Van Gen tot Geneesmiddel: Nuclear Imaging techniques

Part 1.
Techniques: cyclotron and imaging

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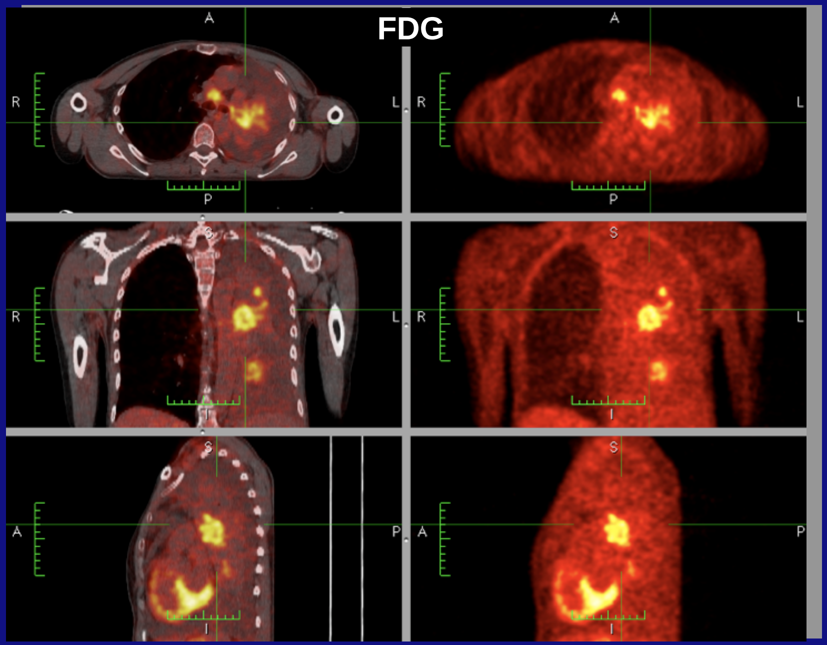
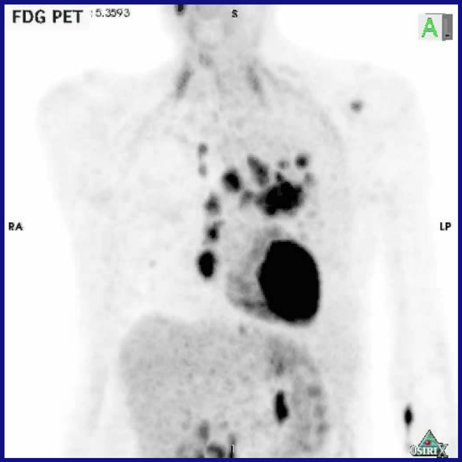
VU University Medical Center Amsterdam

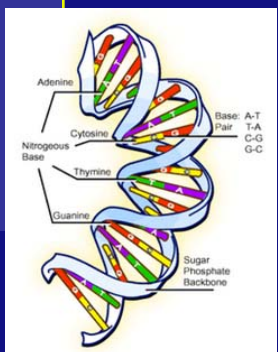
Imaging

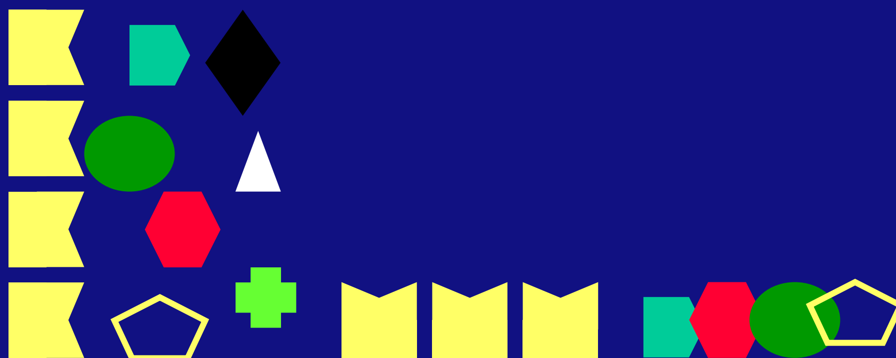


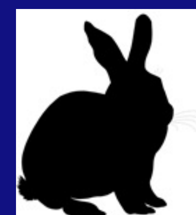


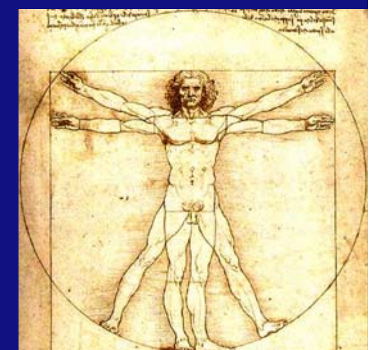
The Gene-to-Medicine paradigm

Target discovery | Chem diversity | Hit | optimise | safety | efficacy







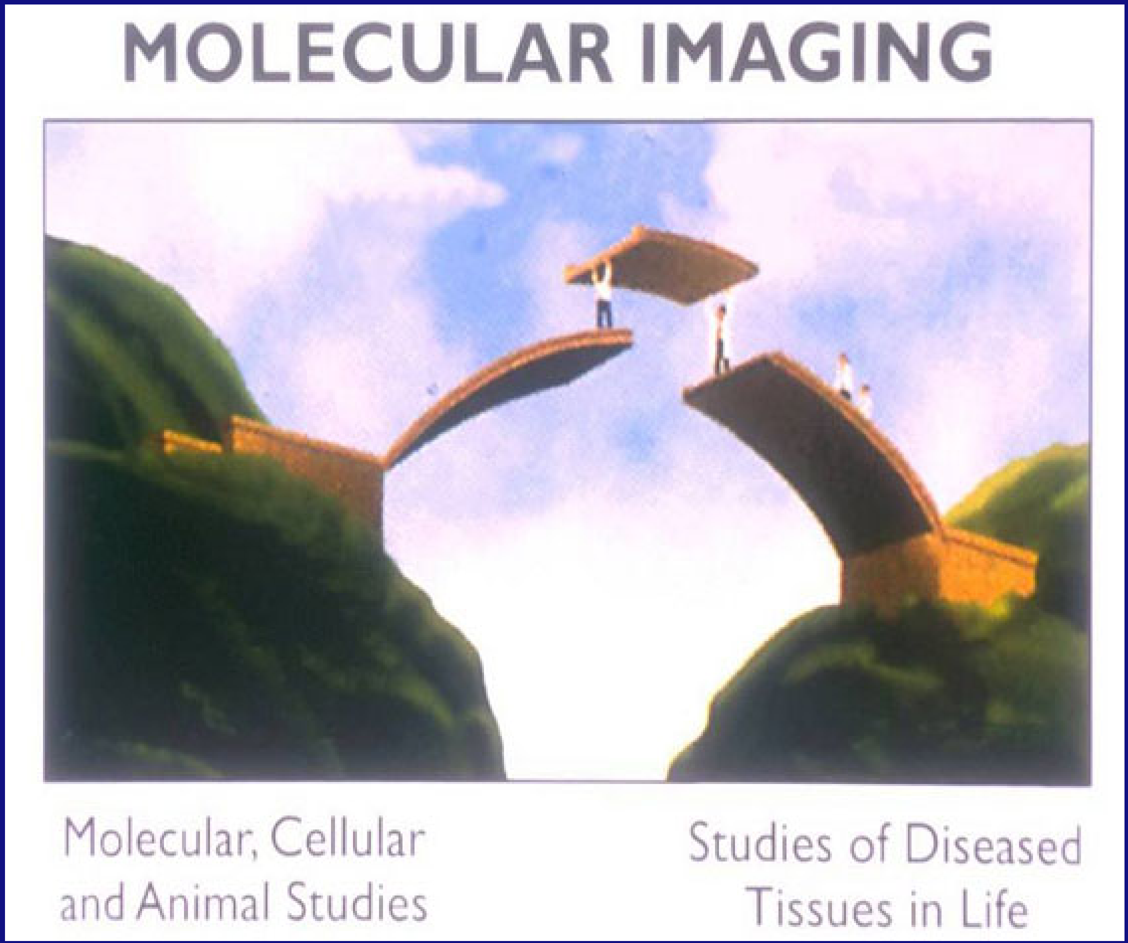


genomics | Lead chem | HTS | SAR | Pre clinical | human

$\underbrace{\text{genomics} \quad \text{Lead chem} \quad \text{HTS}}_{\text{bio informatics}}$

