From Isotopes to Images: Applications in Nuclear Medicine

Part 1: Accelerator Production of Isotopes and Imaging Basics

Suzanne Lapi, PhD

Associate Professor of Radiology and Chemistry

Director, UAB Cyclotron Facility

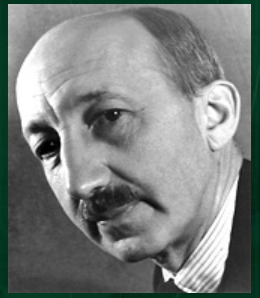
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Knowledge that will change your world

What are isotopes used for?
The tracer principle

- In Nuclear Medicine and many areas of basic science, radioactive atoms are used as tracers.
- Tracer behaves in a similar way to the components of the system to be probed.
- Tracer does not alter the system in any measurable fashion.
- Tracer concentration can be measured.

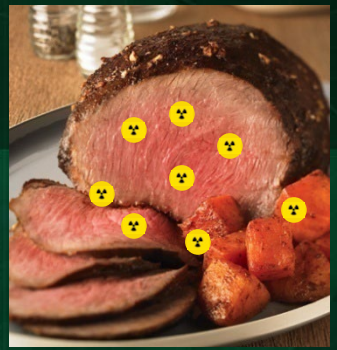
The first tracer experiment?



- George de Hevesy was a pioneer in radiochemistry
- While in Manchester in the early 1910's working with Rutherford, he suspected his landlady was serving recycled food

Sunday night roast

Radium



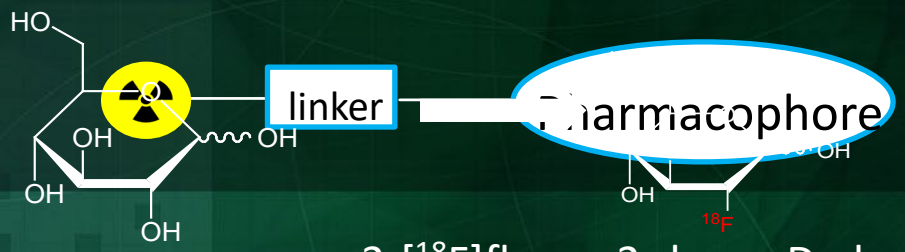
Wednesday hash

Basics of Nuclear Medicine

- Nuclear medicine encompasses most of the medical uses of radioactive substances
  - diagnostic tests
  - imaging studies
  - therapy for certain diseases

Radiopharmaceuticals

- A **radiopharmaceutical** is a drug labeled with a radionuclide to image a biological process or to deliver therapy to a specific disease site
  - the overall chemical structure determines biological properties
  - the radionuclide determines imaging or therapeutic properties

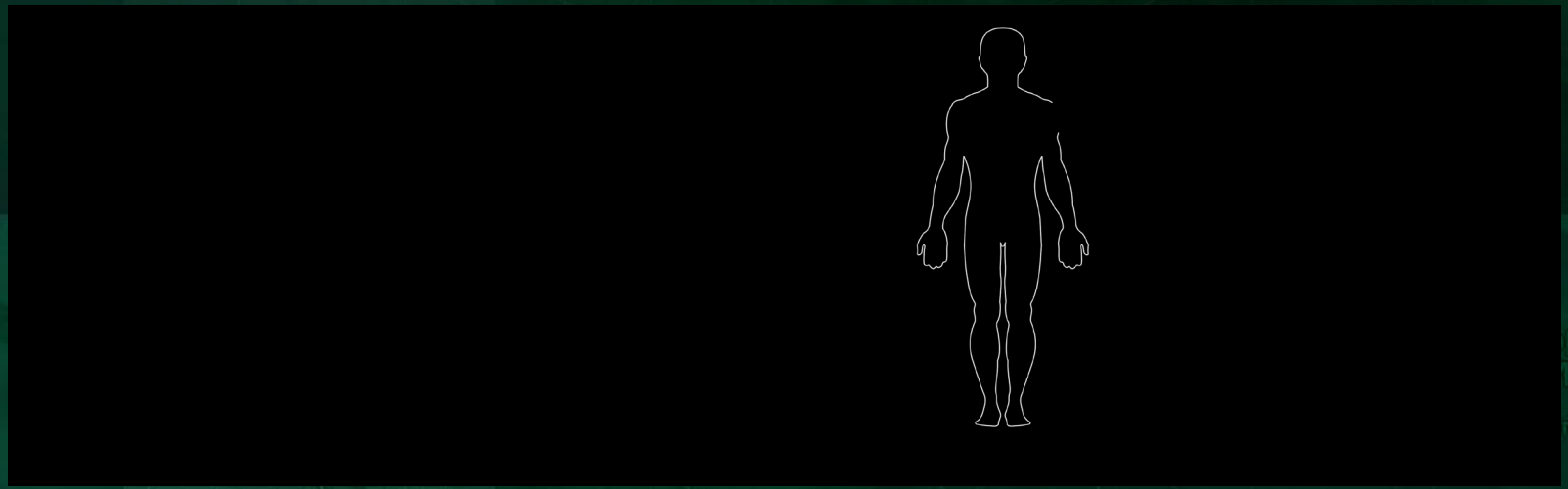


D-glucose

2-[^{18}F]fluoro-2-deoxy-D-glucose
(FDG)

Radiopharmaceuticals

- Radiopharmaceutical: Targeting compound labeled with a radionuclide for imaging or therapy.
- Structure of the compound determines biological properties (targeting, clearance, receptor interactions).
- Radioactive label determine the imaging or therapeutic properties.



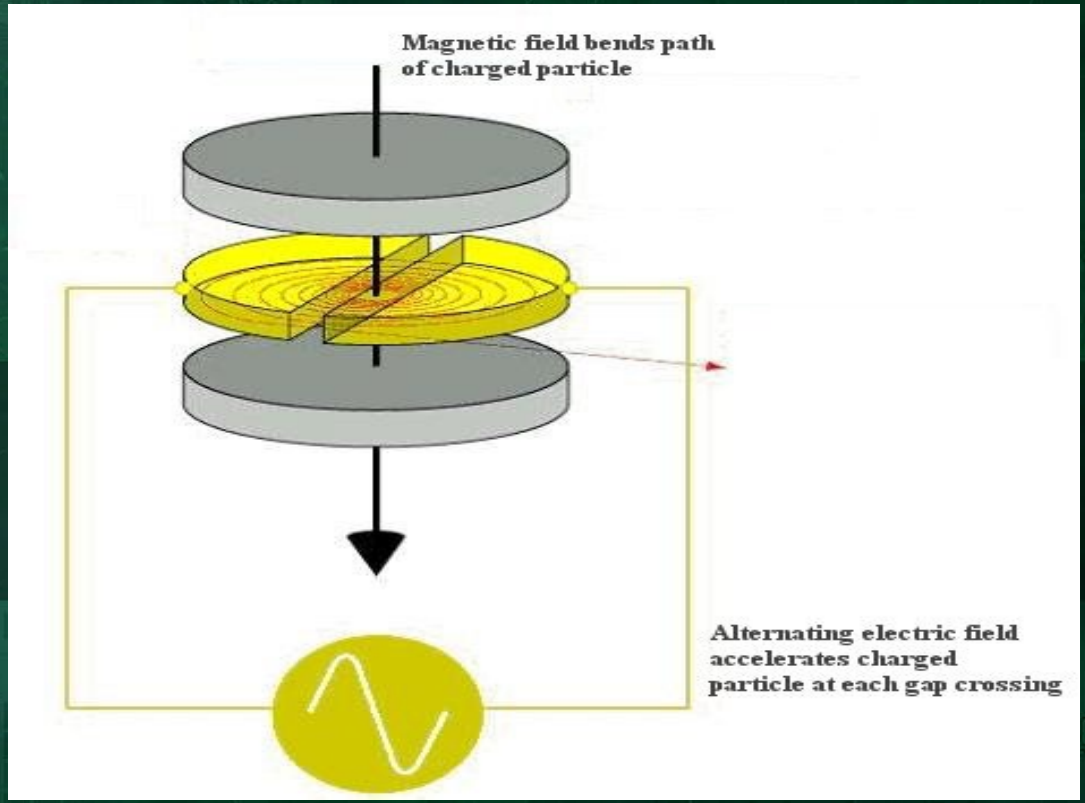
Accelerators for Isotope Production

- Can be protons (most common), ^{2}H, ^{3}He, ^{4}He or heavier ions
- Some machines are single particle, other can accelerate 2 or more
- Typically accelerated by electric fields

Cyclotron

- Cyclic or repetitive application of force
- Allows small force to be used many times
- Small device
- High power

Overview

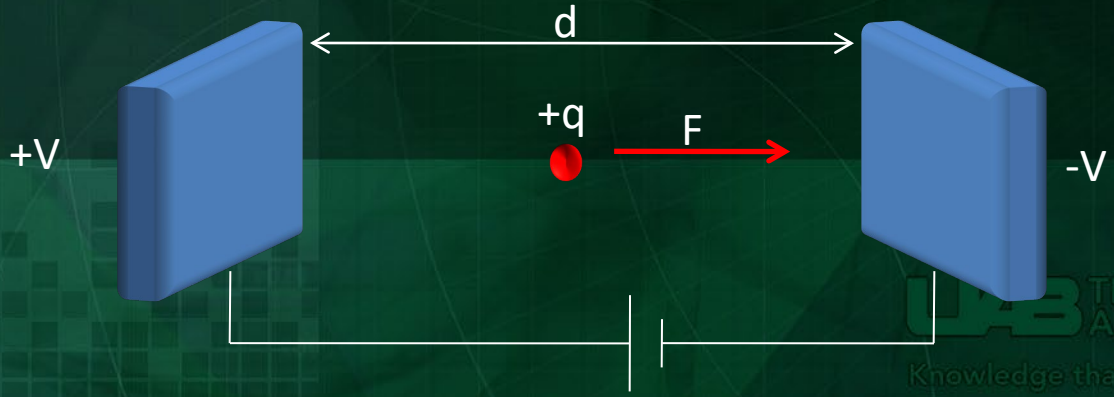


Essential Cyclotron Criteria

- Source of ions
- Accelerating force
- Constraining force
- Vacuum
- Phase stability

Acceleration of charged particles

The acceleration of a charged particle in an electric field, created in the space between two plates by connecting a voltage source between them.



$E = V/d$

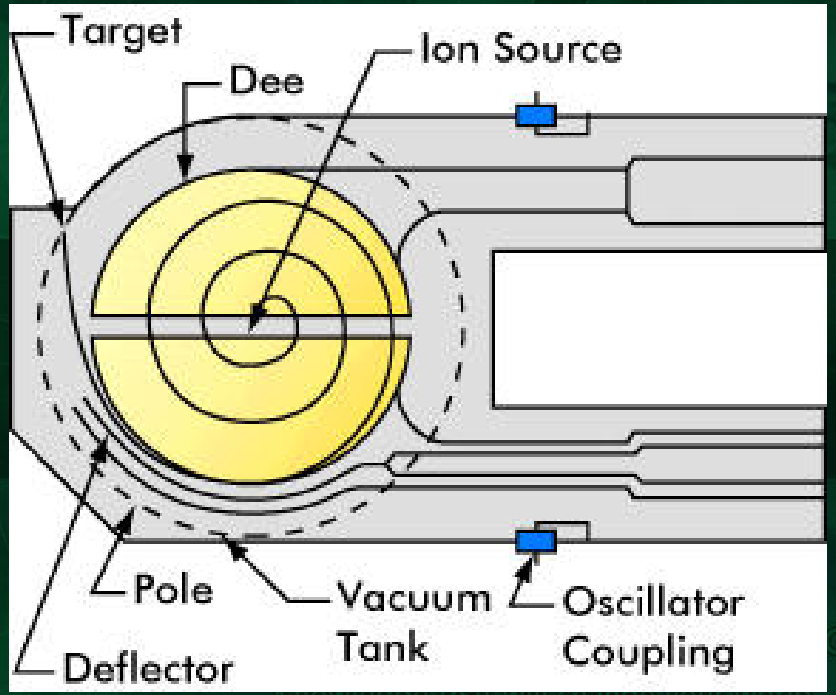
$F = qE$

Vacuum

- Avoid molecular collisions
  - Ion losses from neutralization, trajectory changes
  - Unnecessary radioactivation of components
- Oil diffusion pumps – backing pump
- Turbopumps –backing pump
- Cryopumps – no backing pump
- Mechanical (roughing/backing) pump

Dees

- Acceleration at gap due to alternating electric field
- No field inside conductor

