Overview of the A-BNCT System in Korea

Jan. 30th, 2018

D.S. Kim

A-BNCT Project
Dawonsys

Contents

BNCT (Boron Neutron Capture Therapy)

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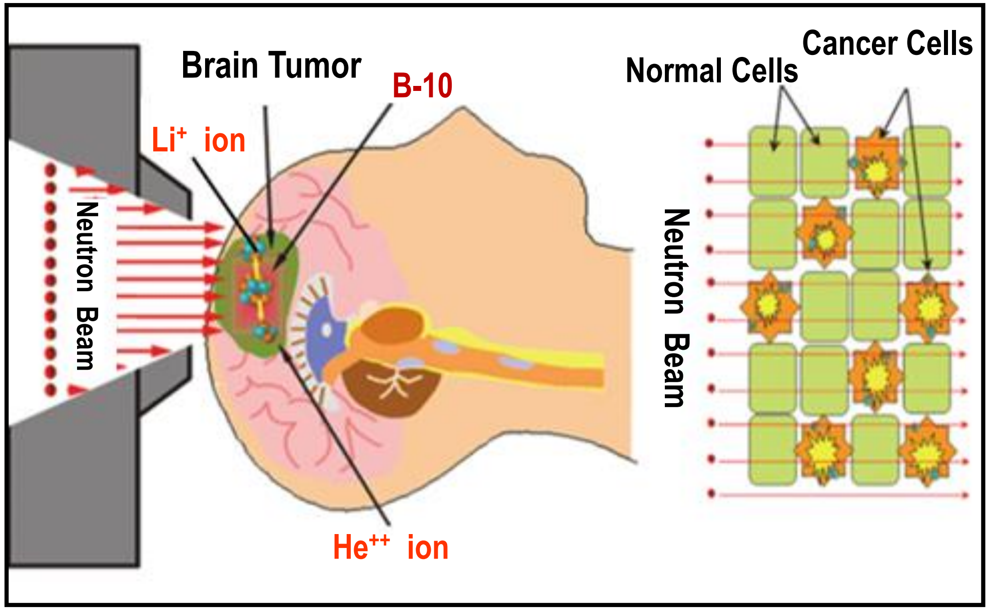
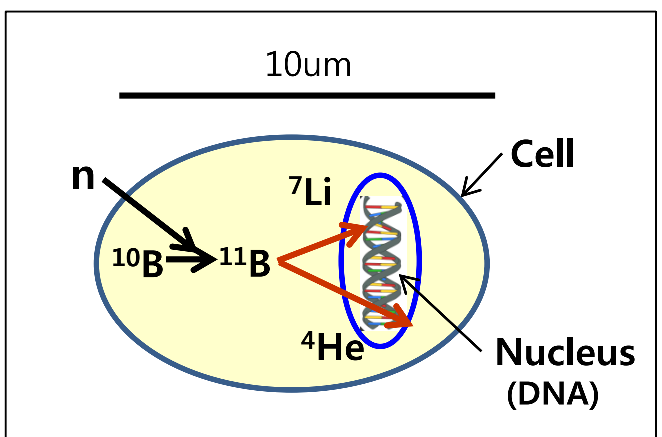
❖ Principle of BNCT



❖ Cell death by 2ndary ions from NR



❖ Therapeutic Features of BNCT

- Clarity of therapeutic principles
- Treatment unit of cell size
- Minimization of radiation exposures for normal tissues
- Reduction of side effects
- Treatment of malignant cancers which are not effective with conventional treatments
  (Brain Tumor, Head & Neck Cancer, Malignant Skin Cancer, Recurrent Cancers, Radiation Resistant Cancers)

❖ Clinical Trials of BNCT

Stage	Fields	Name of diseases	Treatment Effects
Clinical Trials & Treatment	Brain Tumor	Glioma GlioblastomaMutiforme(GBM) Astrocytoma	good
	Head-Neck Tumor	Carcinoma	good
	Skin Cancer	Malignant Melanomas Mesothelioma	good
Under Clinical Trials	Recurrent Cancer	Recurrent Breast Cancer	good
	Thyroid Cancer	Undiffertial Thyroid Cancer	Fair

Brief History of BNCT R&D Activities in Korea

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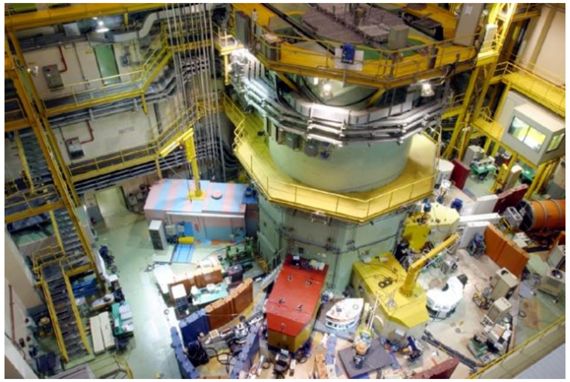
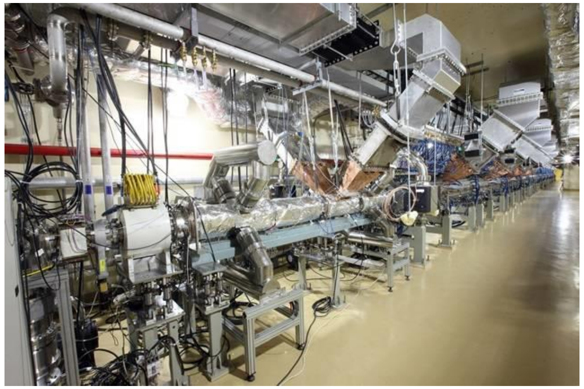
❖ 25 years to study on BNCT : Neutron Sources, Boron Compounds, Biological Effects, TPS

1. **Survey study of BNCT**: KIRAMS ('92-'96)
2. Establishment of basic technology of BNCT: KAERI ('96-'99)
3. **Building a thermal neutron beam port at 30MW Hanaro reactor**
   : KAERI ('97-'02)
4. Development of Boron labeled compound (^{18}F-BPA, ^{123}I-BPA)
   : KIMAMS ('02-05)
5. **Biological studies on cells & rats with boron compounds and thermal neutrons**: KAERI('02-'07)
6. Design study of an accelerator based BNCT
   : Hanyang Univ. ('02-'07)
7. Development of new boron compounds,
   : Wonkwang, Chosun & Korea Univ. ('02- '12)
8. **Construction of a 100MeV Proton Linac, KOMAC,**
   (Korea Multipurpose Accelerator Complex) KAERI ('02-'12)
9. **Establish of A-BNCT project : Dawonsys Consortium** ('16-'20)

☐ **Hanaro** (30MW Reactor)



☐ **KOMAC** (100MeV Linac)



