PET Radionuclides Production

Cyclotron Selection and Location

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3. PET Radionuclides Production
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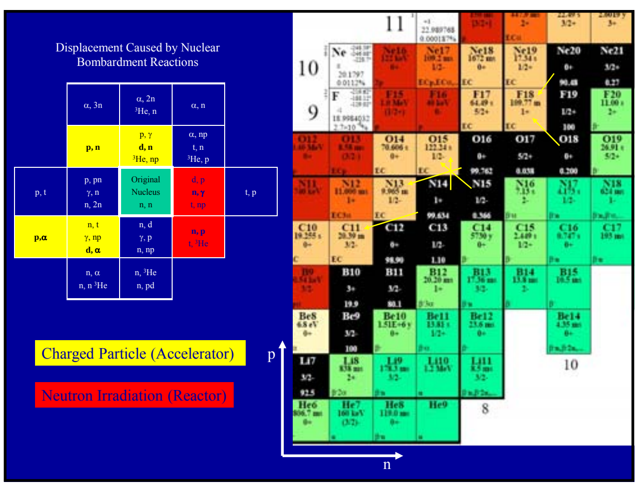
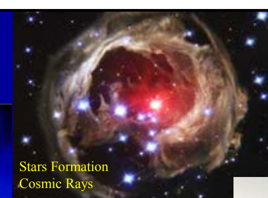


Radionuclides Production



Common PET Radioisotopes

Radioisotope	Half-life	Decay (%)	β^+ Endpoint (MeV)	Principal Nuclear Reactions
^{11}C	20.3 min	β^+ 99.8, EC 0.2	0.961	$^{14}N(p,\alpha)^{11}C$
^{13}N	9.96 min	β^+ 100	1.190	$^{16}O(p,\alpha)^{13}N$
^{15}O	122 sec	β^+ 99.9, EC 0.1	1.723	$^{14}N(d,n)^{15}O$ $^{15}N(p,n)^{15}O$
^{18}F	109.8 min	β^+ 96.9, EC 3.1	0.635	$^{18}O(p,n)^{18}F$ $^{20}Ne(d,\alpha)^{18}F$
^{61}Cu	3.41 hr	β^+ 62, EC 38	1.205	$^{60}Ni(d,n)^{61}Cu$ $^{61}Ni(p,n)^{61}Cu$
^{62}Cu (gen.)	9.73 min	β^+ 97.8, EC 2.2	2.934	$^{63}Cu(p,2n)^{62}Zn(9.1\ hr) \rightarrow {}^{62}Cu$
^{64}Cu	12.7 hr	β^+ 19, EC 41, β^- 40	0.657	$^{64}Ni(p,n)^{64}Cu$, $^{64}Zn(n,p)^{64}Cu$
^{82}Rb (gen.)	75 sec	β^+ 96, EC 4	3.35	$^{85}Rb(p,4n)^{82}Sr(25\ d) \rightarrow {}^{82}Rb$
^{86}Y	14.7 hr	β^+ 34, EC 66	1.248, others	$^{86}Sr(p,n)^{86}Y$
^{124}I	4.15 d	β^+ 25, EC 75	1.533, 2.134	$^{124}Te(p,n)^{124}I$

$ Cyclotron Selection Criteria $

Purpose	Commercial Distribution	Distribution & Research	Clinical Research	Pre-Clinical Research
Radionuclide	^{18}F	^{11}C, ^{13}N, ^{15}O, ^{18}F, solid	^{11}C, ^{13}N, ^{15}O, ^{18}F, solid	^{11}C, ^{15}O, ^{18}F
Activity	~ 10 Ci/batch	> 1 Ci/batch	~ 1Ci/batch	< 1 Ci/batch
Particles	H^-	H^-, D^-	H^-, D^-	H^-
Energy	≥ 15 MeV	≥ 15 MeV	≥ 15 MeV	≥ 7 MeV

Shielding options: Self + Vault (~30 cm concrete)
Vault (~ 200 cm concrete)

Long term investment >10 years ⟶ Long term needs

Radionuclide Production Yields

Disintegration Rate: (Activity) $D = N \cdot \lambda_A$

N : Number of atoms
λ_A : Probability of decay
$\lambda_A = \ln(2)/T_{1/2}$

Bateman's equation (balance) for growth of daughter radionuclide *B* from parent *A*

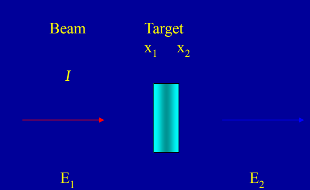
$$B \cdot \lambda_B = (A \cdot \lambda_A)\frac{\lambda_B}{\lambda_B - \lambda_A}\left(1 - e^{-(\lambda_B - \lambda_A)t}\right)$$

A : Number of target atoms. *A >> 1*
λ_A: Probability of transforming target atom A into B $\lambda_A << 1$
The product $A.\lambda_A$ remains finite.

