MIRION Connect AMERICAS 26

Annual Users' Conference

ADVANCING RADIATION SAFETY. EMPOWERING PROGRESS.

M Resort, Henderson, NV | June 15 – June 18

MIRION TECHNOLOGIES

Advancing Radiation Safety.
Empowering Progress.

Challenges and Opportunities in Radiopharmacies and Cyclotron Facilities
SHS MI Radiopharma

Mandy Dubuc, Pharm D

Radiation Safety Officer/Project Health Physicist

Mirion Connect | Annual Users' Conference 2026

Henderson, NV

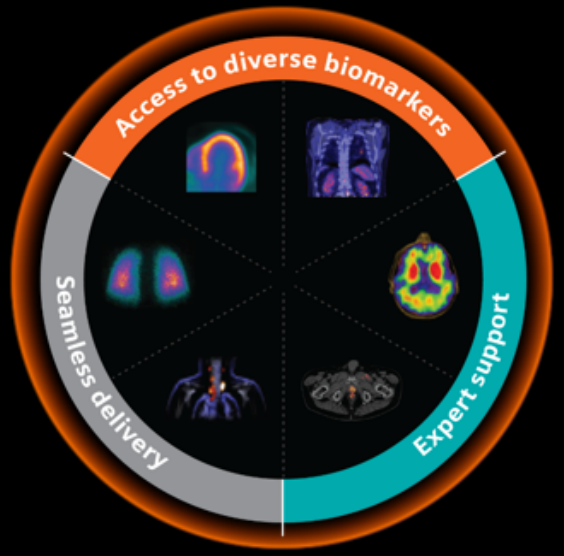
MIRION Connect 26 AMERICAS
Annual Users' Conference

Advancing Radiation Safety.
Empowering Progress.

Global leader in PET radiopharmaceutical manufacturing and distribution

SIEMENS Healthineers

Siemens Healthineers fuels the power of PET by delivering high-quality radiopharmaceuticals to advance patient outcomes



Partnership delivering outcomes

CDMO plus

CDMO of choice for IP holders bringing novel PET radiopharmaceuticals to market

Manufacture and distribute the broadest portfolio of PET radiopharmaceuticals.

- **Alzheimer's disease**
- **Prostate cancer**
- **Breast cancer**
- **Other indications**

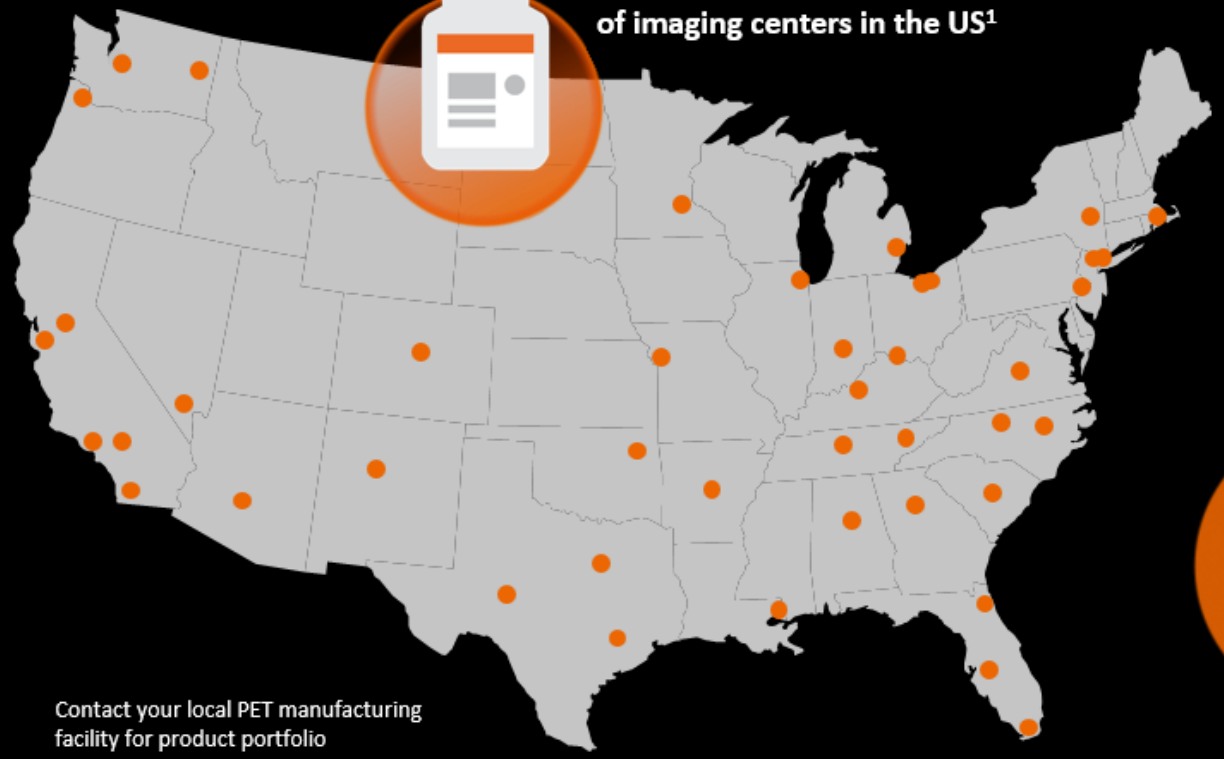
> 2,100,000 doses delivered annually[1]

Broadest network of PET manufacturing facilities for PET imaging in the United States and internationally

[1] FY25 total dose delivery, data on file.
*Not available in all countries.

Largest global PET manufacturing facility network: USA

SIEMENS Healthineers



Contact your local PET manufacturing facility for product portfolio

The largest cyclotron-equipped network of PET manufacturing facilities for PET radiopharmaceuticals in the United States

- **43 US PET manufacturing facilities** with continuous investment
- Over **14.5 million US patient doses** delivered since 2011

More than **1,500,000** patient doses delivered annually in the US[2]

[1] Based on commercially available PET IMV 2025 study results compared with internal data, on file.
[2] FY25 US dose delivery, data on file.