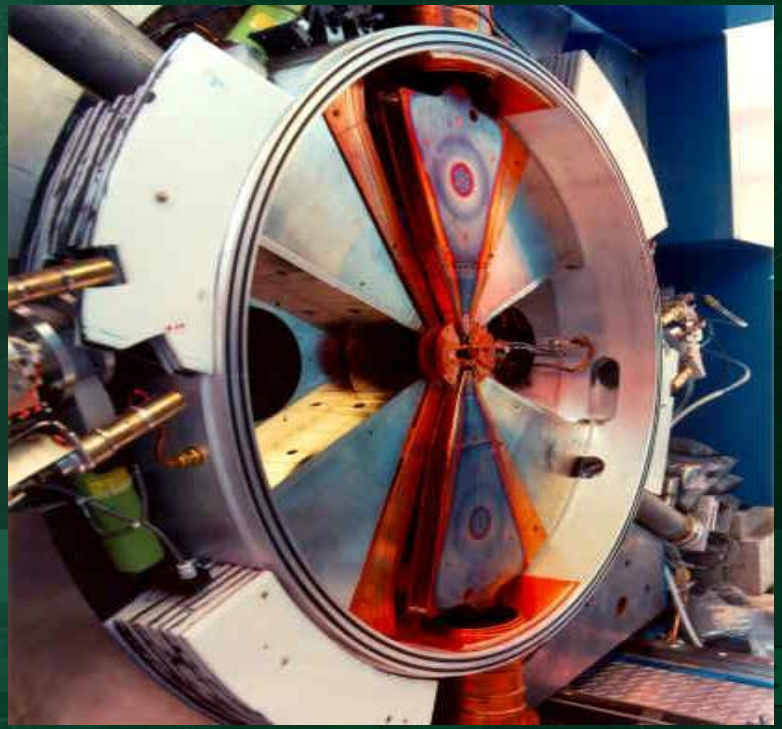


Accelerating Force

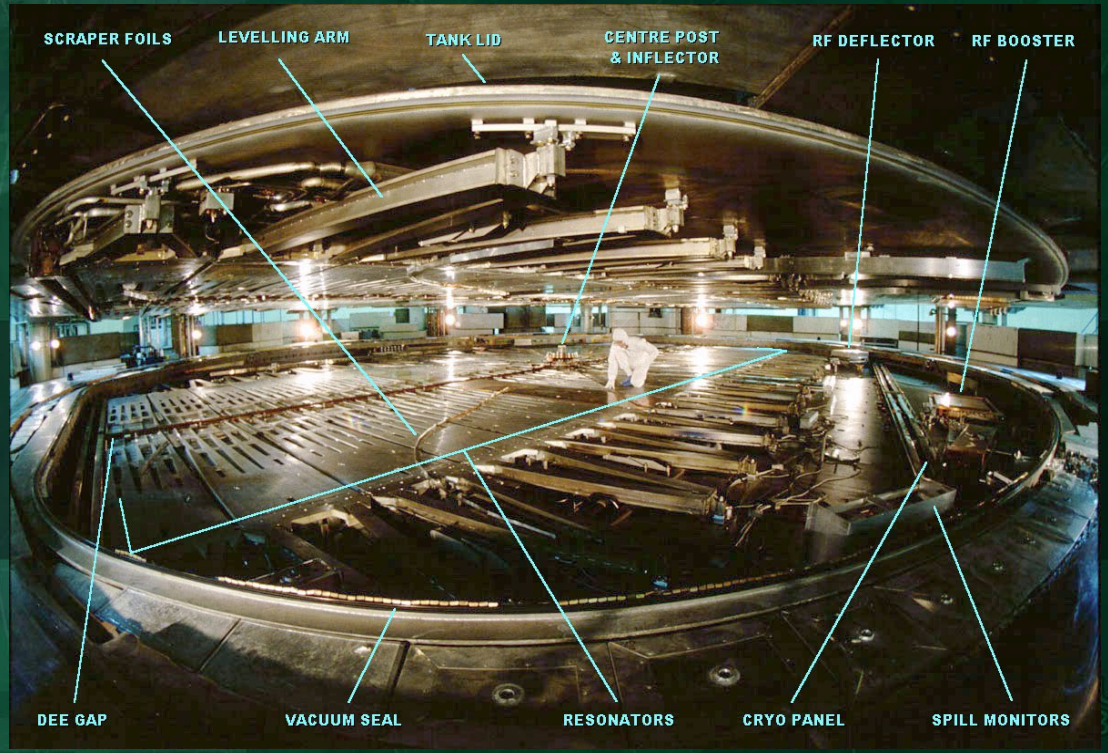
- Electric potential
- Applied repetitively
  - Radio frequency (10's of megahertz)
  - High voltage (10's of kilovolts)

UAB TR24 Dees

TRIUMF TR13 Dees



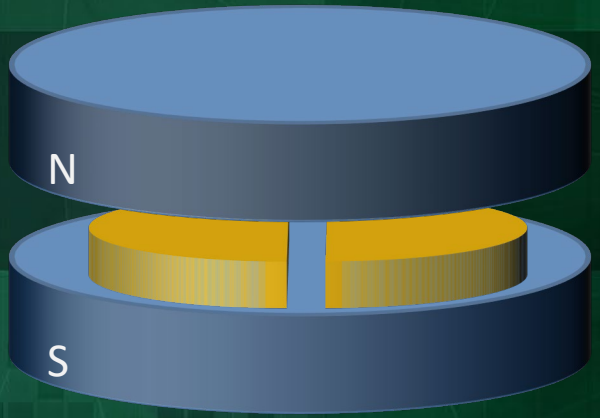
TRIUMF 500 MeV cyclotron

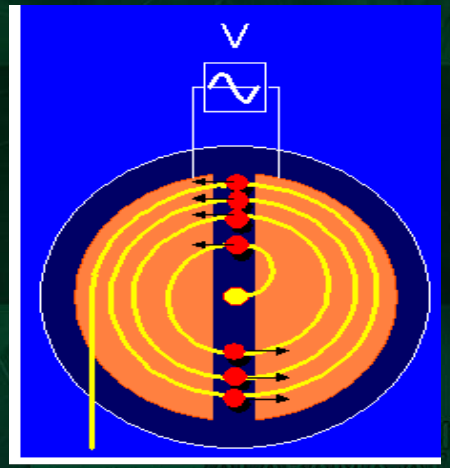


UCSF GE PETtrace

The Cyclotron Principle

An alternating voltage with a frequency equal to the orbital frequency of the particles is applied between the dees.





Particle motion

- Circular motion F = Mv^2/r
- Magnetic force F = qvB
- $v=qBr/M$
- Time to traverse a circle $t = 2pr/v$
- $t = 2pM/qB$ (period)
- $f = qB/2pM$ (cyclotron frequency!!)

Phase Stability

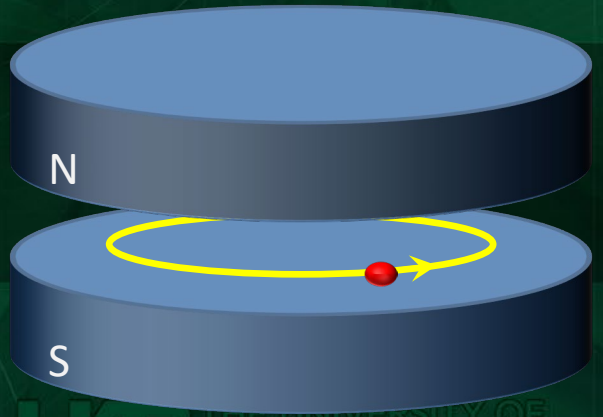
- Isochronous cyclotron
- Particle arrives at the accelerating gap at the same point in the voltage oscillation.
- Time to traverse path between applications of accelerating voltage must be constant

Magnet

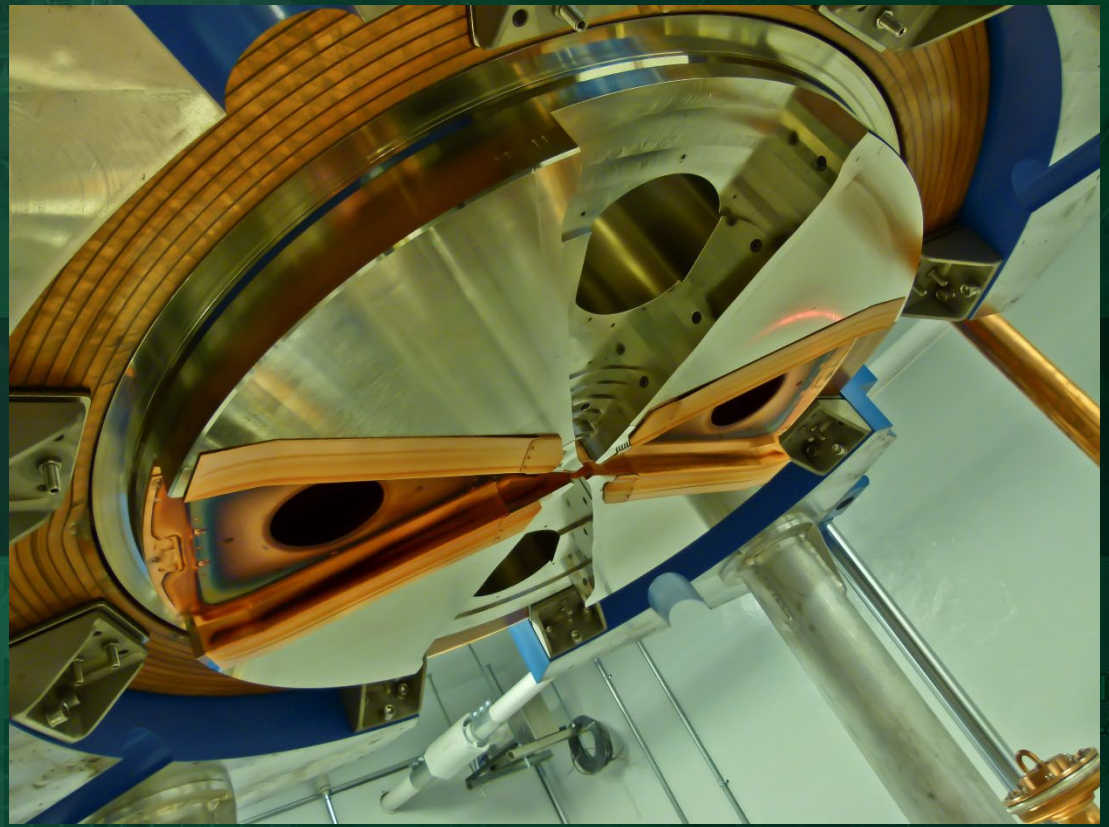
- Constrains particle to circular orbit
- Increasing momentum, increasing radius
- Increasing radius, increasing path length
- Synchronous
- Magnet tricks for
  relativistic mass increase

$$M=M_o/(1-v^2/c^2)^{1/2}$$

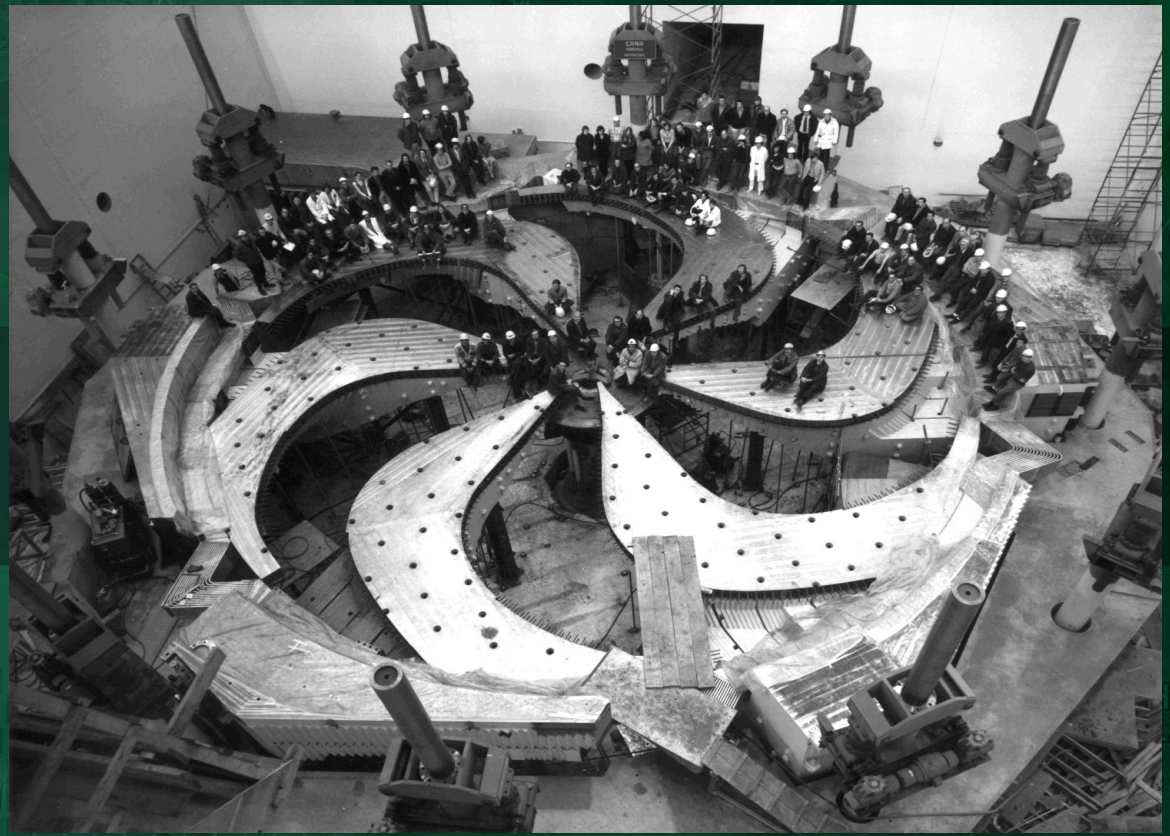
- Focusing:
  hills and valleys



UAB TR24 Magnet



TRIUMF 500 MeV cyclotron



Extraction

- Negative ions : carbon foil ~200 ug/cm^2
  - >99% efficiency
- Positive ions : deflector
  - Electric/magnetic perturbation
  - 20-30% efficiency (70%)
  - Or internal targets

