



Commercial Production and Distribution of **Astatine-211** for Targeted Alpha Therapy

Astatine-211 User Group Meeting
September 6, 2022

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VP, Medical Affairs

IONETIX CORPORATION

Ionetix Corporation was founded in 2010 with a revolutionary concept to create a new paradigm for **isotope access** centered on proven superconducting cyclotron technology developed at the MIT Plasma Fusion Laboratory.

Lansing, Michigan - Company HQ and home of the DoE's Facility for Rare Isotope Production

Production and Supply Platform

Cyclotron Technology: In-house expertise to design, engineer, build, and service "next generation" cyclotrons.

Isotope & Radiopharmaceutical

Manufacturing: Vertical integration - cyclotron deployment, isotope production, drug manufacturing and "white glove" distribution.

Quality & Regulatory: Highly experienced regulatory affairs team with a proven track record with the FDA and NRC agencies.

Achievements and Milestones

Cyclotron Technology: Two cyclotrons, one for short-lived positron-emitting and now one for therapeutic alpha-emitting radioisotopes.

- **12 MeV Cyclotron** – 2013
- **30 MeV Cyclotron** – 2021

Isotope & Radiopharmaceutical

Manufacturing: **9 locations**, including new alpha isotope facility.

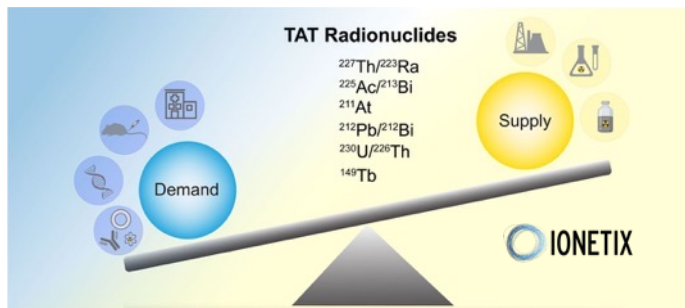
- **ANDA for N-13 Ammonia** (210524) – approved 2018
- NDC: 71162-0001-10 & 71162-0001-05

Quality & Regulatory: **8 Successful FDA inspections** to date across all manufacturing sites.

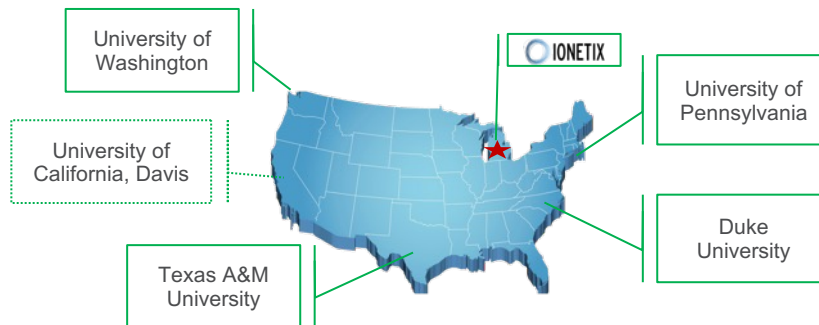


Targeted Alpha Therapy Radionuclide Supply: Astatine-211

Growing demand in TAT raises need for supply

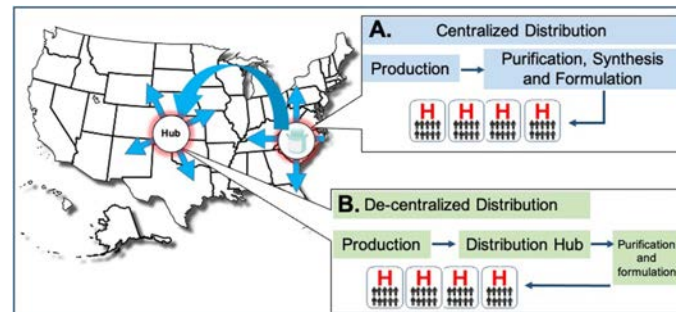


Astatine-211 production in the U.S.