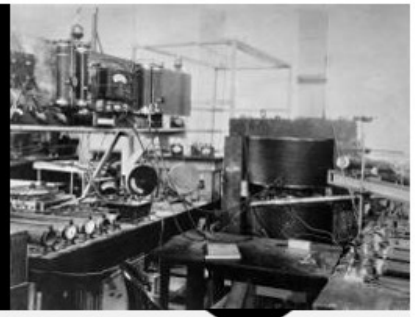
Map source date: April 2026

History of pioneering of modern-day PET

SIEMENS Healthineers

OLD MODEL

Must own a cyclotron to access PET imaging



Cost-prohibitive to **BUY**

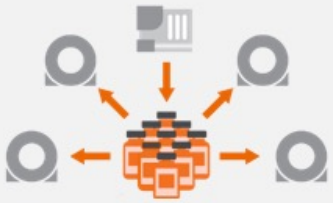
Cost-prohibitive to **HOUSE**

Cost-prohibitive to **OPERATE**

CURRENT MODEL

Facility with a cyclotron delivers doses to multiple* imaging sites

** Fixed delivery distance from manufacturing facility, limited by isotope half-life*



1990

CTI built the 1st commercial distribution site for PET imaging agents in Tampa, Florida

1996

CTI and Syncor found P.E.T.Net Solutions

2002

Advanced Accelerator Applications was founded as a spinoff of CERN (European Organization for Nuclear Research)

2006

ADACAP MI's first cyclotron built in St. Genis-Pouilly, France

Who is Radiopharma?

RADIATION PROTECTION PROGRAM – US

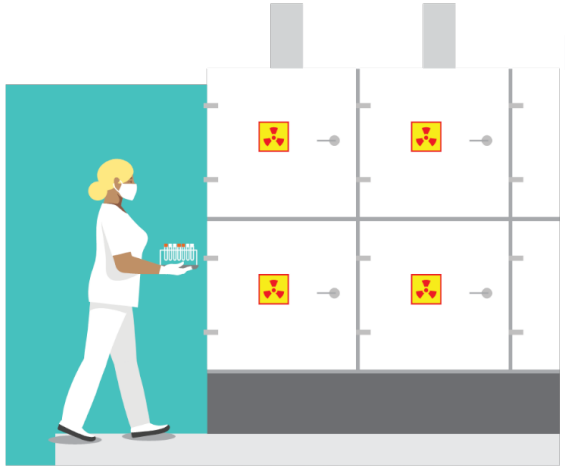
- *~100 RAML & Cyclotron Registrations*
- *86 EHS permits including waste, biohazard, and fire*
- *>30 separate regulatory jurisdictions*
- *cGMP RPP requirements – FDA, BOP, OSHA, EPA, DOT, FFA*
- *Dosimetry Program*
  - *~600 monitored employees*
  - *InstadoseVUE*
  - *Weekly extremity dosimeters*
  - *Electronic Personal Dosimeter (EPD)*

What is it we do?

What is it we do?

Radinouclide Production

- *Cyclotron Produced F-18*
- *Up to 16.5 MeV*



Radiopharmaceutical Manufacturing

- *Chemical Synthesis of Drug*
- *Sterile Manipulation of the Drug*
- *Quality Control Testing*
- *Sterility Testing*

Drug Dispensing & Packaging

- *350+ patient doses dispensed daily per facility*
- *~10-15 mCi per patient dose*
- *FDG batches ~15 Curies*

Delivery To Customer

- *1.5M patient doses every year*
- *Contract Couriers*

Radiation Protection Challenges

- *Radionuclide Production*
- *Radiopharmaceutical Manufacturing*
- *Radiopharmaceutical Dispensing*

