After these nice talks yesterday and today, such as

- Manjit’s - from HEP to Medical (therapeutic applications)
- Georgio’s – how to apply physics in medicine
- Suzie’s - introduction to particle therapy
- Thomas’(ok, ok, Christians’) – how GSI pioneered particle therapy
- Marco’s – CNAO has a center, treated 1000 patients, so eat my dust talk

I am here to say "HELLO WORLD, Dallas in Texas GOT IT! We are working on it, and here is where we stand"

Experience from Dallas: building a new heavy therapy center “What system to put in an what building to build for it”

Arnold Pompoš PhD

UT Southwestern Medical Center

Dallas, TX

Work Supported by NCI P20 planning grant and by

State of Texas Matching Grant for Planning The Heavy Ion Research and Therapy system

IONS2017, χανιά, Greece

Motivation

- Photons
  - – Undershoot and overshoot target - yet, MDs are not sitting in jail
  - – In the last 100 years they perfected the techniques to adapt to an imperfect tool

Motivation

- Photons
  - Undershoot and overshoot target - yet, MDs are not sitting in jail
  - In the last 100 years they perfected the techniques to adapt to an imperfect tool

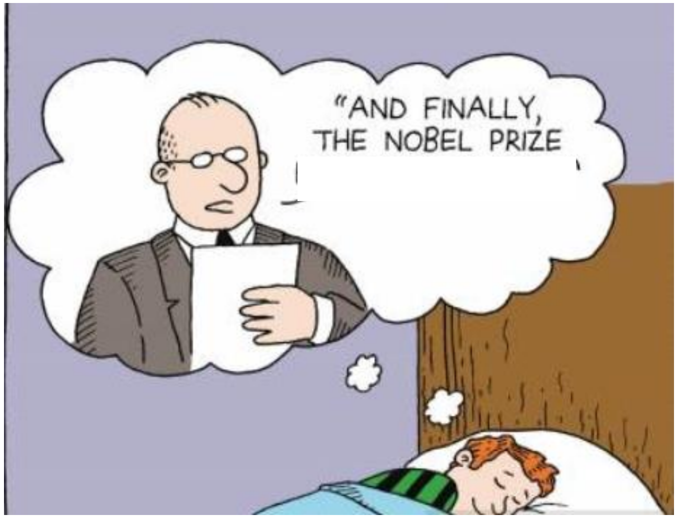
Motivation

- Heavy ions - sounds like a dream opportunity
  - Bragg peak,
  - low lateral scatter,
  - low ionization density in healthy tissue
  - high ionization density in tumor
- Reality
  - Uncertainties exist, image guidance is poor, dose rate is low, organs are moving, staring cost is relatively high
- And of course, the ultimate question should not be neglected either: does the patient benefit?
- **Conclusion: heavy ions offer great opportunity for a lot and lot of research and a lot and lot and lot of good things for cancer patients and it is time to bring it back to USA.**

What System to Build?

- Medical doctors and administrations dream is a money maker machine

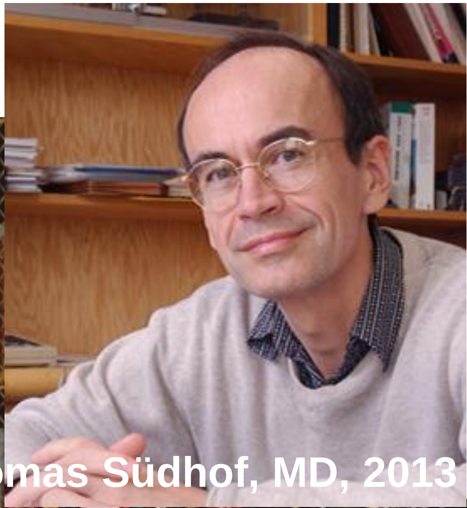
(please do not quote me on this. I will deny I ever said this ☺)



- Academic institutions press for research device.

UT Southwestern is an Academic Institution

Our Nobel Prize winners



Academic Ranking of World Universities

ACADEMIC RANKING OF WORLD UNIVERSITIES SINCE 2003

Global leaders driv… world-class innova…

…me About Rankings Universities GRUP Initiative Conference Resou…

>> ARWU-FIELD 2014>> ARWU-MED 2014

…demic Ranking of World Universities in Clinical Medicine and Pharmacy - 2014

…I ENG LIFE MED SOC Methodology Statistics

…orld Rank	Institution	Country	Total Score	Score on Alumni
1	Harvard University		100	100
2	University of California, San Francisco		78.5	0
3	University of Washington		76.1	42.6
4	The Johns Hopkins University		75.2	30.2
5	Stanford University		72.8	42.6
6	University of Cambridge		70.5	67.4
7	Columbia University		70.1	52.2
8	The University of Texas Southwestern Medical Center at Dallas		66.8	52.2
9	University of California, Los Angeles		66.2	42.6
10	Yale University		65.2	67.4
11	University of Pittsburgh-Pittsburgh Campus		62.9	30.2
12	Karolinska Institute		62.8	30.2
13	University of North Carolina at Chapel Hill		62.3	0
14	University of Oxford		62.1	0
15	Mayo Medical School		61.4	0

ACADEMIC RANKING OF WORLD UNIVERSITIES SINCE 2003

Educating

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…me>> ARWU-FIELD 2014>> ARWU-LIFE 2014

…cademic Ranking of World Universities in Life and Agriculture Sciences - 2014

SCI ENG LIFE MED SOC Methodology Statistics

World Rank	Institution	Country	Total Score	Score on Alumni
1	Harvard University		100	100
2	University of Cambridge		82.3	67.4
3	Stanford University		79.3	42.6
4	Massachusetts Institute of Technology (MIT)		77.8	67.4
5	University of California, San Francisco		76.1	0
6	University of Washington		73.9	42.6
7	Yale University		72.6	67.4
8	University of California-Berkeley		71.2	67.4
9	Rockefeller University		67	30.2
10	University of Oxford		66	0
11	University of California, San Diego		65.8	60.3
12	Columbia University		65	52.2
13	The Johns Hopkins University		64.3	30.2
14	The University of Texas Southwestern Medical Center at Dallas		64.2	52.2
15	University of California, Los Angeles		62.9	42.6

The US federal government also noticed the lack of therapeutic heavy ions in the country

IS USA INTERESTED????

