Medical Cyclotron: Physics and Instrumentation

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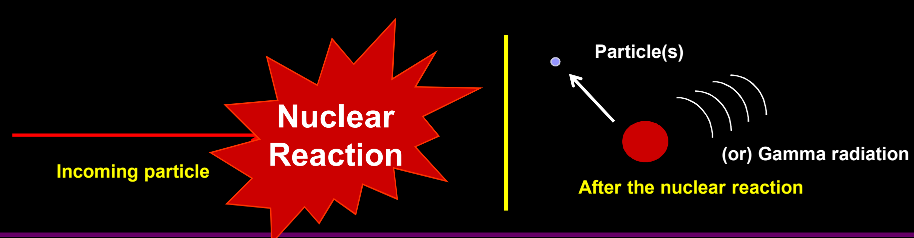
Nuclear Reactions : How does it works ?

During a nuclear reaction a target nucleus is bombarded with some particles : the atomic numberZ is changed (adding or removing particles) and the final nucleus is 'unstable' i.e. radioactive. A radioactive nucleus always get out energy, in form of particles or EM radiation.



Atomic number for the reacting nucleus

Atomic number for the formed nucleus

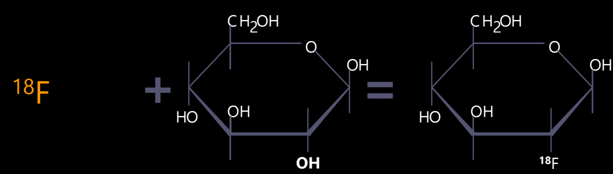
$^{Z1}A\ (p,n)\ ^{Z2}B$

Incoming particle

Expelled particle

Radioisotopes and Radiopharmaceuticals

- **Radioisotope** is the radiation source (radioactive atom)
- **Pharmaceutical** is the vector molecule that targets the organ
- Radioisotope + pharmaceutical = radiopharmaceutical (radiotracer)



Fluorine-18 + Glucose = ^{18}F-FDG

Particle Accelerators

HIGH VILTAGE ACCELERATOR

1- ELECTROSTATIC
2- ELECTRODYNAMIC

RF ACCELERATOR

1- LINEAR ACCELERATOR (LINAC)
2- CYCLOTRON

Motion in electric and magnetic fields

$$F_L = qVB$$

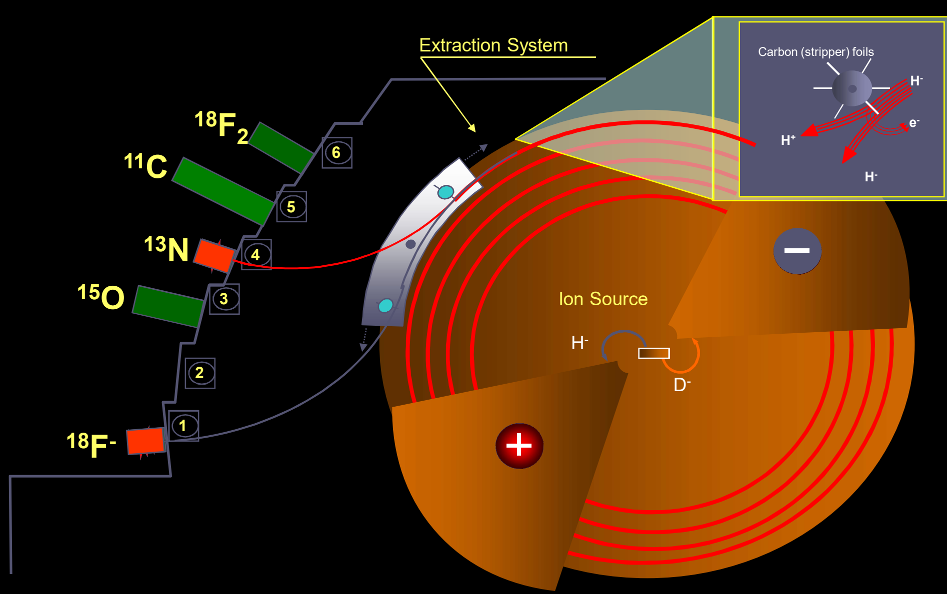
$$F_L = F_0$$

$$qVB = \frac{mV^2}{r} \Rightarrow qBr = mV = P$$

$$T = \frac{2\pi r}{V} = \frac{2\pi m}{qB} \Rightarrow f = \frac{1}{T} = \frac{qB}{2\pi m} = \frac{\omega}{2\pi}$$

$$\omega_s = \omega \Rightarrow \omega_s = \frac{qB}{m}$$

Basic Principal of Acceleration



What is the Size of Baby Cyclotron?

