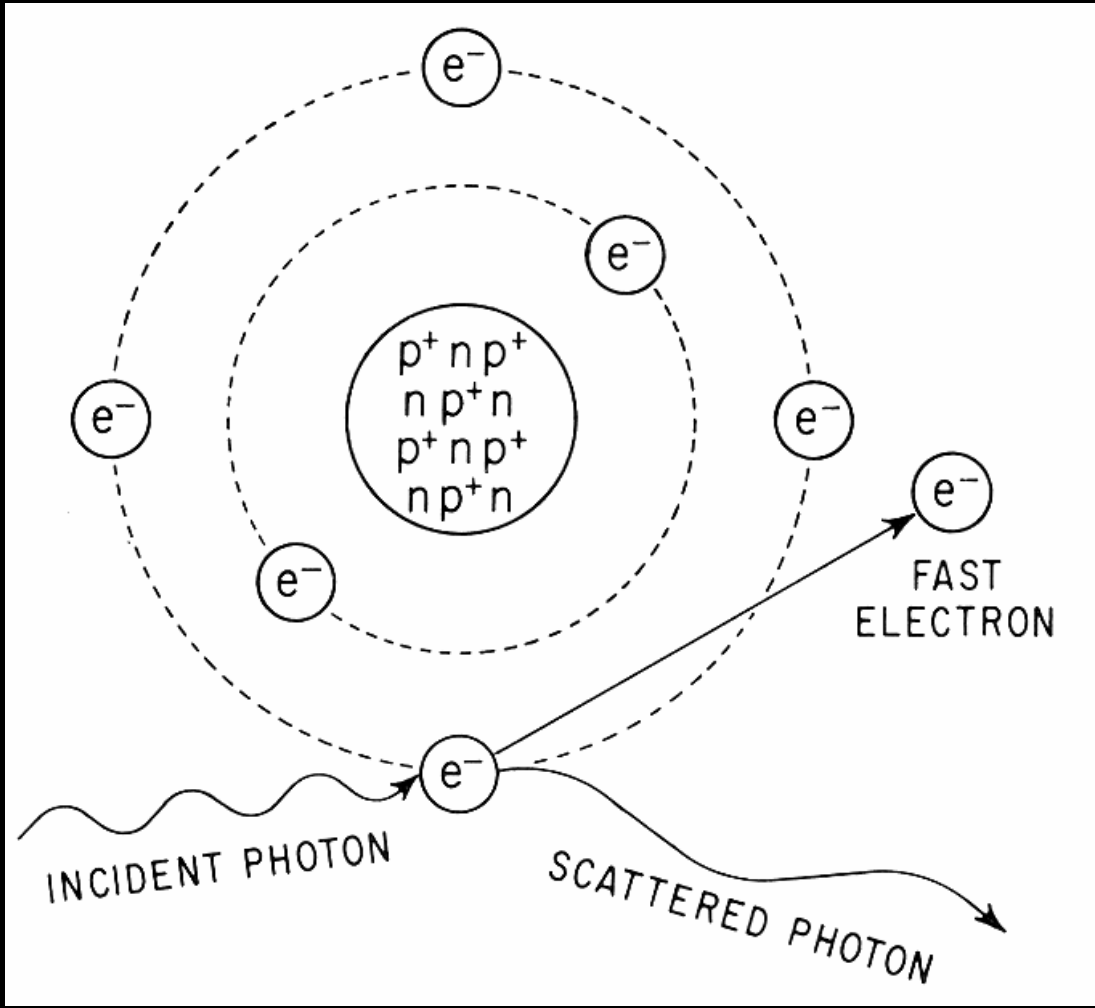
proportional to Z^3.



診斷用X-光因原子序及密度　同而形成對比（光電效應與Z^3成正比）

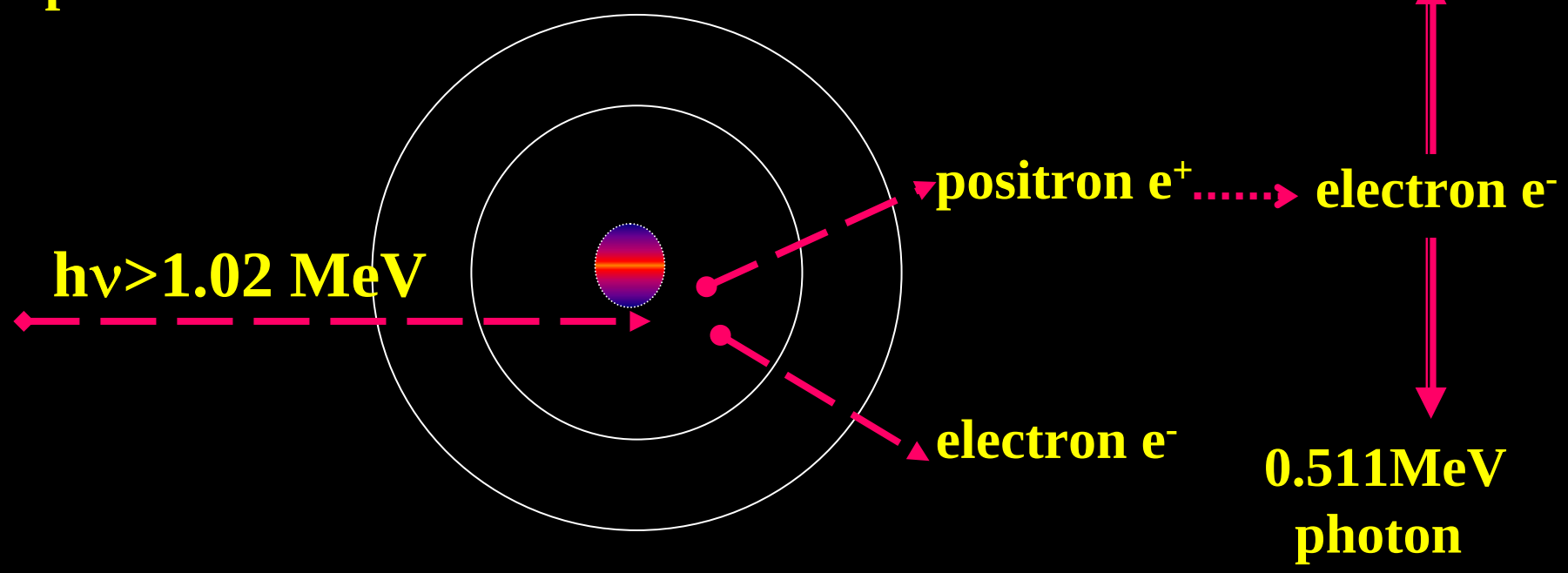
Absorption of X-rays

2. 康普吞效應(Compton process):
higher energy range, independent of Z.



Absorption of X-rays

3. 成對效應 (Pair production):
>0.51 MeV,
proportional to Z



電子游離的後續效應
(Consequences of ionizing event)

eg. 70-80% body content is water

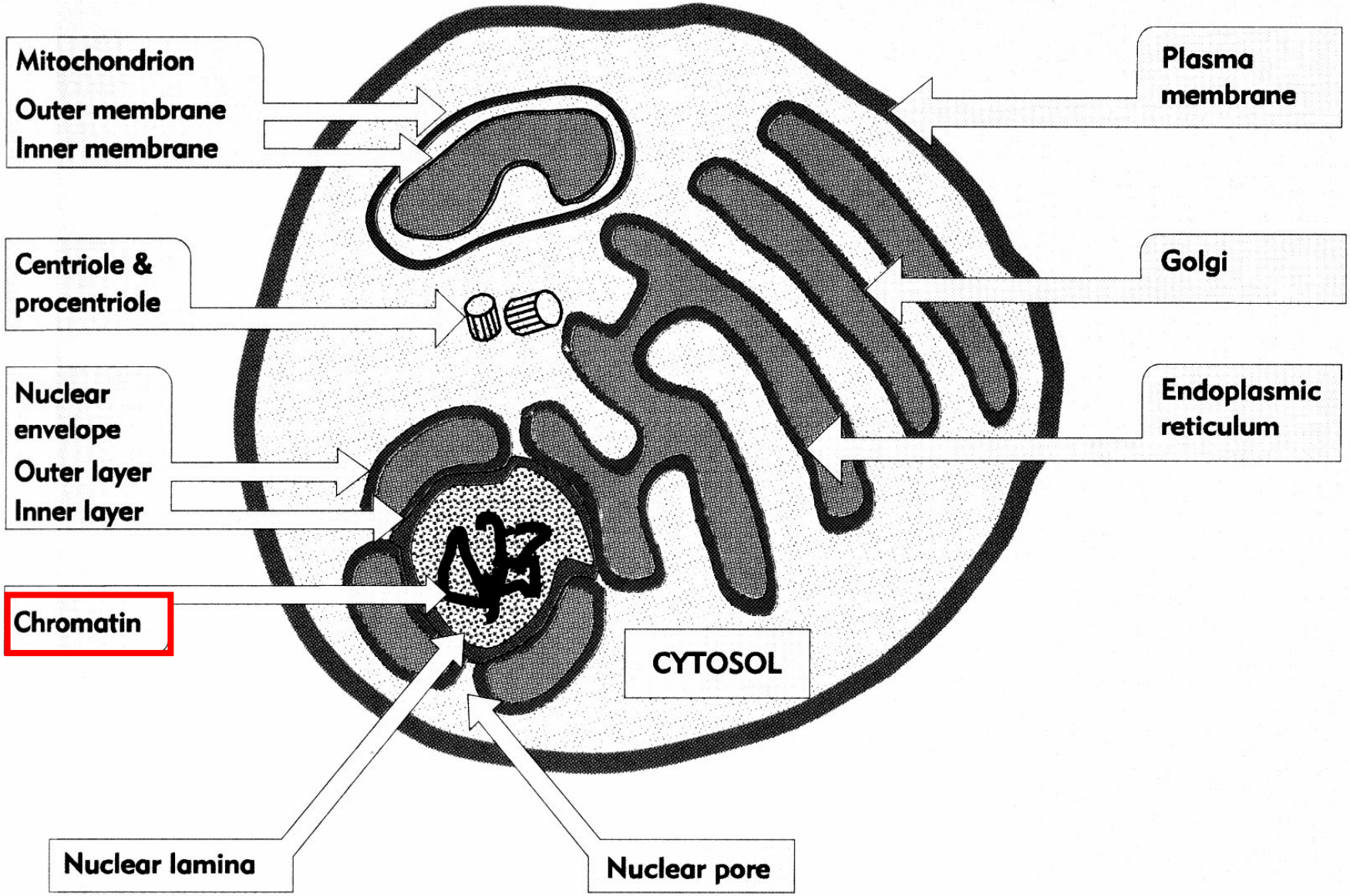
$H_2O \rightarrow H_2O^+ + e^-$

$H_2O^+ \rightarrow OH^{\cdot} + H^+$

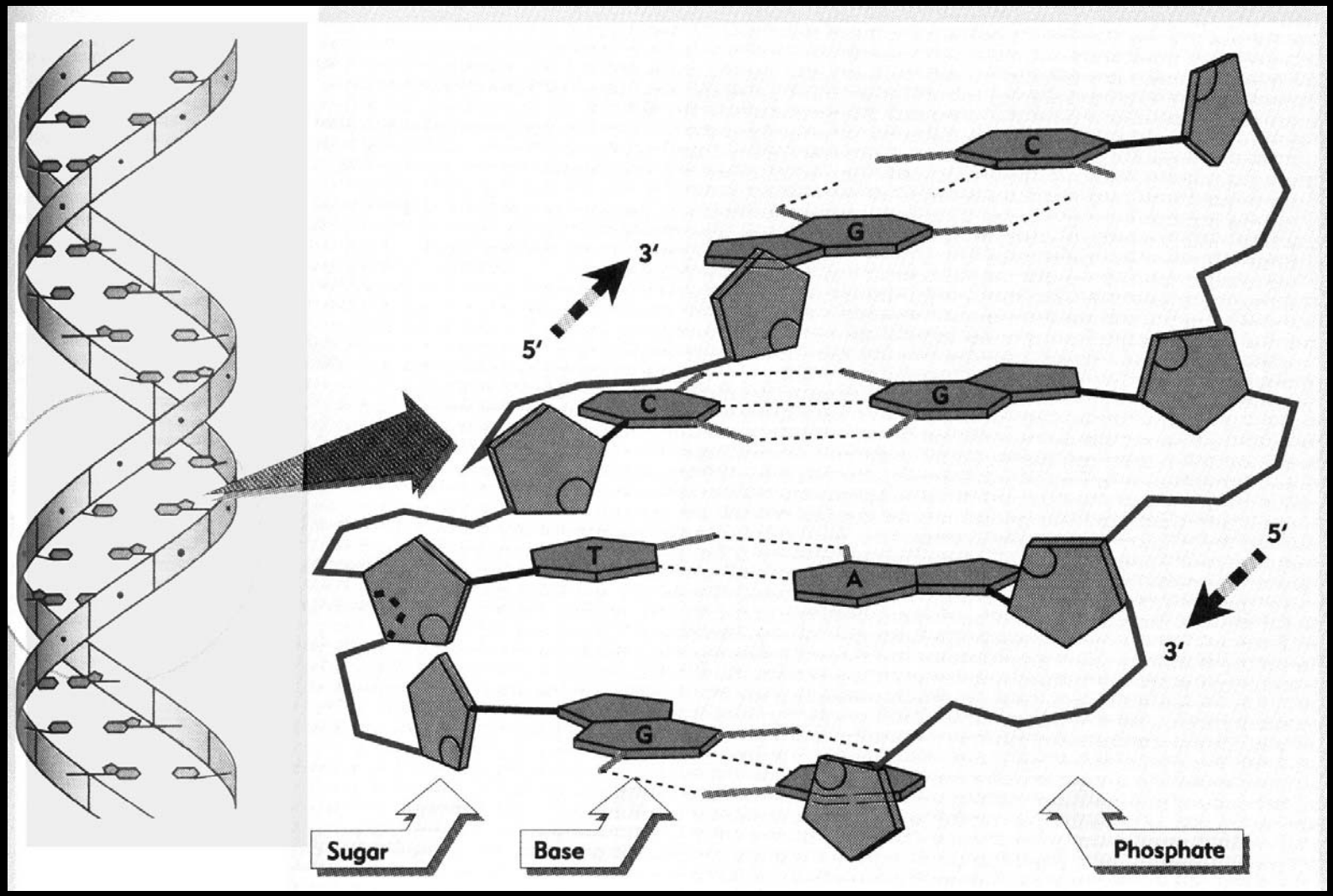
$H_2O^+ + H_2O \rightarrow H_3O^+ + OH^{\cdot}$

- **Formation of free radicals is the major biochemical consequence**
- **X-ray damage to DNA: 2/3 caused by hydroxy radicals**

Components of an eukaryotic cell



What is Deoxyribonucleic acid (DNA) ?

