Dr. Se Byeong Lee
Proton Therapy Center / NCC, Korea

On behalf of the FKPPL collaborators
(LPC-CENBG-NCC)

Med 1.

Proton Therapy and microdosimetry simulations using G4/G4DNA/GATE

Impact of radiations on bacteria and DNA samples

FJKPPL LIA Workshop in Clermont-Ferrand
May 28 – 30, 2012

Collaboration member

French Group			Korean Group		
Name	Title	Affiliation	Name	Title	Affiliation
Leader: Incerti, Sebastien	Dr	IN2P3 – CENBG	Leader: Lee, Se Byeong	Dr	NCC
Breton, Vincent	Dr	IN2P3 – LPC Clermont	Jae Ik Shin	Mr	NCC
Champion, Christophe	Dr	Metz U.	Park, Sey-Joon	Mr	NCC.
El Bitar, Ziad	Dr	IN2P3 – IPHC	Kim, Dae Hyeon	Mr	NCC.
Maigne, Lydia	Dr	IN2P3 – LPC Clermont	Kyung-Hoon Kwon	Dr	KBSI
Perrot, Yann	Dr	IN2P3 – LPC Clermont	Hyun Sik Kim	Dr	KBSI
Pham, Trung	Mr	IN2P3 – LPC Clermont	Kyu Hwan Park	Dr	KBSI
Micheau Pierre	Mr	IN2P3- LPC Clermont			

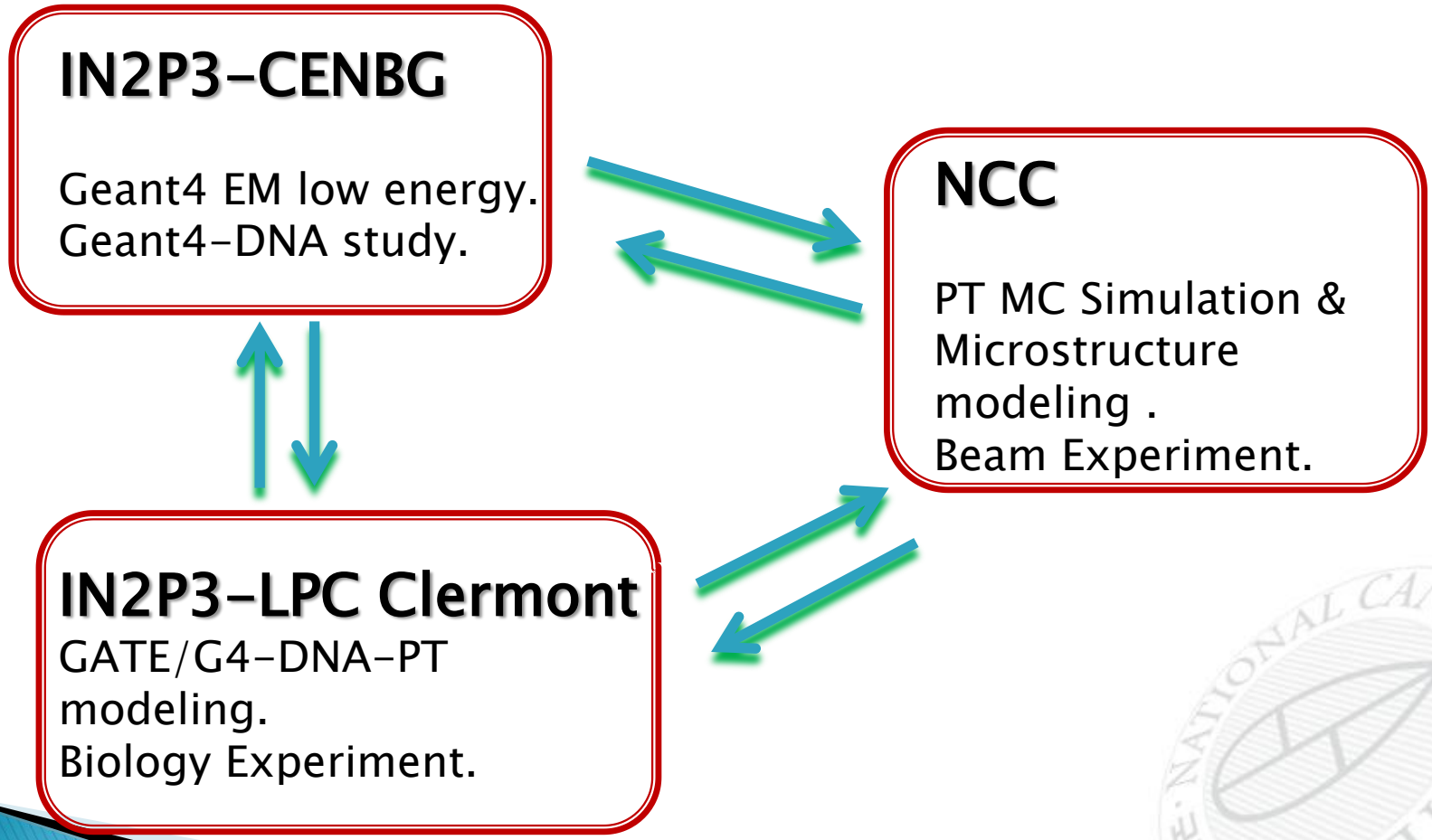
Activities & Proposals for FKPPL-Med1

- **Monte Carlo modeling activities using Geant4/GATE**
  - Geant4 Modeling of the NCC proton beam line for Proton therapy
  - Experimental validation of Geant4 physics models through Geant4/GATE using recommended Geant4 physics lists and experimental dose profile measurements performed at NCC
    (Nuclear Emulsion Experiment, Radiobiology Experiment)
  - Modeling of direct biological damages using the Geant4-DNA extension
  - Modeling of non-direct biological damages using the Geant4-DNA extension
  - Combination of GATE and Geant4-DNA

- **Geant4/GATE Tutorial for Korean Medical Application User Group**
  - Annual Joint Tutorial Course / Korean Group Workshop

- **Radiobiology experiments**
  - Plasmid DNA & Bacteria irradiations.
  - E. coli and linear DNA irradiations (Experiment in NCC / Analysis in Clermont-Ferrand)

FKPPL-Med 1 collaboration



Proton beam facility in NCC

Proteus 235 Specification

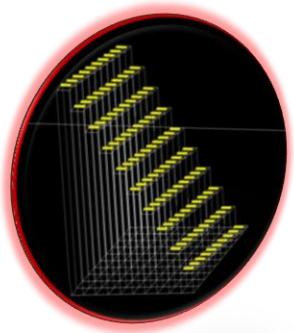
Weight : 220 ton Height : 210 cm Diameter : 434 cm