$\lambda_A << \lambda_B \Rightarrow$

$$B \cdot \lambda_B = A \cdot \lambda_A\left(1 - e^{-\lambda_B \cdot t}\right)$$

Probability of transforming atom A into B



$$\lambda_A = I \cdot \sum_{x_1}^{x_2} \sigma(x) \cdot dx \quad \Rightarrow \quad \lambda_A = I \cdot \int_{E_1}^{E_2} \frac{\sigma(E)}{(dE/dx)} \cdot dE$$

Radionuclide Production Yield

$$B \cdot \lambda_B = I\left(1 - e^{-\lambda_B \cdot t}\right) \cdot \frac{N_A \cdot \rho}{M} \cdot \int_{E_i}^{E_{th}} \frac{\sigma(E)}{(dE/dx)} dE$$

Yield (mCi)

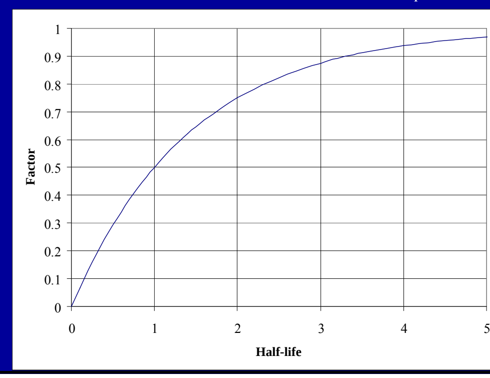
(I) Beam Current (μA)

Build-up (irradiation time)

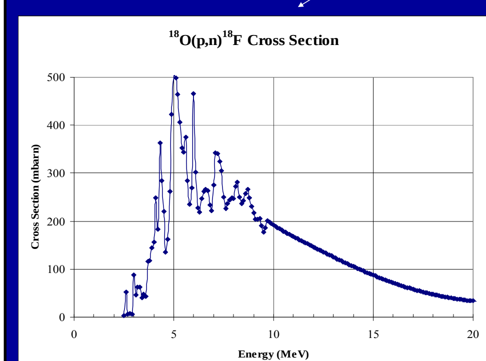
Saturation Yield (mCi/μA)

$B\lambda_B = I\,(1- e^{-\lambda_B t})\,\mathbf{N}_A\rho / M \int \sigma(E)$
$dE/(dE/dX)$

Irradiation Build Up

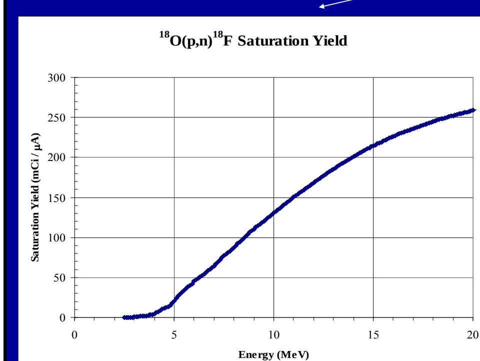


$B\lambda_B = I\,(1- e^{-\lambda_B t})\,\mathbf{N}_A\rho / M \int \sigma(E)$
$dE/(dE/dX)$



1 mbarn = 10^{-27} cm^2

$B\lambda_B = I\,(1- e^{-\lambda_B t})\,\mathbf{N}_A\rho / M \int \sigma(E)$
$dE/(dE/dX)$



Production Efficiency

How many protons per produced ^{18}F atom are needed?

