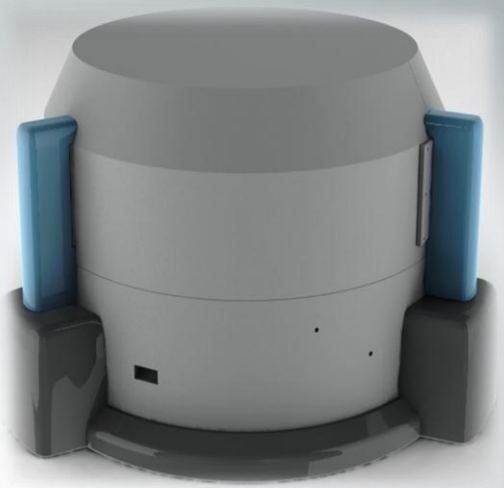
ABT “Dose on Demand” Biomarker Generator



The Vision

Increasing the use and usefulness of PET throughout the world through our small, simple Biomarker Generator

The Principle

Single operator produces individual doses "on demand" verified by automated Quality Control, with a system that can fit next to the PET/CT

SIMPLE SMALL ACCESSIBLE

Advantages

Simplicity - Integrated accelerator, micro-chemistry and quality control with one button operation

Efficiency - Economic, rapid production of individual doses of FDG

Small size - Easier and more cost effective installation

Flexibility - Capable of producing other important [^{18}F]fluoride based research biomarkers

Less Radiation - Lower energy provides lower exposure to environment, public and users, and self shielding eliminates the need for mini-cell containment.

Regulatory Benefits

- Reduced Radiation – Single dose production lowers radiation burden.
- No Dispensing - (or traditional sub-division of batches). A single injectable dose is manufactured in a grade D room.
- Cartridge based chemistry - Dose Synthesis Cards provide a closed and sterile fluid pathway with reaction vessel, sterile filter, and final product vial, in a single use consumable.
- Simple, consistent operation, with minimum operator manipulations.
- Patient injection occurs less than 1 hour from end of synthesis.

ABT Molecular Imaging

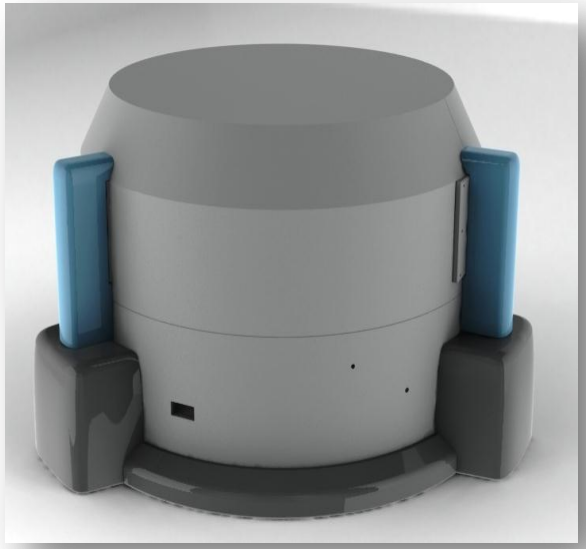
ABT was started in 2006 and is located in Knoxville, Tennessee where clinical PET was developed beginning in the early 1980's. Dr. Ronald Nutt, Chairman of the Board, began ABT with the vision of expanding the utilization of PET throughout the world.

The prototype Biomarker Generator was operational in the factory in early 2009. The production version of the "Dose on Demand" Biomarker Generator became commercially available in 2010.

