2012 :15th SESSION of ESMP

Lecture presented in Archamps (Salève Building) by :

Gerd-Jürgen BEYER (CHU-Geneva)

RADIOISOTOPES in MEDICINE:

Requirements - Production - Application and Perspectives

1

History

Gerd-Jürgen BEYER

Prof.Dr.rer.nat.habil.

Cyclotron Unit, University Hospital of Geneva, Switzerland

GSG-Int. GmbH, Switzerland

gerd.beyer@cern.ch

gerd.beyer@gsg-int.com

Lecture

ESI

Week 1

Archamps (France) October 19, 2012

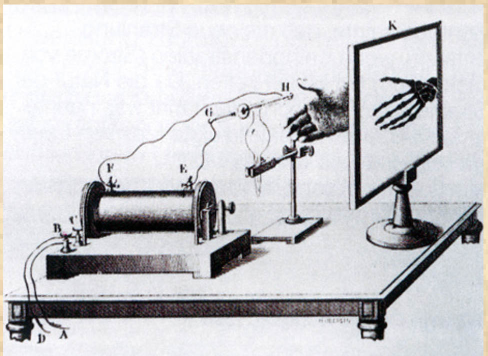
European School of Medical Physics - Archamps

NUCLEAR MEDICINE – HOW IT BEGAN

• 1789	Klaproth	Uran
• 1895	Conrad Roentgen	X-Ray
• 1896	Henry Becquerel	Radioactivity
• 1898	M.&P.Curie	**Po** und **Ra**
• 1923	G.Hevesy	Tracer Principle
• 1932	Lawrence	Cyclotron
• 1934	I.&F.Juliot-Curie	Artif.Radiactivity
• 1938	Hahn / Strassmann	U-Fission

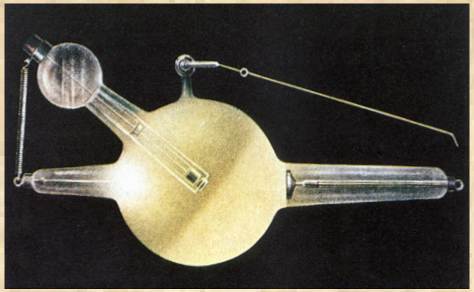
W.C. Roentgen discovers X-rays

Nov.8, 1895



W.C.Roentgens experiment
in Würzburg

Radiograph of
Mrs.Roentgens hand,
the first x-ray image
ever taken,
22.Dec.1895, published in
The New York Times
January 16, 1896



An early XX[th] century

X-ray tube

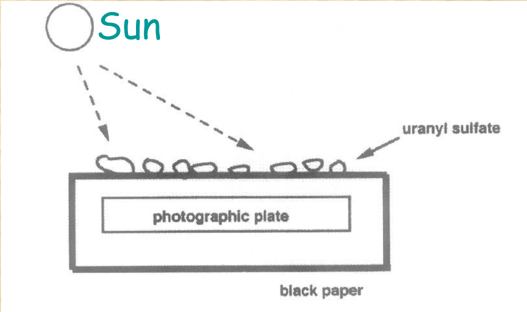
The Académie of Sciences in Paris Monday Meetings in early 1896:

Monday, January 20: Poincaré's Hypothesis:

„... Since Roentgen rays seem to emerge from the fluorescence of the wall of the Crookes tube, other fluorescent substances may emit both visible and invisible X-rays.“

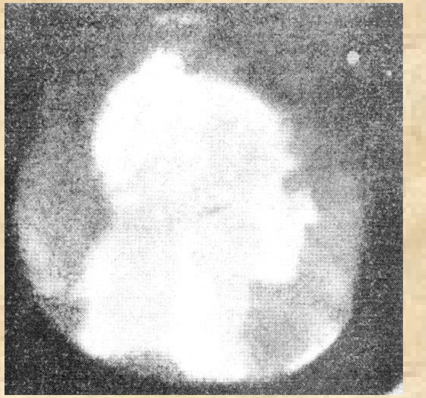
Monday, February 24: First Becquerel Note:

first experiments to verify Poincare's hypothesis:
„On radiation emitted by phosphorescence“,
Comptes Rendus 122 (1896) 420



Monday, March 2: second Becquerel Note:

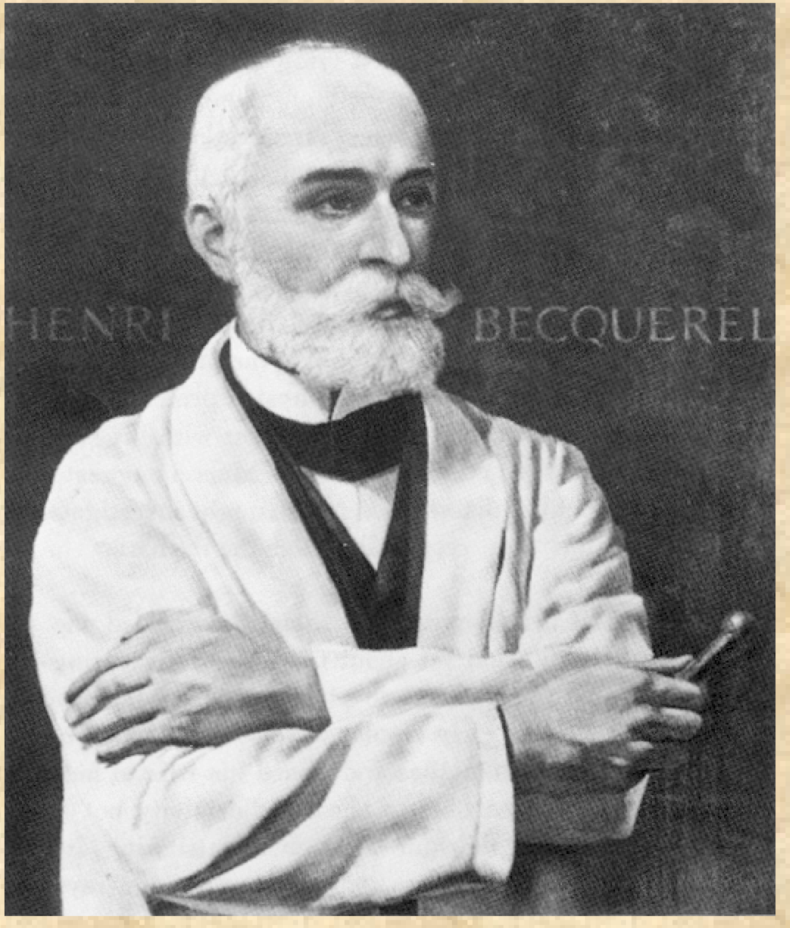
„On the invisible radiation emitted by phosphorescent substances“,
Comptes Rendus 122 (1896) 501



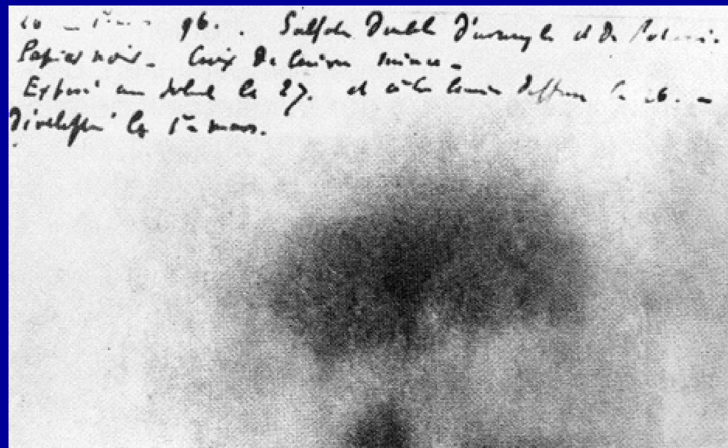
„I had prepared some plates on Wednesday, February 26 and some more on Thursday February 27. Because the sun appeared only intermittently on those days, I had saved the experiments, completely assembled, and returened the plateholders to the darkness of a drawer, leaving the uranium crystals in place. .... Sinse the sun did not reappear during the following days, I did develop the plates on March 1, expecting to find very week images. On the contrary, the silhouettes appeared with great intensity...“

Taken from J.P.Adloff: „Milestones in History of Radioactivity“

1896 RADIOACTIVITY



First image of
potassium uranyldisulfate
on **24 February 1896**
was the discovery of
natural radioactivity



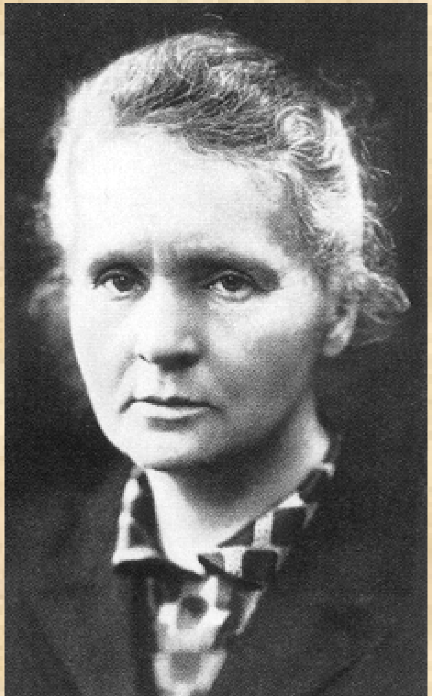
Antoine Henry Becquerel

RADIOACTIVITY

Marie and Pierre Curie
with their daughter Irene

Marie Curie (1867 – 1934) **Pierre Curie** (1859 – 1906)

1898 **Polonium**
Radium
1903 **Nobel Prize**
together with Pierre and H.Bequerel
1911 **Nobel Prize**
alone



Marie Curie

1897 Becquerels friend, Pierre Curie, also Prof. of physics in Paris suggested to his young wife, Marie, that she study the phenomena discovered by H.Becquerel for her thesis. She found soon that some components of Uranium minerals were much more radioactive than Uranium itself. "**We shall call the mysterious rays 'radioactivity'**," she told to her husband Pierre, and the substances that produce the rays "**radioelements**".

1898 Pierre started to join Marie in the study of the mysterious rays. In **July** that year they reported the discovery of **Polonium** (^{210}Po) and in **December** they announced the discovery of the **Radium** (^{226}Ra)

THE TRACER PRINCIPLE 1923

G.V.Hevesy:
The Absorption and Translocation of Lead (ThB) by Plants [ThB = ^{212}Pb]
Biochem.J. **17**, 439 (1923)

Measurements of the tracer's Radioactivity provided thousand fold increases in sensitivity and accuracy over existing chemical assays. The foundation and basic rationale of much of Hevesy visualized that **a radioactive atom might be used as a "representative" tracer of stable atoms of the same element** whenever and wherever it accompanied them in biological systems.

1943 Nobel Prize Chemistry

the father of Nuclear Medicine

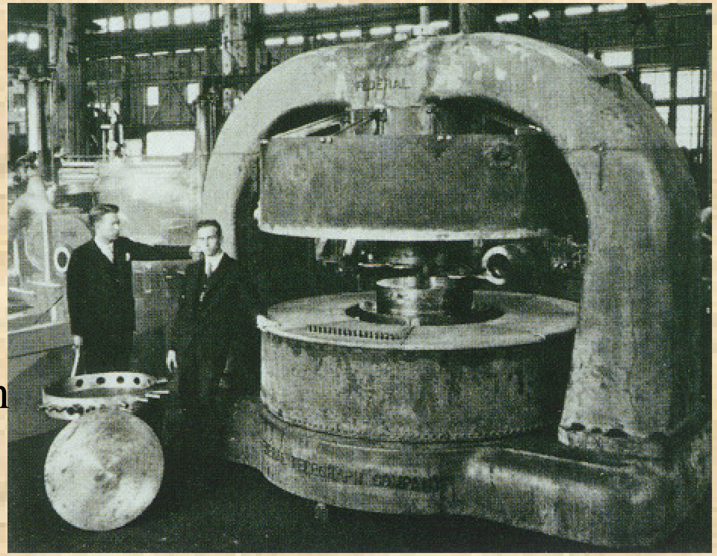
INVENTION of the CYCLOTRON

Ernest O Lawrence and his
First cyclotron 1932

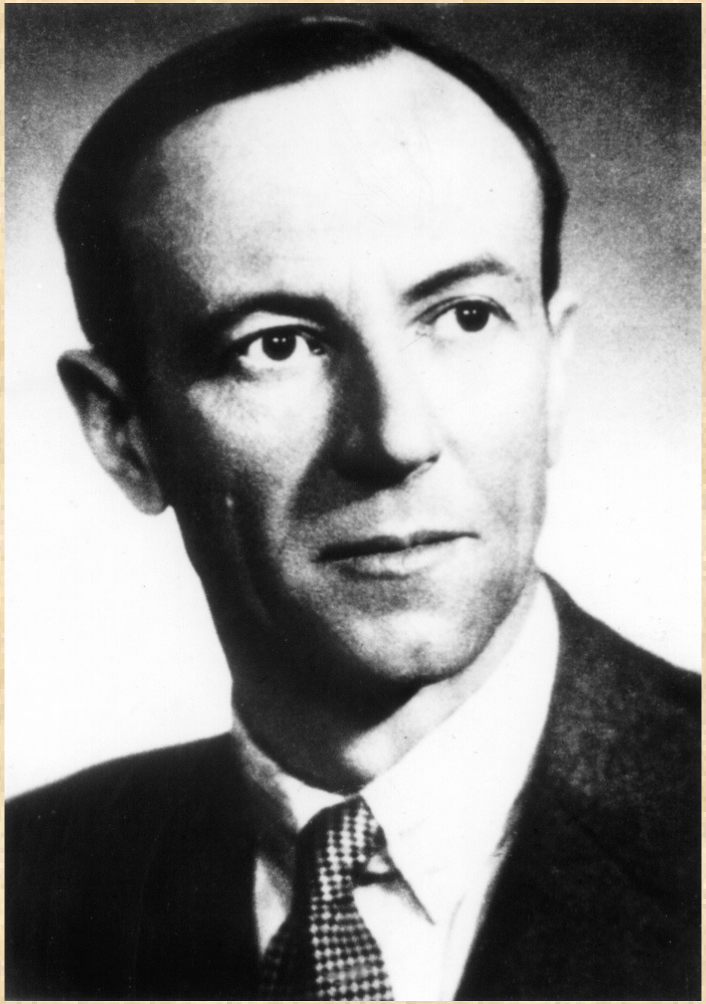
1932

E.O.Lawrence and M.S. Livingston
“The production of high speed Light ions without the use of High voltages”,
A milestone in the production of usable quantities of radionuclides.

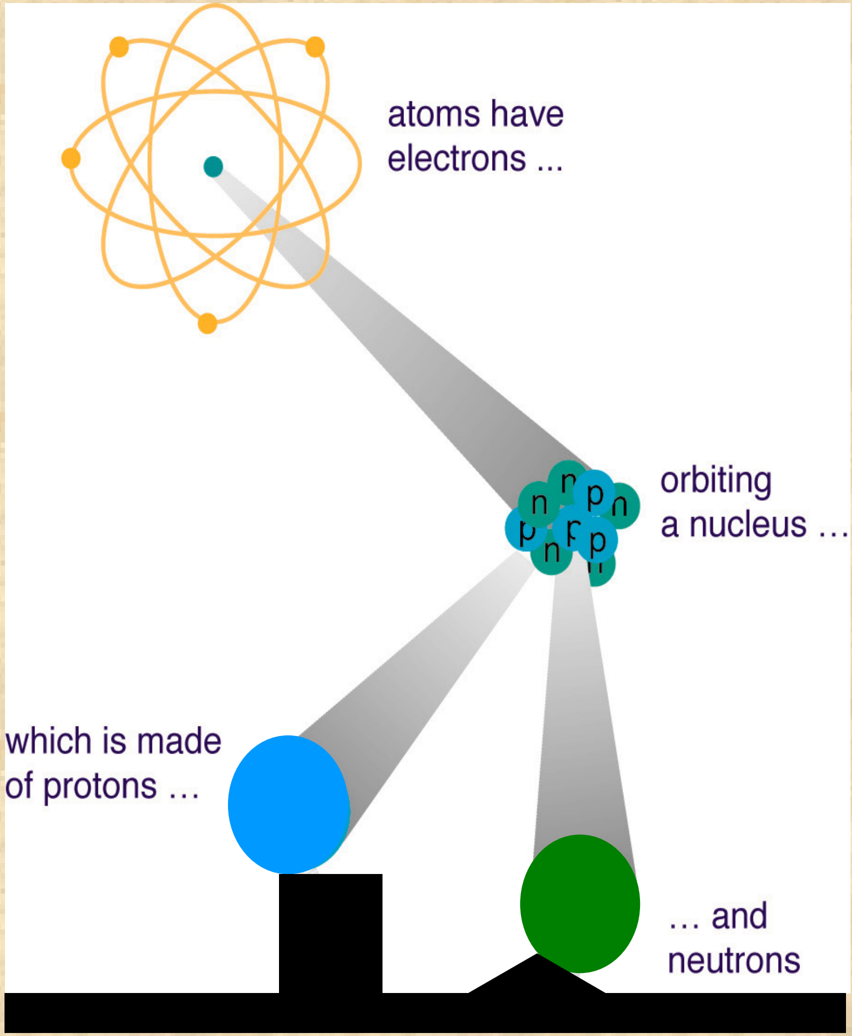
E.O Lawrence and M.S.Livingston with the 27-inch cyclotron at Berkeley 1933, the first cyclotron that produced radioisotopes