$\underbrace{\text{Lead chem} \quad \text{HTS} \quad \text{SAR}}_{\text{chemo informatics}}$

$\underbrace{\text{genomics} \quad \text{Lead chem} \quad \text{HTS} \quad \text{SAR} \quad \text{Pre clinical} \quad \text{human}}_{\text{imaging}}$



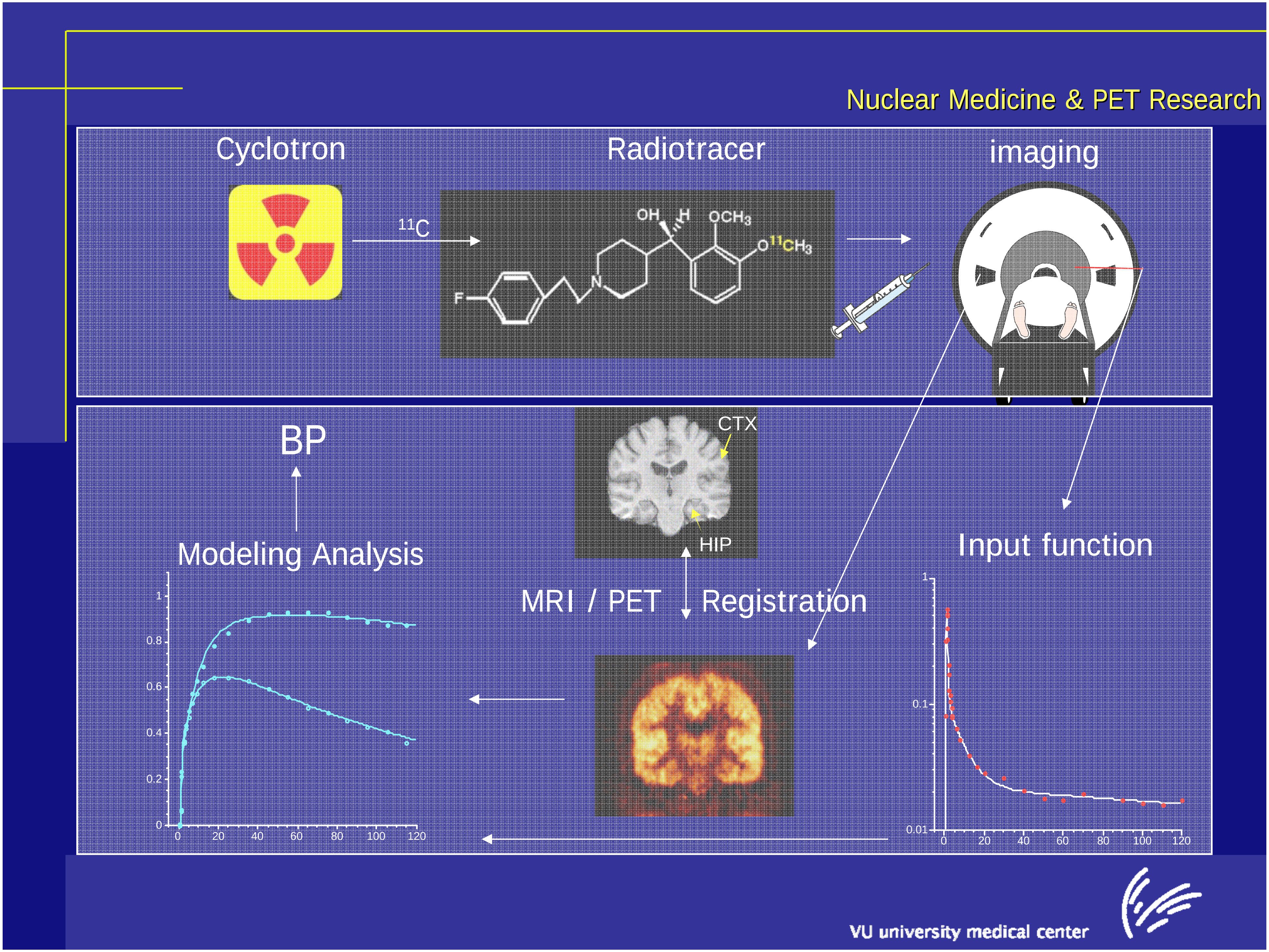
Goal this week: provide overview

VGTG : Imaging

Dinsdag 24 februari
Deel 1: techniek
Deel 2: radiochemie

Donderdag 26 februari
Deel 3: casus neuroimaging
Deel 4: casus alzheimer en borstkanker

Dinsdag 3 maart rondleiding op RNC: inschrijven



Nuclear Medicine & PET Research
Cyclotron
Radiotracer
imaging
11C
OH H OCH3
O11CH3
F
N
BP
CTX
HIP
Modeling Analysis
MRI / PET Registration
Input function
0 0.2 0.4 0.6 0.8 1
0 20 40 60 80 100 120
0.01 0.1 1
0 20 40 60 80 100 120
VU university medical center