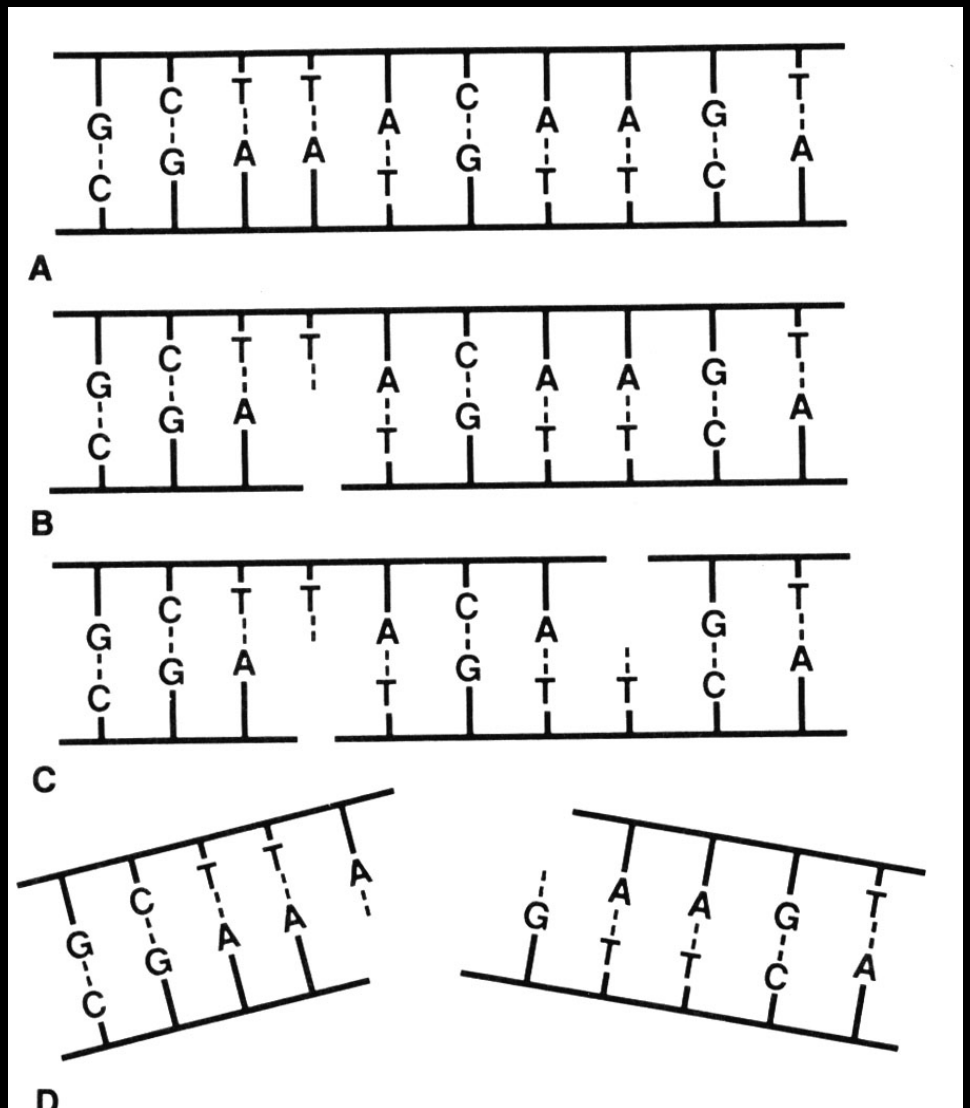


Adenine pairs thymine， Guanine pairs cytosine

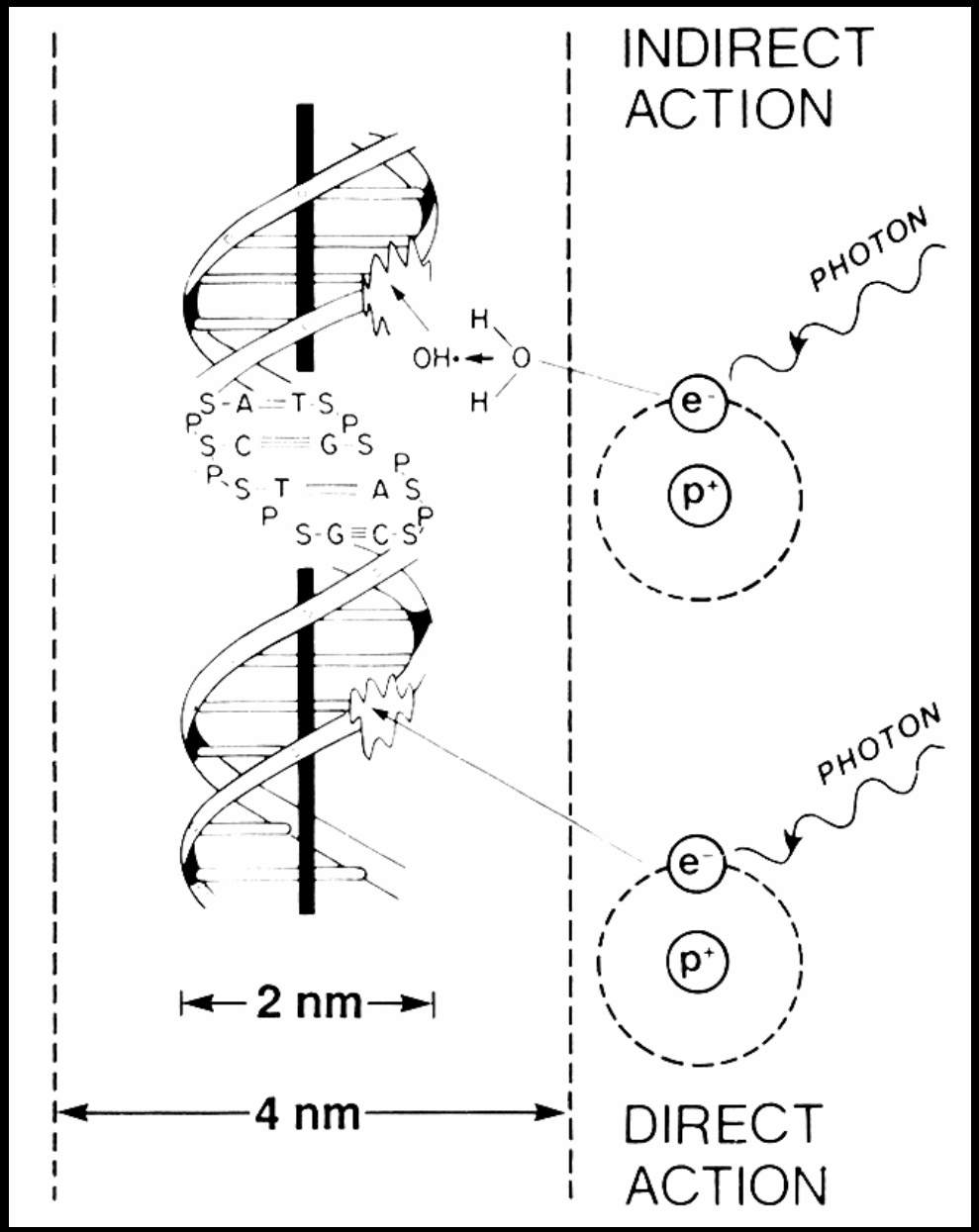
Function of DNA:
carry genetic code.

DNA strand break

- 單股斷裂 (Single strand break) vs.双股斷裂 (double strand break)



DNA 傷害



單股斷裂 (Single-strand breaks, ssb’s)

雙股斷裂 (Double-strand breaks, dsb’s)

DNA傷害後細胞的命運

- 死亡
- 存活
  - 完全修復
  - 不完全修復
    - 未在重要部位
    - 在重要部位：突變、致癌

Time Scale of Radiation Effects

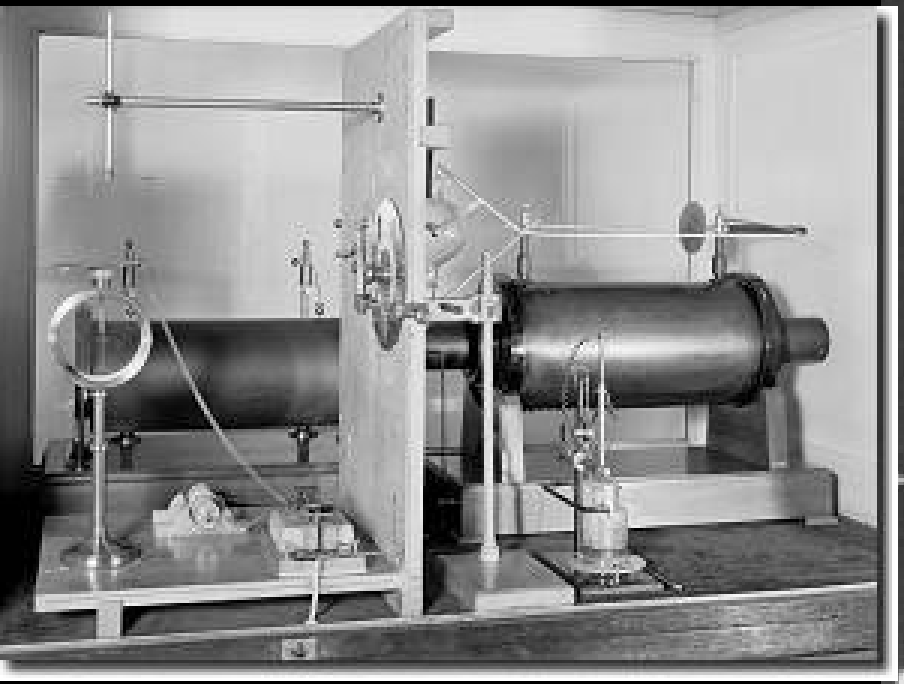
Sec		
	INCIDENT PHOTON	
10^{-18}	IONIZATION AND EXCITATION	Physical effects
10^{-12}	ION RADICAL LIFETIME	Chemical effects
10^{-6}	FREE RADICAL LIFETIME	
10^{0}	BREAKAGE OF BONDS CHEMICAL REPAIR / MISREPAIR ENZYMIC REPAIR / MISREPAIR	Biochemical effects
Mins-Hrs	EARLY BIOLOGICAL EFFECTS	Cellular effects Tissue effects Systemic effects
Hrs-Days		
10^{6}	LATE BIOLOGICAL EFFECTS	
Days-Years		

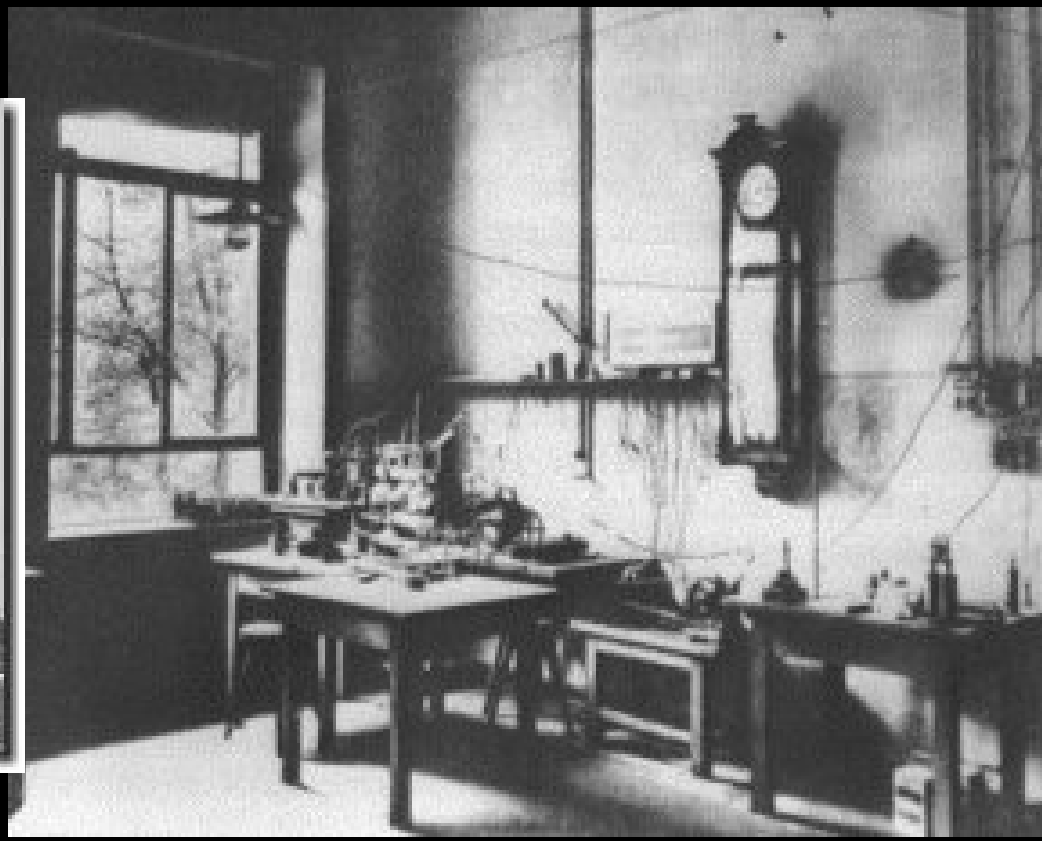
游離輻射之歷史

- **X-ray:**
  - **discovered by Roentgen in 1895.**
  - **“a new kind of ray” emitted by a gas discharge tube. X: unknown**
- **First radiography: hand**
- **First application: published in Lancet in 1896, located a piece of knife in the backbone.**
- **Radioactivity:**
  - **by Becquerel in 1898.**
- **Radium:**
  - **by Piere and Marie Curie, 1898**