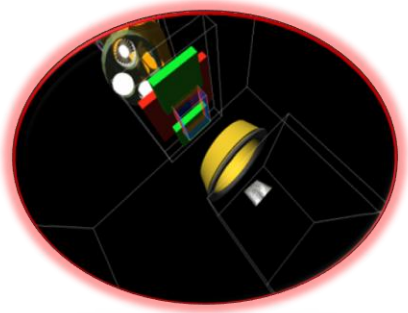
Energy : 230MeV

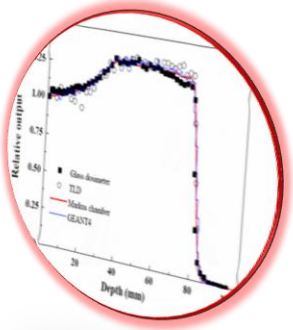
Max. extracted beam current : 300nA

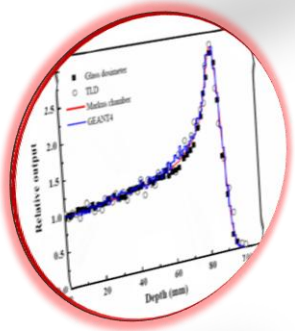
RF frequency :106 MHz

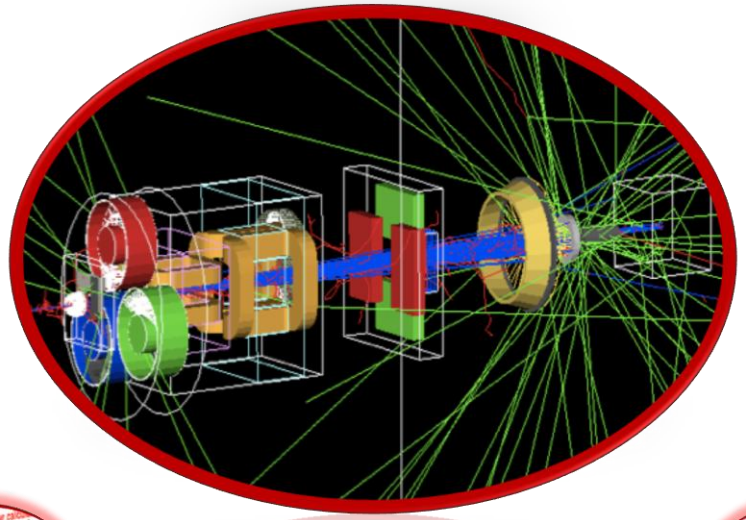
Proton Treatment Beam Simulation

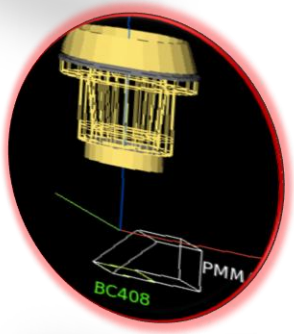


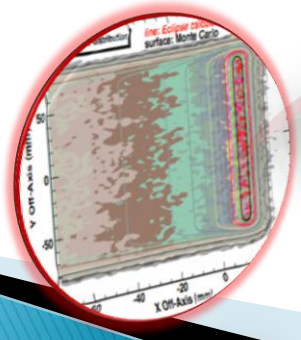


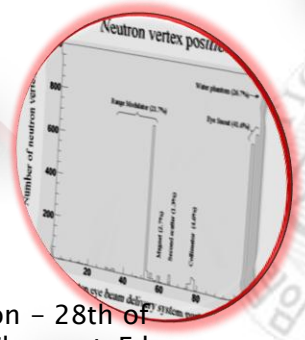








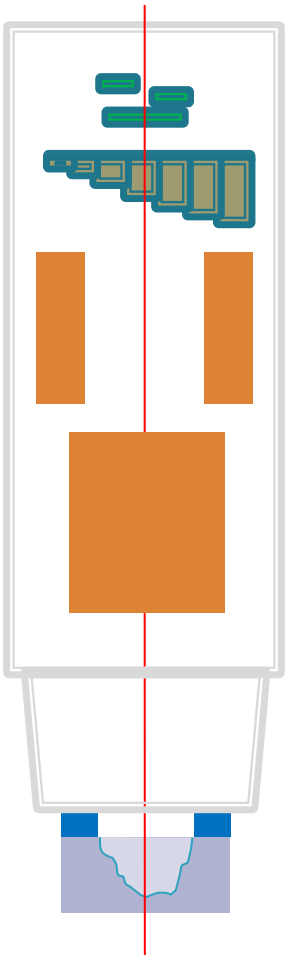