- **USA pioneered the heavy ion therapy**
  - **Clinical trials ran at Lawrence Berkeley National Lab**

1. Office of Science and Technology Policy (OSTP) at the White House
2. National Cancer Institute
3. Department of Energy(DOE)

"All understand the need of Heavy Ion Therapy Center for patient Care and Research" in US.

- **Almost 40 years after the first heavy ion patient, there is still no heavy ion therapy center in the USA**

Planning for a National Center for Particle Beam Radiation Therapy Research (P20)

Key Dates

Posted Date	January 28, 2013
Letter of Intent Due Date(s)	April 21, 2013; December 21, 2013
Application Due Date(s)	May 21, 2013; January 21, 2014
AIDS Application Due Date(s)	Not Applicable
Scientific Merit Review	October 2013; June, 2014
Advisory Council Review	January 2014; October 2014
Earliest Start Date	April 2014; December 2014
Expiration Date	January 22, 2014
Due Dates for E.O. 12372	Not Applicable

FINANCIAL ASSISTANCE
FUNDING OPPORTUNITY ANNOUNCEMENT

U. S. Department of Energy
Office of Science
Office of High Energy Physics

FY2015 Research Opportunities in Accelerator Stewardship

Funding Opportunity Number: DE-FOA-0001142
Announcement Type: Initial
CFDA Number: 81.049

Issue Date:	**June 13, 2014**
Letter of Intent Due Date:	**July 3, 2014, at 5 PM Eastern Time (A Letter of Intent is required)**
Encourage/Discourage Response:	**July 10, 2014, at 5 PM Eastern Time**
Application Due Date:	**September 4, 2014, at 11:59 PM Eastern Time**

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Buyers: Login | Register Vendors: Login | Register Accessibility

A Prospective Randomized Phase 3 Trial of Carbon Ion versus Conventional Radiation Therapy for Locally Advanced, Unresectable Pancreatic Cancer

Solicitation Number: HHS-NIH-NCI-ETSB-51007-51
Agency: Department of Health and Human Services
Office: National Institutes of Health
Location: National Cancer Institute, Office of Acquisitions

Notice Details | Packages | Interested Vendors List | Print | Link

Original Synopsis
Dec 10, 2014
2:52 pm

Return To Opportunities List | Watch This Opportunity | Add Me To Interested Vendors

Solicitation Number:
HHS-NIH-NCI-ETSB-51007-51

Notice Type:
Sources Sought

ALL FILES

Sources Sought Notice
Dec 10, 2014
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Attachment_1-Backgro...

Targeting Tumors with Particle Beams

Today, the National Cancer Institute (NCI), part of the National Institutes of Health, and the Department of Energy (DOE) are each announcing the selection of several new research awards to advance particle beam therapies for the treatment of cancer. Particle beam approaches use directed protons — or heavier ions, such as carbon ions — to target and kill cancerous tissue. Because the delivered particles interact strongly with tissue at a certain distance within the body that depends on the energy of the beam, the damage to surrounding healthy tissue can be minimized, offering an important possible alternative or supplement to more conventional radiotherapy (using x-rays or gamma rays), chemotherapy, and surgery. At present, there are 14 proton therapy centers in the United States; there are only a few carbon ion therapy facilities worldwide, but none are in the United States. The NCI awards announced today support planning for the establishment of a Center for Particle Beam Radiation Therapy as a national research resource, and the DOE awards address development of improved hardware that could shrink the size, increase the maneuverability, and considerably reduce the steep costs of particle beam therapy equipment.

The Planning Grant awards for the national research center are being made by NCI. The planned center would serve as a research adjunct to an independently created and funded, sustainable clinical facility for particle beam radiation therapy. Ultimately, the proposed center is expected to perform clinically relevant research using ion beams. The planning grants include pilot projects that will enable a research agenda in particle beam delivery systems, dosimetry, radiation biology, and/or translational pre-clinical studies. NCI encourages other researchers to collaborate with the awardees in advancing the capabilities for particle beam therapies.

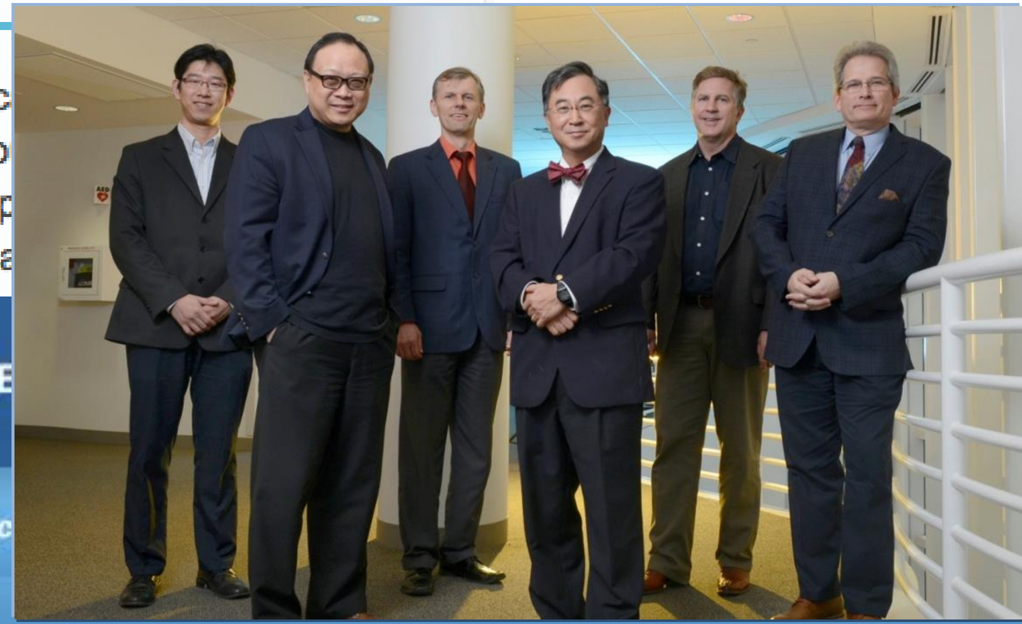
The DOE awards are being made under the Accelerator Stewardship Program. The machinery needed to produce and control particle beams, such as synchrotrons, cyclotrons, and related beam delivery systems, is expensive and complex. This machinery, however, can be used in a variety of fields, ranging from high-energy physics to materials science to medical treatment. The DOE program has the responsibility for long-term, fundamental research and development of such instrumentation. The new efforts will support improvements in the generation of the accelerated particles and in the powerful magnets that direct the charged particle beams, aiming to make these key components smaller, lighter, more versatile, and potentially less expensive.