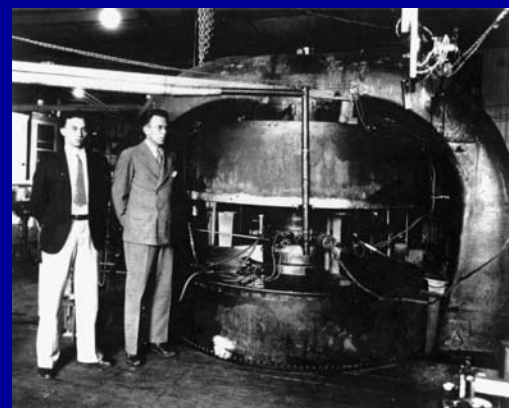
$^{18}O(p,n)^{18}F$

Protons Energy [MeV]	Yield* [mCi/μA]	^{18}F at EOB [mCi]	Protons/^{18}F
10.5	120	950	1700
18	200	1583	1020

Irradiation conditions : 25 μA x 60 min

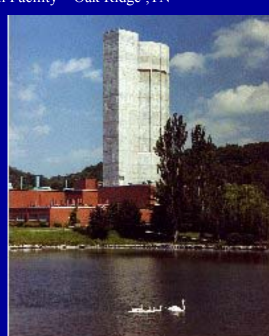
* Typical production yields using >95% enriched ^{18}O-Water

Ernest Orlando Lawrence and M. Stanley Livingston



Holifield Radioactive Ion Beam Facility – Oak Ridge ,TN

25 MV Terminal

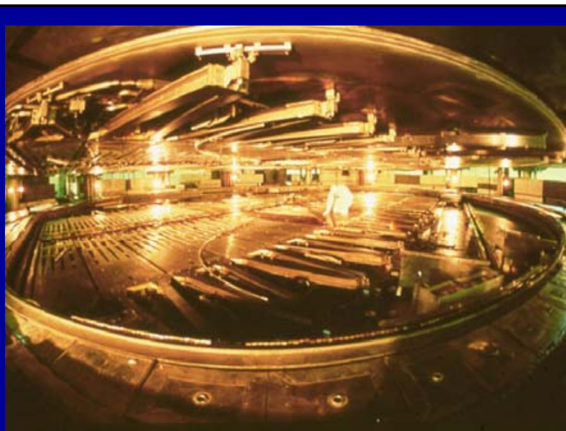


Building

Comparative size for electrostatic accelerator with similar final proton energy as 40 MeV cyclotron

UT Houston – Scanditronix MC40

T R I U M F
T R
5 0 0
M e V



CYCLOTRON MENU

Sizes:

Small (PET):	$K(p) < 19$ MeV	self-shielded option
Medium (SPECT):	$K(p) < 30$ MeV	vault required
Large (Therapy):	$K(p) > 30$ MeV	up to few hundred MeV

Flavors:

Ion	*Positive*	*Negative (p, d only)*
Ion Source	*Internal*	*External*
Magnet	*Conventional*	*Superconducting*
Plane	*Horizontal*	*Vertical*
Shielding	*Self*	*Vault*
Particles	*Single*	*Multiple (p,d,α,He3)*
Energy	*Fixed*	*Variable (steps-cont.)*

Siemens Eclipse HP

11 MeV protons
60 µA (x2)max. current

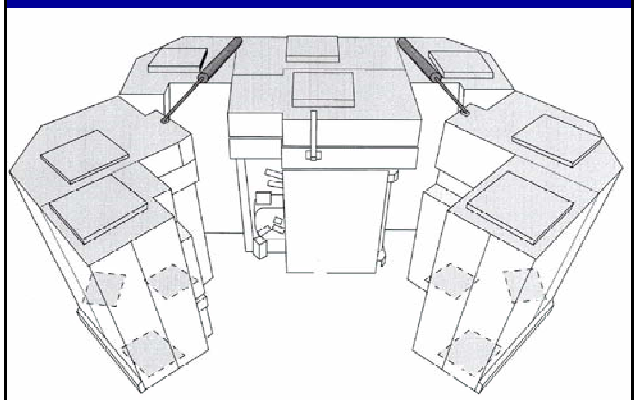
MAX. POWER: 660 W (x2)