Extraction

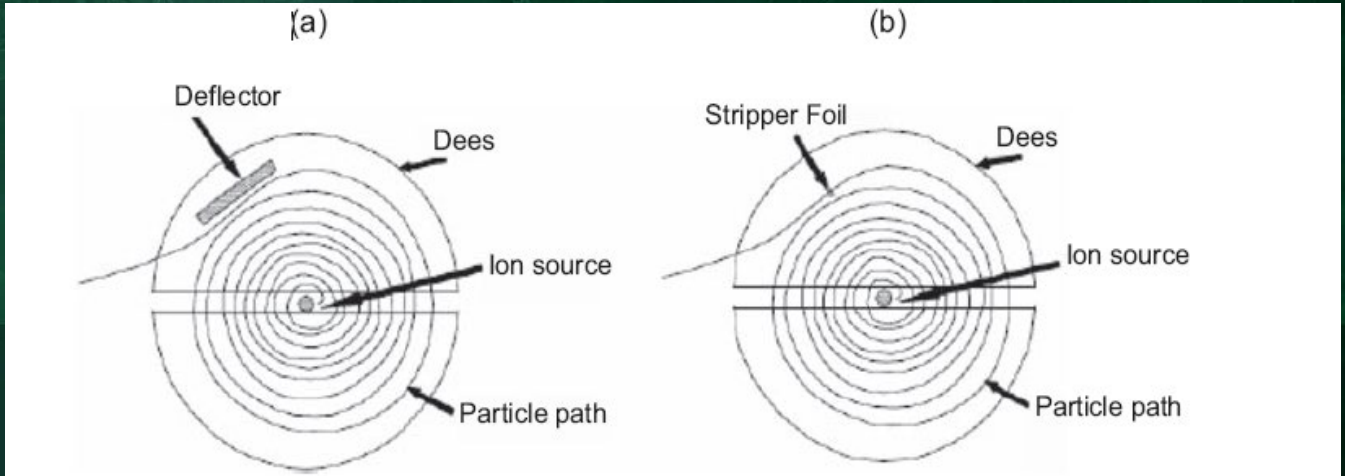
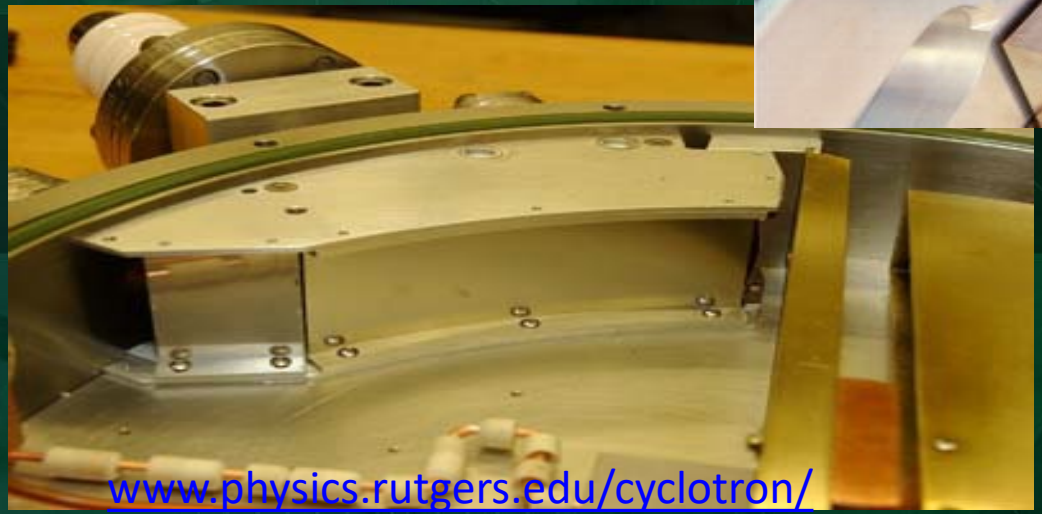


FIG. 3.7. Extraction process in modern cyclotrons using either (a) a deflector for positive ions or (b) a stripper foil for a negative ion source.

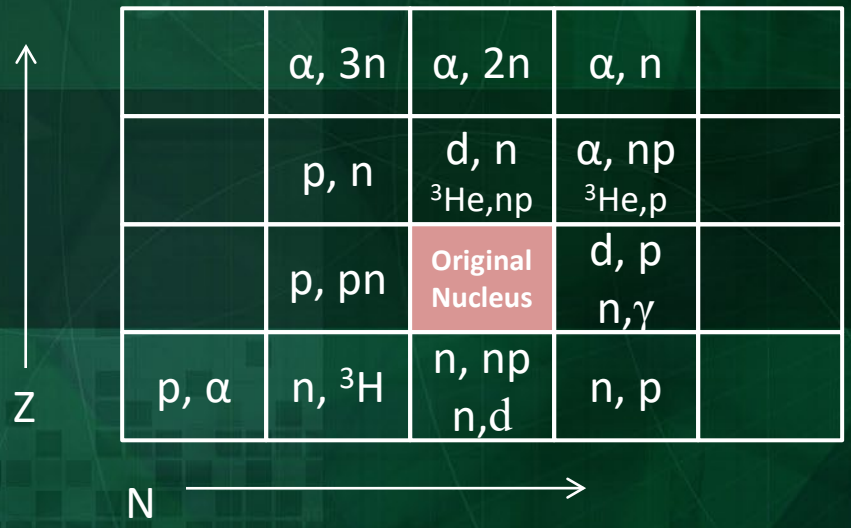
http://www-pub.iaea.org/MTCD/publications/PDF/trs465_web.pdf



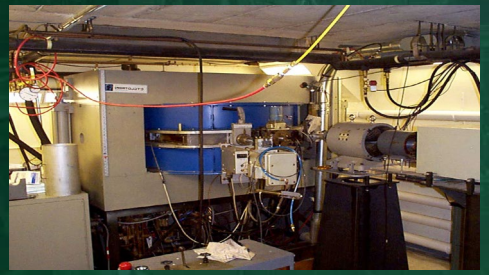
www.physics.rutgers.edu/cyclotron/

Reaction Channels

Many possible outcomes from the interaction of an incoming particle with a target nucleus:
- reaction channels.



Thin Targets - Reaction Rates



Assumptions:

1. There is no appreciable decay of the product during the irradiation period.
2. The number of target atoms is not greatly depleted during the course of irradiation (no burn up).
3. The cross section is constant.

Thin Targets - Reaction Rates

$R = I x \sigma N_{tgt}$

Where

R = reaction rate

σ = cross-section (cm^2)

I = flux = incident particles per second

x = target thickness (cm)

N_{tgt} = number of target nuclei/cm^3

Thick Targets - Reaction Rates

The particle beam can be significantly attenuated:

1. Flux of particles varies at different depths in the target.
2. Neutrons – less interaction with matters, most targets are "thin" unless very high σ.
3. Protons and other charged particles interact with matter and thus targets need to be considered "thick".

Thick Targets - Reaction Rates

It is often helpful to think of a thick target as a series of thin targets.

Each may have a different

- flux
- incoming particle energy
- cross section.

Charged Particle Excitation Functions

- All charged particle reactions have a threshold (for neutrons this can be zero).
- Low energies – low σ
- Usually σ increases to a maxima and then decrease due to competing reaction channels.
- Usually much lower σ than for neutron reactions.

Charged Particle Excitation Functions

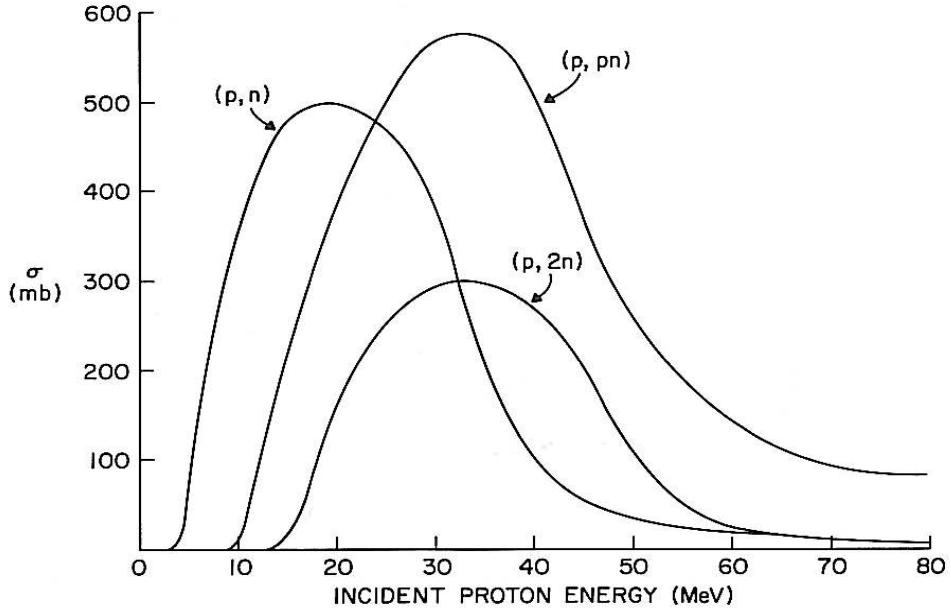


Figure 4.4. Excitation functions for several common proton-induced reactions on the same low-Z target nuclide.

Production of Radioactive Nuclei

- Often we are looking at reactions to produce radioactive nuclei.
- Rate of increase of radioactive nuclei:

$$\frac{dN}{dt} = R - \lambda N$$

Production Rate Decay rate

Rate of increase = production – decay

$$\frac{dN}{dt} = \sigma\Phi N_{tgt} - \lambda N$$

Rearranging gives:

$$\frac{dN}{\sigma\Phi N_{tgt} - \lambda N} = dt$$

Take the integral of both sides:

$$\int \frac{dN}{\sigma\Phi N_{tgt} - \lambda N} = \int dt$$

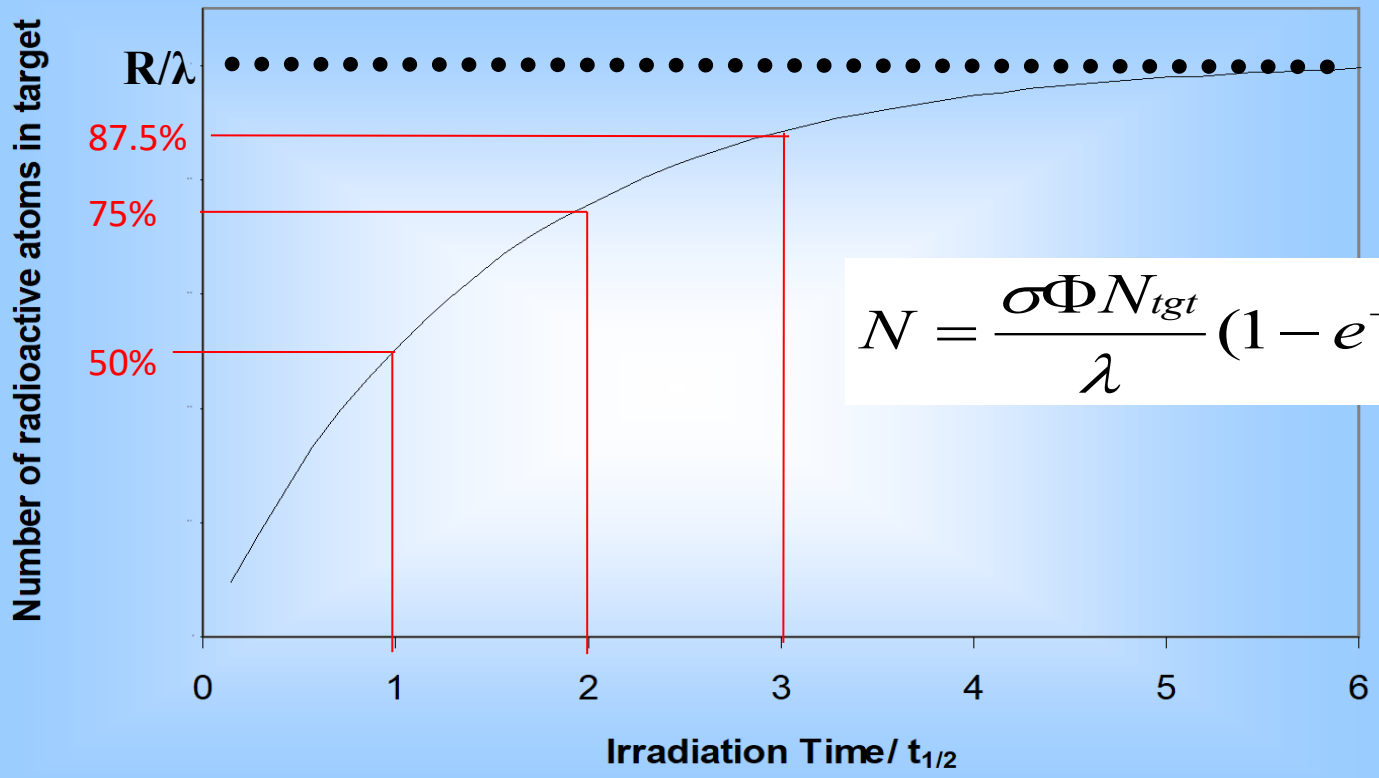
This is a standard form integral of the type

$$\int \frac{dx}{a+bx} = \frac{1}{b}\ln(a+bx)$$

Solving and simplification yields :

$$N = \frac{\sigma\Phi N_{tgt}}{\lambda}(1 - e^{-\lambda t})$$

Saturation Effects



$$N = \frac{\sigma \Phi N_{tgt}}{\lambda}(1 - e^{-\lambda t})$$

Accelerator Targets

1. Gases:

$^{14}N(d,n)^{15}O$	($^{14}N_2$)
$^{14}N(p,\alpha)^{11}C$	($^{14}N_2$)

2. Liquids:

$^{16}O(p, \alpha)^{13}N$	($H_2{}^{16}O$)
$^{18}O(p,n)^{18}F$	(enriched $H_2{}^{18}O$)

3. Solids:

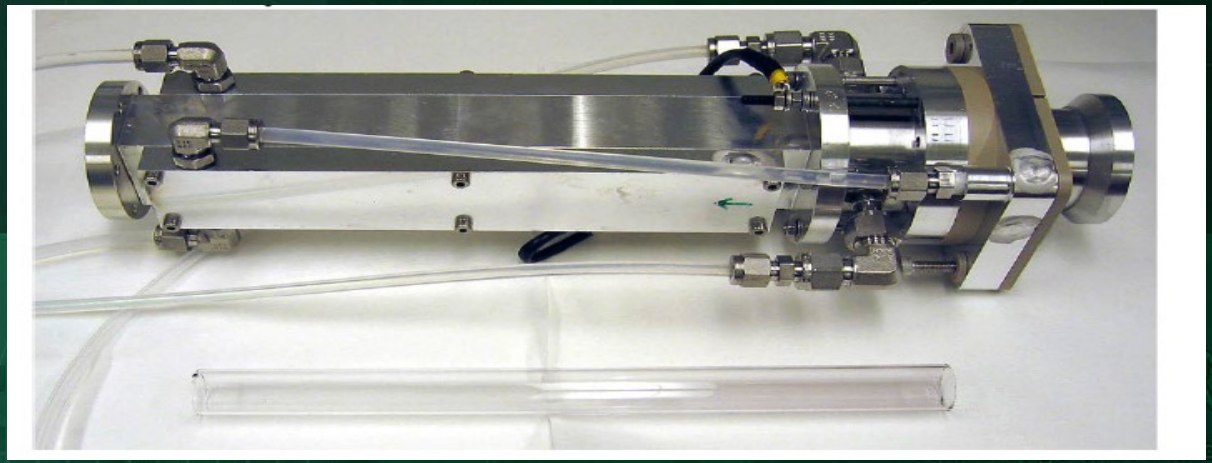
$^{64}Ni(p,n)\ ^{64}Cu$	(enriched metallic ^{64}Ni)
$^{89}Y(p,n)^{89}Zr$	(metallic ^{89}Y)
$^{68}Zn(p,2n)^{67}Ga$	(enriched metallic ^{68}Zn)