http://m.whitehouse.gov/blog/2015/02/10/targeting-tumors-particle-beams

Posted by Tof Carim on February 10, 2015 at 11:15 AM EST

UTSW receives key NCI funding to plan first U.S. Center for Heavy Ion Radiation Therapy Research

DALLAS – Feb. 10, 2015 – UT Southwestern Medic
Texas consortium of researchers to establish the co
Center for Heavy Ion Radiation Therapy that could p
research using heavy particles for innovative new ca



BRIEFING ROOM | ISSUE

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Targeting Tumors with Particle Beams

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Posted by Tof Carim on February 10, 2015 at 11:15 AM EST

In addition the State of Texas issued a 2:1 matching grant to UT Southwestern to plan the therapeutic component as well.

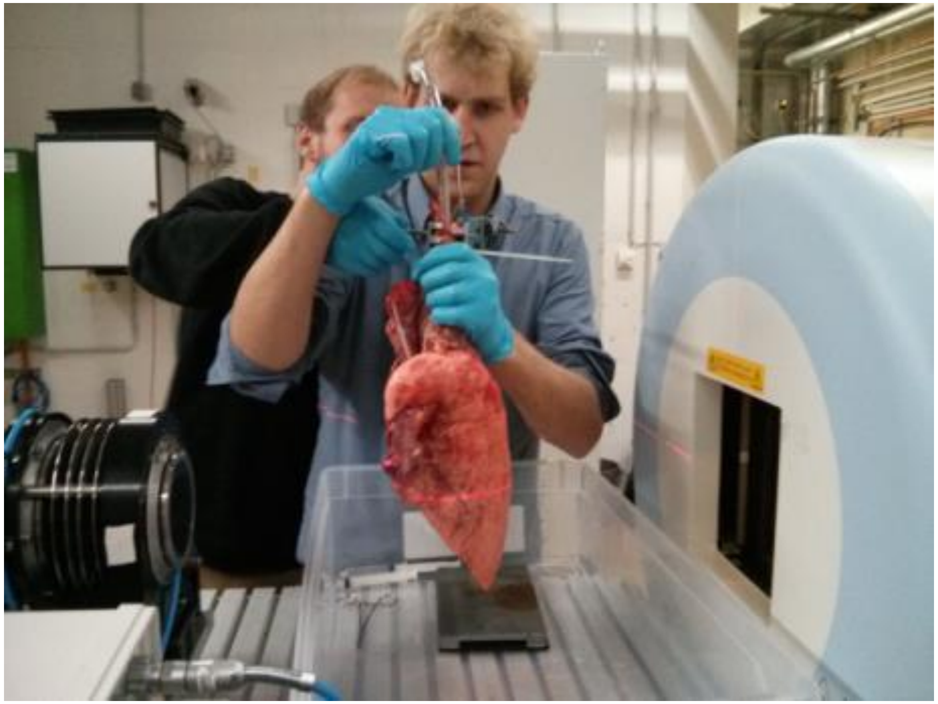
The Most Important Components

- Particle Accelerator System
- Particle delivery system
- Building
- Business Plan (not discussed here due to high uncertainties)
  - Needs estimation of annual number of patients as a function of time
  - Needs reimbursement model input
  - Needs research income modeling
  - Needs facility running cost understanding
  - Needs service contract estimation
  - Needs staffing information

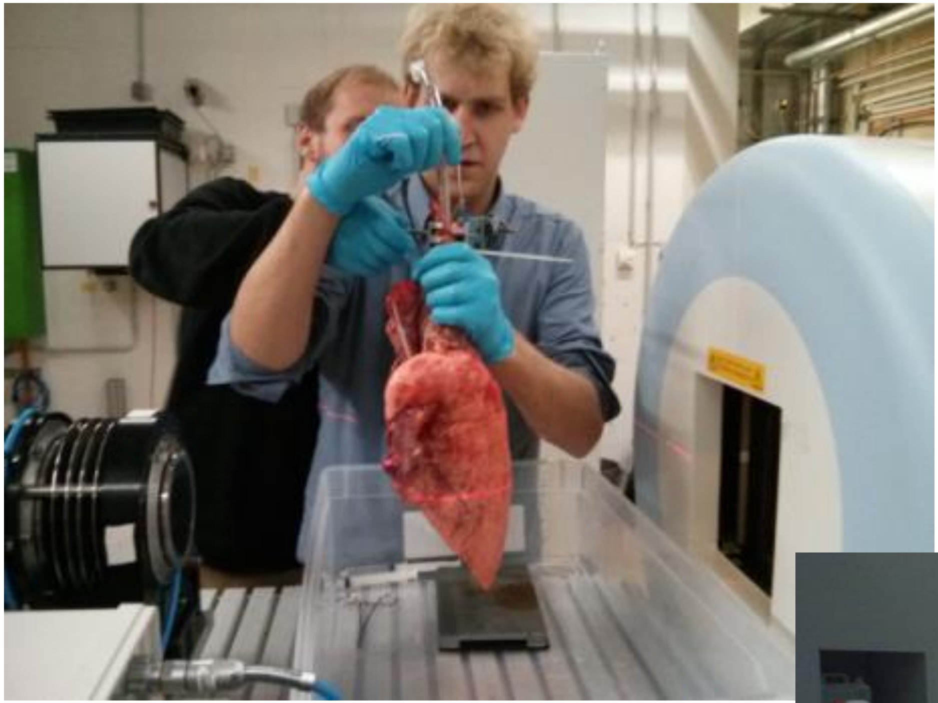
Investigators and Users of a heavy ion therapy and research facility

- Clinical and Pre-Clinical Research (therapeutic or not, for humans or not)
  - Medical Doctor
  - Translational radiation Biologist
  - Medical Physicist
- Fundamental Biologists
- Fundamental Physicists
- Fundamental Chemists
- Extraterrestrial Researchers
  - Mostly Radiation biologists and physicists
- Industry
  - Space and aeronautics

What is it that these various species of humans would like to do with the beam?