Outline

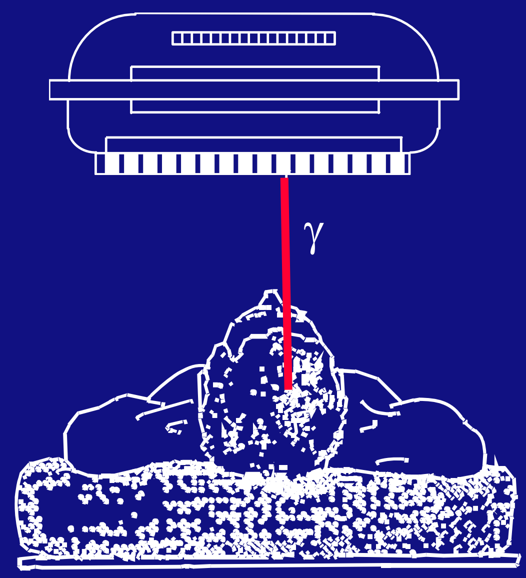
Nuclear Imaging: PET and SPECT

Cyclotron technique

Targetry

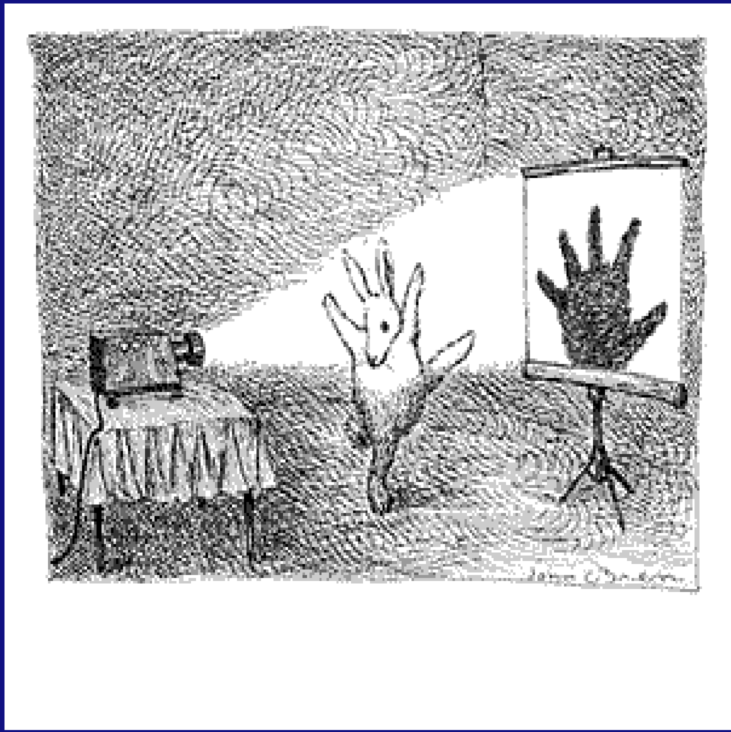
SPECT

Planar detection

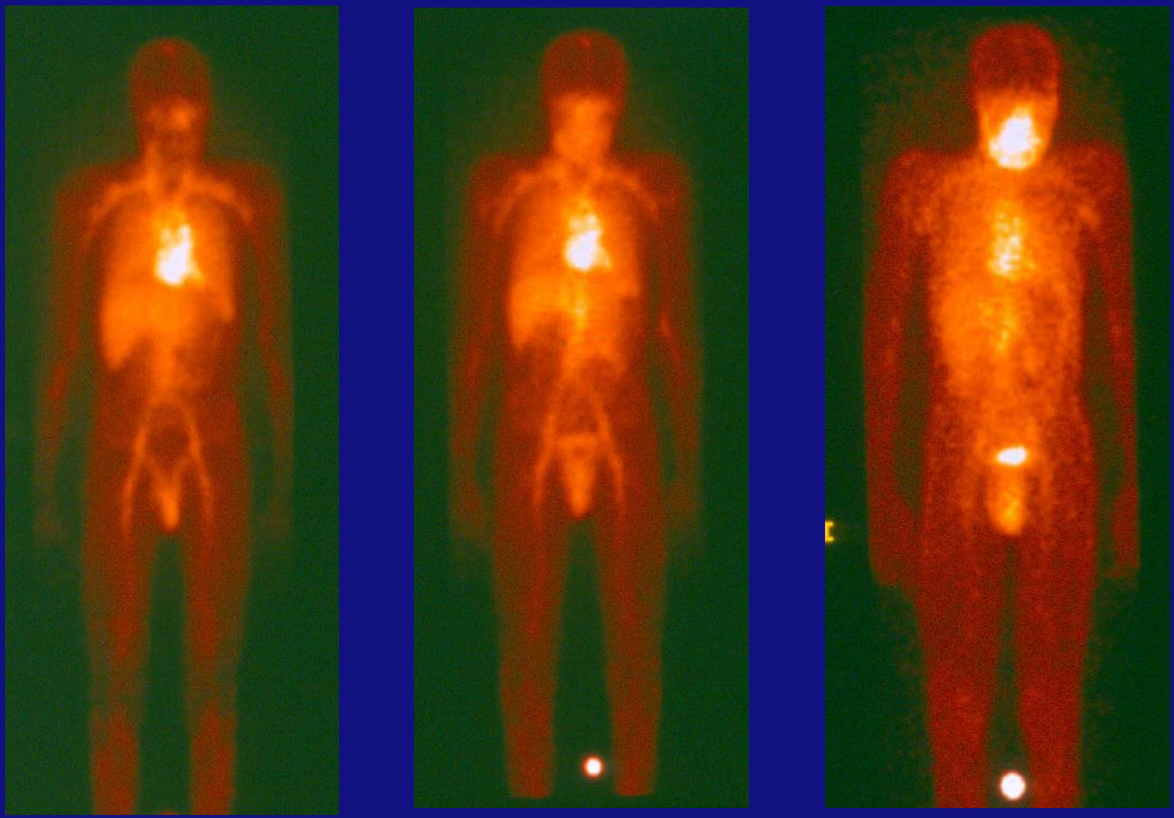


SPECT

Planar detection



SPECT

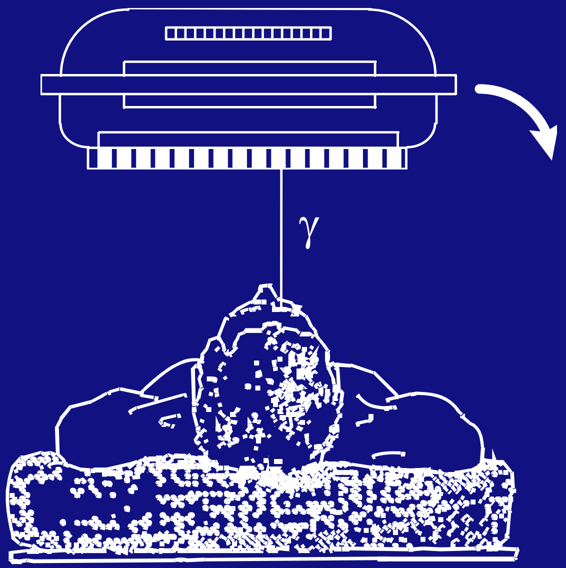


1 hr 24 hr 6 days

^{186}Re-mab

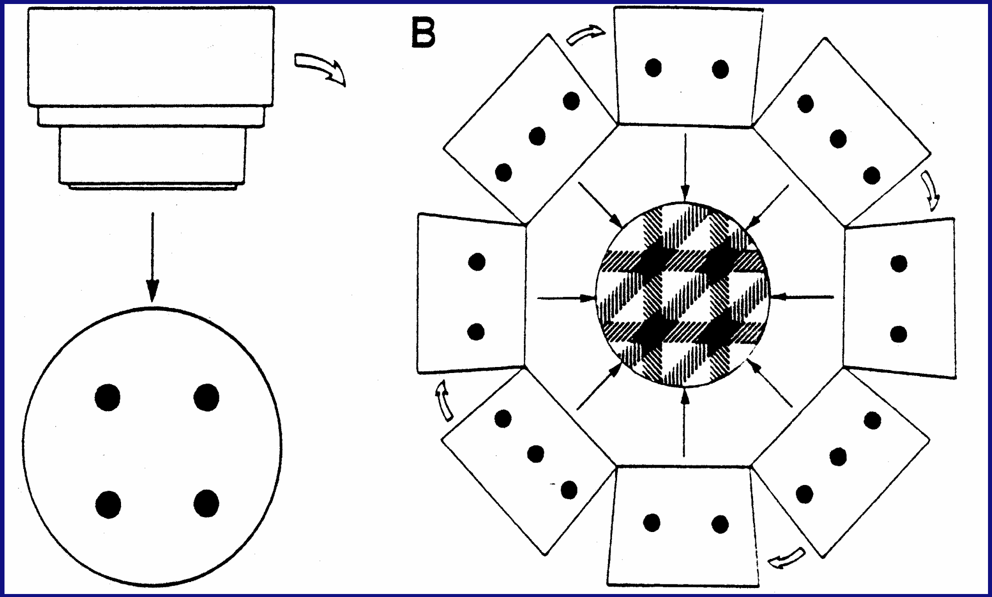
SPECT

Turning camera



SPECT

Reconstruct : (filtered) backprojection



Positron Emission Tomography