Accelerator Targets

- Target Body Materials:
  - Thermally conducting
  - High melting point
  - Low amount of “activation”
  - Easy to machine

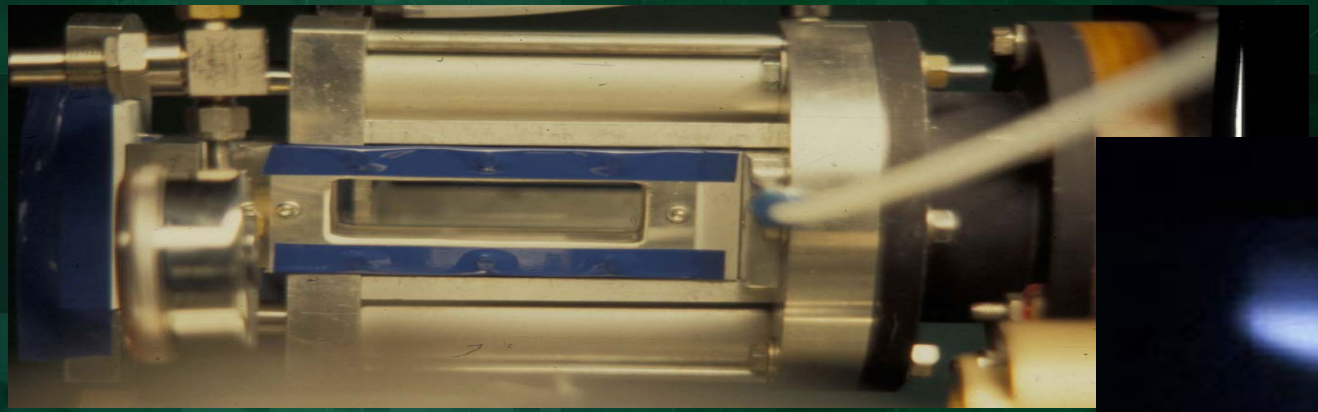
Gas Targets

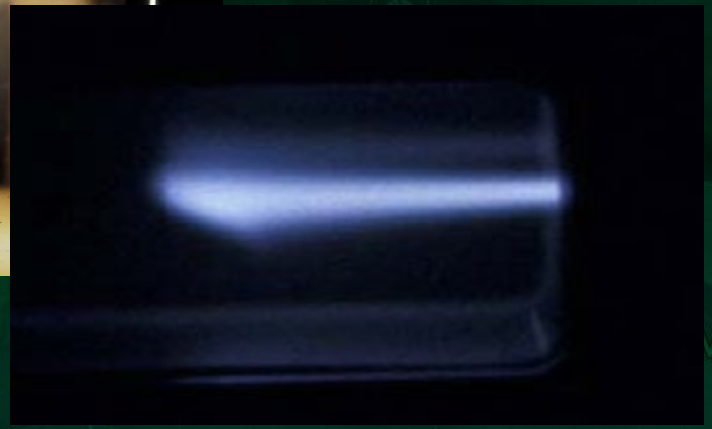
- Most common $^{14}N(p,\alpha)^{11}C$ $[t_{1/2} = 20\ min]$
- Cooling is important
- Transfer to chemistry area



Gas Targets

- Heat effects:
  - Gas expands when heated
  - Wall interactions





Gas Targets

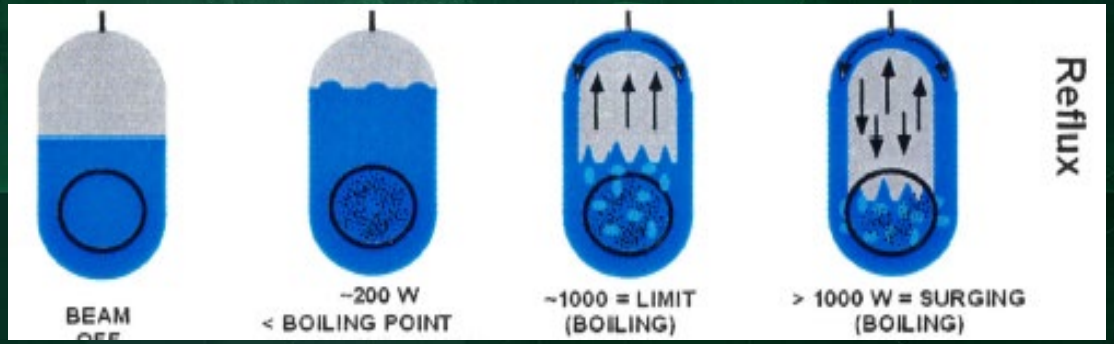
- In target chemistry (“Hot-atom chemistry”)
- Daughter nucleus is formed with some energy
- Can make $^{11}CO_2$ or ^{11}CO by addition of O_2 to the target gas
- Can make $^{11}CH_4$ by addition of H_2 to the target gas

Liquid Targets

- Most common $^{18}O(p,n)^{18}F$ [$t_{1/2}$ = 110 min]
- For clinical [^{18}F]FDG production [water target]
- Usually He on the front and water cooled on the back
- Can be “gridded”

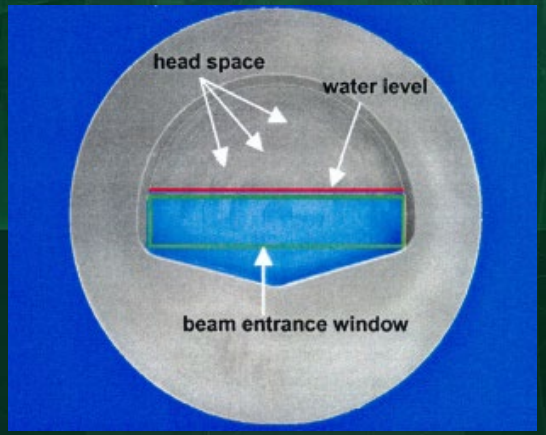
Liquid Targets

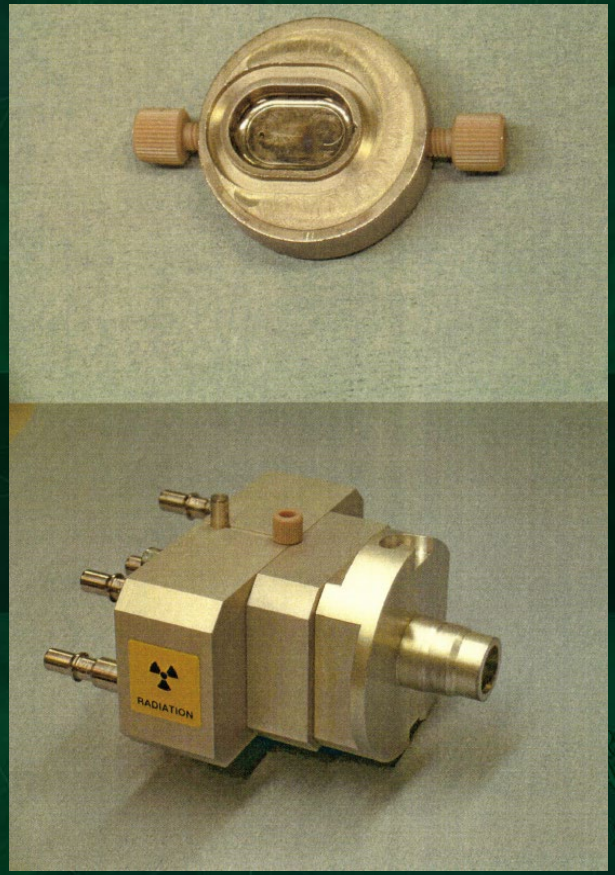
- Heat effects: the water boils!



- Chemistry: F^- is very reactive

Liquid Targets





Solid Targets

- Less common
- Often use enriched materials ($$$)
- Heating issues
- Wide variety of isotopes possible
- Usually more chemistry required for the separation (begin with dissolution or distillation)

Solid Targets

Radionuclide	Half-life	Decay	Production Reaction	Medical Use
Copper-64	12.7 h	EC/β^-/β^+	Cyclotron	Imaging/Therapy
Copper-67	2.58 d	β^- (γ, 184.6 keV)	High Energy Accelerator	Therapy
Gallium-67	3.26 d	EC (γ, 184.6 keV)	Cyclotron	Imaging
Strontium-82	25.4 d	EC → ^{82}Rb(β^+)	High Energy Accelerator	Generator for ^{82}Rb (Imaging)
Yttrium-86	14.7 h	EC/β^+	Cyclotron	Imaging
Zirconium-89	3.27 d	EC/β^+	Cyclotron	Imaging
Indium-111	2.80 d	EC (γ, 171.3 keV)	Cyclotron	Imaging
Thallium-201	3.04 d	EC (γ,167.4 keV)	Cyclotron	Imaging
Actinium-225	10.0 d	α	High Energy Accelerator	Therapy

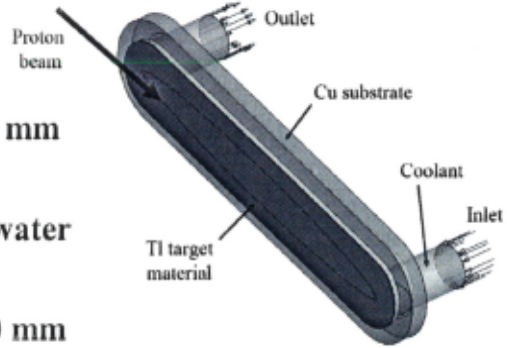
Solid Targets

^{201}Tl Radionuclide Production Target

- ^{203}Tl enriched solid target (melting point : 304 °C)
- ^{203}Tl(p,3n)^{201}Pb($\rightarrow^{201}$Tl) reaction
- Conditions of proton beam : 28 MeV, 200 μA

Target and Cooling System

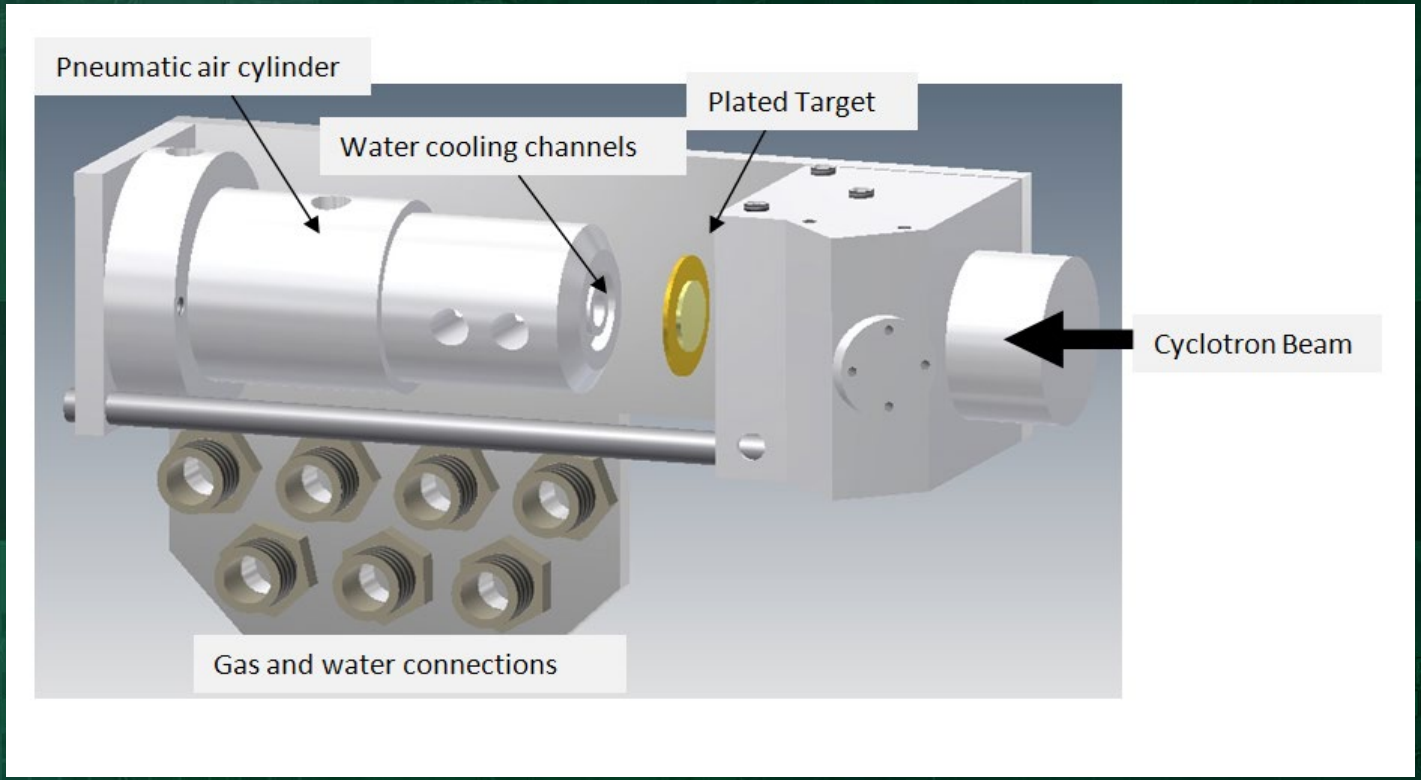
- Electroplated Tl (80 mg/cm^2) on Cu substrate (500 μm)
- Aperture size of beam collimator : 10 mm
- Incident angle : 6°
- Cross sectional dimension of cooling water : 1.5 mm × 12 mm
- Inner diameter of inlet and outlet : 60 mm