GE PETtrace

16 MeV protons
8 MeV deuterons (option)
60 µA max. current

MAX. POWER: 960 W

GE PETtrace Self-Shielded



IBA Cyclone® 18/9 -HC

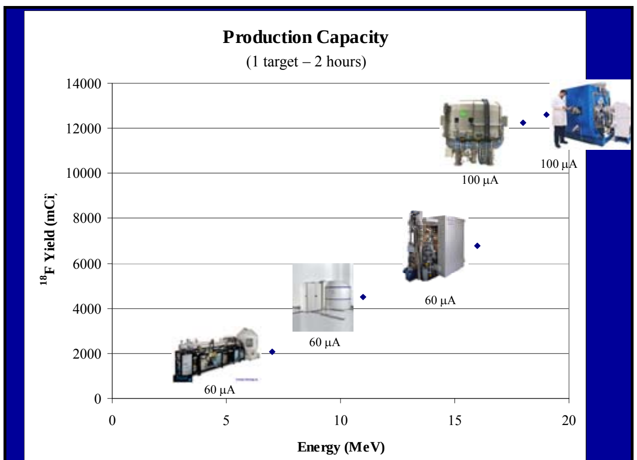
18 MeV protons
9 MeV deuterons
150 μA max. current

MAX. POWER: 2700 W

ACS TR 19/9

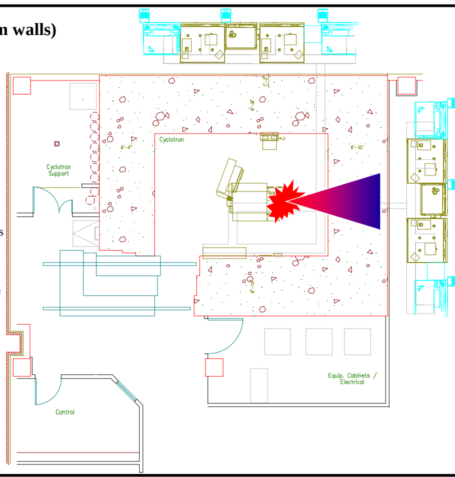
19 MeV protons
9 MeV deuterons
>300 μA current

MAX. POWER: ~ 6000 W



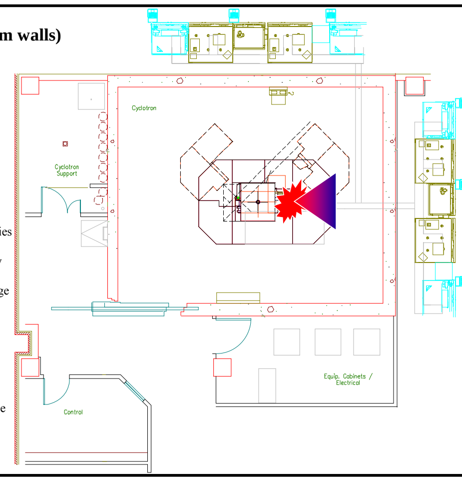
Large Vault (~190 cm walls)

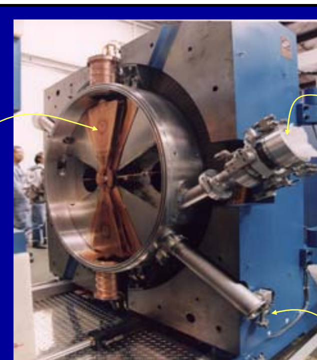
- Shielding (neutrons)
- NCRP 144
- Reinforce floor
- Beam direction
- Negative pressure
- Conduits – Power and utilities
- Trenches – Product delivery
- Corner Pit – Decay in storage
- Power supply room
- Support room
- Control room – Vault door
- Work bench – targets service
- Product distribution valves



Self-shielded (~30 cm walls)

- Shielding (neutrons)
- NCRP 144
- Reinforced floor
- Beam direction
- Negative pressure
- Conduits – Power and utilities
- Trenches – Product delivery
- Corner Pit – Decay in storage
- Power supply room
- Support room
- Control room – Vault door
- Work bench – targets service
- Product distribution valves

