Medical Accelerators

Applications of Particle Accelerators in Europe
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Medical Accelerators now:

- *30,000 particle accelerators are in operation world-wide*
- *Discovery Accelerators are less than 0.1% of this total- the balance are industrial and medical* - we have heard about many of these already at this meeting yesterday
- *About ½ of this balance are Medical X-ray Radiotherapy Systems* that treat around 3 million patients a year world-wide
- *About 1500 (0.5%) are Cyclotrons* dominated by isotope production (IBA, GE, Siemens, Best), with 100 used for discovery science (mainly heavy ion nuclear science) and about 50 now used for Proton Therapy (2/3 IBA)

[DL Friesel & TA Antaya *Medical Cyclotrons* RAST **02** 133 (2009); JR Alanso & TA Antaya *Superconductivity in Medicine* RAST **05** 227 (2012); US DOE Accelerators for America's Future; Future Supply of Medical Isotopes for the UK 2014]

I can best characterize the situation in 2015 for *Medical Cyclotrons*:

- *In terms of installed base and sales, this field is dominated by the European company IBA*- both Isotope Production and Proton Radiotherapy
- *Isotope Production is somewhat static (topology, technology)* but that could change as the SPECT Isotope (Technetium) supply challenge is addressed over the next 2-3 years
- *Proton Radiotherapy is rapidly changing at the moment* with superconducting cyclotron based systems entering the market place, lead by the European Particle Therapy unit of Varian Medical Systems

Cyclotrons, for me, start with Michael Faraday, *in the 1840s*:

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- *But not for what you think when you think about Faraday* motor, generator, diamagnetism, Induction law, displacement current...

- *Instead it was his mostly for concealed heresy* what he called the "Electro-tonic State" ...
  - That lines of force existed between to centers of electric force
  - Where the 'strain' in any region was proportional to the density of lines of force in that region

- *The prevailing theory about electromagnetic forces was a mathematics based 'action at a distance'* staunchly and successfully defended by folks such as George Biddle Airy

- What Faraday, the great experimentalist, had discovered was the concept of a Conservative Electromagnetic Field, itself carrying Momentum and Energy-

And every modern field theory (gravity, QED, QCD, Higgs) follows!

The problem- you couldn't do anything with this Electro-tonic State concept even if it *were* true:

- William Thompson the hero of long distance telegraphy, did something even more incredible than solving current propagation over long distances on transmission lines- he suggested that a young professor at Aberdeen, an unknown named James Maxwell, look at Faraday's **Experimental Researches on Electricity**

- Faraday had only finished Vol. 3 of this work in 1855

- Maxwell just two years later in 1857, published a small but momentous paper "On Faraday's Lines of Force..." where he stated his aim to put mathematics behind the concept:

> "I hope to discover a method of forming a mechanical conception of this electro-tonic state adapted to general reasoning"

- Oliver Heaviside would later codify Maxwell's unified E&M field theory as what we now know as 'Maxwell's Equations' in the 1890s.

To get to Cyclotrons we need also time varying E&M Fields for acceleration:

- RF Frequencies of order ~100 MHz are about right these days
- Heinrich Hertz fortunately solved this problem over the period 1886-1889 by demonstrating the transverse propagation of electromagnetic waves at... 100 MHz !
- Verifying Faraday’s conception of, and Maxwell’s mathematics for, the Electromagnetic field

To make a cyclotron as we know it today, we need one more bit of Modern Science... Special Relativity:

- Length contraction and time dilation were already built into the Lorentz transformations of the electromagnetic wave equation ...
- Special Relativity in 1905, in “The Electrodynamics of Moving Bodies”, Einstein postulated that the “c” in the wave equation was an absolute constant, and that the laws of physics were invariant in any inertial frame (Galilean transformations of Newtonian Mechanics he replaced by the Lorentz transformations of E&M)

That is, by 1905, we had everything we needed to make a cyclotron...

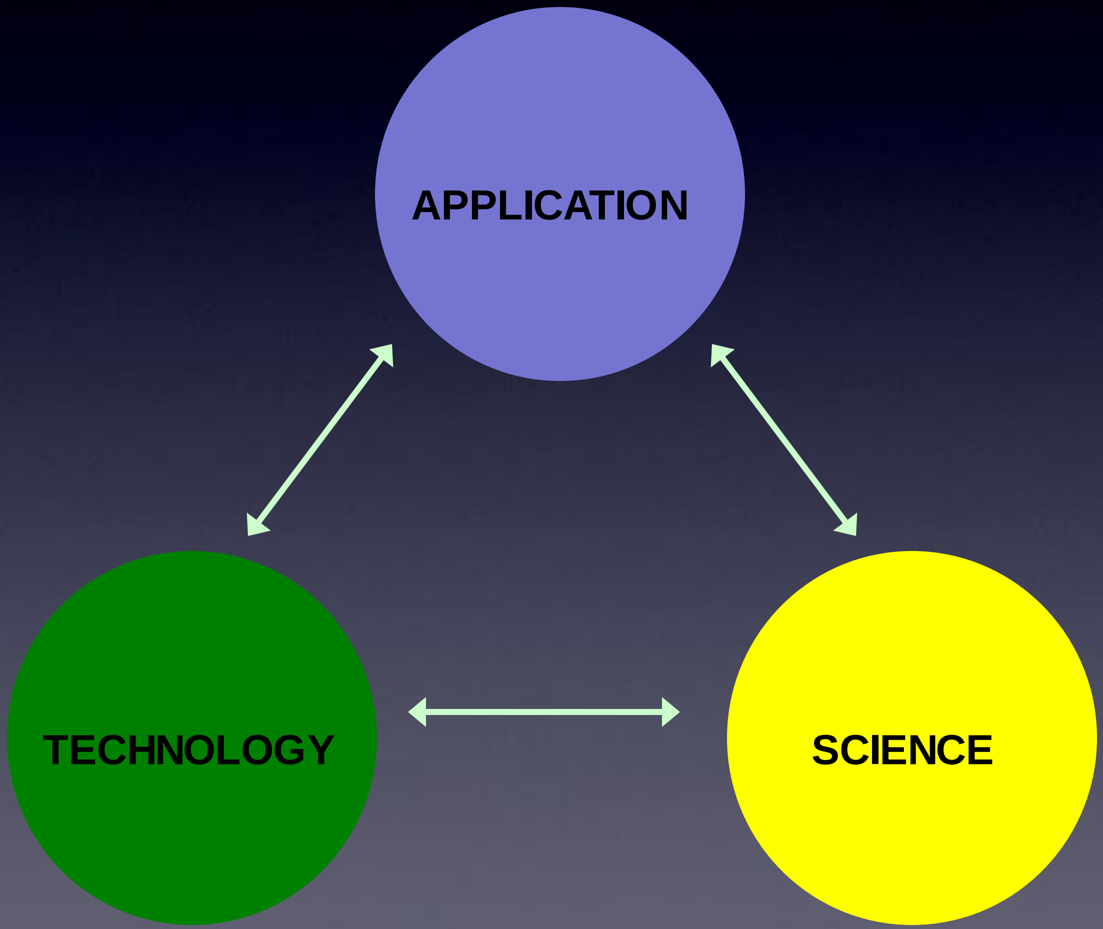
No! The first cyclotron would not come until 1931... Why so long?