Evolution of BNCT Facilities – Neutron Source

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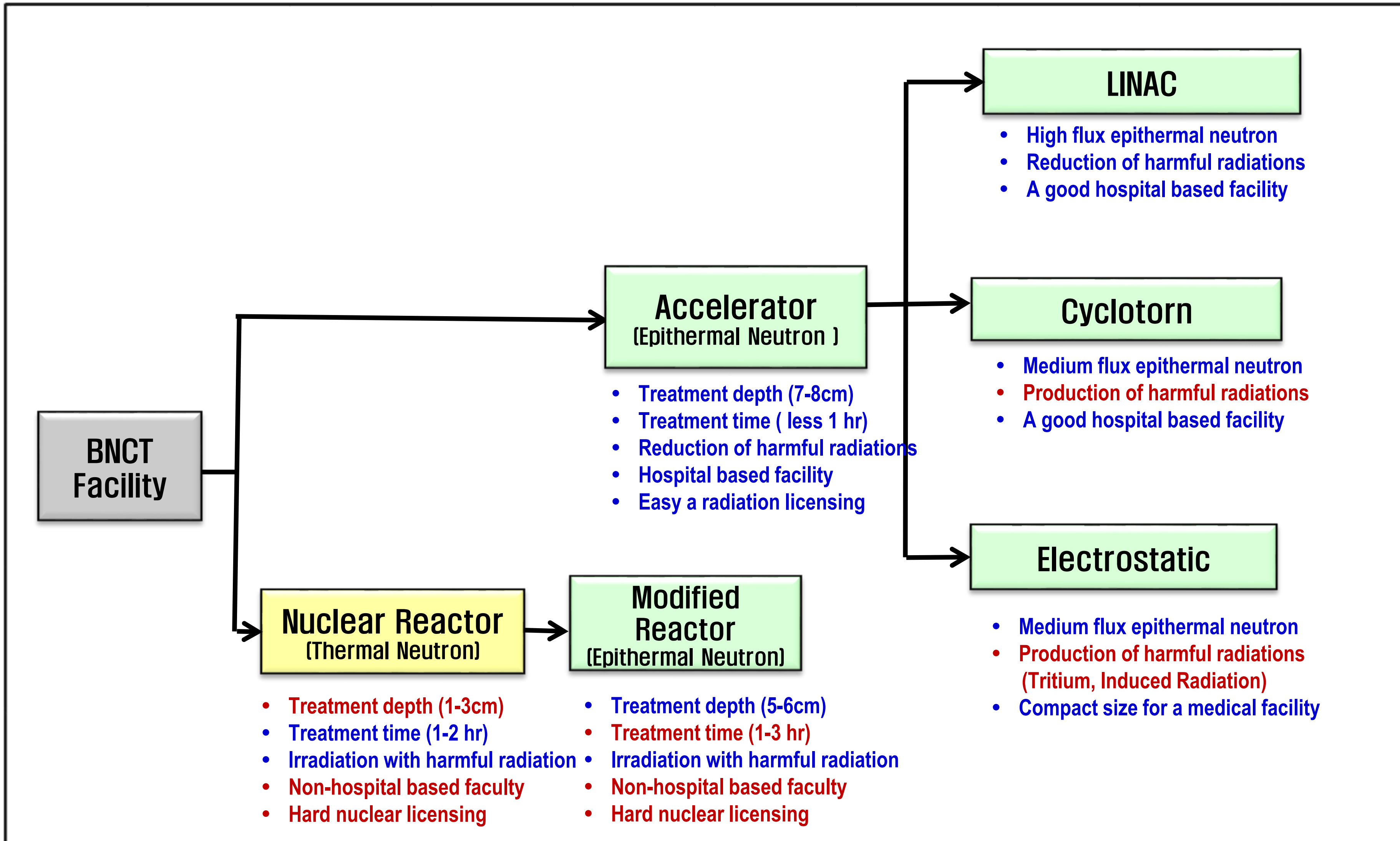
❖ Development of BNCT systems



Requirements of Accelerator based BNCT System

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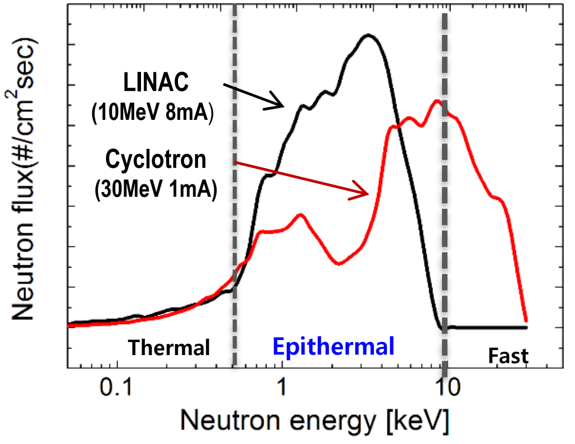
❖ Requirements for Neutron Sources

1. Quality of neutron beam
   - Epithermal neutron spectrum
2. Quantity of neutron beam
   - Epithermal neutron flux
3. Reduction of harmful radiation doses
   - Fast neutrons / thermal neutrons
   - Prompt gamma radiation
4. Elimination of induced radiations dose
   - Induced radiations from

Distribution of moderated neutron energy



❖ Considerations as a Medical Facility

1. Hospital based facility
   - Small size & area
   - Connection with other diagnostics
   - Easy operation (automatic controll)
2. Safety
   - Radiation safety
3. RAM
   - Reliability, availability, maintainability
4. Cost Effectiveness
   - Machine costs
   - Operation costs

2. Introduction to the A-BNCT Project

Technological Bases for a BNCT system at Dawonsys

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❖ Accelerator & Fusion Projects

Large Accelerator Project in Korea

❐ **Light Source Projects**
- Modulator & MPS for PLS
- Modulator & MPS for Pohang XFEL

❐ **Medical Heavy Ion Accelerator Project**
- Investment Agreement to develop heavy ion accelerator
- Precision Dipole MPS

❐ **Heavy Ion Accelerator Project (RAON)**
- Precision MPS

❐ **Intense Neutron Source Project at KBSI**
- RFQ RF Power System

Nuclear Fusion Project

❐ **KSTAR Project of NFRI**
- NBI Power Supply
- ECH Power Supply
- PF & TF Magnet Power Supply

❐ **ITER**(International Thermonuclear Experiment Reactor) **Project**
- ITER Converter Module
- ITER Superconducting Magnet PS

❖ Participating Foreign BNCT Projects

❐ **iBNCT Project** at Tokai, Japan.

- **Business ;**
  ① Development & Delivery of a modulator for high power RF Source
  ② Maintenance Project for RF System

- **Collaboration** :
  ① Contribution to a foreign BNCT project using Dawonsys' Technologies.
  ② Construction of international network to develop the Accelerator Based BNCT.

❐ **OIST-BNCT Project** at Okinawa, Japan

- **Business** :
  ① Design of New type Klystron Modulator
  ② Solenoid Magnet & Its Power Supply

- **Collaboration** :
  Participation and contribution to a commercial BNCT project.

History of A-BNCT Project at Dawonsys

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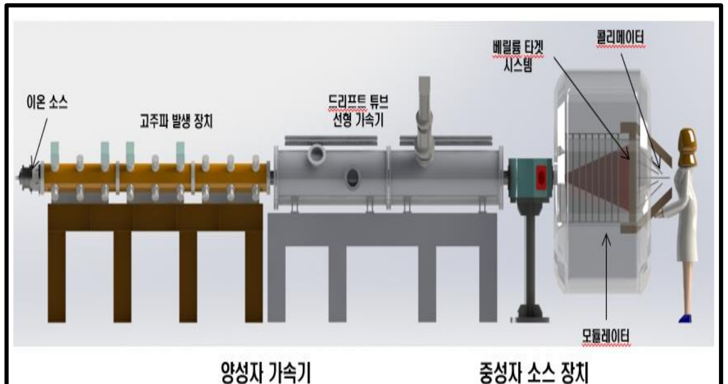
Year Month	A-BNCT Development Activities	Results
15. 03	BNCT commercialization plan passed the board of directors of Dawonsys	· Overall planning of BNCT business
15. 05	Composition of a consortium of A-BNCT	· Organizing cooperation activities among industry, institutes, universities and hospitals.
15. 06	Start A-BNCT system design	· Design injector/RFQ/DTL · Design target assembly · WBS project management system · Design building and utility
15. 10	Investment agreement for A-BNCT	· Attract investment of building & utilities from BRC/Gachon Univ.
15. 11	Agreement on utilization of A-BNCT	· Dawonsys – Gil Hospital
16. 03	Agreement on boron drug development	· Dawonsys – Gachon University
16. 03	Propose a government project to develop & Commercialize A-BNCT	· Review & evaluation process