Ionetix commercial Astatine-211 supply

1. New facility in **Lansing, Michigan** dedicated to high-yield alpha isotope production and distribution
2. Optimization of **existing cyclotron** technology for improved At-211 production
3. Planned growth for **Regional Production Facilities** for expanded access & availability
4. Development of **new cyclotron** system to support regional growth



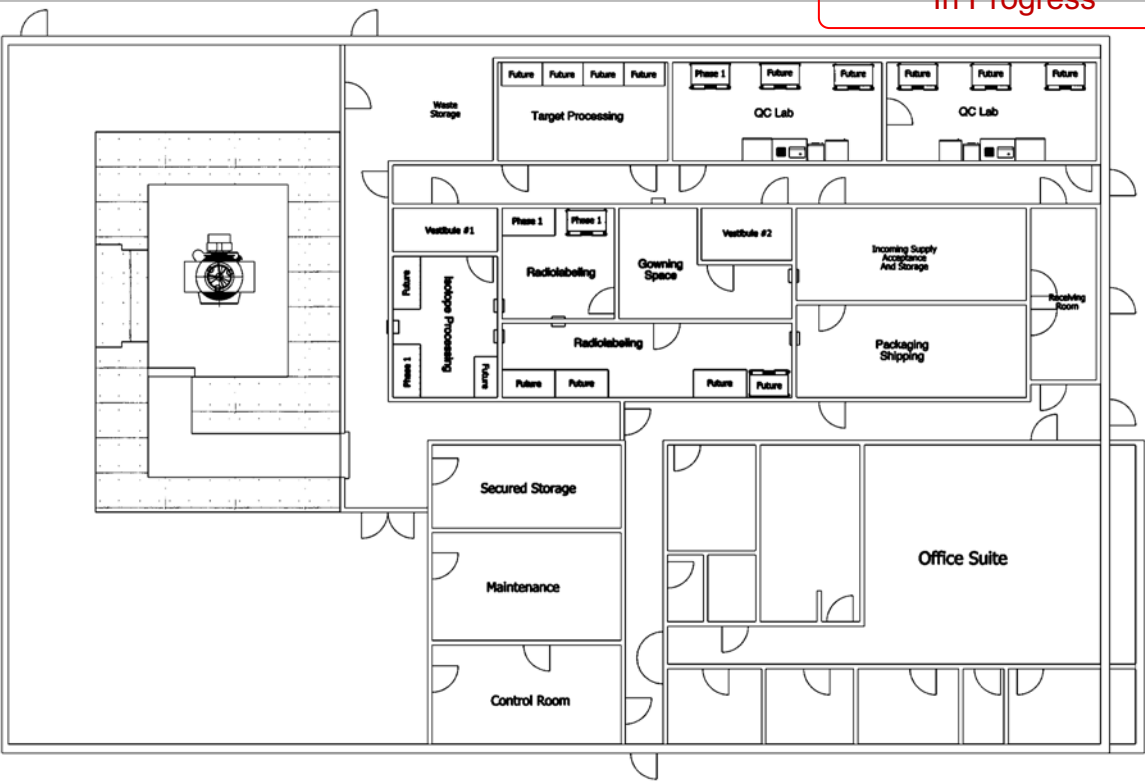
Radchenko, V. et al. "Production and Supply of alpha-Particle-Emitting Radionuclides for Targeted Alpha Therapy". J Nucl Med. 2021 Nov;62(11):1495-1503.

Feng Y. et al. "Production, Purification and Availability of ^{211}At : Near Term Steps Towards Global Access". Nucl Med Biol. 2021 Sep-Oct; 100-101: 12-23.

Targeted Alpha Therapy Manufacturing Services and Solutions – New Facility

Lansing, Michigan

In Progress



Google Maps

Targeted Alpha Therapy Manufacturing Services and Solutions – Cyclotron and Vault