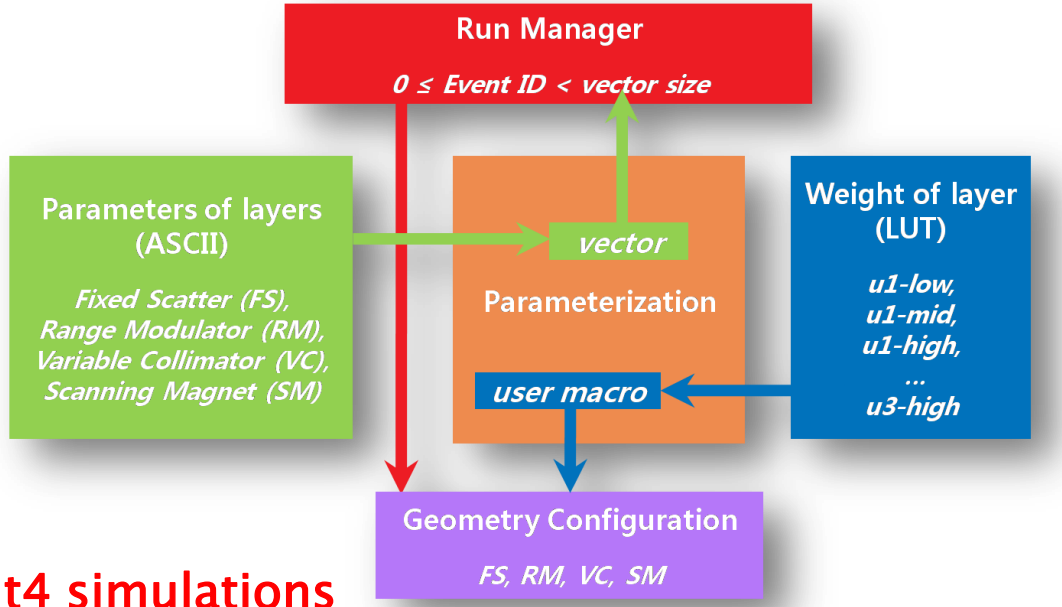


First scatterer

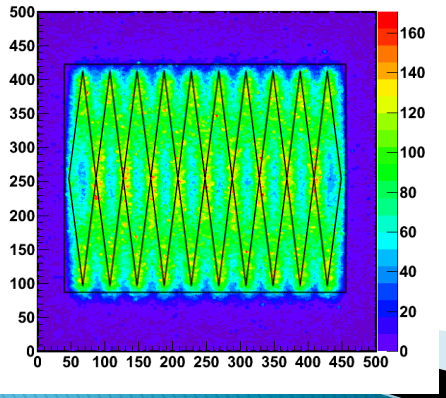
Range modulator

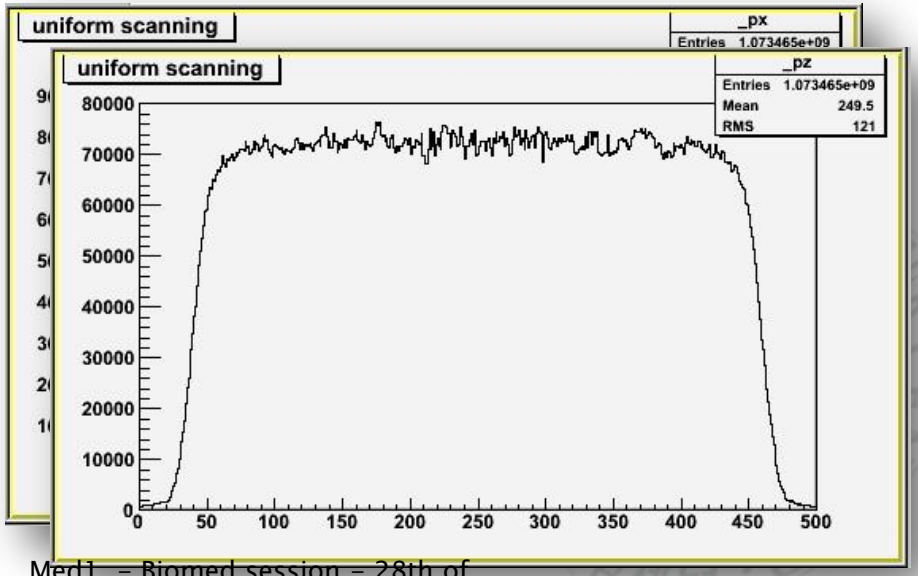
Scanning magnet



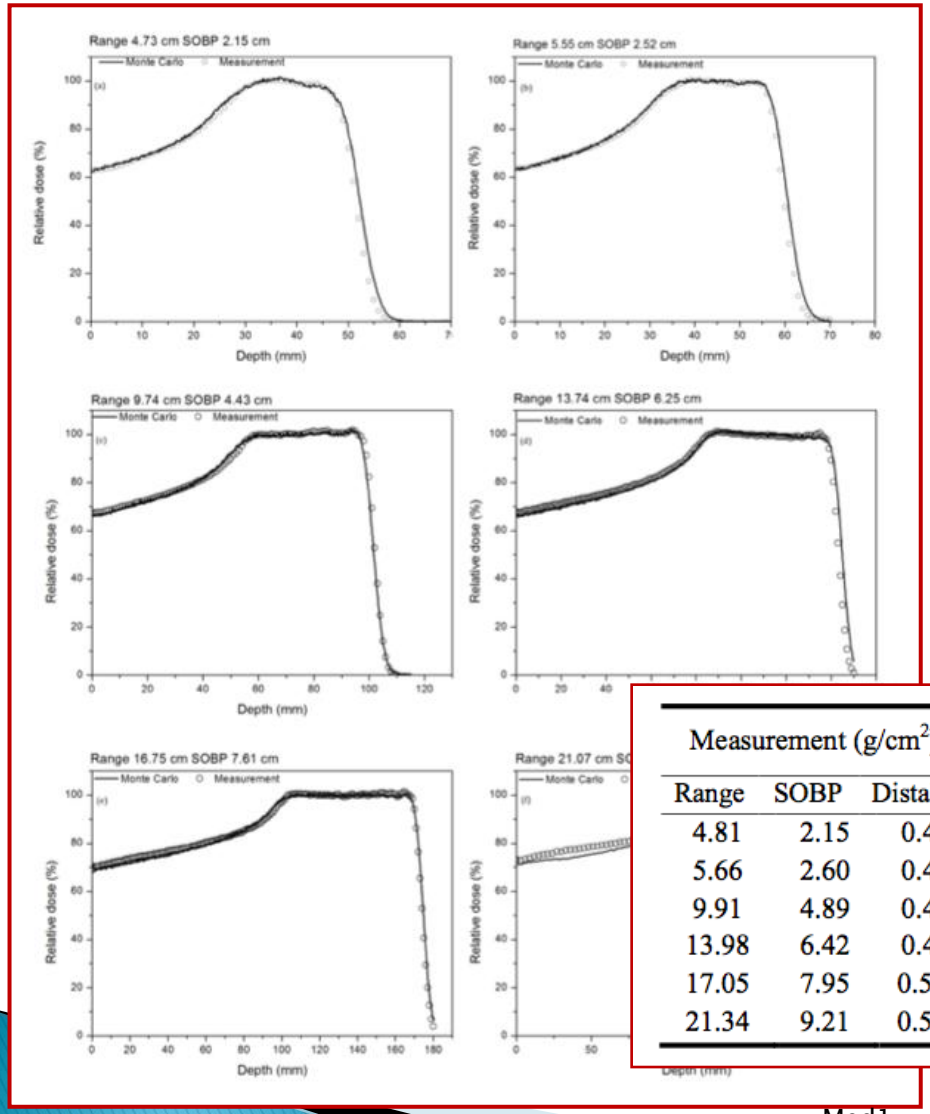


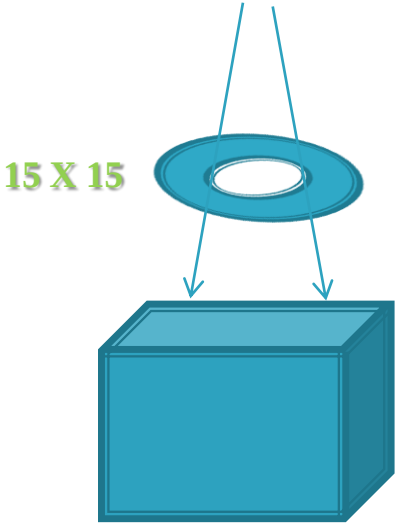
Geant4 simulations





Validation of Proton Nozzle Sim.

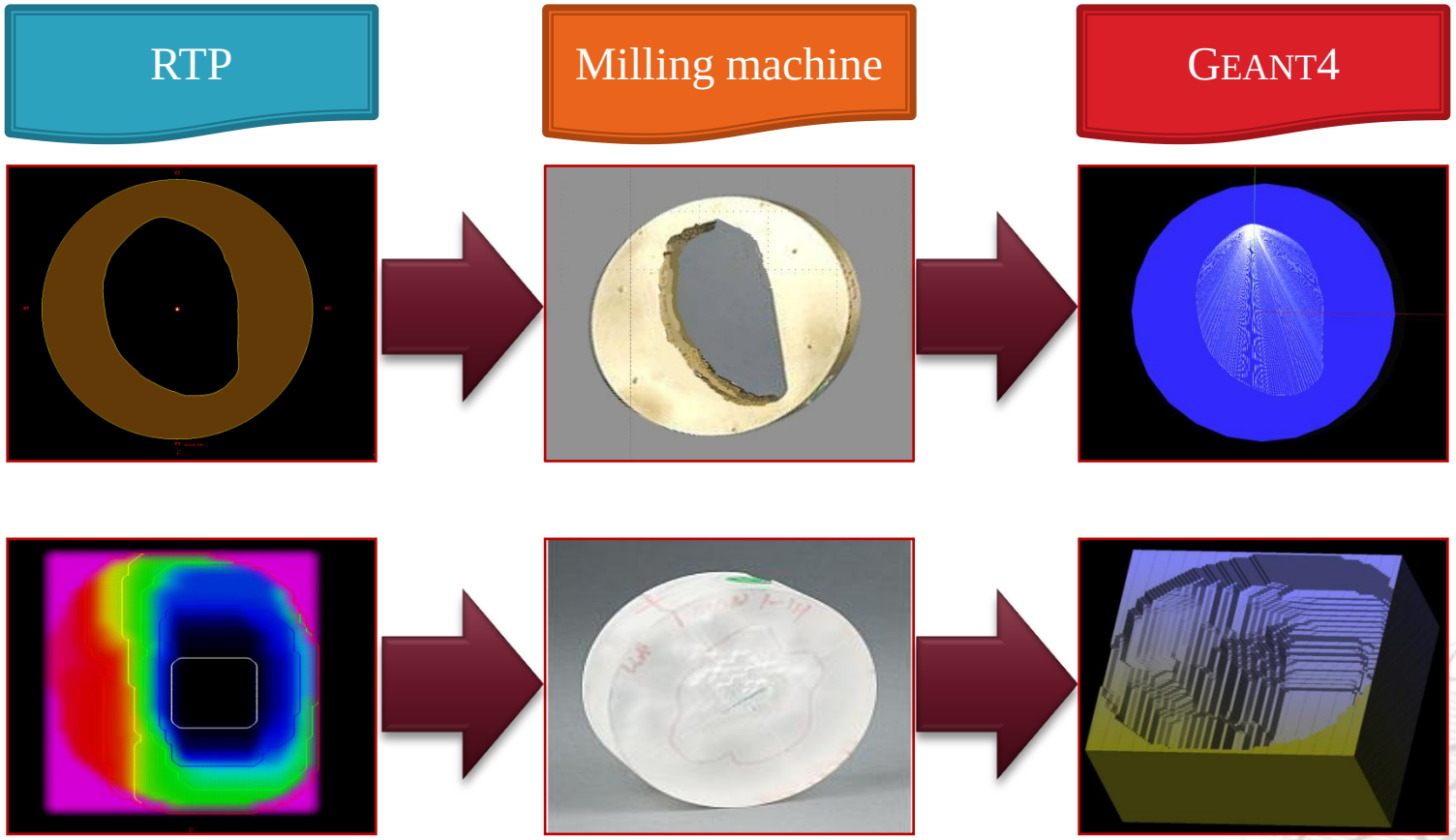




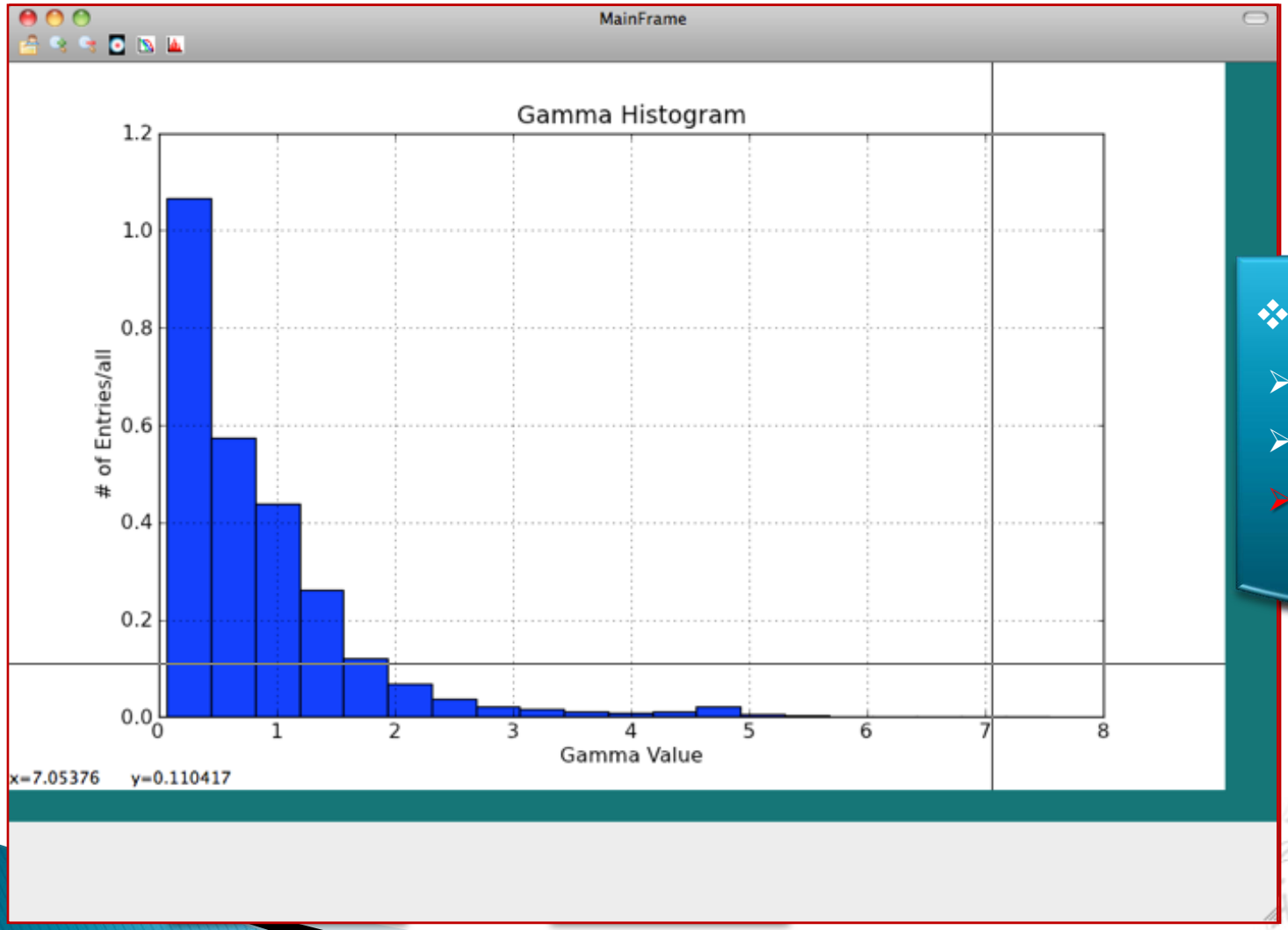
Voxelized Water Phantom
Voxel size: 1x1x1 mm^3