ABT Biomarker Generator

Compact Accelerator

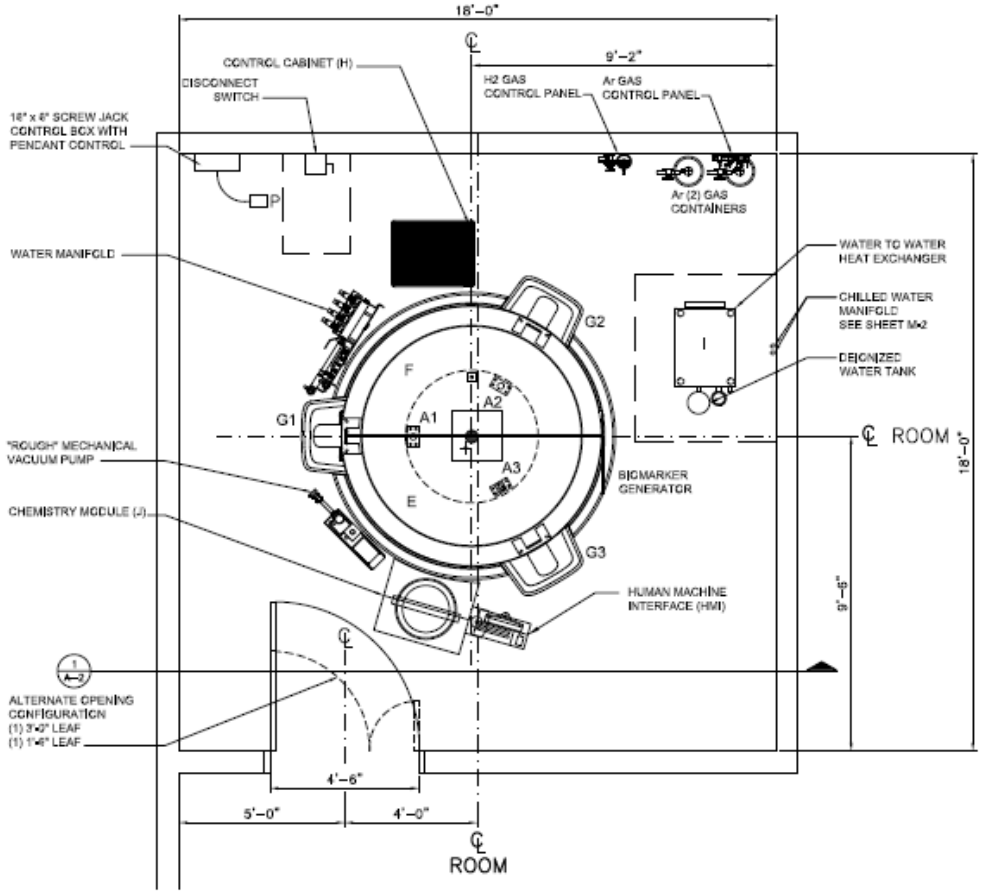
+ Micro-Chemistry/
Automated Quality Control