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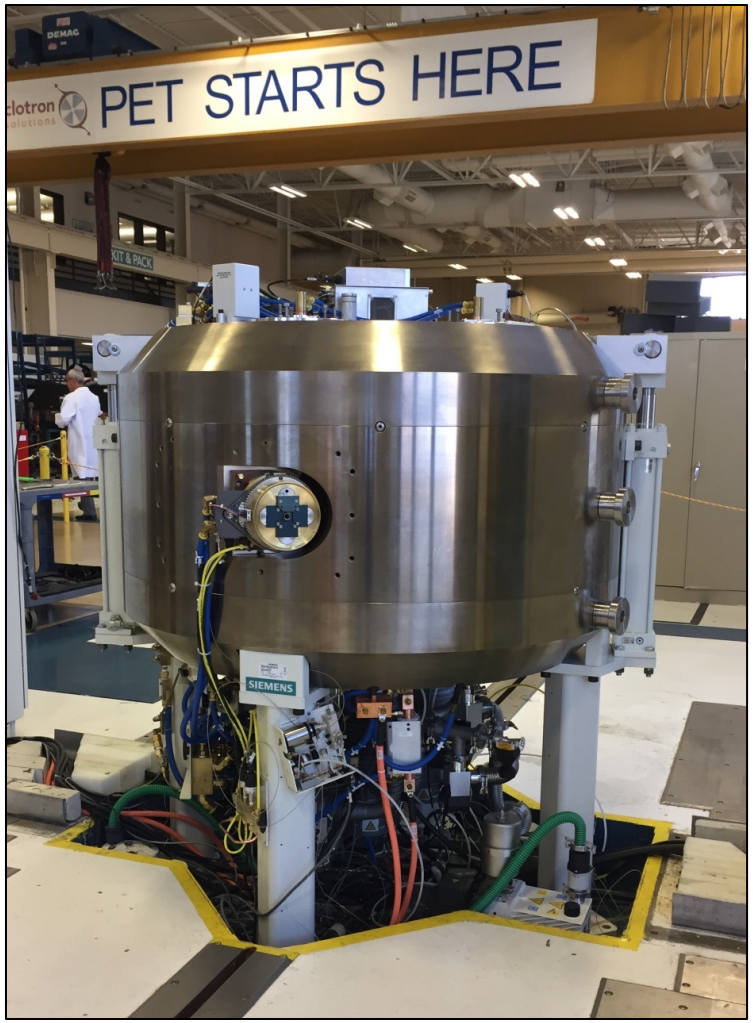
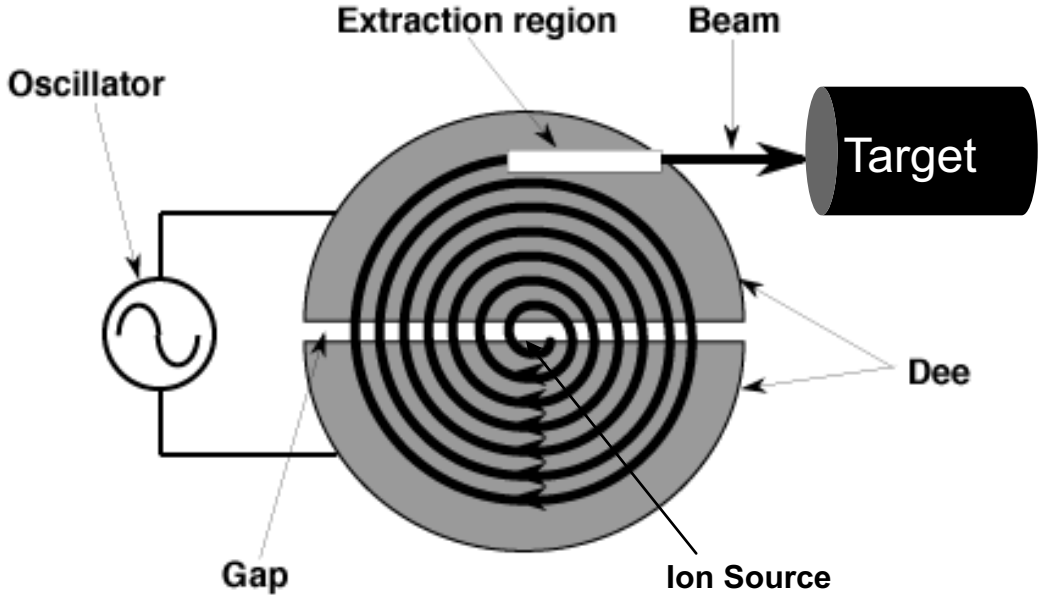
Empowering Progress.

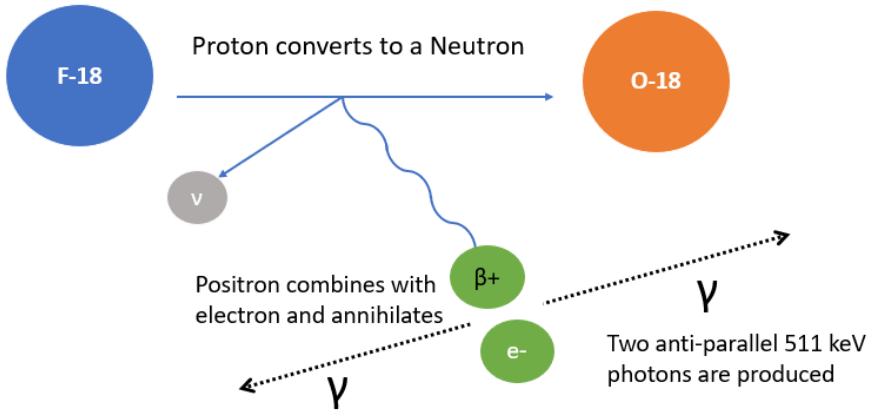
Radionuclide Production

Radionuclide Production



- O^{18} (p, n) F^{18}
- 110-minute half-life
- Beta ~636 keV
- Annihilation reaction





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Radionuclide Production

MATH ON F-18

Gamma dose rate of F-18: 6 R/hr at 1 cm from 1 mCi

** Assume 1 R = 1 rem*

A typical target unload of F-18 can be as much as 10,000 mCi in a 10 mL vial. Average patient dose is 15 mCi.

Direct handling of an unshielded vial for as little as 5 seconds can result in an extremity dose in excess of the annual occupational exposure limit.

$$Gamma\ Dose = 6\ \frac{rem}{hr\ mCi} \times 10{,}000\ mCi \times \frac{1\ hr}{3600\ sec} \times 5\ sec = \mathbf{83\ rem \rightarrow 830\ mSv}$$

Exposure from contamination also a significant concern as even small quantities of material can result in high skin dose.

Uniform deposit of 1 uCi per cm2 = skin dose of **7200 mrem/hr**

Radionuclide Production

SIEMENS ECLIPSE RDS

- *11 MeV Proton Beam Energy*
- *120 uA Beam Current*
- *Tantalum Targets*
- *1 Ci F^{18} in a 15-minute run*
- *Maintained under negative pressure*