Measurement (g/cm^2)			Monte Carlo (g/cm^2)			Difference (g/cm^2)		
Range	SOBP	Distal P.	Range	SOBP	Distal P.	ΔRange	ΔSOBP	ΔDistal P.
4.81	2.15	0.44	4.91	2.32	0.47	0.10	0.17	0.03
5.66	2.60	0.43	5.74	2.70	0.51	0.08	0.10	0.08
9.91	4.89	0.42	9.88	5.00	0.46	-0.03	0.11	0.04
13.98	6.42	0.48	14.07	6.40	0.54	0.09	-0.02	0.06
17.05	7.95	0.54	17.06	8.14	0.55	0.01	0.19	0.01
21.34	9.21	0.56	21.40	9.54	0.66	0.06	0.33	0.10

Aperture and Compensator Modeling Module development



Radiation Dose Analysis Toolkit Development in NCC



- **Plan Evaluation**
  - Dose Differencce
  - Dose Volume Histogram
  - **Gamma Index**

Proton Beam Linear Energy Transfer Simulation Study

- Nuclear Emulsion Experiment in PT facility (OPERA Experiment Emulsion)
- 4 firm in a sealing pack & Each firm surface size is 2.5cm x 2.5cm
- Total number of Emulsion layer is 8 layer in a pack.
- NCC proton beam exposure on the emulsion stack with Bragg Peak Range 14cm (~180MeV) & proton density $10^4/cm^2$.
- Emulsion sample scanning and analysis is on going at Korean opera group.
- Geant4 MC simulation of Emulsion experiment will be tried with new physics list.

OPERA Emulsion

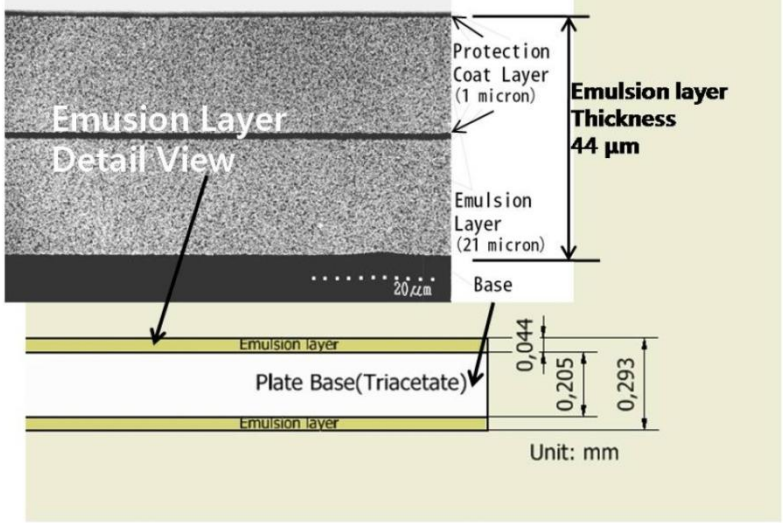


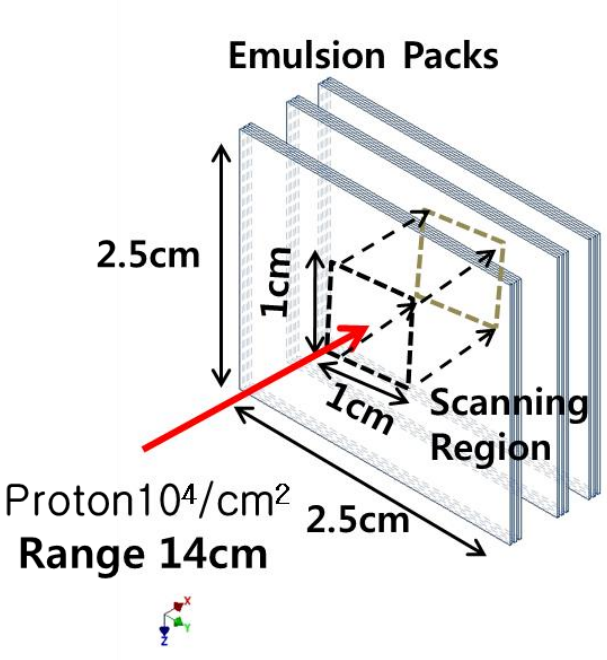
Fig. 1. Schematic drawing of cross secion in the emulsion plate

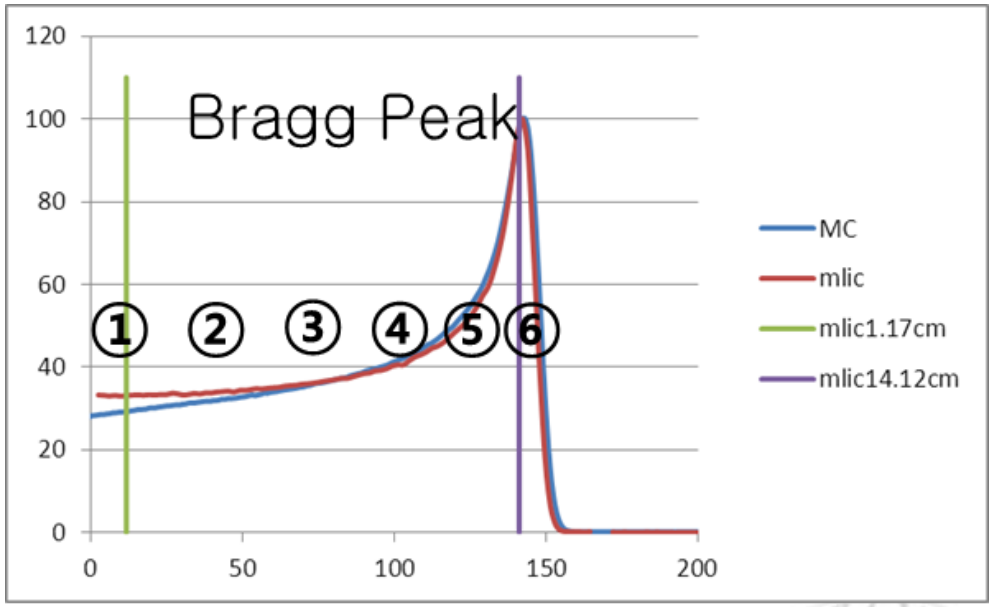
Table 1. Gel parameters. The diameter and the divergence were measured on the images taken by an electron microscope

	Fuji ET7B	OPERA film
Average diameter of the crystal	0.240 μm	0.200 μm
Divergence of the diameter	0.078 μm	0.016 μm
Volume occupancy of AgBr	0.50	0.31
Number of crystals per100μm	262	230
Grain density for MIP(/μm)	38	36
Detection efficiency per crystal	0.14	0.17
Machine-coating possibility	X	O

- This figure is a cross-sectional view of the film. The thickness of the plastic base (black part) is 0.205um.
- Emulsion layers were created on both sides of the base. Double layer structure of the emulsion layer can be seen. Two layers are separated by a protection coat (thickness of 1um).