- Accelerator Physics   the notion of a circular particle accelerator, and an underlying quantitative physics basis for it, was missing in 1905

- A Driving Need (Application) there was none in 1905- the atom was not yet explained: it's nucleus has not yet been been discovered by Rutherford, or it's quantum mechanics postulated by Bohr.

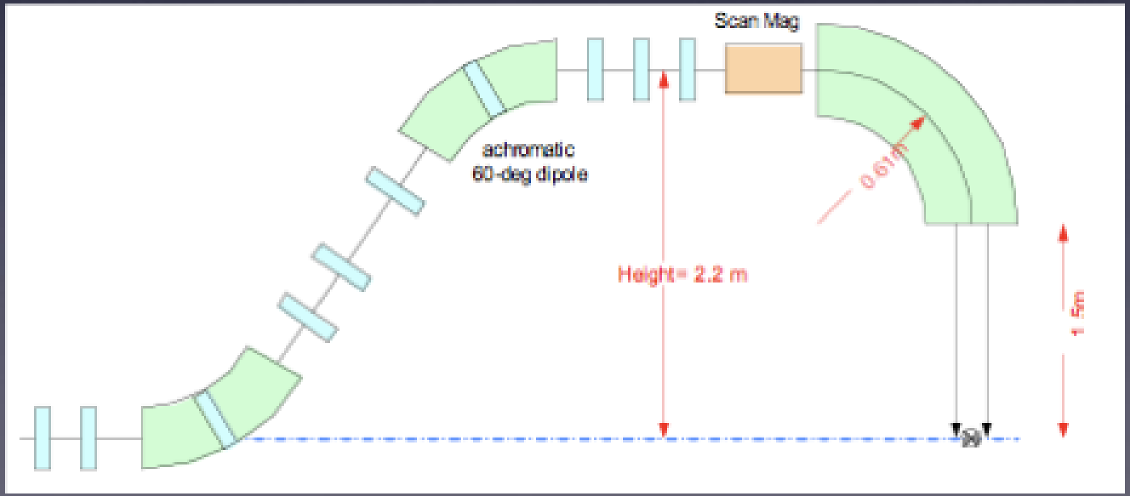
- Supporting Technology was not yet available: vacuum pumps, ion sources, RF amplifiers, magnets were all yet to come *from the general advance of technology in other areas* like power transmission, radio transmission, telephone, lighting, electrical process control, gas separation and gas exhaust

When I design a new particle accelerator,
I am mindful of this very paradigm
as the necessary conditions for success:



An example... I design particle accelerators, but sometimes advances are required in other areas to move an important application forward:

- Hospitals are expensive real estate- PT gantries need to be more compact too
- Procure Double Bend Achromat Gantry- Cameron, Anferov (ProCure) and Antaya (MIT)
  - Each bend is independently an achromat allowing flexible layout to accommodate other medical systems while providing some insensitivity to momentum spread
  - Field level 2-4 T reduce the gantry diameter by a factor of two for the same rigidty
  - Cryogen Free operation
- ProCure licensed this DBA Gantry to ProNova in 2012 for use with a Sumitomo Sc Cyclotron



Cyclotrons in general:

- Can Accelerate all ions: H^+,H^-,H_2^+ and highly charged heavy ions
- Intensities: highly charged heavy ions to ~ 1 mA and H^+,H^- to ~few mA
- Advanced cyclotrons are possible in all three Cyclotron Flavors: Lawrence, Synchronous, Isochronous

Key Characteristics of Cyclotron Flavors:

- Lawrence and Synchrocyclotrons are weak focusing and have longitudinal phase stability like synchrotrons and linacs
- Isochronous are strong focusing (AVF) and have no relation between period and momentum (sit at the synchronous transition energy for the full acceleration)
- Isochronous share many key beam physics properties with FFAGs (they are derived from the same set of equations)

How the Cyclotron Flavors scale with Energy and Field:

- Lawrence have a simple uncritical field scaling but energy is limited to 20 MeV or less by an accumulating ion phase error (with respect to acceleration gap crossing)

- Synchrocyclotrons - share the same field scaling simplicity with Lawrence but have unlimited final energy – the frequency synchronously declines with increasing mass-energy

- Isochronous $T \sim r^2$ has no limit but you have to simultaneously solve the vertical focusing limit in the AVF field that scales as $1/B^2$

Cyclotron Flavors and Intensity:

- Lawrence no real limit but with internal ion sources a few hundred microamps have been demonstrated

- Synchrocyclotrons – low intensity (enA): Low duty factor ~1000 acceleration cycles per second, with a full acceleration cycle of order few hundred microsecond and the same ‘bucket’ space charge limits as the other flavors

- Isochronous are the highest intensity CW ion accelerators – milliamps protons at both low energy and high energy have been achieved

Cyclotrons 2015:

- *The bulk of the discover cyclotrons (~40-50) do heavy ion nuclear science* nuclear stability on the proton and neutron drip lines

- *There are still a few large Heavy Ion Cyclotron Facilities* RIKEN, GANIL and NSCL ;*the megawatt power Neutron Science PSI Ring Cyclotron is still in operation*

- *Isotope Production Cyclotrons are all isochronous H^- machines*

  + stripping extraction, variable energy, multiple targets

  - gas stripping losses, low field / large footprint & power consumption

- *Radiotherapy Cyclotrons*
  - IBA ~25 C230 cyclotrons provide beam for most of the PT Radiotherapy Centers in use W-W
  - VMS is coming on strong with more than 10 orders for Probeam Sc Cyclotron based multi-room PT Centers
  - Transition to compact PT Centers with Sc Cyclotrons is in progress: Mevion, IBA, ProNova (Sumitomo)

Cyclotron development *Drivers* 2015:

- *Medical Isotopes- Technetium 99m Supply Instabilities and Shortages*

- *Proton Radiotherapy- Affordable Local PT Centers* that actually exploit the intrinsic physics advantage of particle radiotherapy

- *Medical Isotopes- enabling emerging transformational isotope imaging and therapy concepts* while development resources continue to diminish