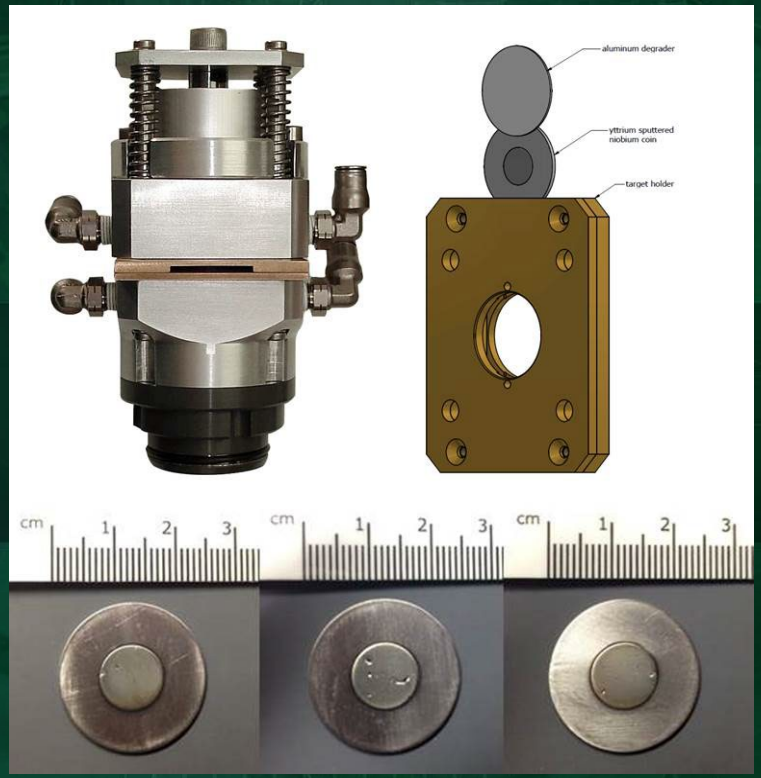
KIRAMS

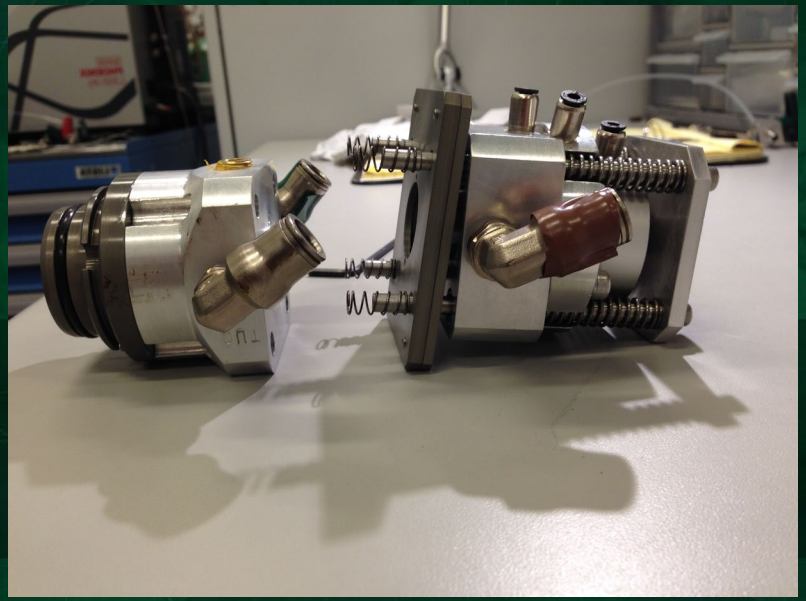
Seoul National University
Dept. of Nuclear Engineering

Solid Targets



Solid Targets





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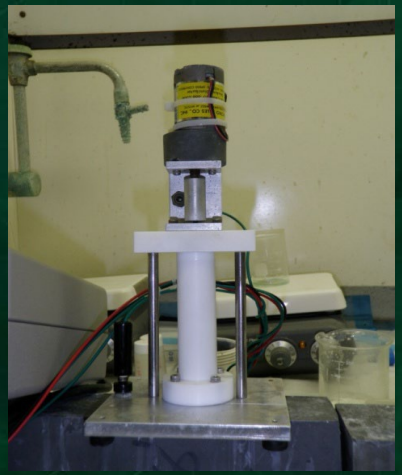
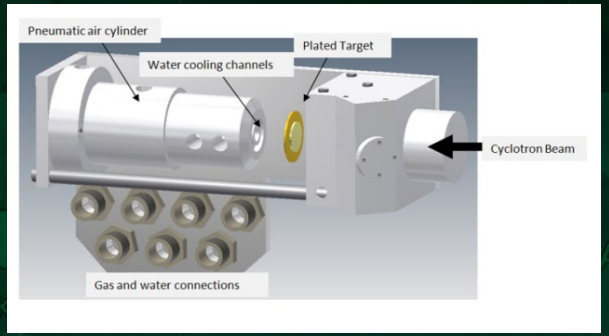
Knowledge that will change your world

Copper-64

64Zn STABLE 48.63%	65Zn 243.66 D ε: 100.00%	66Zn STABLE 27.90%
63Cu STABLE 69.17%	64Cu 12.701 H ε: 61.50% β-: 38.50%	65Cu STABLE 30.83%
62Ni STABLE 3.634%	63Ni 100.1 Y β-: 100.00%	64Ni STABLE 0.926%



- $T_{1/2}$ 12.7 hours
- β^+ (17.8%) β^- (38.4%)
- Produced by $^{64}Ni(p,n)$ reaction
- Target material electroplated on gold backing



Innovative Targetry

- Historical Example:
- Two-shoot method for producing $^{18}F_2$
  - Shoot 1: $^{18}O_2$ gas to produce $^{18}F^-$
  - Shoot 2: Ar/F_2 mixture
  - During Shoot 2 plasma causes F_2 to exchange with $^{18}F^-$ on walls of target chamber

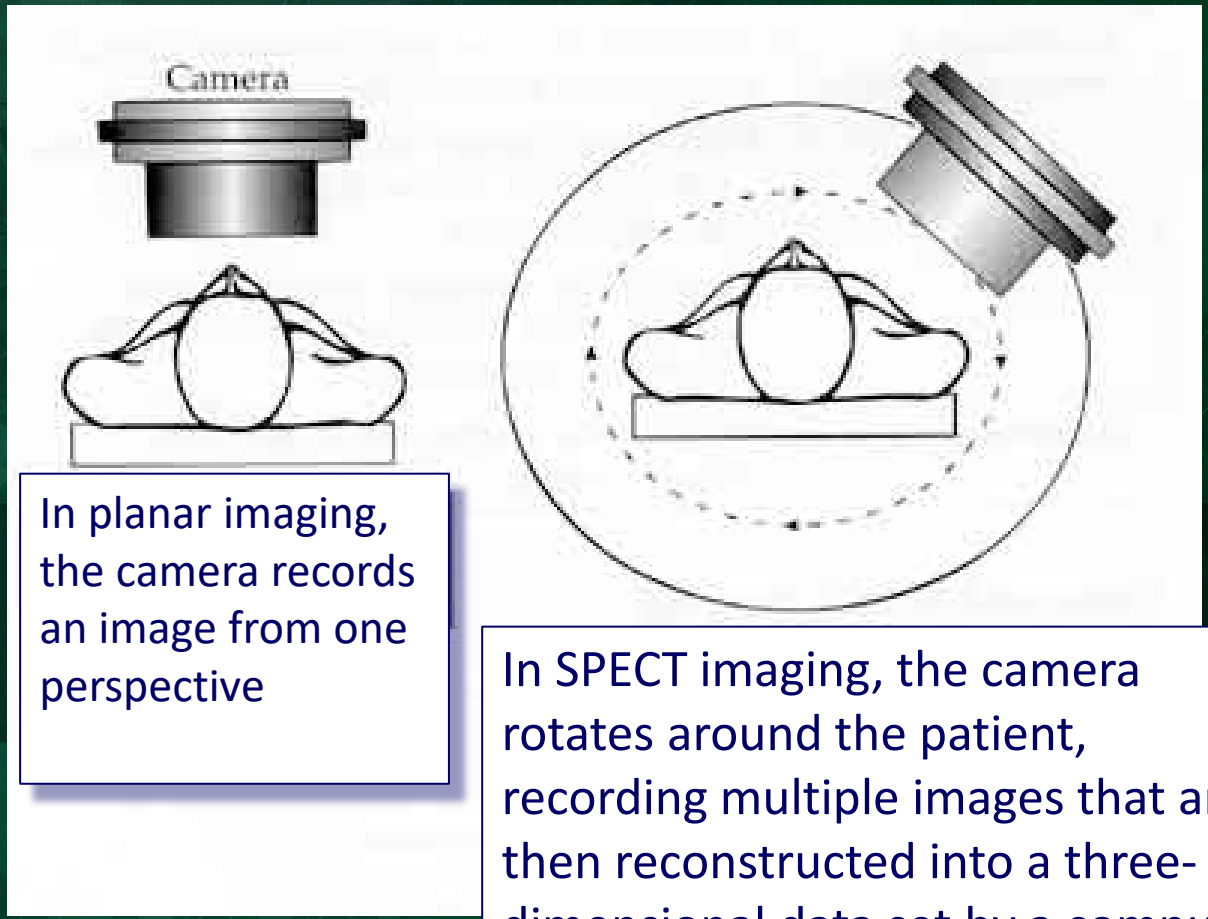
Innovative Targetry

- Liquid Solid Targets:
  - Irradiation a solution of metal salt.
  - Skip dissolution step (easier to automate)
  - Lower density of target atoms.

Nuclear Imaging

SPECT: Single Photon Emission
Computed Tomography

PET: Positron Emission Tomography



In planar imaging, the camera records an image from one perspective

In SPECT imaging, the camera rotates around the patient, recording multiple images that are then reconstructed into a three-dimensional data set by a computer

Gamma camera imaging

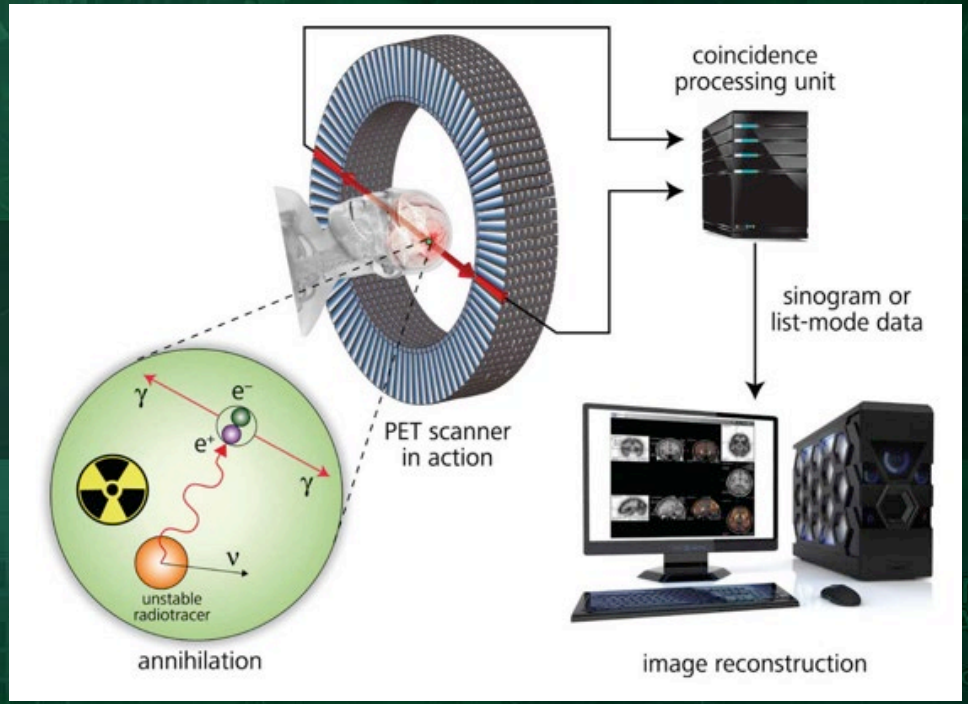
Gamma cameras are used for planar and SPECT imaging

^{99m}Tc-radiopharmaceuticals are imaged with gamma cameras

From http://www.upc.com.mx/img/imagenologia/cardiodiagnostico/e_cam3.jpg

Positron Emission Tomography

PET imaging is a very sensitive tool capable of providing quantitative information about biochemical and physiological processes in a non-invasive manner.



PET-CT

PET cameras use radionuclides that emit positrons

Images formed using photons from annihilation events

From http://www.medical.siemens.com

The ideal imaging radiopharmaceutical

- Radionuclide considerations:
  - Half-life matched to biological process of interest and radiopharmaceutical kinetics
  - Monochromatic γ-ray production for planar and SPECT imaging
  - γ -ray energy high enough to escape from patient but low enough to be easily stopped by the detector
  - High fraction of low energy positron emission for PET imaging
  - Minimal production of particle radiation (β^-, internal conversion and Auger electrons) to minimize dose

The ideal imaging radiopharmaceutical

- Radiopharmaceutical considerations:

  - Localization to the organ of interest with clearance from non-target tissues
  - Distribution of radioactivity reflects biological process of interest
  - Non-toxic, often through high specific activity
  - High radionuclidic, radiochemical and chemical purity
  - Inexpensive, readily available, short imaging time
  - Suitable for quantification

Radiopharmaceutical localization

- Compartmental
  - Blood pool imaging for GI bleeding : ^{99m}Tc radiolabeled red blood cells (RBCs)
- Simple diffusion and bulk flow
  - Ventilation imaging: ^{133}Xe, ^{99m}Tc DTPA aerosol
- Capillary blockade
  - Perfusion imaging: ^{99m}Tc macro-aggregated albumin (MAA)