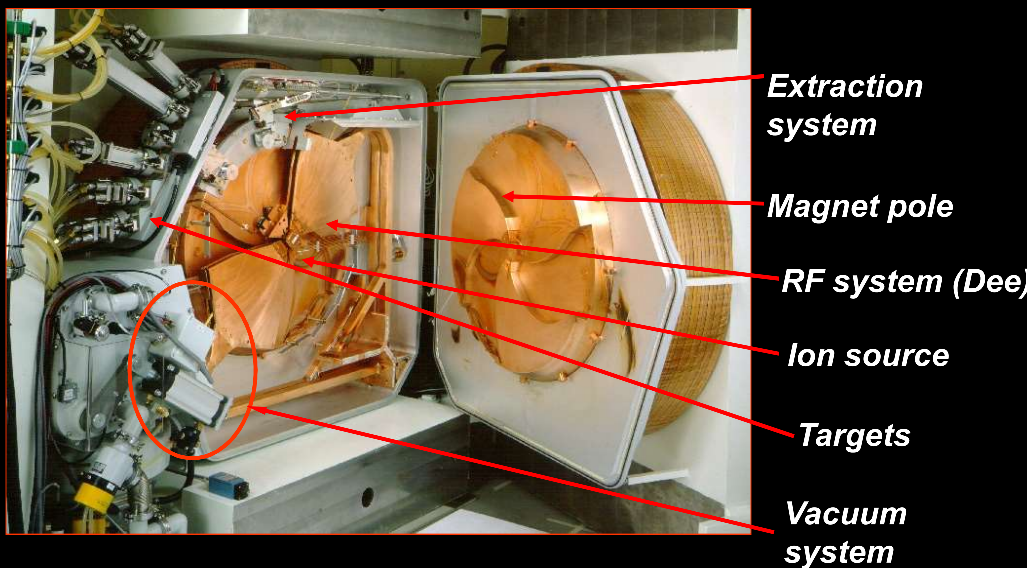
High Energy

Medium Energy

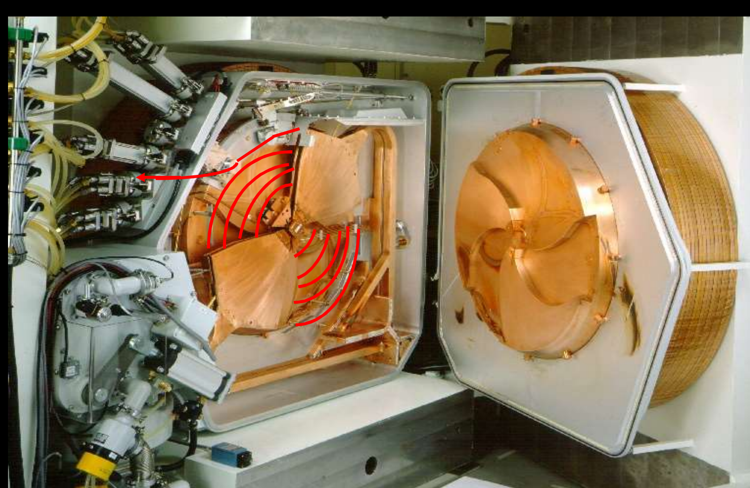
Cyclotron subsystems

- ***Magnet system***
- ***RF system***
- ***Ion source system***
- ***Extraction system***
- ***Diagnostic system***
- ***Vacuum system***
- ***Control System***
- ***Target system***
- ***Cooling system***

Cyclotron Subsystems



Beam Acceleration

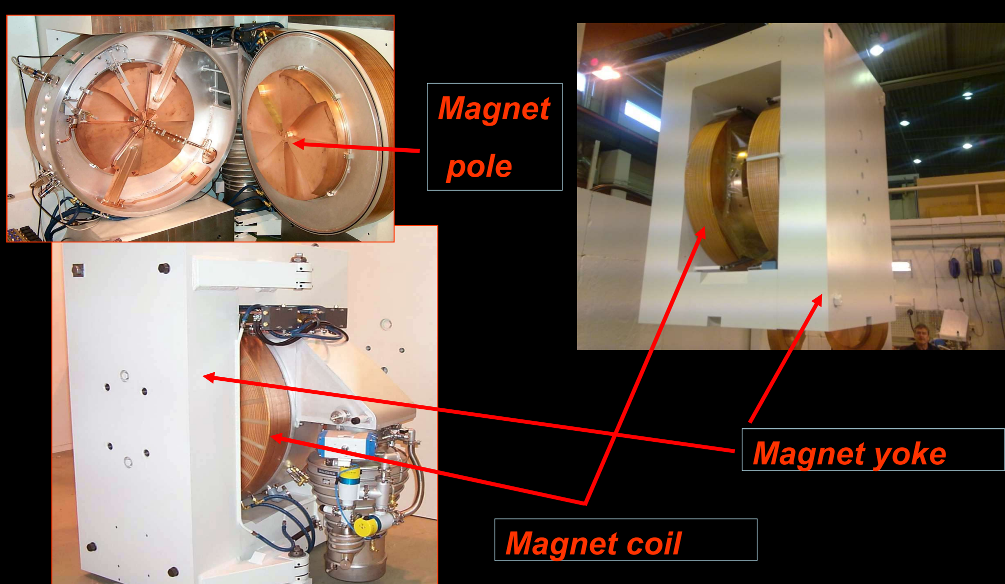


Magnet system

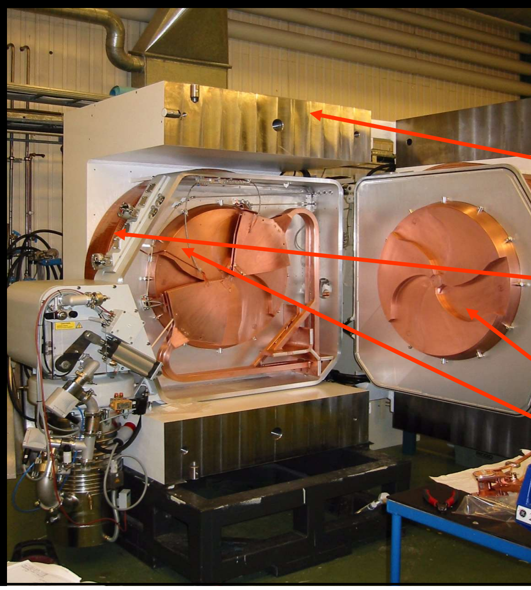
- *The main function is to keep the particles in circular orbits.*
- *The magnet field is also needed to get a plasma in the Ion Source.*
- *The Magnet field is achieved with a large electromagnet.*

Typical Magnetic field 1.5 - 2.5 T

Magnet System



Magnet System

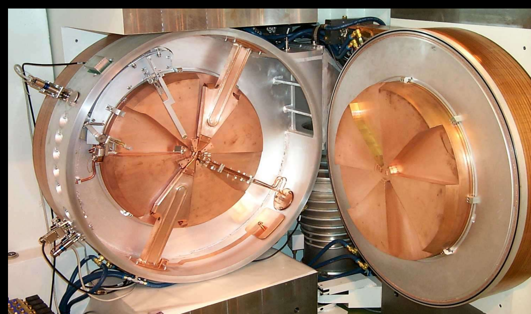


Magnet System

Magnet Coils,
Preparation in the Factory

Magnet System

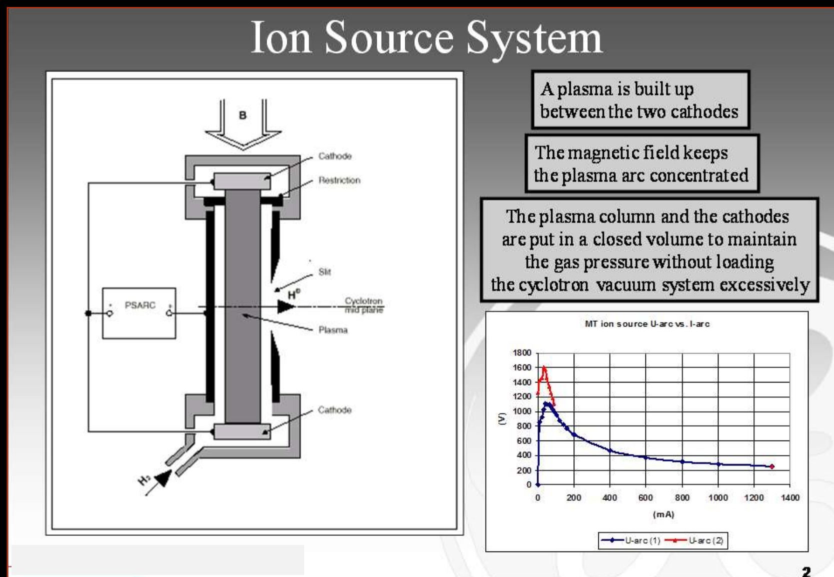
- Magnet weight (coils included) 10,450 tons
- Dimensions (height x width x depth) 1,64 x 1,12 x 0,7 m
- Number of sectors 4
- Average field (at extraction) 1.66 T