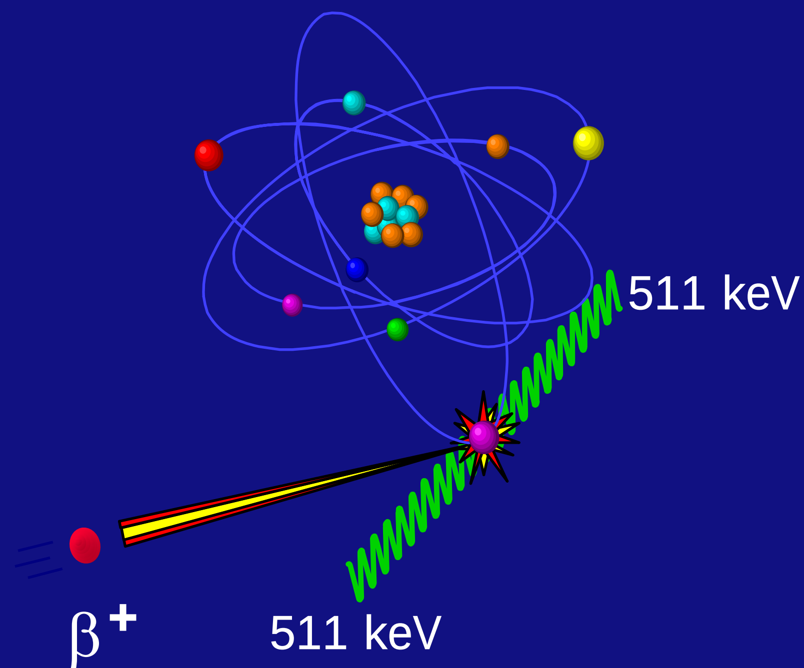
Makes use of positron decay

Requires special radio isotopes

Images in 3D

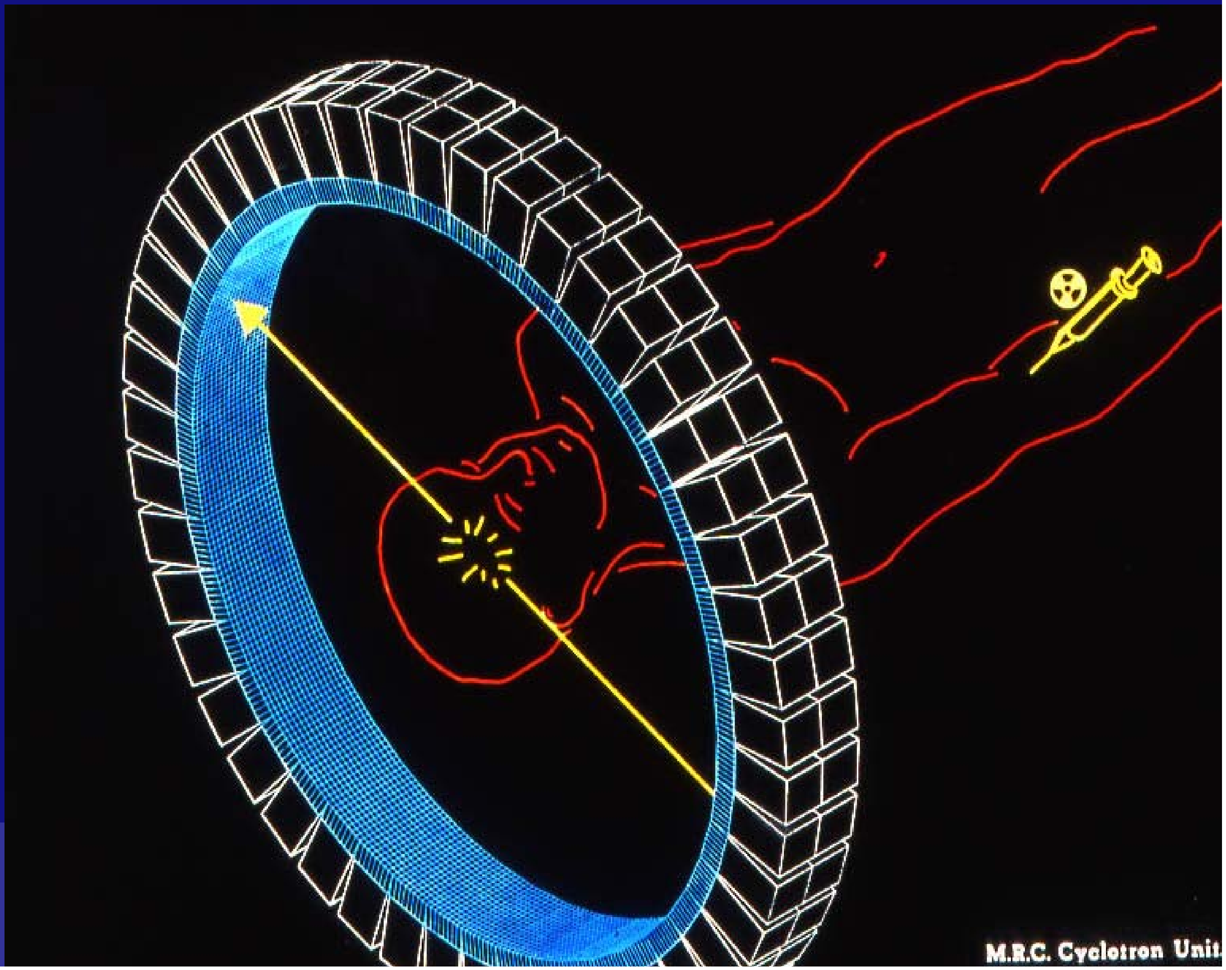
positron decay

Decay
Loss kinetic energy
Annihilation
511 KeV
180°

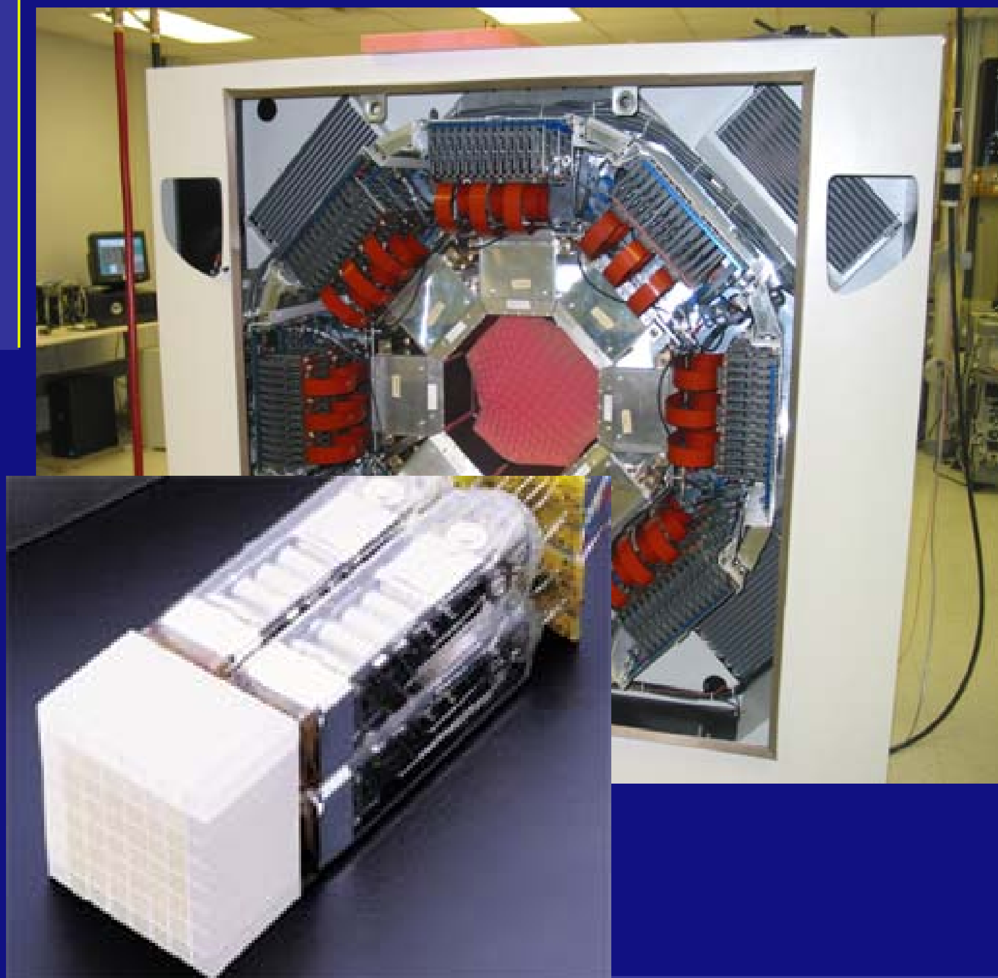


Positron Emission Tomography

Co-incidence detection



PET Camera



HRRT
8 blocks
9x13 detectors

8x8 crystals
59904 crystals in total

Fast data collection
4-D matrix of data:
X, Y, Z, time

PET animation

Loss of kinetic energy

Annihilation