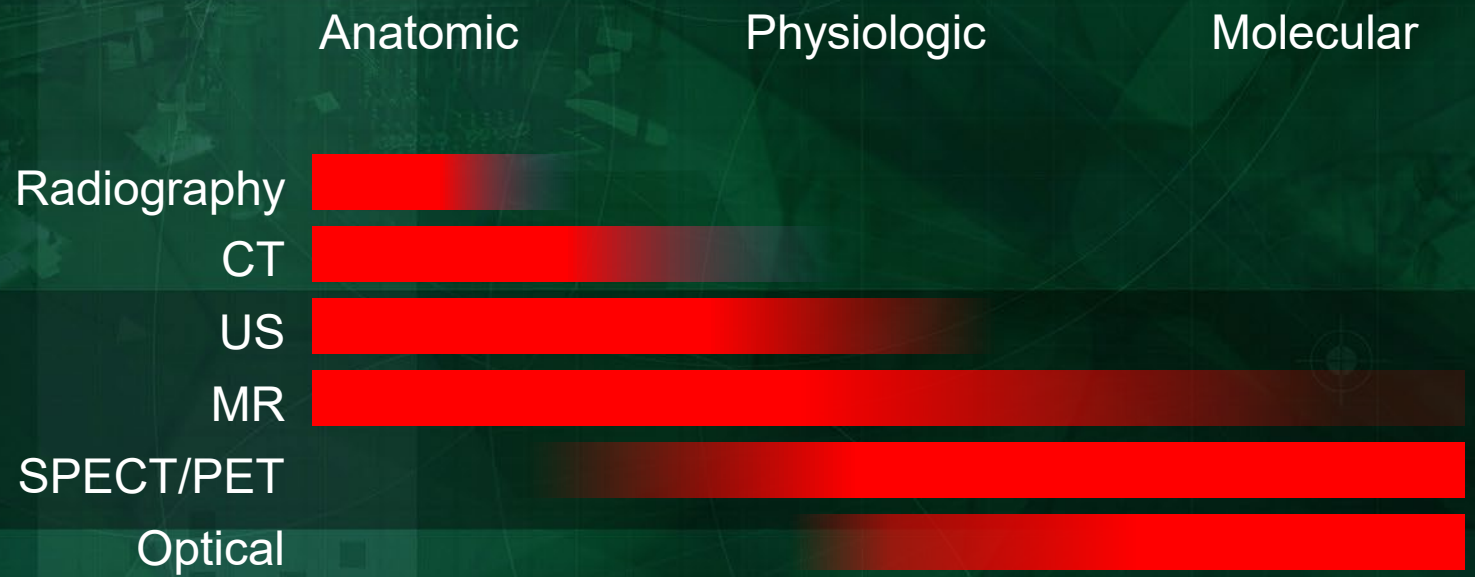
Radiopharmaceutical localization

- Biological transport
  - Norepinephrine transporter: ^{123}I MIBG
  - Glucose transport: ^{18}F FDG
  - Renal tubular secretion: ^{99m}Tc MAG-3
  - Potassium analogues: ^{201}Tl, ^{82}Rb
  - Iodide transport: $^{123}I^-$, $^{131}I^-$, $^{99m}TcO_4^-$
- Receptor binding
  - Somatostatin receptor binding: ^{111}In Octreoscan

Radiopharmaceutical Localization

- Chemisorption (bond formation at material surface)
  - Bone scintigraphy: ^{99m}Tc MDP
- Phagocytosis of particles or cells
  - Reticuloendothelial imaging: ^{99m}Tc sulfur colloid
  - splenic imaging: heat damaged Red Blood Cells (RBCs)
- Hypoxia
  - Trapping in hypoxic tissues: [^{18}F]FMISO and [^{64}Cu]ATSM
- Protein binding
  - Amyloid plaque binding: [^{11}C]PIB

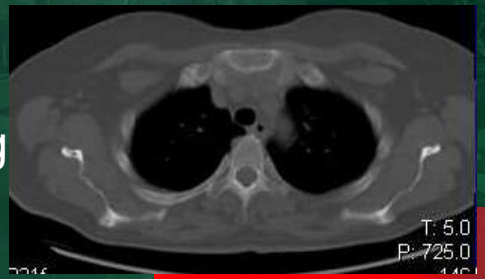
Comparison of imaging modalities

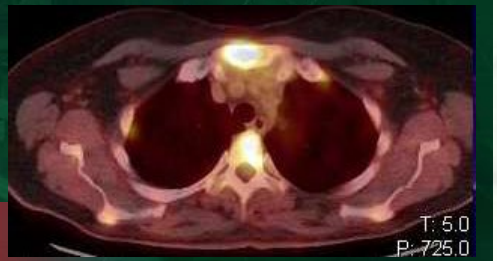


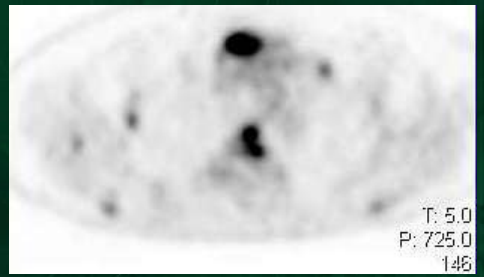
Weissleder R and Mahmood U. Radiology 2001; 219:316–333.
Hoffman JM and Gambhir SS. Radiology 2007; 244: 39-47.

Anatomic Physiologic Molecular

Radiog

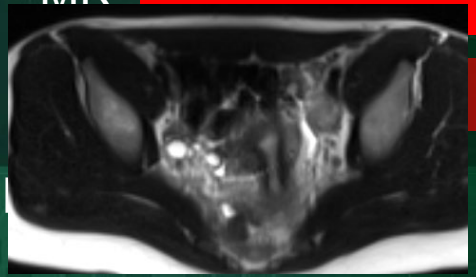


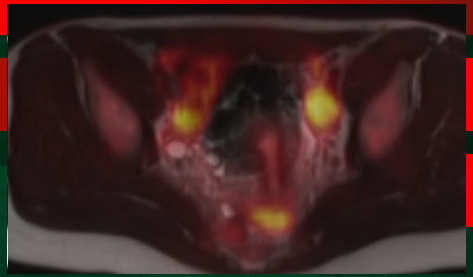


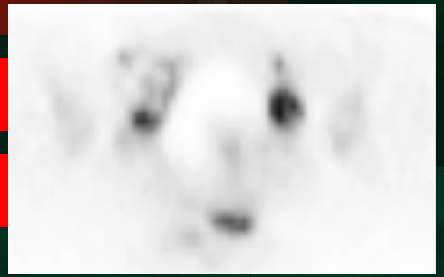


- US

MR







O

-

Common PET Radioisotopes

$^{14}N(p,\alpha)^{11}C$	$t_{½}$ = 20.3 min.
$^{18}O(p,n)^{18}F$	$t_{½}$ = 109.7 min.
$^{16}O(p,\alpha)^{13}N$	$t_{½}$ = 9.97 min
$^{14}N(d,n)^{15}O$	$t_{½}$ = 2.0 min

$^{14}N(p,\alpha)^{11}C$ and ^{11}C Chemistry

- Typically irradiate ^{14}N as N_2
- Add trace O_2 → $^{11}CO_2$
- $^{11}CO_2$ is the starting point for chemistry
- Transferred in gas phase to chemistry module
  - →$^{11}CH_4$ → $^{11}CH_3I$
- A few groups have tried in-target production of $^{11}CH_4$ (lower yields)

$^{18}O(p,n)^{18}F$ and ^{18}F Chemistry

- Typically irradiate ^{18}O as H_2O
- ^{18}F is the starting point for chemistry
- Transferred in liquid phase to chemistry module

- Several groups have tried in target production of ^{18}F as F_2 using the two shoot method described

$^{16}O(p,\alpha)^{13}N$ and ^{13}N Chemistry

- Typically irradiate ^{16}O as H_2O
- Additional of trace ethanol as a reducing agent to yield ^{13}N as $^{13}NH_3$
- Rare to try additional chemistry ($t_{1/2}$ = 9.93 min!)

$^{14}N(d,n)^{15}O$ and ^{15}O Chemistry

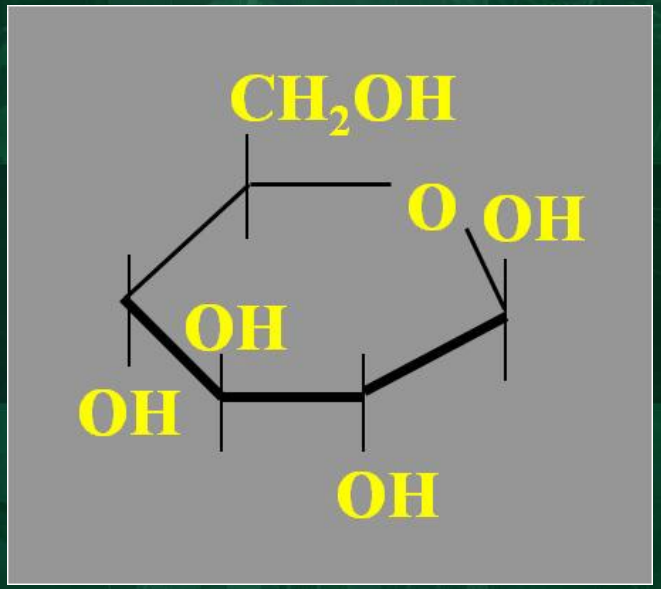
- Typically irradiate ^{14}N as N_2
- Additional of trace O_2 to yield ^{15}O as O_2
- Addition of trace H_2 to yield ^{15}O as H_2O
- Fast gas phase chemistry ($t_{1/2}$ = 2.0 min!) for CO, CO_2

PET in Oncology…

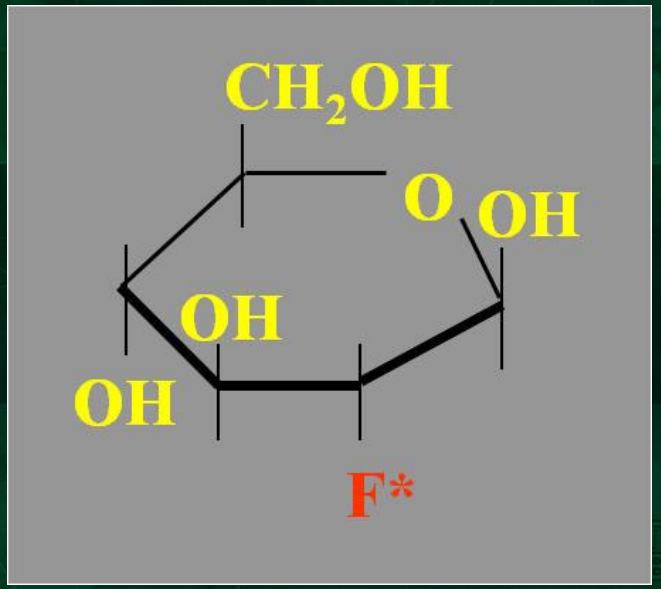
- diagnosis
  - location and extent of disease
  - general (FDG) or tumor-specific probes
- prognosis
  - size, stage, grade of disease
  - proliferation (FLT) and/or hypoxia (EF5, etc)
- “real-time” therapy evaluation
  - customizing treatment could increase efficacy, decrease toxicity, and improve economics

PET Radiopharmaceutical: FDG

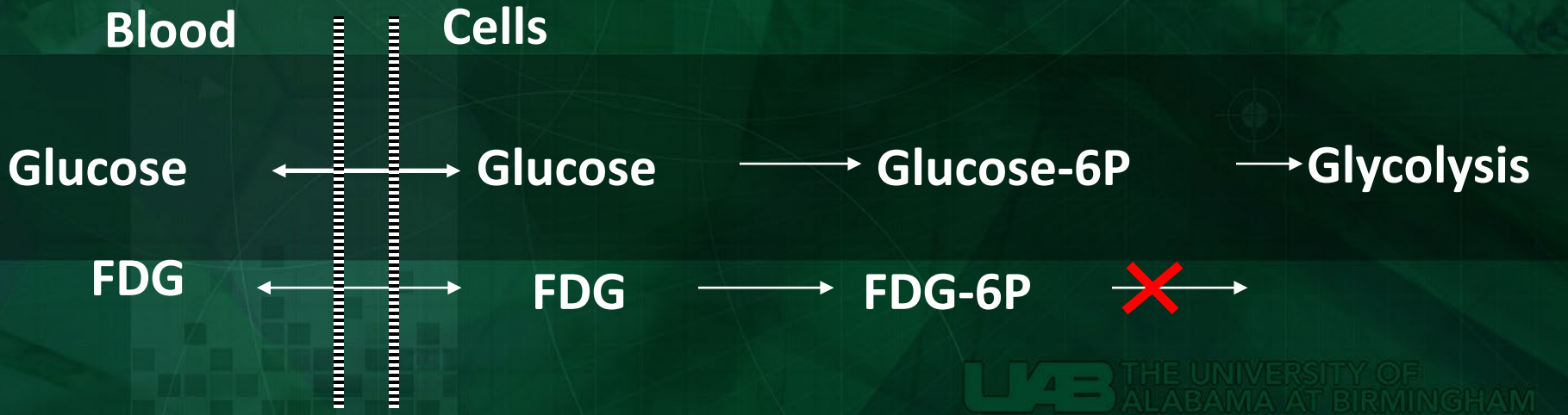
Glucose



Fluorodeoxyglucose (FDG)