Discovery of the neutron 1932

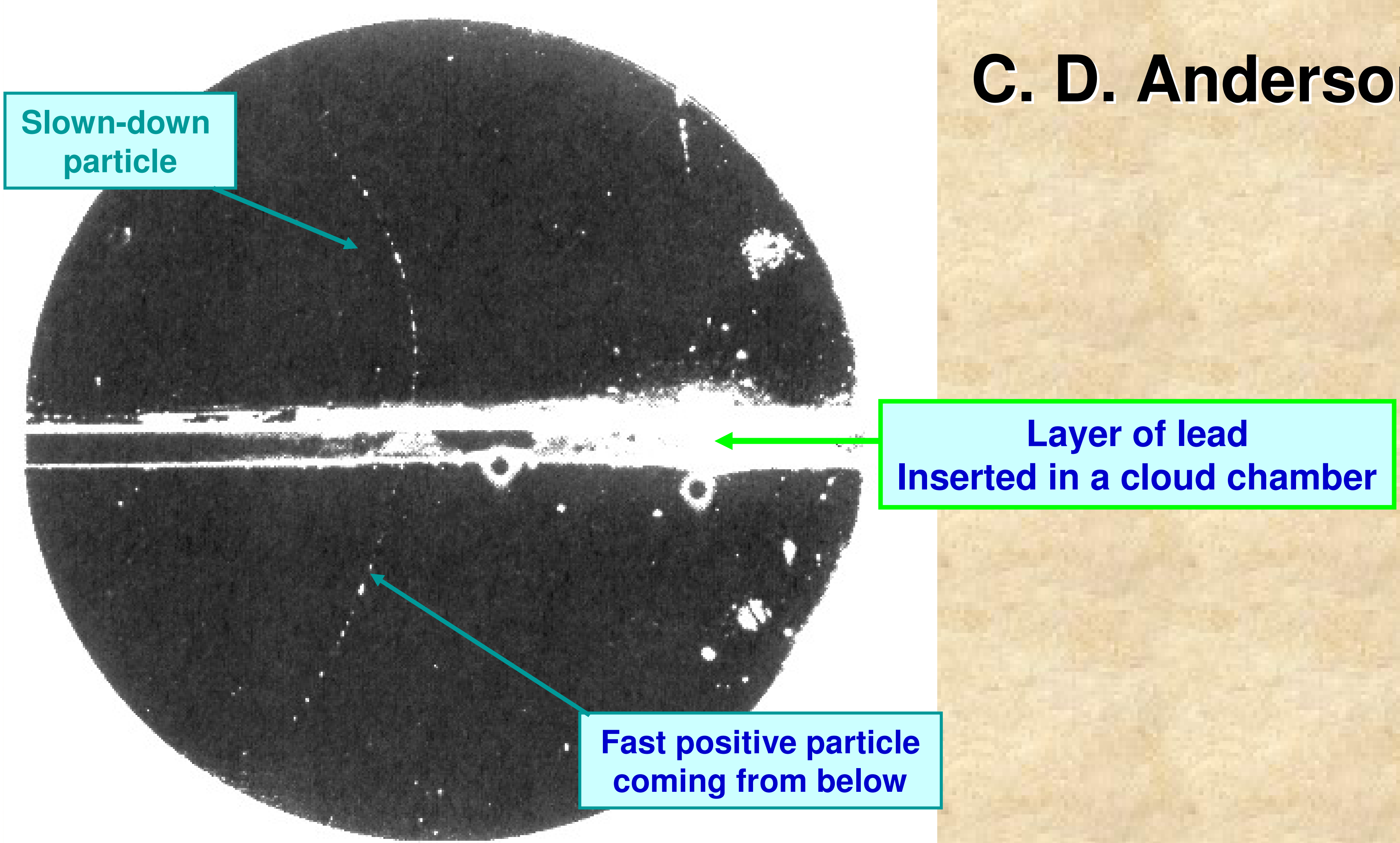


James Chadwick
(1891 – 1974)



1932 Discovery of the Positron

C. D. Anderson



1934 Artificial RADIOACTIVITY

Irene and Frédéric Joliot-Curie

1934 Nature, February 10
1935 Nobel Prize

"Our latest experiments have shown a very striking fact: when aluminum foil is irradiated on a polonium preparation, the emission of positrons does not cease immediately when the active preparation is removed. The foil remains radioactive and the emission of radiation decays exponentially as for an ordinary radioelement. We observed the same phenomena with boron and magnesium."

$^{27}Al\ (\alpha,n)\ ^{30}P$ and **$^{10}B\ (\alpha,n)\ ^{13}N$**

The discovery of artificial radioactivity in combination with the cyclotron opened the door to the production of a variety of useful radio-indicators. Practically any element could be bombarded in the cyclotron to generate radioactive isotopes.

1935 Nature **136**, 754 O.Chievitz and G.V.Hevesy
Radioactive indicators in the study of phosphorus metabolism in rats **(^{32}P**)

1937 Radiology **28**, 178 J.G.Hamilton, R.S.Stone:
The administration of radio-sodium (**^{24}Na**)

1938 Proc.Soc.Exp.Biol.Med. **38**, 510 S.Hertz, A.Roberts, R.D.Evans
Radioactive iodine (**^{128}I**) – Study of thyroid physiology

1939 Proc.Soc.Exp.Biol.Med. **40**, 694, J.H.Lawrence, K.G.Scott:
Metabolism of phosphorus (**^{32}P**) in normal and lymphomatous animals

1940 Am.J.Physiol. **131**, 135 J.G.Hamilton, M.H.Soley:
Studies of **iodine** metabolism by thyroid in situ

1940 J.Biol.Chem. **134**, 543 J.F.Volker, H.C.Hodge, H.J.Wilson
The adsorption of fluoride (**^{18}F**) by enamel, dentine, bone and hydroxyapatite

1945 Am.J.Physiol. 145, 253 C.A.Tobias, J.H.Lawrence, F.Roughton
The elimination of 11-C-Carbon monoxide from the human body

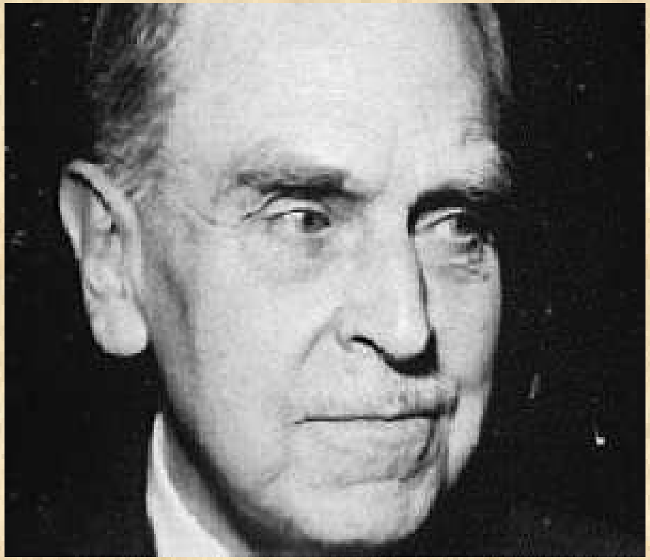
FISSION of Uranium

1938, 17. Dec.

Naturwissenschaften **1**, (1939) 1

O.Hahn und F.Straßmann

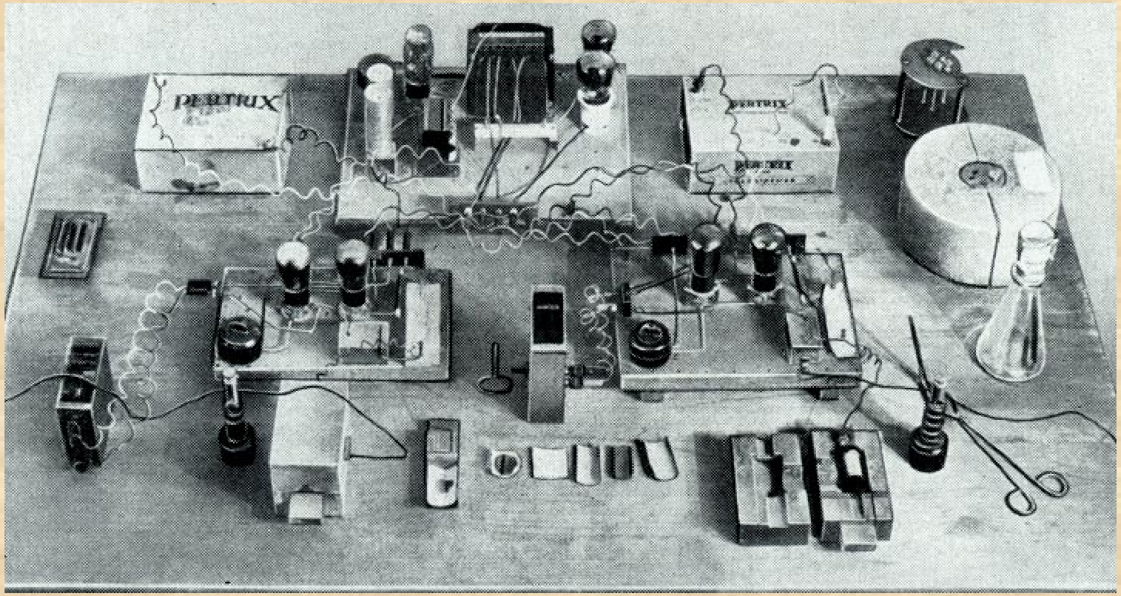
Über den Nachweis und das Verhalten der bei der Bestrahlung des Urans mittels Neutronen entstehenden Erdalkalimetalle



Otto Hahn, 1944 Nobel Prize

Lise Meitner and O.R Frisch described the Explanation and defined the terminus "FISSION"

Als Chemiker müßten wir … statt
Ra, Ac und Th die Symbole Ba, La und Ce einsetzen. Als der Physik in gewisser Weise nahestehende Kernchemiker können wir uns zu diesem, allen bisherigen Erfahrungen der Kernphysik widersprechenden Sprung noch nicht entschließen. Es könnten doch vielleicht eine Reihe seltsamer Zufälle unsere Ergebnisse vorgetäuscht haben.



Laboratory table of Otto Hahn

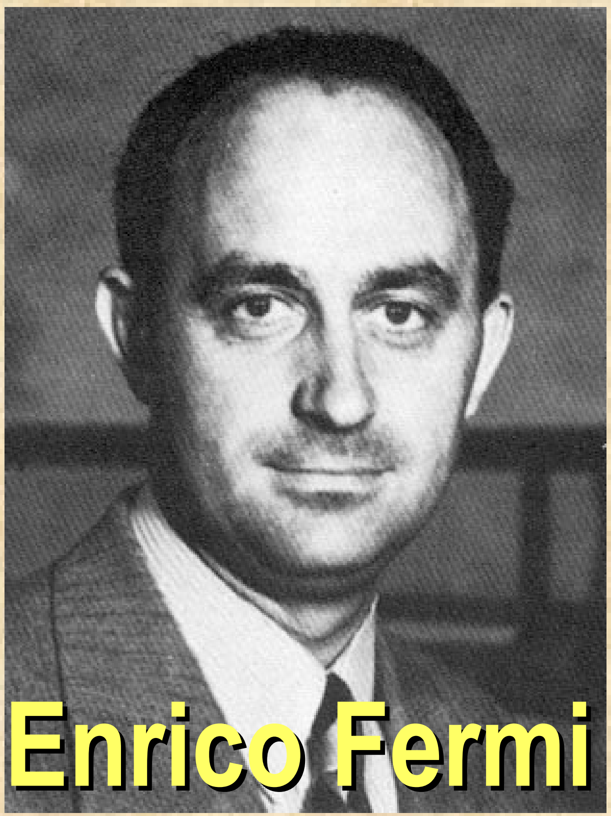
Niels Bor (Jan.1939)

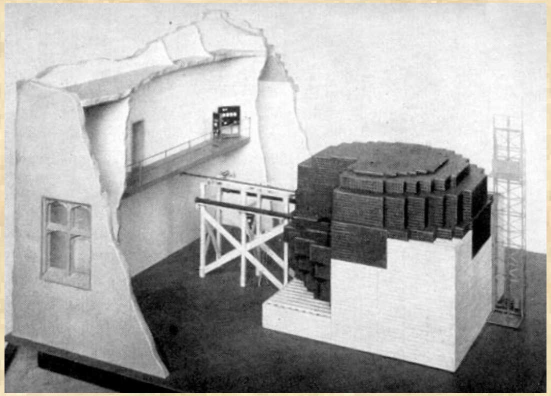
Mein Gott, wie haben wir das nur so lange übersehen können

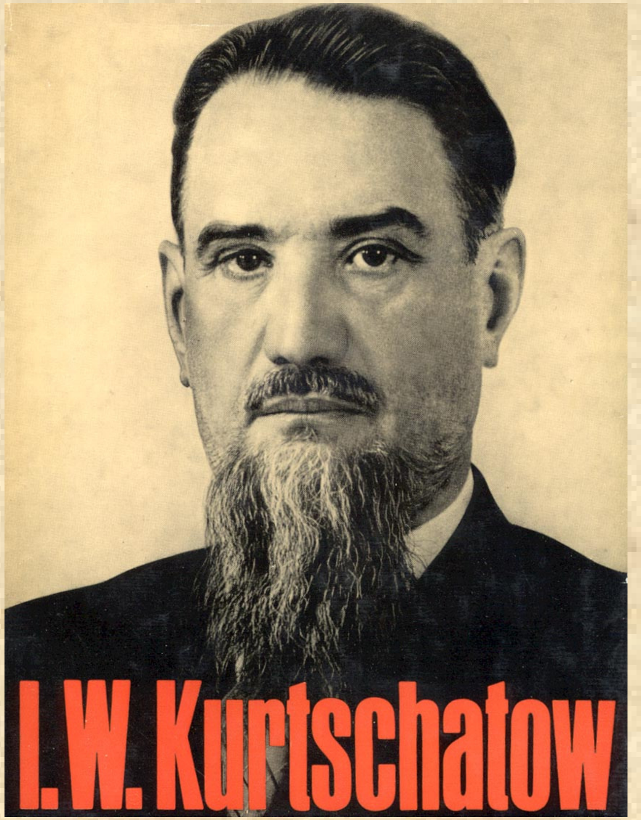
FISSION of Uranium

$^{235}\mathrm{U} + \mathrm{n} = [^{236}\mathrm{U}] \longrightarrow {}^{140}\mathrm{Ba} + {}^{94}\mathrm{Kr} + 2\,\mathrm{n} + \gamma + \text{Energy}$