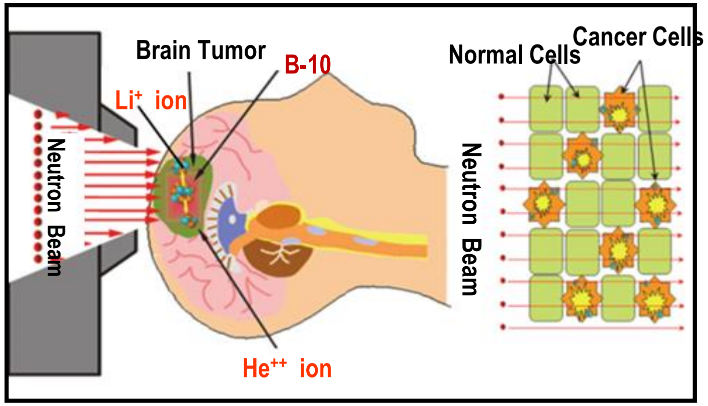
Summary of A-BNCT Project

- ❒ **Project Name :** Development of the accelerator based Boron Neutron Capture Therapy system for the cancer treatment within "1 hour" therapeutic time
- ❒ **Project Period :** 2016 . 5 ~ 2020 . 12
- ❒ **Leading Organization :** Dawonsys Inc.
- ❒ **Participating Organizations :** Gil Hospital, Gachon Univ., PAL, KAERI and KBSI
- ❒ **Developed Items :** Proton Linac, Be Target / Moderator Assembly, Dosimetry (Neutron & Gammas), Radiation Safety & Licensing, Boron Compounds, TPS(Treatment Planning System), Clinical Trials, Government Approvals of Boron Compounds & BNCT Treatment

A-BNCT Facility



BNCT TPS

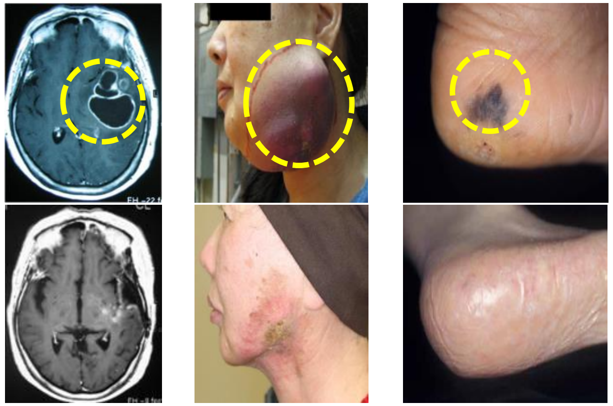


BNCT Treatment

Brain Tumor

Head &Neck Cancer

Malignant Skin Cancer



Set up Goals for A-BNCT facility

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❖ Qualitative Goals

1. To achieve and exceed characteristics of neutron source for BNCT recommended by "IAEA"

2.. To reduce a treatment time, less than 1 hour by delivering high flux of epi-thermal neutrons over 2 X 10^9 [n/cm^2.s]

3. To establish and implement a precise treatment planning system through real time measurements of radiation doses and boron concentration for each patient.

4. To realize safety, reliability, availability, maintainability and easy operation of the system as a medical facility.

5. To prepare 2 treatment rooms and a research room for effective utilizations of the facility

❖ Performance Goals

❑ Neutron Source

- Epithermal Neutron Flux : more than 2 X 10^9 [n/cm^2.S]
- Ratio of Epithermal Neutrons / Thermal Neutrons : more than 20
- Fast Neutron Dose / Epithermal Neutron Dose: less than $2x10^{-13}$
- Gamma Dose / Epithermal Neutron Dose : less than $2x10^{-13}$
- Neutron Irradiation Field: about 15 x 15 cm^2

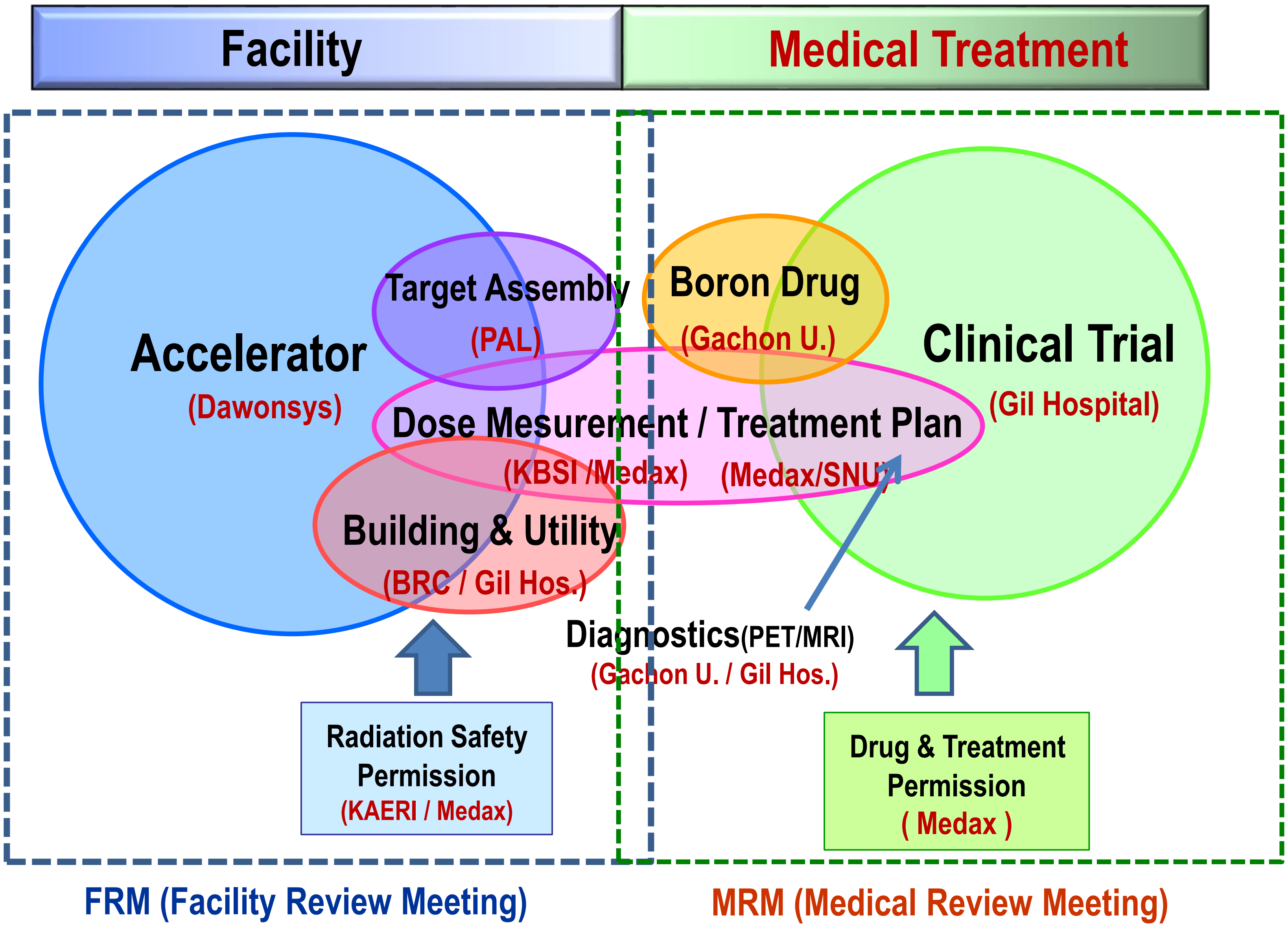
❑ Accelerator & Target

- Type : High Power Proton LINAC
  (50kV Injector + 3MeV RFQ + 10MeV DTL+ BT)
- Beam Energy : Two Operation Modes
  10MeV (for a high neutron flux operation)
- Beam Current (Average / Peak) : 10 / 50 mA
- Beam Power : max 80 kW
- Target / Cooling : Be / Water

❑ Treatment Ancillary Facilities

- Rooms : 2 treatment rooms, 1 research room
- Treatment Planning System : S/W, H/W
- Diagnostics : MRI, F^{18}-FET, CT
- Patient Positioning & Alignment Devices

Fields and Interfaces of A-BNCT Collaboration



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Objectives & Schedule of A-BNCT

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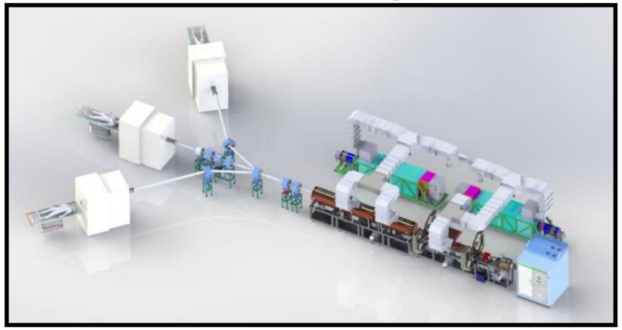
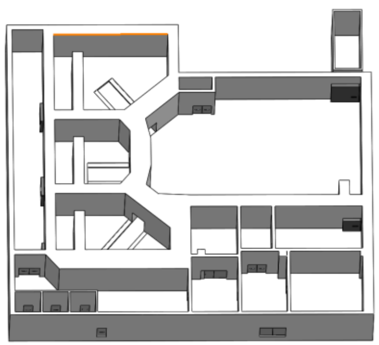
Fabrication of Components (1st -2nd yr.)