2 Fotons, 511 KeV

Opposite direction

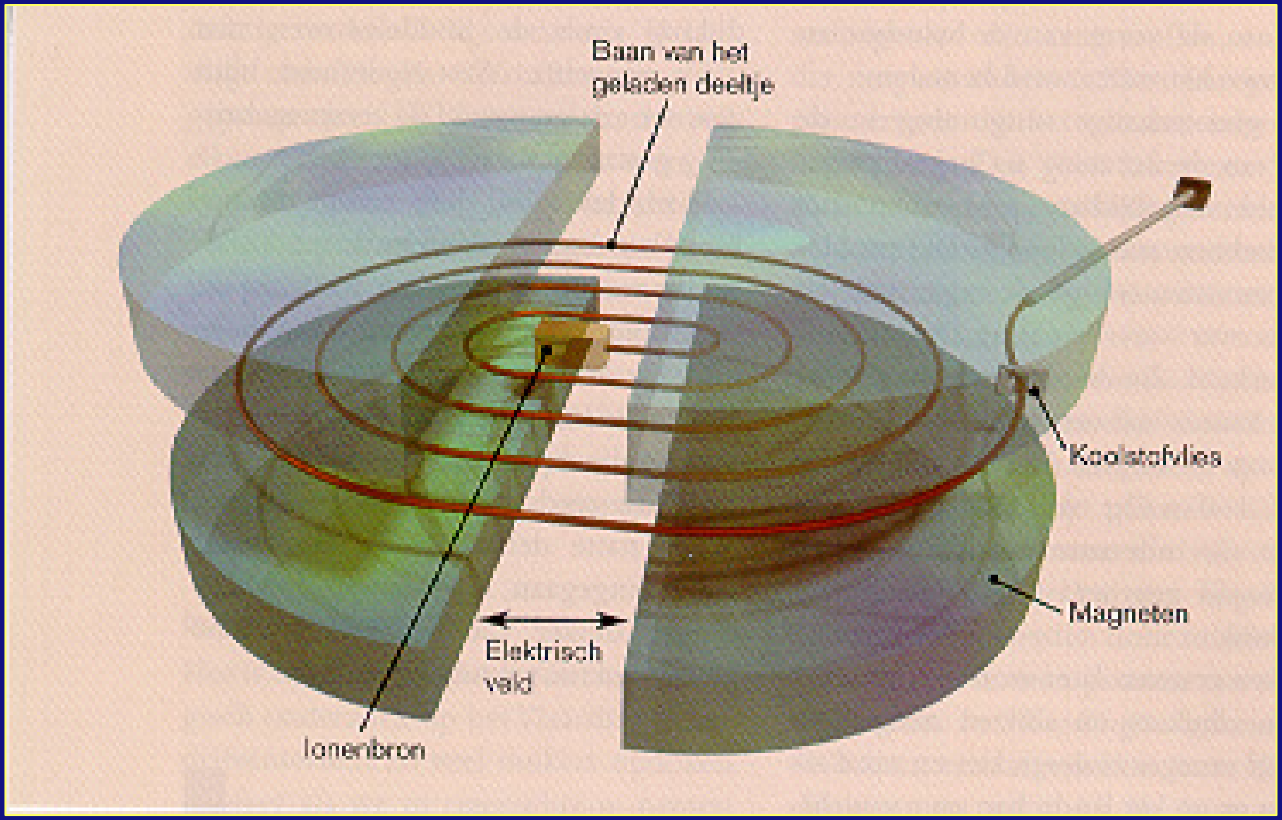
PET Isotopes

^{11}C : 20 min, β^+ (970 KeV), $^{14}N(p,\alpha)^{11}C$

^{18}F : 110 min, β^+ (635 KeV), $^{18}O(p,n)^{18}F$

^{89}Zr : 78 hrs, β^+ (900 KeV), $^{89}Y(p,n)^{89}Zr$

Cyclotron production



30.000 volt between D’s
300 circles, 600 accelerations of 30.000 volt = 18 MeV

Cyclotron animation

IBA 18/9

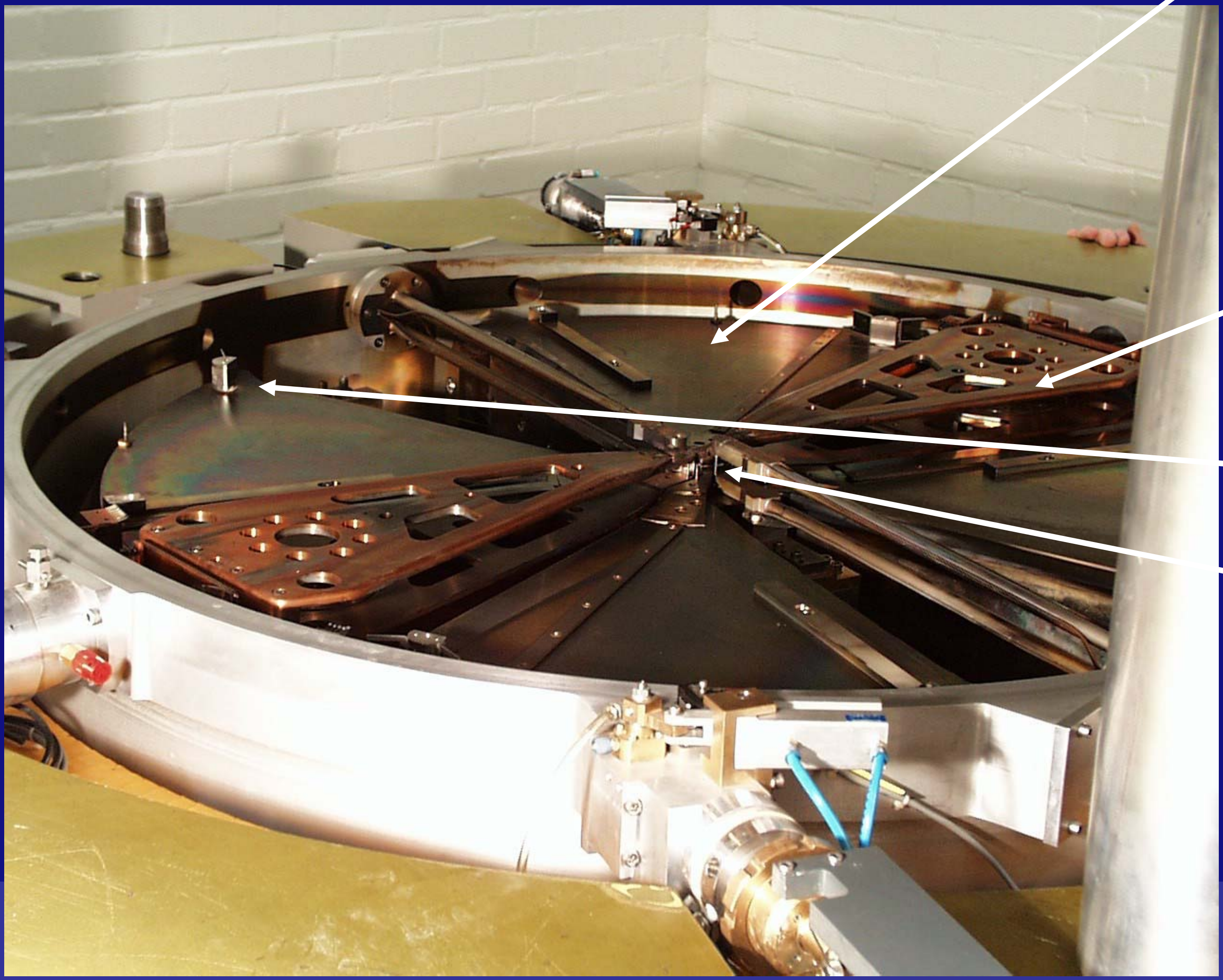
Cyclotron inside

magnet

E-field

stripper

Ion source