1942 Dec.2, first graphite miler in Chicago

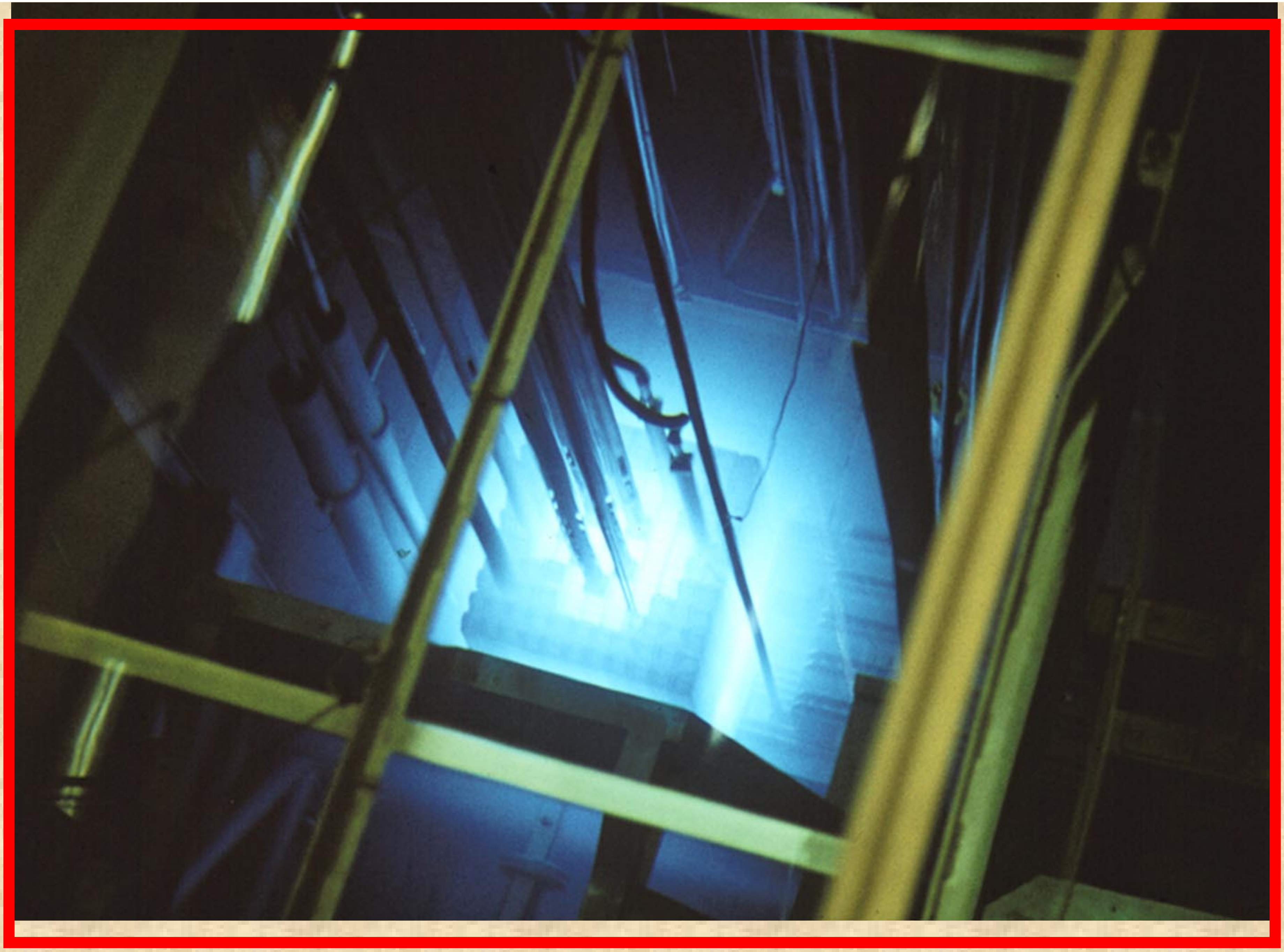






1946 Dec.25, first graphite miler in Moscow

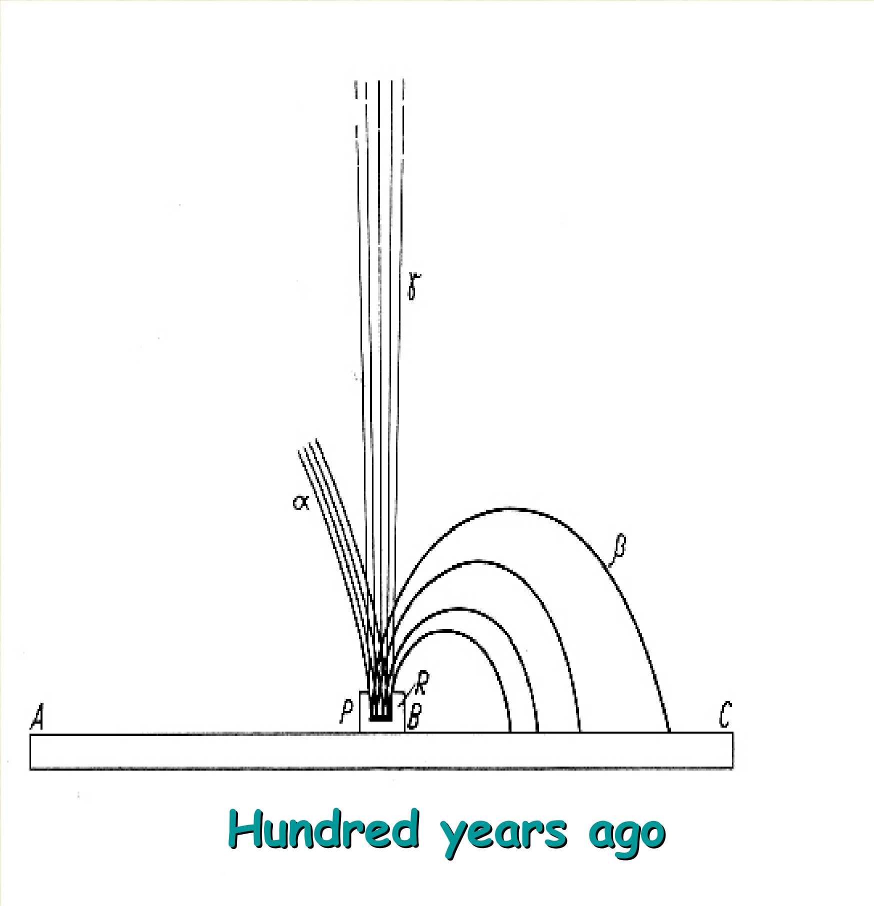
Note: first A-Bomb 1945/1949, first atomic E-power station 1954

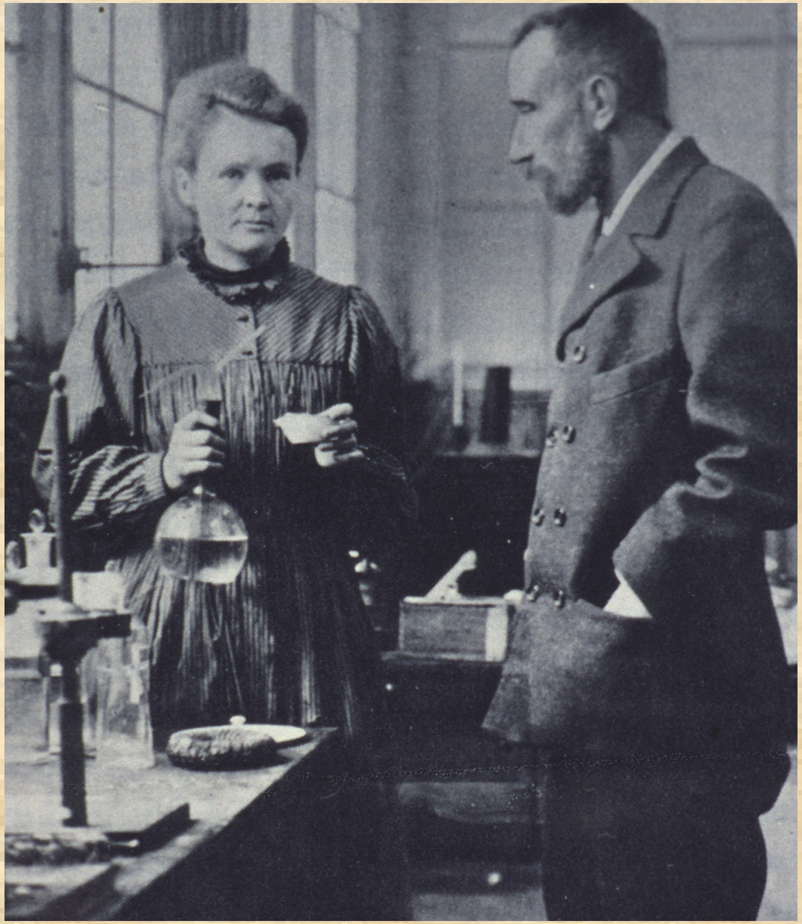


10 MW swimming pool reactor, Geesthacht (D) **European School of Medical Physics - Archamps** Foto: G.Beyer, 1973

RADIOACTIVITY

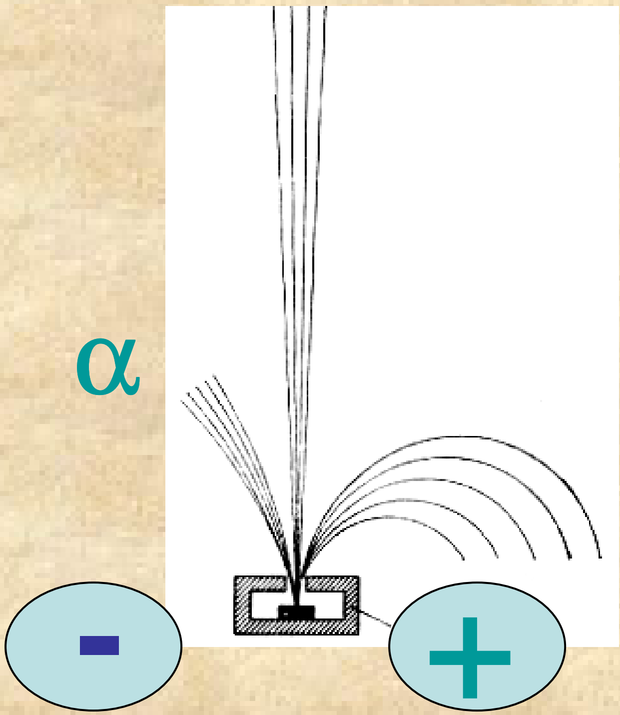
Marie Curie (1867 – 1934) Pierre Curie (1859 – 1906)

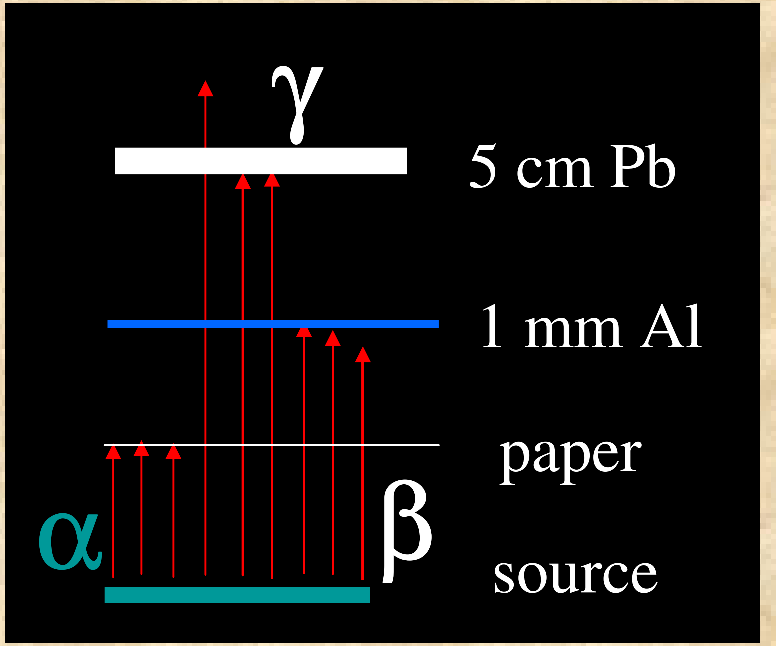




RADIOACTIVITY

The radiation characteristics of an isotope determines where and how it can be used in medicine





DECAY MODES

		Energy	Range in water	/ Pb
ß⁻, ß⁺		~ 0.2 – 4 MeV	~ 1 cm	
EC, X-ray	f(Z)	Fe: 7 keV	$d_{1/2}$ ~ 1 mm	
		Ra: 100 keV	$d_{1/2}$ ~ 4 cm	
α		4 - 8 MeV	28 – 80 µm	
γ		50 keV	$d_{1/2}$ ~ 3 cm	0.01 mm
		140 keV	**$d_{1/2}$ ~ 5 cm**	**0.4 mm**
		1 000 keV	$d_{1/2}$ ~ 10 cm	1 cm
		2 000 keV	$d_{1/2}$ ~ 15 cm	1.5 cm
conversion electrons		$E\gamma$ - Ee	~ mm range	
Auger electrons			~ µm range	
IT		like γ		

exotic decay modes, spontaneous fission

1946, June 14

Nuclear Medicine's modern era began

Availability of Radioactive Isotopes,

Announcement from Headquarters, Manhatten Project, Washington D.C.:

Production of tracer and therapeutic radioisotopes has been heralded as one of the greatest peacetime contributions of the uranium chain-pile. This use of the uranium pile will unquestionably be rich in scientific, medical, and technological application.

On 1.Aug.1946 the Atomic Energy Act
passed the congress,
releasing radioisotopes from military control.

RADIOISOTOPES in MEDICINE:

Requirements - Production - Application and Perspectives

2

Imaging with Radiotracers

Gerd-Jürgen BEYER
Prof.Dr.rer.nat.habil.
Cyclotron Unit, University Hospital of Geneva, Switzerland
GSG-Int. GmbH, Switzerland
gerd.beyer@cern.ch
gerd.beyer@gsg-int.com

Lecture
ESI
Week 1
Archamps (France) October 19, 2012

ISOTOPES IN MEDICINE

DIAGNOSIS

in vitro

^{14}C
^{3}H
^{125}I
others

in vivo

^{99}Mo-^{99m}Tc

^{201}Tl
^{123}I
^{111}In
^{67}Ga
^{81}Rb-^{81m}Kr
others

ß+ emitters for PET

^{18}F, ^{11}C, ^{13}N, ^{15}O
^{86}Y, ^{124}I, ^{64}Cu
^{68}Ge - ^{68}Ga
^{82}Sr - ^{82}Rb
^{44}Ti - ^{44}Sc

THERAPY

internal

systemic

^{131}I, ^{90}Y
^{153}Sm, ^{186}Re
^{188}W-^{188}Re
^{166}Ho, ^{177}Lu,
others

α-emitters:

^{225}Ac-^{213}Bi
^{211}At, ^{223}Ra
^{149}Tb

e^--emitters:

^{125}I

sources

sealed sources
^{192}Ir, ^{182}Ta, ^{137}Cs
many others

needles for brachytherapy:
(^{103}Pd), ^{125}I
many others

stands
^{32}P and others

seeds
^{90}Sr or ^{90}Y, others

applicators
^{137}Cs, others

external

tele radio

^{60}Co

gamma knife

^{137}Cs
blood cell irradi-ation

European School of Medical Physics - Archamps

G.J.BEYER, Geneva, 2011

THE TRACER PRINCIPLE 1923

G.V.Hevesy:
The Absorption and Translocation of Lead (ThB) by Plants [ThB = ^{212}Pb]
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1943 Nobel Prize Chemistry

the father of Nuclear Medicine

NUCLEAR MEDICINE =
in vivo APPLICATION of RADIOTRACERS

1923 First tracer study with $^{210}Pb/^{210}Bi$ G.Hevesy

1925 ^{214}Bi arm-to-arm circulation time, H.Blumgart

1935 ^{32}P renewal of mineral constituents of bone, O.Chieivitz & G.Hevesy

1937 dynamics of sodium transport in vivo, J.G.Hamilton

1937 ^{128}I, thyroid physiology, R.Hertzs, A.Roberts, R.Evans

1938 ^{131}I discovered by G.T.Seeborg, 1939 first diagnostic use J.G.Hamilton et al.

1947 ^{131}I –Fluorescine, 1950 ^{131}I –HSA, 1955 ^{131}I-rose bengale & hippurane, …

1957 ^{99}Mo-^{99m}Tc generator (1960 first sale), ^{133}Xe for lung ventilation

1969 ^{67}Ga accumulation in cancer, C.L.Edwards

1970 Instant KIT's for ^{99m}Tc

1973 ^{201}Tl, ^{123}I, ^{111}In, many other isotopes and tracer compounds

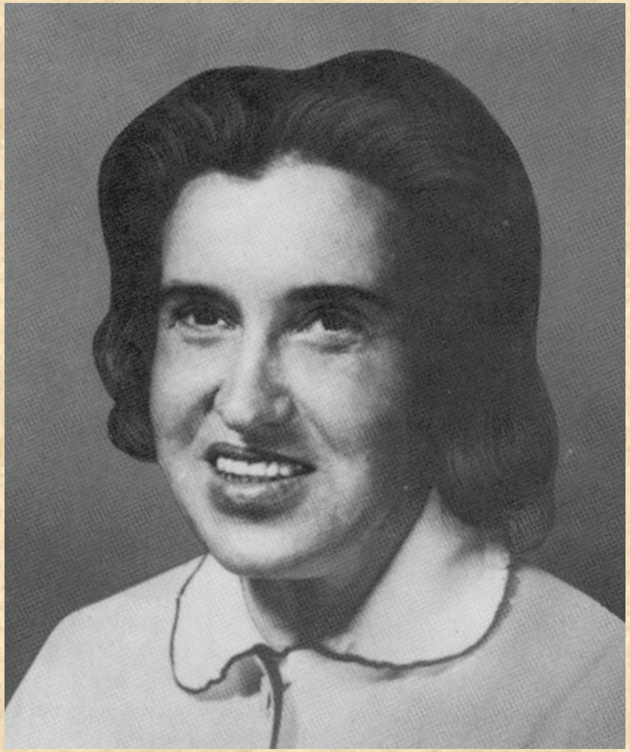
1978 first ^{18}FDG PET scan

> 30 million individuals receive every year a radiotracer for diagnosis

ISOTOPES in MEDICINE

Application	Requirement	Isotope
DIAGNOSIS **in vitro**	**$T_{1/2}$ = long** **biogenic behavior**	**^{3}H, ^{14}C** **^{125}I**
DIAGNOSIS In vivo SPECT	single photons no particles biogenic behavior $T_{1/2}$ = moderate	^{99m}Tc, ^{123}I, ^{111}In, ^{201}Tl,
DIAGNOSIS in vivo PET	β^{+}-decay mode biogenic elements $T_{1/2}$ = short	^{11}C, ^{13}N, ^{15}O, ^{18}F

Diagnostic in vitro RIA



Rosalyn S.YALOW

S.A.BERSON

Nobel Prize 1977

Introduced the radioimmunoassay (RIA)

assay for insulin based on the principle of competitive binding by antibody of natural and radioactive labeled hormone)