***F-18 is volatile*

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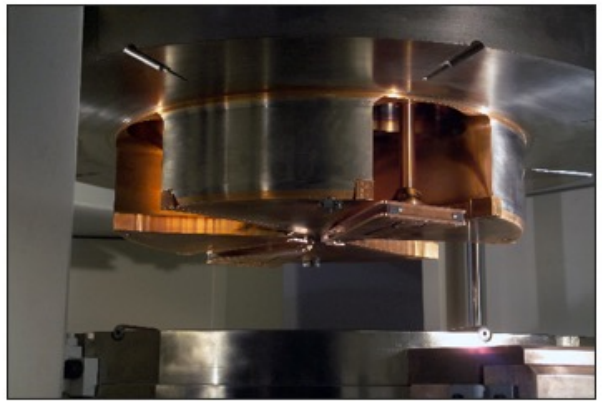
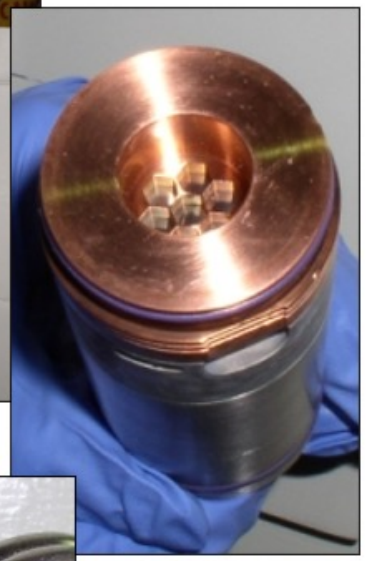
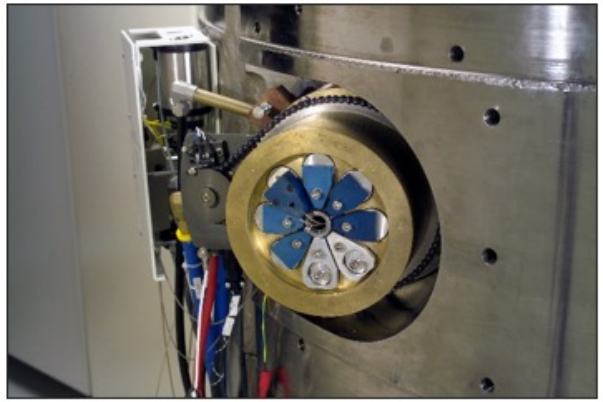
Radionuclide Production

SIEMENS ECLIPSE RDS

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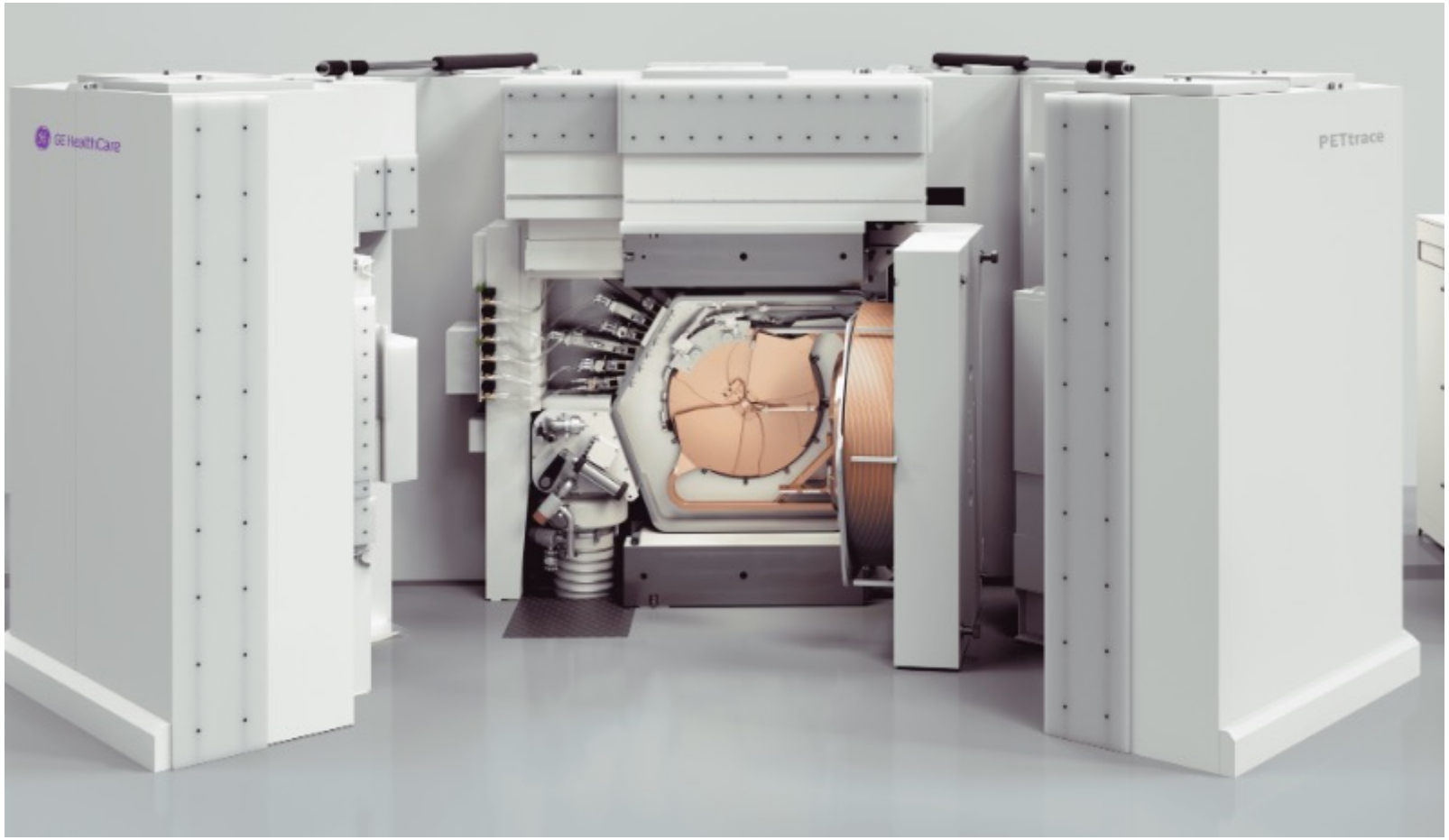
Radionuclide Production