Medical Isotopes- Technetium 99m Supply Instabilities and Shortages

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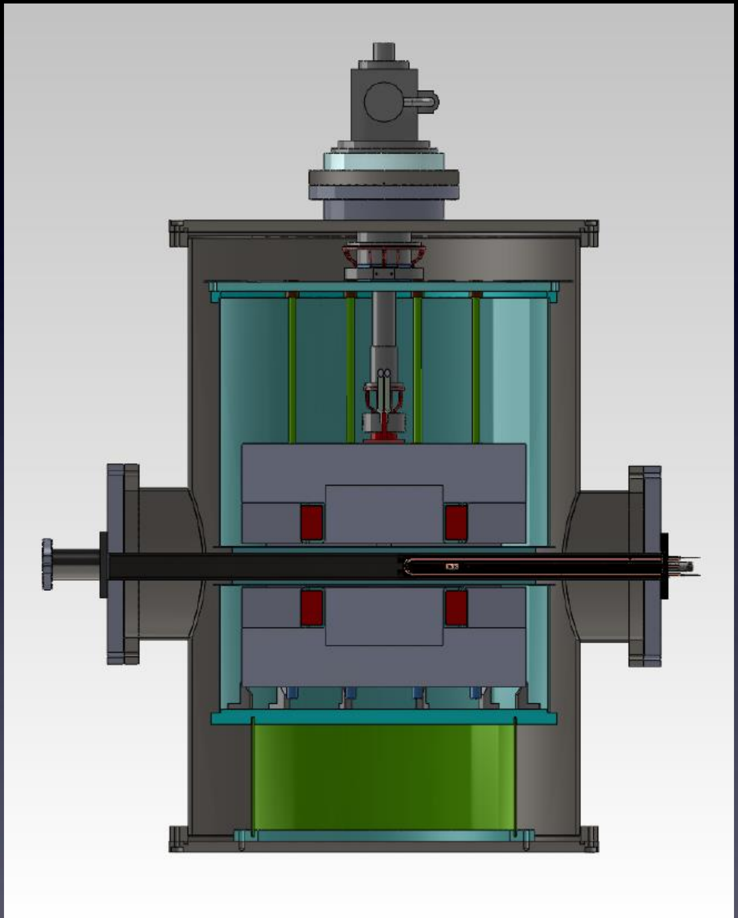
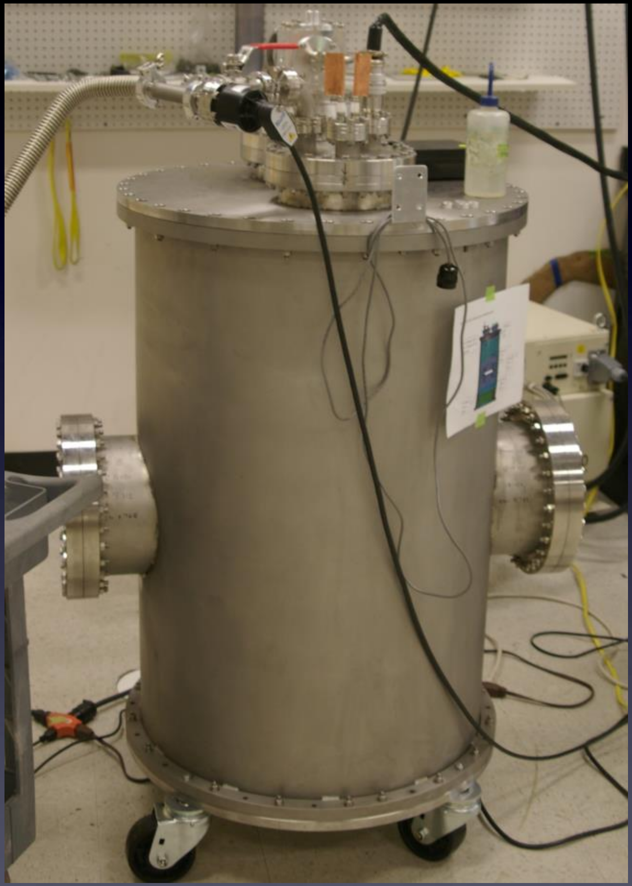
- *Dominant Cardiac Imaging Radioisotope ^{99m}Tc (~20M doses/y)* comes from the fission of weapons grade ^{235}U in a set of aging reactors
- *At any given time there is only a 1 week supply available* having a difficult to replace *continental scale* supply chain with many dependencies and issues yet is fully medically compliant and doctors dominantly have the SPECT cameras based infrastructure in-house
- *Continental Scale Solutions* new reactors, high power photo-fission accelerators... may not happen quick enough
- *Cyclotrons can solve this* there are two choices – regional supply and Point-of-use Unit Dose
  - Regional – have the regulatory pathway but not the development funds at present
  - Point of Use – largely means shifting to PET isotopes (high res, excess oncology imaging capacity

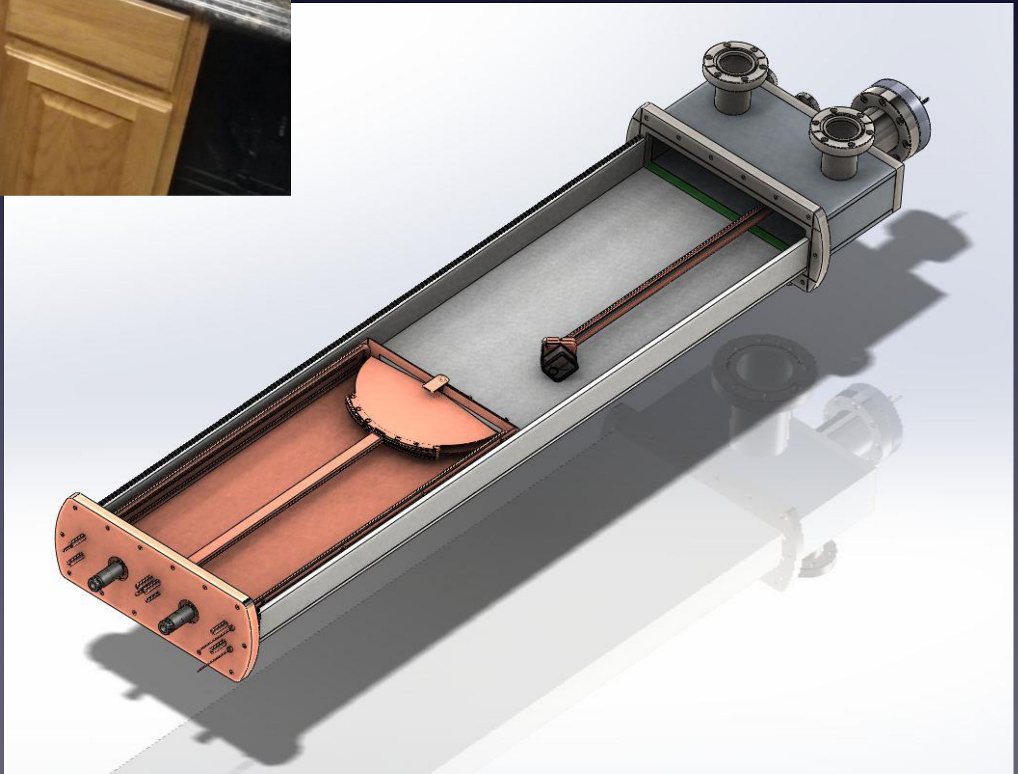
Isotron Prototype Topology





Isotron scale?

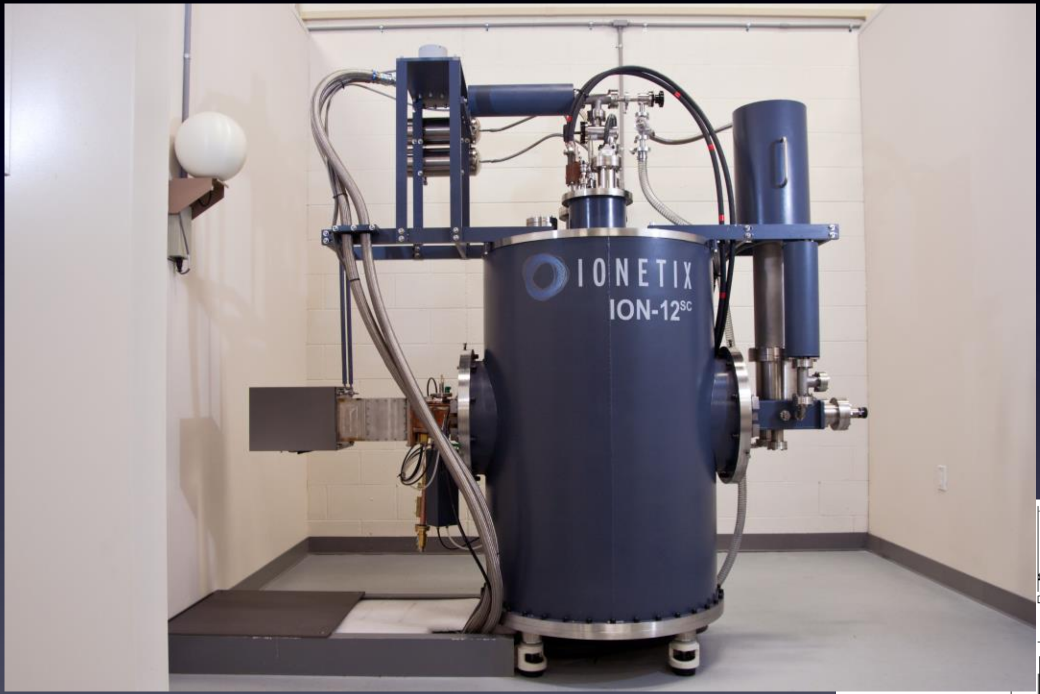
- About the same pole size as the 1932 Cyclotron but 160 times higher final proton energy