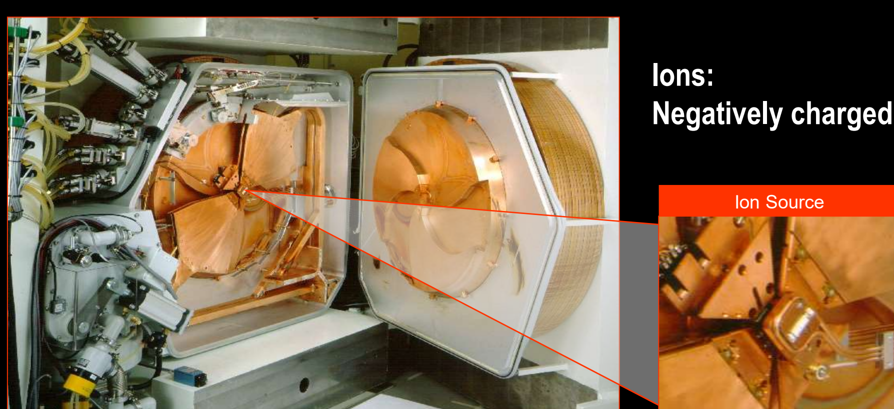
Ion Source System

- *The Ion Source generates the ions that will be accelerated.*
- *The Ion Source is of Penning Ionisation gauge type (PIG) with cold cathodes.*
- *The Ion Source is mounted in the centre of the cyclotron.*

Ion Source System



Ion Source System



Ions:
Negatively charged Protons

RF System

- *Pulls the ions out of the Ion source.*
- *Accelerates the ions to the specified energy.*
- *The two Dees are oscillating at high frequency and voltage.*

RF System in Vacuum Tank

Dee's

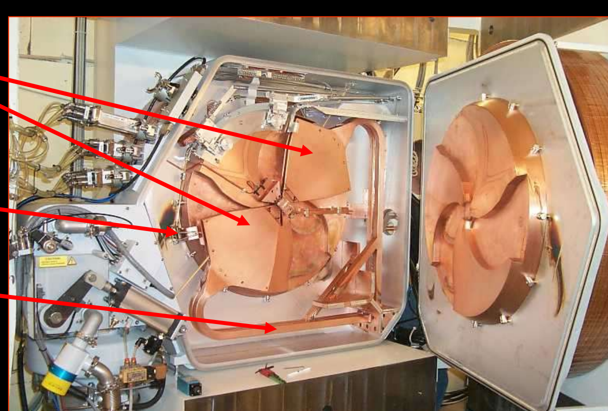
Acceleration Plates

Flaps

Fine tuning RF frequency

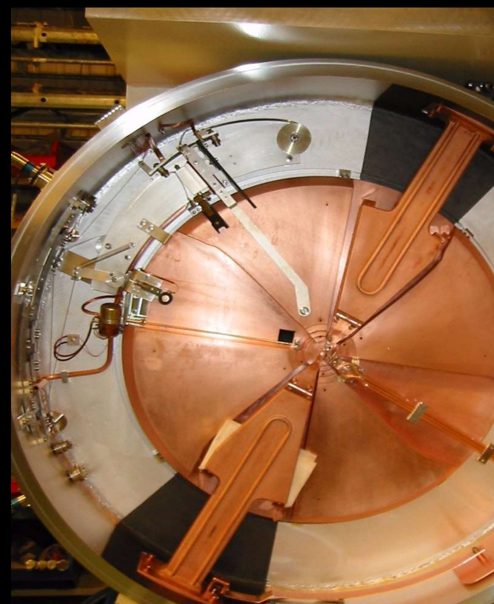
Stem

Supplying RF power to Dee's



RF System

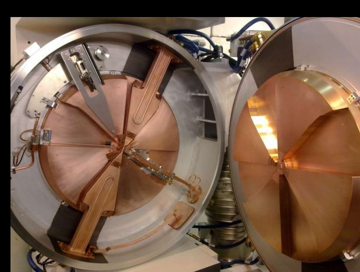
- Dees 2
- Dee voltage 35 kV
- Frequency 101 MHz



Different Dee Configuration

Number of Acceleration per Rotation: 2

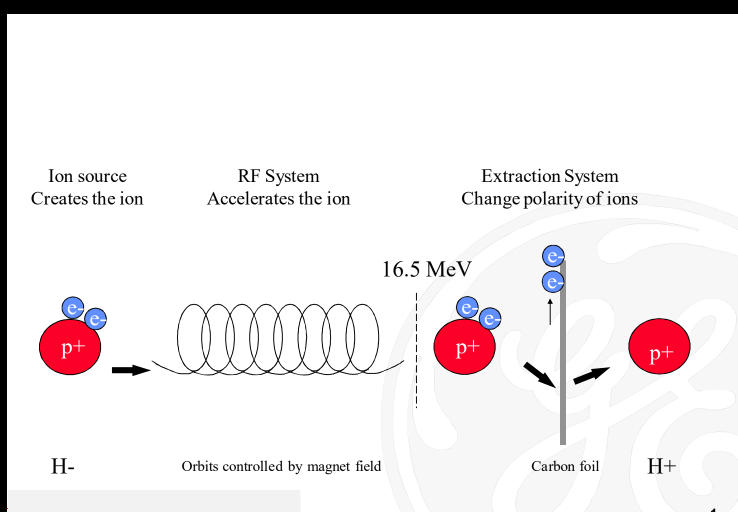
Number of Acceleration per Rotation: 4



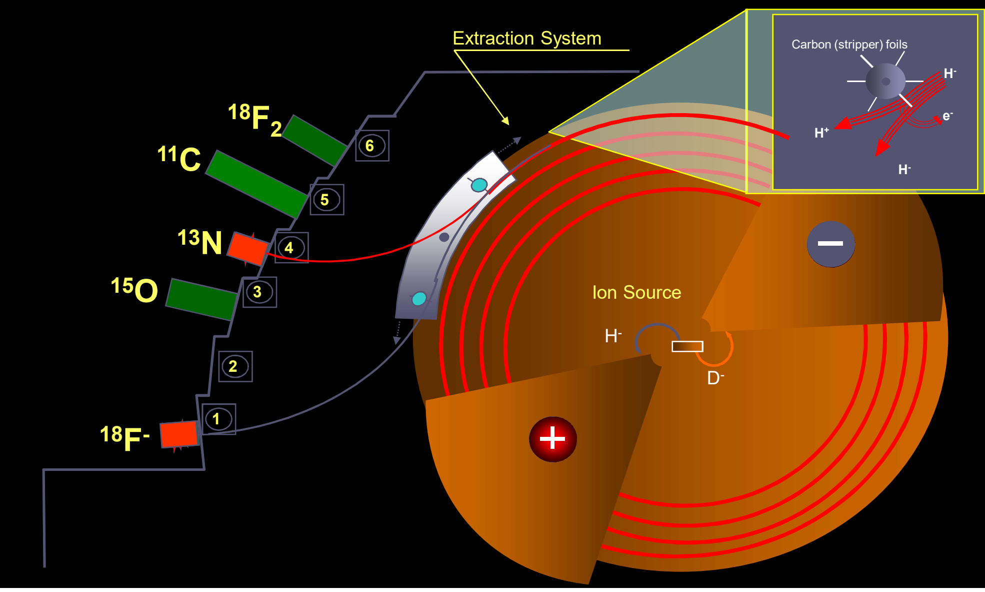
Extraction system

- *The H- beam strikes the thin carbon foil at extraction radius. The negative charged ion will lose two electrons, become positive and bend out from the centre of the cyclotron*
- *This method allows dual beam operation.*
- *The extraction efficiency is about 100%.*