ISOTOPES in MEDICINE

Application	Requirement	Isotope
DIAGNOSIS **In vitro**	$T_{1/2}$ = long biogenic behavior	**^{3}H, ^{14}C** **^{125}I**
DIAGNOSIS **In vivo** **SPECT**	single photons no particles biogenic behavior $T_{1/2}$ = moderate	**^{99m}Tc,** **^{123}I, ^{111}In,** **^{201}Tl,**
DIAGNOSIS **in vivo** **PET**	β^{+}-decay mode biogenic elements $T_{1/2}$ = short	**^{11}C,** **^{13}N, ^{15}O,** **^{18}F**

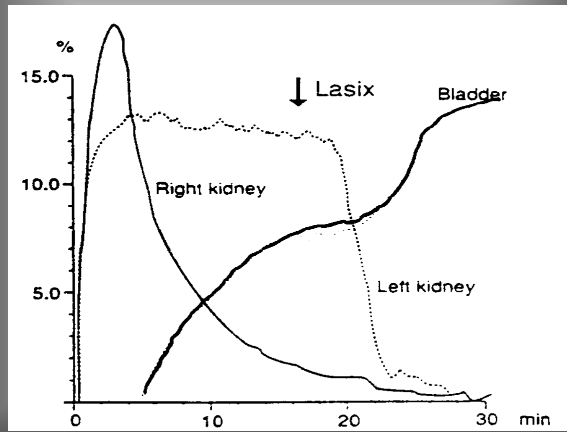
Photo published 1942

J.G.Hamilton, M.H.Soley:

"Studies of **iodine** metabolism by thyroid in situ"

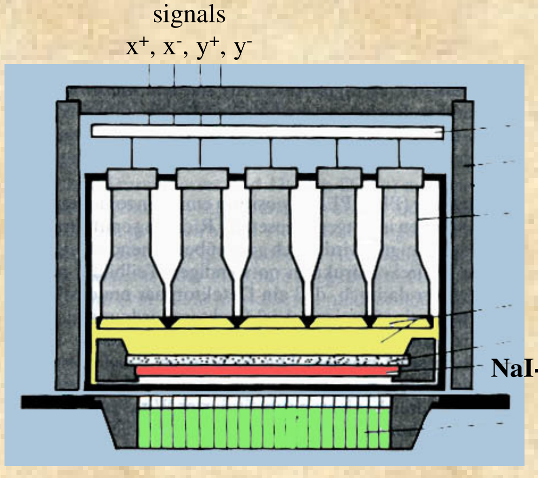
1940, Am.J.Physiol. **131**, 135

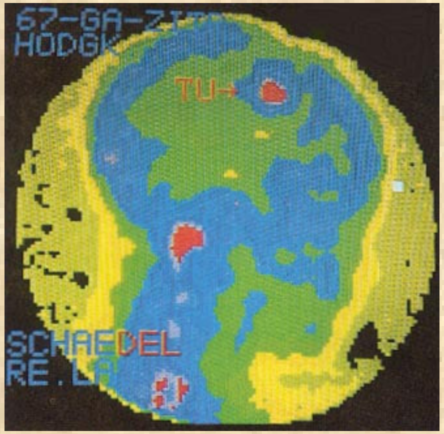
Kidney Isotope Nephrogram

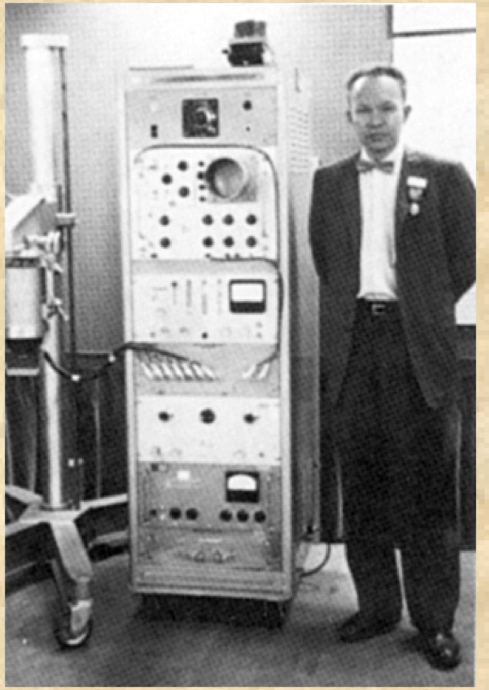


GAMMA CAMERA

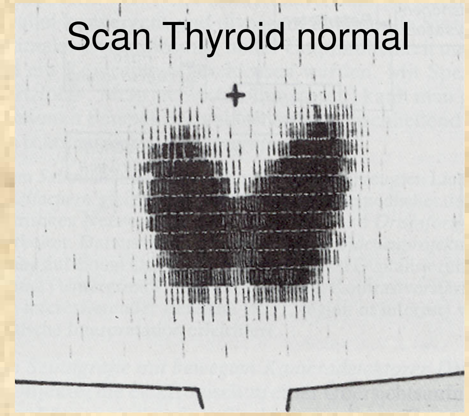
H.O.ANGER

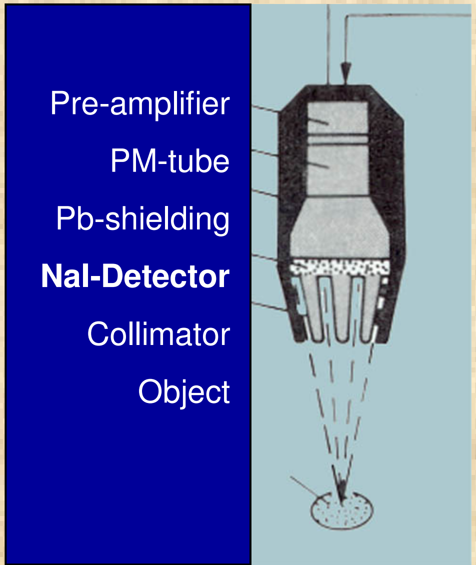






1958 Planar scintigram





1951

B.CASSEN

SCANNER

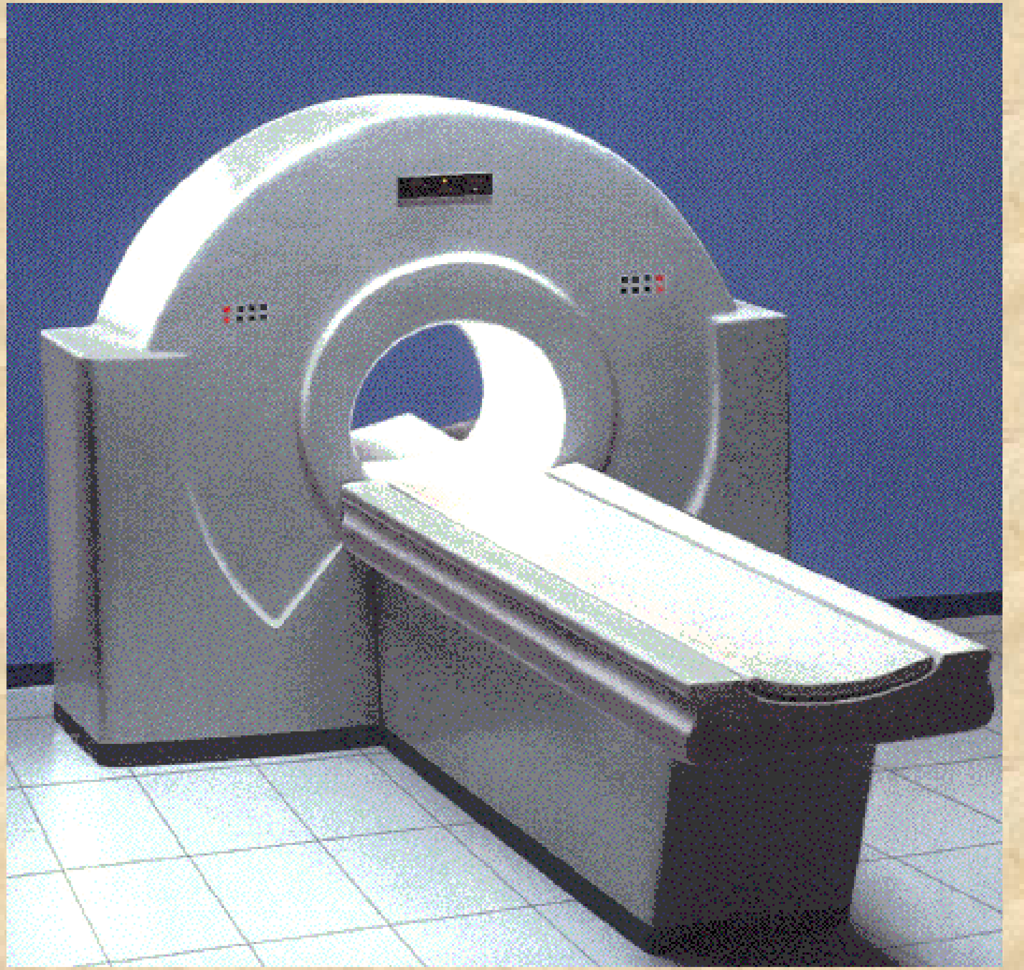
The scanner was designed for 131-I

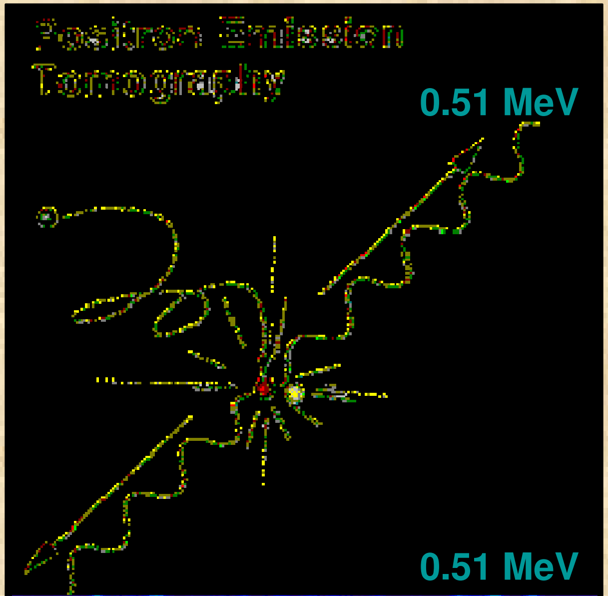
Modern SPET

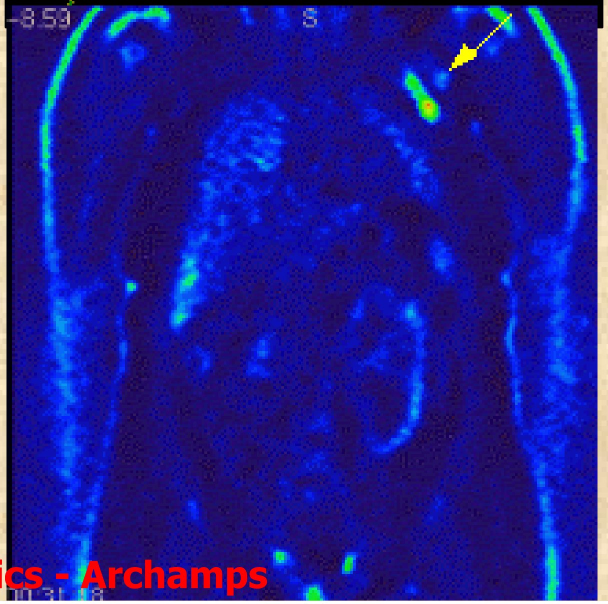
Cameras

(GE Medical Systems)

PET = Positron Emission Tomography



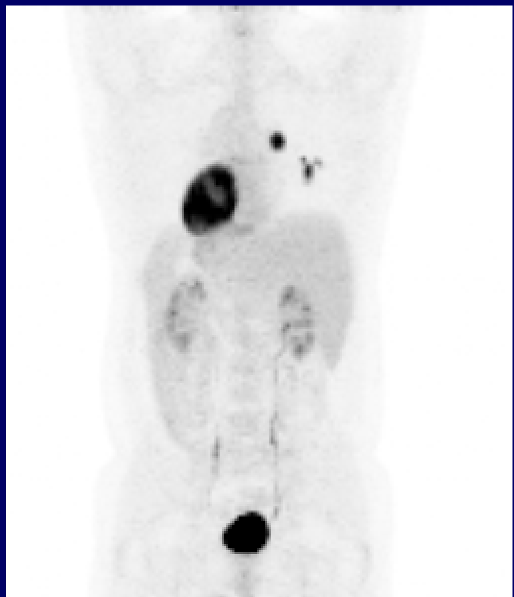




3D whole-body PET

ECAT HR+

25 year-old male with Melanoma,
71 kg, 178 cm, 625 MBq FDG, 45 min p.i.



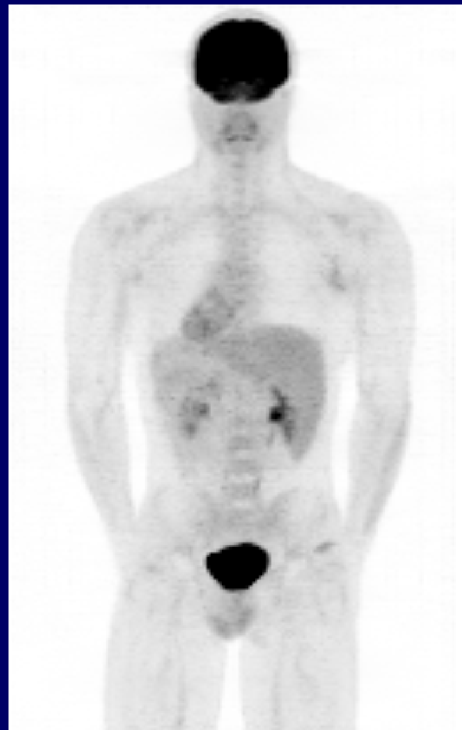
Emission scan time: 54 min
Transmission scan time: 18 min

Data courtesy of
Kettering Memorial Hospital, Kettering, USA

year 2000

ECAT ACCEL

50 year-old male with colon CA
91 kg, 183 cm, 720 MBq FDG, 162 min p.i.



Emission scan time: 27 min
Transmission scan time: 18 min

Data courtesy of
NC PET Imaging Center, Sacramento, USA

PET/CT concepts **1998-2000**

^{18}FDG-PET/CT of a patient w/ ENT

INVENTORS & INVENTIONS

INVENT-ORS

1+1=3

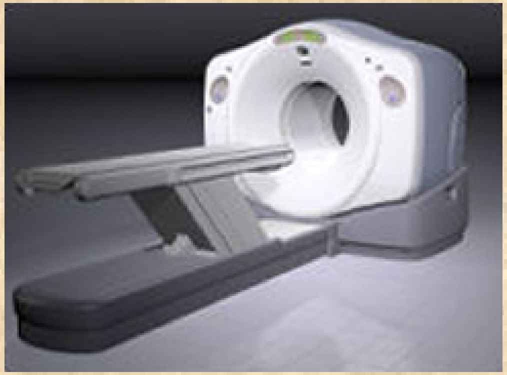
Accidents plus luck: the sum of innovation is greater than its parts

BY JAMES BURKE

INVENT-&IONS

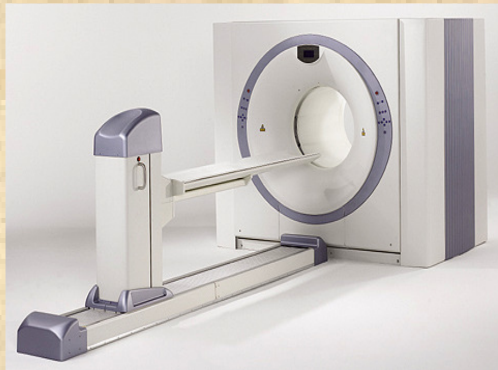
TIME, 04-Dec-2000

PET/CT today

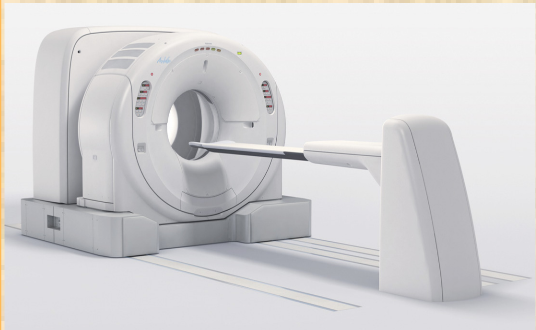


Discovery ST, STE, RX

Gemini GXL, TF



Biograph HiRez, TruV



Aquiduo

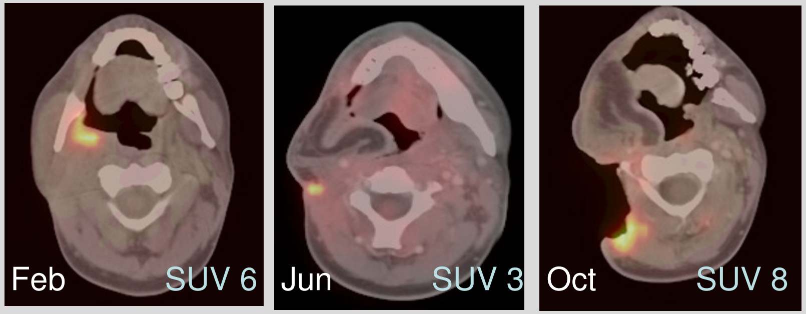
Sceptre P3

AnyScan PC

Trend: New PET components in combination w/ high-performance CT

PET/CT 2009: routine application

Oncology



35 y/o M w/ malignancy in mandibula

Feb: ^{18}FDG-PET/CT identified disease

Mar: right mandibulectomy and maxillectomy

Jun: PET/CT identified recurrent disease

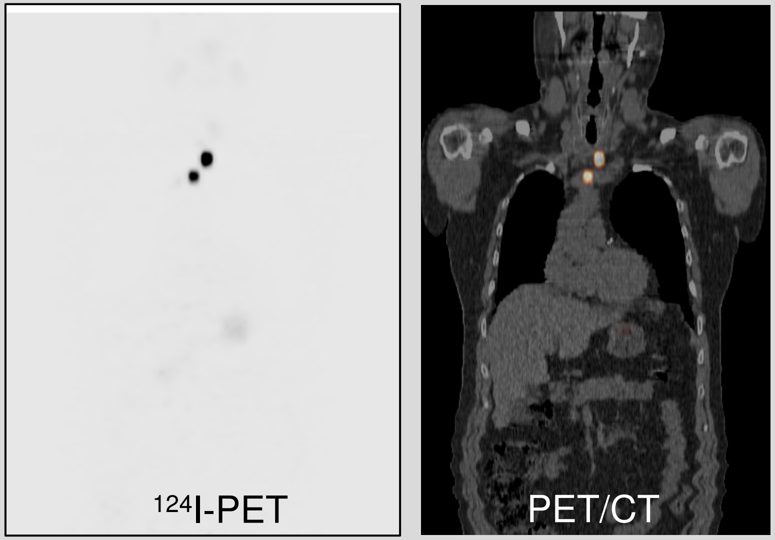
Jun: Extensive surgery

Oct: PET/CT showed recurrent disease

UPMC, Pittsburgh

Anatomy
CT-based AC

Oncology - Specific tracer



45 y/o M w/ papillary thryorid CA (pT4)

^{124}I-PET/CT

→ mediastinal LN metastasis w/o CT correlate

UH Essen-Duisburg

Anatomy
CT-based AC

Structure without function is a corpse,
… function without structure is a ghost.