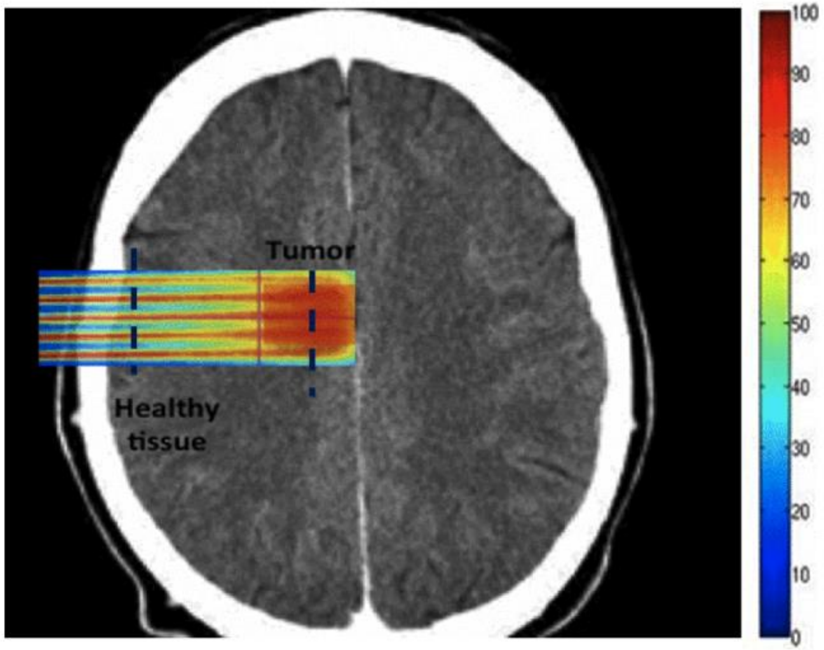


What is it that these various species of humans would like to do with the beam?



Medical Doctors (few main selected needs)

- Treat patients, treat patients, treat patients (humans or not)
- Design clinical trials to fully exploit the advantages of heavy ion therapy.
  - comparative randomized clinical trials
  - dose escalation for novel heavy ion irradiation sites.
  - high linear energy transfer (LET), in combination with low LET radiation
  - combination with surgery, chemotherapy, immunotherapy
  - normal tissue response
  - hypofractionation benefits
  - hypoxia overcome
  - treat large tumors with minibeams
  - Benign tumors
  - Non-cancerous conditions
  - Secondary cancer generation



Radiation Biologists (few selected needs)

- Understand RBE
  - in tumors, various endpoints
  - normal tissue, various endpoint
- reduction of RBE uncertainties
- biology of irradiation by heavy ions
- biology of combining cancer care modalities
- immunological consequences
- ions effectiveness with hypoxia
- micro and nano dosimetric parameters influencing biology
- exploration of genomics
  - To develop biomarkers
  - To develop personalized treatment selections for cancer
  - To enable more accurate cancer diagnosis
- modeling tumor control probability in TPS
- modeling normal tissue complication probability in treatment planning systems
- biology experiments to study cocktail beam effects

Physics (few selected needs)

- Reduction of physical dose calculation uncertainties
- Reduction of uncertainties during physical dose delivery
- Fast & robust dose calculation engines & optimization algorithms & their verification in heavy ion beams
- Micro and nano-dosimetr
- Functional imaging to produce images for better biological targeting or delivered dose
- Physical characteristics of microbeams.
- Development and testing of novel shielding materials for heavy ion therapy rooms
- Develop and test beam detectors that are very fast and very precise as far as their response time goes.
- Develop and test novel magnet designs that would allow low loss and low power operation and would enable very fast heavy ion beam energy change
- Study interaction of ions beyond the therapeutic ones

Extraterrestrial Interest (few selected needs)