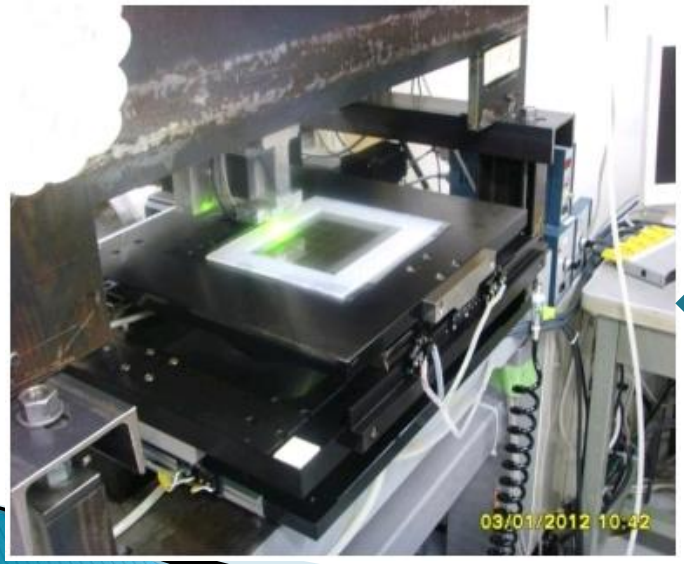
Experiment Setup



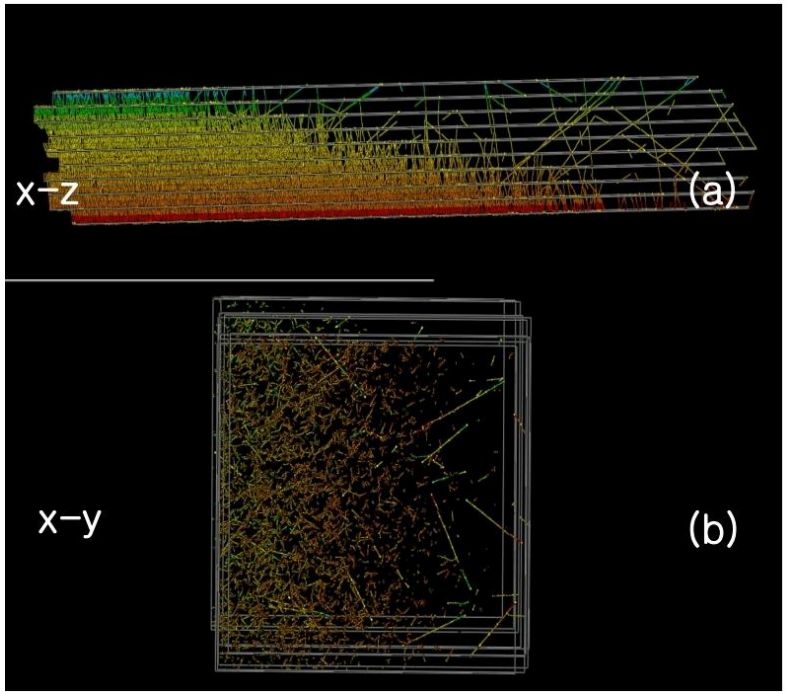


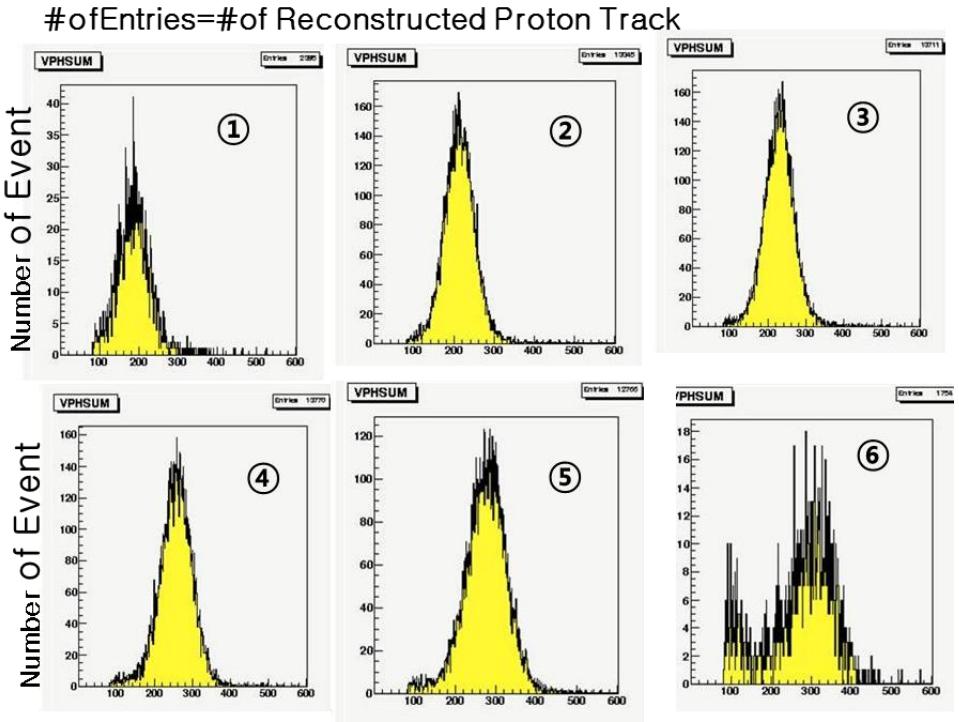
Packaging Emulsion
At Pusan University

Beam Exposure At
NCC



Developing and Scanning At Nagoya
Univ[illegible]





We measured “VolumePulseHeight” and compared several region in Bragg Peak.
It show particle flux. For LET measurement, we will analyze LET using measurement data.

Developement of Geant4-DNA cross section models for DNA material

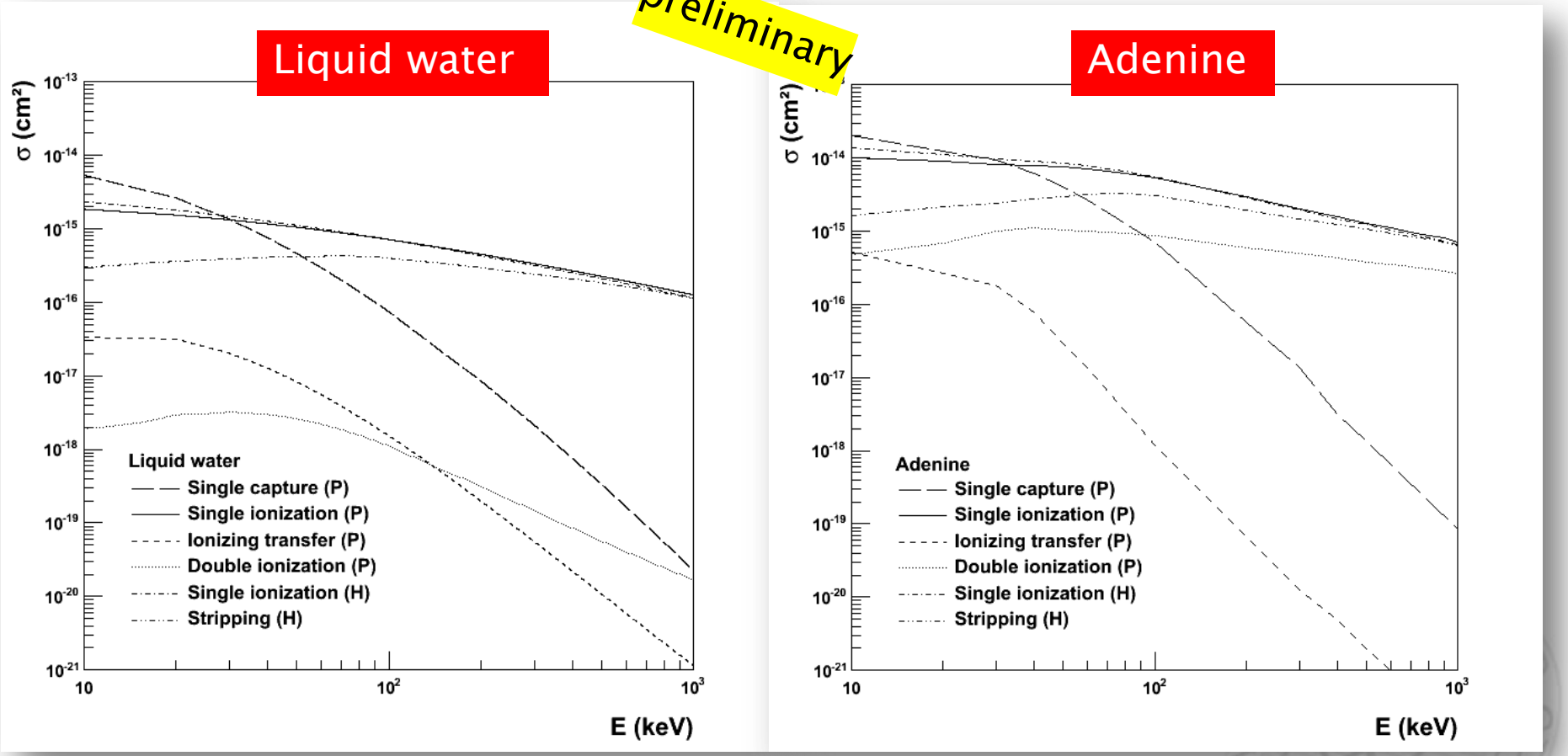
- Geant4-DNA Physics models are currently limited to liquid water only. We would like to propose alternative interaction processes for DNA nucleobases and investigate their influence on energy deposition.
- The physics models adopted in this work follow the Classical Trajectory Monte Carlo – Classical Over Barrier (CTMC-COB) approach and are fully described in the theoretical work of Lekadir et al. 2009.
- Principle
  - large number of trajectories for ion-molecule impacts are calculated and all particle movements are described by Newtonian laws.
  - for each trajectory, occurring ionising processes are determined using specific energy criteria of COB
    - relative position of the binding energy of the "impacted" target electron and the maximum of the Coulomb potential barrier existing between the ion projectile and the molecular target
- Interesting alternative since
  - it can be applied to colliding systems which are difficult to model using quantum mechanics (such as the ones involving large molecules)
  - it can handle multiple collisions (such as double ionization and ionisation transfer)