Stephen Wainwright, Duke Dept Biology

RADIOISOTOPES in MEDICINE:

Requirements - Production - Application and Perspectives

3

Medical Isotope Production

Gerd-Jürgen BEYER

Prof.Dr.rer.nat.habil.

Cyclotron Unit, University Hospital of Geneva, Switzerland

GSG-Int. GmbH, Switzerland

gerd.beyer@cern.ch

gerd.beyer@gsg-int.com

Lecture

ESI

Week 1

Archamps (France) October 19, 2012

European School of Medical Physics - Archamps

NUCLEAR MEDICINE 2009

DIAGNOSIS

SPECT (SINGLE PHOTON EMISSION TOMOGRAPHY)

- → ^{99m}Tc still working horse
- → Increase of diagnostic value
- → New radiopharmaceuticals
- → New instrumentation & quantification

PET became a clinical tool

- → [^{18}F] FDG is the working horse
- → **ONCOLOGY (80 %)**
- → Neurology
- → Cardiology

Molecular Imaging

PET is a powerfull R&D tool

- → clinical research
- → Drug development
- → invivo biochemistry

Multi-Modality Imaging

- → SPECT - PET
- → PET – CT, SPECT - CT
- → PET – MRI
- → Animal PET-CT, SPECT-CT, PET-MRI

THERAPY (RIT)

New Approaches in Radionuclide Therapy

- → free chelates (EDTMP, others)
- → bio-selective antibody conjugates (mab)
- → bio-specidfic peptide conjugates
- → Lyposomes
- → Nanoparticles
- → others

New Radionuclides for Therapy:

- → Beta-Emitters with different energies
- → Alpha emitters
- → Auger electron emitters
- → Research isotopes

PET for individual invivo dosimetry

- → Quest for metallic positron emitters
- → longer lived positron emitters
- → PET imaging with „durt“ isotopes
- → Simmulatne Multi-tracer studies

ISOTOPES IN MEDICINE

DIAGNOSIS

in vitro

^{14}C
^{3}H
^{125}I
others

in vivo

^{99}Mo-^{99m}Tc

^{201}Tl
^{123}I
^{111}In
^{67}Ga
^{81}Rb-^{81m}Kr
others

ß+ emitters for PET
^{18}F, ^{11}C, ^{13}N, ^{15}O
^{86}Y, ^{124}I, ^{64}Cu
^{68}Ge - ^{68}Ga
^{82}Sr - ^{82}Rb
^{44}Ti - ^{44}Sc

THERAPY

internal

systemic

^{131}I, ^{90}Y
^{153}Sm, ^{186}Re
^{188}W-^{188}Re
^{166}Ho, ^{177}Lu,
others

α-emitters:
^{225}Ac-^{213}Bi
^{211}At, ^{223}Ra
^{149}Tb

e^{-}-emitters:
^{125}I

sources

sealed sources
^{192}Ir, ^{182}Ta, ^{137}Cs
many others

needles for brachytherapy:
(^{103}Pd), ^{125}I
many others

stands
^{32}P and others

seeds
^{90}Sr or ^{90}Y, others

applicators
^{137}Cs, others

external

tele radio

^{60}Co

gamma knife

^{137}Cs
blood cell irradi-ation

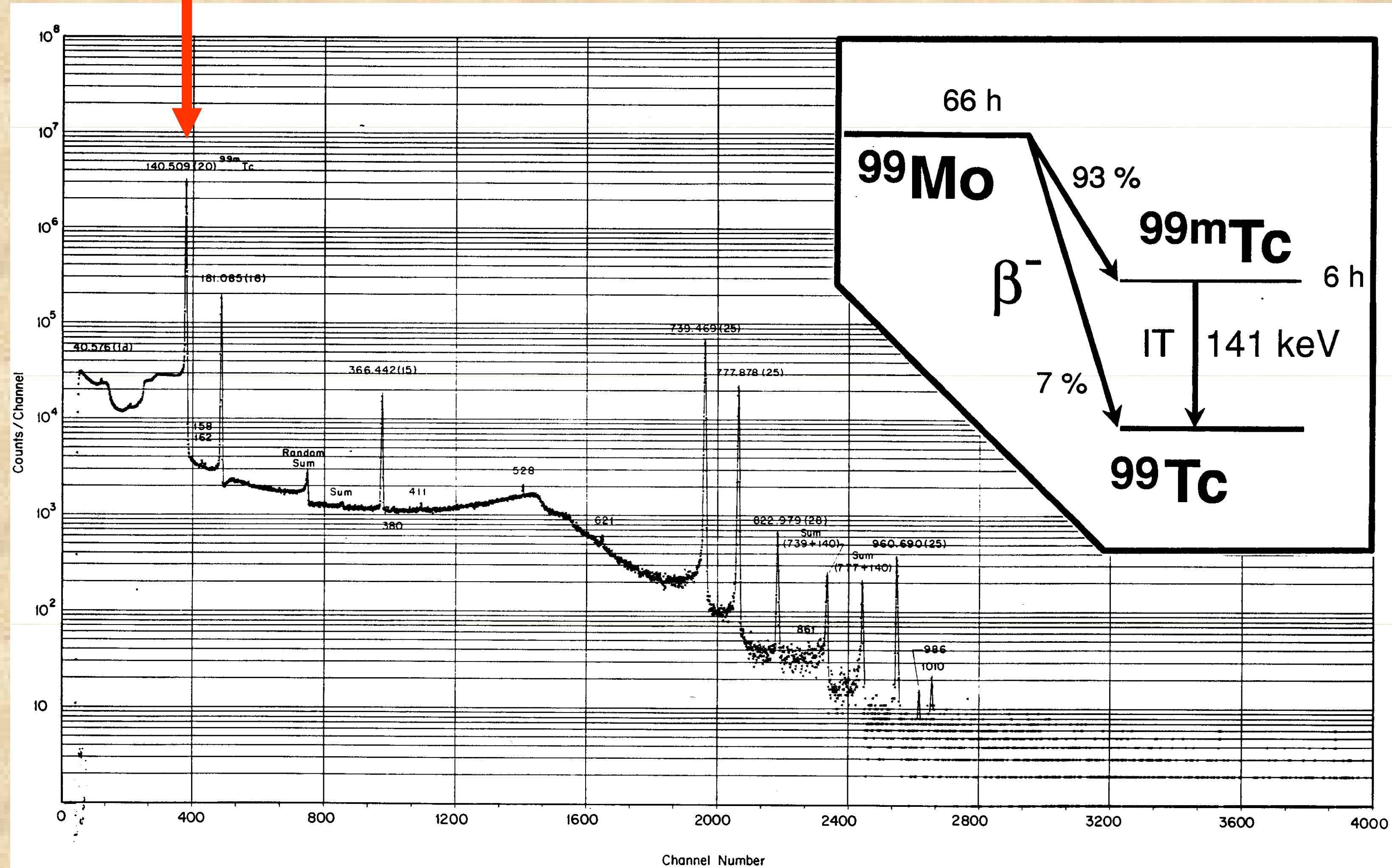
G.J.BEYER, Geneva, 2012

Why 99m-Tc

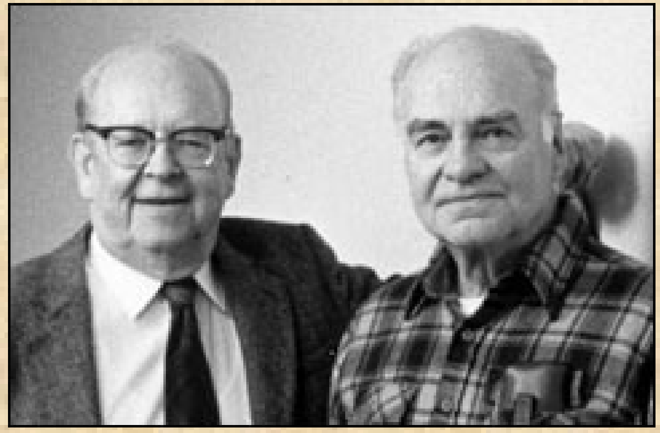
Three Aspects:

1. Nuclear properties
2. Generator principle (availability)
3. Sn(II) as reducing agent opened the door for KIT Technology

141 keV photons - the strength of ^{99m}Tc



Discovery of ^{99m}Tc generator in 1957 in BNL



^{99m}Tc detected while refining ^{132}I from ^{132}Te → ^{99}Mo-^{99m}Tc generator → Stang, Tucker, Greene,

Richards

BNL declined to file a patent for this device - ^{99m}Tc generator!

BNL memo in 1958:

"We are not aware of a potential market for technetium-99 great enough to encourage one to undertake the risk of patenting in hopes of successful and rewarding licensing."

Slide from Ramamoorthy, IAEA Vienna

Sn(II) as reducing agent

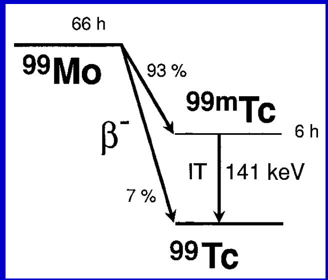
1962: The 99-Mo / 99m-Tc Generator introduced into clincal practice:
Harper P.V., G.Autors, K.A.Latrhrop, W siemens, L Weiss:
Technetium-99m as a biological tracer, J.Nucl.Med. **3** (1962) 209

1969: **Introduction of Sn(II) as reducing agent:**

Dreyer R. & Muenze R. (Dresden, Germany);
Markierung von Human Serum Albominw with 99m-Tc
Wiss.Z.K-Marx Uni Leipzig Nat.Wiss.R. **18** (1969) 629-633
Zur Tc-99m-Markierung von Serumalbumin; Isotopenpraxis **5** (1969) 296

2009: **Eckelmann W.C.:** JACC cardiovascular Imaging **2**, (2009) 364-368:

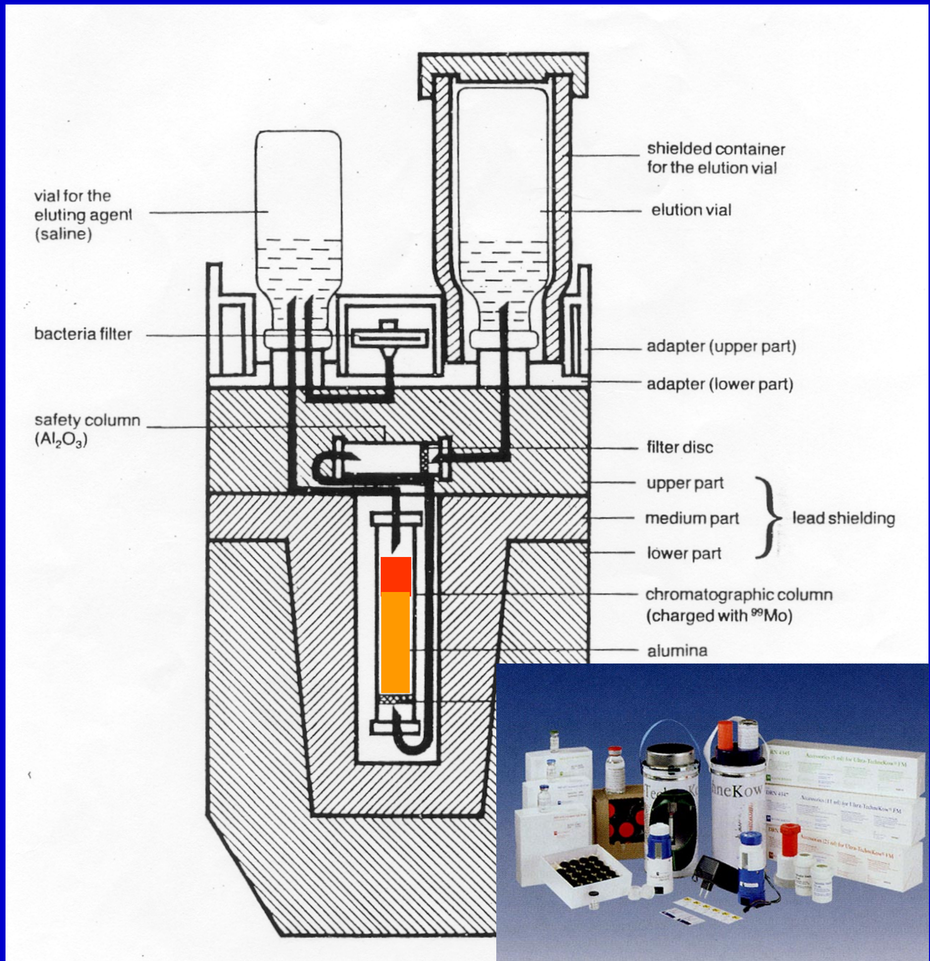
"…On a practical level, the use of stannous ion was a key development and current radiopharmaceutical kits employ the stannous reduction technique. With the advent of the Mo-99/Tc-99m generator in the 1960s followed by the development of "instant" kits, the use of Tc-99m–labeled compounds expanded rapidly"



$^{99m}TcO_4^-$

0.9 % NaCl solution

\+

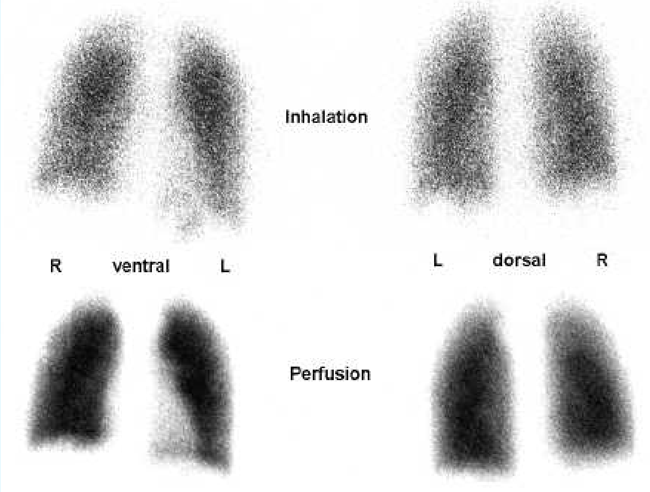


many different

^{99m}Tc-tracer

for

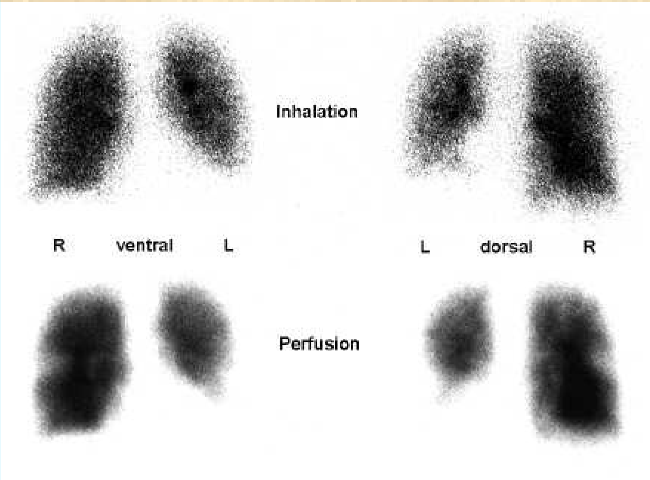
imaging of many different organ and tissue functions