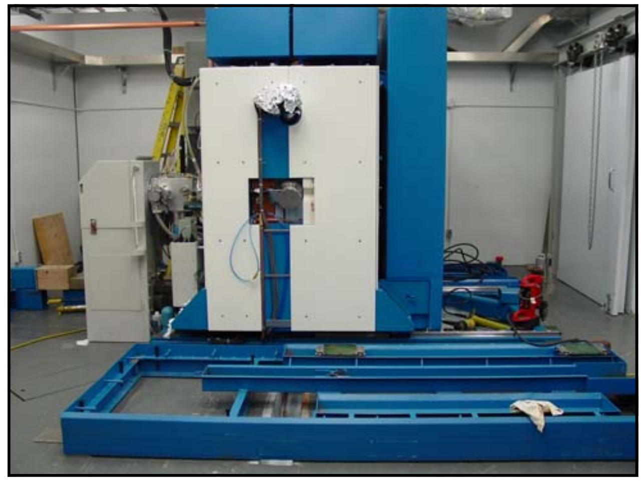


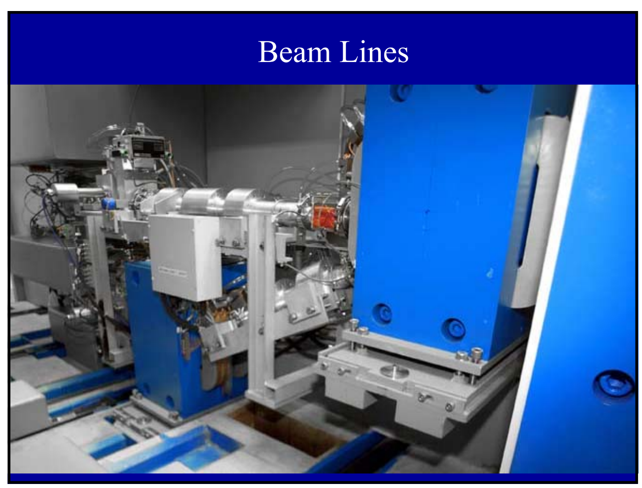


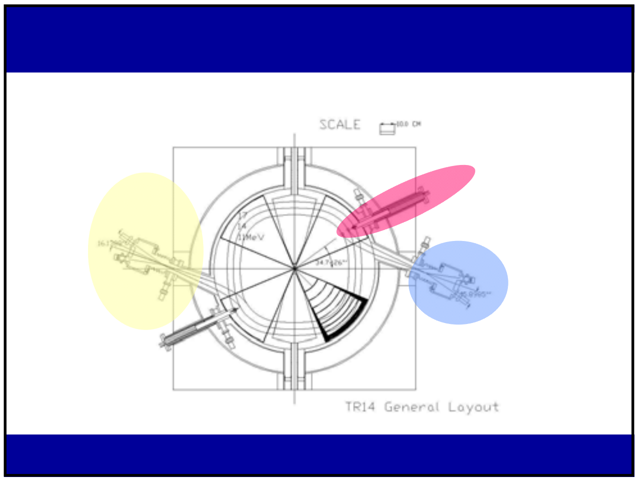
Open Cyclotron

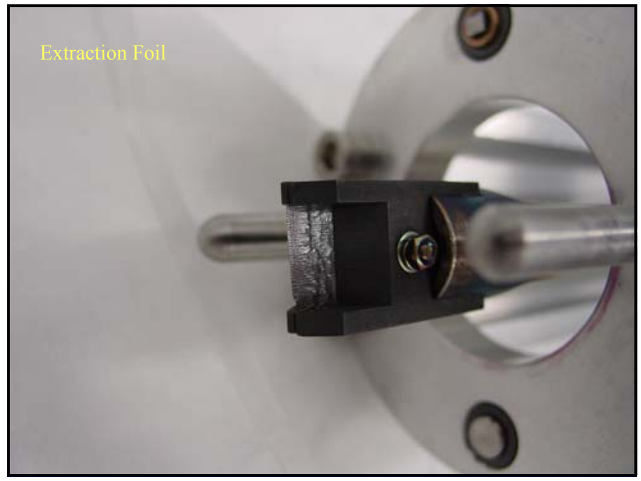
All parts requiring maintenance can be isolated from the cyclotron vacuum