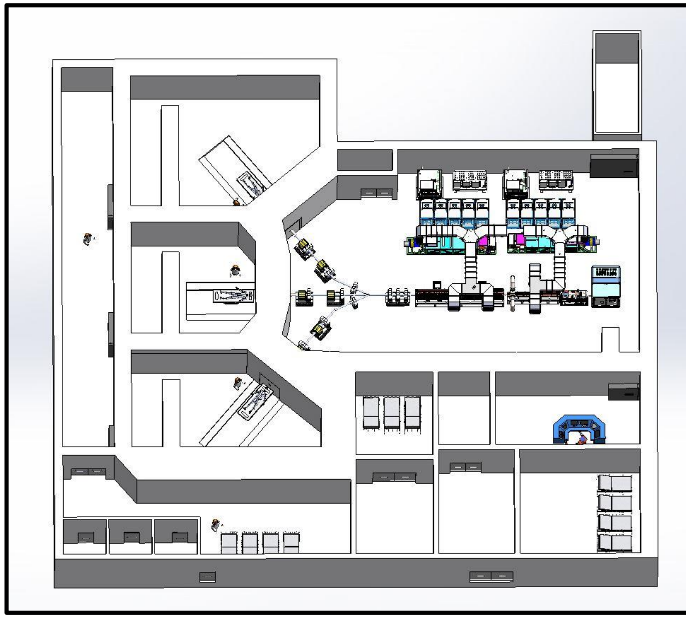
Proton Linac : Injector + RFQ + DTL + BL
Target System : **Be Target** + Assembly

Constr. of Building & Utility (1st -2nd yr.)



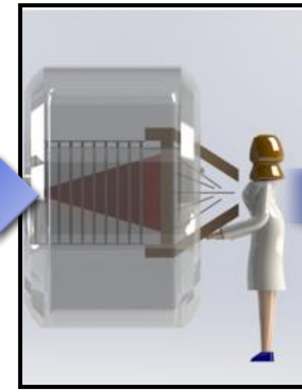
Building: 35.3 x 21.8 m^2 , Radiation Shielding
Utility: Electricity, Cooling Water, Air Cond. etc

Installation & Commissioning (3rd - 5th yr.)



Proton Beam : Energy 7~10 MeV, Power 1→20→80 kW
Epithermal Neutron Flux : 0.03→ 0.5→ 2 x10 ^{9} n/cm^2s

Clinical Trial (3rd - 5th yr.)



1st Stage Trial
2nd Stage Trial

Final Goal

- **BNCT 3rd Stage**
- **Facility Transfer to the Hospital**

Development of Boron Compounds (1st -3rd Yr.)

Synthesis of B Compounds ⇨ **In-Vitro Exp. (Cell, Animal)** ⇨ In-Vivo Exp. (Man)

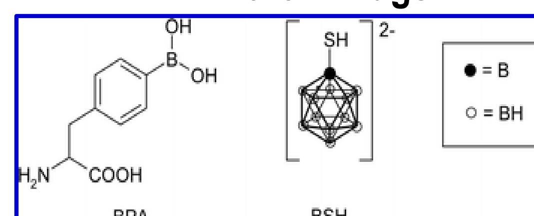
Boron Drugs : BPA. BSH, ^{18}FBPA

Report on In-Vitro Experiment

Cancer Cell Uptake of B-10 : 10→25 μg/g
Boron Ratio of Cancer/Normal Cell : 2→4

Entrance

Boron Drugs



Road Map & Milestones

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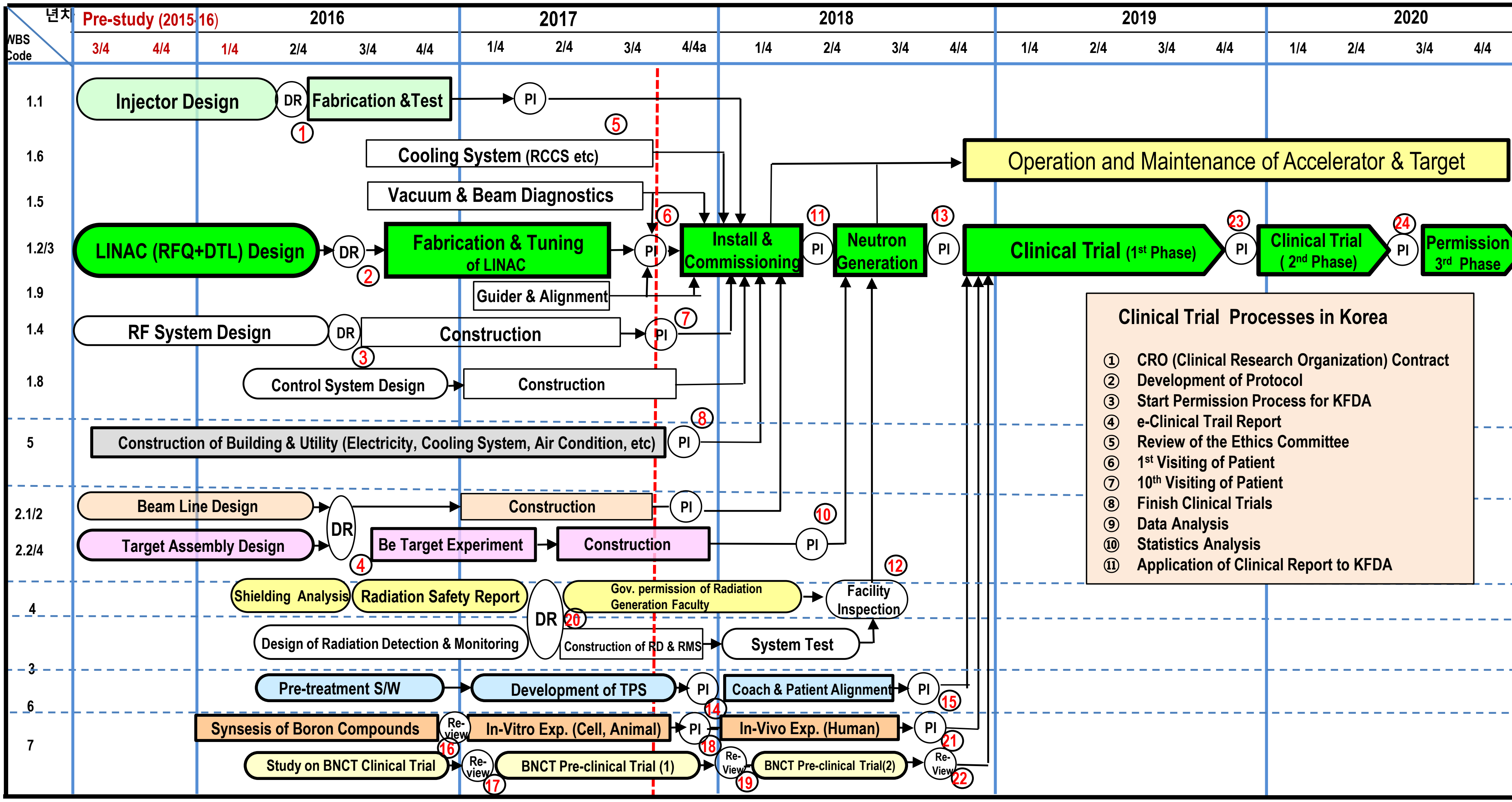
❖ Component Development and Review Process