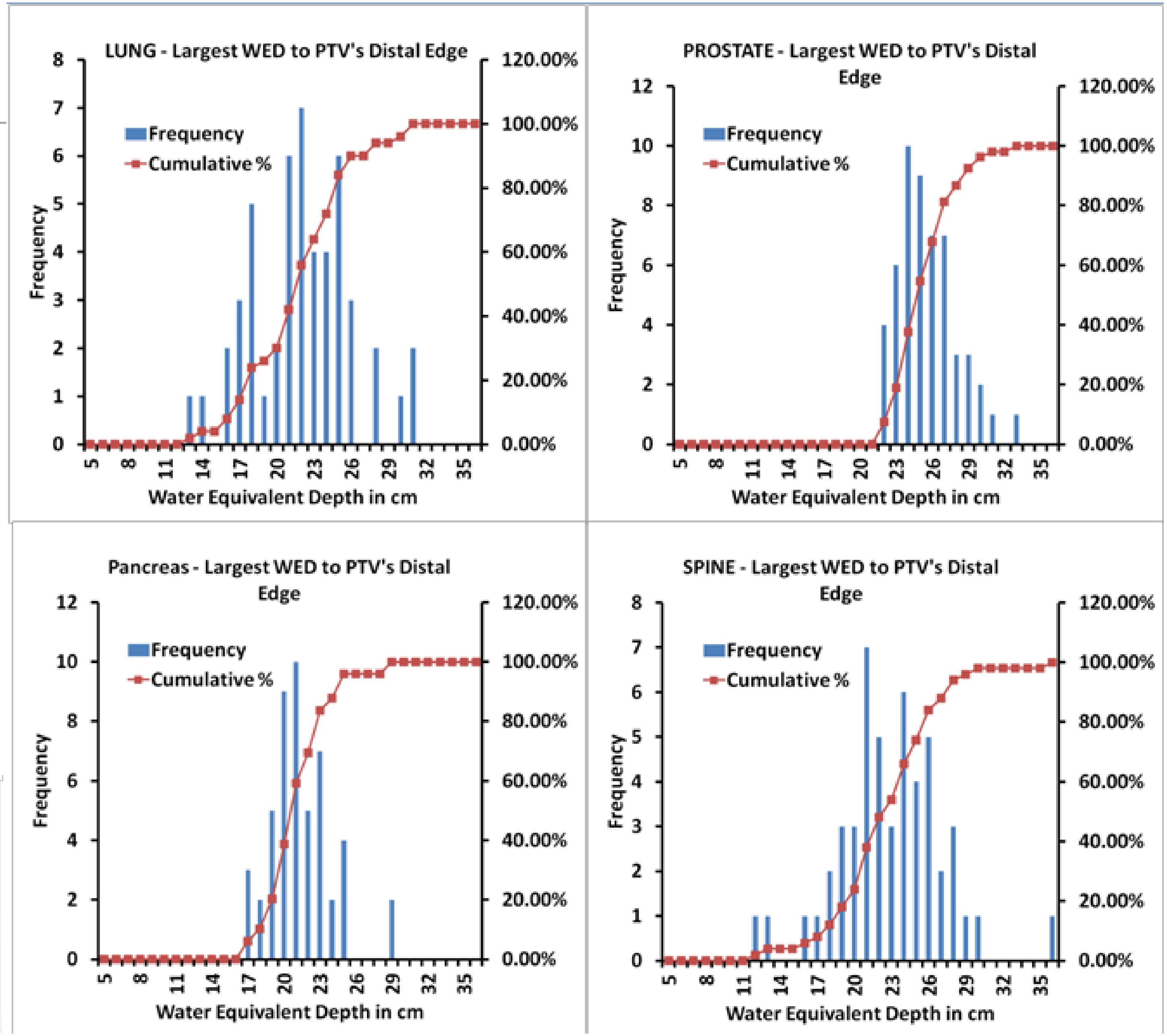
- Space radiation protection/simulation
  - Biodosimetry,
  - radiation quality factors
- Electronic testing for space applications
  - Data corruption: single and multiple bit upsets (SEU and MBU)
  - Device failure: single event latchup (SEL) and single event gate rupture (SEGR), etc.

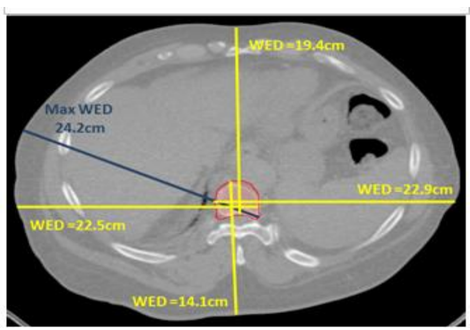
Industrial Applications (few selected needs)

- Ion implantation
- Calibration of dosimeters

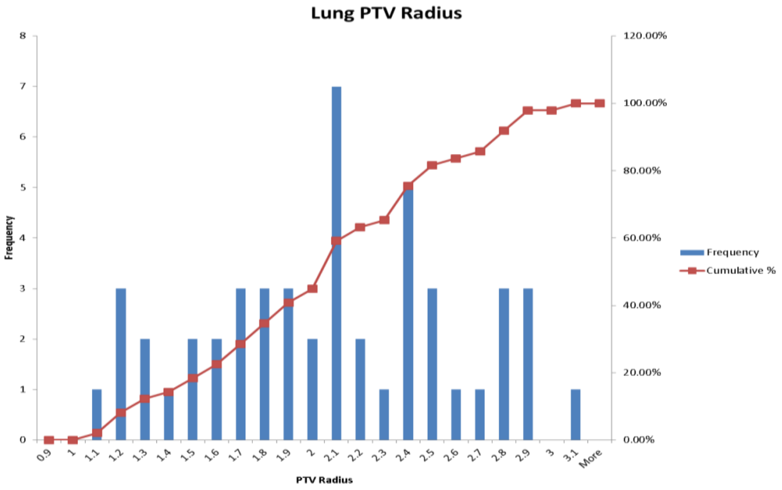
What is that the heavy ion facility should provide in order to be able to conduct the above mentioned research directions?