Lansing, Michigan

In Progress

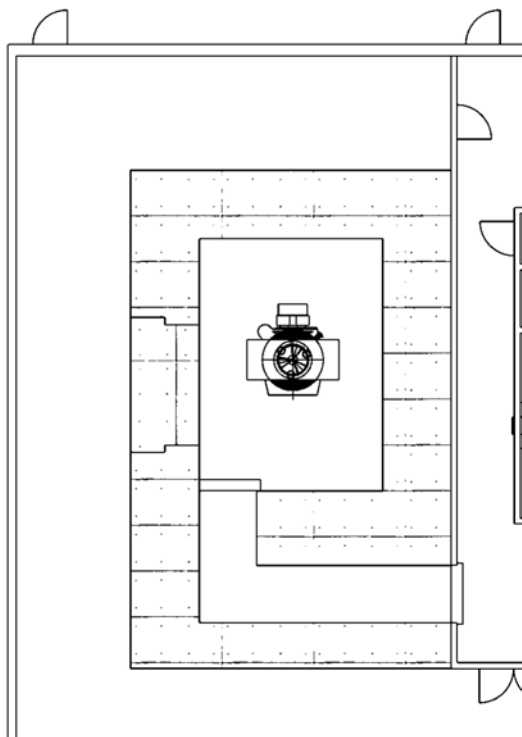
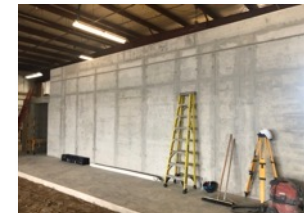
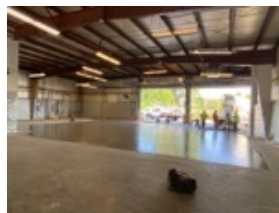
Cyclotron Assembly and Installation

Magnet Installation and Magnetic Field Mapping Completed in May 2022



Cyclotron Vault

Vault Completed in August 2022




Google Maps


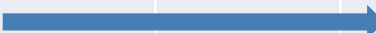
Alpha Facility Timeline and Astatine-211 Drug Development Collaboration

Lansing, Michigan

Facility Project Timeline

	Completion
Cyclotron	December 2022
Radiochemistry Lab	March 2023
Astatine-211 Production – Distribution Ready	April 2023 
Astatine-211 Drug Master File (DMF)	July 2023

Customer At-211 Pipeline

Program	Lead Compound	Indication	Discovery	Preclinical	IND-Enabling	Phase I	Phase II	Phase III
PMI21	PSMA	Prostate Cancer						
ATO-101	Girentuximab	Bladder Cancer						

PRECISION
MOLECULAR



Ionetix 30 MeV Cyclotron Development Roadmap – Astatine-211 Production Cyclotron

30 MeV, Alpha Particle Cyclotron

- 2019 + **CS-30 Cyclotron** – Duke University
- Contracted to support cyclotron upgrades

- 2021 + **CS-30 “Upgraded” Cyclotron** – Ionetix Alpha Facility, Lansing
- Modified CS-30 – **Optimized for Alpha Particles**. (University of Michigan 1982)
 - Internal Target
 - New main coils, trim coils, central region, magnet sectors, power supply, operating system, target



- 2024 + **R&D ION-30 Cyclotron** – Ionetix Manufactured Cyclotron
- 4-sector magnet
 - Internal Target



- >2024 + **R&D ION-30X Cyclotron** – Ionetix Manufactured Cyclotron
- High Intensity
 - 4-sector magnet with central hole of 30 mm in radius
 - External ion source: Injection line/Spiral inflector

Ionetix 30 MeV Cyclotron Development Roadmap: Technical Specifications

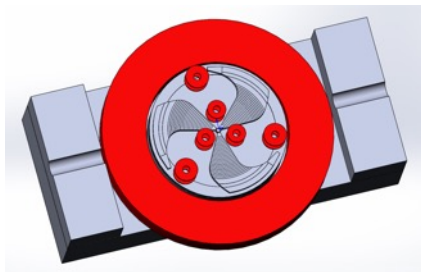
30 MeV, Alpha Particle Cyclotron

Manufacturer	Cyclotron	Ion Source	Central Region	Magnet	Target	Current (alphas)	Energy (alphas)
The Cyclotron Corporation (TCC)	CS-30	Internal	Factory Original	Factory Original 3-sectors	Internal	90 μ A	~28.7 MeV
The Cyclotron Corporation (TCC) – Ionetix Upgrade	CS-30 “Upgraded”	Internal	New	New 3-sectors	Internal	90 μ A	~28.7 MeV
Ionetix – R&D	ION-30	Internal	New	4-sectors	Internal	~150 μ A	30 MeV
Ionetix – R&D	ION-30X	External Injection Line Spiral Inflector	New	4-sectors, Central hole Radius 30mm	Internal/ External	~400 μ A	30 MeV