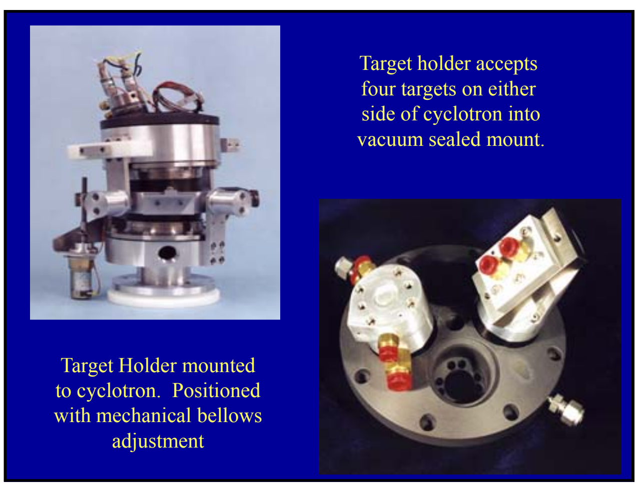

TR-19
HOUSTON
TEXAS
JUL 16 2002

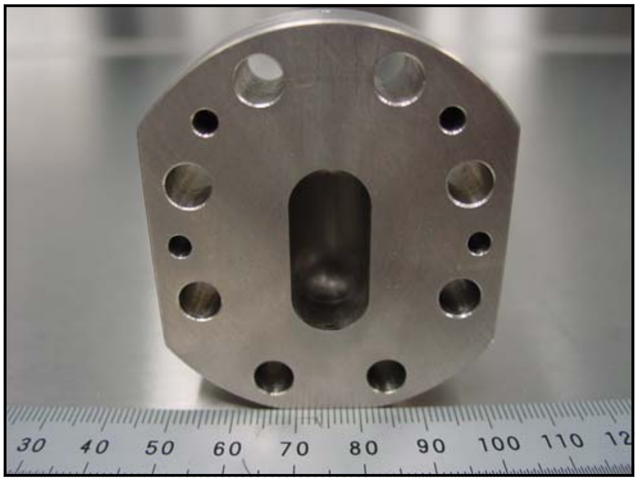


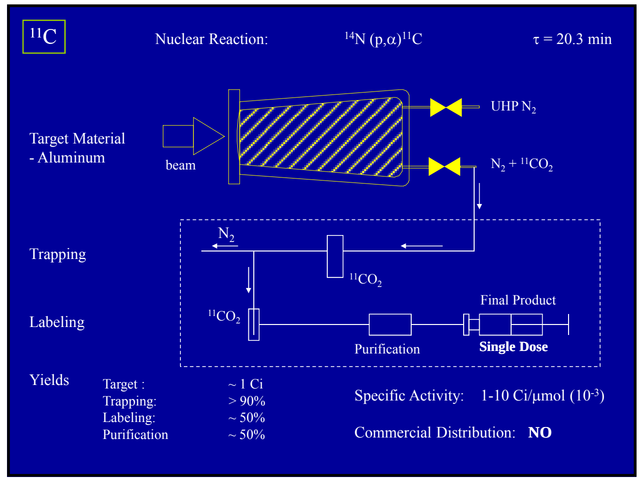

Beam Lines

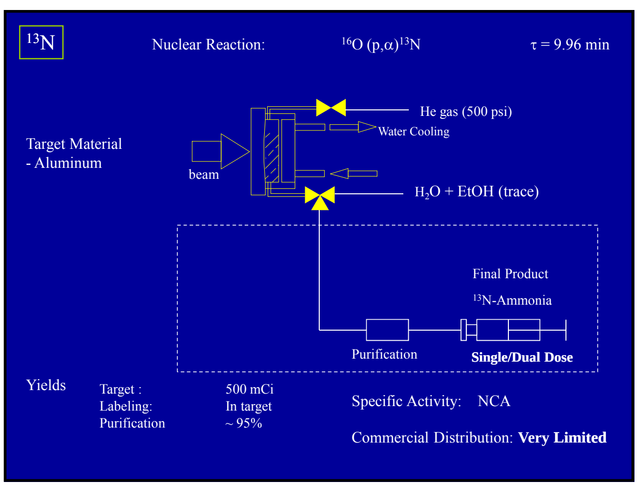

SCALE
TR14 General Layout

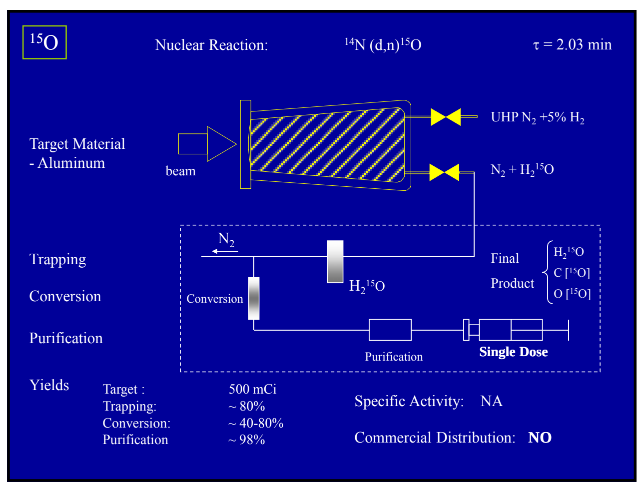

Extraction Foil

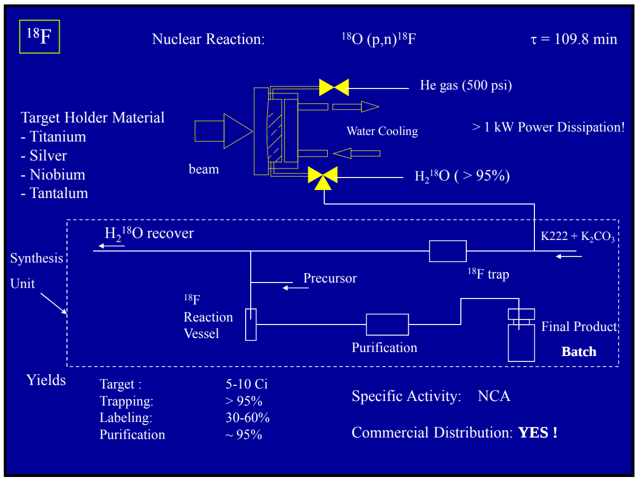

Target holder accepts four targets on either side of cyclotron into vacuum sealed mount.
Target Holder mounted to cyclotron. Positioned with mechanical bellows adjustment