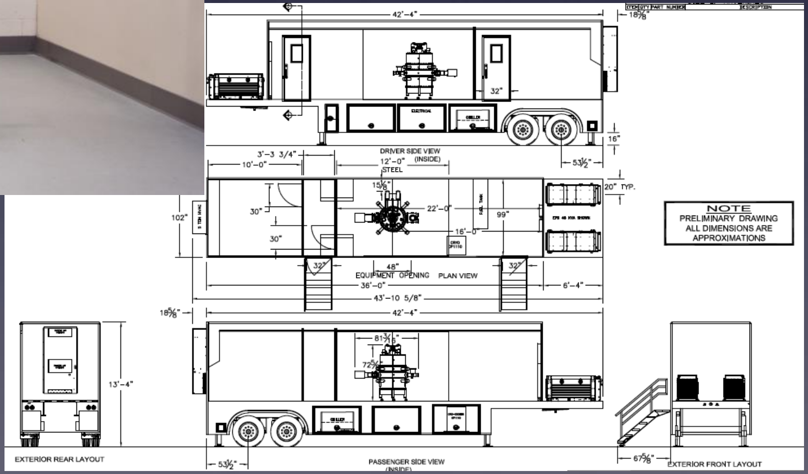


Isotron Dee /Resonator

Ionetix production model ION-12^{SC}

12 MeV 1800 kg cyclotron + target + chemistry self-shielding unit dose

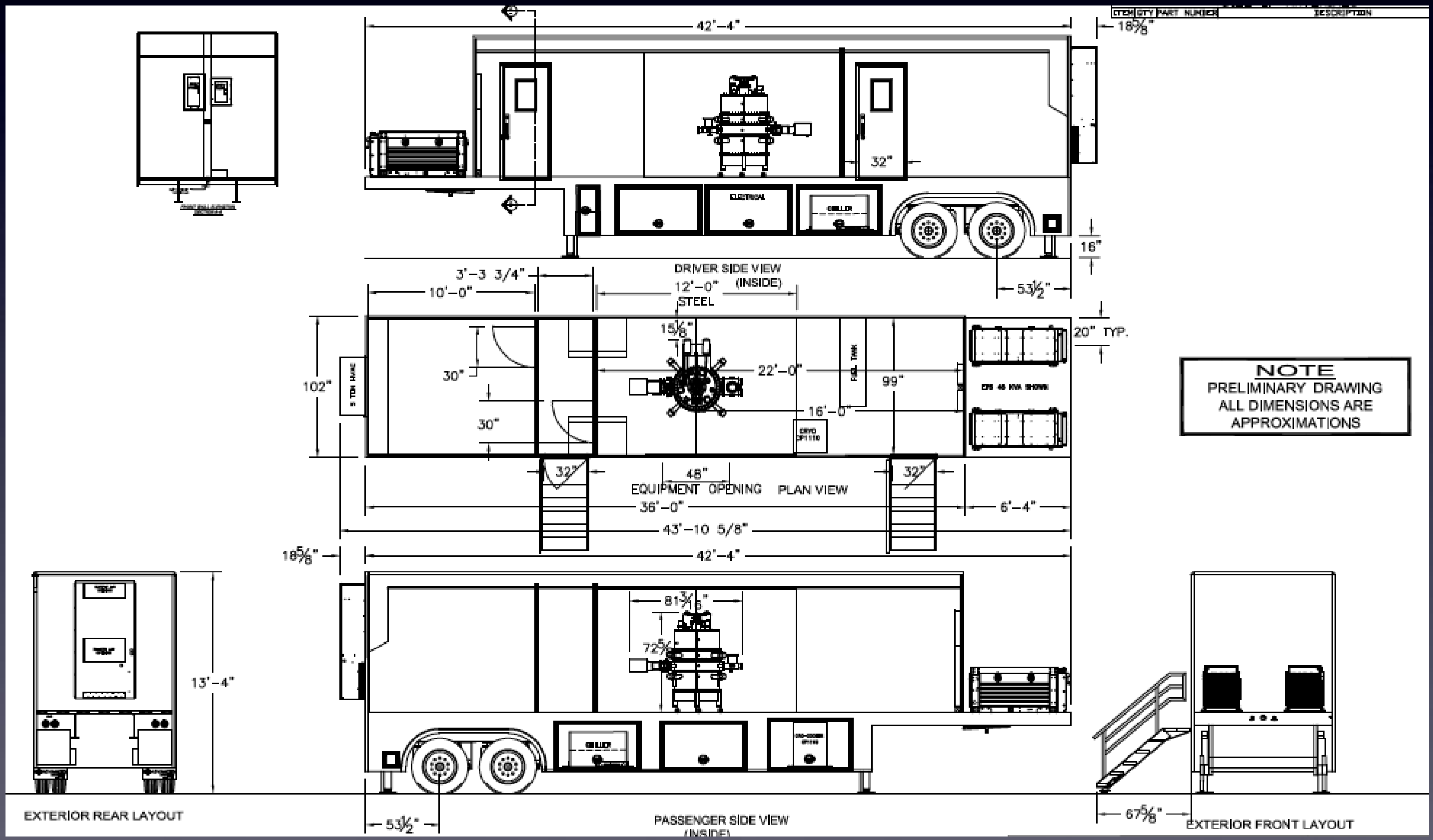




Ionetix N13 Ammonia Generator Status – 3 installs so far planned in 2015:

- First ION-12^{SC} is going to the University of Michigan Medical School Cardiology Department
- Second system is to be installed on the fourth floor offices of a 15 doctor cardiology practice in Sarasota Florida ... this is what I was trying to do
- The third to Wisconsin where it will be installed in a track and moved around to medium size hospitals

Ionetix ION-12SC is fully portable and transportable:



The Isotron has an Active Detection variant- fully portable Nanotron:

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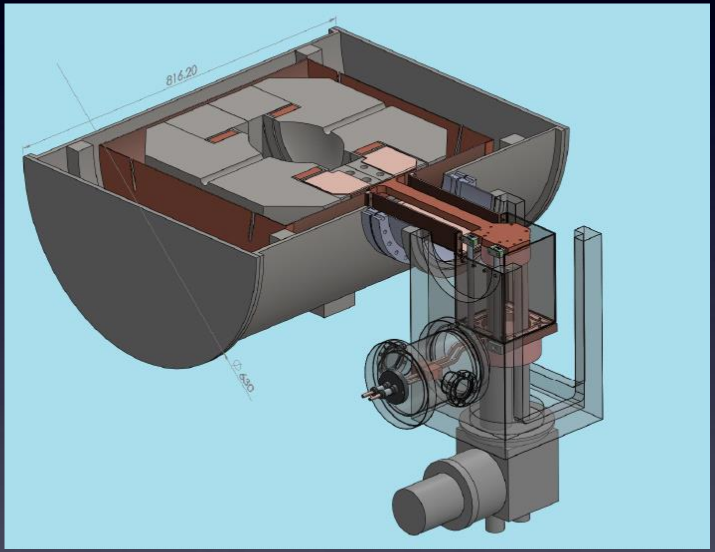
- 2008-2011 MIT Nanotron Design Studies for portable Active Interrogation Systems
  - Lawrence B_0~ 6T
  - Portable, transportable weak focusing cyclotron for Active Interrogation; persistent mode, cryocooled
  - Simple field, RF and T~10 MeV

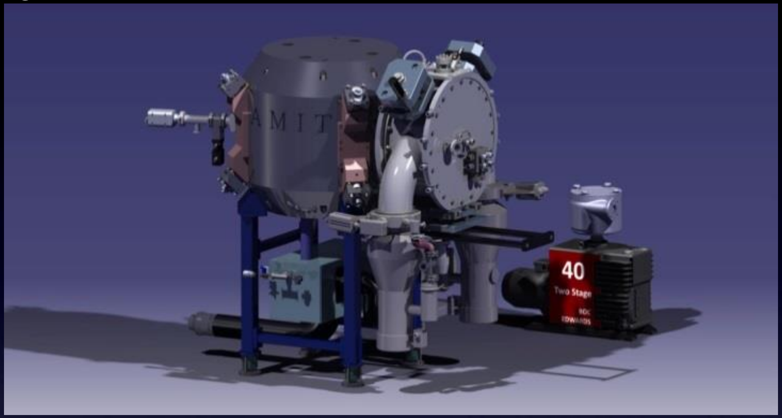


Isotron/Nanotron is not the only Point of Use Cyclotrons under development at the Moment:

- 2009-2012 MIT / CIEMAT Design Studies for a weak focusing compact isotope generator
  - CIEMAT approached me and others to propose new accelerator initiatives for them to develop
  - I proposed high field cyclotrons and this is in fact the accelerator class they chose for development
  - But MIT Nanotron IP limited what they could do with compact high field H^+ cyclotrons

- I had felt that H^- at high field, missed by others, was possible, and this would give CIEMAT a unique 'space' of their own to develop
  - 1T is no real hard limit for probabilistic Lorentz Stripping
  - D. Obradors came to MIT and we found a H^- solution ~4T at ~10 MeV in early 2010
- C. Oliver also came to MIT and began the quantitative Beam Dynamics effort

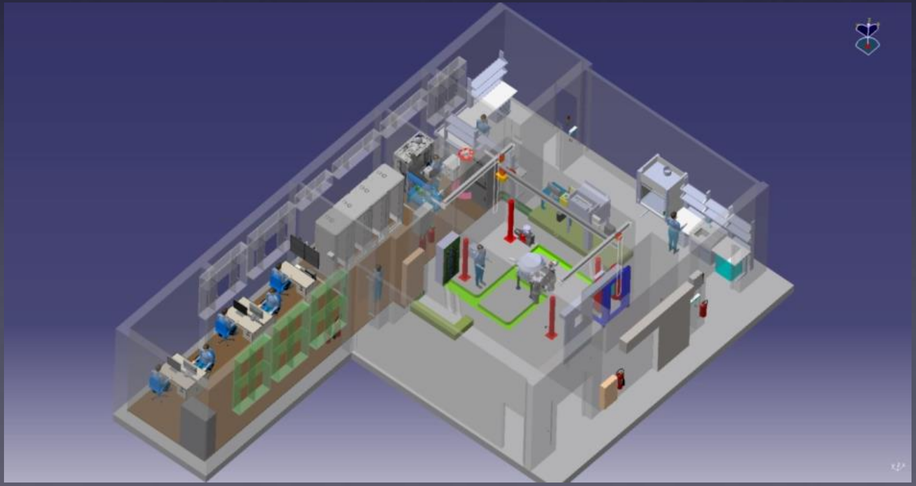
Isotron is not the only Point of Use PET cyclotron under development at the moment- here si the Highest Field H^- Compact Superconducting Lawrence Cyclotron:



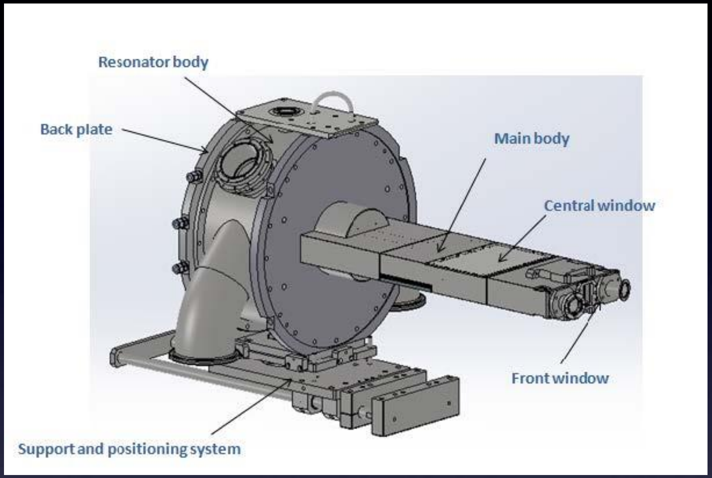
- CIEMAT AMAT in 2015 is now well underway...
  - Complete systems design for a stand alone isotope generation is a hospital has been completed
  - T>8.5 MeV and I~10 eμA
  - For C11 and F18 radioisotopes

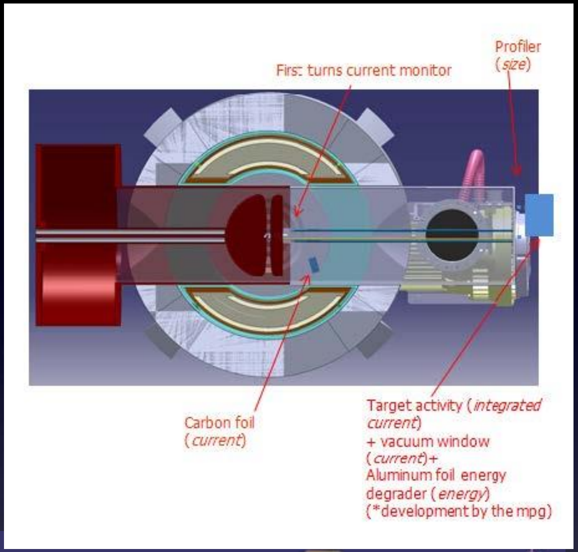
- It is an impressive large & successful collaboration: 10 companies, 14 Research Labs