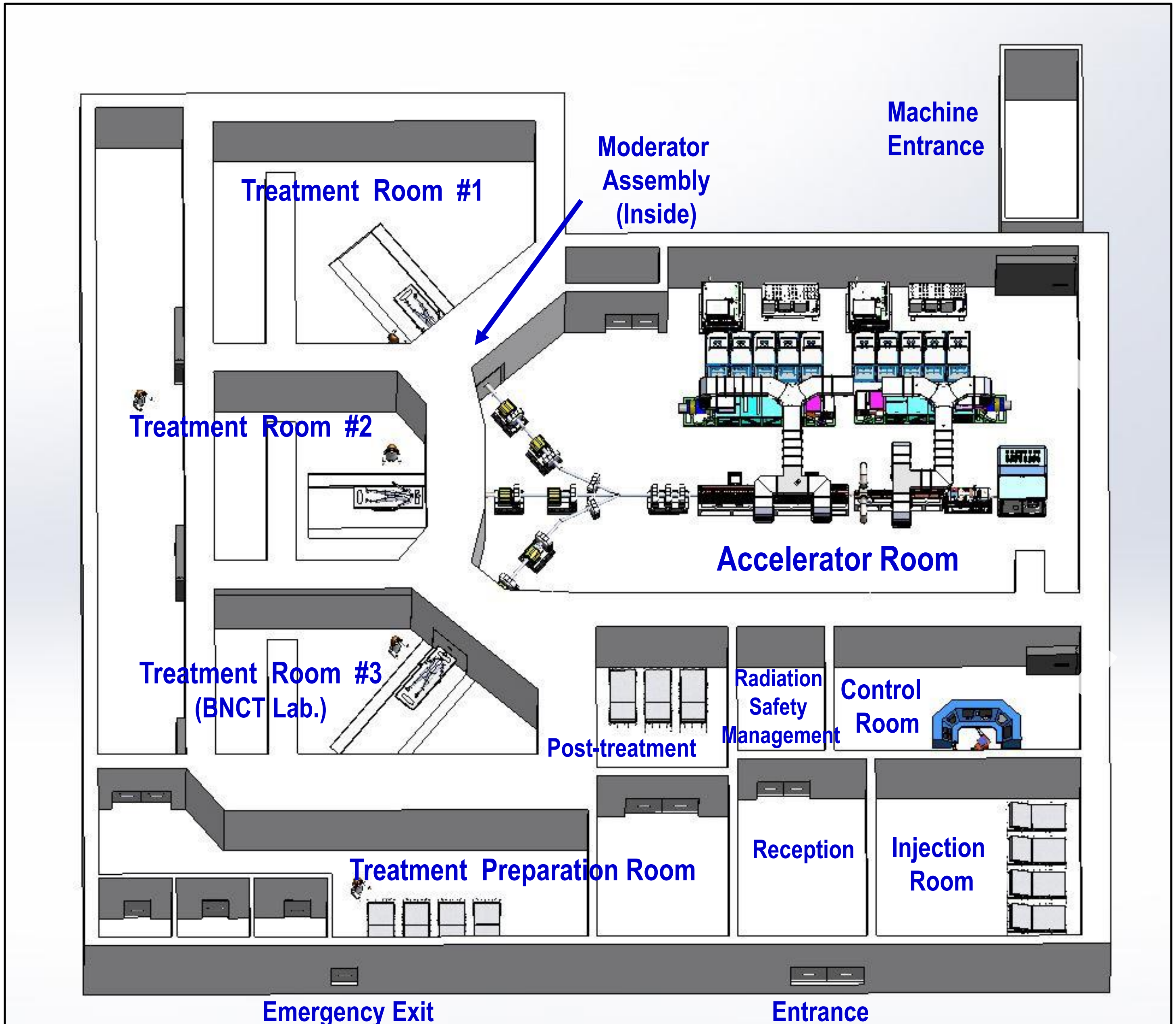
S/W
H/W
Review : MRM & FRM



DR : Design Review **PI** : Performance Inspection

3. Development Status of the A-BNCT Facility

Layout of A-BNCT Facility



Building : 35.3 x 21.8 m^2 with shielding

Utility : Electricity, Cooling, Air Cond.

A-BNCT Facility

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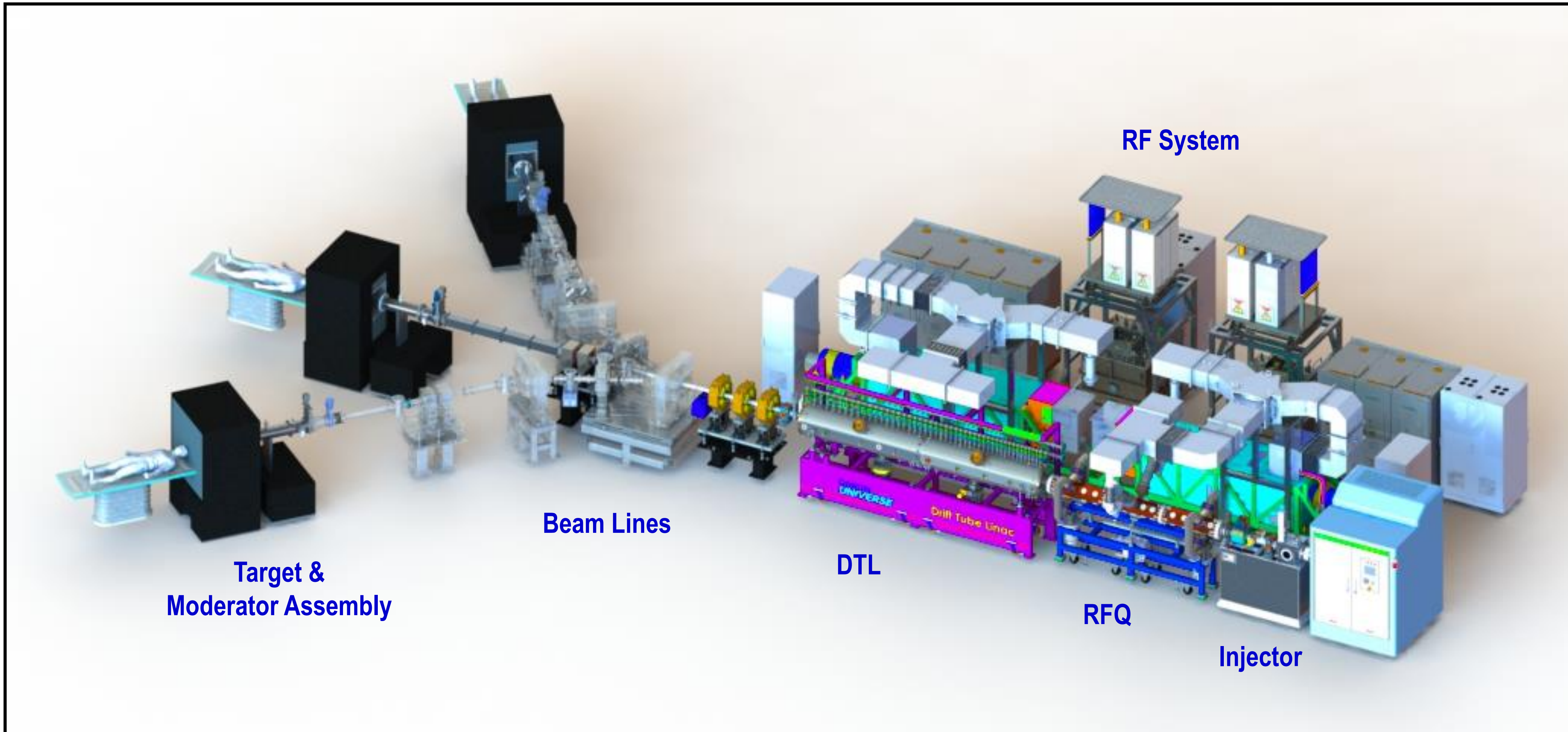
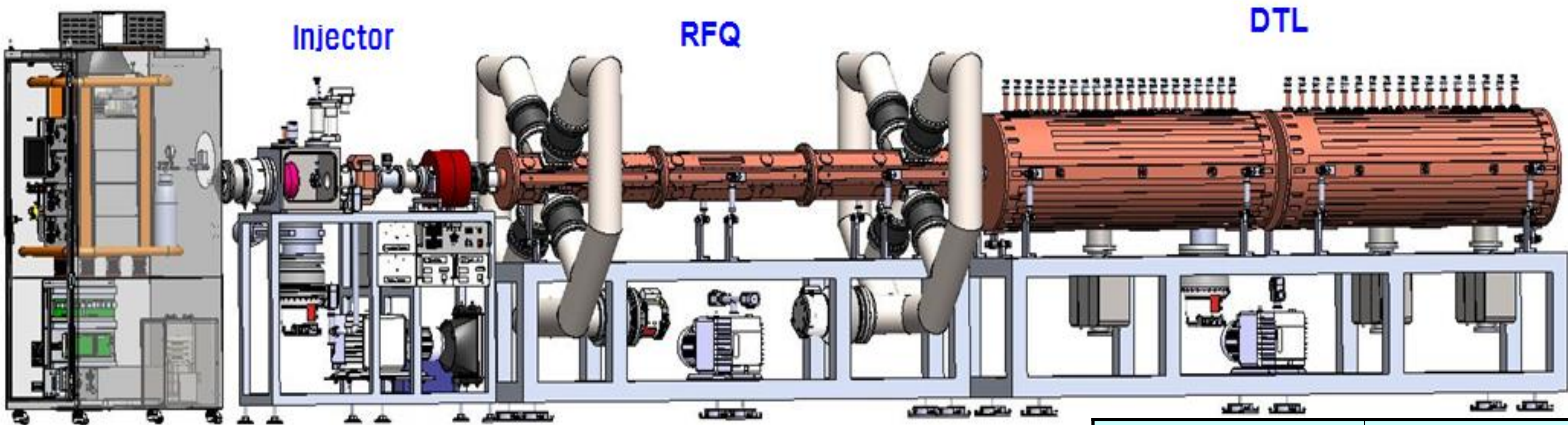