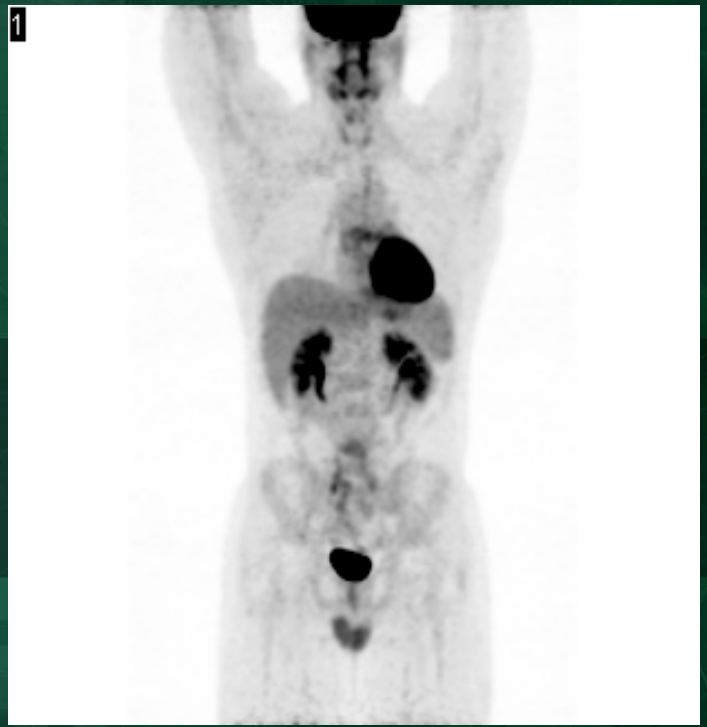
FDG Uptake and Retention



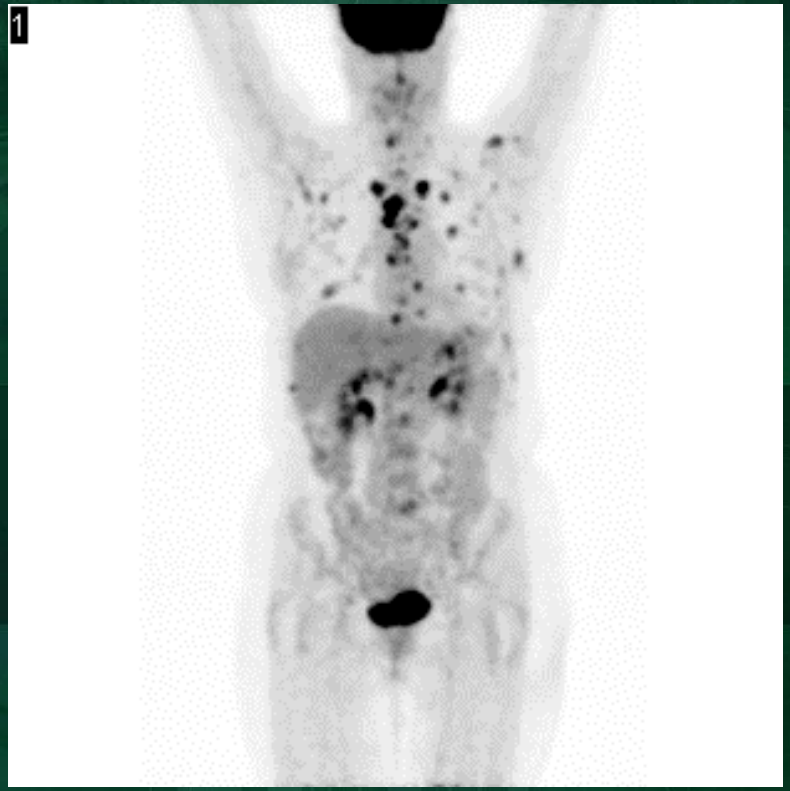
FDG-PET

- Used for diagnosis, staging and treatment monitoring for many types of cancer
- 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG)
    - glucose analogue that measures the transport and phosphorylation of glucose (1st steps in glycolysis)
- Higher FDG uptake is typically associated with more aggressive malignancies
- FDG uptake also occurs in inflammation and infection which can lead to false positives

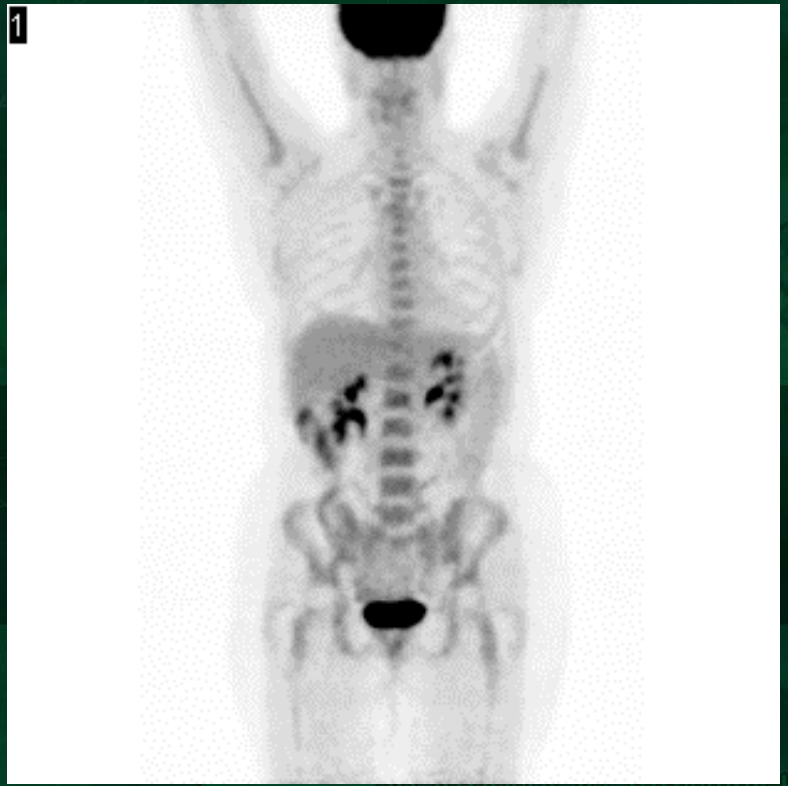
Normal FDG-PET study



59 year old woman with T-cell lymphoma



Initial study



4 months later,
after chemotherapy

PET in Oncology…Beyond FDG

FDA News Release

FDA approves new diagnostic imaging agent to detect recurrent prostate cancer

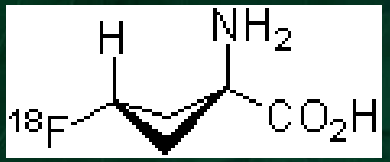
For Immediate Release May 27, 2016

Release

The U.S. Food and Drug Administration today approved Axumin, a radioactive diagnostic agent for injection. Axumin is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated prostate specific antigen (PSA) levels following prior treatment.

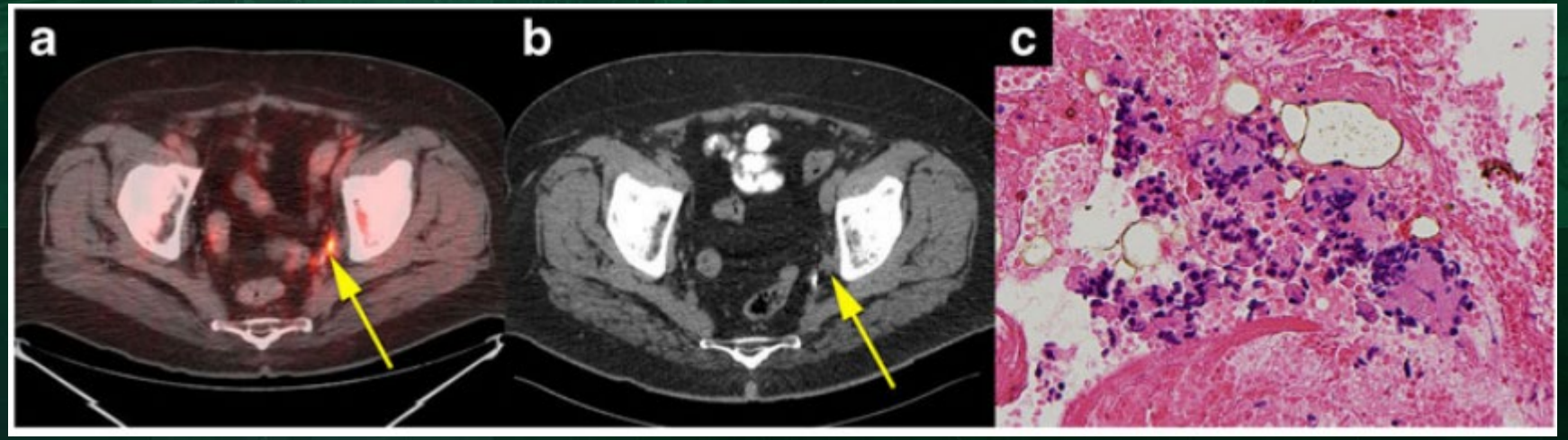
Prostate cancer is the second leading cause of death from cancer in U.S. men. In patients with suspected cancer recurrence after primary treatment, accurate staging is an important objective in improving management and outcomes.

"Imaging tests are not able to determine the location of the recurrent prostate cancer when the PSA is at very low levels," said Libero Marzella, M.D., Ph.D., director of the Division of Medical Imaging Products in the FDA's Center for Drug Evaluation and Research. "Axumin is shown to provide another accurate imaging approach for these patients."



[^{18}F]-Fluciclovine
1-amino-3-[^{18}F]-fluorocyclobutane-1-carboxylic acid
[^{18}F]FACBC

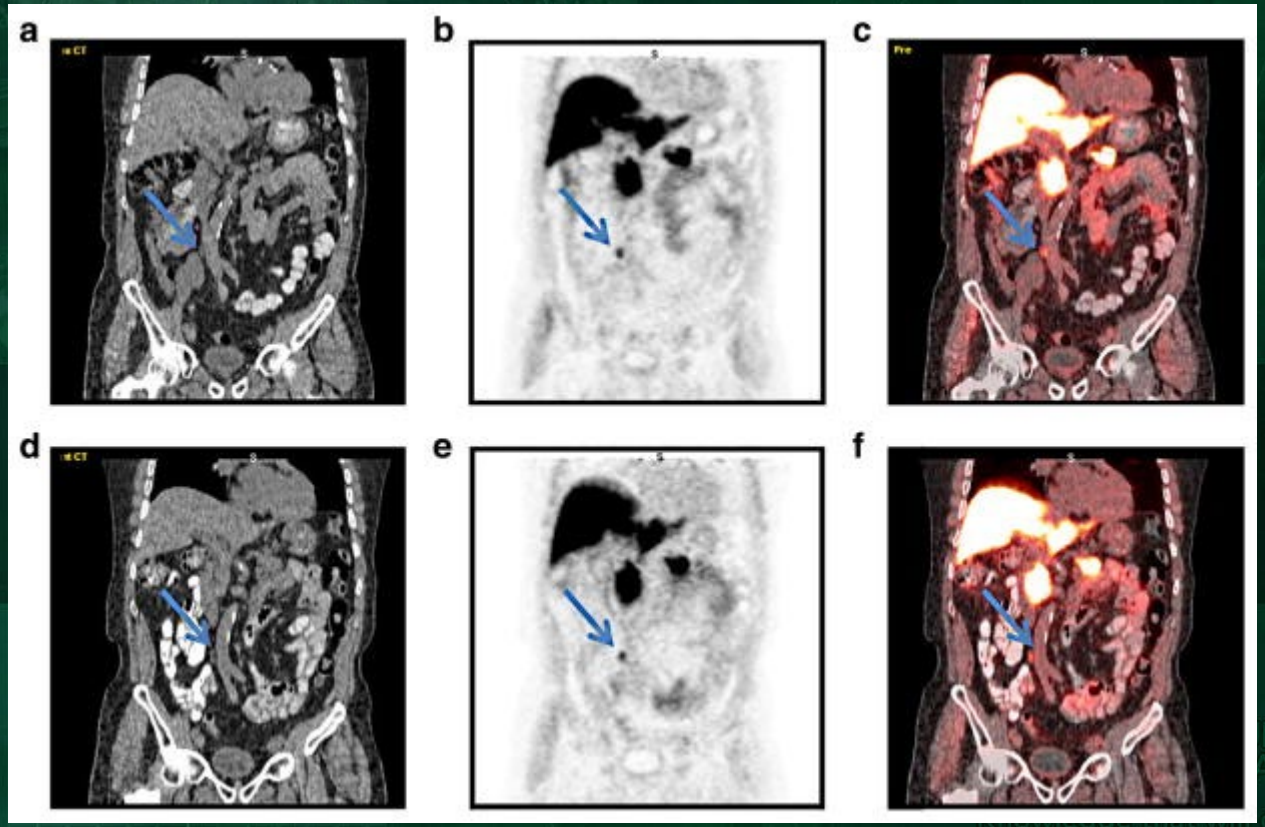
[^{18}F]Fluciclovine/[^{18}F]FACBC



Subcentimetre lymph node true-positive on the fluciclovine PET

Odewole et a Eur J Nucl Med Mol Imaging 2016

[^{18}F]Fluciclovine/[^{18}F]FACBC



Odewole et al Mol Imaging Biol. 2015 Apr;17(2):277-83.

PET in Neurology…

- SPECT agents for multiple indications
- FDG for brain tumors
- PET imaging in dementia

FDA Approves Amyvid for Clinical Use

ARTICLE | COMMENTS | R

09 Apr 2012

The Food and Drug Administration (
Pharmaceuticals/Eli Lilly and Comp
imaging in cognitively impaired pati
compound will be available for use i
—the disease.

FDA PRESS RELEASE

For Immediate Release: Oct. 25, 2013
Media Inquiries: Stephanie Yao, 301-796-0394, stephanie.yao@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA approves second brain imaging drug to help evaluate patients for Alzheimer's disease, dementia

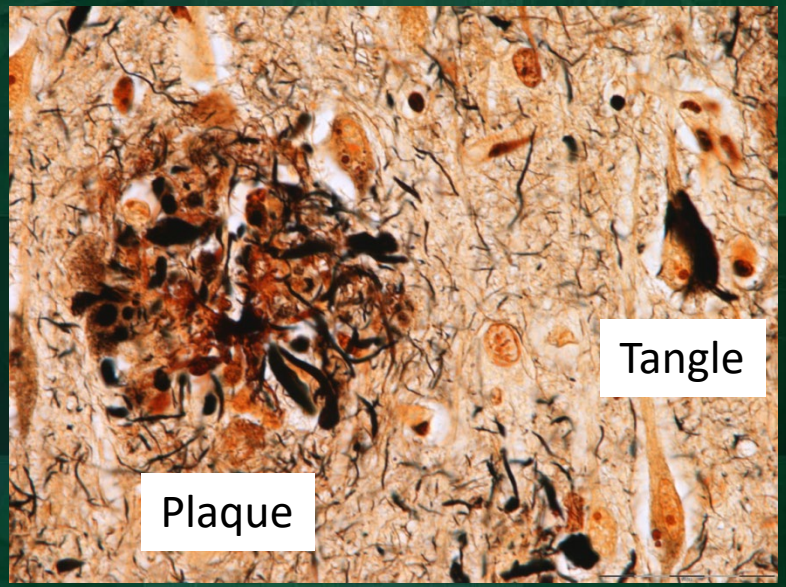
The U.S. Food and Drug Administration today approved Vizamyl (flutemetamol F 18 injection), a radioactive diagnostic drug for use with positron emission tomography (PET) imaging of the brain in adults being evaluated for Alzheimer's disease (AD) and dementia.