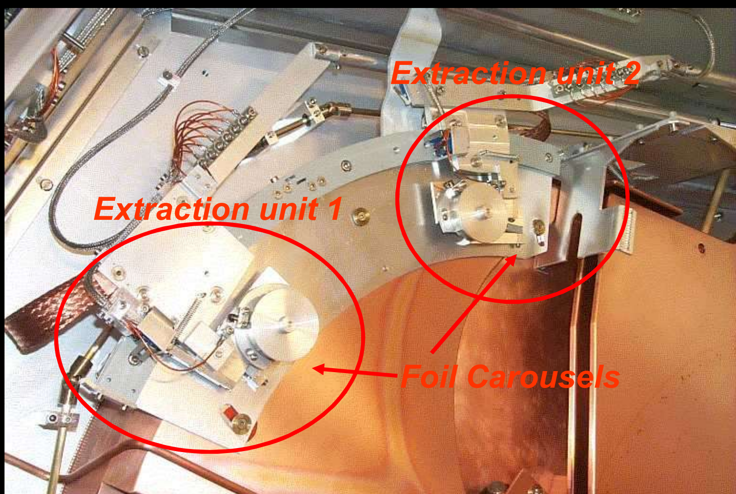
Extraction system



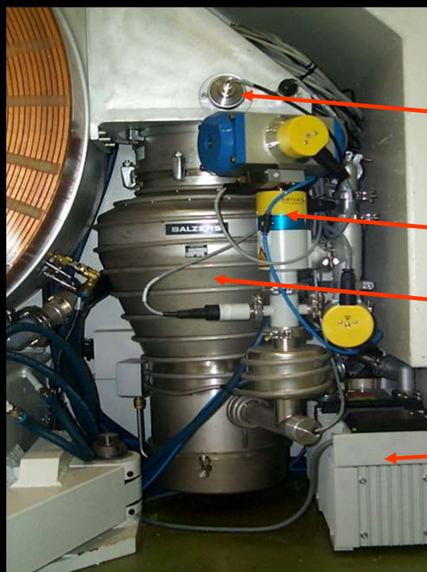
Extraction System



Extraction System



Vacuum system

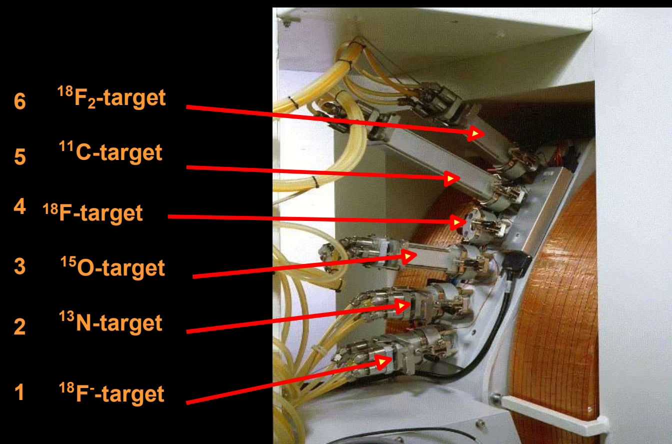


Targets

- Targets are located on the accelerator/cyclotron where the desired isotopes are formed
- The produced high energy particle beam hits the nucleus (within the target) causing a nuclear reaction (transmutation)
- The target material can be gas, liquid or solid The nature of the molecule is determined by the composition of the target material elements (the chemical environment)

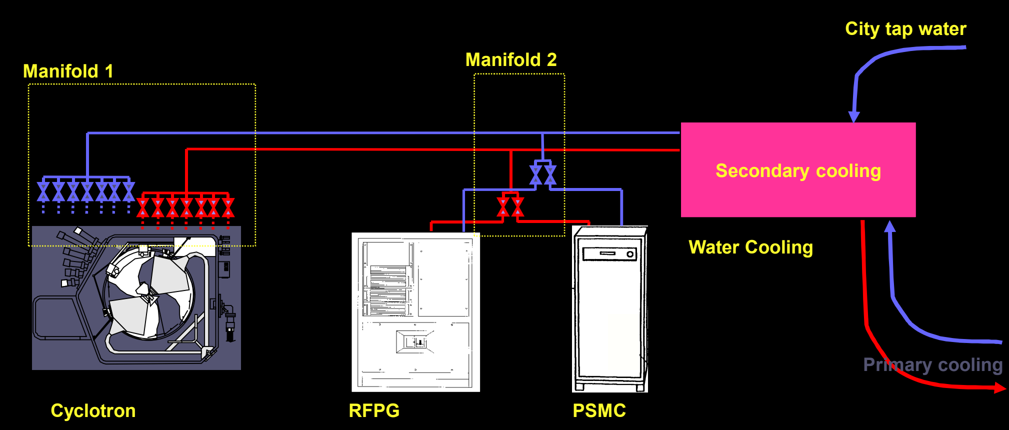
Radioisotope	Half life	Nuclear Reaction	Target Media
Carbon-11	20 min	$^{14}N\ (p,\alpha)\ ^{11}C$	Nitrogen gas + 0.5% oxygen
Nitrogen-13	10 min	$^{16}O\ (p,\alpha)\ ^{13}N$	^{16}O-Water
Oxygen-15	2 min	$^{14}N\ (d,n)\ ^{15}O$	Nitrogen gas + 1% oxygen
Fluoride-18	110 min	$^{18}O\ (p,n)\ ^{18}F$	^{18}O-enriched water
Fluorine-18	110 min	$^{20}Ne\ (d,\alpha)\ ^{18}F$	Neon gas + 0.3% fluorine