Proposed developements

- Able to model 5 physical interaction processes
  - Single ionisation (p, H)
  - Single capture (p)
  - Double ionisation (p)
  - Ionisation transfer (p)
  - Stripping (H)
- Applicable to protons and neutral hydrogen
- Covering the energy range 10 keV – 1 MeV
- Materials include
  - Liquid water
  - DNA nucleobases: Adenine, Thymine, Cytosine and Guanine
- Their implementation started at CENBG during Spring 2012 and the venue of Jae Ik Shin
  - Computation of total cross sections
  - Computation of final state

Examples of cross section models

preliminary

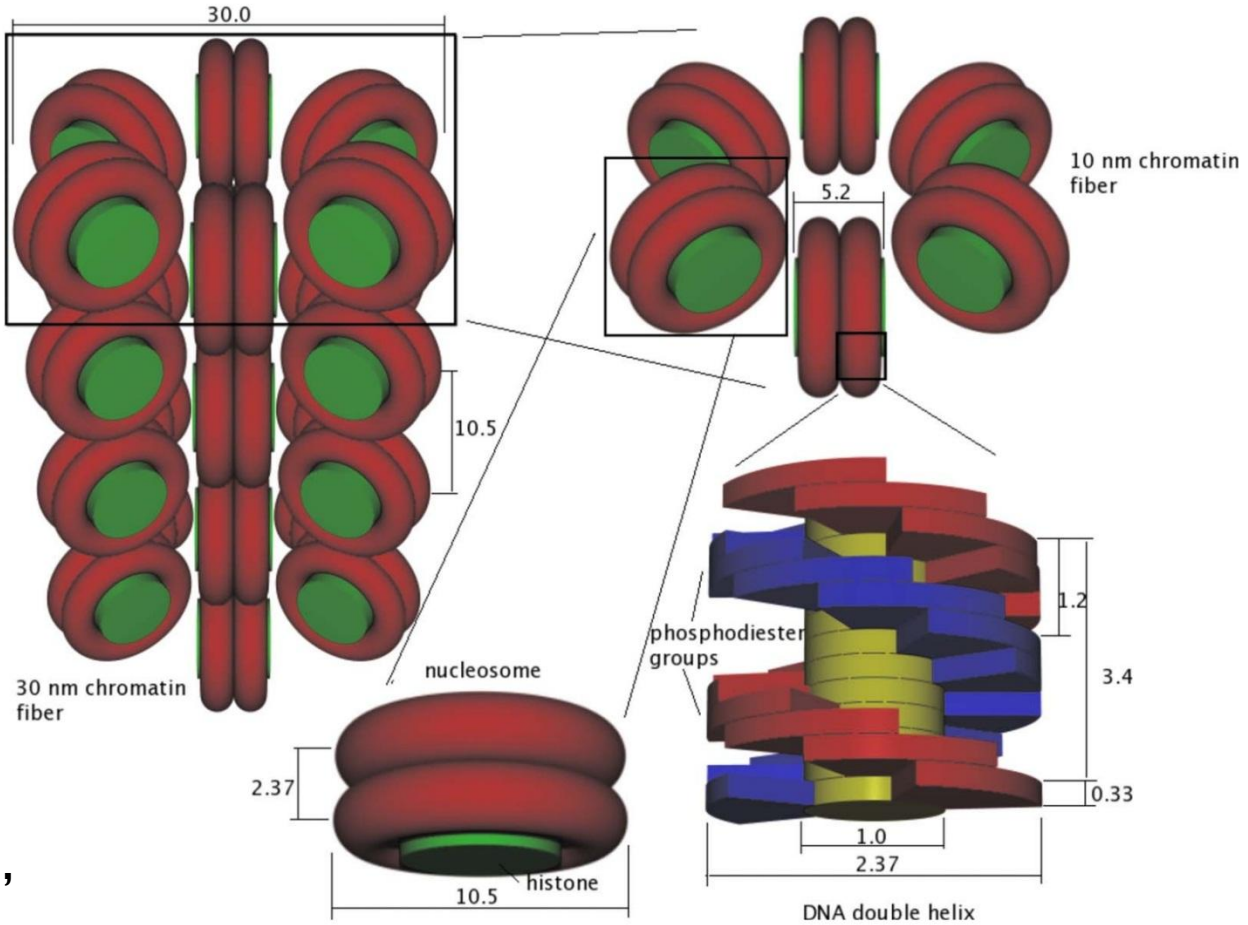


- One order of magnitude difference for dominant processes (SI, SC)
- Two orders of magnitude for DI

To be combined with DNA geometries

- These cross section models will be combined with a geometrical model of a cellular nucleus including DNA structures, containing
  - Either pure liquid water
  - or liquid water and DNA material (A-T-G-C)
- These models have been developed by Mr J. I. Shin
  - Nucleotides
  - Nucleosomes
  - Chromatin fiber

Example of biological geometry



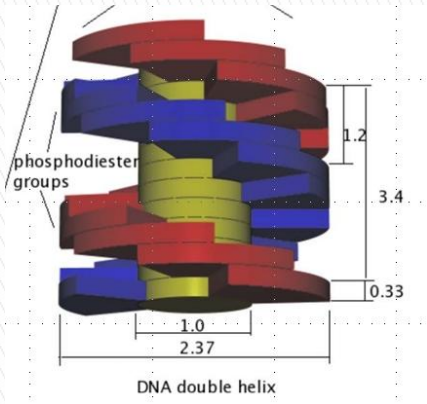
Nucleosomes Nucleotides

Ref.
An investigation on the capabilities of the PENELOPE MC code in nanodosimetry,
M. A. Bernal and J. A. Liendo,
Medical Physics, Vol. 36, No. 2, February 2009

Simple geometry for A,T,G,C materials

by J.I.Shin(NCC)

Make simple geometry having ratio of ATGC materials



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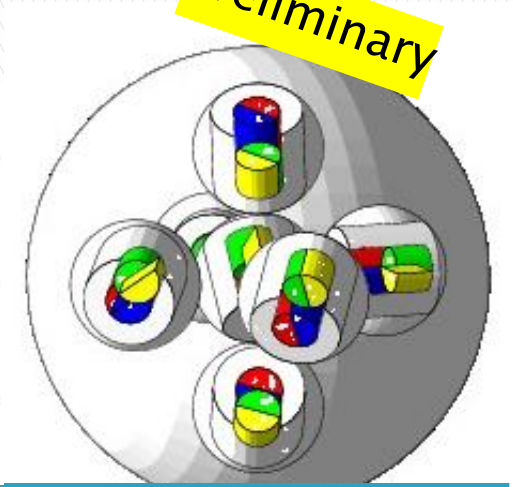
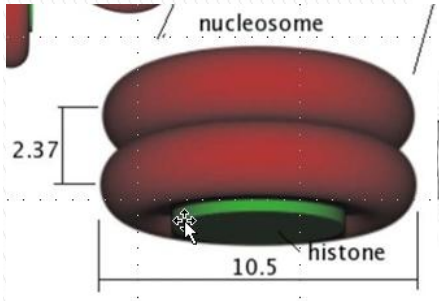