Roentgne’s laboratory

1895-11-08; University of Wurzburg

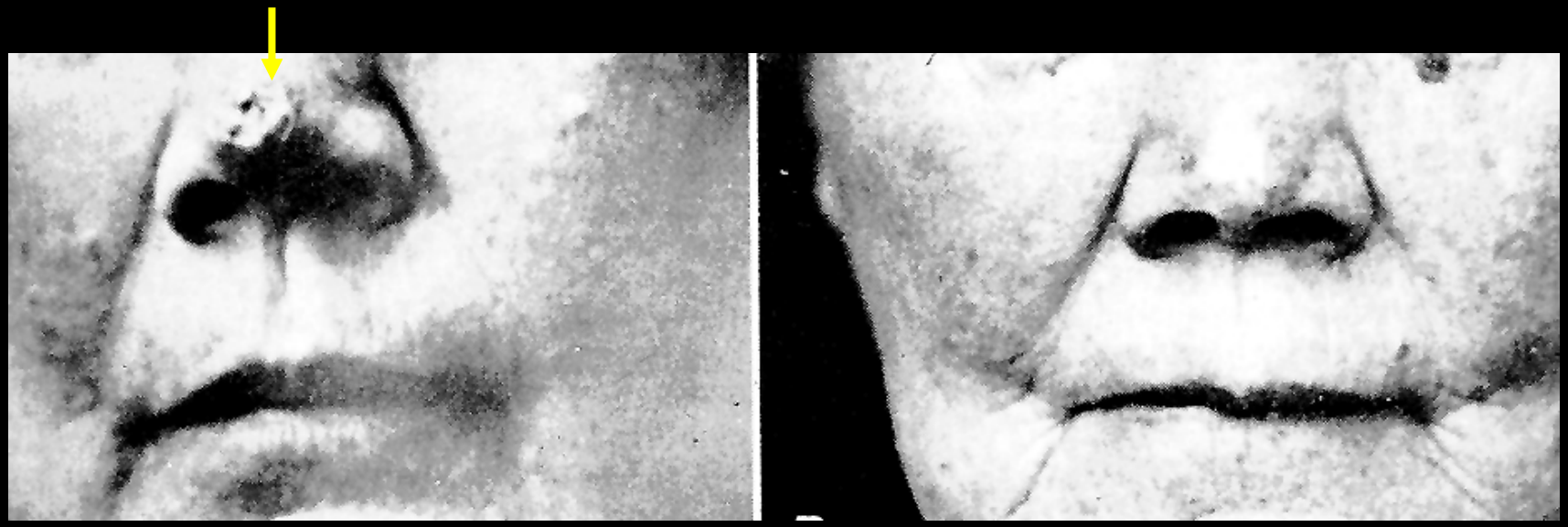




The first X-ray – Roentgne’s wife’s hand

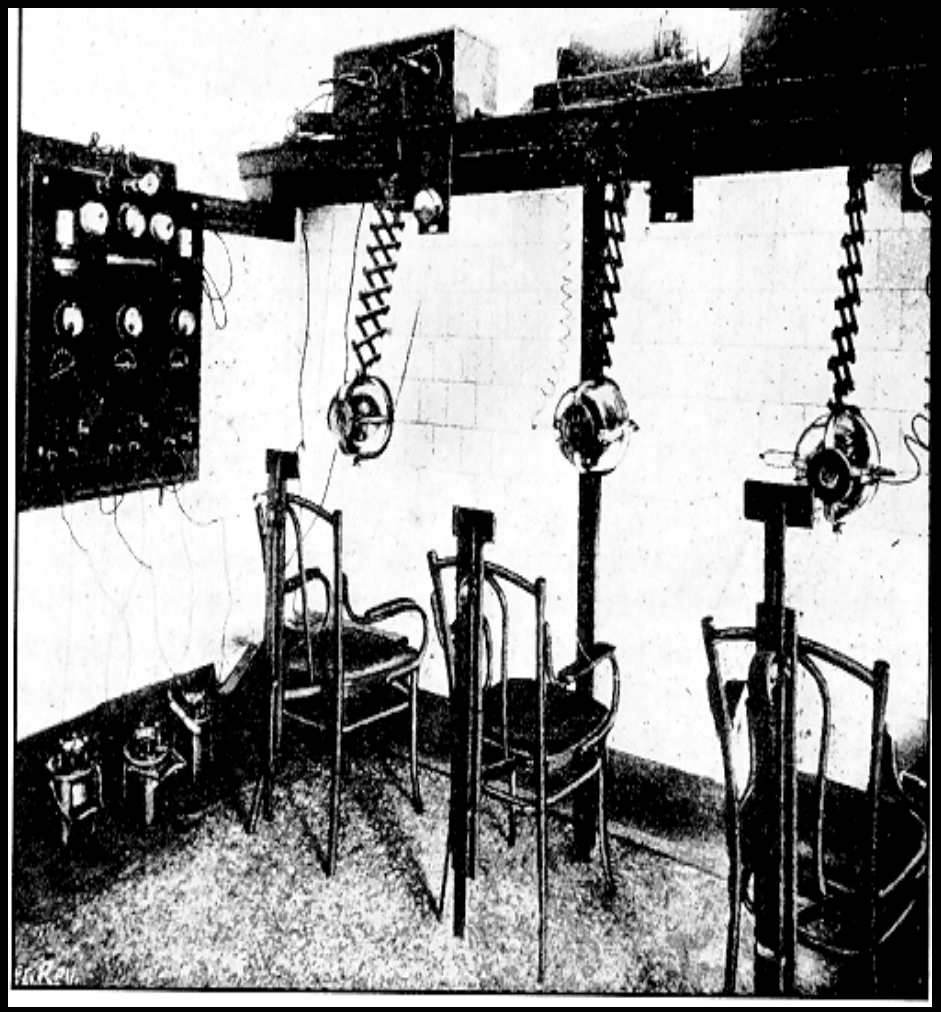
1895-12-22

第一個治癒個案



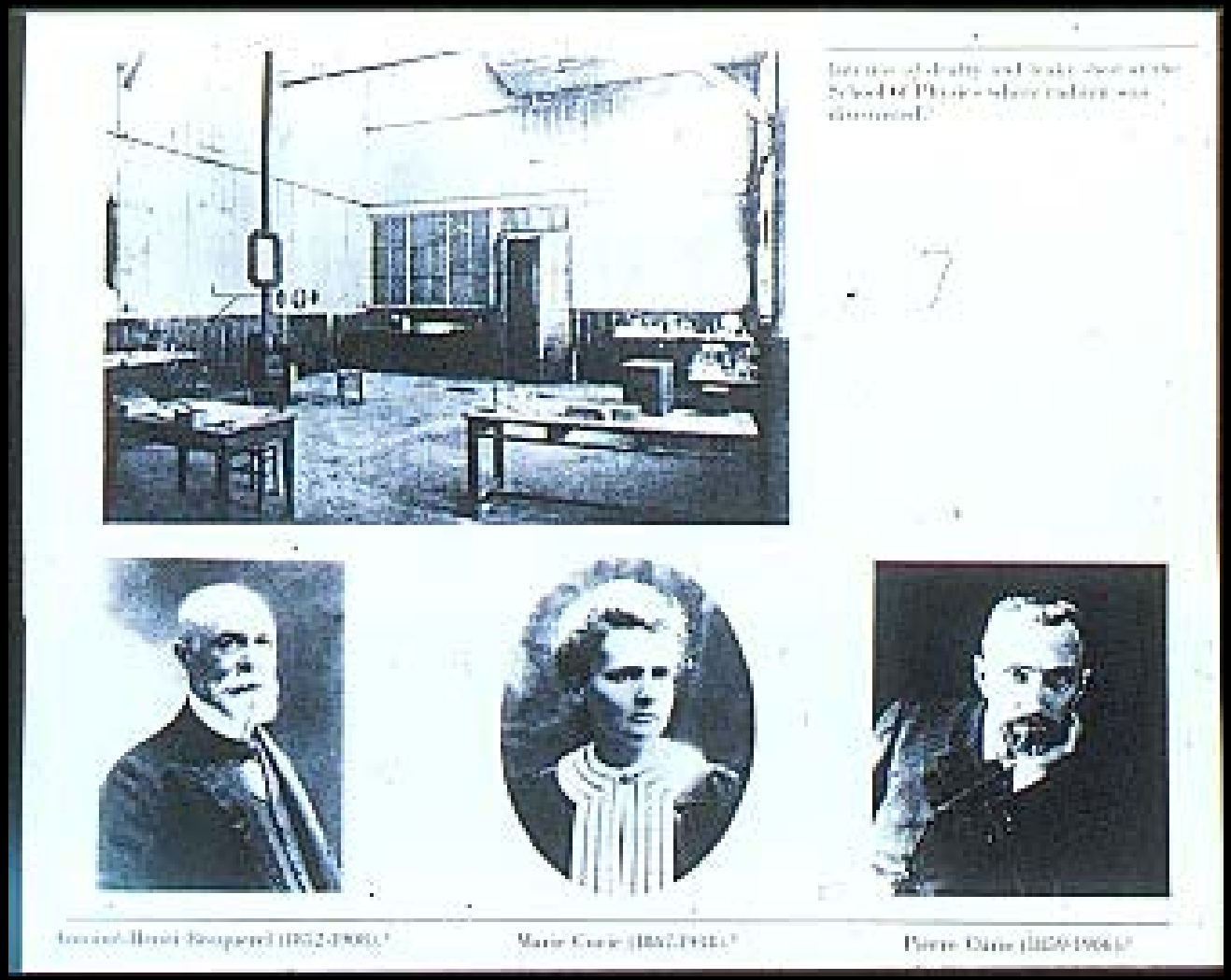
1899年治癒 basal cell carcinoma

Office-based therapy



Hammersmith Hospital, London, 1905

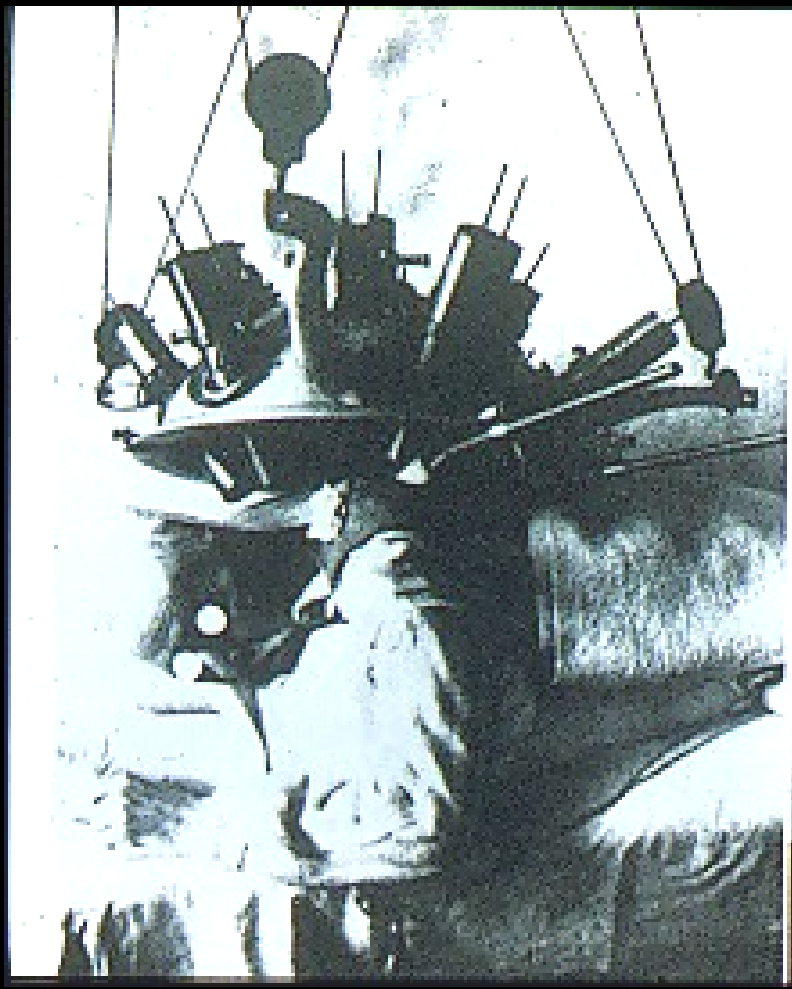
Radioactivity and radium

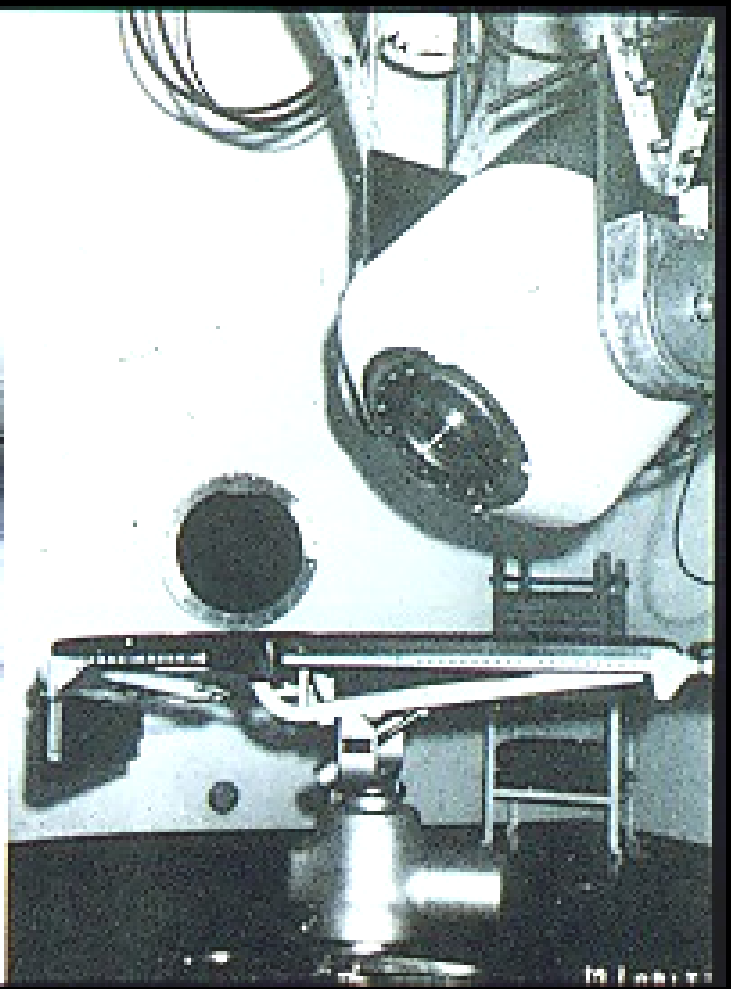


1896
Antoine Henri Becquerel: Uranium

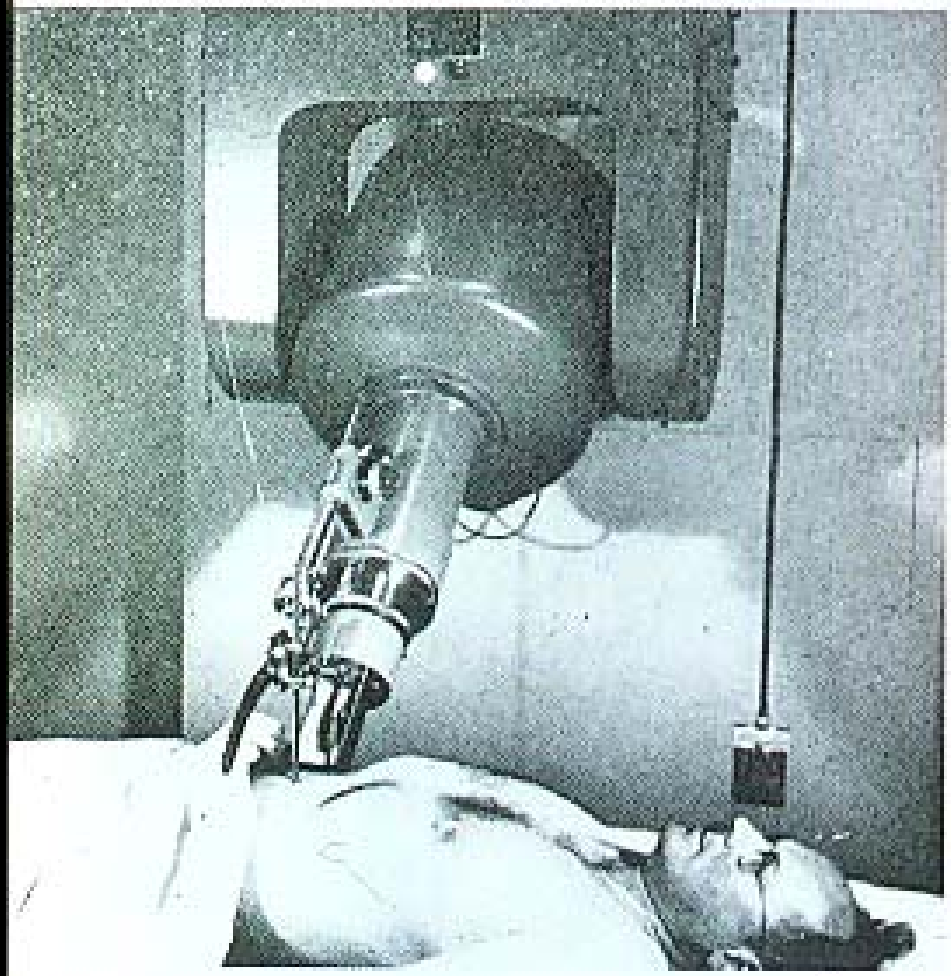
1898
Marie and Piere Curie: Radium and polonium

Radium bomb
1930



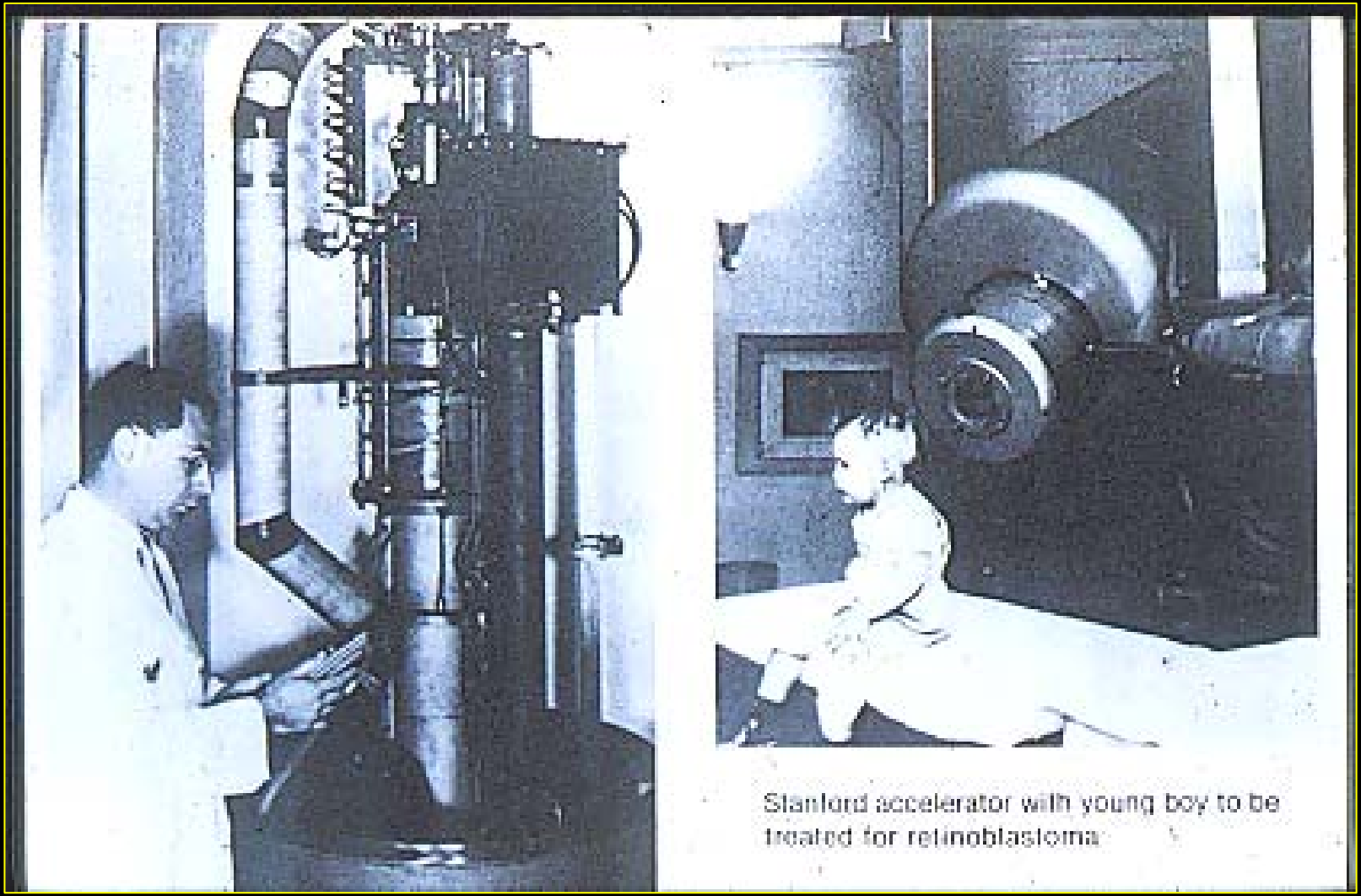


First Co-60 machine: 1951



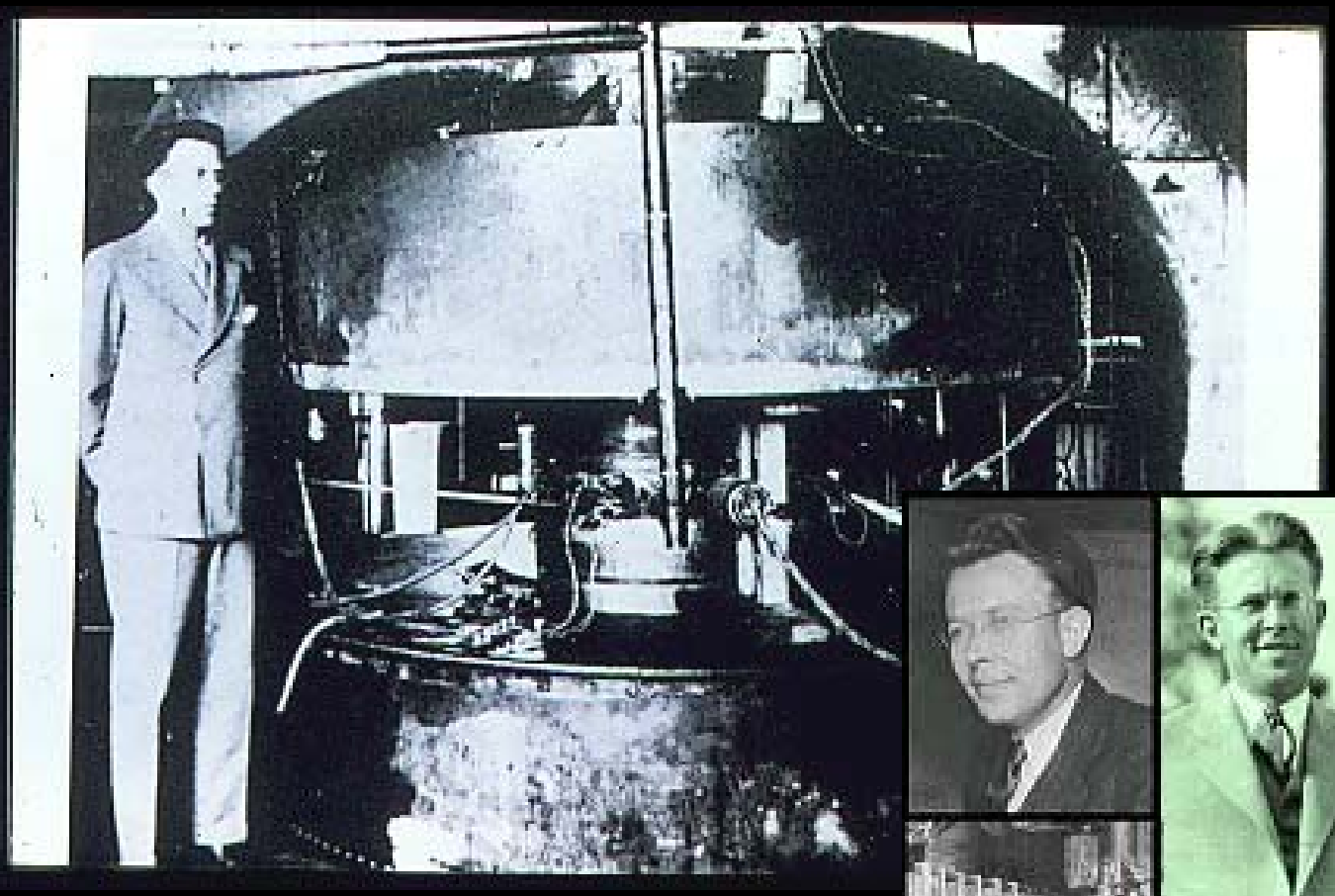
First cobalt-60 radiation therapy unit (1951).