Target System

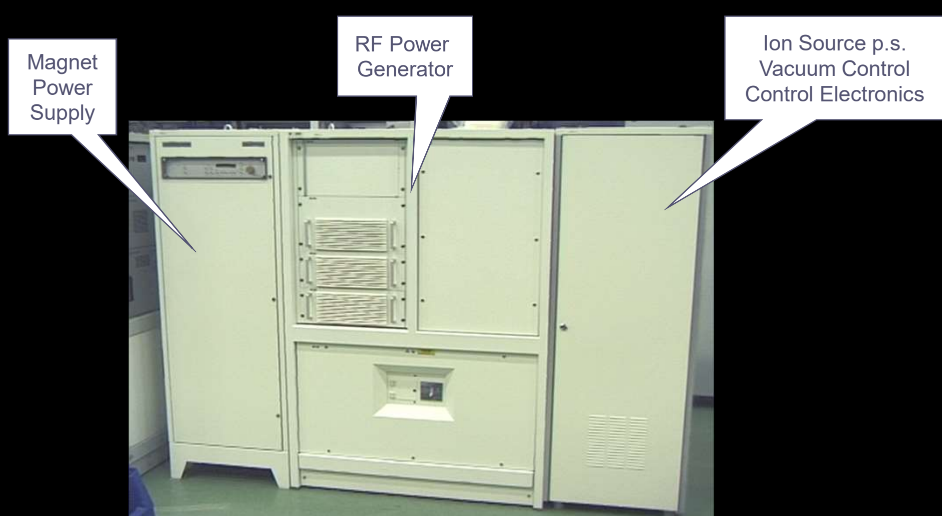


Targets Assembly

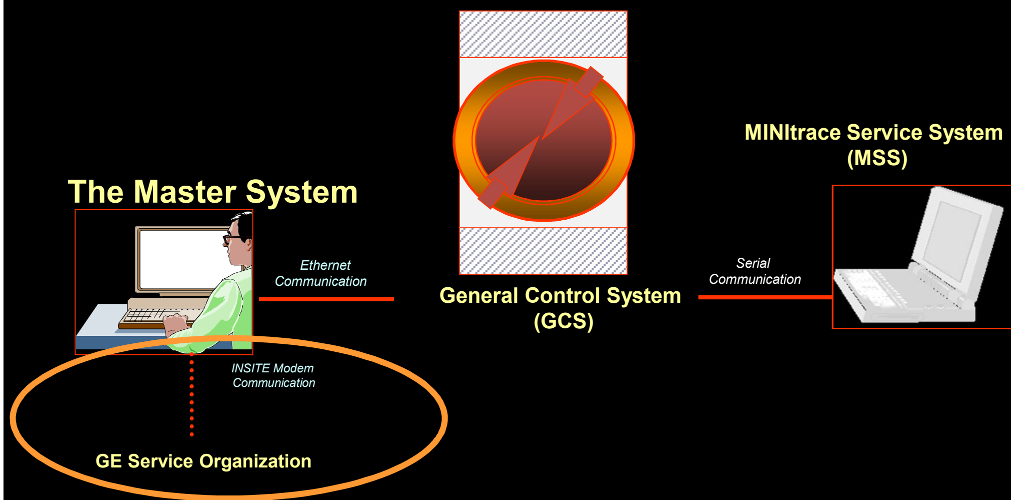
Water cooling system



Electronic Cabinets



Control System



Radiation Sheild

PINLab
PET Instrumentation & Neuroimaging Lab

Planning a Cyclotron Facility

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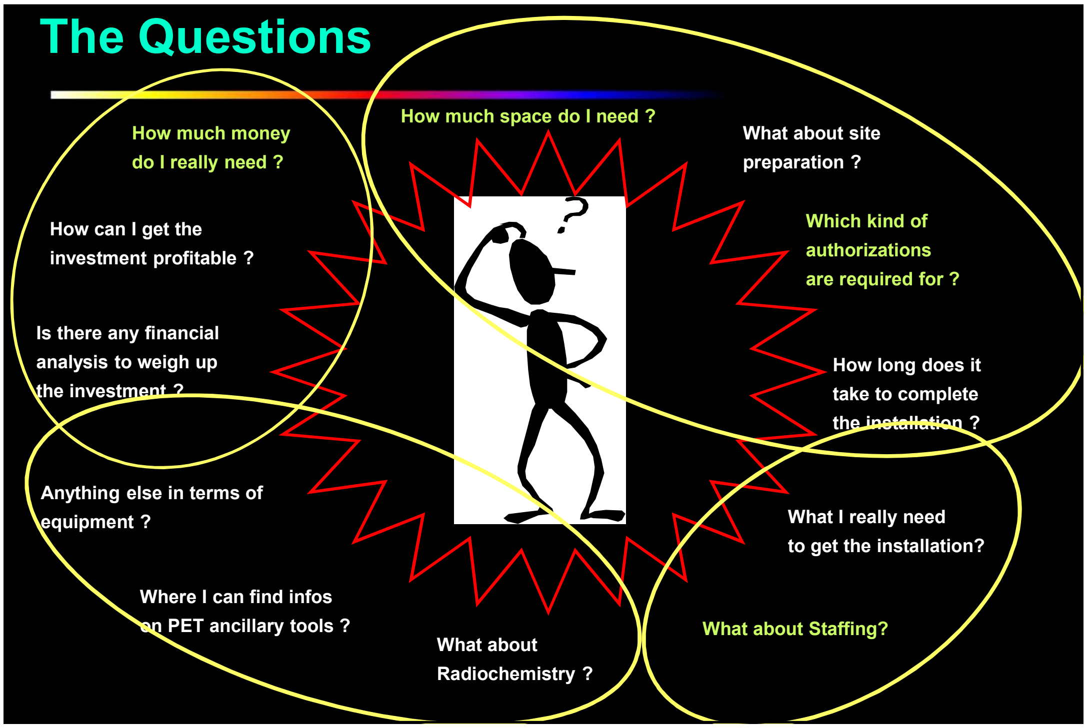
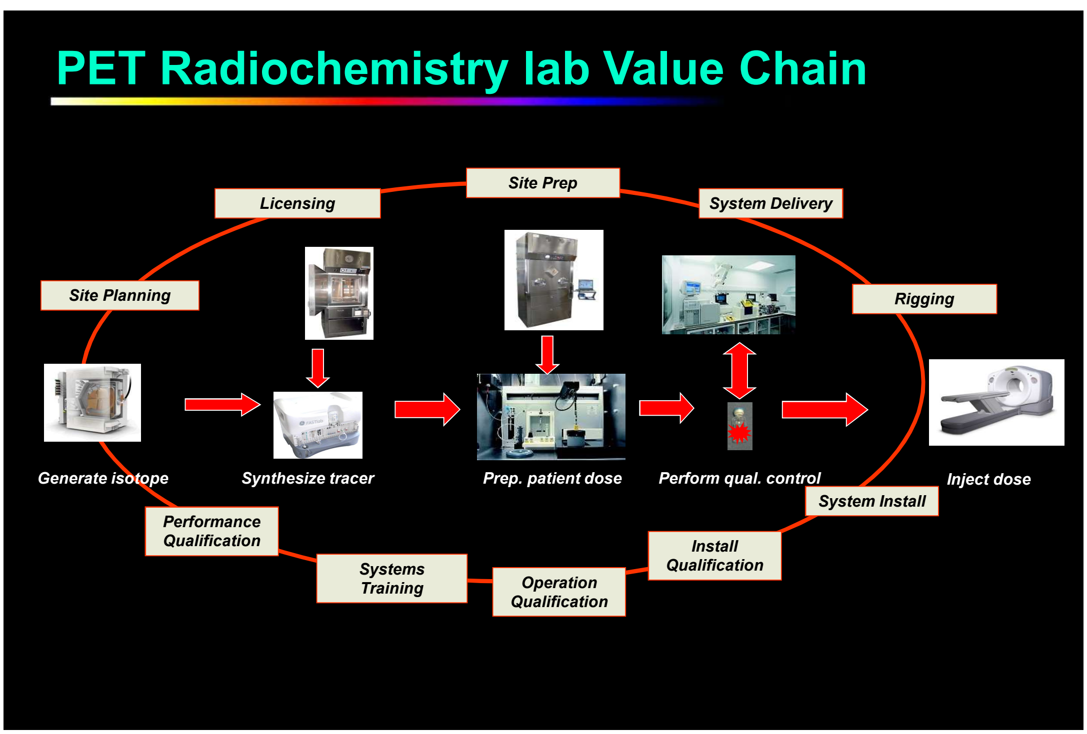
How Difficult is The Project?!!!