Ventilation study

LUNG Function

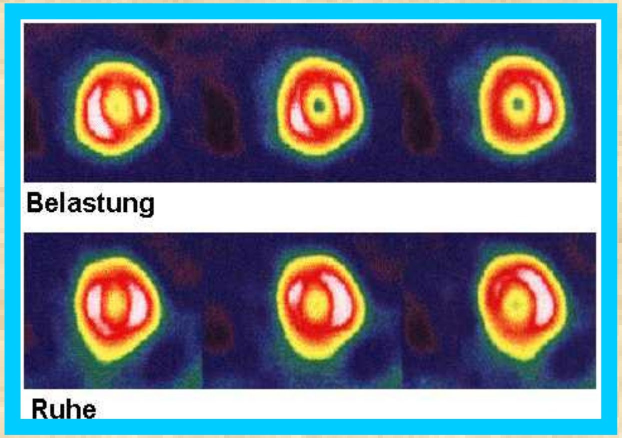
Perfusion Study



^{99m}Tc TRACER

Examples

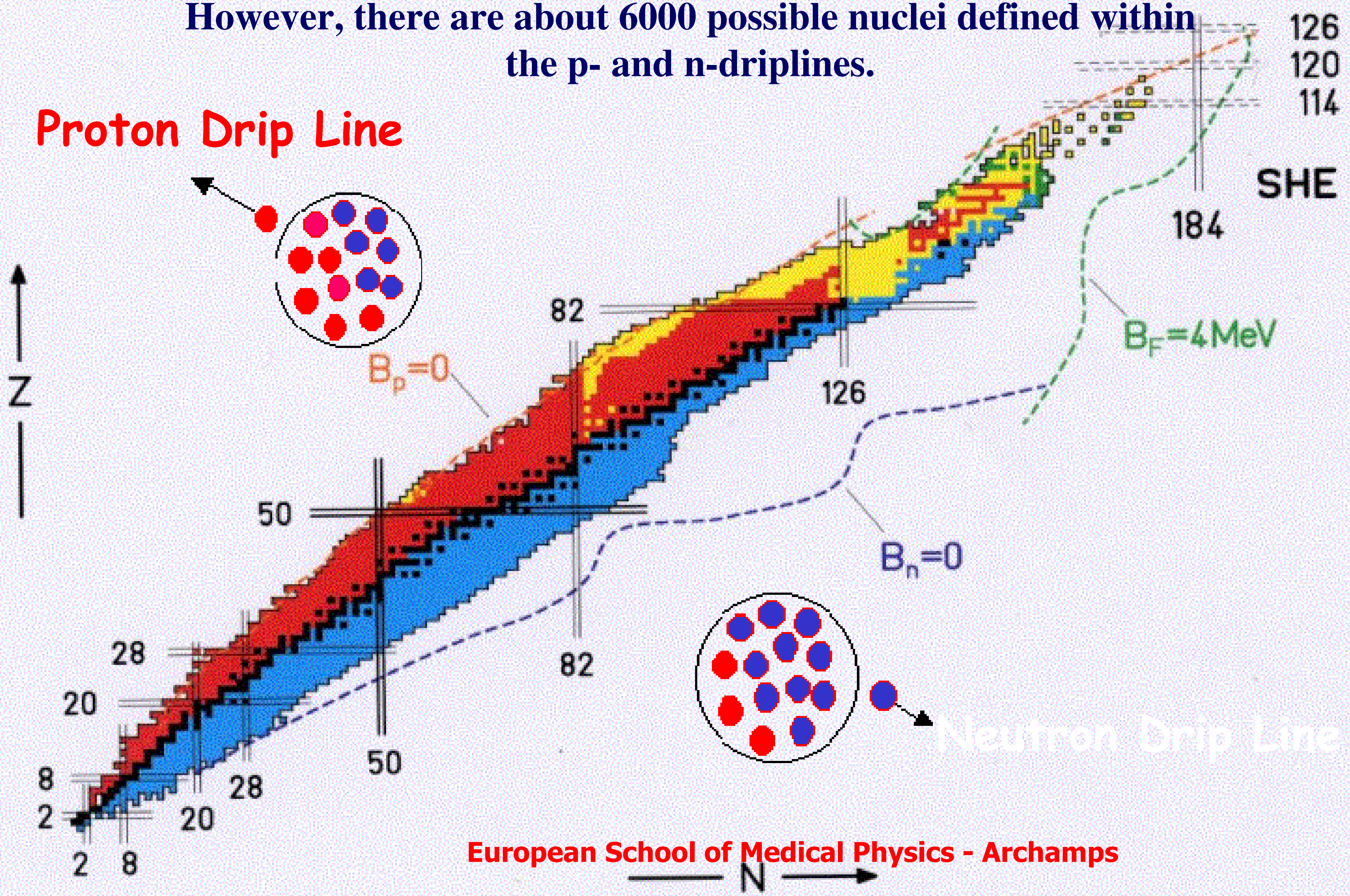
HEART Perfusion



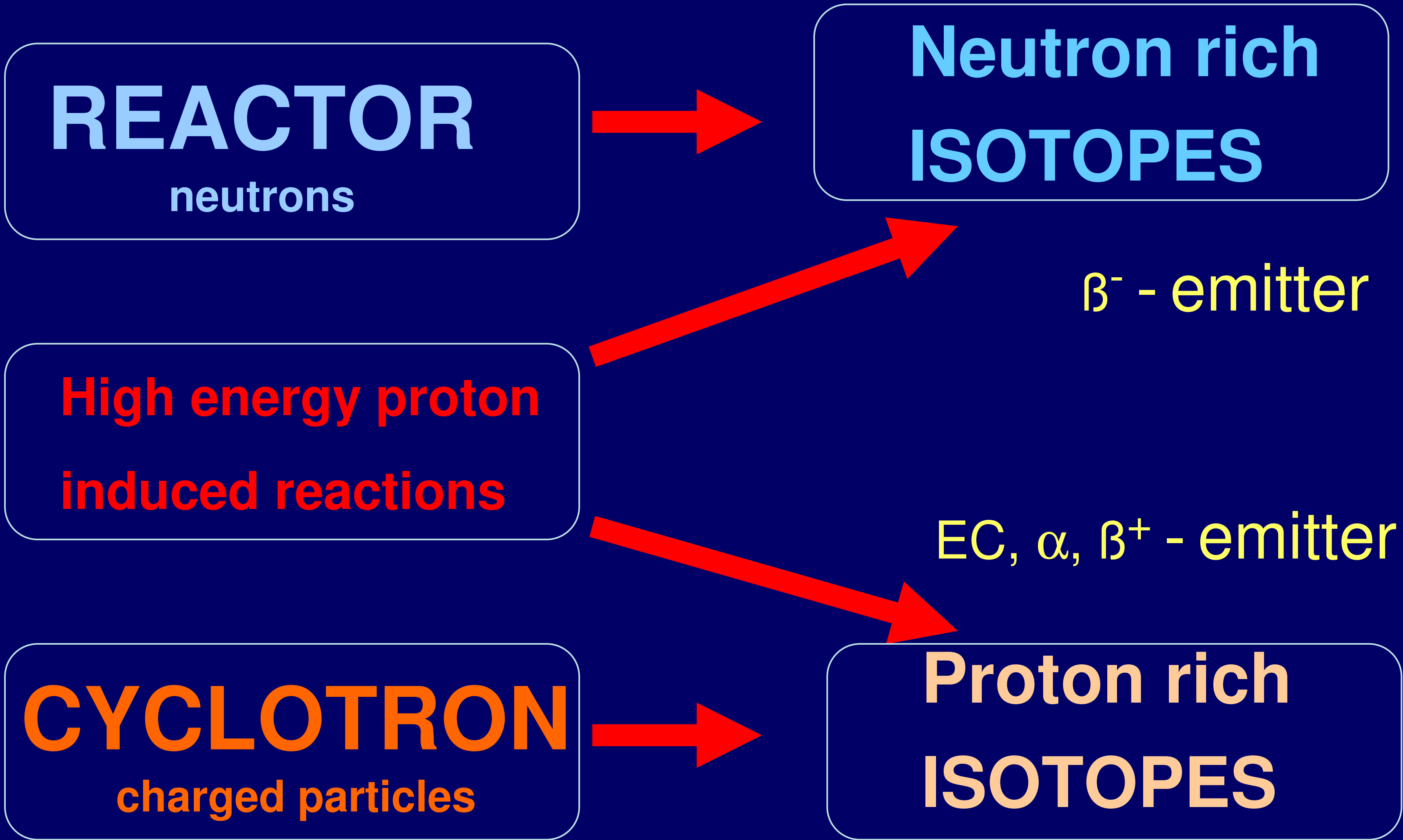
BONE metabolic activity

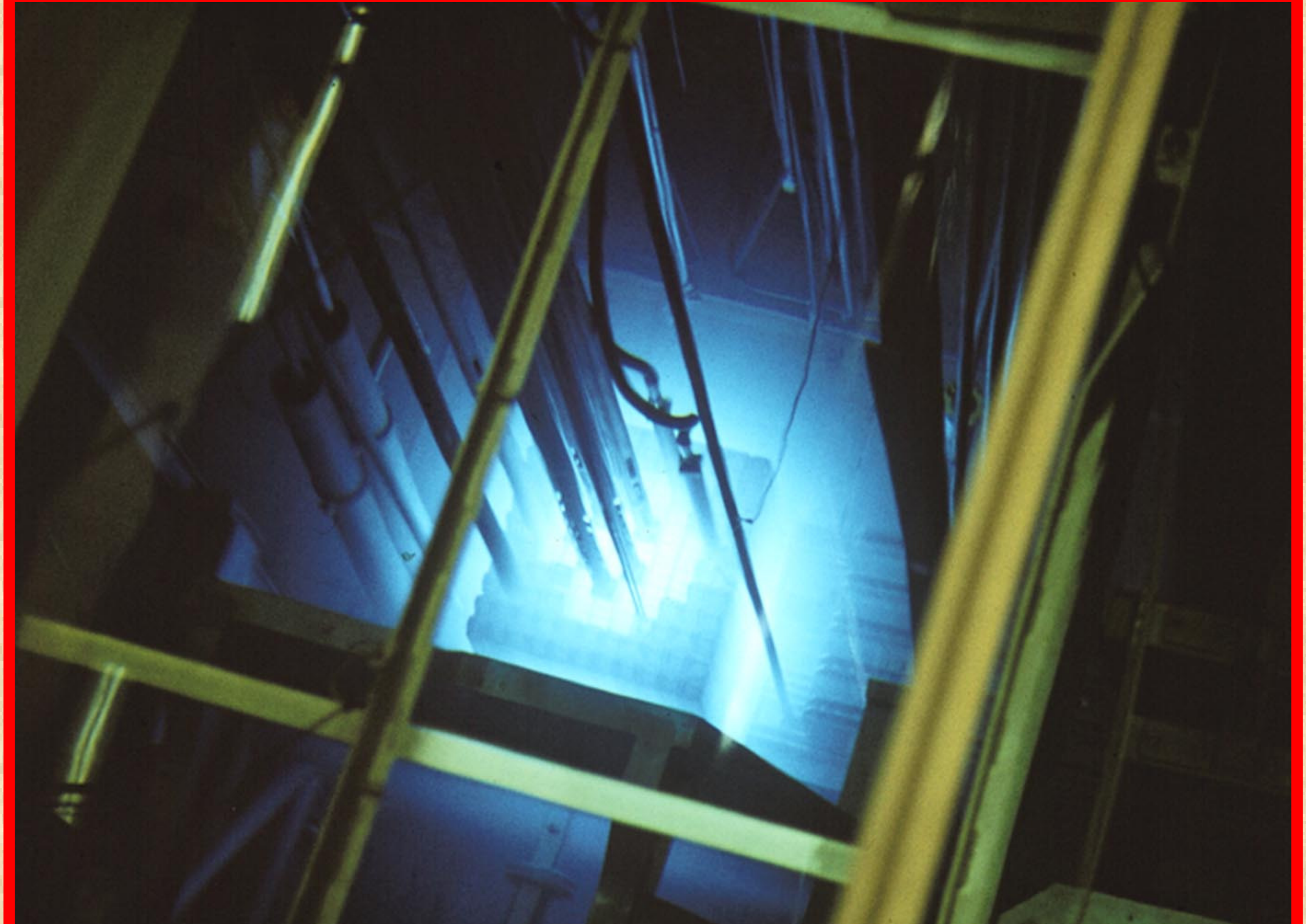
Naturally found on our planet are 265 stable plus 60 radioactive nuclei
About 3000 isotopes are synthesised in laboratories

However, there are about 6000 possible nuclei defined within the p- and n-driplines.



ISOTOPE PRODUCTION





10 MW swimming pool reactor, Geesthacht (D)

Foto: G.Beyer, 1973

^{99}Mo: PRODUCTION ROUTES

$^{98}Mo \quad (n, \gamma) \quad ^{99}Mo$

σ = 0.130 b

1 g ^{98} Mo, $\Phi_{n^{th}}$ = 1 * 10^{13} $cm^{-2}s^{-1}$

8 GBq $^{99}Mo/g\ ^{98}Mo$ (**low specific activity**)

$^{235}U \quad (n; f) \quad ^{99}Mo$

σ = 586 b

^{99}Mo - fission yield = 6.15 %

1 g ^{235} U, $\Phi_{n^{th}}$ = 1 * 10^{13} cm^{-2}

914 GBq ^{99}Mo/ mg Mo (**high specific activity**)

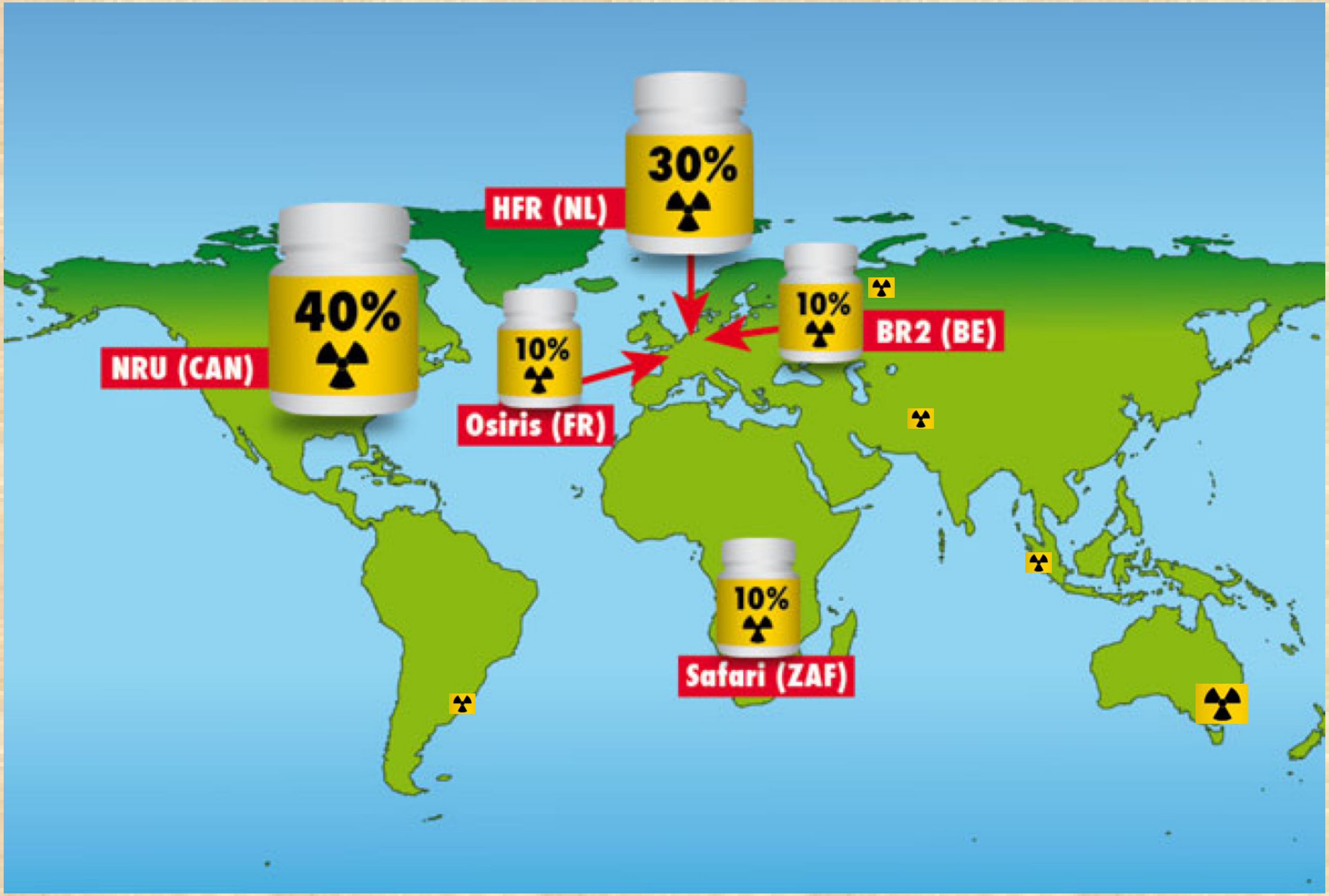
NRU Reactor, Canada

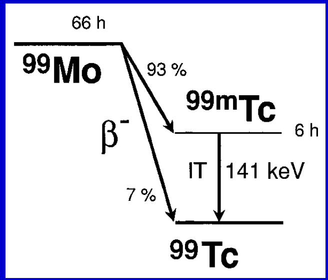
- 15 May 2009: D_2O leak
- stopped till spring 2010+
- license till October 2011