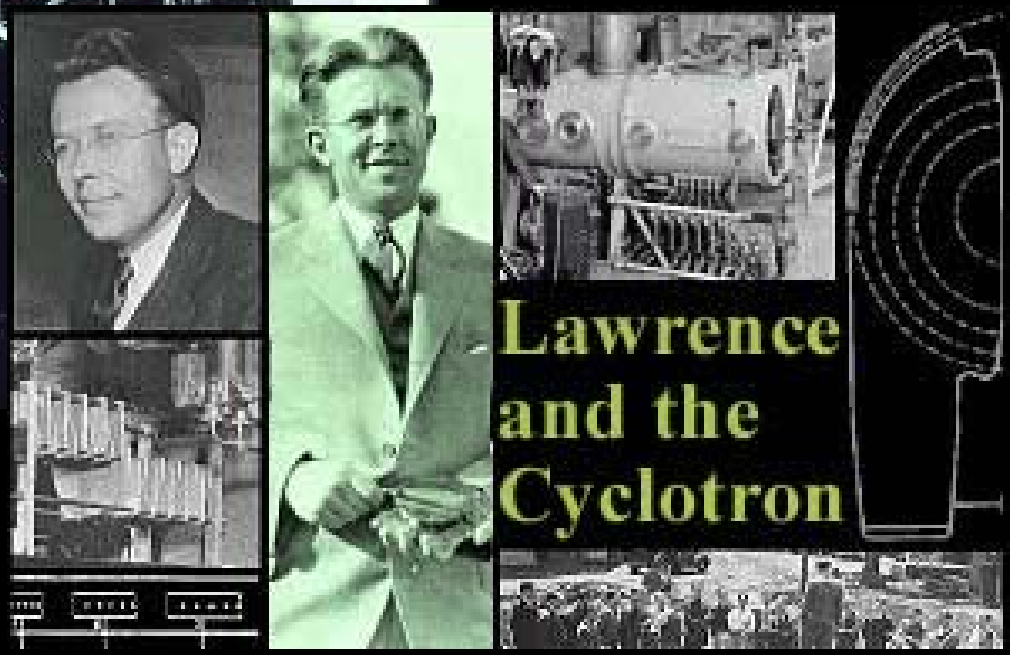
6 MV Stanford Linac and first treatment –year 1955



Stanford accelerator with young boy to be treated for retinoblastoma

Ernest O. Lawrence
Cyclotron, 1931



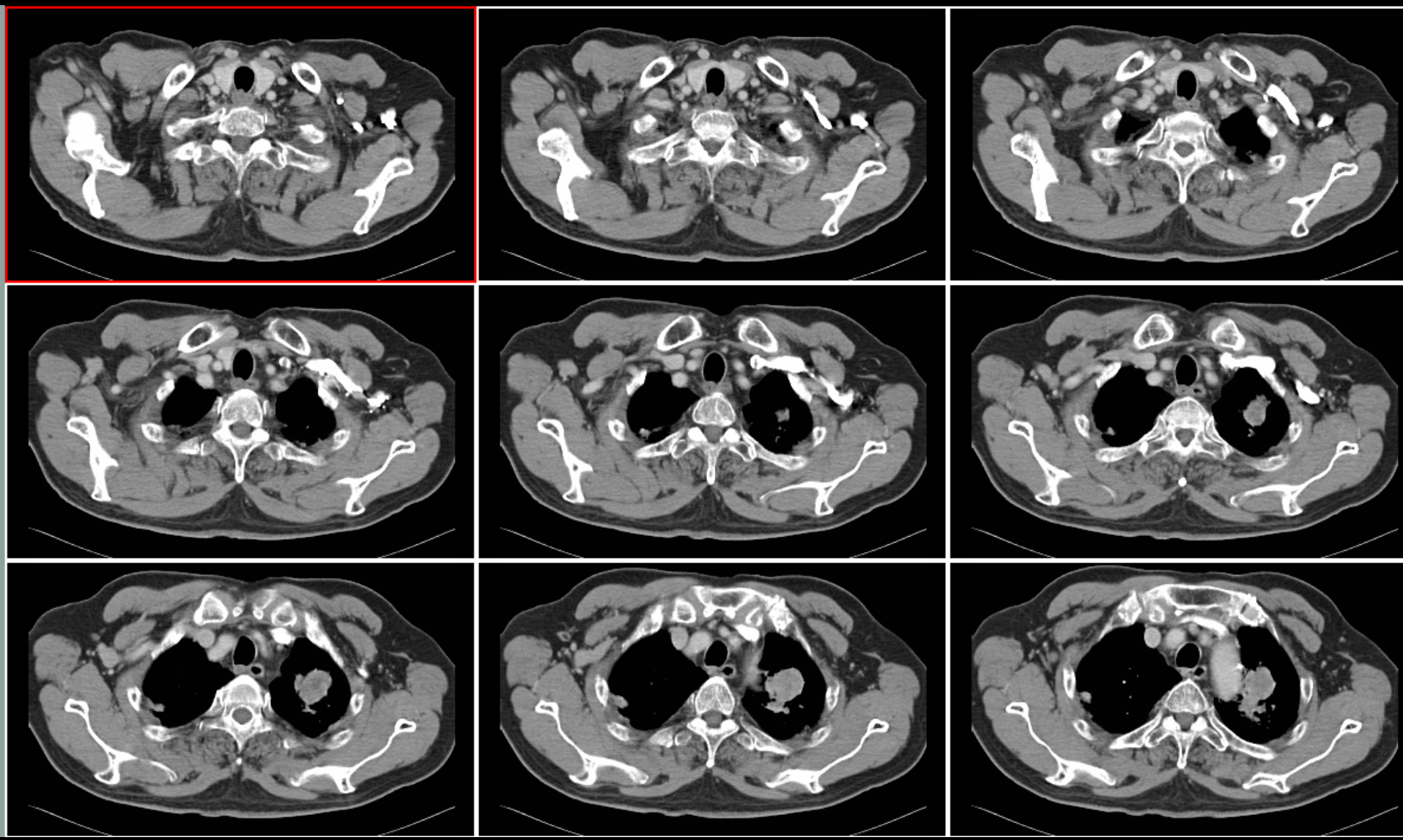


游離輻射之醫學應用

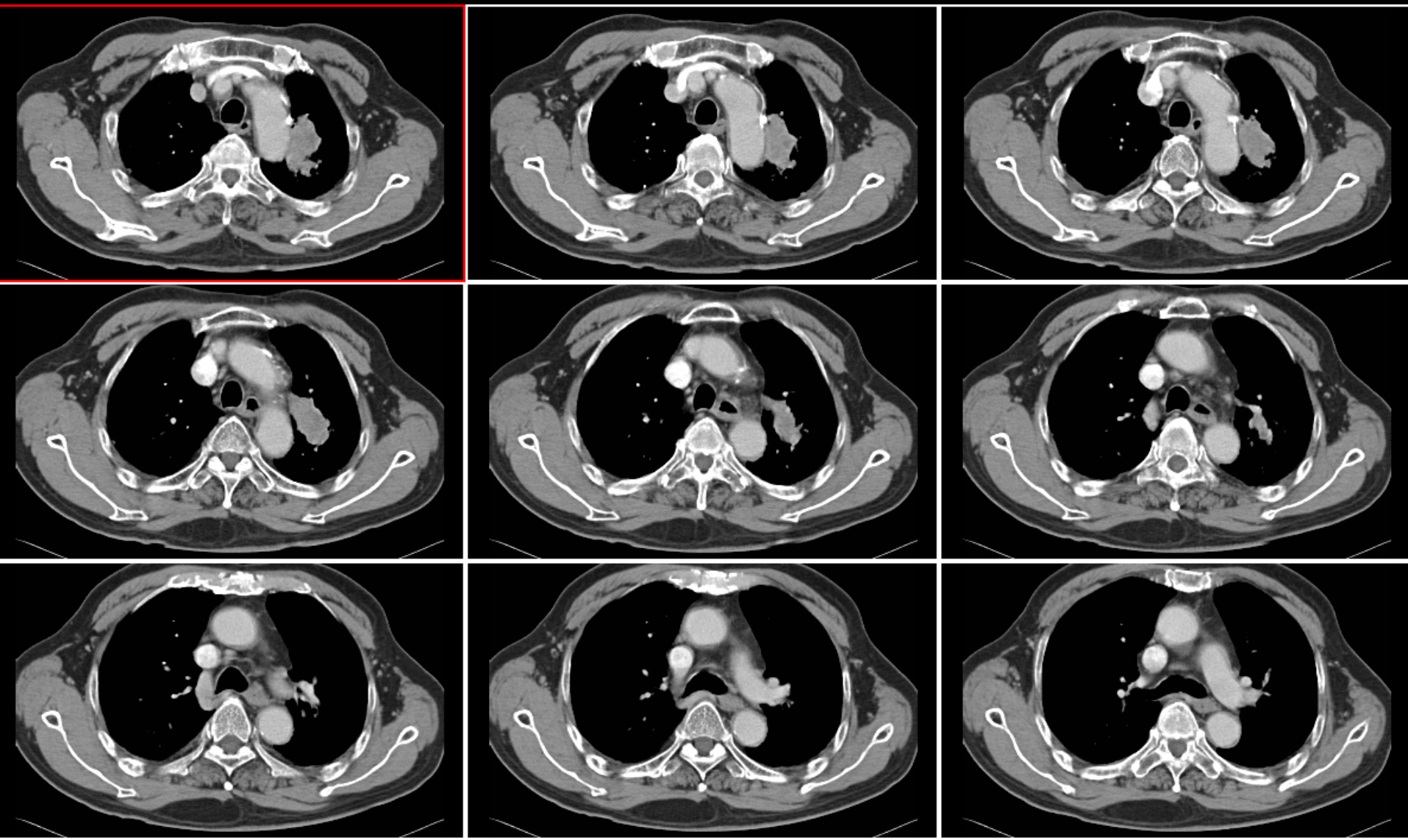
- 診斷
  - X-ray
    - X-ray tube
    - 電腦斷層
  - Isotope
    - 核醫
- 放射治療
  - 體外
    - Co-60, X-ray, 質子(proton), 重粒子..
  - 體內
    - Isotope

胸部X-光

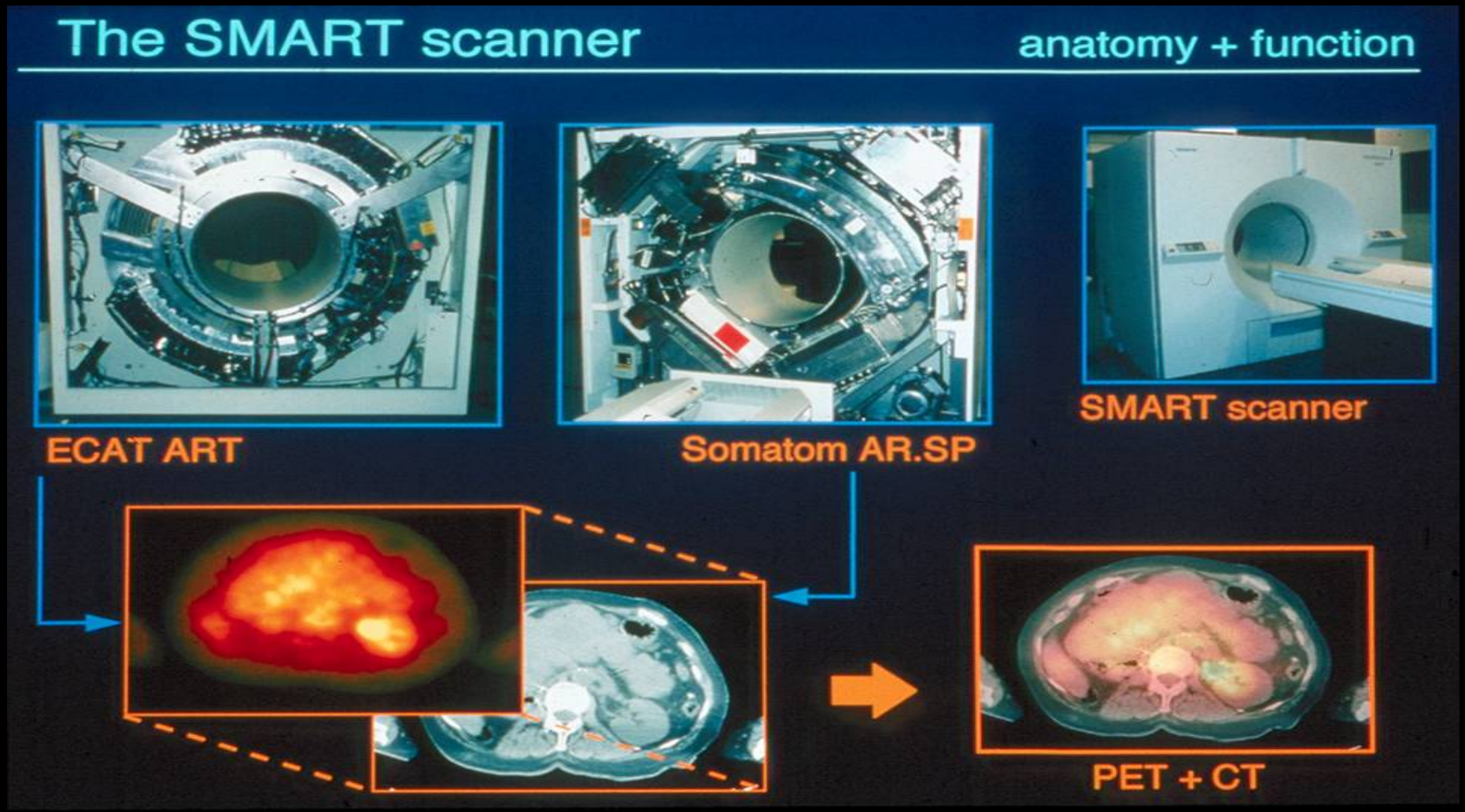
電腦斷層 (CT scan)