The Questions
How much money
do I really need ?
How can I get the
investment profitable ?
Is there any financial
analysis to weigh up
the investment ?
How much space do I need ?
What about site
preparation ?
Which kind of
authorizations
are required for ?
How long does it
take to complete
the installation ?
Anything else in terms of
equipment ?
Where I can find infos
on PET ancillary tools ?
What about
Radiochemistry ?
What I really need
to get the installation?
What about Staffing?


PET Radiochemistry lab Value Chain
Site Prep
Licensing
System Delivery
Site Planning
Rigging
Generate isotope
Synthesize tracer
Prep. patient dose
Perform qual. control
Inject dose
System Install
Performance
Qualification
Systems
Training
Operation
Qualification
Install
Qualification

Qualifying The Site

1 – Clinical Applications	Oncology (90-95% total applications) Oncology + Cardiology Oncology + Cardiology + Neurology
2 – Clinical + Applied Research	Oncology Cardiology Neurology
3 – Research	Tracers Development Physiology and Metabolism
4 – Clinical + FDG Distribution	Clinical Satellite centers
5 – FDG Distribution	FDG (main activity) Pharmaceutical + Industrial Activity

Instrumentation

PET/CT with accessories

Cyclotron with options

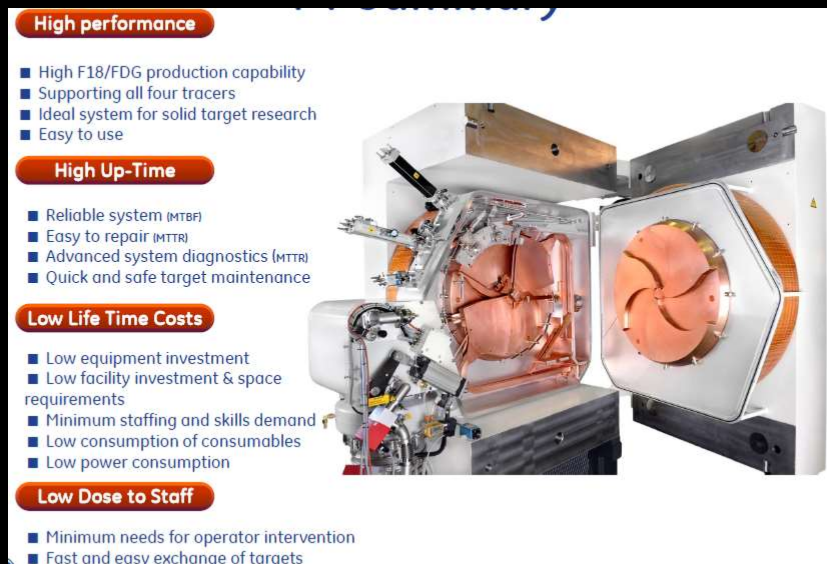
Synthesis Modules based on production demand

QC Tools and Lab Instruments

Hot Cells and Dispensing Units

Radiation Monitoring System

Cyclotron Important Parameters

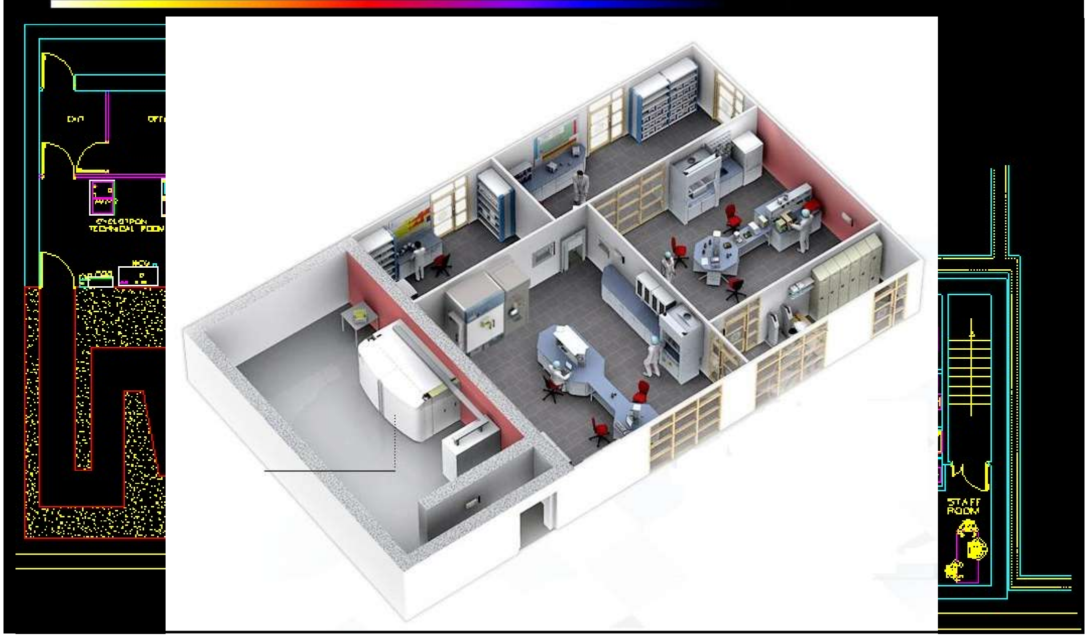


What do we need?