GE PETTRACE 800

- *16.5 MeV Proton Beam Energy*
- *160 uA Beam Current*
- *Shielded Niobium Targets*
- *17.5 Ci F^{18} in a 2hr run*
- *Maintained under negative pressure*
- *More N-13 production vs Eclipse*



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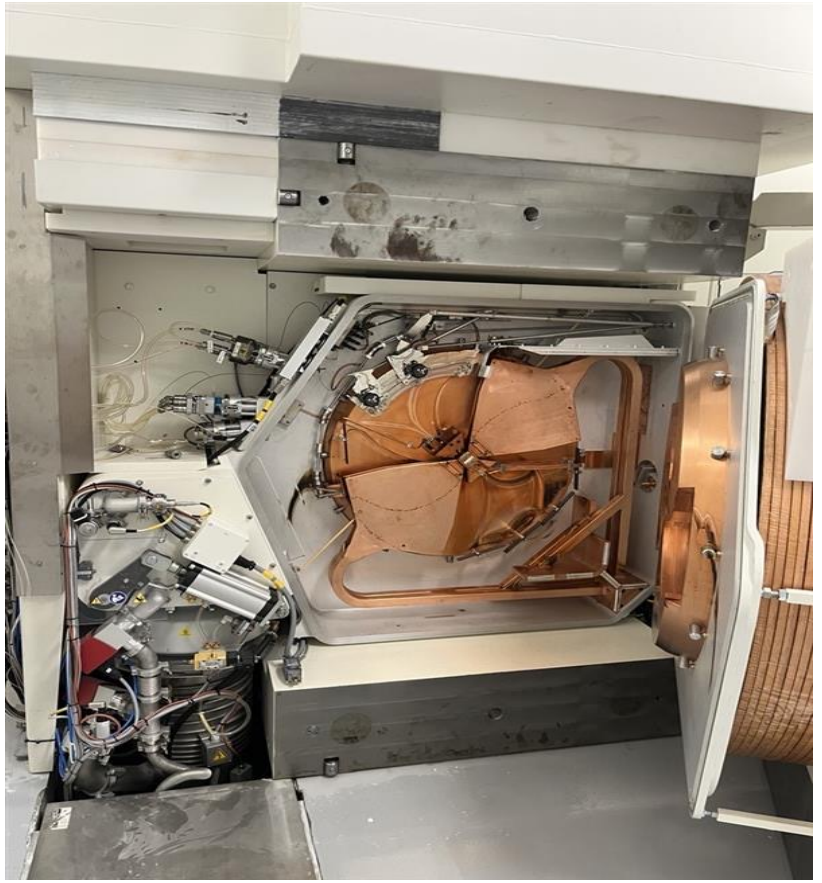
Radionuclide Production

GE PETTRACE 800



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Radionuclide Production

RADIATION PROTECTION CHALLENGES

Havar															
Element	Naturally-Occurring Isotope		Weighted Amount (%)	Activation Reaction	Activation Product	Half Life	Half-life in hours	Cross Section (mb)	Decay Mode	TTY (mCi/uA hr, 25 u of Havar)	TTY (mCi/uA at sat, 25 u of Havar)	activity produced per run (mCi)	activity 3 hours later (mCi)	activity 24 hours later (mCi)
Cobalt	59	100%	42.00%	(p,n)	Ni-59	8e4 y	7.01E+08	400		2.08E-08		0.0	0.00	0.000
42%														
Chromium	50	4%	0.80%	NA	NA	NA	NA	NA						
20%	52	84%	16.80%	(p,n)	**Mn-52m**	21 m	3.50E-01	370	EC, Beta		5.74E+00	**337.8**	**0.89**	0.000
	52	84%	16.80%	(p,n)	**Mn-52g**	5.6 d	1.34E+02	80	EC, Beta	7.24E-03		**0.9**	**0.86**	**0.768**
	53	10%	2.00%	(p,n)	Mn-53	2e6 y	1.75E+10	200	NA					
	54	2%	0.40%	(p,n)	Mn-54	312 d	7.49E+03	100	EC	3.13E-05		0.0	0.00	**0.004**
Iron	54	6%	1.08%	NA	NA	NA	NA	NA						
18%	56	91%	16.38%	(p,n)	**Co-56**	77 d	1.85E+03	450	EC, Beta	1.75E-03		**0.2**	**0.21**	**0.208**
	57	2%	0.36%	(p,n)	Co-57	272 d	6.53E+03	400	EC	2.16E-05		0.0	0.00	**0.003**
Nickel	58	68%	8.84%	(p,a)	**Co-55**	17.5 h	1.75E+01	11	EC, Beta	4.23E-03		**0.5**	**0.45**	**0.196**
13%	60	26%	3.38%	(p,a)	Co-57	272 d	6.53E+03	11	EC	9.77E-06		0.0	0.00	**0.001**
	62	4%	0.52%	(p,n)	**Cu-62**	10 m	1.67E-01	770	Beta		3.10E-01	**18.6**	0.00	0.000
Tungsten	182	27%	0.81%	(p,n)	Re-182	2.3 d	5.52E+01	NA	EC					
3%	183	14%	0.42%	(p,n)	Re-183	70 d	1.68E+03	NA	EC					
	184	31%	0.93%	(p,n)	Re-184	38 d	9.12E+02	NA	EC					
	186	28%	0.84%	(p,n)	Re-186	3.8 d	9.12E+01	NA	Beta					
Manganese	55	100%	2.00%	(p,n)	Fe-55	2.7 y	2.37E+04	NA	EC					
2%														
Molybdenum	92	15%	0.30%	NA	NA	NA	NA	NA	NA					
2%	94	9%	0.18%	(p,n)	**Tc-94m**	53 m	8.83E-01	430	EC, Beta		3.59E-02	**1.7**	**0.16**	0.000
	94	9%	0.18%	(p,n)	Tc-94g	293 m	4.88E+00	90	EC, Beta		7.91E-03	**0.1**	**0.08**	**0.004**
	95	16%	0.32%	(p,n)	Tc-95m	61 d	1.46E+03	280	EC	1.97E-05		0.0	0.00	**0.002**
	95	16%	0.32%	(p,n)	**Tc-95g**	20 h	2.00E+01	700	EC		9.87E-02	**0.4**	**0.36**	**0.173**
	96	17%	0.34%	(p,n)	**Tc-96m**	52 m	8.67E-01	1000	EC		1.55E-01	**7.4**	**0.67**	0.000
	97	10%	0.20%	(p,n)	Tc-97	3e6 y	2.63E+10	NA	NA					
	98	24%	0.48%	(p,n)	Tc-98	4e6 y	3.50E+10	NA	NA					
	100	10%	0.20%	NA	NA	17 s	4.72E-03	NA	NA					
Total			99.58%									**367.7**	**3.68**	**1.358**