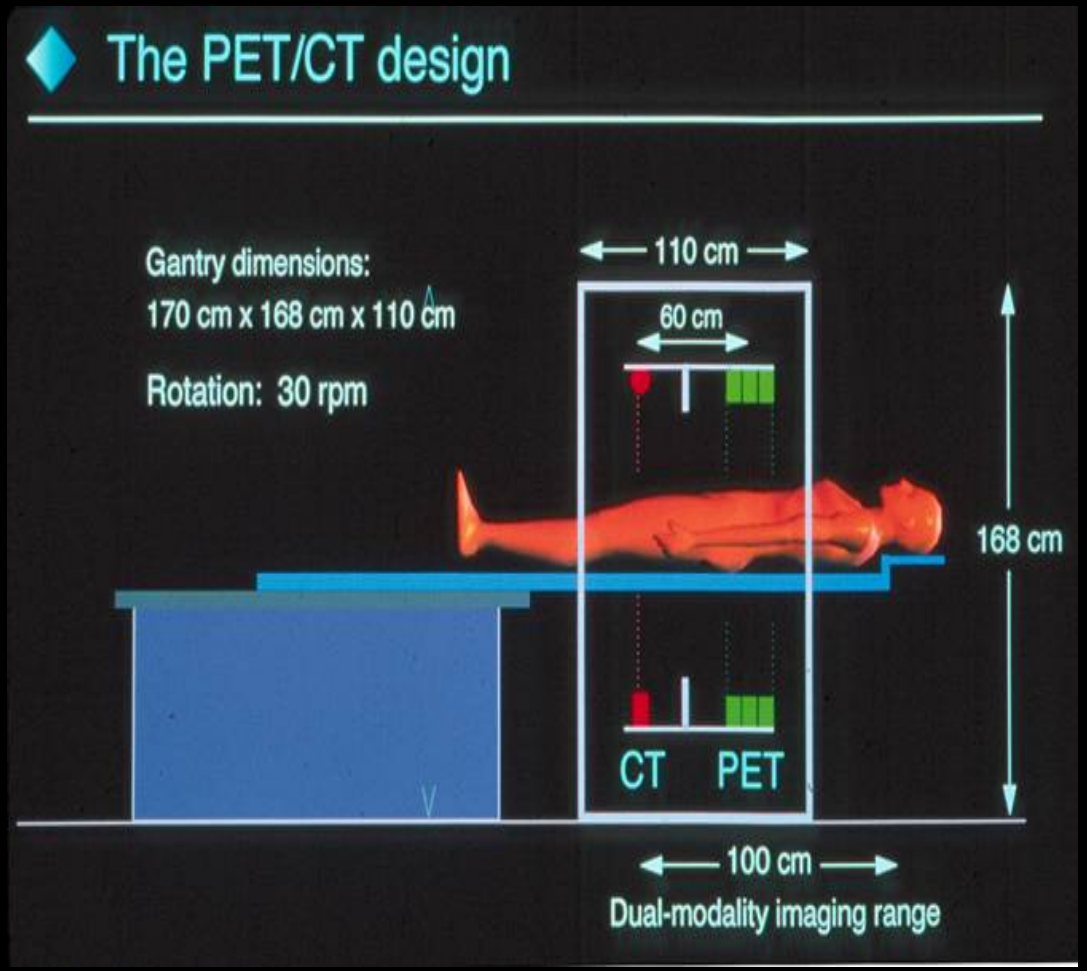
電腦斷層（CT scan）

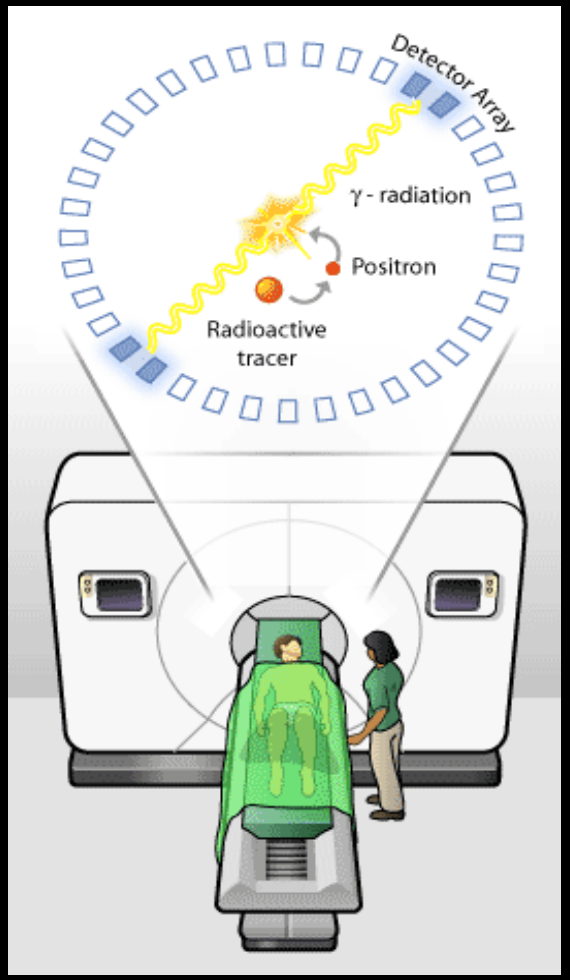


分子影像 – 正子照影

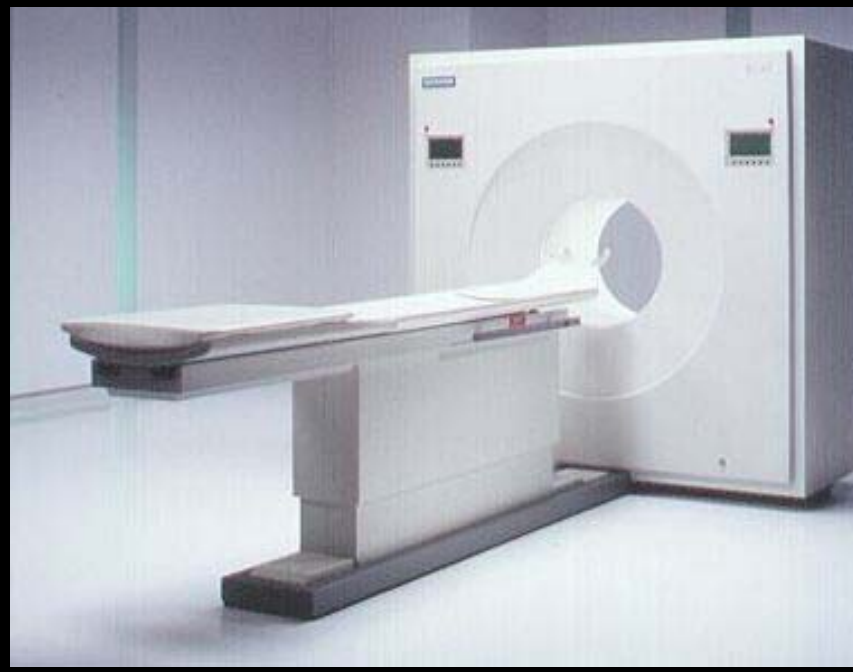

The SMART scanner
anatomy + function
ECAT ART
Somatom AR.SP
SMART scanner
PET + CT

如何做？

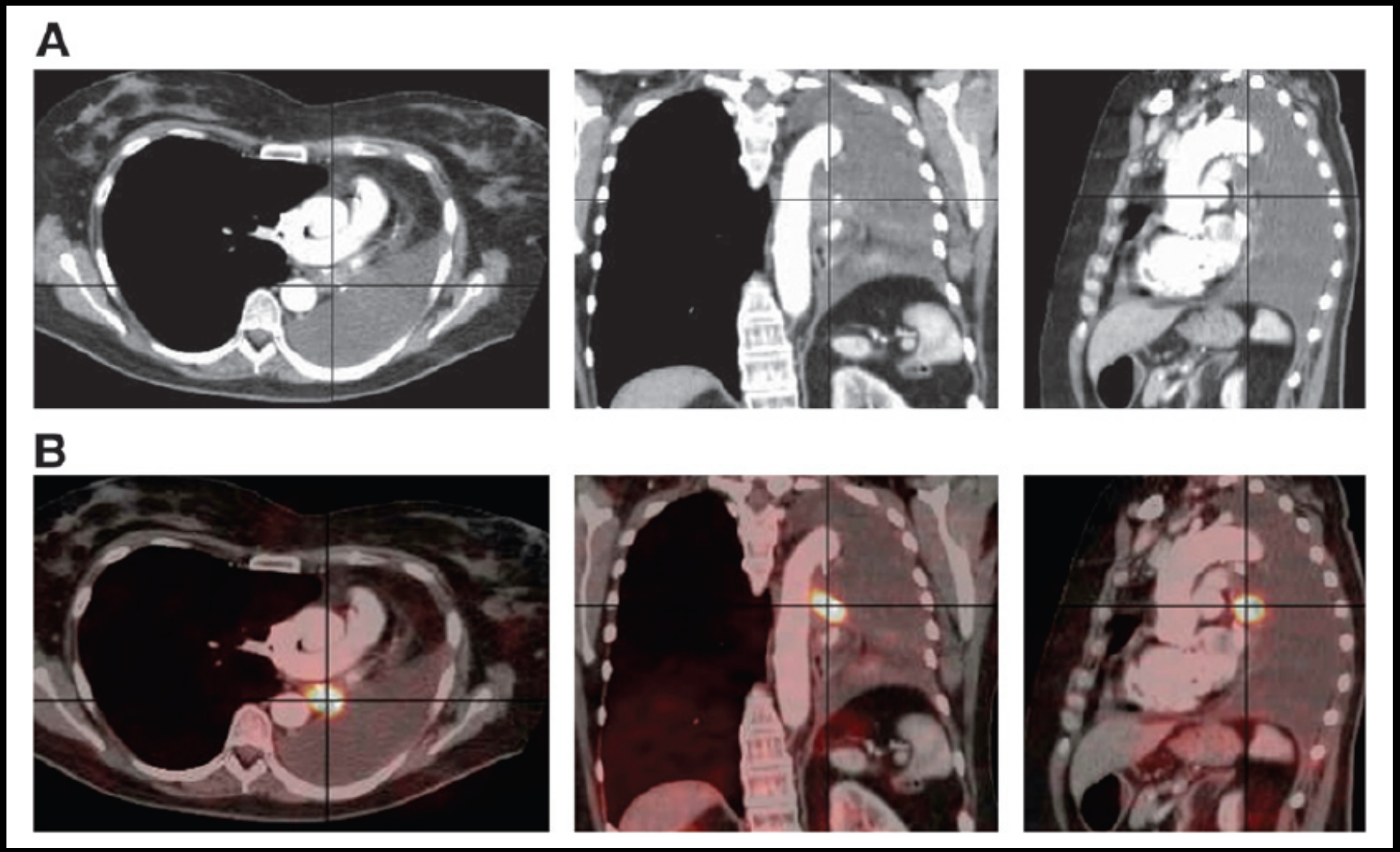

The PET/CT design
Gantry dimensions:
170 cm x 168 cm x 110 cm
Rotation: 30 rpm
110 cm
60 cm
168 cm
CT
PET
100 cm
Dual-modality imaging range

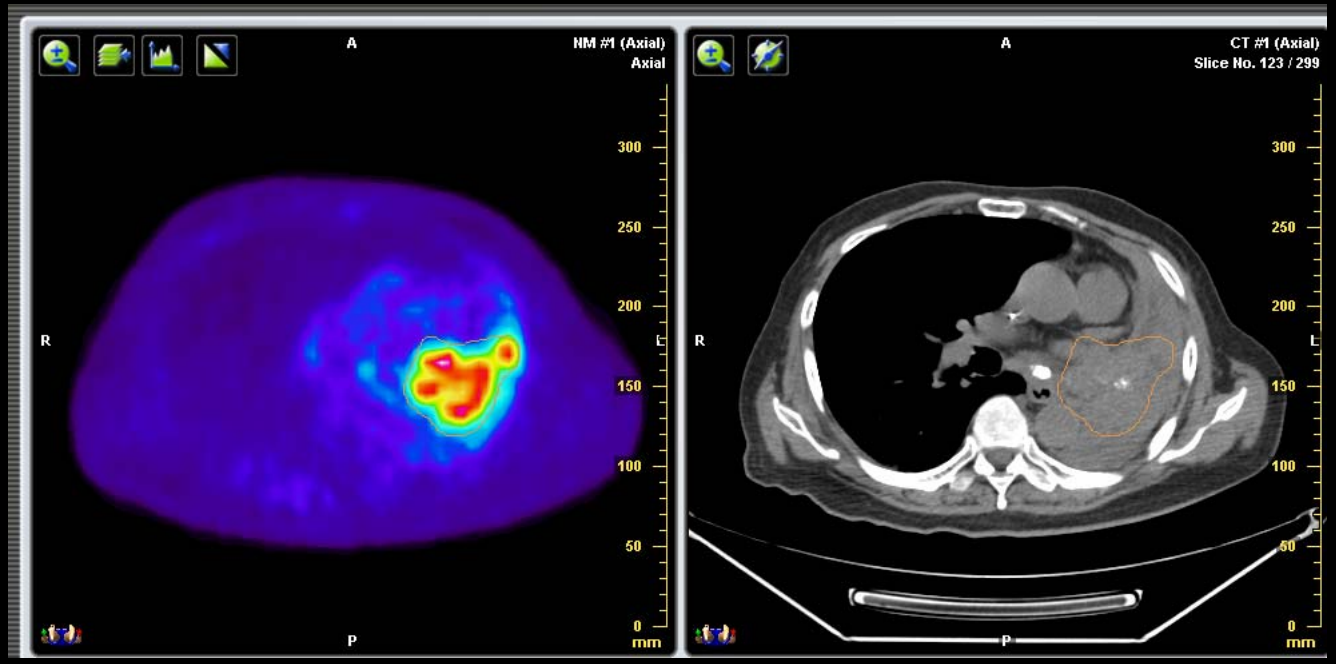

Detector Array
γ - radiation
Positron
Radioactive
tracer

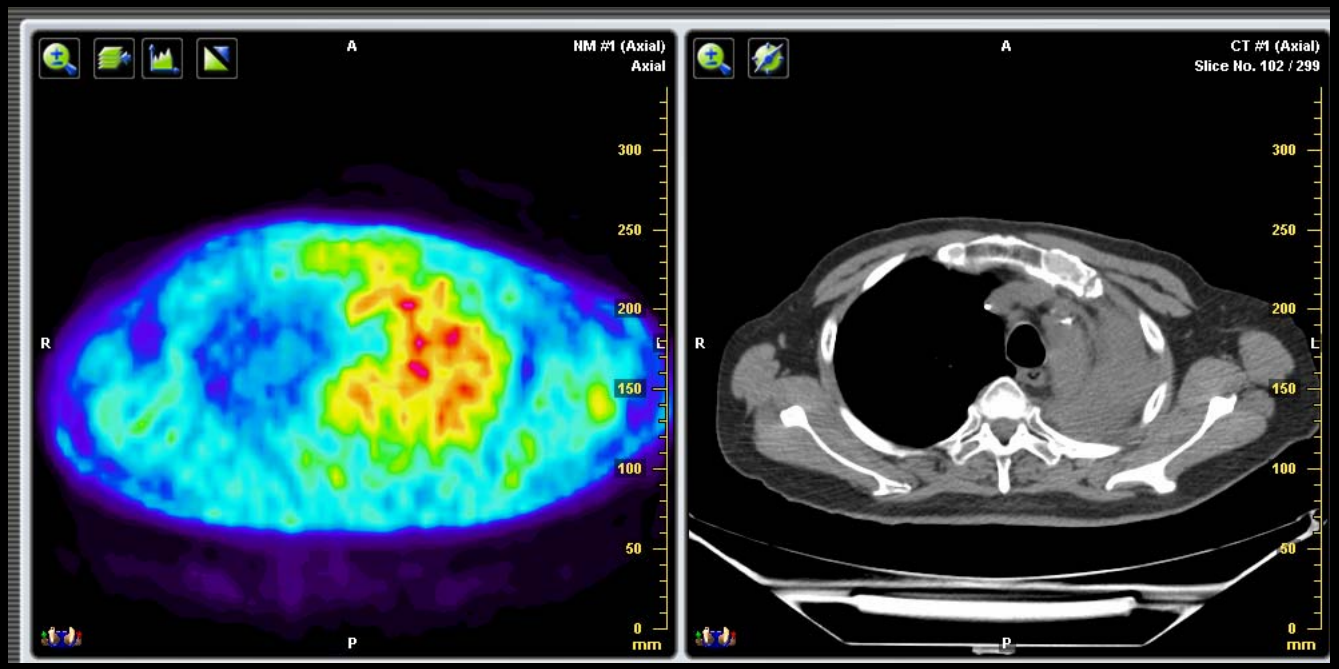
PET camera



分子影像 – 葡萄糖正子照影




A
NM #1 (Axial)
Axial
R
L
P
300
250
200
150
100
50
0
mm
A
CT #1 (Axial)
Slice No. 123 / 299
R
L
P
300
250
200
150
100
50
0
mm

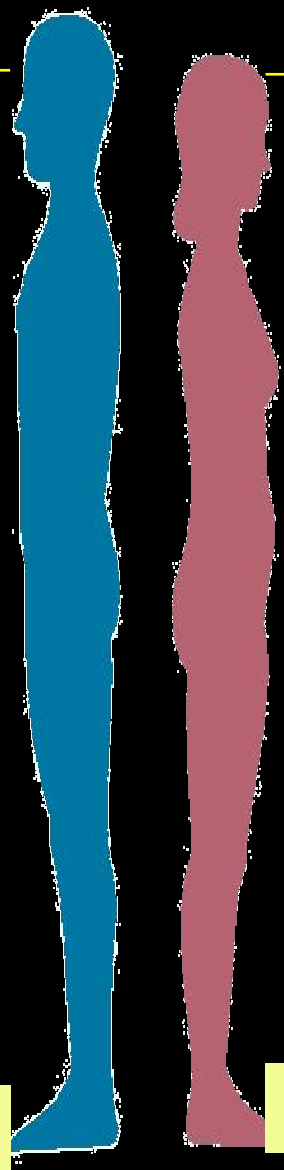

A
NM #1 (Axial)
Axial
R
L
P
300
250
200
150
100
50
0
mm
A
CT #1 (Axial)
Slice No. 102 / 299
R
L
P
300
250
200
150
100
50
0
mm

游離輻射之醫學應用 – 癌症治療

台灣男女性10大癌症發生分率, 民國93、94年

（發生人數）部位	百分比
(7,051、 7,159)肝	18、18
(5,426、5,497)結腸及直腸	14、14
(5,537、 5,566)肺	14、14
(4,363、4,310)口腔	11、11
(2,660、2,704)攝護腺	7、7
(2,380、2,288) 胃	6、6
(1,374、1,403)食道	4、4
(1,380、1,363)膀胱	4、3
(1,196、1,139)皮膚	3、3
(1,123、1,123)鼻咽	3、3
(6,585、6879)其他癌症	16、17

男性共（39,075、 39,431人）



百分比	部位（發生人數）
21、22	乳房 (6,176、6593人)
14、14	結腸及直腸(4,109、4107人)
10、9	肝(2,779、 2,757人)
9、9	肺(2,605、 2,746人)
8、7	子宮頸(2,292、 1,977人)
5、4	胃(1,338、 1,292人)
4、4	甲狀腺 (1,132、 1,146人)
3、4	皮膚(965、 1,039人)
3、3	子宮體(877、 987人)
3、3	卵巢 (841、 894人)
20、20	其他癌症(5,707、5,938人)

女性共（28,821、29,476人）

備註:口腔癌含下咽及口咽

男性10大癌症90-94年新發個案存活率(追蹤至95年)

	全癌症	肝	肺	結直腸	口腔	胃	攝護腺	膀胱	食道	鼻咽	皮膚
一年	64	48	36	82	77	59	94	88	39	88	94
二年	52	36	20	71	62	46	89	82	21	78	90
三年	46	29	15	65	56	41	84	78	16	70	88
四年	43	24	12	60	52	37	81	75	13	66	86
五年	40	20	10	57	49	35	78	73	12	61	84

女性10大癌症90-94年新發個案存活率(追蹤至95年)