HFR Petten, NL

- extended maintenance stop from 19 February 2010

Main ^{99}Mo-Production Sites

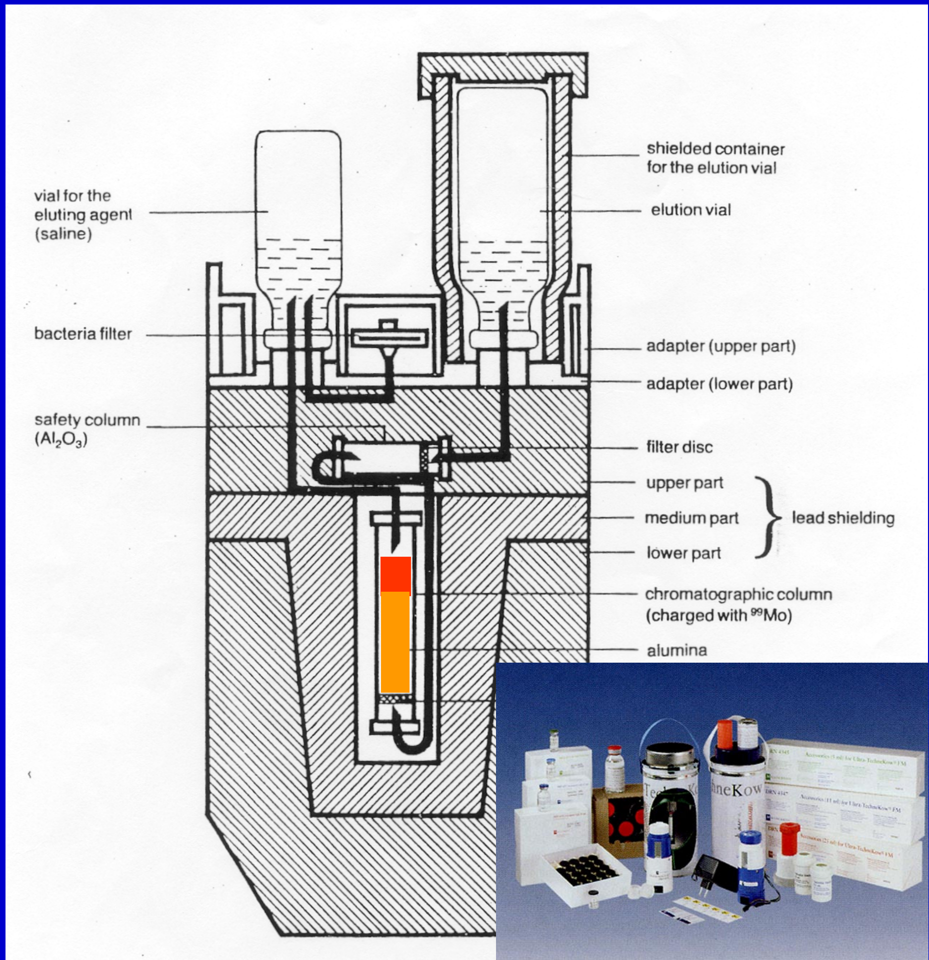




$^{99m}TcO_4^-$

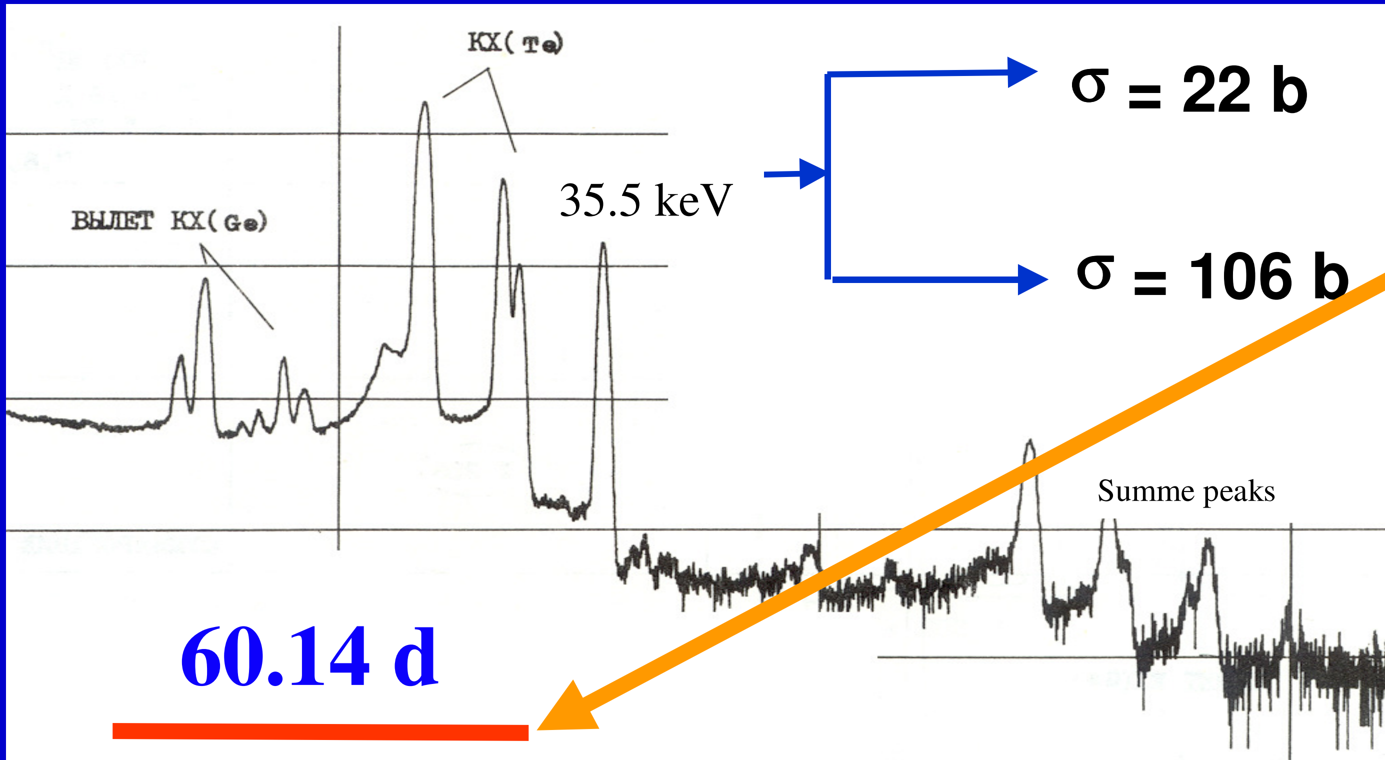
0.9 % NaCl solution

\+



many different ^{99m}Tc-tracer for imaging of many different organ and tissue functions

$^{124}Xe\ (n,\gamma)\ ^{125}Xe \xrightarrow{EC} {}^{125}I$



σ = 22 b

σ = 106 b

57 sec

16.8 h

^{125}Xe

60.14 d

^{125}I

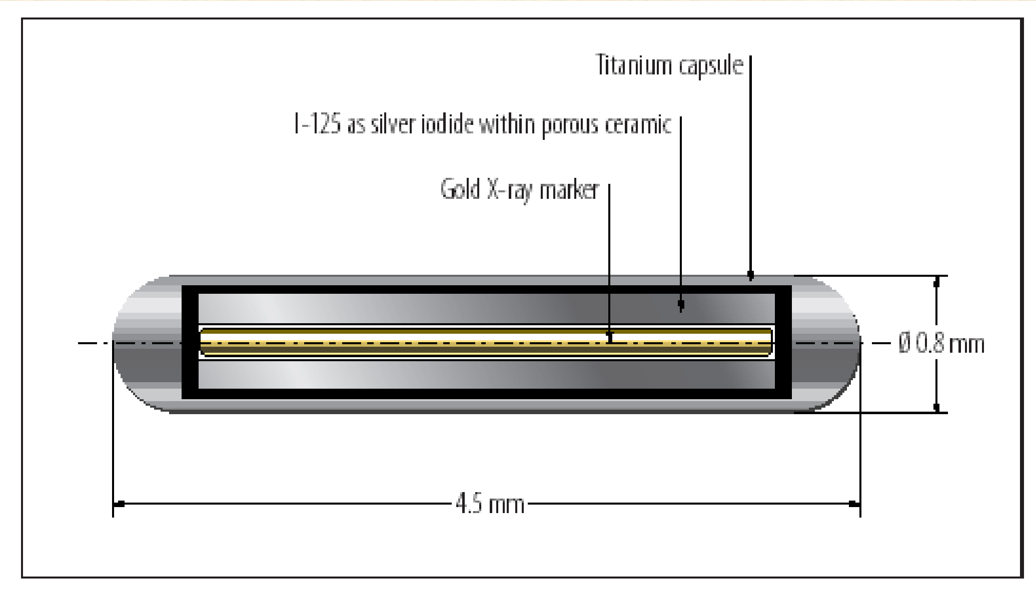
(n, γ)

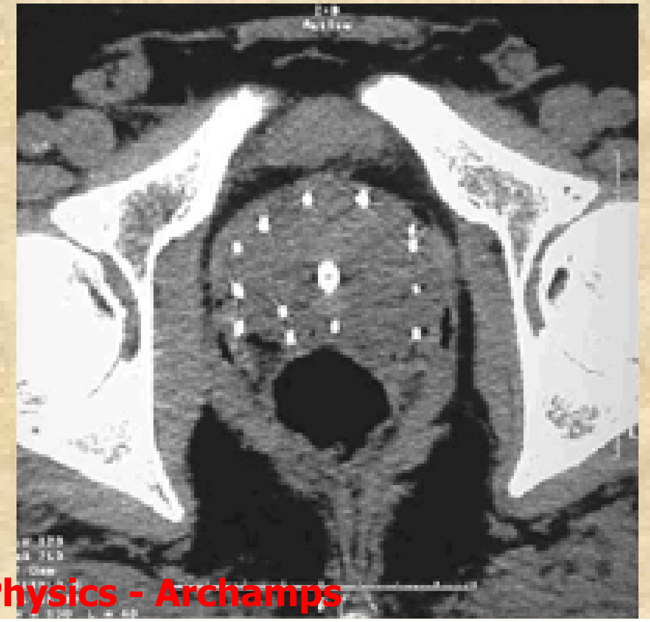
σ = 894 b

^{126}I (13.6 d)

BEBIG
An Eckert & Ziegler Company

IsoSeed I-125





The IsoSeed is equipped with a high-density gold marker providing excellent CT visibility. The full-length marker allows easy and precise location of each seed and produces minimal artefacts. This enhances the precision of the post-implant quality control.

$^{130}Te\ (n,\gamma)\ ^{131}Te \xrightarrow{\beta^-} {}^{131}I$

$\sigma = 0.02$ b

$\sigma = 0.27$ b

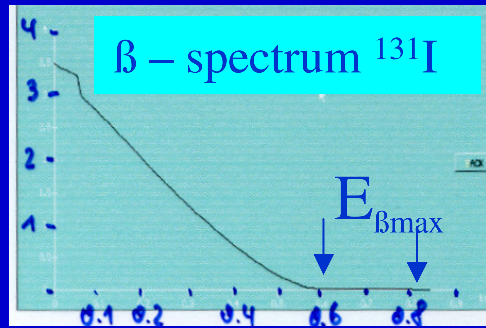
182 keV

IT

22 %

30 h

25 min



22 %

78 %

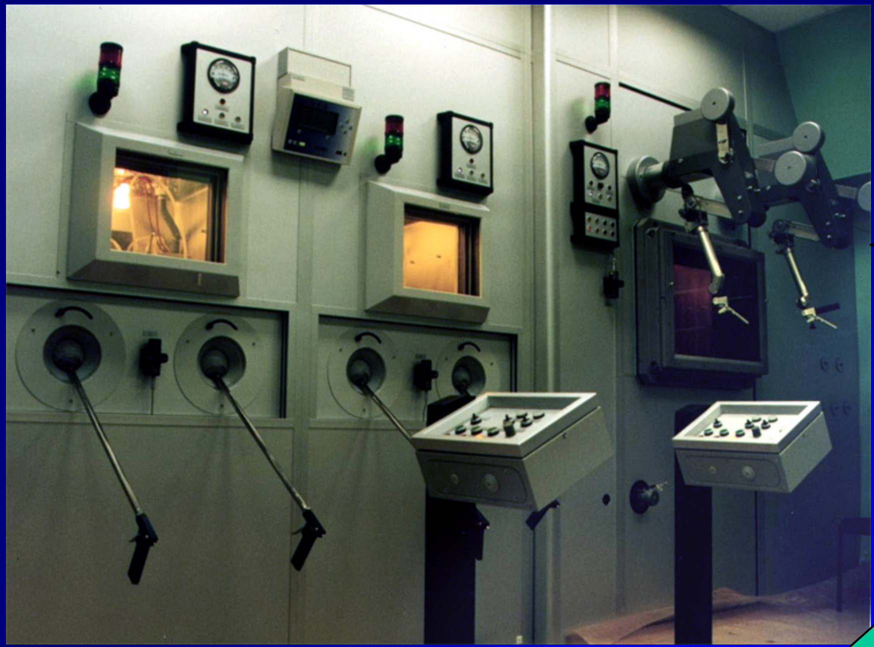
8.04 d

β^-

^{131}I

Simplified scheme for ^{131}I-production via thermal neutron irradiation of natural TeO_2

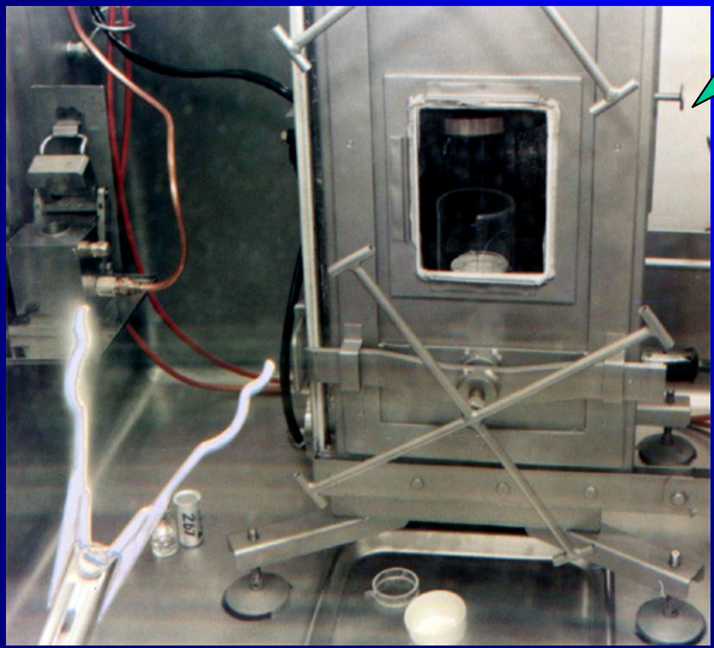
^{131}I Production Technology

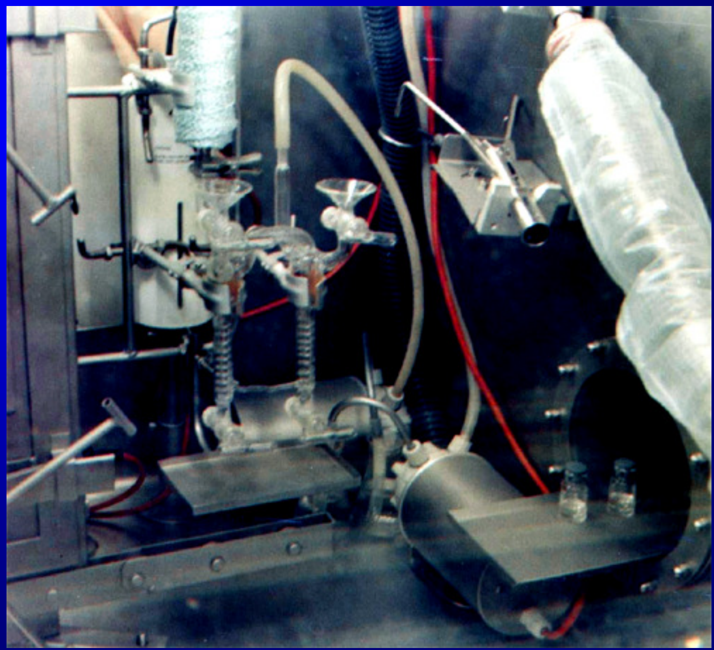


Hot Cell Facility

Target Processing

Iodine Trapping





Problems of medical RI Production with CYCLOTRONS

- **Short range of the particle beam**

Range: 30 MeV p about 1 mm
15 MeV d about 0.3 mm
30 MeV a about 0.1 mm

small target - high thermic energy deposition!