Nucleotides



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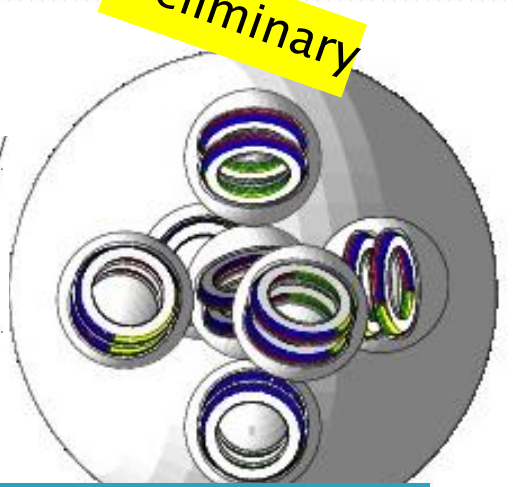


Nucleosomes

Radiobiology Experiments

- 1st Experiment (Feb. 2011)
  - DNA breaks vs. Proton with Plasmid DNA sample: NCC
- 2nd Experiment (Nov. 2011)
  - Cell survival exp. With alive E. coli bacteria samples
- 3rd Experiment (May. 2012)
  - Radiation response between Proton & Photon with linear DNA from E.coli strain(MG1655)

Simulation vs Experiment validation

- **Modeling radiation effects on a bacteria model**

- **Link between energy deposition – biological effects**
  - µm scale: bacteria (survival rate)
  - nm scale: DNA (DSB, SSB and base pair oxydation)
  - **Bacteria model : *Escherichia coli***
    - Safe to manipulate (present in human gut)
    - Easy to grow-up (~10^9 bacteria/ml after 16h of culture 37°C)
    - Genome are sequenced, protein functions are identified

- **IBA Pencil Beam simulation using GATE6.1**
  - **Validation in water conditions**: depth dose profiles

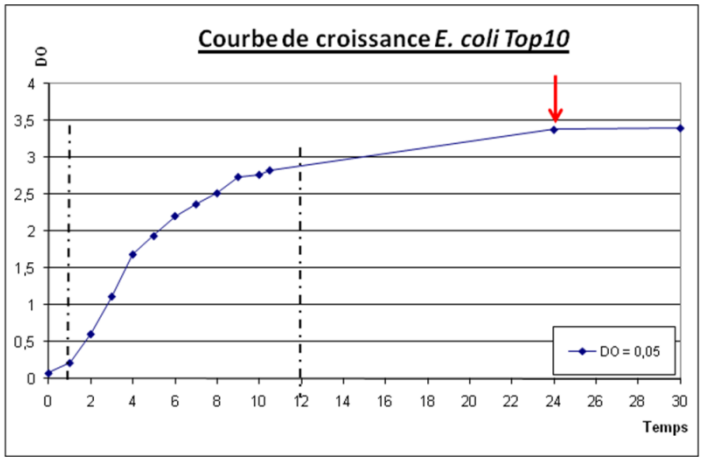
- **Integration of G4 DNA processes into GATE 6.1 (in progress)**
  - **Validation**: calculations of energy distributions in small cylinders mimic king DNA fragments

1°) Experiment: Bacteria survival rates

protocol

Culture in LB medium

10^5 *E. coli*/membrane are put on each fibber glass m embrane.
2 sets of membranes: 3 non irradiated membranes (control) and 3 irradiated membranes.



Packaging in steril plastic bags

3 Controls **3 Irradiated**

Protons Irradiation

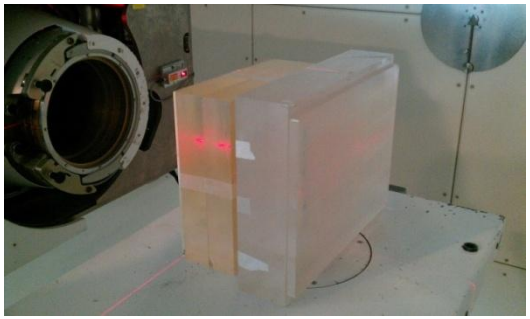
Photons Irradiation

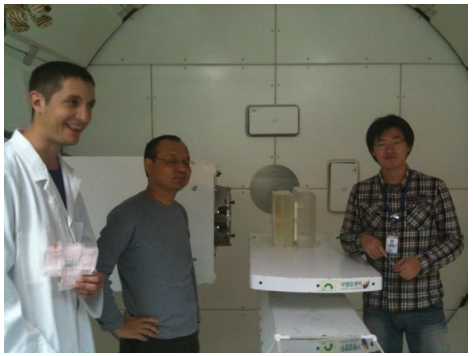
1°) Experiment: Bacteria survival rates irradiation

Sample processing for irradiation

Photon Irradiation conditions:
- Doses: 10, 20, 30, 40, 50 Gy
- Field size: 20 x 20 cm
- Energy: 18 MV

Centre JEAN PERRIN





Proton Irradiation conditions:
- Low LET: 0.1 keV/nm
- High LET: 3 keV/nm
- Doses: 10, 20, 30, 40, 50 Gy
- Field size: 20 x 20 cm
- Energy: 235 MeV

국립암센터 NATIONAL CANCER CENTER

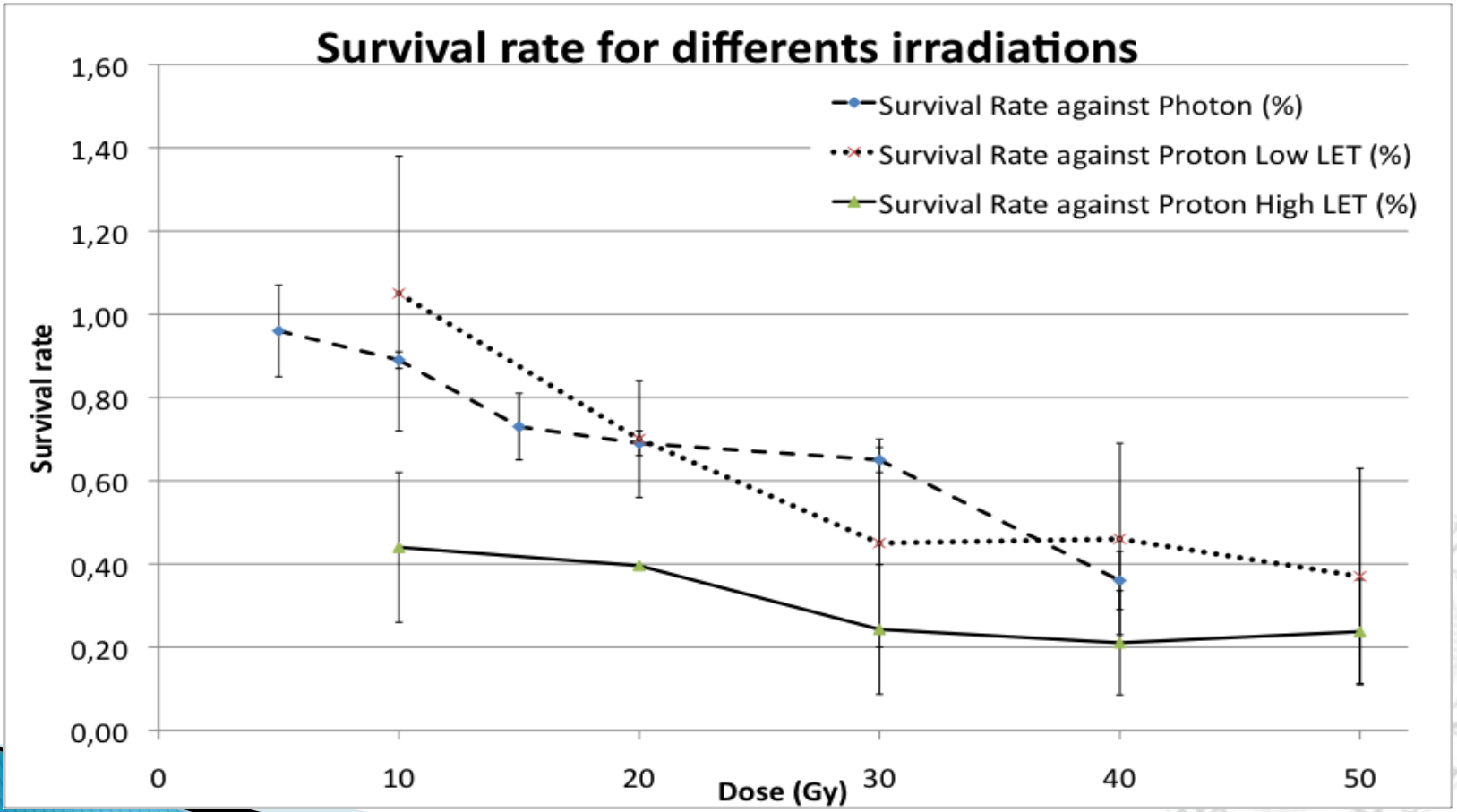
Bacteria are directly put on LB plates (3 plates / membrane)
Incubation of LB plates overnight at 37°C

Dilution in 20 ml of physiologic ser um.
Strong skaking with glass beads.