	全癌症	乳房	子宮頸	結直腸	肝	肺	胃	甲狀腺	皮膚	子宮體	卵巢
一年	80	97	91	82	53	48	62	96	96	92	84
二年	72	93	84	72	40	30	49	96	93	87	75
三年	68	90	79	66	32	22	44	95	91	84	68
四年	65	87	76	62	26	17	41	95	89	82	63
五年	63	85	74	59	22	15	40	94	88	80	61

備註:子宮頸癌僅限侵襲癌

如何根治腫瘤治療

- 早期發現 – 診斷
- 早期治療
  - 精準掌握病情 – 診斷
  - 最佳的治療
    - 手術
    - 放射治療
    - 化學治療

第一目的：局部腫瘤控制

- 腫瘤治療失敗
  - 1/3 死於遠側轉移。
  - 1/3 死於局部失敗。
  - 1/3 死於局部復發加，遠側轉移→>>局部失敗。
- 腫瘤治療失敗
  - 死亡。
  - 生活品質損害代價高。
- 放射治療根治不同腫瘤
  - Eg. 子宮頸癌、鼻咽癌、頭頸癌、乳癌、攝護腺癌等

放射治療的目的

- *根治*：根治腫瘤。
  - 第一目的：局部腫瘤控制。
  - 第二目的：功能保留。

- *疏緩*：
  - 不能根治腫瘤，延長生命或改善生活品質。

第二目的：功能保留

- 不只根治腫瘤，同時保留器官功能.
- 主要部位:
  - Eg: 早期乳癌、喉癌、下咽癌、攝護腺癌、膀胱癌等

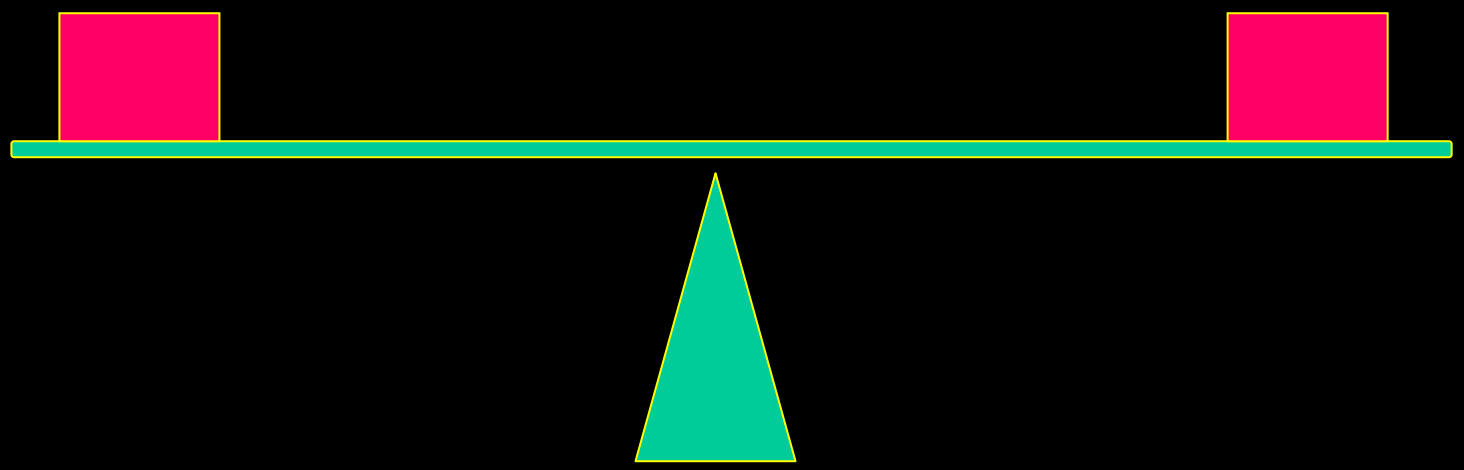
放射治療基本原則

精準定位
劑量

劑量和體積

腫瘤控制

副作用



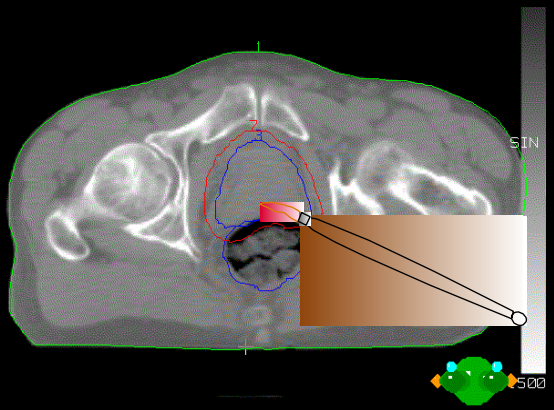
三度空間順形治療 (3-D conformal RT)

Immobilization

Image acquisition

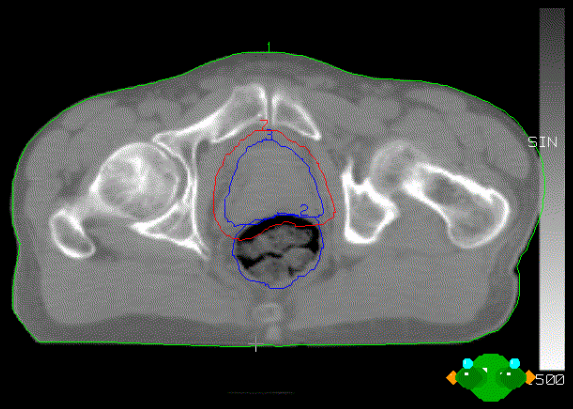
3-D treatment planing and treatment

Contour delineating

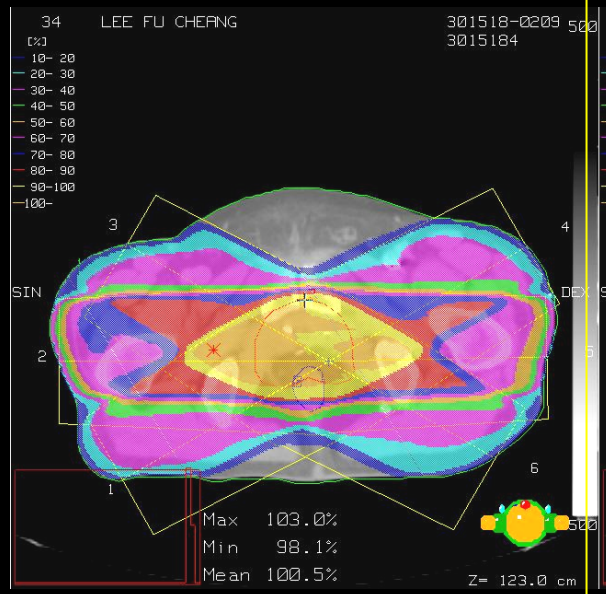


三度空間順形治療之限制

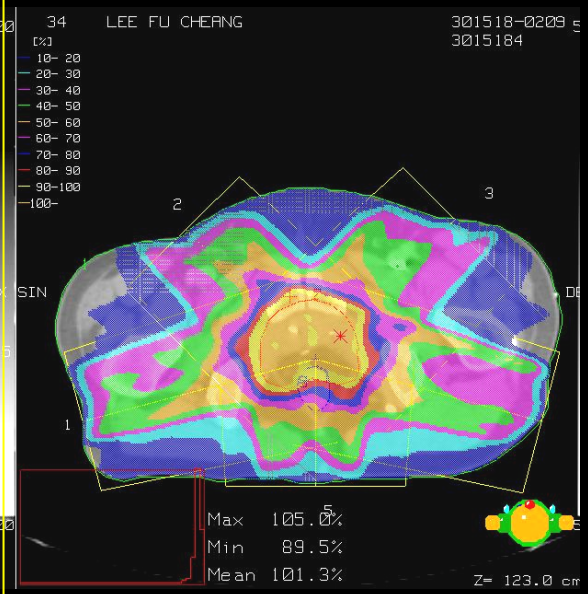
Dose = 70-72 Gy



Really

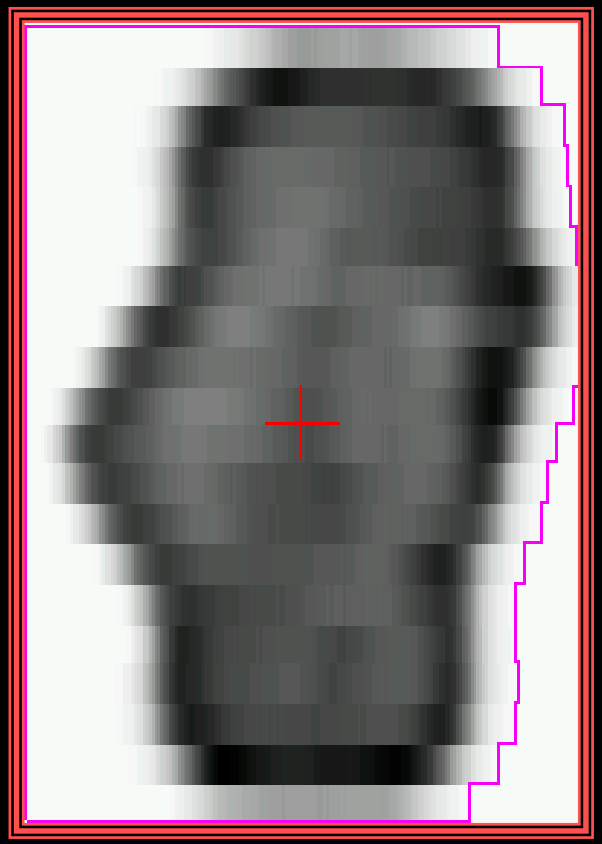


Ideally

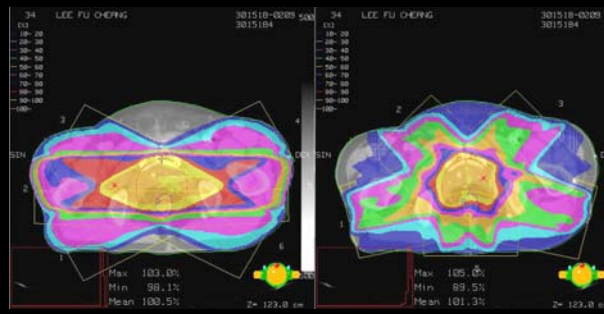


強度調控放射治療

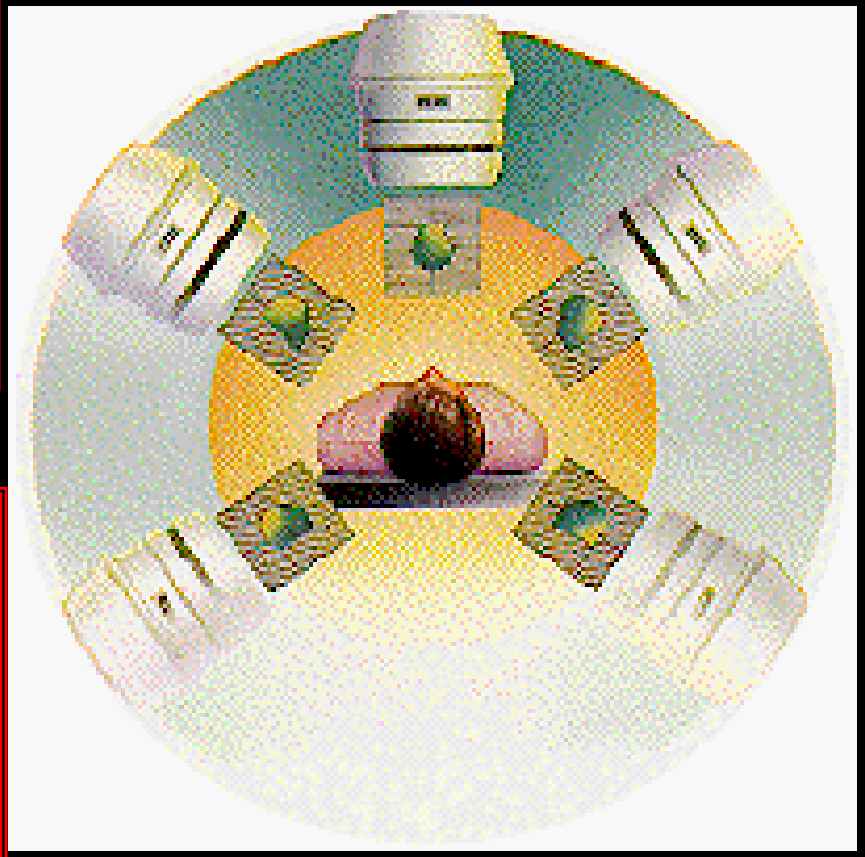
Conventional field

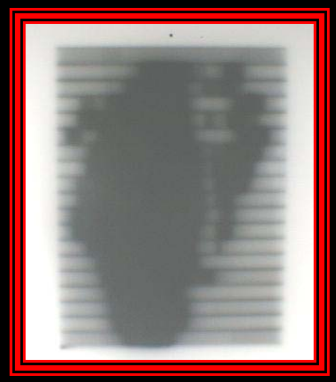


Intensity modulation field



Conventional field

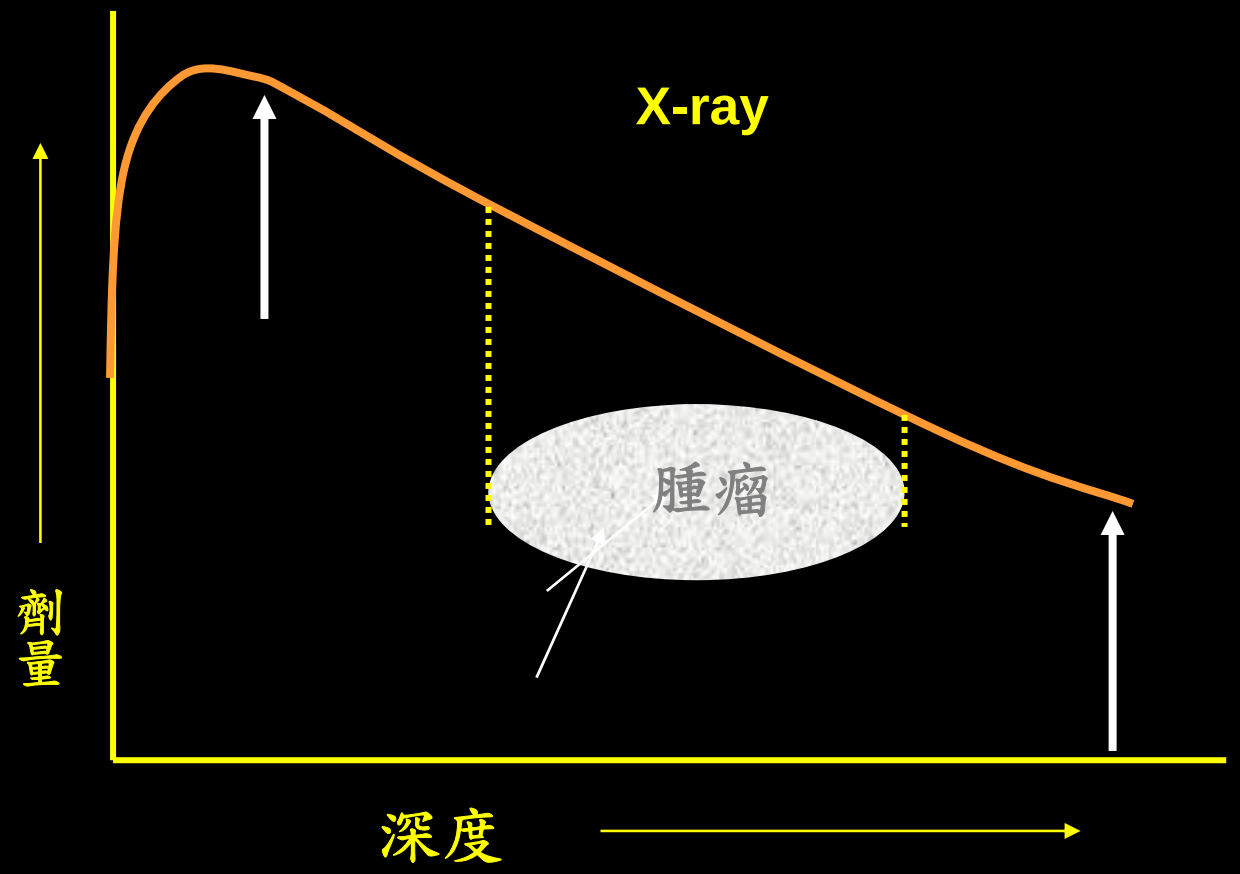




強度調控放射治療

放射治療新趨勢與局限

- 精準：影像導引 **(Image-guided radiotherapy, IGRT)**
- 順形：強度調控 **(Intensity-modulated RT, IMRT)**
- 分散劑量：多角度照射