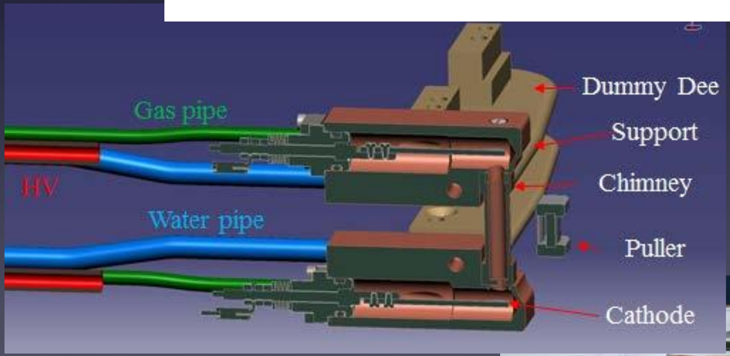
- It has a ‘beautiful’ quantitative weak focusing cyclotron beam dynamics design (C. Oliver and collaborators)



Some CIEMAT AMAT Hardware: ANTAYA







Proton Radiotherapy – Affordable Local PT Centers

- *The target for the last Decade has been to get to IMRT Per Room Cost (~$10M)* while not losing the Bragg Curve advantage

- *Everything in a PT System has to scale down in size, cost and complexit yto meet this target* footprint, number of rooms, staffing, wall plug power cyclotron, beam transport, treatment rooms (gantries)

- *Compact High Field Superconducting Cyclotrons* can help do this

Compact High Field Cyclotrons in general:

- Are necessarily about going to high magnetic guide field: p/q=rB
  - This scaling characteristic is shared with synchrotrons (also betatrons and microtrons)
  - Synchrotrons operate essentially on one fixed equilibrium orbit by ramping B
  - Cyclotrons contain a nested set of EOs from T=0 to $T=T_{final}$ in a fixed B field
- Can Accelerate all ions: H^+,H^-,H_2^+ and heavy ions
- Are possible in all three Cyclotron Flavors: Lawrence, Synchronous, Isochronous

Why high field? ***We found already with the first Sc Ccyclotron, the K500 at NSCL, that a 2X increase in average field results in a facility cost (cyclotron, vault, services) decrease of 3X***

Compact High Field Superconducting Cyclotron Development Timeline:

- 1982 - K500 at MSU was the first compact high field superconducting Cyclotron
  - It is Isochronous with B~3-5T and fully saturated AVF poles (very important)
  - With iron AVF poles high energy and focusing are not compatible
  - Heavy ion acceleration represents a ‘sweet spot’ where both work well enough
  - Demonstrated that when you double B the cost declines by $/3

- 1980s-1990s - Many Compact Heavy Ion Superconducting Cyclotrons for heavy Ions were built- only 1, AGOR, could also accelerate protons directly.

- 2000s (finally) Protons- Mevion 9T Synchrocyclotron, Varian 3T Probeam CW Isochronous, IBA 6T S2C2 Synchrocyclotron, Sumitomo 3.5T CW Isochronous

The first Compact High Field Superconducting Cyclotron for PT:

- 2003-2007 – MIT High Field Synchrocyclotron commercialized by Mevion
  - It is the highest field particle accelerator B_0~ 9T
  - T=250 MeV and I~40 enA
  - It was my first attempt to make a compact proton therapy machine using superconducting magnet technology
  - The field scaling solution came in 2004
  - The full quantitative beam dynamics solution with self-extraction was achieved in 2007

- For Single room PT, to date, Mevion has orders for about 10 installations

However the next Step forward should be a Compact
CW Superconducting isochronous Cyclotron

"TAAC Compact High Field Isochronous Cyclotron for Ultra-Fast Pencil Beam Scanning Proton Therapy"

Antaya Science and Technology (USA) & Co-Development Partners

AS&T Technically Advanced Affordable Cyclotron

- Origins of this Cyclotron:
  - General problem of the cost of PT
  - The challenging problem of Organ Motion that obscures PT precision

- January 2103 NIH Experts Meeting in Bethesda
  - Many researchers were at this meeting were looking for ways to track organ motion (MR, CT, in patient PET, proton radiography)
  - As a development path this 'felt' hard to me
  - Still, with so many good people looking at tracking organ motion, it seemed this development path was properly 'covered'

- What should I look at?
  - Everyone knows how to hold their breath for a few seconds- So I put up a nice challenge for my team at AS&T
  - Could we develop a system (cyclotron and fast gantry) that could treat a 10x10x10 cm^3 tumor in the rest portion of a single breath hold?

Compact High Field Superconducting CW Isochronous Cyclotron for Ultrafast Pencil beam Scanning

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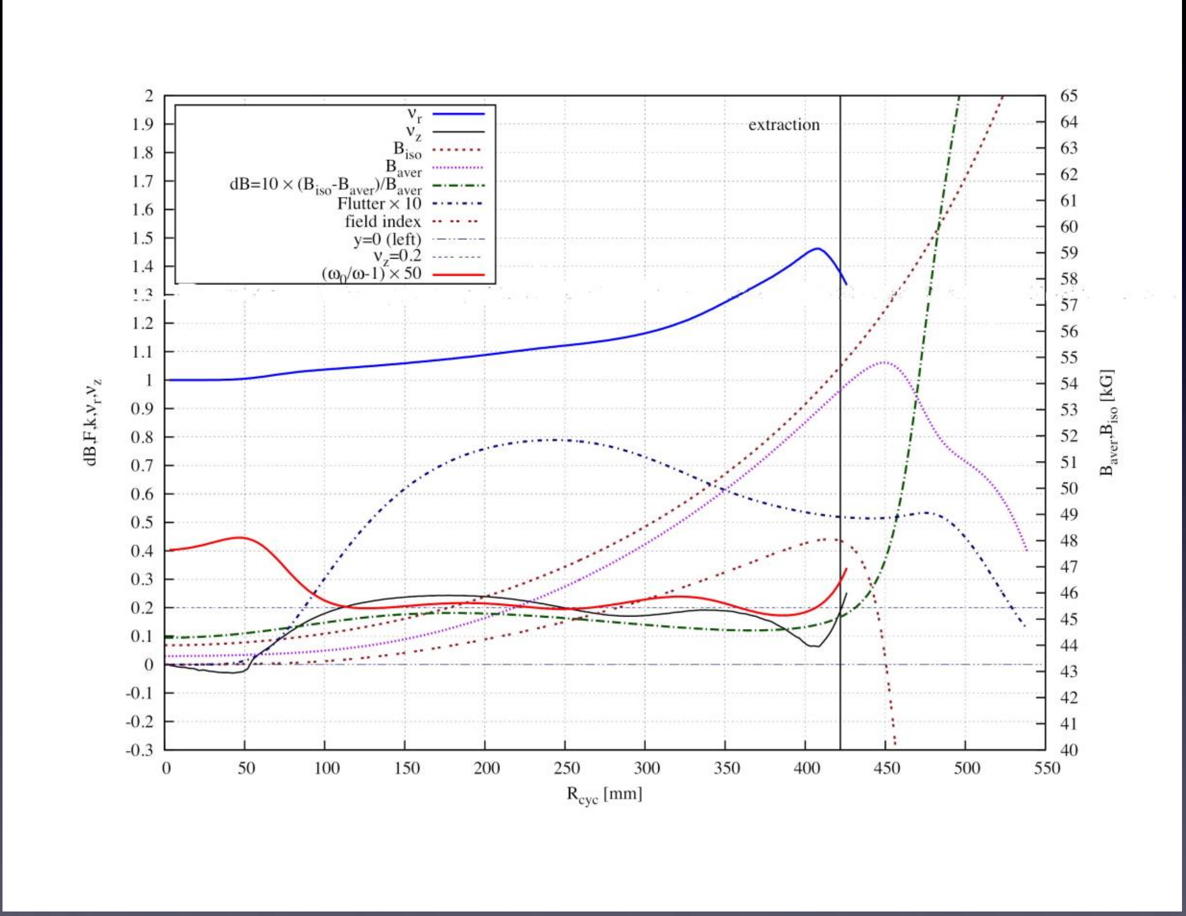
A 2X increase in B field over existing proton cyclotrons to get $/3 cost reduction while making Ultra-fast Pencil beam scanning possible?