+ Self-Shielding

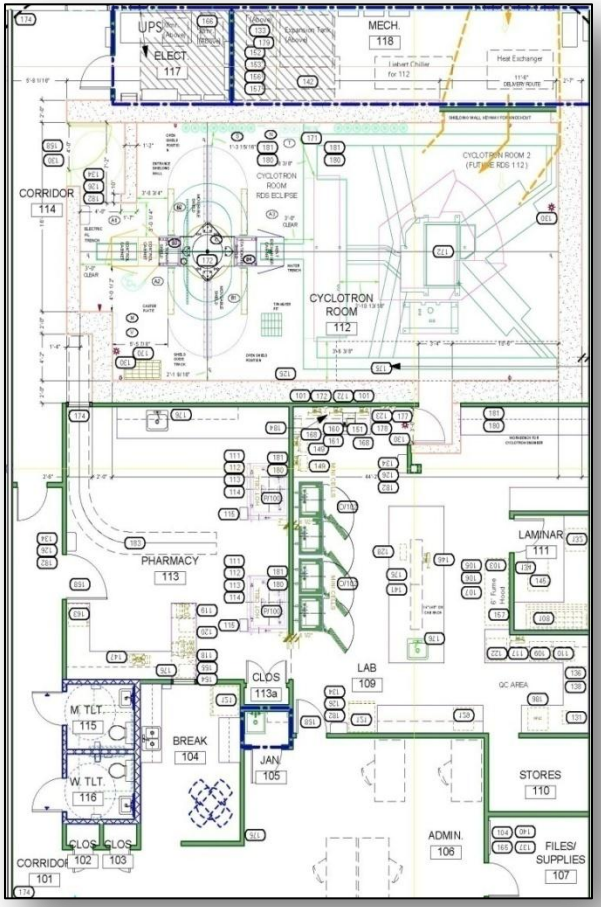
= PET Biomarker Production

ABT Biomarker Generator

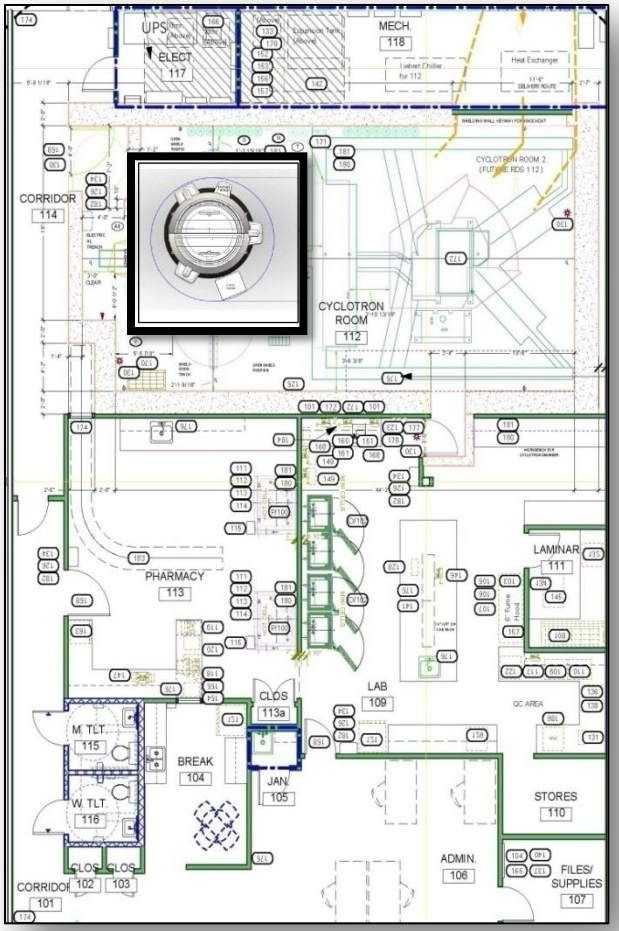


.....in a 30 m² room

Conventional Cyclotron Facility



Biomarker Generator Room



Distribution Solutions

- Requires $4.0-6.0M in working capital
- Requires 5-10 network sites to break-even
- Requires staff of 3-5
- High Radioactivity Regulatory Burden
- Transportation Logistics

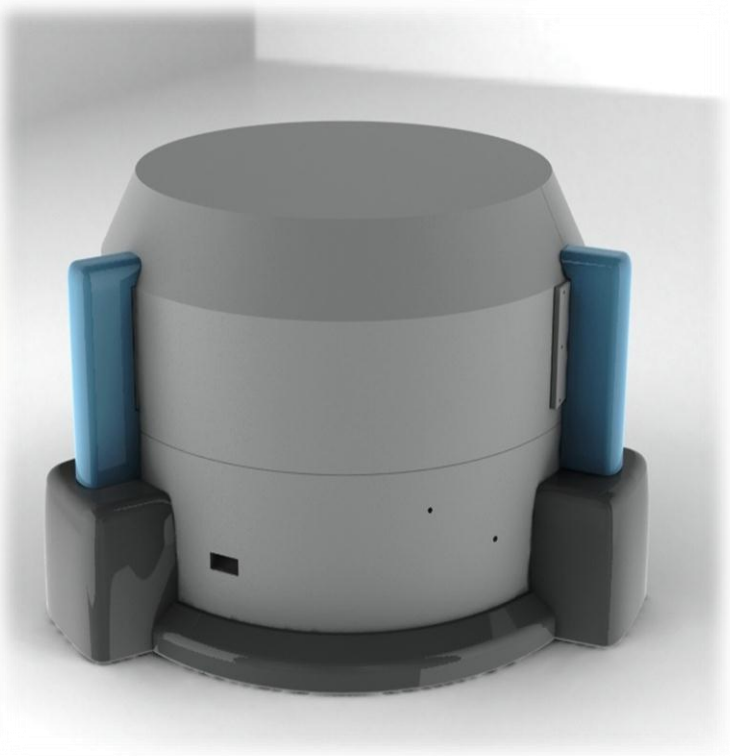
ABT Biomarker Generator

- Low operating costs requirement.
- Fits into small room: 18’ by 18’ (30^2 meters).
- Minimal facility alterations
- FDG dose every 30 minutes
- Flexibility to produce other important [^{18}F]fluoride based research biomarkers. (NaF, FLT, FMISO)
- Fully automated process– one button operation.