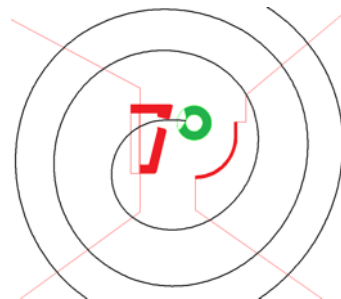
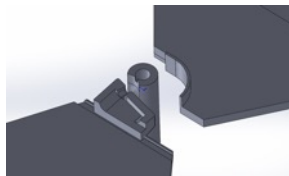
Ionetix Upgraded CS30 for Astatine-211 Production: New Central Region

30 MeV, Alpha Particle Cyclotron

Complete electrical and magnetic field analysis of the CS-30.

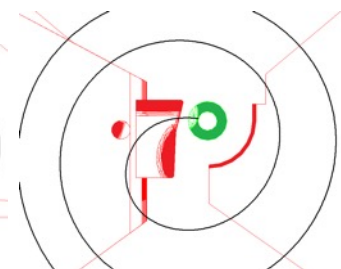
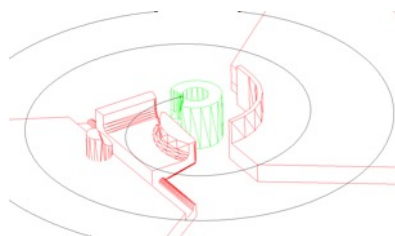


TCC CS-30
Factory Central Region

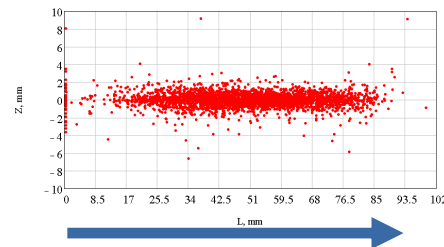


- Objective: Precisely calculate beam transmission and delivery on target.
- Result: Redesign of the central region and sectors.
- Impact: **Improved beam capture efficiency** to accelerate more particles to the target while maintaining consistency of beam spot and spread on target.