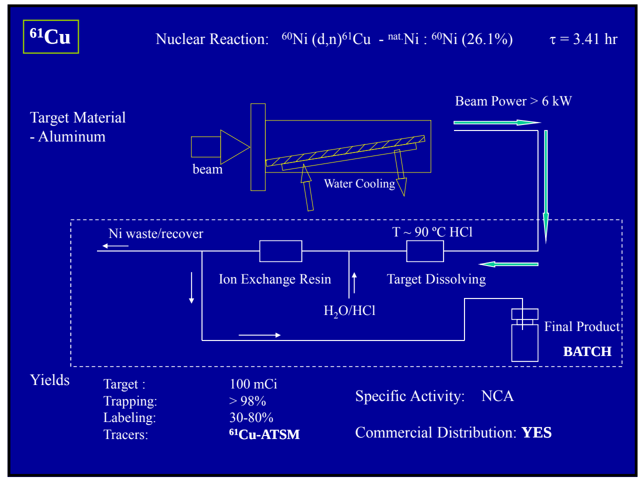


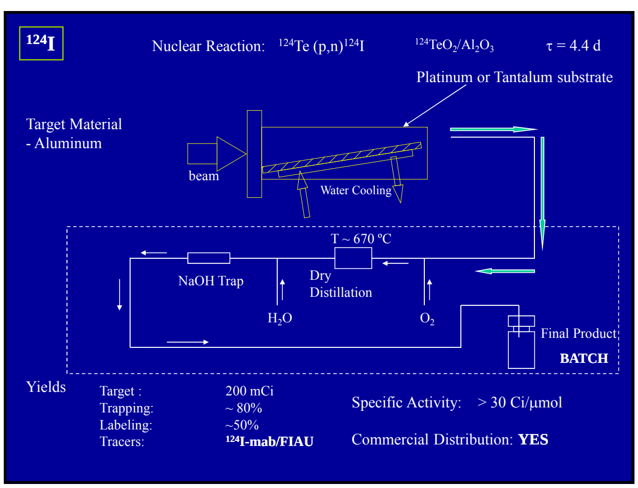

^{11}C
Nuclear Reaction:
$^{14}N\ (p,\alpha)^{11}C$
τ = 20.3 min
Target Material
- Aluminum
beam
UHP N_2
$N_2 + {}^{11}CO_2$
Trapping
N_2
$^{11}CO_2$
Labeling
$^{11}CO_2$
Final Product
Purification
Single Dose
Yields
Target : ~ 1 Ci
Trapping: > 90%
Labeling: ~ 50%
Purification ~ 50%
Specific Activity: 1-10 Ci/μmol (10^{-3})
Commercial Distribution: NO