^{18}F Fluoride production

Nuclear reaction

$^{18}O(p,n)^{18}F$, obtained as Fluoride in water

Proton energy from 10 MeV

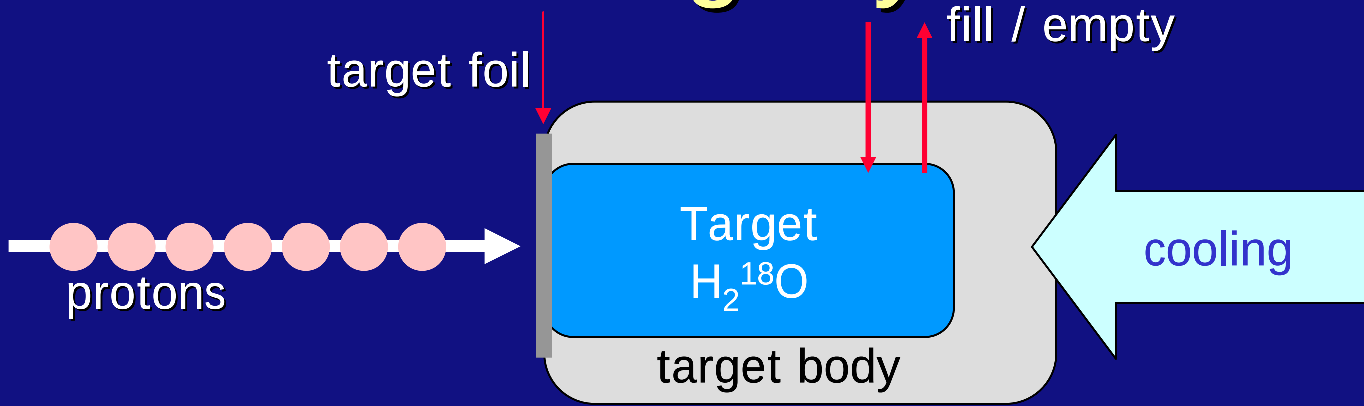
Side reaction

$^{16}O(p,\alpha)^{13}N$, obtained as nitrates in water

Work up

anion exchange column

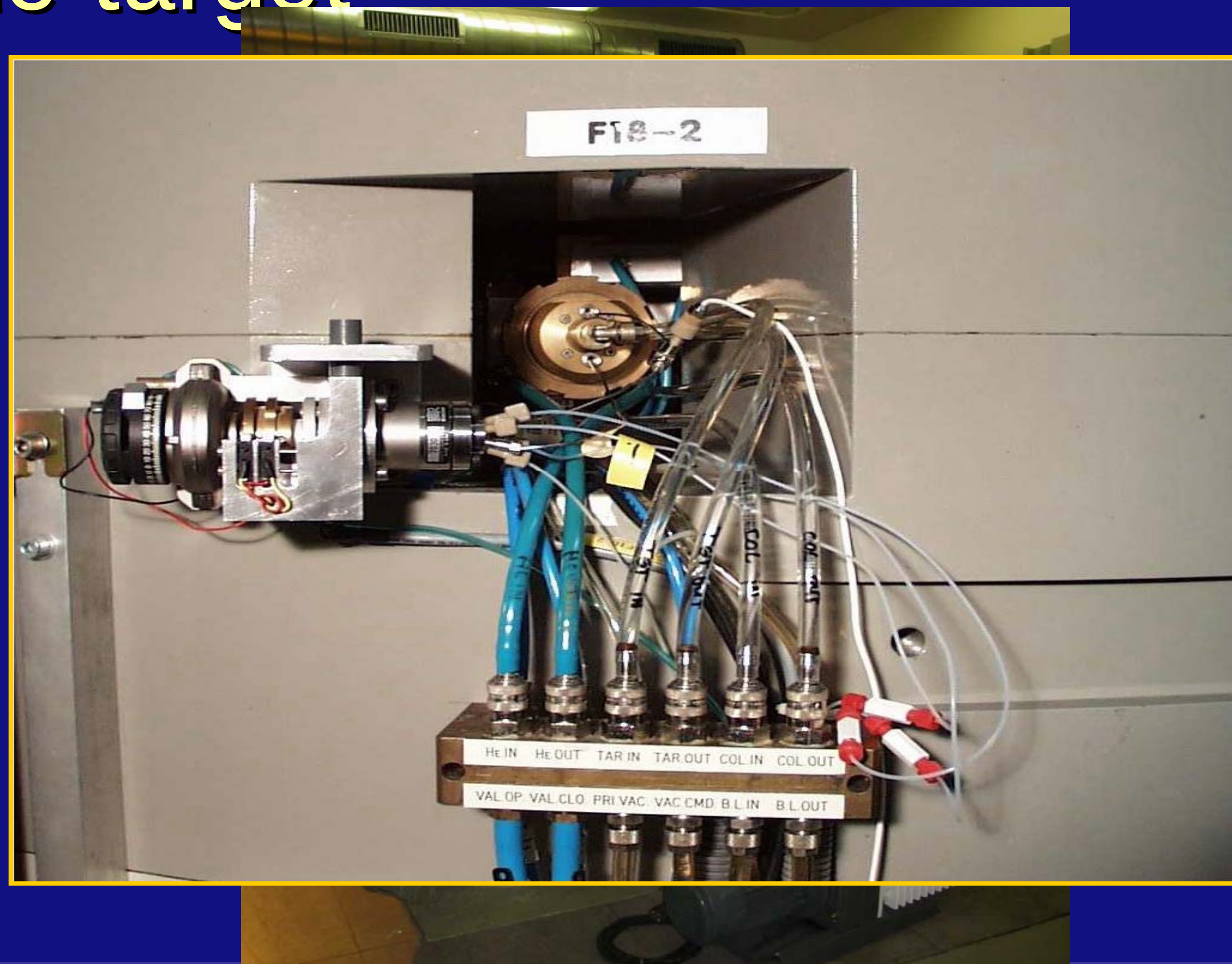
^{18}F Fluoride targetry



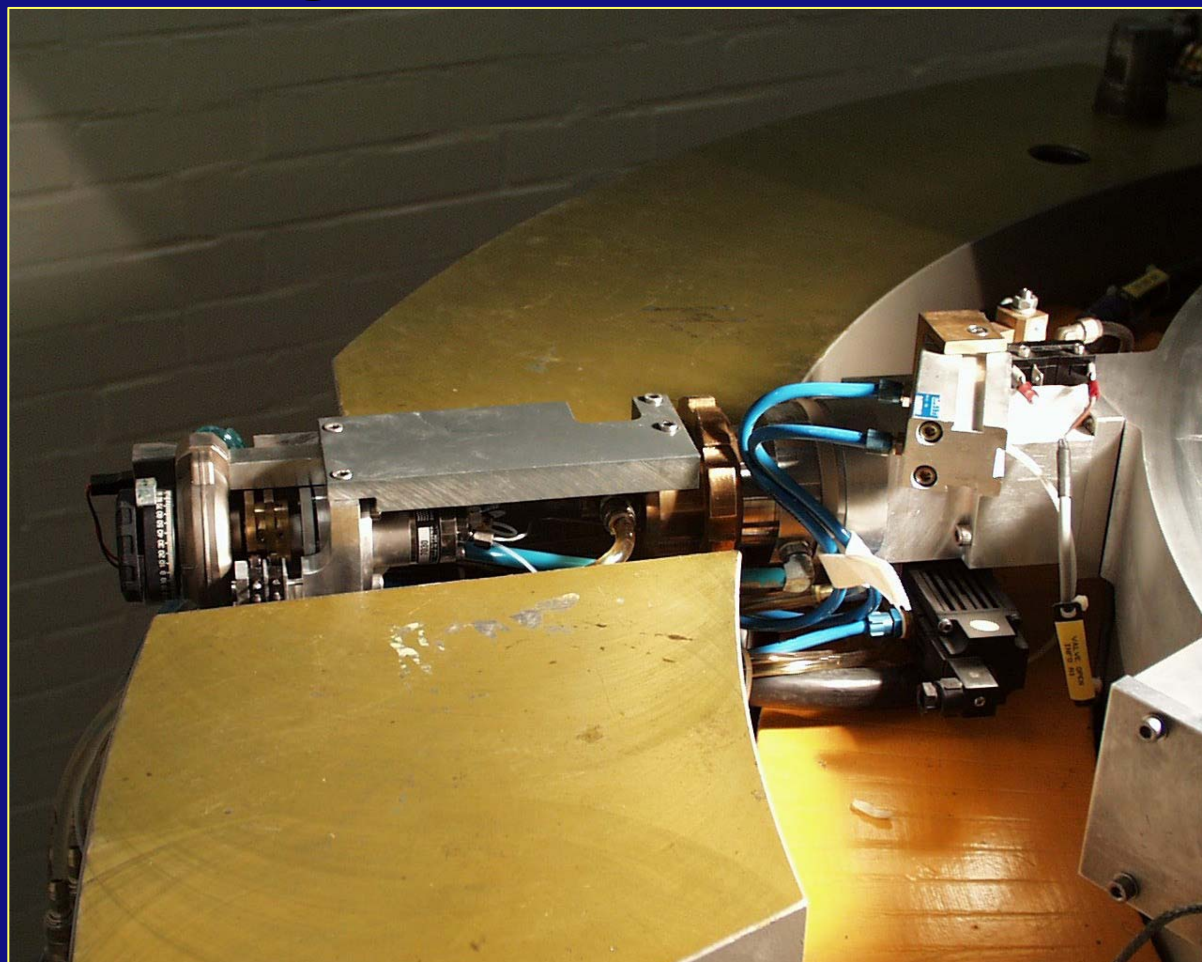
Important chracteristics for target body material:

- Heat capacity coefficient
  - (limiting factor for high beam currents: high pressure in target)