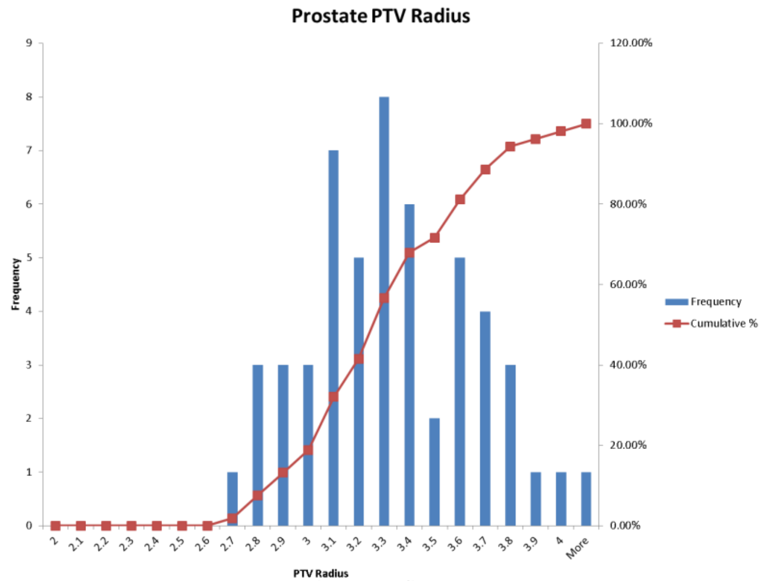
Energy needed – tied to depth of tumor

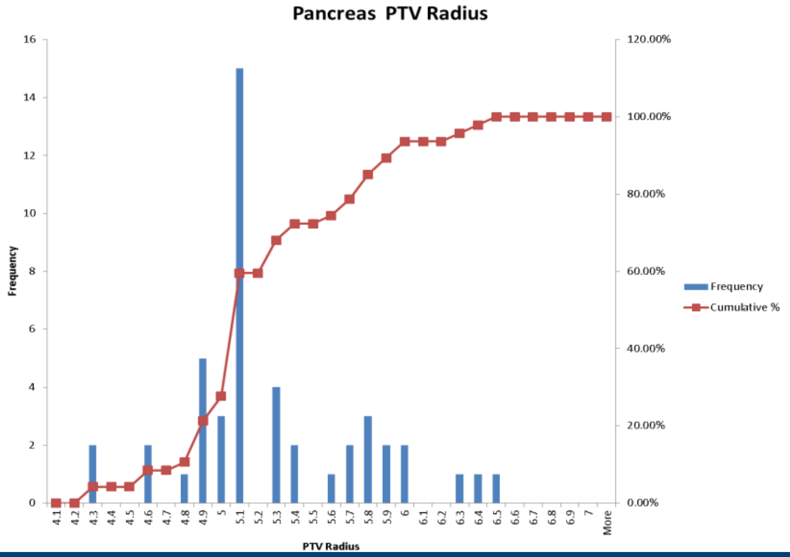


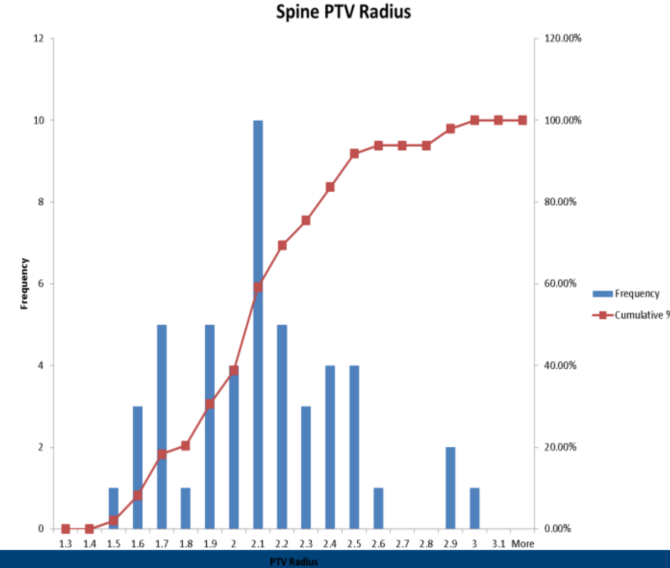


Tumor size


Lung PTV Radius
Frequency
PTV Radius
Frequency
Cumulative %


Prostate PTV Radius
Frequency
PTV Radius
Frequency
Cumulative %


Pancreas PTV Radius
Frequency
PTV Radius
Frequency
Cumulative %


Spine PTV Radius
Frequency
PTV Radius
Frequency
Cumulative %

Requirements

- Ions from Z=1 to Z= 26, including Si, Ti and Fe (simulate Galactic Cosmic Rays)
  - For therapy up to potentially Ne
  - For extraterrestrial research – higher (carcinogenic risks)
- Energies
  - Therapeutic, to reach 30cm depth, means ~ 430 MeV/n for C12
  - Extraterrestrial, to mimic what is out there ~ 1GeV/n (GCR)
- Beam intensities - high stability
  - Therapeutic – 2Gy physical dose per 10cm x10cm x10cm per minutes
  - Extraterrestrial – low dose rates 0.01 cGy/min
  - Possibility low fluence (down to ~100 -500 ions / spot, (radiography, single particle experiments)
  - 10 Gy per second for a single 0.5 mm pencil beam (minibeam research)
  - 200 Gy per second for planar minibeam of 10 mm length
  - kGy dose (dry layers, molecular chemists, free radical studies)