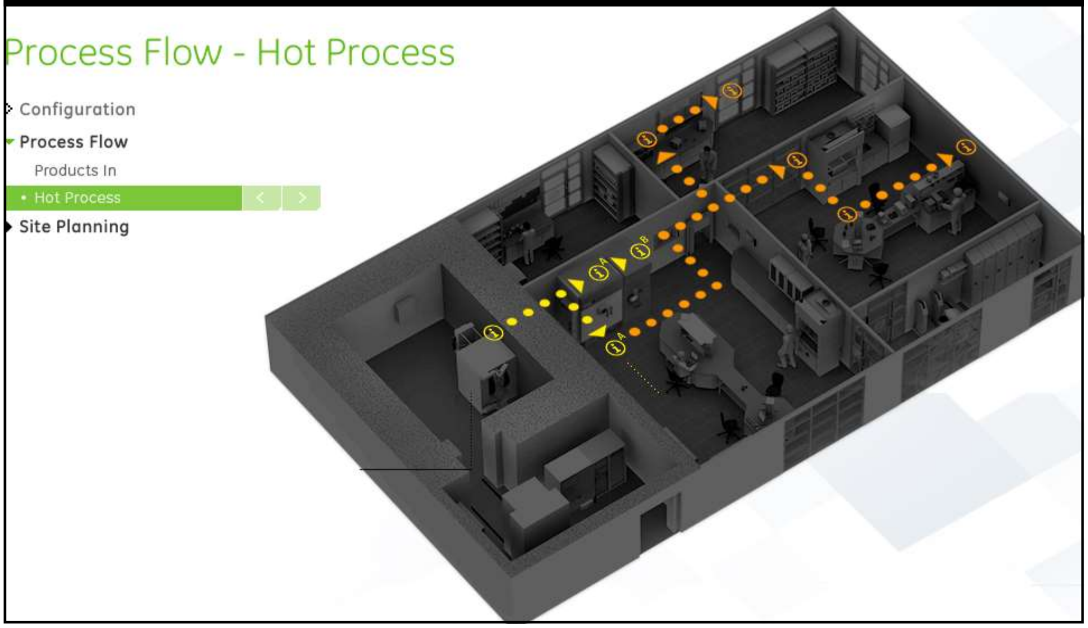
Typical Performance

Radiochemical	Target Material	Bombardment Time	End of Bombardment Yield (EOB)
$^{18}F^-$ Fluoride PETtrace 840 PETtrace 860 PETtrace 880	^{18}O-Water	120 min – dual target	 6500 mCi 10800 mCi 14000 mCi
^{18}F-F_2	Deuteron based Neon gas	60 min	300mCi
^{18}F-F_2	Proton based Method: Two Shoot 1 = $^{18}O_2$ 2 = Ar + F_2	60 min	1800mCi
^{11}C-CO_2	N_2 + 1% O_2	30 min	4500mCi
^{11}C-CO	-	30 min	1500mCi
^{11}C-HCN	-	30 min	1300mCi
^{11}C-CH_4	N_2 + 10% H_2	30 min	1300mCi
^{13}N-NH_3	Distilled Water	30 min	900mCi EOS
^{15}O-O_2	N_2 + 1% O_2	6 min	1200mCi
^{15}O-CO	-	6 min	700mCi
^{15}O-CO_2	-	6 min	700mCi
^{15}O-H_2O	-	6 min	1200mCi

Typical Cyclotron Site Planning



Process Flow in Tracer Production



Site Planning Requirements

Hot Lab

QC Lab

Air Lock

Product In

Product Out

Small Animal Research

Cyclotron Technical Specifications

- Energy of Particle
- Type of Accelerate Particle (Proton and Deuteron)
- Beam Current
- Dual Irradiation Option
- Production Yield (EOB and EOS)
- Research Beam line Option
- Number of Target Port
- Target installation (Ease of Use)
- Dose Load to Operator During target Installation
- Time to Beam on Target
- Ion Source Life Time
- Set Up Time
- Power Consumption
- Up Time in High Beam Current Mode
- Upgradeability
- Reproducibility
- Reliability
- Serviceability

cti + petnet solutions = SIEMENS

CTI Eclipse ST, RD, HP

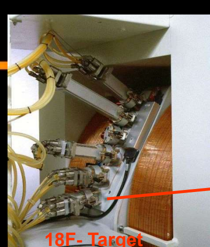
10/5, 18/9

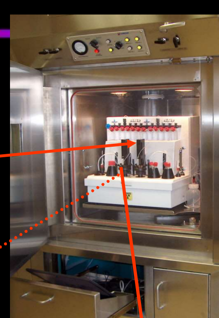
IBA

Eastern Isotopes

FDG Production Cycle

Target Irradiation, (generally referred per hour) → 18F- Production





18F- is automatically transferred in to the synthesis unit →FDG Production

Synthesis is completely automated

A small amount is moved to the QC Lab to check final Quality of the Product

Finally FDG is transferred to the manual (or automatic) dispenser unit

Synthesis Module

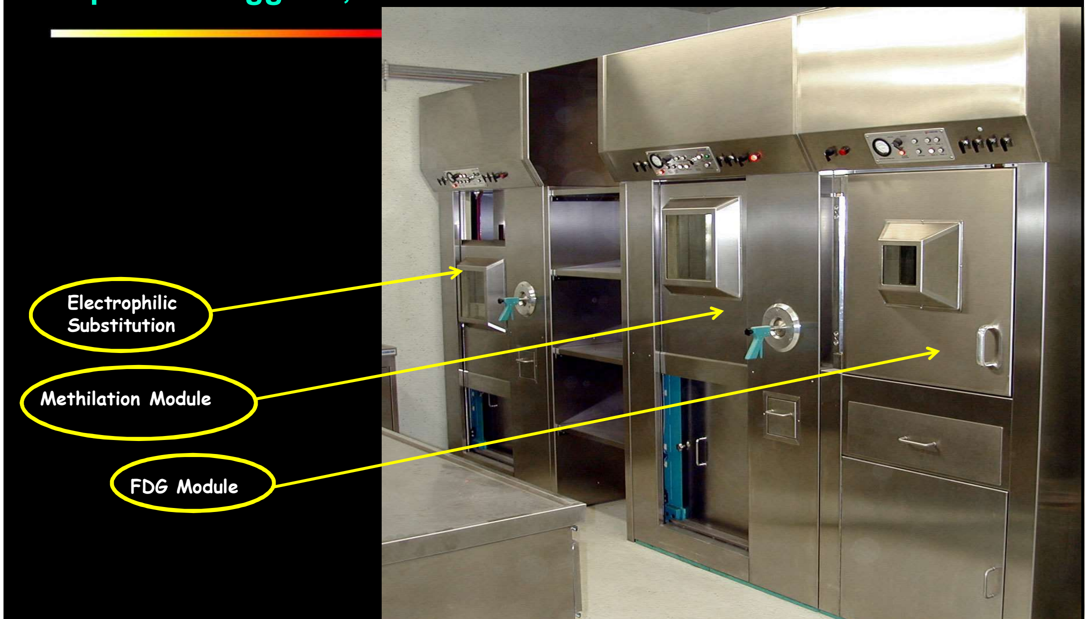
In almost all cases the produced isotope in the target require a chemical transformation to become a usable tracer. This is done in a chemical system (or by a radio chemist by hand).