Neutron Generator

Proton Linear Accelerator

A-BNCT Proton Linear Accelerator

❐ A-BNCT Accelerator System (50keV Injector + 3MeV RFQ + 10MeV DTL)



Injector Parameter	Value
Beam Energy	50 keV
Beam Current (peak)	60 mA
Proton Ration	> 80%
Pulse Length	1.7 ms
Repetition Rate	120 Hz
Emittance	0.11 π mm mrad
Length	**1.85 m**

RFQ Design Parameter	Value
Frequency	352 MHz
Beam input / output energy	0.05 / 3.0 MeV
Beam current (average)	8 mA
Peak surface electric field	31.73 MV/m
Input emittance (rms, norm)	0.2 π mm mrad
Transmission	93.96 %
Length	**3.18 m**

DTL Design parameter	Value
Frequency	352 MHz
Beam input / output energy	3.0 / 10.0 MeV
Input beam current(average)	8 mA
Length	**4.85 m**
Number of DT	50
Peak surface electric field	12 MV/m
Magnetic gradient	50 T/m
Total power (wall + beam)	900 (540 + 360) kW

❐ Features & Achievements

1. High beam power of 80kW (10MeV, 8mA) with a compact machine size of 10m length for in-hospital facility
2. design & construction through domestic collaboration using domestic accelerator technology
3. design focus : reliability, availability, maintainability and economic consideration

Progress of the Linear Accelerator

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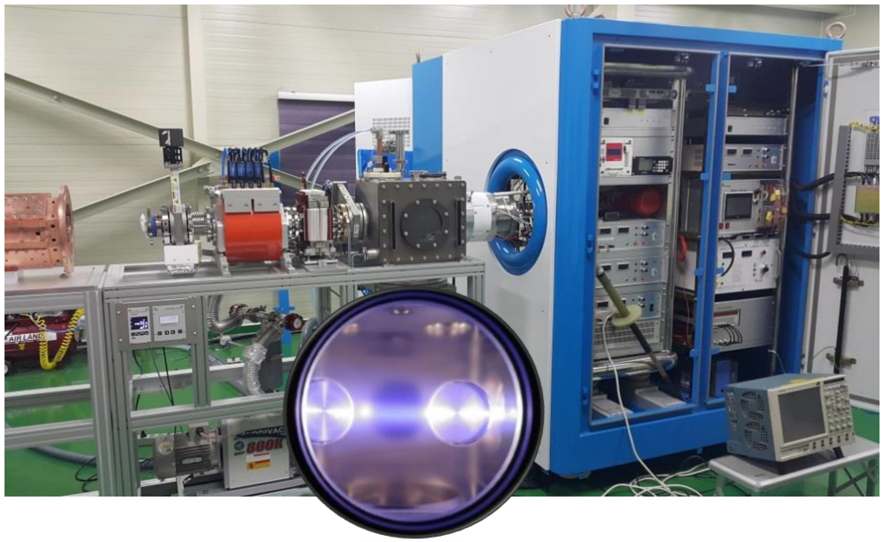
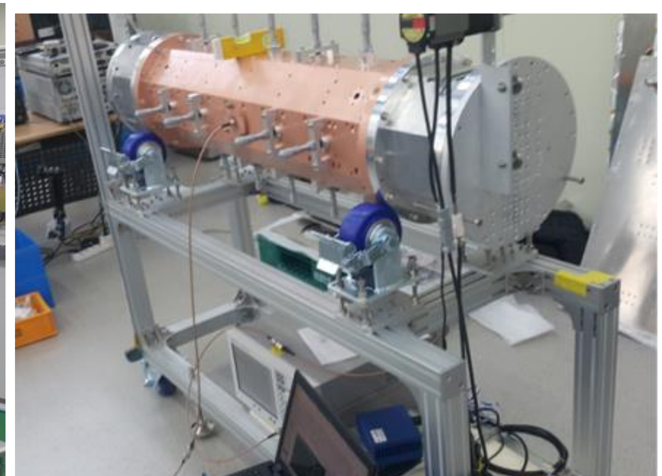
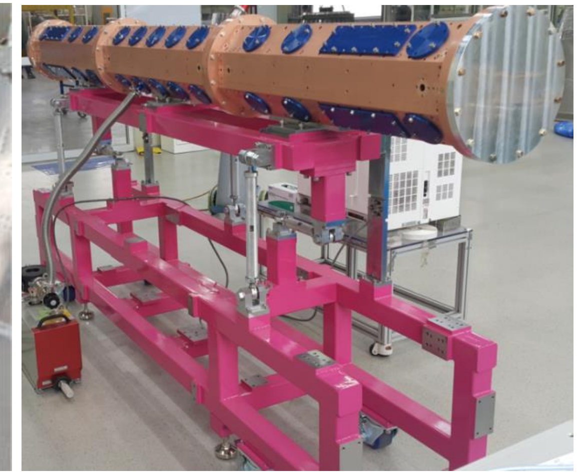
❐ Proton Injector (Under Beam Test)

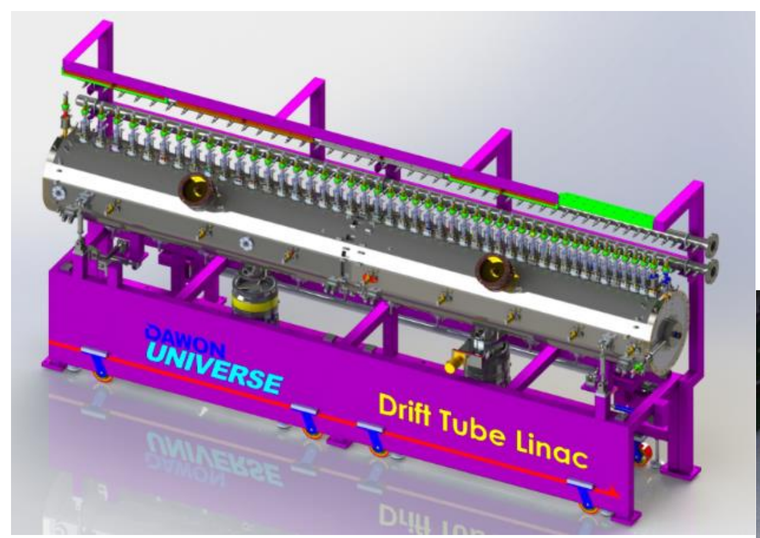


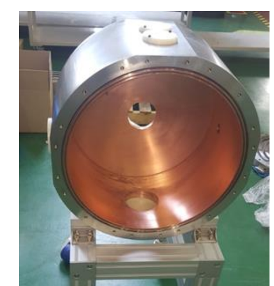
❐ RFQ (under Fabrication)