Table 9: Havar activation products

APPENDIX B: Secondary Neutron Activation Products

Table 8 lists a number of pertinent neutron activation reactions for reference.

Table 8: Neutron Activation Reactions

Element	Component	Reaction	Product	Half-Life	Gamma Energy MeV
Copper	Magnet Coils	^{63}Cu (n, a)	Cobalt 60	5.27 yr	1.15. 1.33
Copper	Magnet Coils	^{63}Cu (n, g)	Copper 64	12 hr	8β
Iron	Magnet Yoke	^{54}Fe (n, p)	Manganese 54	312 day	.835
Iron	Magnet Yoke	^{56}Fe (n, a)	Manganese 56	2.58 hr	.847
Aluminum	Vacuum Tank Concrete	^{27}Al (n, a)	Sodium 24	15 hr	2.75
Aluminum	Vacuum Tank Concrete	^{27}Al (n, p)	Magnesium 27	9.5 month	.844
Silicon	Concrete	^{28}Si (n, p)	Aluminum 28	2.25 month	1.78
Sodium	Concrete	^{23}Na (n, g)	Sodium 24	15 hr	2.75
Antimony	Lead Shielding	^{121}Sb (n, g)	Antimony 122	2.7 day	.56
Antimony	Lead Shielding	^{123}Sb (n, g)	Antimony 124	60 day	.6, .7, 1.7

Radionuclide Production

RADIATION PROTECTION CHALLENGES

- *Cyclotron Break- Fix & Repair*
- *Cyclotron Routine Preventative Maintenance*
- *High effluent releases*
- *Waste Management – Solid & Mixed Liquid Waste*

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Radiopharmaceutical Manufacturing

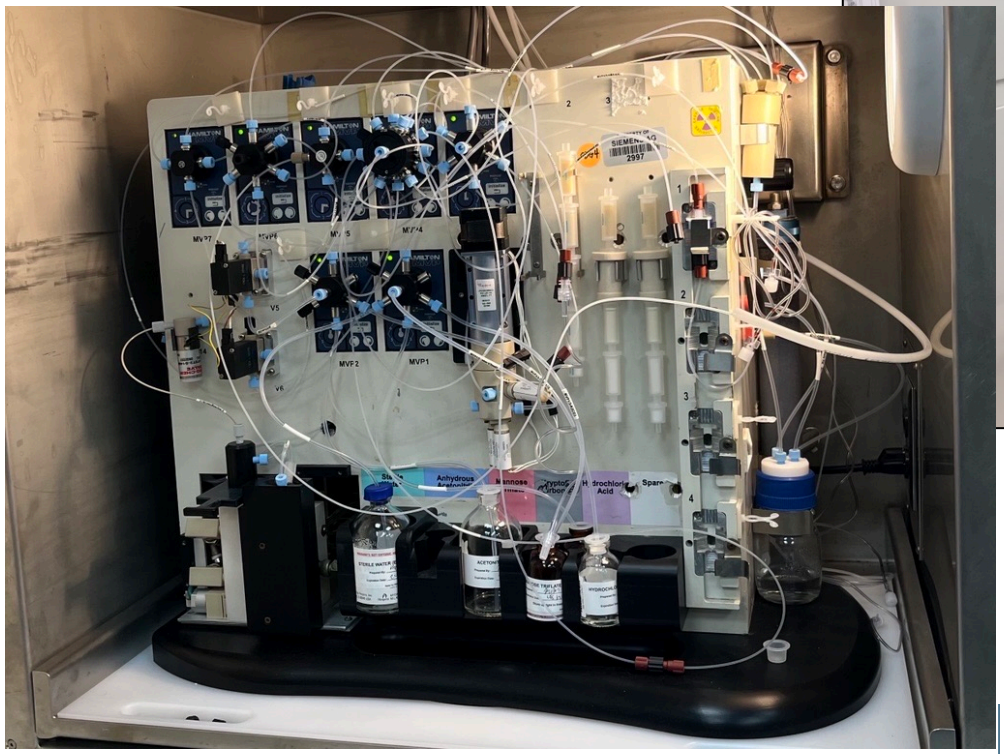
Radiopharmaceutical Manufacturing

Chemical Synthesis of Drug

- *Shielded automated chemistry module, known as a mini-cell.*
- *Maintained under negative pressure to the surrounding room.*
- *Door must be closed prior to delivery of material from the cyclotron.*