Compact Accelerator

- 7.5 MeV Positive Ion Cyclotron
- Internal targets
- F-18, C-11 in development
- Production Rate of 1.0 mCi/min [^{18}F]fluoride
- 1.16 T Magnet
- <5 μA Beam current
- <300 μL Target Volume

Self-Shielding

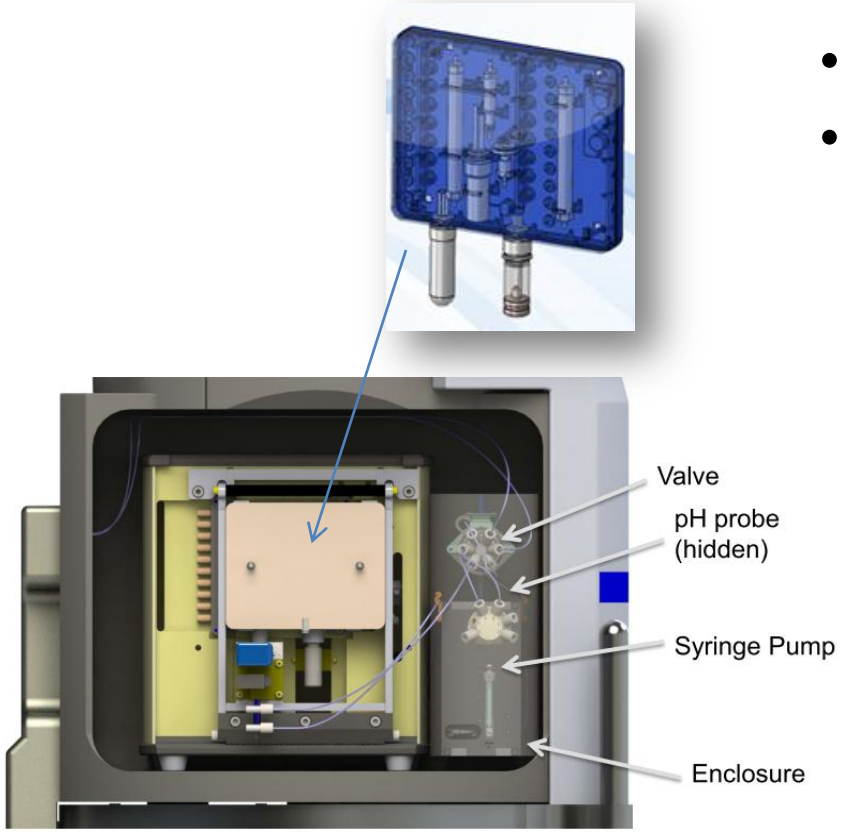


- Steel shell with gamma and neutron shielding
- Rigging through 54” doorway
- Vertical lift for servicing
- Enables operator to work in room while accelerator is operating
- Reduces radiation to less than1 mR/hr at room boundary

Micro-Chemistry Module

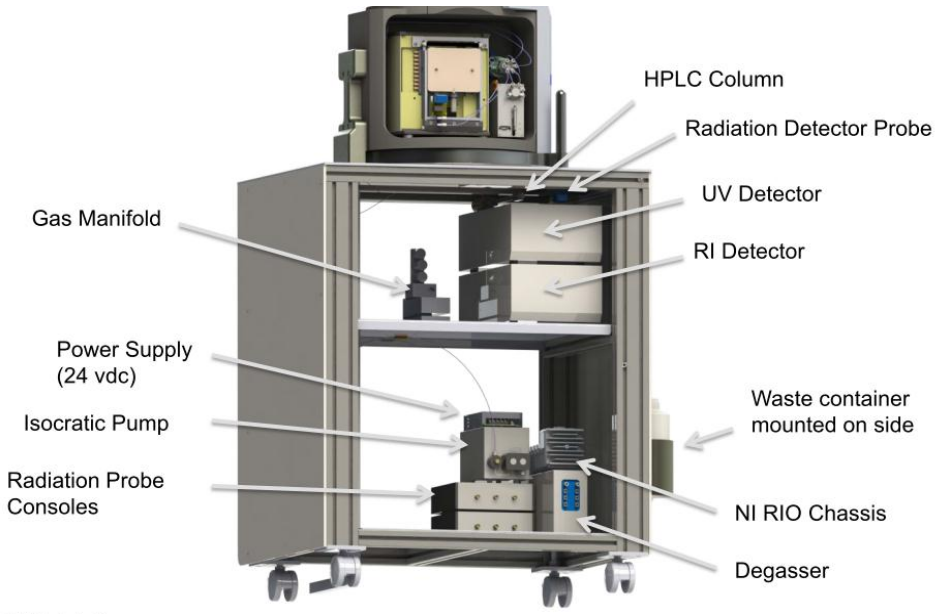
- Closed, cartridge based system
- No dispensing, Grade D room
- Single use card for biomarker synthesis
- Reagent Kit Interface
- Self Shielded - no hot cell required
- Integrated Quality Control