- Solve the problem of scaling the Isochronous AVF Flutter field to High Energy for very compact proton cyclotrons while preserving isochronism, and minimizing the integral phase error for acceptable betatron tunes

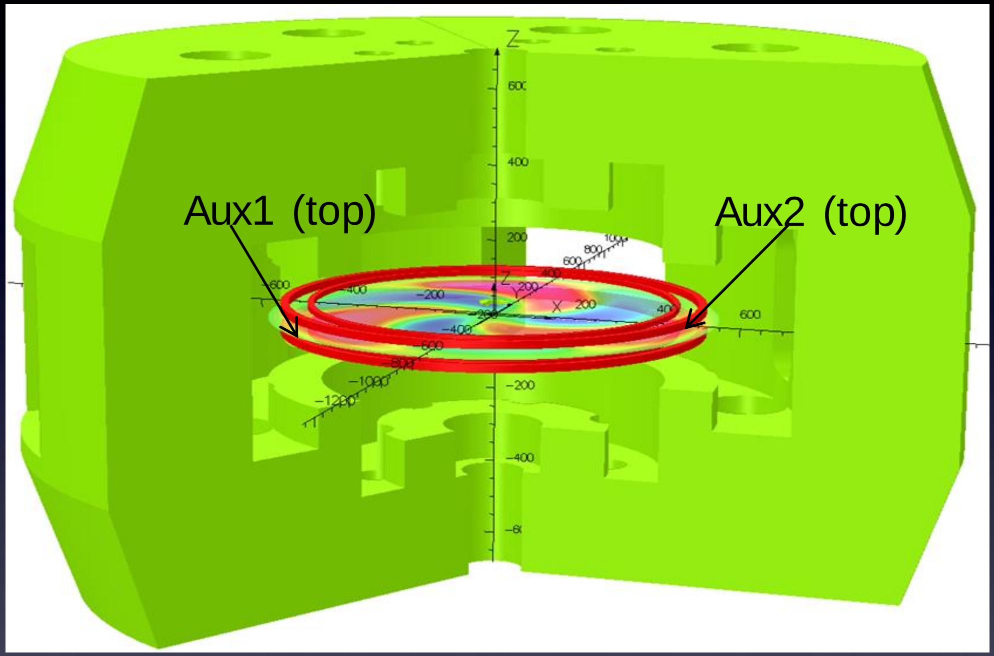
- Sort out how to do high extracted beam intensities and fast time based intensity modulation in high field conduction cooled compact superconducting cyclotrons

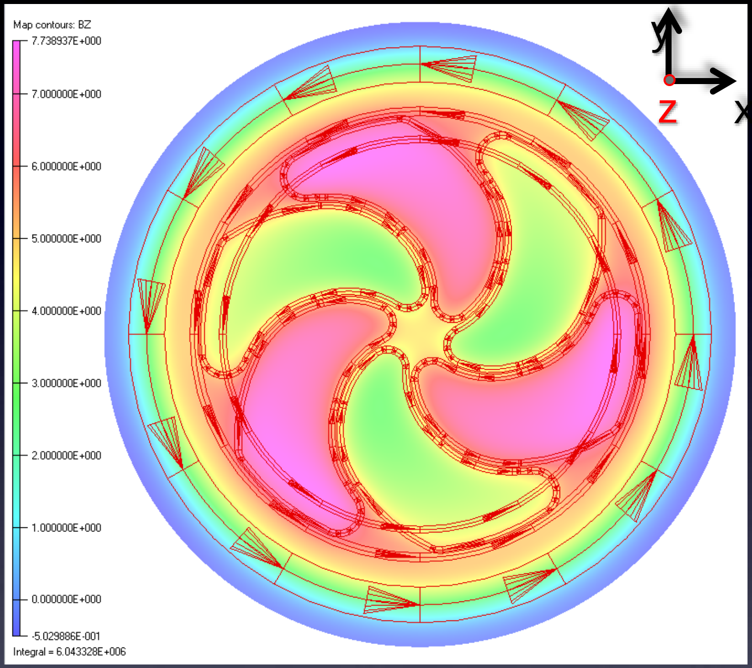
TAAC Tune Diagram...



Isochronous, CW, 3 Sector, 230 MeV, 0.42 m extraction radius... Impossible!

TAAC Field design:





Simple return yoke, superconducting coils, modest spiral, average field 4-7T

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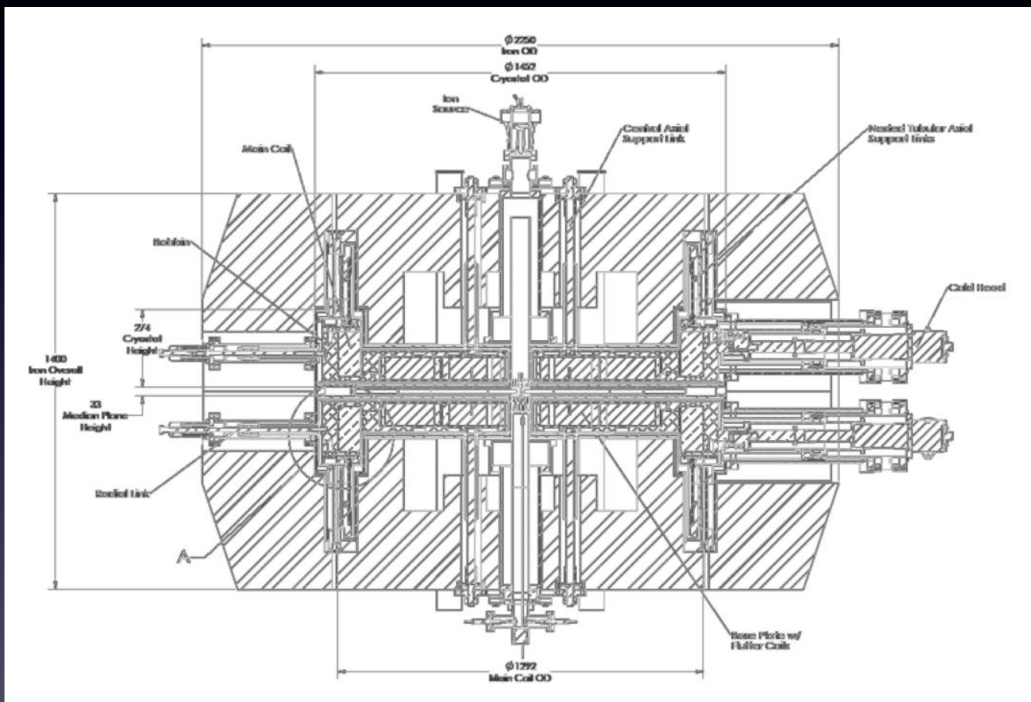
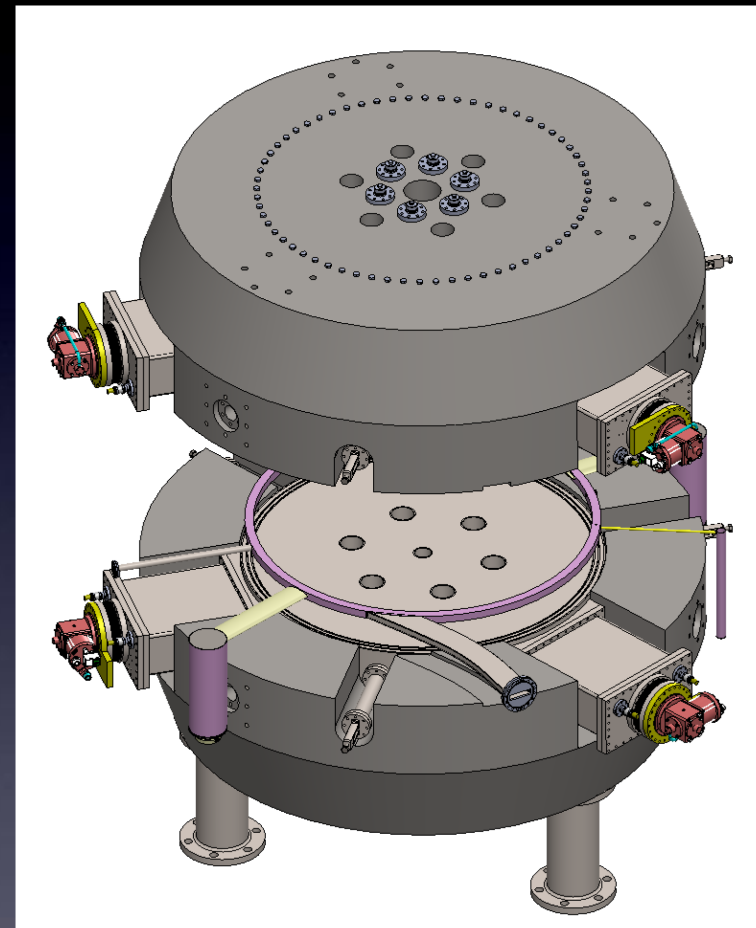
TAAC engineering design:





2.2m diameter, 1.6m tall, 30 tonnes, dry cryo-cooled, warm median plane- key technology proof-of-concept demonstrations (magnet, RF, high intensity injector) are now in progress

Medical Isotopes- enabling emerging transformational isotope imaging and therapy concepts

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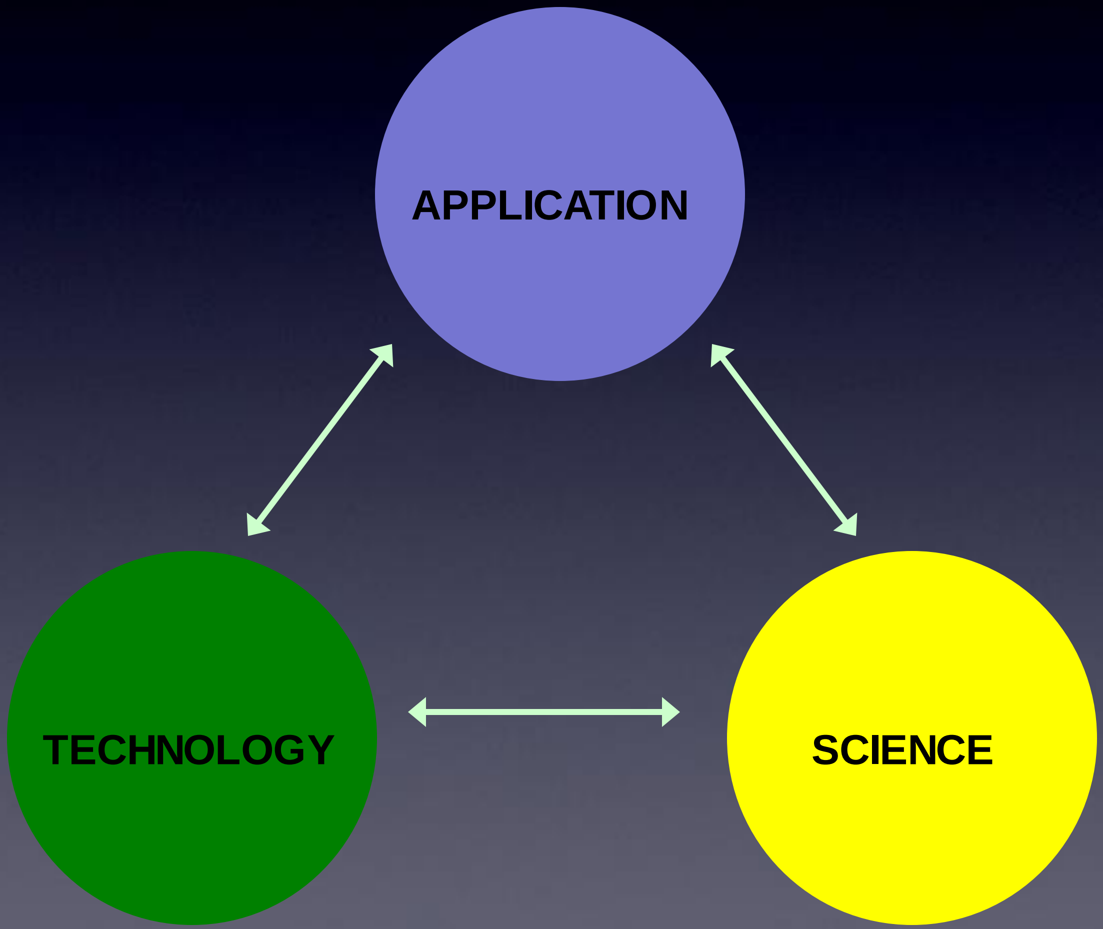
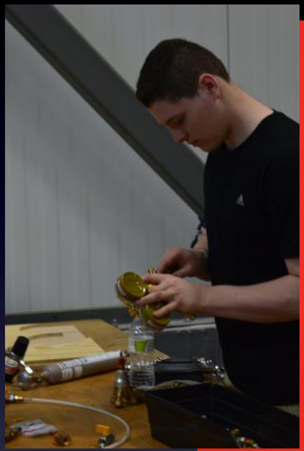
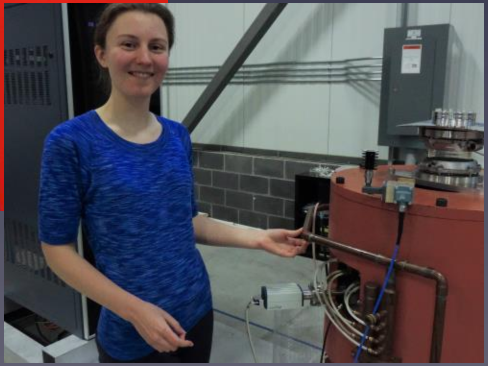
- *The TAAC is scalable over the energy range 1-230 MeV* quantitative design basis
- *Isotope production* any ion species, compact point-of-use, or regional high production – it is a platform
- *(Active interrogation too)*

I come back to the particle accelerator paradigm to make one more point about our field– because of the richness of this space I find I can plunk a smart people in the middle of a new accelerator development, regardless of their background and experience, and they will find their place:



An example... Here are 8 talented High Schoolers (~16-17y) working at AS&T developing the proton injector for fast Pencil Beam Scanning PT TAAC:





Thank you. Onward. TAA