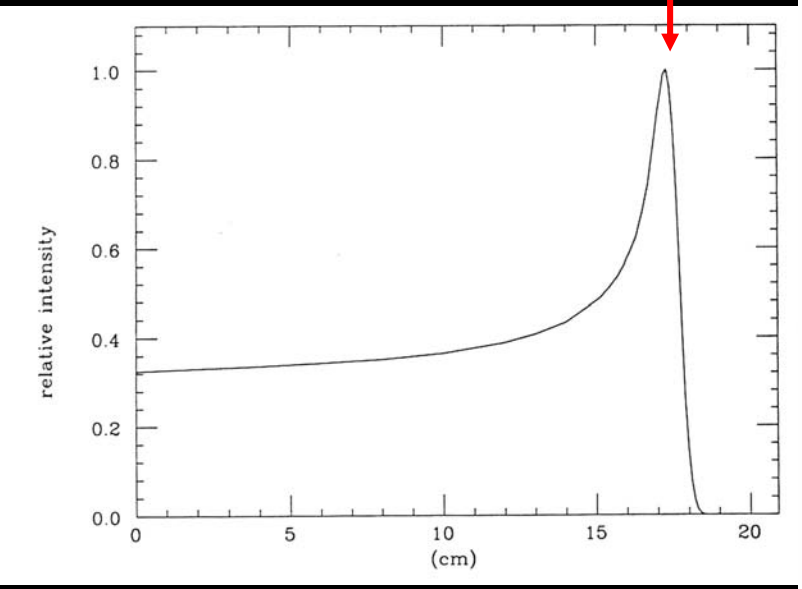


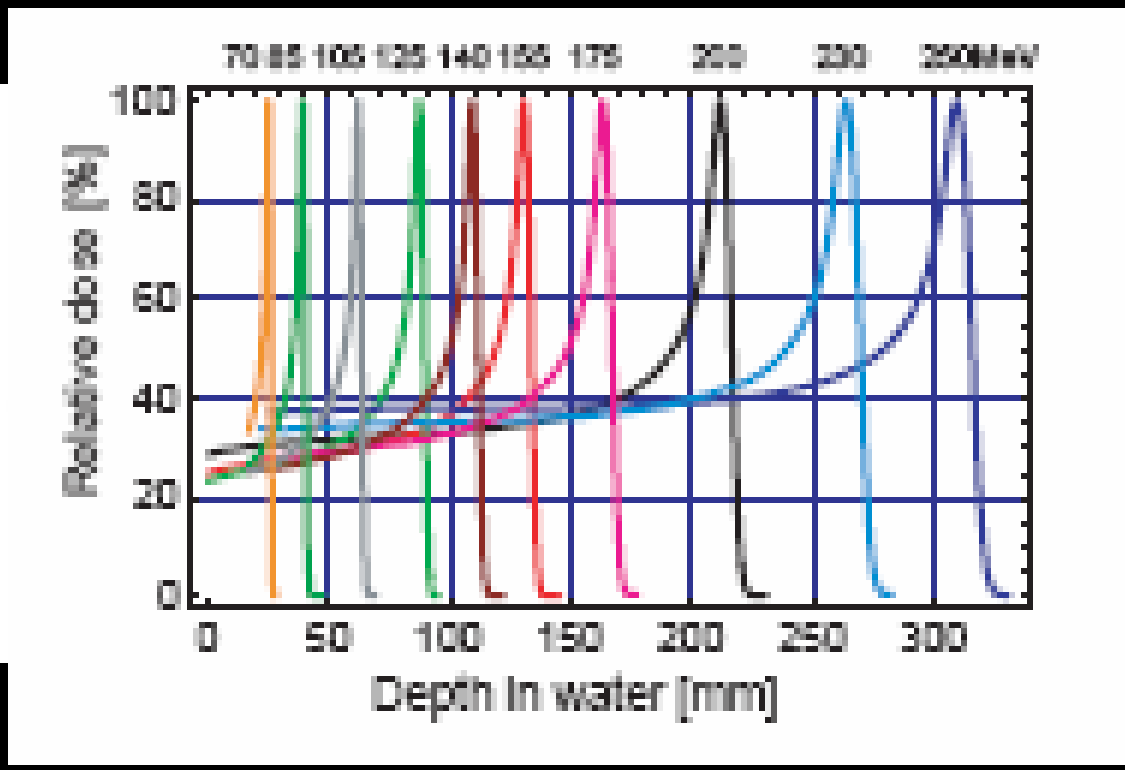
Do not decrease integral dose to body, but reduce dose/per unit area

粒子治療?

Dose profile of proton

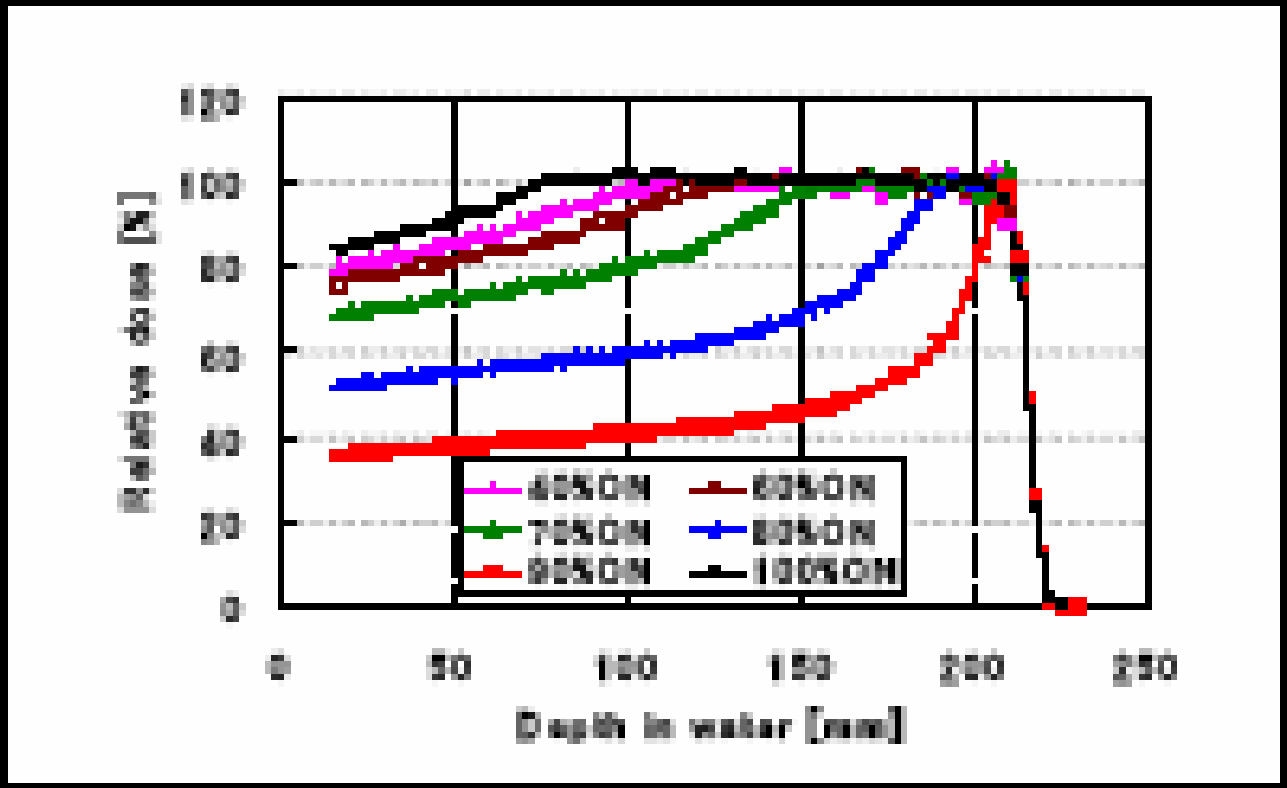
Bragg peak





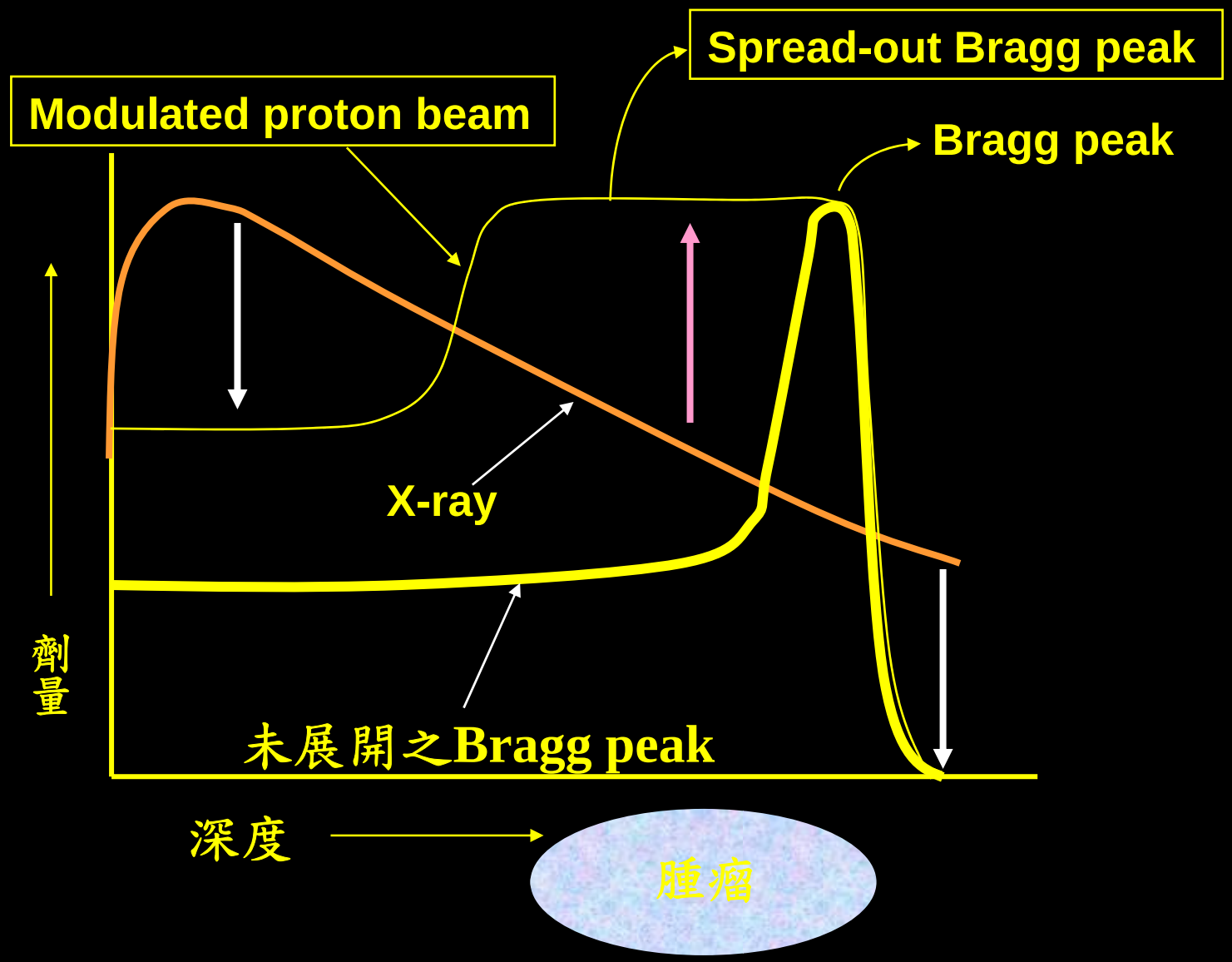
- Less dose at the entrance.
- Nearly no dose at the distal sites

Spread of Bragg Peak (SOBP)



- Entrance dose is increased as the SOBP, but still less than tumor dose and that by X-ray.
- Still nearly no dose at distal sites.

質子之物理特性


Spread-out Bragg peak
Modulated proton beam
Bragg peak
X-ray
劑量
未展開之Bragg peak
深度
腫瘤

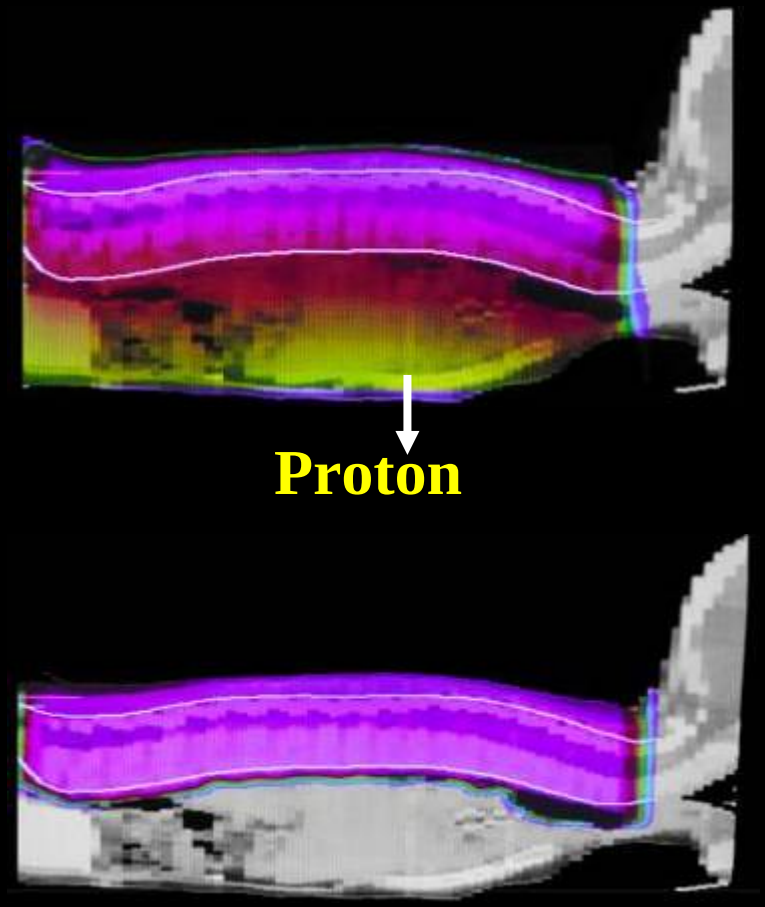
其他腫瘤

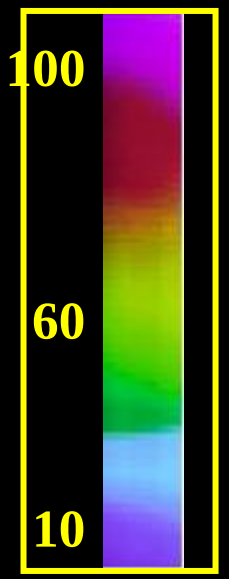
- 食道癌、軟組織腫瘤、小兒腫瘤、任何靠向單側之腫瘤……..

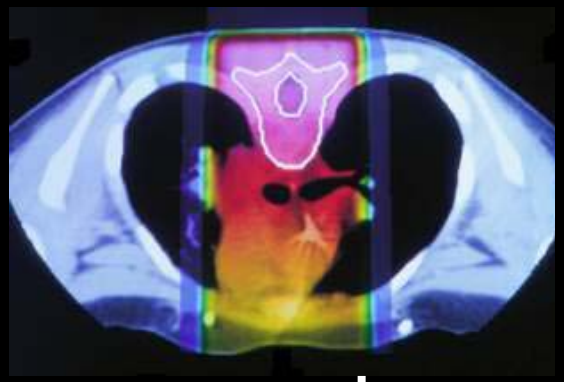
X-ray

Medulloblastoma

X-ray

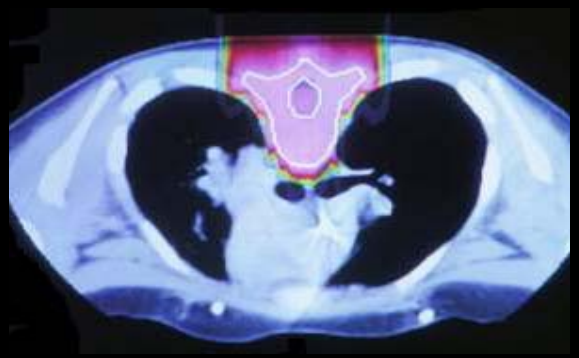






Proton

Proton



粒(質)子治療所需之設備

- 加速器

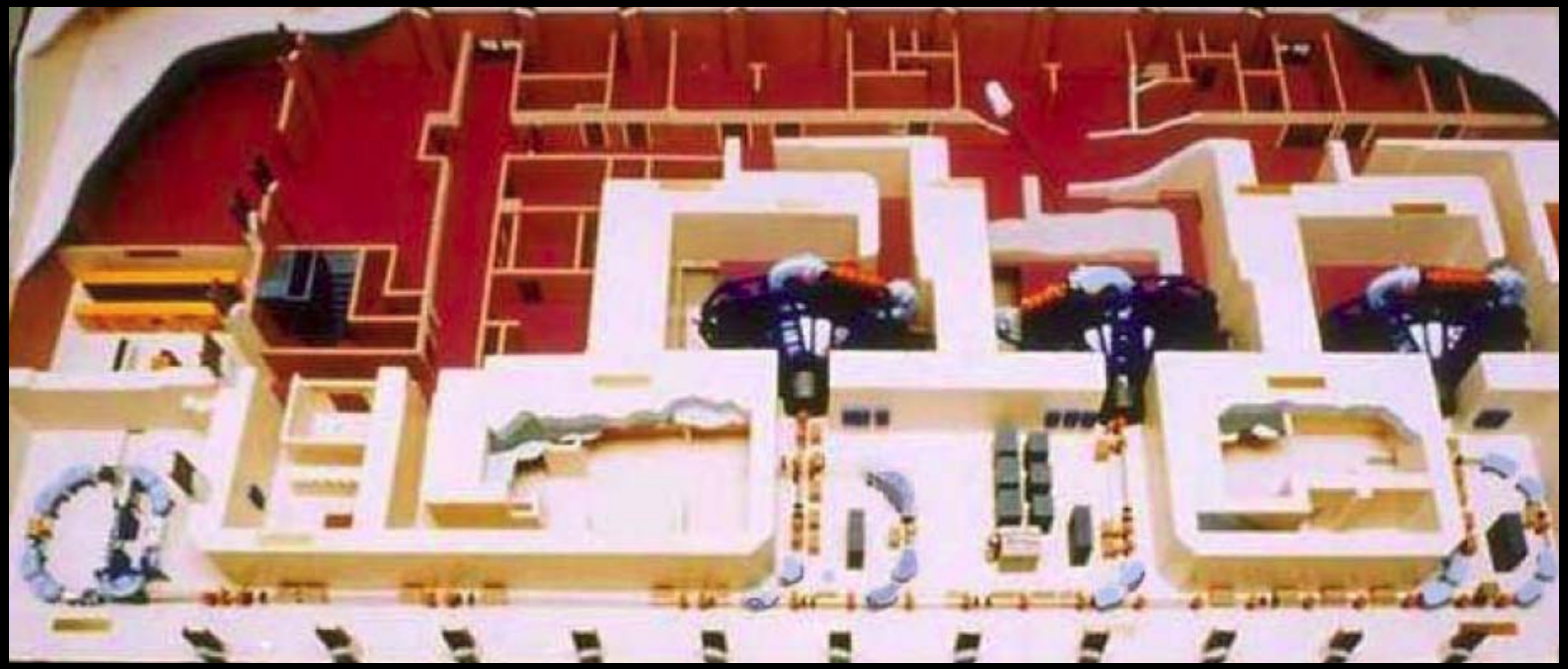
  同步加速器(Synchrotron)