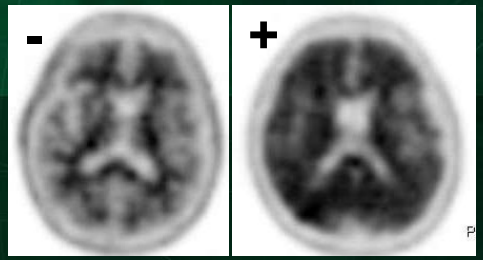
Dementia is associated with diminishing brain functions such as memory, judgment, language and complex motor skills. The dementia caused by AD is associated with the accumulation in the brain of an abnormal protein called beta amyloid and damage or death of brain cells. However, beta amyloid can also be found in the brain of patients with other dementias and in elderly people without neurologic disease.

Diagnosis of Dementia

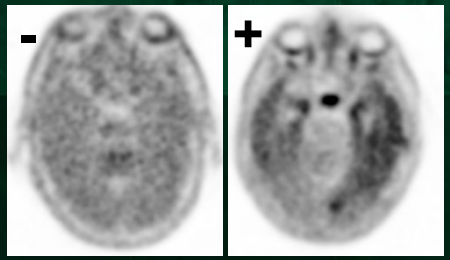
- Clinical diagnosis requires multiple clinical and neuropsychological exams over years to establish the diagnosis
  - estimated rate of misdiagnosis in Alzheimer's disease is ~20% based on autopsy studies
- MRI is normal or shows non-specific lesions
- FDG-PET often shows characteristic pattern for different dementias
- Amyloid-PET can identify the presence of beta-amyloid plaques in the brain

Protein misfolding plays key roles in many neurodegenerative diseases(e.g. amyloid, tau)





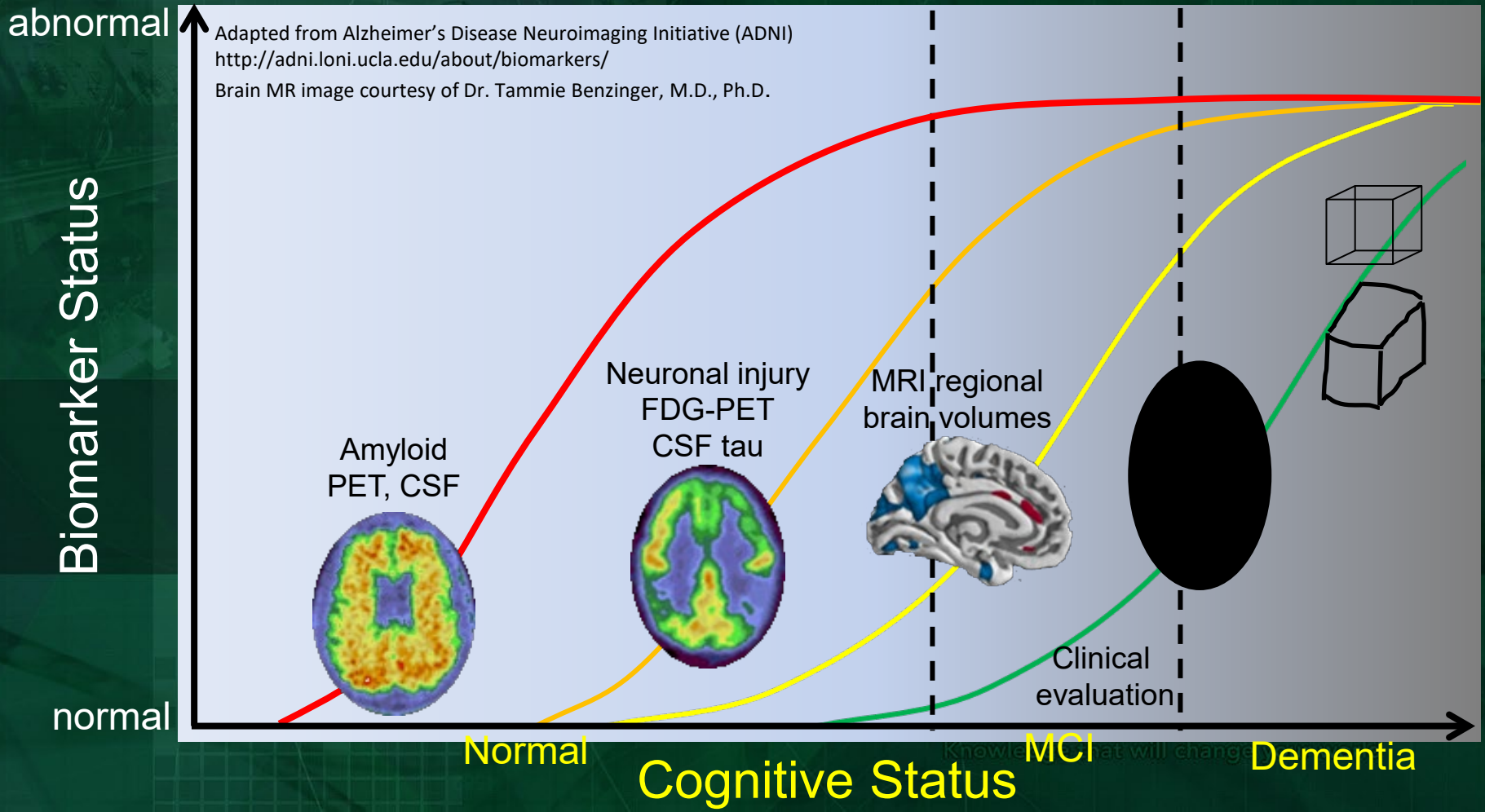
Amyloid-PET



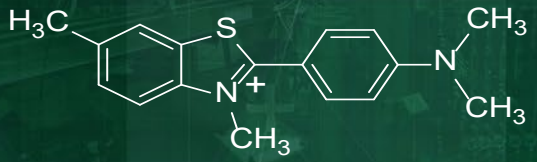
Tau-PET

http://neuropathology-web.org/chapter9/chapter9dPD.html

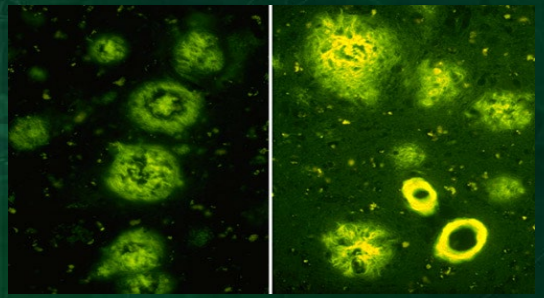
Time Course of Biomarkers in AD



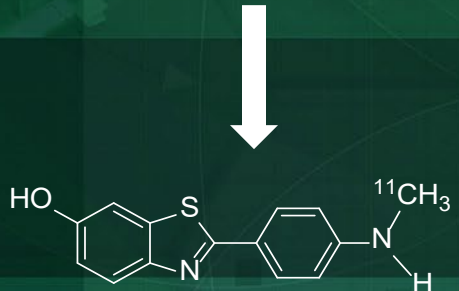
Amyloid plaque imaging agents



Thioflavin T



Thioflavin S staining of amyloid plaques and amyloid angiopathy in a patient with AD



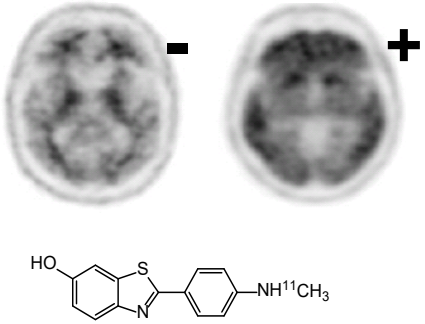
[^{11}C]PIB

[^{11}C]PIB has been used extensively in research studies for amyloid plaque imaging

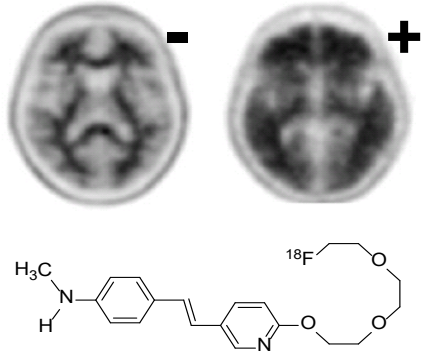
http://library.med.utah.edu/WebPath/COW/COW046.html

PET tracers for amyloid plaque imaging

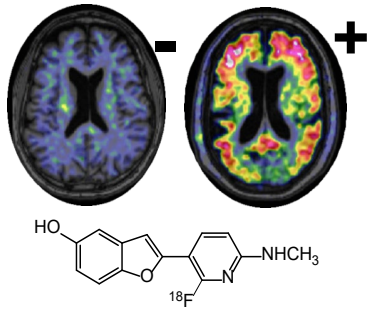
[^{11}C]PiB



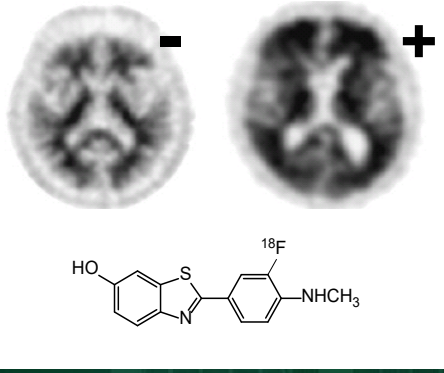
[^{18}F]florbetapir (Ely Lilly/Avid)



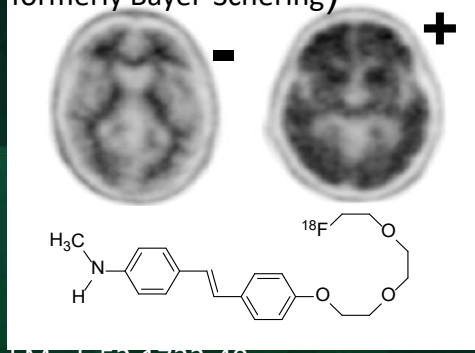
[^{18}F]AZD4694 (Navidea, formerly Astra-Zeneca)



[^{18}F]flutemetamol (GE)



[^{18}F]florbetaben (Piramal, formerly Bayer-Schering)



Rowe CC et al., 2011. Brain amyloid imaging, J Nucl Med. 52:1733-40.
Cselenyi Z et al., 2012. Clinical validation of 18F-AZD4694, an amyloid-beta-specific PET radioligand, J Nucl Med. 53:415-24.

Controversies regarding amyloid-PET

- How much will imaging contribute above clinical assessment?
- Will imaging tests be used in a reasonable, cost-effective manner?
- What will the clinical impact be?

Therapy

- Radiopharmaceuticals can be used for therapy
  - Radioactive iodine-131 for thyroid disease
    - hyperthyroidism
    - thyroid cancer
  - Radiolableled antibodies for non-Hodgkin lymphoma
    - Bexxar, Zevalin (target CD-20 on B-cells)
  - ^{131}I MIBG for certain cancers
    - neuroblastoma in kids
    - pheochromocytoma in adults

Traditional Radiotherapy

- The use of external beam radiotherapy is the most frequently used approach for tumor cell killing
- A major disadvantage is high radiation dose to healthy cells

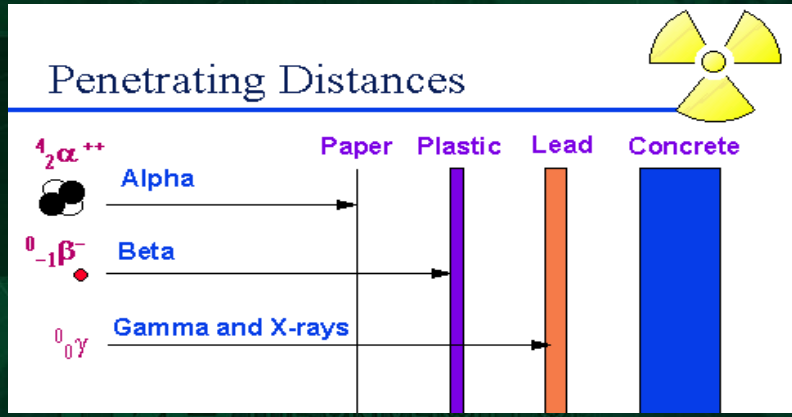
Targeted Radiotherapy

- Uses a targeting moiety (small molecule, peptide, antibody) to deliver a radioactive payload (therapeutic isotope) to a specific disease site.

- Localized high dose of radiation
  → “Magic Bullet”

Targeted Radionuclide Therapy

- Reduces exposure to normal tissue by irradiating tumors from within the body
- 3 types of radionuclides suitable for therapy :
  1. β-particle emitters
  2. α-particle emitters
  3. Auger electron emitters



Isotope Pairs

- Using structurally identical (or similar) compounds for imaging and therapy
- Information about the biodistribution of therapeutic compound can be determined before administering a large dose of radioactivity to the patient

Why Use Isotope Pairs?

- Therapeutic isotope not suitable for imaging
- Need to learn biodistribution or dosimetry prior to treatment
- During development of new radiotherapeutics
- Imaging response to therapy

Isotope Pairs

Therapeutic Isotope	Imaging "Surrogate(s)"
^{131}I ($t_{1/2}$ = 8d)	$^{124/123}I$
^{90}Y ($t_{1/2}$ = 2.7d)	$^{86}Y/^{111}In/^{68}Ga/^{64}Cu/^{89}Zr$
^{177}Lu ($t_{1/2}$ = 6.7d)	$^{111}In/^{68}Ga/^{64}Cu/^{89}Zr$
^{186}Re ($t_{1/2}$ = 3.7d)	^{99m}Tc
^{77}Br ($t_{1/2}$ = 2.4 d)	^{76}Br
^{67}Cu ($t_{1/2}$ = 2.6 d)	^{64}Cu

Isotope Pairs: Considerations

- May or may not be the same element
  - Chemistry/Structural variations
    → Biology variations
- Varying Half-life
  - Usually imaging surrogate has shorter half-life
  - Can you image for as long as the therapeutic isotope is contributing dose?
  - Do you need to?
- Availability

Theranostics

- Imaging strategies for new radiopharmaceuticals are required to calculate dosimetry
- Isotope pairs offer an excellent opportunity to image the biodistribution of these new compounds
- Care must be taken to ensure the biological activity and fate is the same as the compound of interest

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Email: lapi@uab.edu

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