❐ DTL (Under Fabrication)



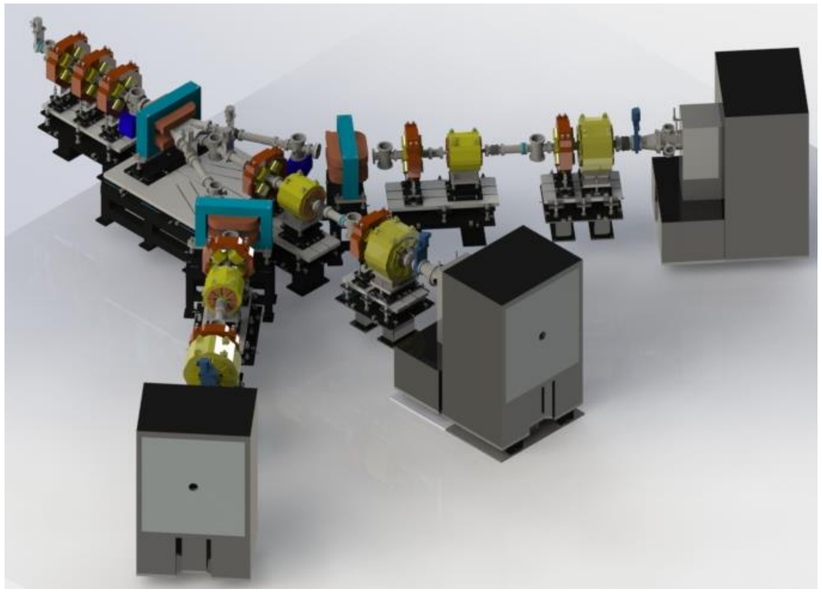


❐ Features & Achievements

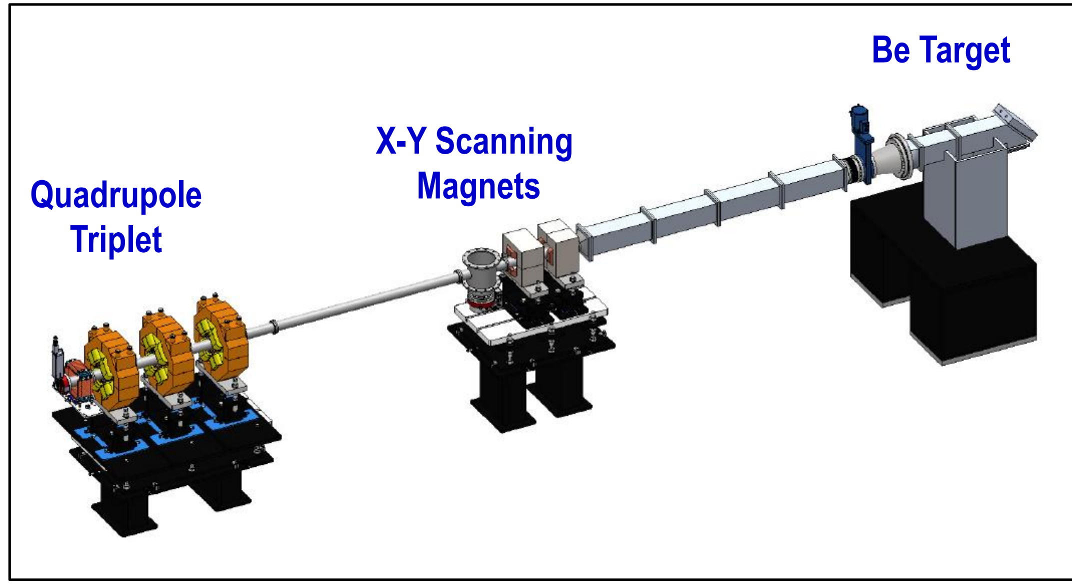
1. Proton injector under beam test has achieved separated machine parameters : 50keV, 60mA, 80% of proton ratio, 1.7mS pulse length etc
2. RFQ under fabrication targets a high beam current of 50mA and high duty of 20%.
3. DTL under fabrication targets also a high averaged beam current of 8 mA to achieve 80kW beam power

Beam Lines & Be Target for A-BNCT

❒ Configurations of 3 Beam Lines



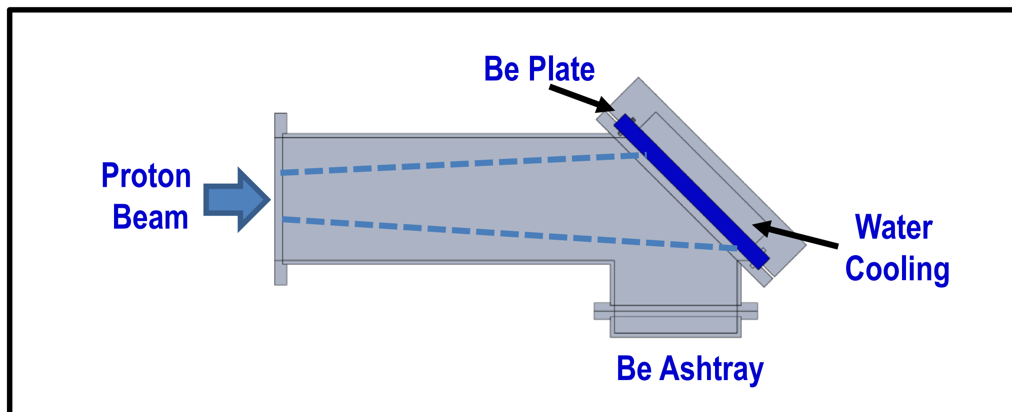
❒ Central Beam Line (1st Stage const.)



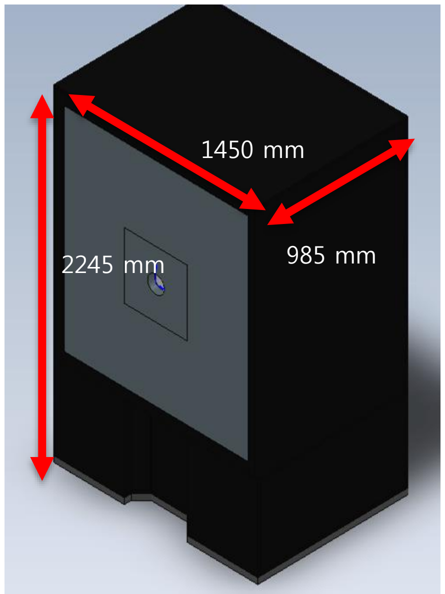
❒ Features & Achievements

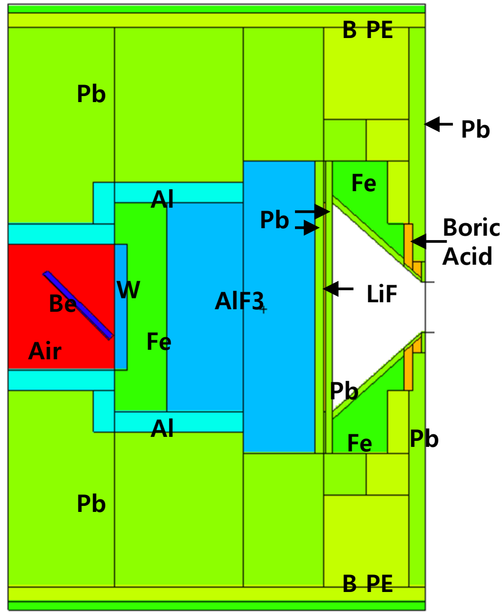
1. Bended beam lines have an achromatic beam optics for minimized beam losses.
2. The central beam line is a simple straight line with a raster beam scanning system for a large area uniform beam
3. Be target system uses a simple thick Be plate of 20mm with back cooling allowing hydrogen blistering