Sterile Manipulation of the Drug

- *Remote manipulation of FPV in HC*
- *Filtration, dilution, sterility testing*



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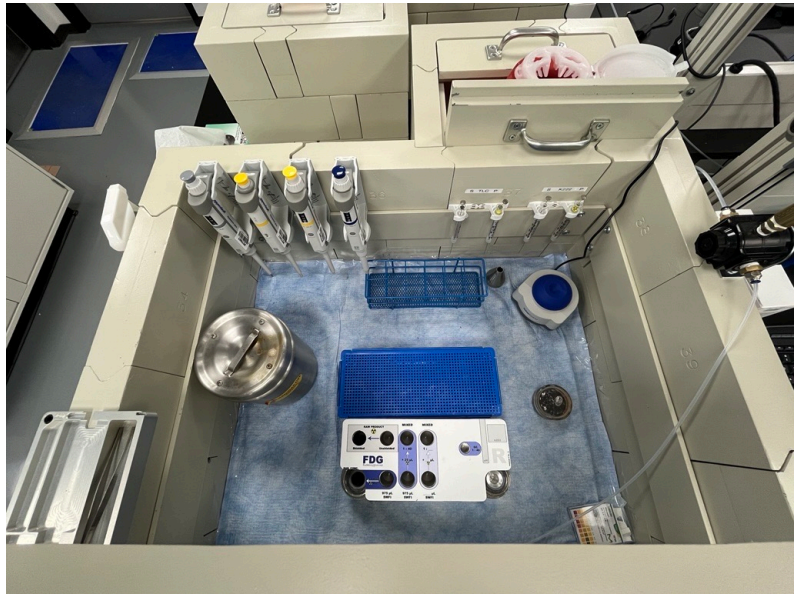
Radiopharmaceutical Manufacturing

Quality Control Testing

- *Each batch tested for radionuclide purity, chemical composition, pH, and other FDA/BOP requirements*
- *Small aliquots handled directly, typically dilute concentrations*
- *Handling performed behind an L-block to minimize whole-body exposure*



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Radiopharmaceutical Manufacturing

RADIATION PROTECTION CHALLENGES

- *Manual QC sample manipulations*
- *Chemistry intervention into mini cells*
- *Residual F-18 and long-lived radionuclides on chemistry components*
- *High background is difficult to differentiate contamination during survey*
- *High Effluent Releases*
- *Waste Management – Solid & Mixed Liquid Waste*

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Radiopharmaceutical Dispensing & Packaging

Radiopharmaceutical Dispensing & Packaging

- *Shielded dose dispensing isolator, known as a hot cell.*
- *Maintained under negative pressure to the surrounding room.*
- *Remote manipulator used by pharmacists to draw individual patient doses per prescription.*
- *Side door opens to withdraw shielded syringes*

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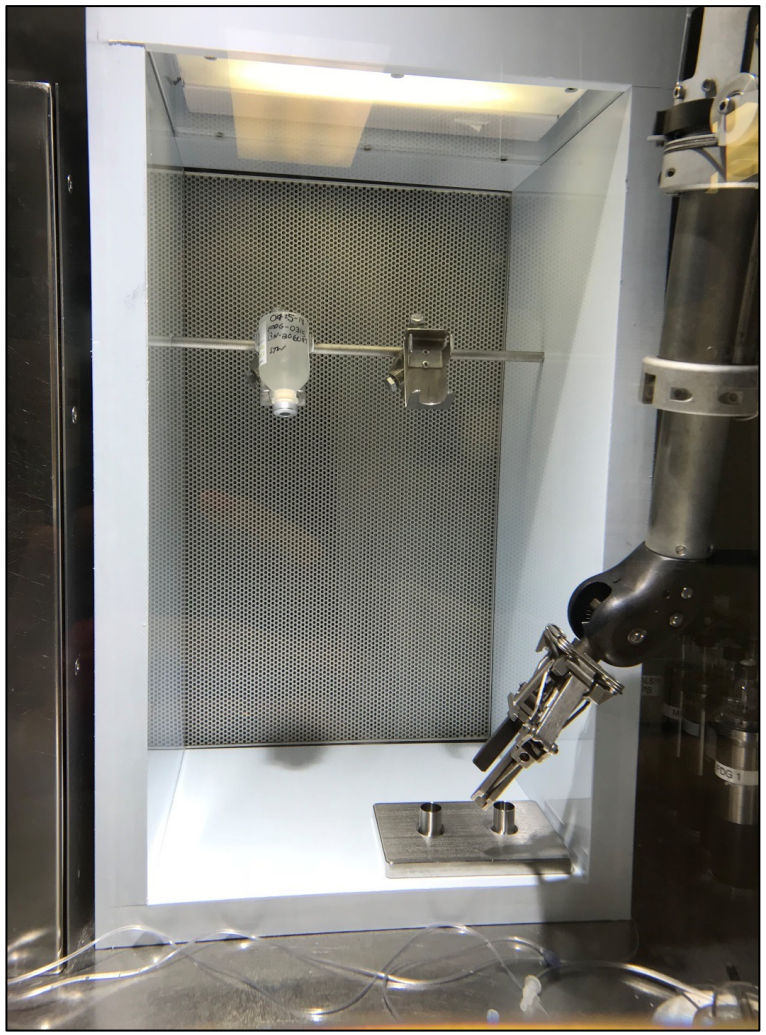
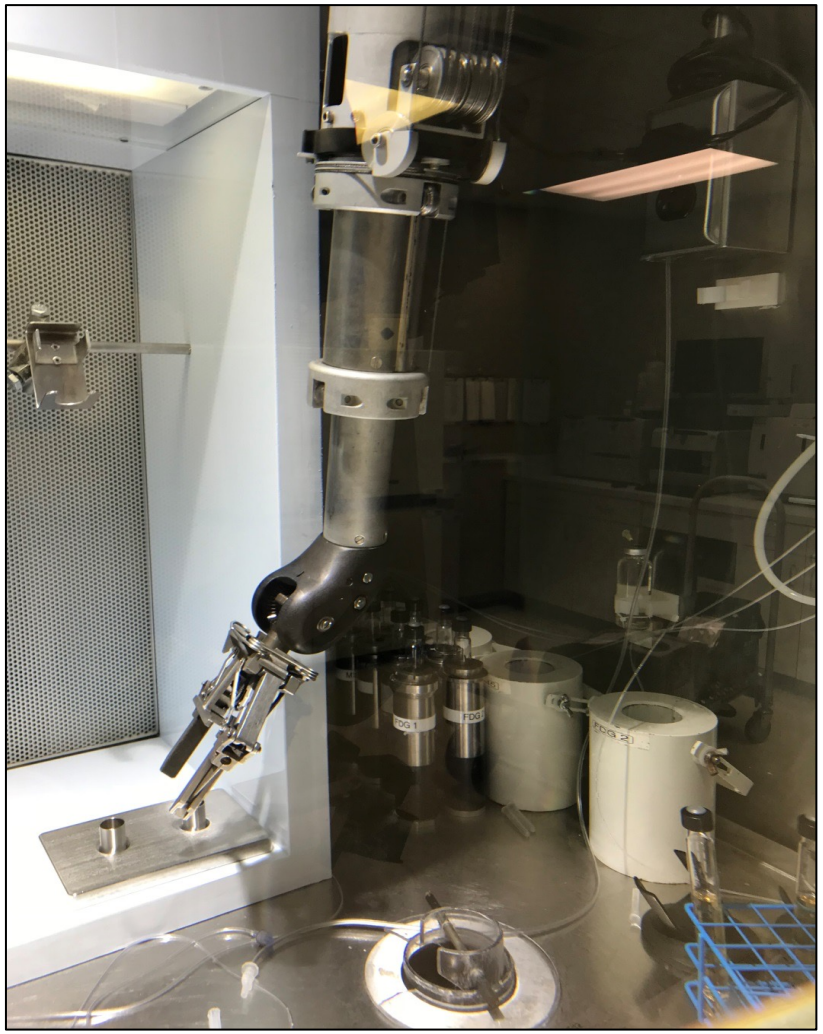
Radiopharmaceutical Dispensing & Packaging