Cartridge Based Chemistry



- Single use Dose Synthesis Card
- Includes:
  - wetted components and delivery lines
  - Purification cartridge
  - 0.22 mm sterile filter
  - Internal waste containment
  - Syringe ready final product vial

Automated Quality Control



- Connected to a micro HPLC with radiation detectors, Refractive Index (RI) and UV/Vis detectors.
- Samples from the Final Product Vial directly.
- Directly measures pH, Radiochemical purity, chemical purity, volatile organic chemicals.
- Loads a sterility sample for further analysis.

USP Release Criteria

	Specification	Conventional QC
Color/Clarity Characterization	Clear/Colorless/Particulate Free	Visual Inspection
Radiochemical Identity	[^{18}F]FDG R_f = ± 10% of FDG standard	(Radio-TLC)
Radiochemical Purity	≥ 95%	(Radio-TLC)
Radionuclidic Identity	$t_{1/2}$ = 105 to 115 min	(Half-Life Determination)
Radionuclidic Purity*	>99.9% F-18	MCA
Chemical Purity K-222	≤ 50 µg/mL	(K-222 Spot Test)
pH	4.5 – 7.5	**(**pH strips)
Residual Solvent Acetonitrile	≤ 0.04% w/w or ≤ 400 ppm	(Gas Chromatography)
Membrane filter integrity	Passes test	(Bubble point test)
Bacterial Endotoxin	< 175 EU Dose	(Endosafe PTS)
Sterility	Sterile	Incubation 14 days

Final Dose Record

ABT Biomarker Generator (BG)
[^{18}F]FDG FINAL PRODUCT QC Test Results

Originator:	Anthony M. Gismis
Process Owner:	Anthony M. Gismis
Mgmt Approval:	
Q&R Approval:	

ABT# 615-99-1622 / Form M-001	
Revision:	A
Supersedes:	
Date Issued:	
Date Effective:	

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Dose Number: MDR-[^{18}F]FDG-_____ Manufacturing Date: _____

Test Description	SOP Reference	Specification	Test Result(s)	Pass / Fail	Performed By/ Date	Supervisor Check By/ Date
Radiochemical ID & Purity (Radio-TLC)	QC-103	Rf > 0.5 Purity ≥ 95%	Rf = _____ Purity = _____%			
Residual Solvent (Gas Chromatography)	QC-104	Acetonitrile < 400 ppm	Acetonitrile = _____ppm			
Radionuclidic ID (Half-Life Test)	QC-105	100-120 minutes	_____ min			
Bacterial Endotoxin (EndoSafe PTS)	QC-100	< 175 EU per dose	Pass Fail (Circle One)			
pH	QC-101	4.5 - 8	_____ pH			
Chemical Purity (K[2.2.2] Color-spot Test)	QC-106	< 50 µg/mL Kryptofix	(> 50 µg/mL) (< 50 µg/mL) Positive Negative (Circle One)			
Chemical Purity (Particulates)	QC-102	Clear, Colorless, No particulates	Pass Fail (Circle One)			
Sterility*	QC-107	Negative/ No Growth	Pass Fail (Circle One)			

*Test Not Required for Preliminary Release

Attach all test results to this QC Form, corresponding to the testing performed for the batch referenced above. Note any outstanding QC Investigations that are outstanding in the comment section below. For all doses, note the volume of each dose and ug in the dose in the comment section below.