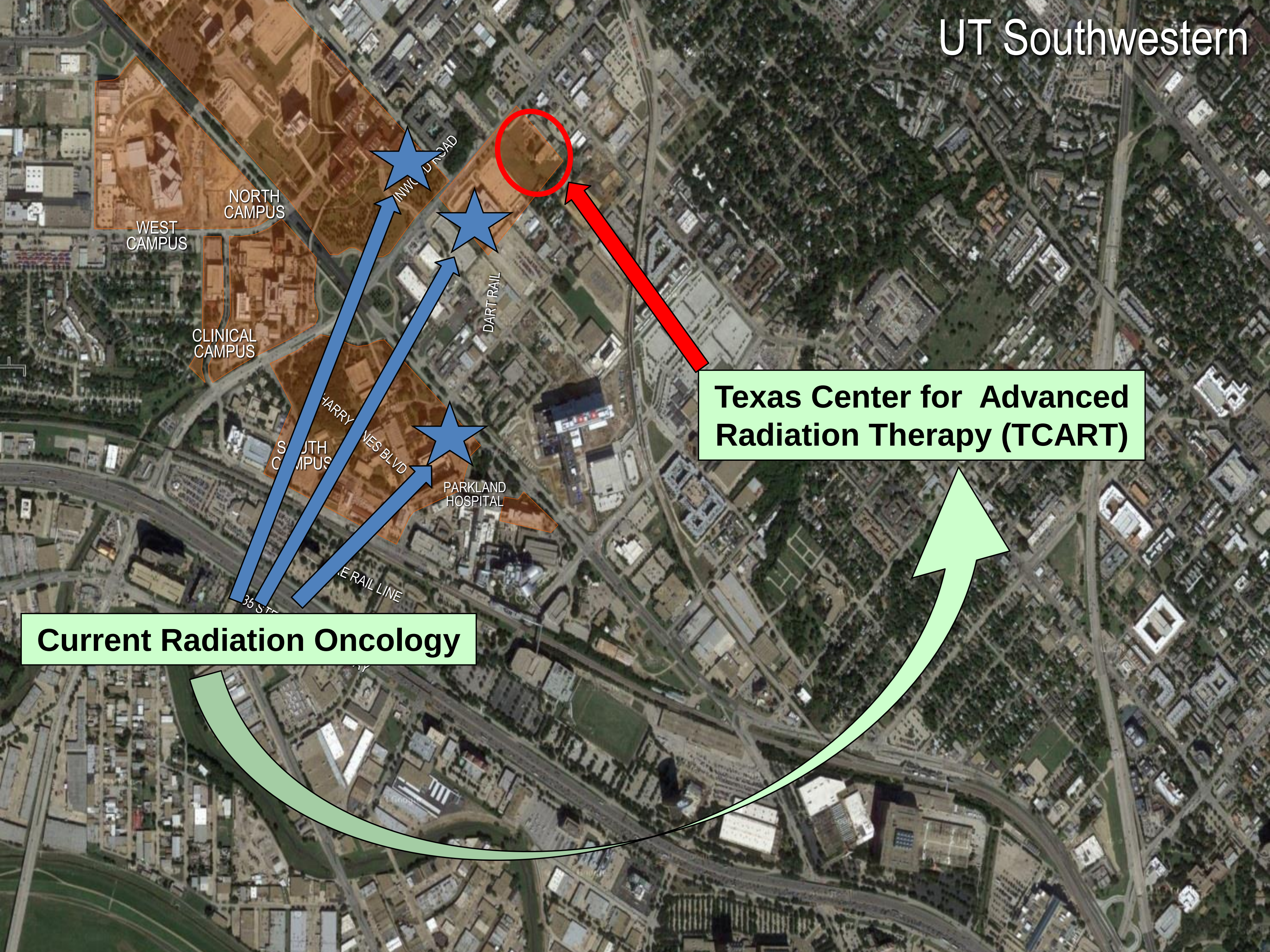
Requirements

- Fast Energy Change – order of tens of miliseconds is desired to switch particle energies
- Fast Ion species change – while patient on table (order of seconds is fine)
- Field size – for patients desired 40 x 40 cm x cm , not because of large tumors, but rather to reach multiple tumors in one patient setup
- Spot size
  – Fine focal beam 1mm FWHM for animal radiography experiments
  – Submilimiter FWHM for minibeam experiments
  – Variable for therapy purpose – small (4mm) on tumor perimeters for sharp penumbra, larger (1cm or larger) inside the tumor for fast delivery
- Research room size
  – Large enough to allow Time of Flight measurements – Target to Detectors ~10m
  – Large enough to fit auxiliary support devices (anesthesia for animals, oxygen control, imaging devices)

Now that we know what we needed, we planned it out

Current Status at Dallas – Part 1

- We have the land
- UT Southwestern allocated the necessary land within currently existing university campus


UT Southwestern
NORTH CAMPUS
WEST CAMPUS
CLINICAL CAMPUS
DART RAIL
PARKLAND HOSPITAL
Texas Center for Advanced Radiation Therapy (TCART)
Current Radiation Oncology

Current Status at Dallas – Part 2

- Issued the “Request for Proposal” for technology
- Received the proposals for Accelerators and Delivery systems
- Ranked them and worked with the top rated ones on morphing their proposal to Dallas needs
  - Gantry (rotating beam line)
  - Dedicated research room
  - High dose rate at acceleration
  - High dose rate at delivery
  - Fast energy switch
  - Fast switch between ions
  - Higher Z than C-12
  - Large field size (35cm circular)

Current Status at Dallas – Part 3

- Issued the “Request for Qualification” for technology
- Hired Architects
- Created a design
- Finished shielding calculations