The high radioactivity require this happen in a protected environment - a hot cell

Hot Cell and Radiation Protection

- Hot cell for Synthesis Modules
- Tungsten shield for syringe
- Shielded container for syringes transportation
- ISOLA WORKBENCH WITH SHELF
- WORKBENCH WITH SINK
- Canister for solid radioactive wastes
- Built-in shields for capillaries and tubes (Cyclotron to Synthesis modules)
- GM for monitoring surface contamination
- Neutron detectior with electrometer
- Hands-Clothes-Feet Monitoring system LEONARDO

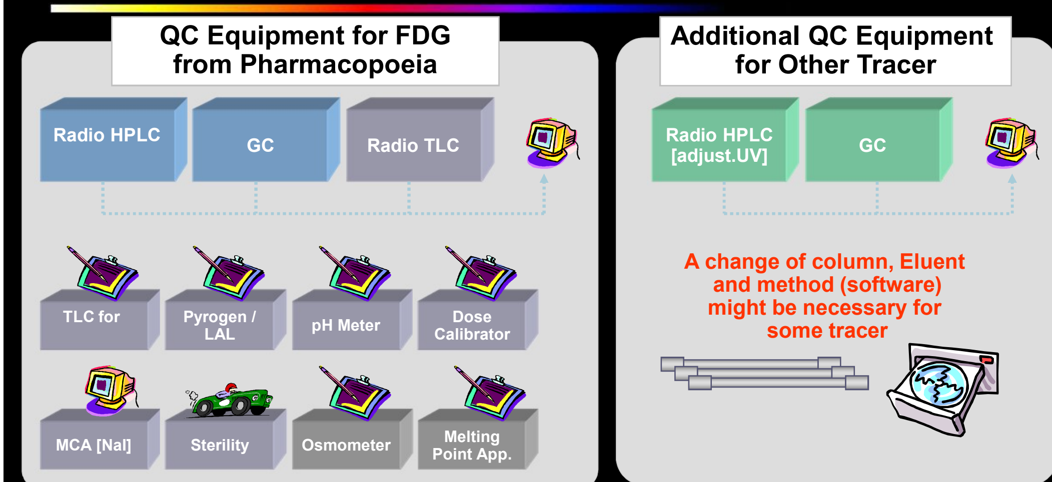
Ospedale Maggiore, Milano



Dispensing Unit

- **Fully Automatic:** Ultra Low Dose to Operator But Expensive
- **Semi Automatic :** Low Dose to Operator Reasonable Price
- **Manual:** More Dose to Operator But Cheaper

Quality Control Equipment



- Equipment dedicated to FDG only; high risk of cross-contamination or damage
- Equipment necessary for FDG, but can be used for other tracer without restriction
- Additional QC equipment necessary for other tracer
- Optional equipment

Computerized test
Manual test, evaluation
External test,

Quality Control Definition

FDG QC Tests Required by USP and EUP	Equipment for EU Pharmacopeia	Equipment for US Pharmacopeia
Endotoxins	LAL Tester	LAL Tester
PH Test	PH Meter	PH Meter
Radio Chemical Purity	HPLC + TLC	TLC
Chemical Purity	HPLC	TLC
Kryptofix test	N/A	N/A
Residual Solvents	GC	GC
Radioactivity	Dose Calibrator	Dose Calibrator
Half-life	Dose Calibrator	Dose Calibrator
Gamma spectrum/Radionuclidic Purity	MCA	MCA
Sterility	Outsource to labs	Outsource to labs
Bubblepoint	Integrity Tester	Integrity Tester
Visual Inspection	N/A	N/A
Particles	N/A	N/A

Chemicals & Reagents for FDG

- Enriched water (cyclotron target material), > 97 purity
- All Chemicals Needed for One FDG Synthesis
- Reagents for FDG Quality Control
- Material for Production of N13, C11 and O15
- All Accessories (Small Hardware) Needed for One FDG Synthesis
- Sterile Kit for Dispenser

Low Cost But Efficient Tracer Production Solution

- Self Shield Cyclotron
- One FDG Synthesizer and one for Spare
- One Single Hot Cell
- Dispensing Unit (Automatic, Semi-Automatic or Manual)
- HPLC, GC and Ph Meter
- Radiation Protection System
- Tungsten Shield and Accessories
- Chemical and Regions for one year FDG Production

Siemens

IBA

Variable and Fixed Costs

VARIABLE COSTS
FDG Production consumables cost
Filming, Archiving, Printing Cost/procedure
Pharmaceuticals, contrast media, ….
Consumables

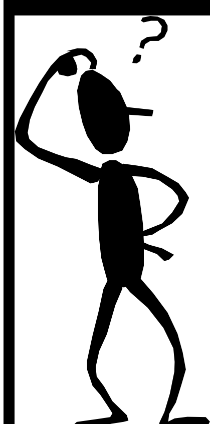
FIXED COSTS
PET/CT Equipment Maintenance
Cyclotron equipment Maintenance
Staffing cost for PET/CT scanner
NM/PET Physicians
Staffing cost for Cyclotron operation
Electricity, Water, Phone & Data costs
Site building/ renewing costs

STAFFING
Physicians
Scanner Operators
Physicists
Admin
Nurses
Cyclotron Operator
Radio Chemist
Radio Pharmacist
Onsite Engineer

Typical Equipment Price

PET/CT	1.4 – 2.4 MUSD (Depending to configuration)
Cyclotron	1.1 – 1.6 MUSD (Depending to configuration)
Synthesis module	250 – 400 KUSD (FDG with hot cell)
QC Equipments	350 – 500 KUSD (for FDG)
Monitoring and Accessories	150 – 350 KUSD (Depending to configuration)
Dispensing Unit	150 – 400 KUSD (Depending to model)
Lab Accessories	150 – 200 KUSD (Depending to configuration)

Summary



How much money do I really need for a PET/CT and Cyclotron facility ? 3.5 – 6.5 MUSD

How much space do I need for a PET/CT and Cyclotron facility ? 600 – 1500 Sq meter

How long does it take to Receive the equipments after ordering? minimum 6 months

How long does it take to complete the installation ? at least 45 days including QC

Which kind of authorizations are required for ? Export License due to the sanctions, MOH License and AEO License


Thank You for Your Kind
Attention