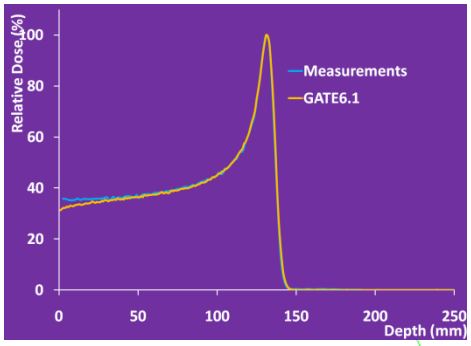
1°) Experiment: Bacteria survival rates

results

- Irradiation with photons (CJP– Clermont Ferrand)
- Irradiation with protons (NCC – Seoul)



2°) GATE-G4DNA simulations



SINGLE SCATTERING MODE

- Gaussian Source: E = 193.1MeV, σ_E = 1.2
- Total Number of Particles: $3x10^8$
- Geometry:
  - First Scatterer
  - Range Modulator
  - Collimator : 10 x 10 cm^2
  - Water phantom: 50 x 50 x 50 cm^3
  - Voxel size: 500 : 500 : 500
- Physics:
  - HadronsTherapyStandardPhysics
- Creation of PhaseSpace files
- Switch to G4DNA processes to obtain dose information into geometry reproducing cells and DNA

PTCOG 51 conference
Seoul May 2012

Geant4, GATE & GRID Tutorial 2011

Oct. 31 – Nov. 4, 2011 KISTI, Seoul

Geant4 Gate and Grid for Medical Applications

10.31-11.4 2011

Monday (Oct. 31)

08:30 ~ 09:00	Registration
09:00 ~ 09:15	Opening addresses (local organizer)
09:15 ~ 09:30	Tutorial Introduction (J. Perl)
09:30 ~ 10:30	Kernel I (T. Sasaki)
10:30 ~ 11:00	**Break**
11:00 ~ 11:30	User Documents and Examples (T. Aso)
11:30 ~ 12:00	User Interface (S. Incerti)
12:00 ~ 12:30	Visualization (J. Perl)
12:30 ~ 14:00	**Lunch Break**
14:00 ~ 14:20	Material Definition (T. Aso)
14:20 ~ 15:00	Geometry I (S. Incerti)
15:00 ~ 15:30	Geometry II (J. Perl)
15:30 ~ 16:00	**Break**
16:00 ~ 16:30	Primary Particle (T. Sasaki)
16:30 ~ 17:30	Hands-on I (J. Shin)
17:30 ~	Reception

Tuesday (Nov. 1)

09:00 ~ 09:45	Physics I (S. Incerti)
09:45 ~ 10:30	Hands On II (J. Shin)
10:30 ~ 11:00	**Break**
11:00 ~ 11:45	Physics II (S. Incerti)
11:45 ~ 12:30	EM Physics (S. Incerti)
12:30 ~ 14:00	**Lunch Break**
14:00 ~ 14:30	Scoring (T. Aso)
14:30 ~ 14:45	Analysis (J. Perl)
14:45 ~ 15:30	Hands On III (T. Aso)
15:30 ~ 16:00	**Break**
16:00 ~ 16:30	Hadronic Physics I (J. Shin)
16:30 ~ 17:30	Hands On IV (J. Shin)
17:30	Done for the day

Wednesday (Nov. 2)

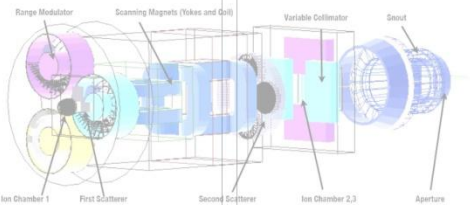
09:00 ~ 09:30	Geometry IV (J. Perl)
09:30 ~ 10:00	Which Physics List to Use (S. Incerti)
10:00 ~ 10:30	Hands On V (J. Shin)
10:30 ~ 11:00	**Break**
11:00 ~ 11:30	Continue Hands On IV
11:30 ~ 11:50	How to Upgrade Your Geant4 Release (J .Perl)
11:50 ~ 12:30	General Geant4 Discussion
12:30 ~ 14:00	**Lunch Break**
14:00 ~ 15:30	PTSim and gMocren talks (T. Sasaki, T. Aso)
15:30 ~ 16:00	**Break**
16:00 ~ 17:30	PTSim and gMocren Demonstrations (T. Sasaki, T. Aso)
17:30	Done for the day

Thursday (Nov. 3)

09:00 ~ 10:30	GATE tutorial part I (L. Maigne)
10:30 ~ 11:00	**Break**
11:00 ~ 12:30	GATE tutorial part II (L. Maigne)
12:30 ~ 14:00	**Lunch Break**
14:00 ~ 15:30	GATE hands on part I (L. Maigne)
15:30 ~ 16:00	**Break**
16:00 ~ 17:30	GATE hands on part II (L. Maigne)
17:30	Done for the day

Friday (Nov. 4)

09:00 ~ 10:30	Grid Introduction (S.
10:30 ~ 11:00	**Break**
11:00 ~ 12:00	Hands-on Exercises o Grid (S. Hwang)
12:00 ~ 13:00	**Lunch Break**
13:00 ~ 14:30	Geant4 Applications Grid (J. Shin)
14:30 ~ 15:00	**Break**
15:00 ~ 16:30	GATE Applications on Grid (L. Maigne)
16:30	Done for the day



KISTI NATIONAL CANCER CENTER

Lecturers(7)

Sebastein Incert (IN2P3, France)
Lydia Maigne (IN2P3, France)
Takashi Sasaki (KEK, Japan)
Aso Tsukasa (Toyama University, Japan)
Joseph Perl (SLAC, USA)
Jungwook Shin (UCSF, USA)
Soonwook Hwang (KISTI, Korea)

35 students

Geant4 User Workshop 2012

2012년 상반기 의학물리전문인 연수교육(안)

일시: 2012년 04월 14일(토)
장소: 풍영 금호리조트

시 간	교육 내용	연자	좌장
1. 의학물리사의 역할과 필수 임상 기초			
08:40–09:20	국내 의학물리학자의 역할과 의무	(전)세브란스병원 추성실 교수	영남대학교 김성규 교수
09:20–09:50	방사선치료 장비 구성목록 작성	한국원자력의학원 김금배 박사	
09:50–10:20	의학물리사를 위한 방사선생물학	양산부산대학교병원 남지호 교수	
10:20–10:40	휴식 시간 (Coffie Break)		
2. Geant4 workshop (의료생명응용을 위한 전산모사)			
10:40–11:00	Monte Carlo의 원리 및 응용	한양대학교 김찬영 교수	국립암센터 이세병 박사 / KISTI 조기현 박사
11:00–11:30	Geant4 HEP Application	Fermi Lab. 장동목 박사	
11:30–11:50	의료분야에서의 Geant4 활용	국립암센터 이세병 박사, 카톨릭대학교 김태현	
11:50–12:10	KISTI 슈퍼컴 Geant4 서비스 소개 및 활용 연구	KISTI 배태길 박사, 김영진 박사	
12:10–12:30	Geant4 연구모임 토의	참가자	
12:30–14:00	점심식사		

- Joint workshop with Korean Society of Medical Physics(KSMP) Program and KISTI Geant4 supporting Program

- Apr. 14, 2012 / Tong Young, Korea
  ~ 100 participants.

Joint communications & perspectives

- PTCOG51 conference (Seoul May 2012)
  - 4 posters
  - 1 presentation for GATE-G4DNA
- PROTEUS project (STAR 2012 proposal in addition to FKPPL collaboration)
  - Partners: NCC – CENBG – LPC (2+2+1 researchers)
  - Fundings 2012: NCC: 7000 €, LPC-CENBG: 6400€
  - Duration: 2 years
  - Workplan:
    - Addition of alternative cross sections models for physical interactions in liquid water (quantum models)
    - Development of voxelized – cellular geometry
    - Simulation of protontherapy direct damages using DNA geometrical models
    - Simulations of non-direct effects and experimental validations
      - requires combination of physics and chemistry
      - Comet assay or other technics

Thank you!


Proton Therapy Center
National Center
for Cancer Prevention
and Early Detection
Research Institute
Hospital