Comments:_____

Preliminary Release By: _____ Date: _____
(Signature)

Dose Labels for Manufacturing Sites

Dose Record label:

Fludeoxyglucose [18F] Injection – [^{18}F]FDG (Site name here)

Lot #: Dose Record # Date: Date Time: Time (EOS)

Activity: QC Measure mCi (QC M * 37 MBq) in 2.0 mL @ EOS

Expiration Date: Date Time: EOS + 2 hrs Initials:_____

Diagnostic – For Intravenous Administration Only

Dose Product (Shield) label:

(Site name here) PET Radiopharmacy:

[^{18}F]FDG, [^{18}F]Fludeoxyglucose, 2-deoxy-2-[^{18}F]fluoro-D-glucose in 0.9% saline.

MDR-[^{18}F]FDG _____ Dose Record # _____

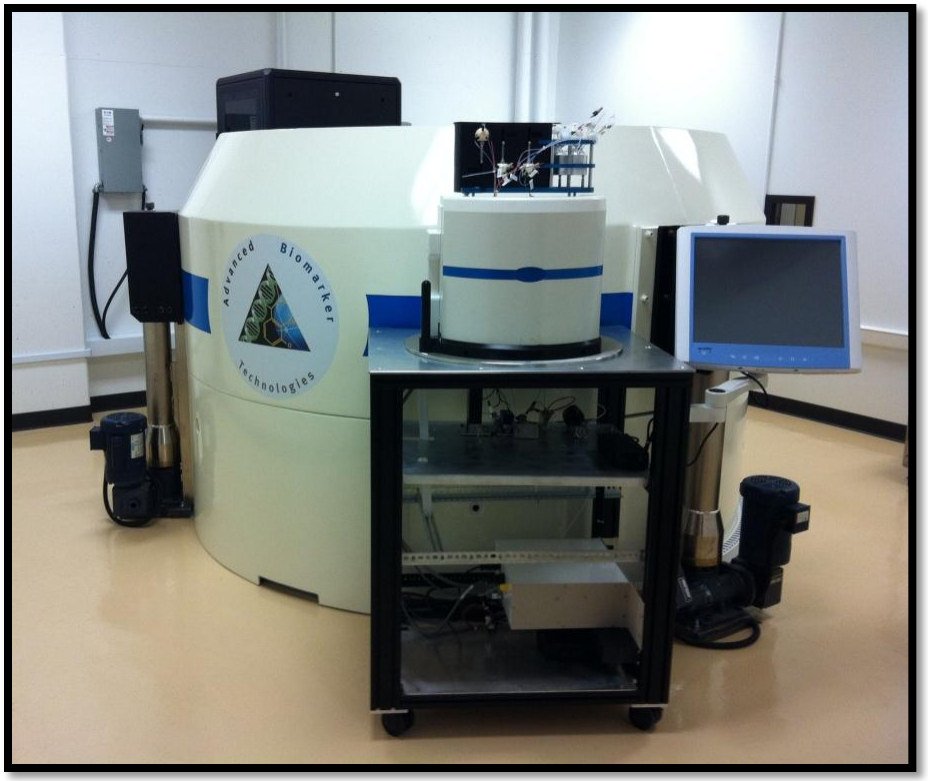
Caution Radioactive Material

Activity: _____ mCi in _____ mL

Calibration Date: _____ Time: ____

This radiopharmaceutical is for intravenous injection by prescription only. Do not use if cloudy or if it contains particulate matter. Expires 2 hours after calibration (EOS). Calculate injection dose from date & time of calibration. $T_{½}$ is 109.8 minutes.

Room Requirements



18’ x 18’ room

54” door entry for equipment entry

2.5 KW HVAC

208V, Single Phase

24T total weight

<1 mR per hour at walls

Summary

Small Size:	- 18’ X 18’ room (30 square meters)
	- Minor facility modifications
Low Power:	- Low radiation burden
	- Low operating costs
	- Self shielded
Simple:	- Push button operation
	- Embedded methods & processes
	- Operated by existing staff
Cost effective:	- Access to advanced biomarkers for 20% of conventional cyclotron investment