- Radionuclidic side products
- Chemical purity of [^{18}F]Fluoride from target

Fluoride target



Fluoride target



Fluoride target

^{18}F Fluorine production

Nuclear reaction

$^{20}Ne(d,\alpha)^{18}F$ or $^{18}O(p,n)^{18}F$

deuterons from 7 MeV

protons from 10 MeV

Side reaction

-

Work up

none

^{18}F Fluorine targets

Target material : Nickel or Monel

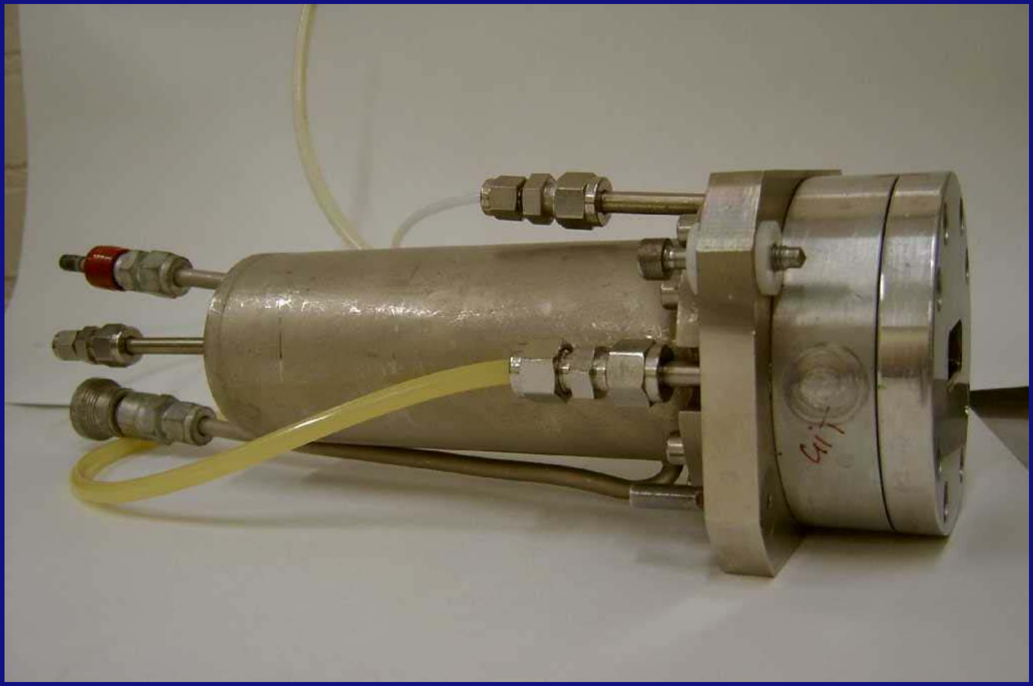
1st irradiation : ^{18}F fluorine deposit on target wall