  迴旋加速器(Cyclotron)

  直線加速器
- 射束傳輸系統(Beam transport)
- 質子射束傳送系統(Beam delivery)
- 病患定位系統(Patient positioning)
- 治療計劃系統(Treatment planning)
- 其他相關系統

Facility Design

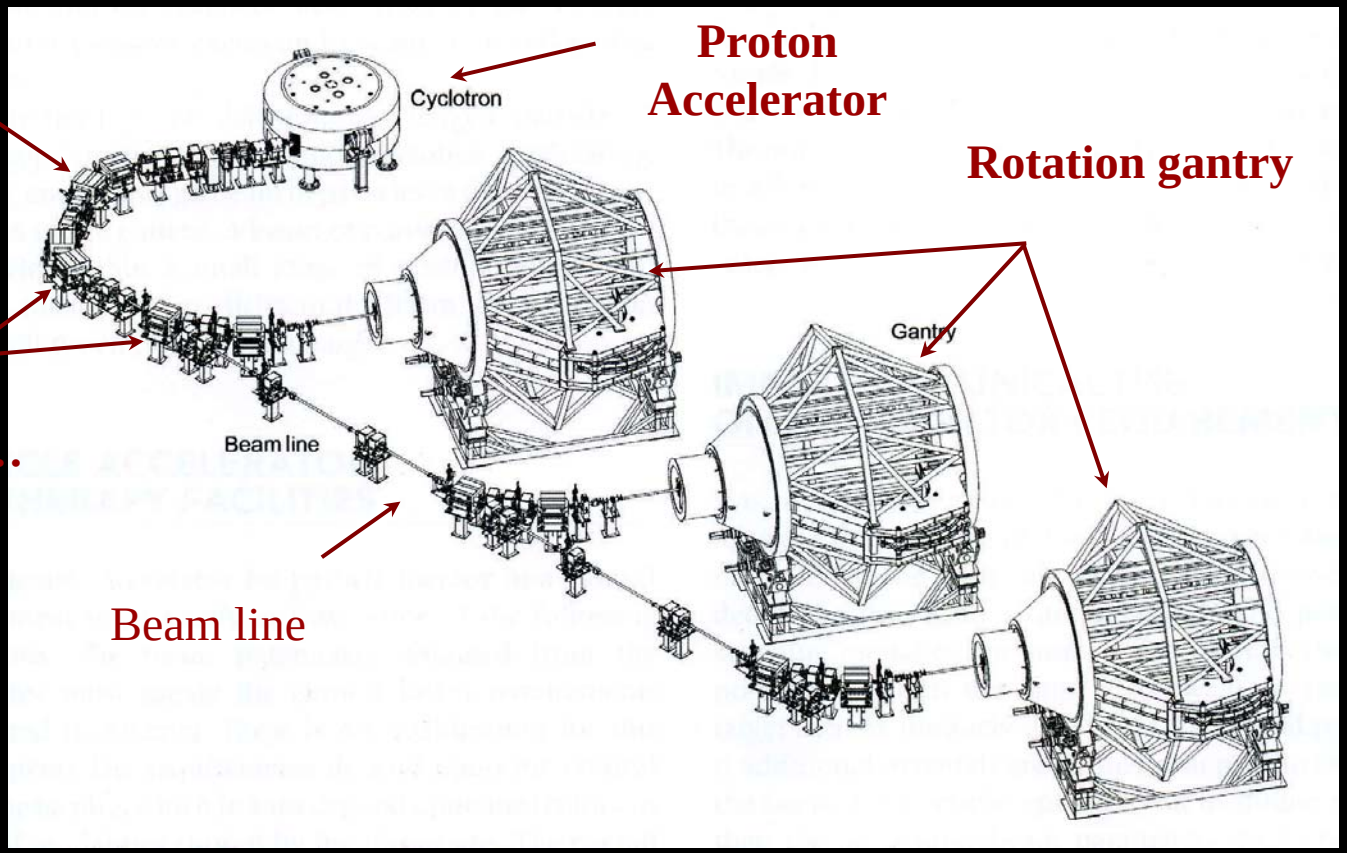
- Loma Linda Medical Centre



(Amaldi et al)

Facility Design

- Typical proton therapy equipments
  - ex. IBA system



Energy Selection System (ESS)

Proton Accelerator

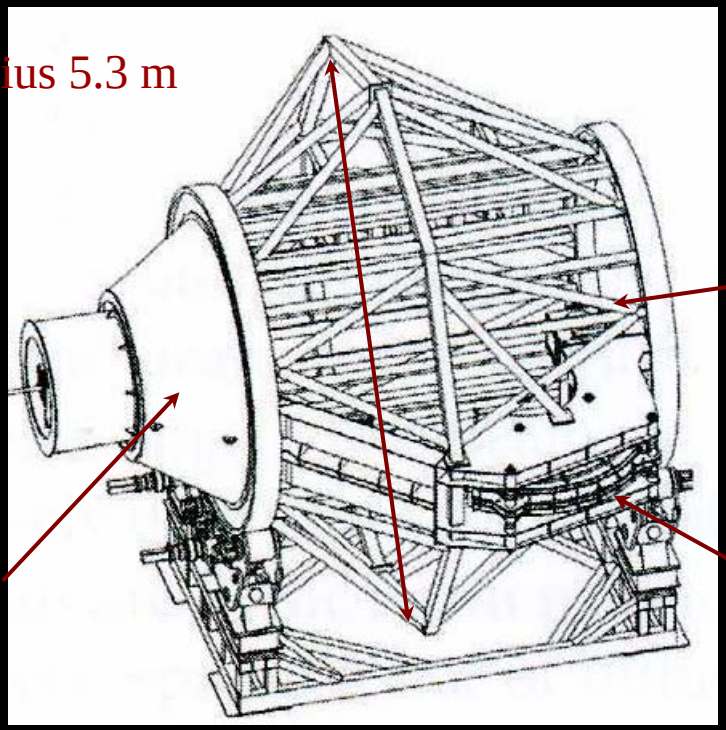
Rotation gantry

Bending magnets Dipole, quadrupole….

Beam line

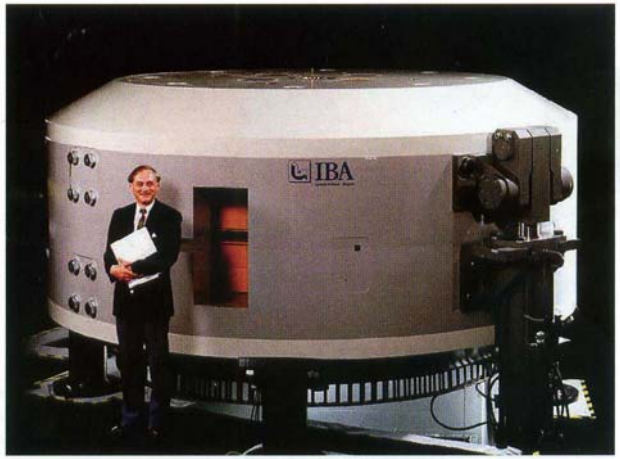
System Overview

- Rotating treatment gantry
  - IBA design



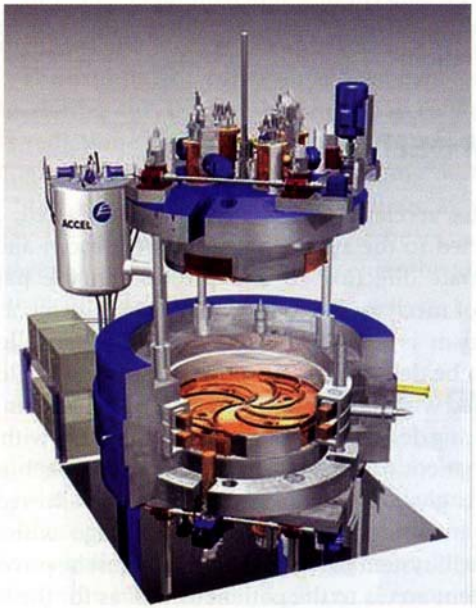
加速器

迴旋加速器



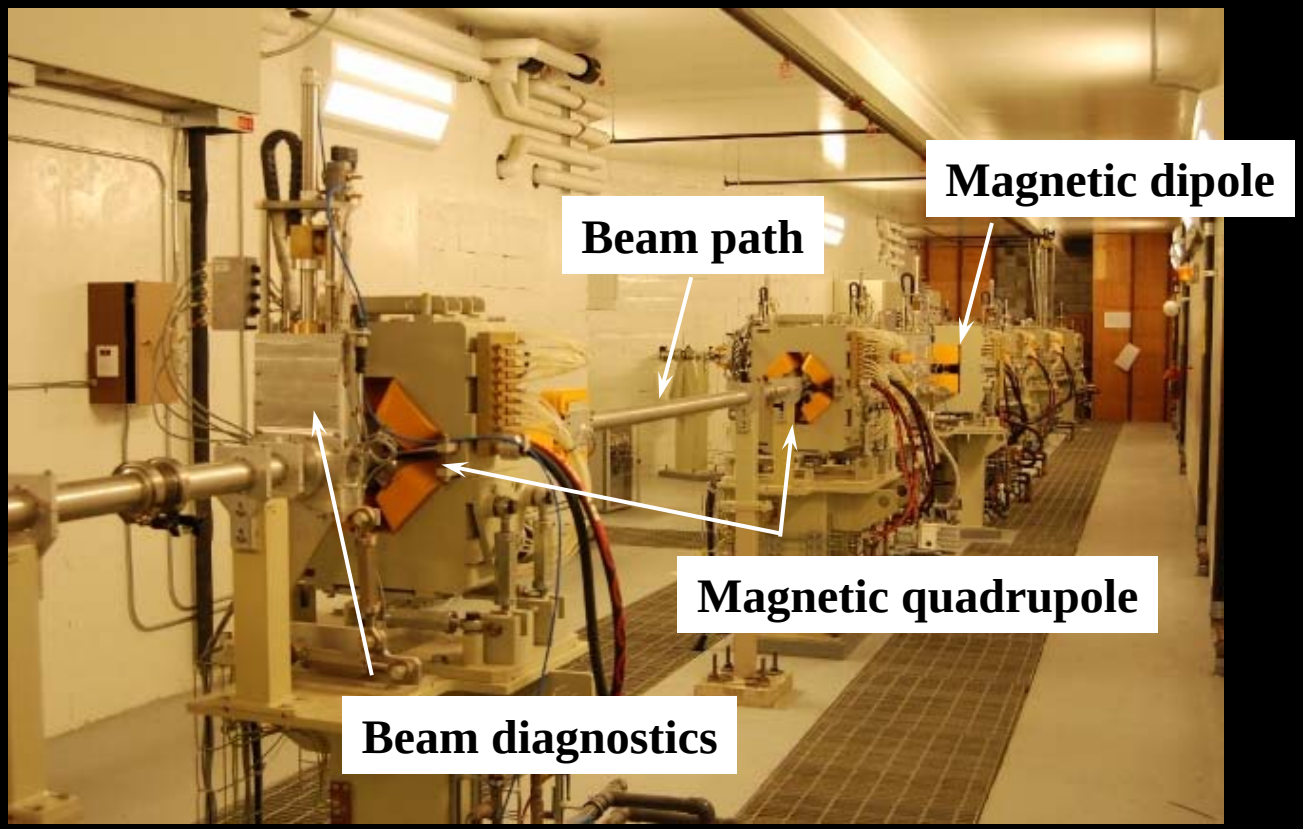
同步加速器

超導體迴旋加速器



Cyclotron

射束傳輸

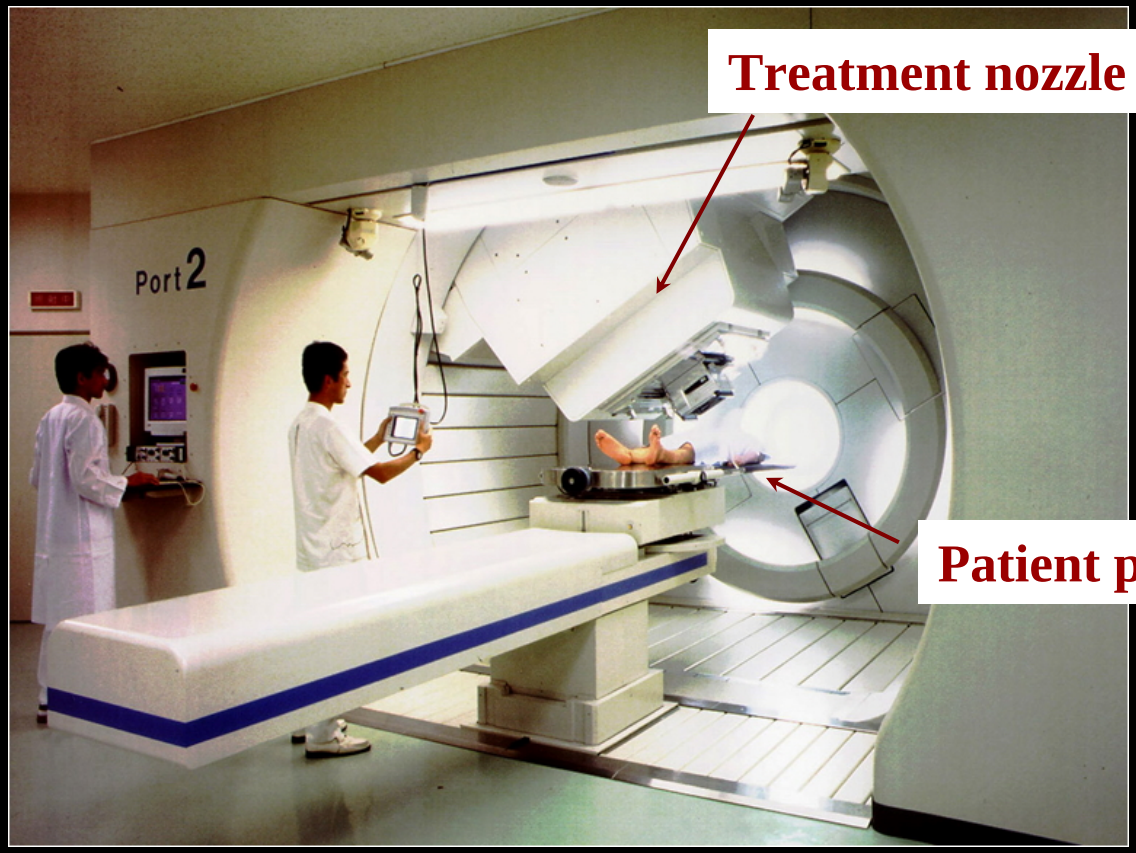

Magnetic dipole
Beam path
Magnetic quadrupole
Beam diagnostics

射束傳輸

- Bending Magnets
  - Quadrupole
    - Beam optics focusing

- Bending Magnets
  - Dipole
    - Beam direction control

治療房

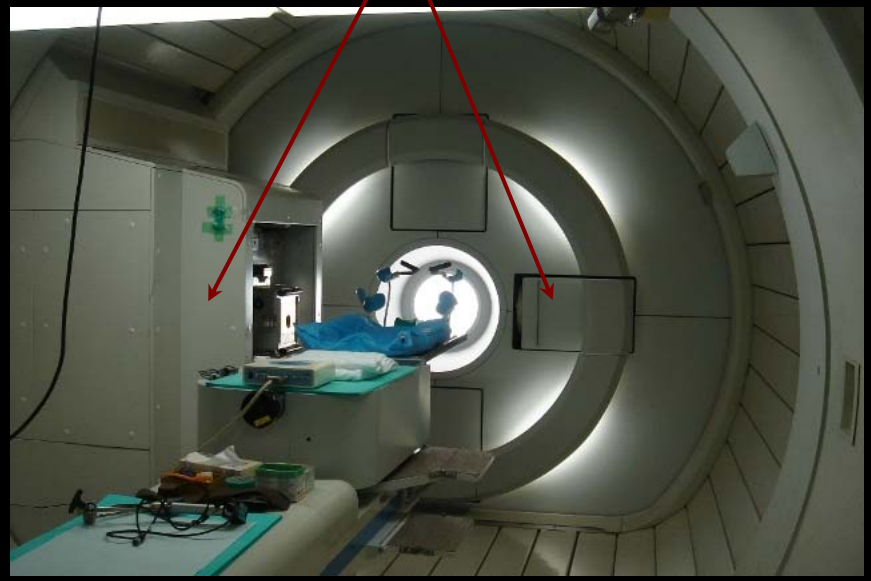


治療房

- Treatment room at NCC, Japan

Dual X-ray positioning system

Dual X-ray positioning system



Gantry