❒ Be Target

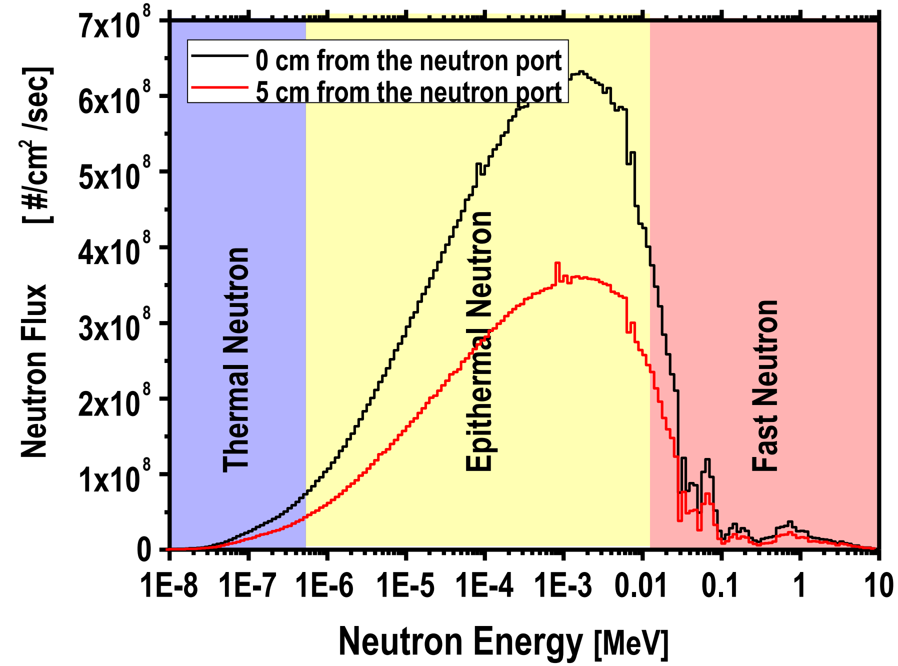


❐ Moderator Assembly





❐ Neutron Spectrum (Calculated)



❐ Characteristics of Neutron Fluxes & Doses

	Epithermal Neutron Flux	Thermal Neutron Flux	Epi / Thermal Ratio (<0.5eV)	> 100keV Fast Neutron Flux	Epi / Fast Ratio (>100keV)	Gamma Dose / Epi Ratio
0 cm	4.15×10^9 /cm^2*s	8.68×10^7 /cm^2*s	47.81	7.56×10^7 /cm^2*s	54.87	7.91×10^{-14} Gy*cm^2
5 cm	2.34×10^9 /cm^2*s	5.11×10^7 /cm^2*s	45.83	4.84×10^7 /cm^2*s	48.32	-
IAEA	> 1.00×10^9 /cm^2*s		> 20			< 2.00×10^{-13} Gy*cm^2

❐ Features & Achievements

1. High epithermal neutron flux to be able to realize treatment time less than 1 hour.
2. Minimization of the fast neutron & gamma doses to reduce radiation side effects.
3. All design parameters of neutron & radiations meet the IAEA recommendations

Radiation Safety & Licensing

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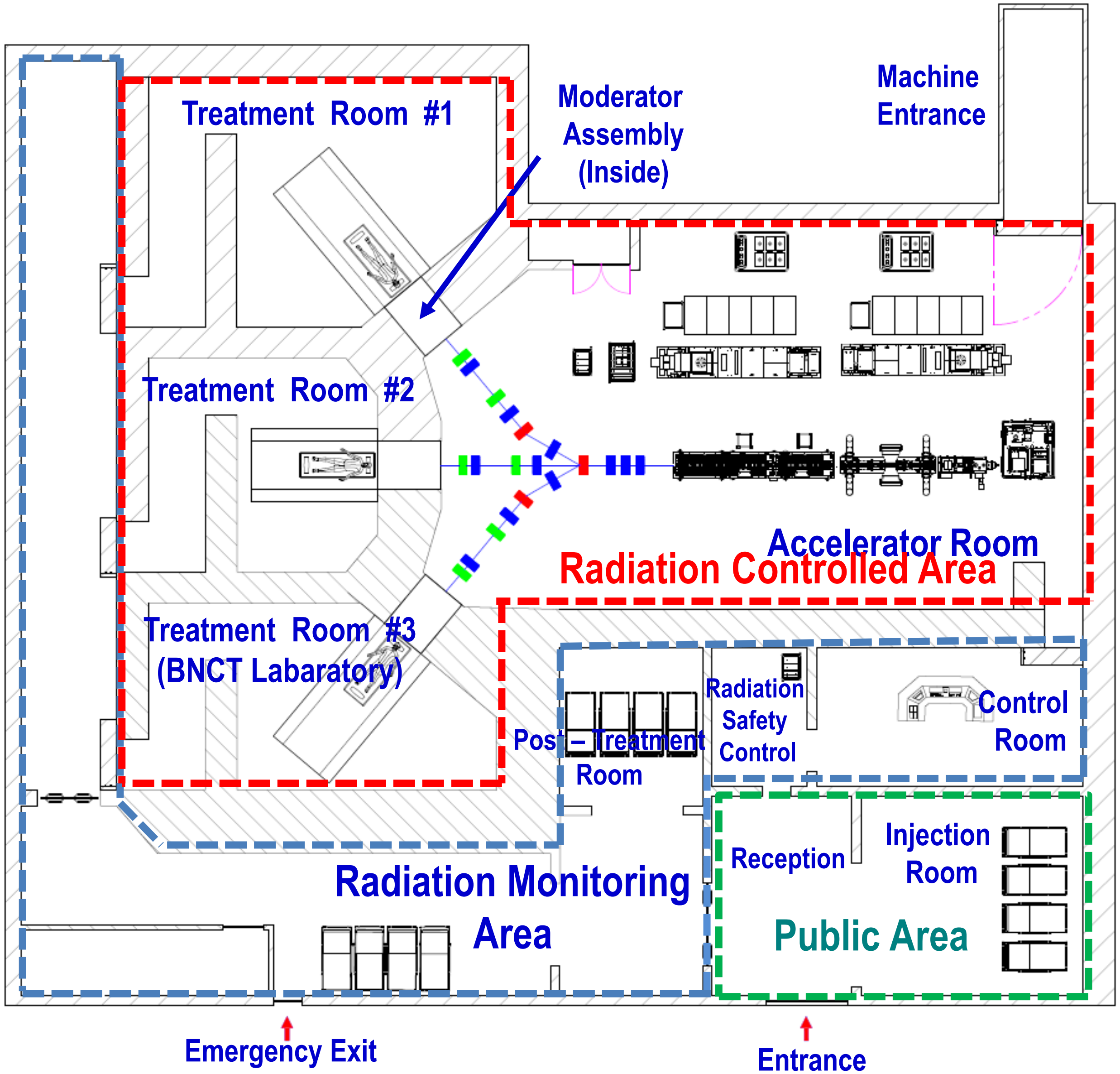
❐ Radiation Controlled Areas



❐ Radiation Licensing Schedule

Year Month	A-BNCT Activities
17. 8	Submitted a radiation safety report of A-BNCT facility to KINS
10-12	Review of the report in KINS
18. 1-2	Evaluation of the facility operation
3	Approval of the radiation safety license
5-8	Inspection of the radiation safety during operation

Construction Progress of A-BNCT facility

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❐ Aerial Photo of A-BNCT building (18. 01)

❐ Rooms inside the building (17. 10)

Accelerator Room

Corridor

Roof

Future Plan of the A-BNCT facility

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❐ Major Milestones of A-BNCT Facility

Year Month	A-BNCT Activities
17.11	Completion of the building and utilities
12	To start Installation of accelerator systems
18. 1	To get a radiation license by the government
3	To start beam commissioning of the accelerator
5	To start experiments of neutron generation
7	To get an operation license of the facility
9	To open neutron beams for BNCT experiments

❐ Configuration of the facility in 1st Stage