- **Small cross sections**

Low productivuity

- **Limited and expensive target material**

enriched isotopes

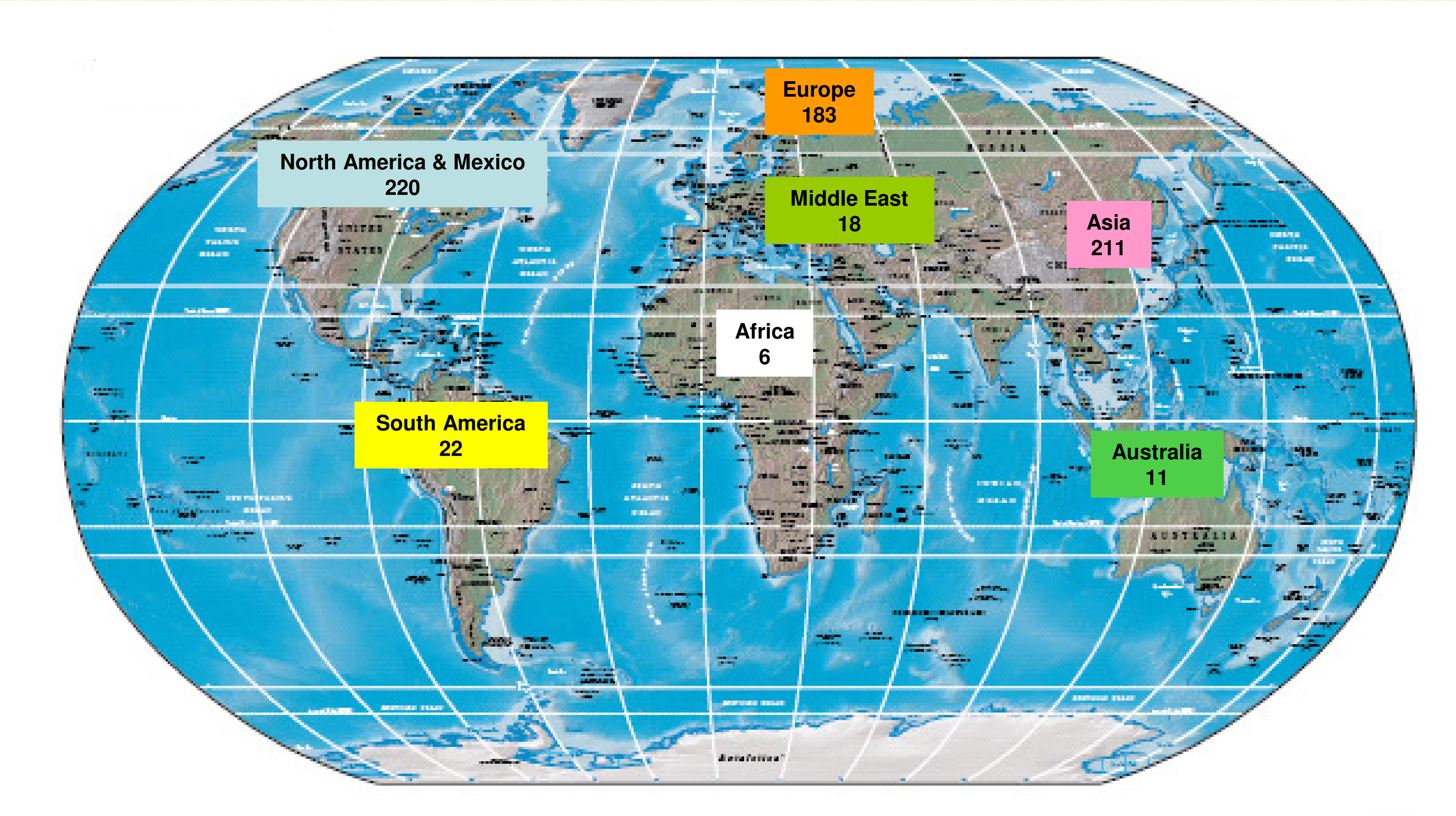
- **Vacuum**

Target window problems, sensitive target material

- **Single target – one isotope**

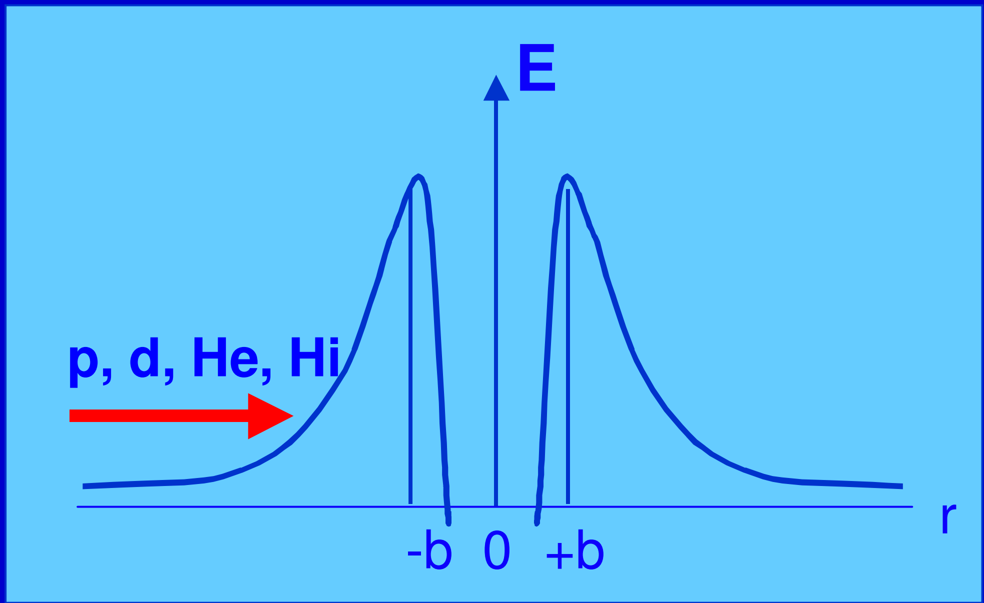
Distribution of cyclotrons for production of PET tracers (2008)

(source: D. Schlyer, BNL/USA, based on inputs of 4 major manufacturers)



Each year: about 40 new installations, PET

Particle Beam Energy



Ep = 30 MeV,

Ip = 100 µA

E_{th} = 3 kW

Area = 1 cm

Range = 1 mm

- at “b” strong nuclear force
- only one particle out of 10^4……10^7 reacts in reality
- full particle beam is stopped inside the target material
- the whole particle energy is transformed into thermic energy (heat)

123-IODINE PRODUCTION ROUTES

^{123}Cs —(5.9 min, EC/β^+)→ ^{123}Xe —(2.08 h, EC)→ ^{123}I

1985 Karlsruhe, Canada	1980 Würenlingen PSI	1975 Many places
^{124}Xe (p,2n)	^{127}I (p,5n)	^{124}Te (p,2n)
20 – 30 MeV p	75 MeV p	22 – 28 MeV
^{125}I < 10-3 %	^{125}I < 1 %	^{124}I = 1 %

ALTERNATIVES:

local ^{123} I production using PET cyclotrons

^{123}Te (p,n) ^{123} I

15 MeV p, 150 MBq/µAh

Fast, easy, reliable, clean product, suitable for direct labeling,

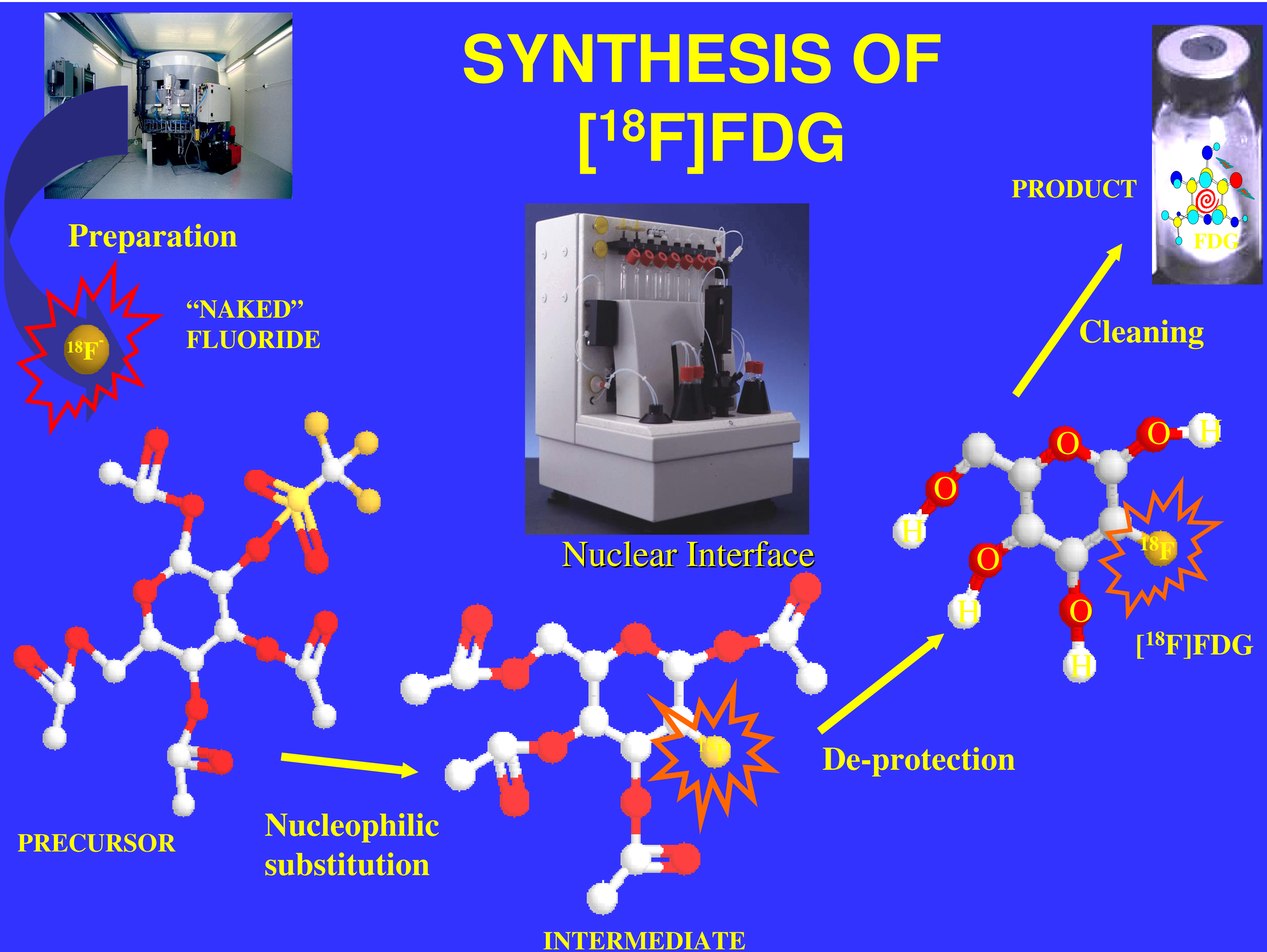
ISOTOPES
for Tracer Synthesis

ISOTOPE	$T_{1/2}$	Reaction	Target	Product
^{11}C	**20 min**	**$^{14}N\ (p,\alpha)\ ^{11}C$**	**N_2**	**unlimited**
^{13}N	10 min	$^{16}O\ (p,\alpha)\ ^{13}N$	**H_2O**	$[^{13}N]NH_3$
^{15}O	**2 min**	**$^{14}N\ (d,n)\ ^{15}O$**	**H_2O**	**$[^{15}O]H_2O$**
^{18}F	110 min	$^{18}O\ (p,n)\ ^{18}F$ $^{20}Ne\ (d,\alpha)\ ^{18}F$	**$[^{18}O]H_2O$** **^{20}Ne**	**$[^{18}F]FDG$** **$[^{18}F]FDOPA$**

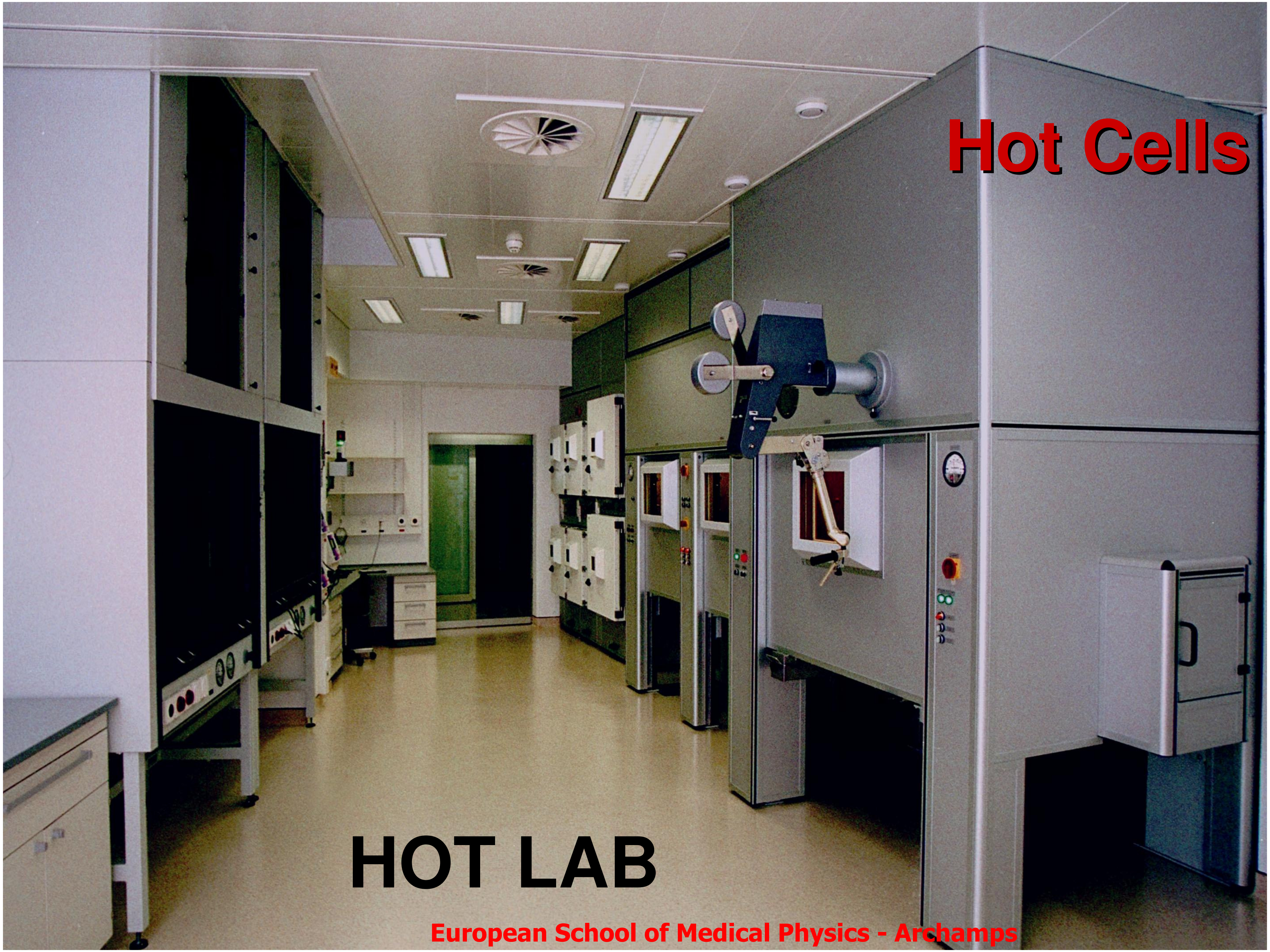
The FIRST FDG SYNTHESIZER

J. Fowler, BNL

SYNTHESIS OF $[^{18}F]FDG$




July.2000


Hot Cells
HOT LAB

ISOTOPES IN MEDICINE

DIAGNOSIS

in vitro

^{14}C
^{3}H
^{125}I
others

in vivo

^{99}Mo-^{99m}Tc

^{201}Tl
^{123}I
^{111}In
^{67}Ga
^{81}Rb-^{81m}Kr
others

ß+ emitters for PET

^{18}F, ^{11}C, ^{13}N, ^{15}O
^{86}Y, ^{124}I, ^{64}Cu
^{68}Ge - ^{68}Ga
^{82}Sr - ^{82}Rb
^{44}Ti - ^{44}Sc

THERAPY

internal

systemic

^{131}I, ^{90}Y
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^{149}Tb

e^{-}-emitters:

^{125}I

sources

sealed sources
^{192}Ir, ^{182}Ta, ^{137}Cs
many others

needles for brachytherapy:
(^{103}Pd), ^{125}I
many others

stands
^{32}P and others

seeds
^{90}Sr or ^{90}Y, others

applicators
^{137}Cs, others

external

tele radio

^{60}Co

gamma knife

^{137}Cs
blood cell irradi-ation

TRENDS

- **Therapy** fast growing demand
  mab, peptides, oligonucleaotides, nanoparticles, seeds

- **PET** cost effective use of [^{18}F] FDG
  new tracer molecules,
  diagnostic support of therapy

- **^{99}Mo/^{99m}Tc** remains working horse in Nucl.Med.
  growing demand, presently shortage in supply

- **Brachytherapy** growing demand
  seeds (^{125}I) spheres (^{90}Y)