Ionetix Upgraded CS-30
New Central Region



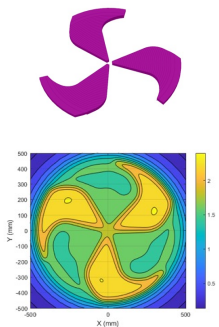
Internal Target
Beam Spot on Target



Ionetix Upgraded CS30 for Astatine-211 Production : New Sectors

30 MeV, Alpha Particle Cyclotron

TCC CS-30 Magnet
Sectors and Field MAP

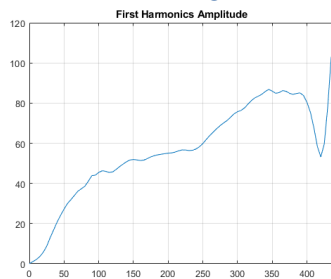


Ionetix Upgraded CS-30
Magnet Sector Shims

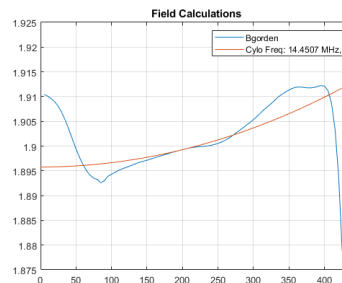


TCC CS-30 Factory Sectors

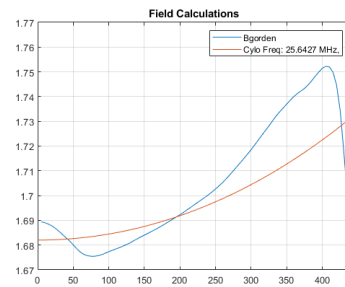
1st Harmonics Magnetic Field



Isochronous Field for Alpha particles

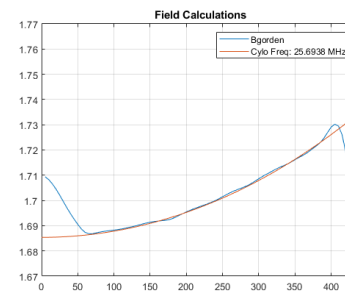
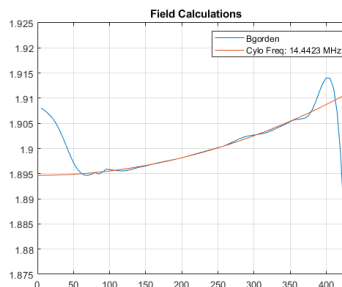
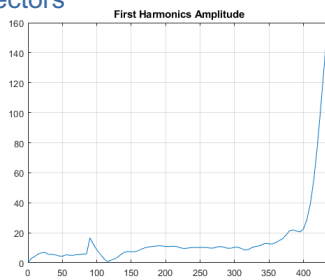


Isochronous Field for Proton particles



- 1st harmonics magnetic field amplitude limited to ~20 gauss in the acceleration region
- Isochronous magnetic field errors reduced significantly for both proton and alpha particles
- Impact: **Improved beam transmissions efficiencies** from the ion source to the target and better beam spot distributions on the target for At-211 production

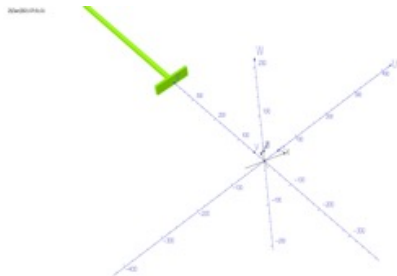
Ionetix Upgraded CS-30 New Sectors



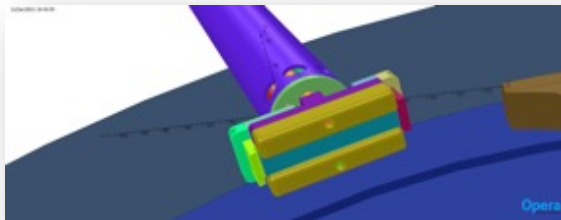
Ionetix Upgraded CS30 for Astatine-211 Production : Astatine-211 Targetry

30 MeV, Alpha Particle Cyclotron

Internal Target



Opera

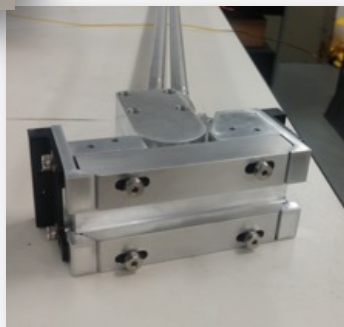


Opera

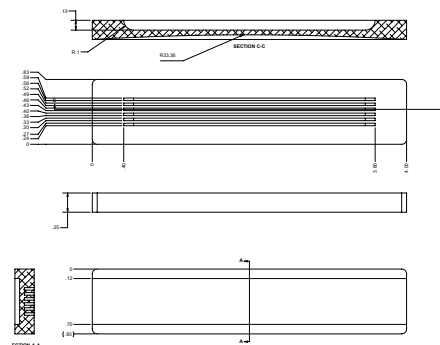
New Upgraded Target Control Arm



- Added additional controls
- The target angle can be change or rotated for improved beam alignment

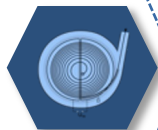


Bismuth-209 Target



Ionetix Alpha Isotope Supply Chain Solution - Summary

Lansing, Michigan



At-211 Production beginning in 2023

- Upgraded CS-30 Cyclotron for near term At-211 Production



Alpha Radionuclide API Supply

- Commercial Processing and Purification Solutions
- DMF for At-211
- Batch Quality Control / Certificate of Analysis release



Full cGMP Facility for Radiolabeling

- Contract Manufacturing
- Manual and Automated Commercial Synthesis Solutions
- Independent Clean Room available for Research Work



Regional Production and Distribution Model

- Ship target, processed At-211 or final drug product

TARGETED- α THERAPY



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Ionetix Alpha-Emitting Radionuclide Production Team

Acknowledgements:

Cyclotron Team

John Vincent, Ph.D. VP of R&D, Project Leader
Xiaoyu Wu, Ph.D., Senior Physicist
Mark Leuschner, Ph.D., VP of Special Projects and Strategy
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