Empty target, fill with Neon + 0.1-0.5% F_2

Irradiate

Electrophilic fluorination, or via intermediate

^{18}F Fluorine target Groningen



Installed in 1992

Design: Robert Dahl

Nickel / 153 ml

30 psi 1% F_2 / 100 psi Neon

^{11}C production

Nuclear reaction

$^{14}N(p,\alpha)^{11}C$, obtained as $^{11}CO_2$ in N_2

Proton energy from 10 MeV

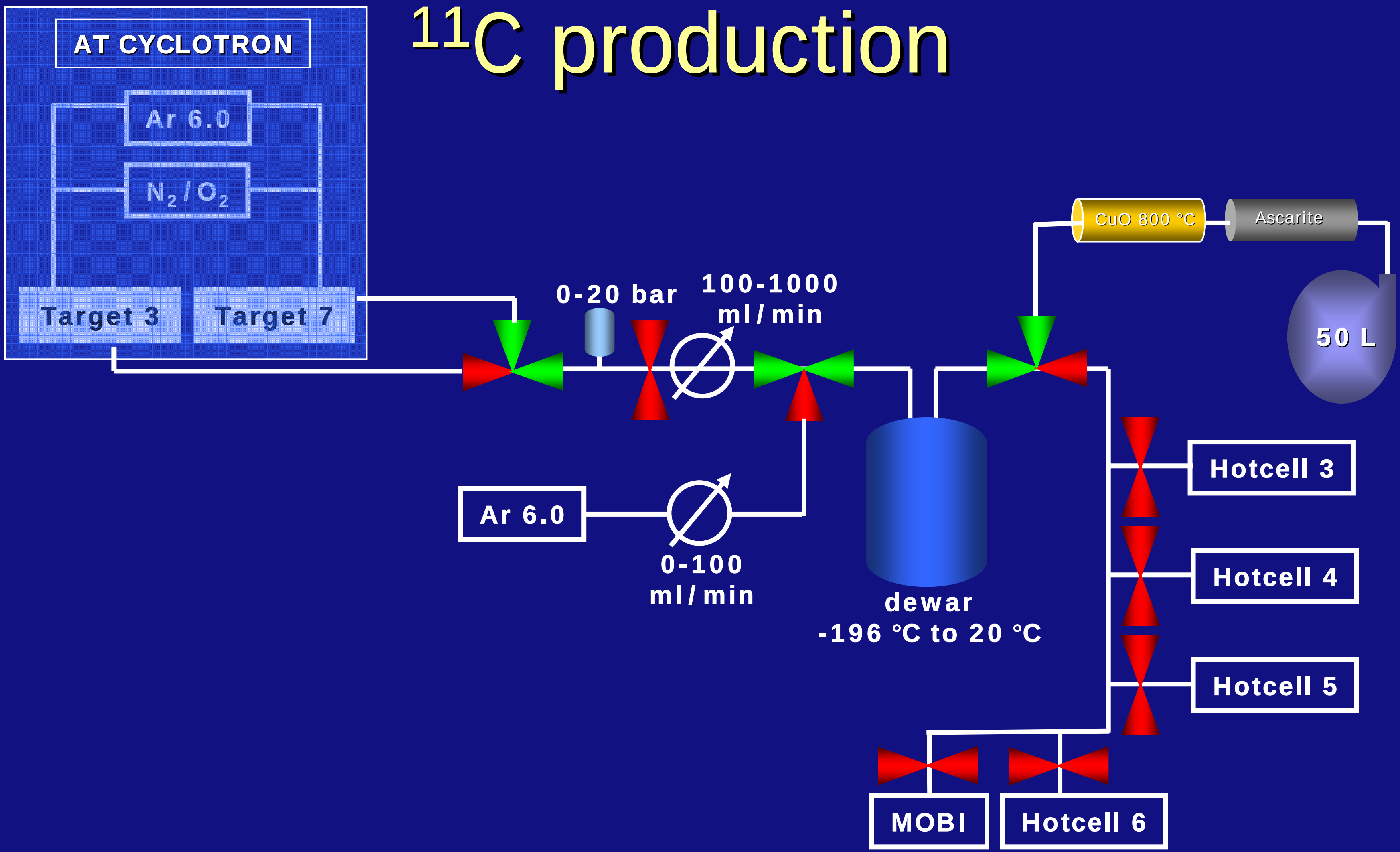
Side reaction

$^{14}N(p,pn)^{13}N$, obtained as $[^{13}N]N_2$

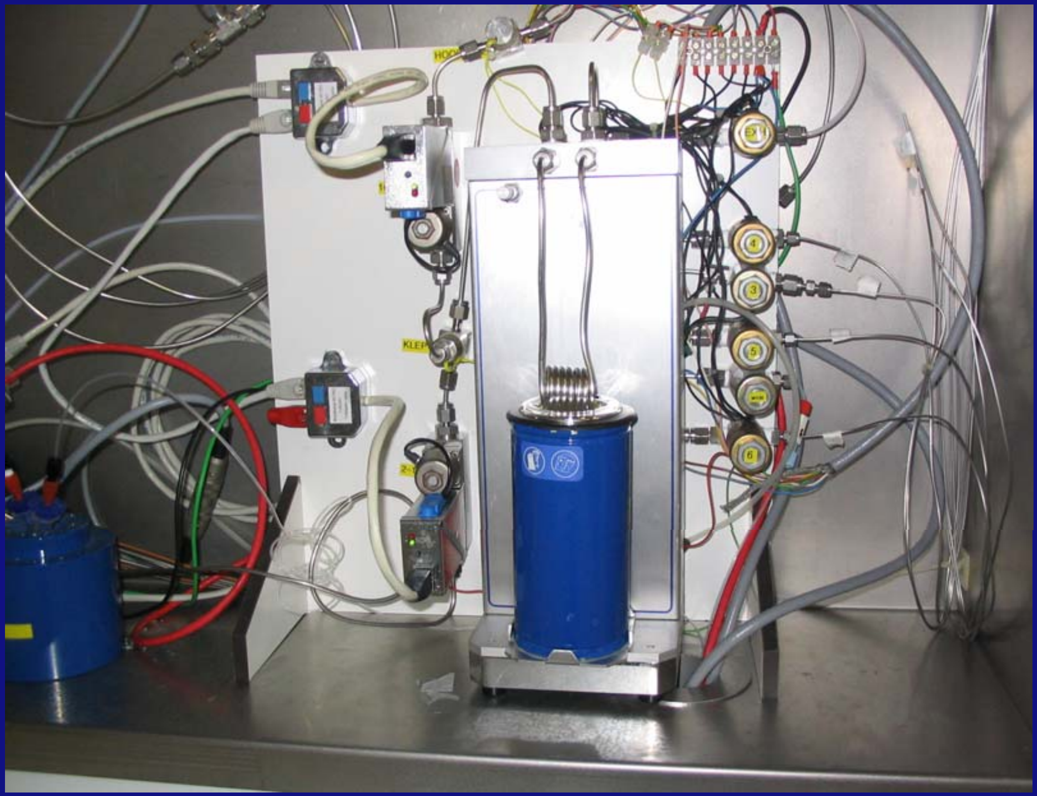
Work up

trap $[^{11}C]CO_2$ below -150 °C

^{11}C production



^{11}C production



^{89}Zr production

Nuclear reaction

^{89}Y (p,n) ^{89}Zr, obtained as ^{89}Zr in Yttrium disk

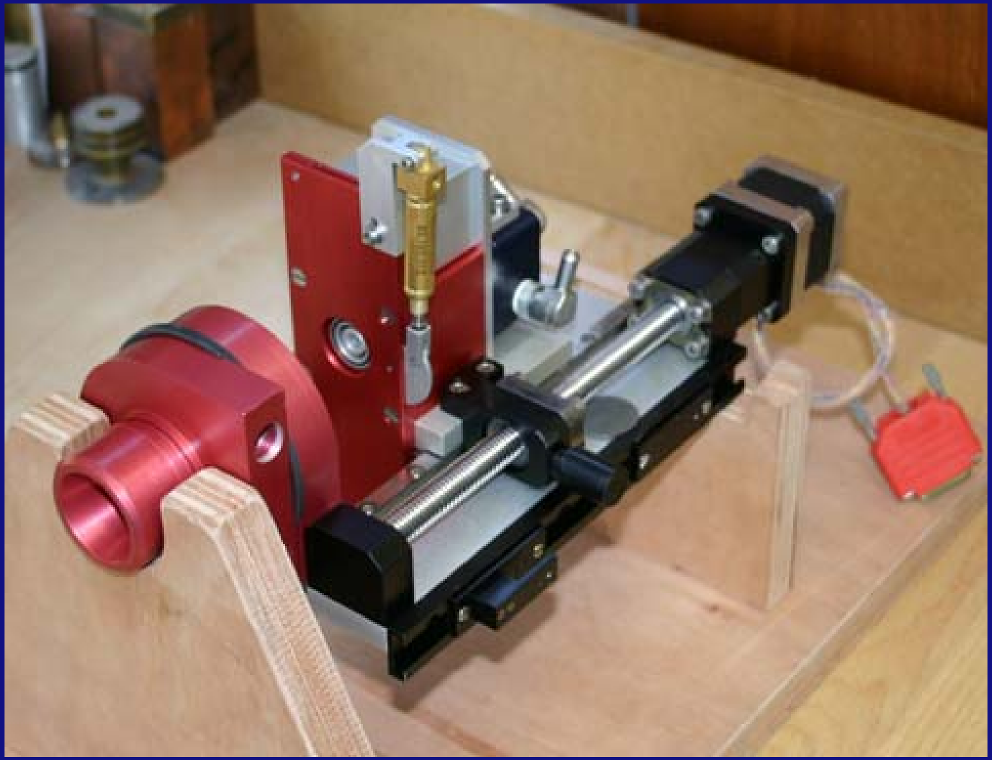
Proton energy 14 MeV optimal

Side reaction

Work up

dissolve in 6M HCl, affinity chromotography

^{89}Zr production



^{89}Zr production

^{89}Zr production

Further reading

Radiopharmaceuticals for Positron Emission Tomography
Ed G. Stöcklin and W.W. Pike
Kluwer Academic publishers, Dordrecht, 1993, isbn 0-7923-2340-8

Handbook of Radiopharmaceuticals : Radiochemistry and applications
Ed MJ Welch, CS Redvanly
Wiley, Sussex, 2003, isbn 0-471-49560-3