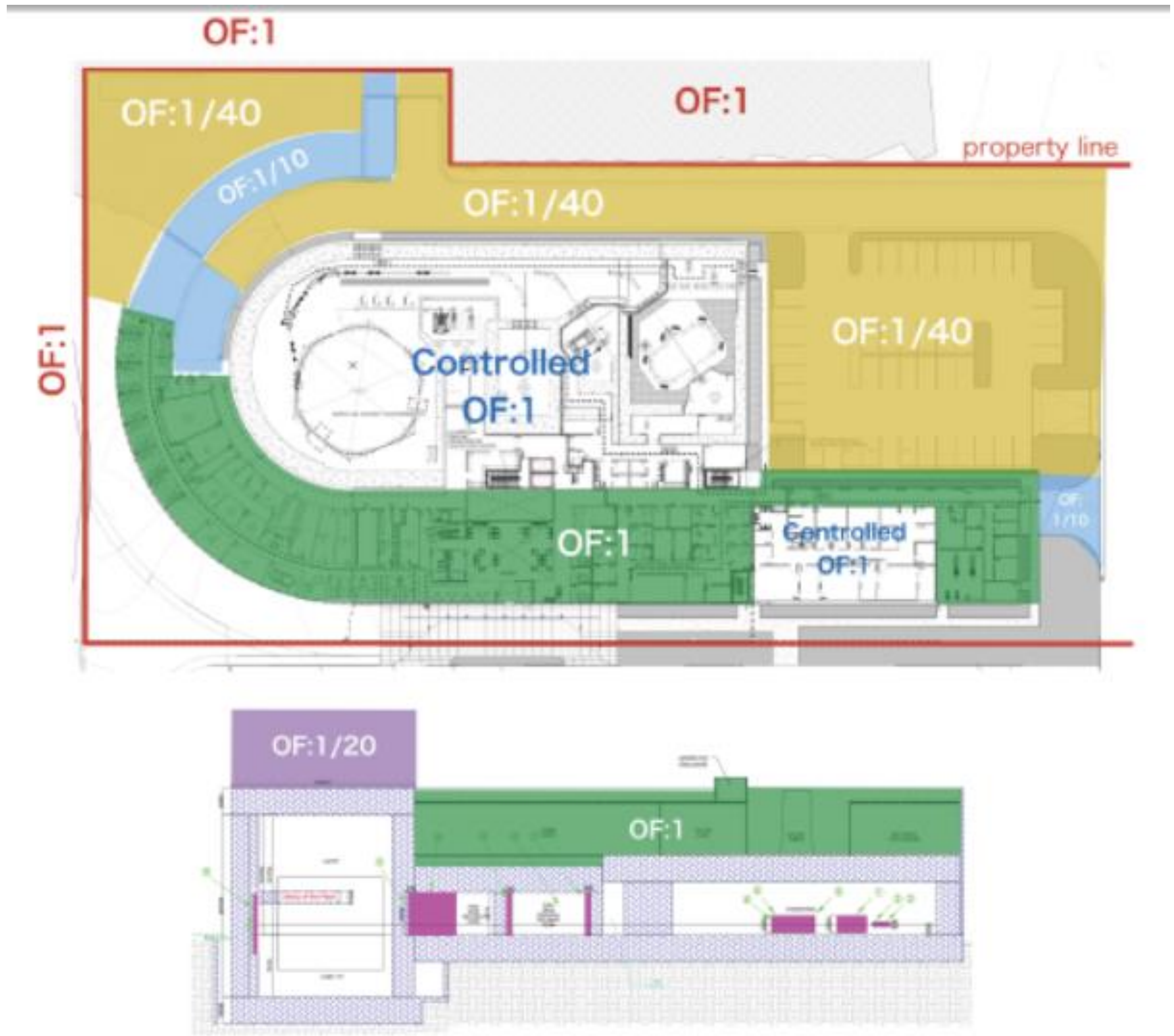
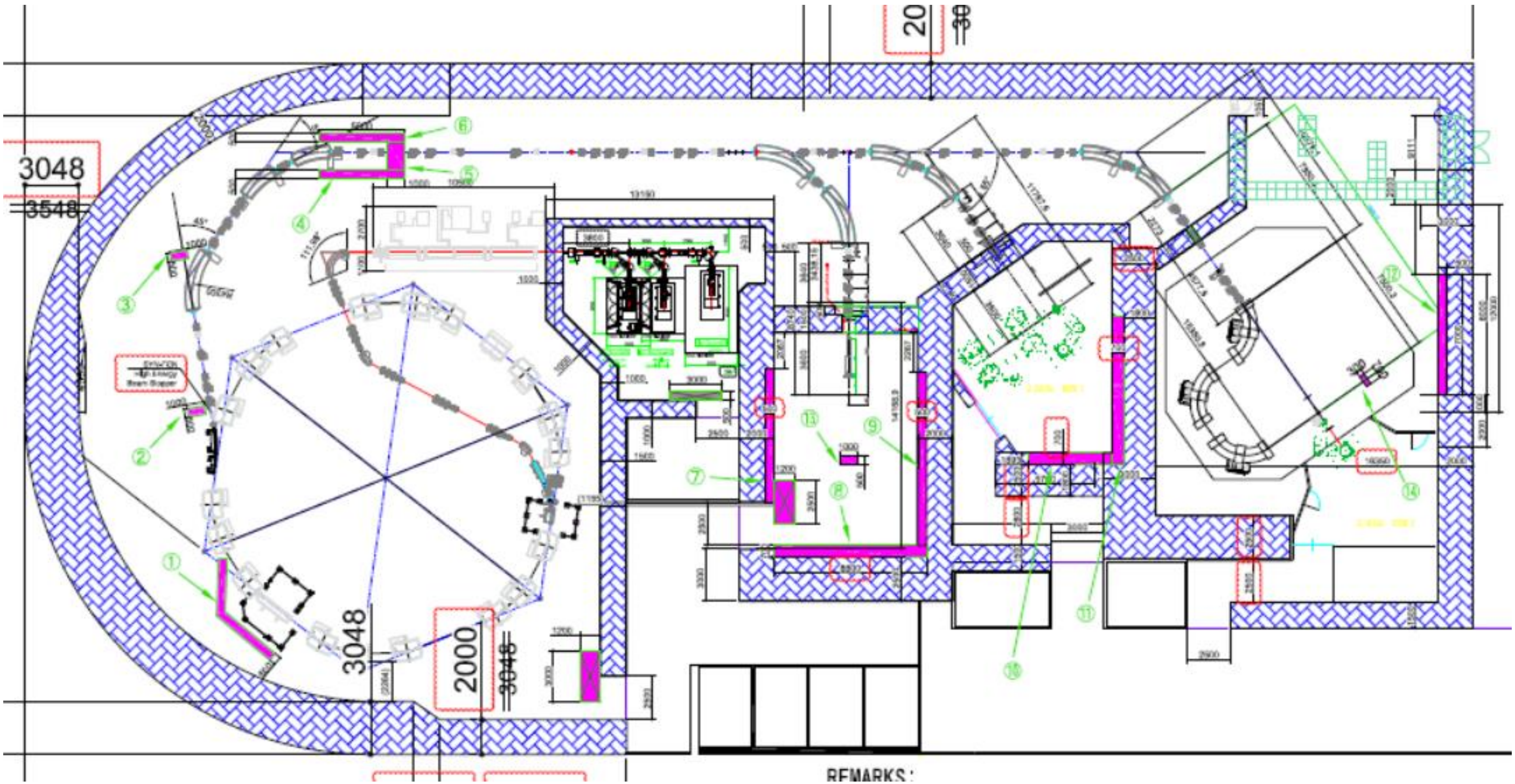


Figure 3: Definition of occupancy factor (OF) in uncontrolled area


20
3048
3548
3048
2000
3048
REMARKS:

- Schematic design documents ready
- Ready for construction documents
- Ready for construction funds

Conclusion

- USA wants to build a heavy ion center
- Texas wants to build a heavy ion center
- NCI awarded funds to plan the research part of the heavy ion system
- State of Texas awarded funds to plan the therapy part of the system
- UTSW identified scientific to do things
- UTSW identified the specs the system must fulfil to meet the needs
- Selected typical expected machine performance parameters
- We created the schematic design documents
- Ready for construction documents
- Ready for construction
- Working on securing construction funds

ISIT

INTERNATIONAL SYMPOSIUM on ION THERAPY

Local Organizing Committee

Hak Choy, M.D.
UT Southwestern

Robert Timmerman, M.D.
UT Southwestern

Michael Story, Ph.D.
UT Southwestern

Steve Jiang, Ph.D.
UT Southwestern

Arnold Pompos, Ph.D.
UT Southwestern

Save the date

ISIT 2017
November 2-3

Preliminary Agenda

- Heavy Ion Related Radiation Biology, Physics & Clinical Research: Results & Discussions
- State of the Art Heavy Ion Therapy Technologies

International Organizing Committee

Marco Durante, Ph.D.
TIFPA & INFN, Italy

Roberto Orecchia, M.D., Ph.D.
CNAO, Italy

Harald Paganetti, Ph.D.
MGH, USA

Quynh-Thu Le, M.D.
Stanford, USA

Hirohiko Tsujii, M.D., Ph.D.
i-ROCK, Japan

Held at
UT Southwestern Medical Center
Dallas, Texas