Doses drawn remotely using manipulator arms inside a small ISO-5 laminar flow hood.

Activity determined with a dose calibrator based on concentration and prescribed dose at injection time.

Localized shielding used in the hot cell during shielded syringe removal to protect staff.



Radiopharmaceutical Dispensing & Packaging

- *Shielded syringe containers, known as pigs.*
- *Pigs are handled remotely (to the extent possible) and placed into shielded Type A shipping containers.*
- *Typically shipped as Yellow II.*
- *1.5M patient doses annually*
- *350+ doses daily future is* **600**

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Radiopharmaceutical Dispensing & Packaging

RADIATION PROTECTION CHALLENGES

- *Manual transfer of high-activity doses from Hot Cell to DOT case*
- *Hot Cell break/fix*
- *Residual F-18 during removal*
- *Package surveys in high-background areas*
- *Case buildup at some sites*
- *No roller track*
- *Challenges meeting MDA limits*

Opportunities for the Future

Opportunities for the Future

DosiServ

- *Dose management with DMC 3000 dosimeters and readers*
- *Data Integration – Dosimetry data from providers*
- *Real-time shift histograms (10-sec updates)*
- *ALARA-focused visibility of work and timing*
- *Automated reporting to RSOs/RPEHS*
- *High-dose alerts with standardized investigations*
- *Network-wide EPD tracking for compliance*
- *Task-level tracking for exposure reduction*
- *Scalable across U.S. and global sites*
- *Future integration with detection systems*
- *Custom dose/dose-rate alarms by task*

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Opportunities for the Future

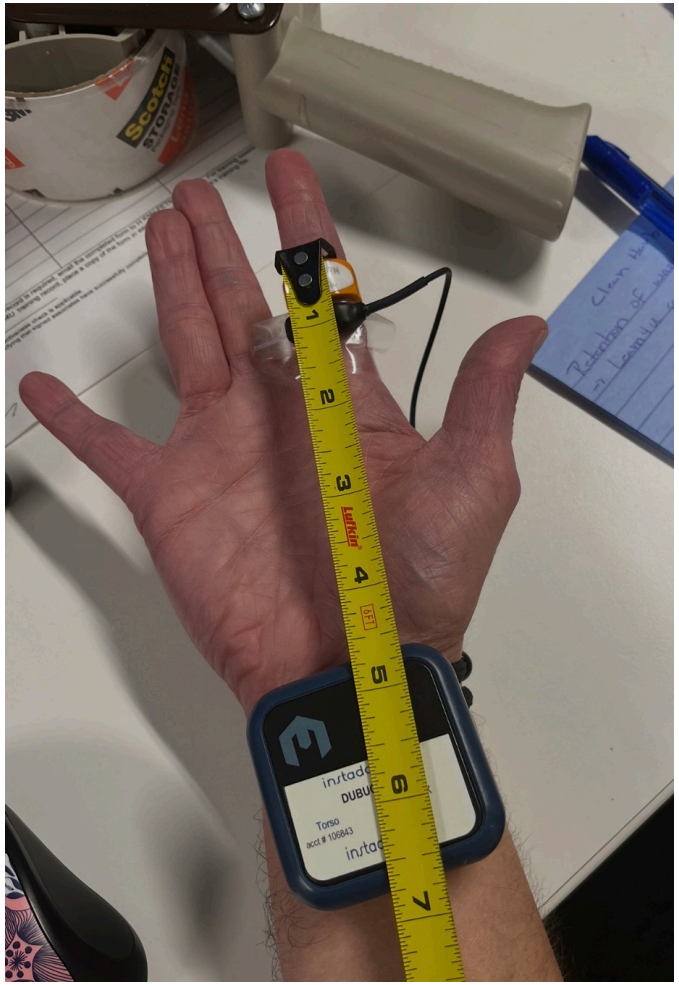
- *Digitalization & Automation*
- *Radiation Protection Program Management System*
- *User friendly for production personnel*
- *Continuous Area Exposure Awareness*

Opportunities for the Future

Mandy's Special Request

1 - Electronic personal dosimeter for EXTREMITIES like a DMC 3000

2 - Real-time EXTREMITY DOSIMETER like Instadose



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Thank you