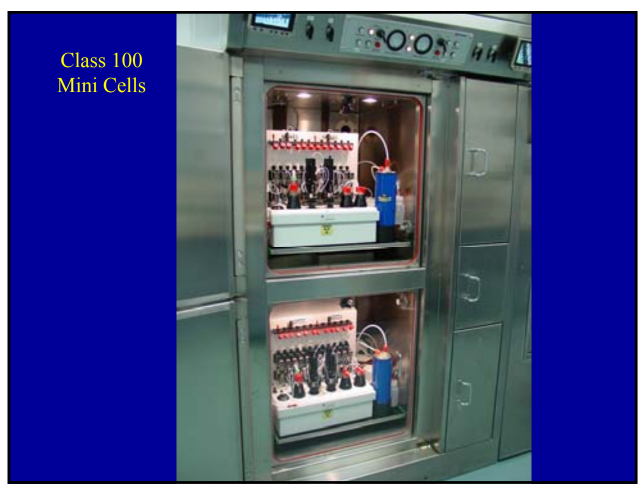

^{13}N
Nuclear Reaction:
$^{16}O\ (p,\alpha)^{13}N$
τ = 9.96 min
Target Material
- Aluminum
beam
He gas (500 psi)
Water Cooling
H_2O + EtOH (trace)
Final Product
^{13}N-Ammonia
Purification
Single/Dual Dose
Yields
Target : 500 mCi
Labeling: In target
Purification ~ 95%
Specific Activity: NCA
Commercial Distribution: Very Limited


^{15}O
Nuclear Reaction:
$^{14}N\ (d,n)^{15}O$
τ = 2.03 min
Target Material
- Aluminum
beam
UHP N_2 +5% H_2
$N_2 + H_2{}^{15}O$
Trapping
Conversion
Purification
N_2
$H_2{}^{15}O$
Conversion
Final Product
$H_2{}^{15}O$
C [^{15}O]
O [^{15}O]
Purification
Single Dose
Yields
Target : 500 mCi
Trapping: ~ 80%
Conversion: ~ 40-80%
Purification ~ 98%
Specific Activity: NA
Commercial Distribution: NO


18F
Nuclear Reaction:
18O (p,n)18F
τ = 109.8 min
He gas (500 psi)
Target Holder Material
- Titanium
- Silver
- Niobium
- Tantalum
Water Cooling
> 1 kW Power Dissipation!
beam
H2 18O (> 95%)
H2 18O recover
K222 + K2CO3
Synthesis
Unit
Precursor
18F trap
18F
Reaction
Vessel
Purification
Final Product
Batch
Yields
Target : 5-10 Ci
Trapping: > 95%
Labeling: 30-60%
Purification ~ 95%
Specific Activity: NCA
Commercial Distribution: YES !


61Cu
Nuclear Reaction: 60Ni (d,n)61Cu - nat.Ni : 60Ni (26.1%)
τ = 3.41 hr
Beam Power > 6 kW
Target Material
- Aluminum
beam
Water Cooling
Ni waste/recover
T ~ 90 ºC HCl
Ion Exchange Resin
Target Dissolving
H2O/HCl
Final Product
BATCH
Yields
Target : 100 mCi
Trapping: > 98%
Labeling: 30-80%
Tracers: 61Cu-ATSM
Specific Activity: NCA
Commercial Distribution: YES


124I
Nuclear Reaction: 124Te (p,n)124I
124TeO2/Al2O3
τ = 4.4 d
Platinum or Tantalum substrate
Target Material
- Aluminum
beam
Water Cooling
T ~ 670 ºC
NaOH Trap
Dry
Distillation
H2O
O2
Final Product
BATCH
Yields
Target : 200 mCi
Trapping: ~ 80%
Labeling: ~50%
Tracers: 124I-mab/FIAU
Specific Activity: > 30 Ci/µmol
Commercial Distribution: YES


Class 100
Mini Cells

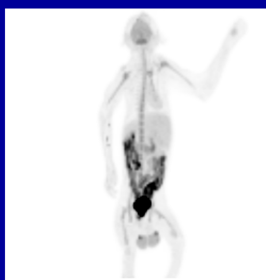
Dose Dispensing

FDA Approved:

- ^{18}F[NaF]
- ^{18}F[FDG]
- ^{13}N-Ammonia
- ^{82}Rb

Potential New Tracers	Primary Application
F18-Acetate	Oncology/Cardiology
F18-Fluorodopa	Neurology -Oncology
F18-FLT	Oncology –DNA marker –Cell Proliferation
C11 – PIB	Detection Alzheimer's disease (F18)
C11 – Acetate	Heart/Prostate
C11 – Palmitate	Fatty Acid Metab – Heart
C11 – Tracers	Brain Receptors
I124 – MoAb	Oncology/Diag.-Treatment
Cu-61/64 ATSM	Hypoxia
Zn62/Cu62 Generator	Heart

FDG



Fluoroacetate

Thank you