FKPPL Project report (2011)

Red info should be replaced by the appropriate text in black

ID: Med_1	Med_1 : Proton therapy and microdosimetry simulations with the Geant4 toolkit

Project Leaders	French Group			Korean Group		
	Name	Title	Affiliation	Name	Title	Affiliation
	Leader: Incerti, Sebastien	Dr	IN2P3 – CENBG	Leader: Lee, Se Byeong	Dr	NCC

Funding from France within LIA

Description	Euro/unit	Nb of units	Total (euros)	Provided by: *
Funding for CENBG : mission to NCC and Geant4 training (28. Oct. – 4. Nov. 2011)	6000 received from IN2P3 1872 euros spent in 2011	1	6000	IN2P3
LPC Clermont-Fd, Workshop LIA FKPPL (07 march – 11 march 2011)	20000€ received from IN2P3 7000€ spent	1	20000	IN2P3
LPC Clermont-Fd, GATE/G4 training + experiments at NCC (28. Oct. – 4. Nov. 2011)	14222€ spent			IN2P3
Total			26000	

Funding from Korea

Description	Won/Unit	Nb of units	Total (Won)	Provided by: **
Experiment for DNA damage produced by Proton beam in Feb, 2011.	3,000,000	1	3,000,000	NCC
Geant4 training(31. Oct. – 4. Nov. 2011) in Seoul	4,000,000	1	4,000,000	NCC
Experiment for Membrane and DNA damage produced by Proton beam in 28. Oct. – 3. Nov. 2011.	4,000,000	1	4,000,000	NCC
FKPPL meeting in Mar. 10 in NCC	600,000	1	600,000	NCC
Total			11,600,000	

Additional funding (outside LIA)	Funding from France			Funding from Korea		
	Provided by: ***	Type	Euro	Provided by: ***	Type	Won

* For example: IN2P3, CEA. ** Korean University or Institute. *** French Embassy, STAR, PICS, other grants…

FKPPL Project report (2011)

Red info should be replaced by the appropriate text in black

Summary of 2011 activities

The following activities took place in 2011 :

- Participation to 3rd FKPPL workshop, March 8-9, 2011 KIAS, Seoul.
- Collaboration meeting, March 10, 2011, at NCC.
- Teaching at the GATE, Geant4 and Grid summer training course, with focus on medical applications, Oct. 31-Nov. 4, 2011, KISTI, Seoul.
- Recruitment of Mr. Jae-ik Shin for FKPPL Project at NCC in 2011.

Research activities were focused on 3 topics :

1) Radiobiology Experiment for measurement of DNA breaks produced by the NCC proton beam.

We performed a radiobiology experiment for measurement of DNA breaks produced by the NCC proton beam. We made sample DNAs using the competent cell called by "DH5alpha" and the plasmid DNA called by "pBS vector". We put antibiotic and antibiotic-resistible DNA into competent cells. Then our cells absorb resistible DNA for survival against antibiotic because they cannot resist themselves. After culturing those cells with LB media in incubator, we could make a lot of competent cells in media which has our plasmid DNA. Using centrifuge, RES, LYS, EQU and NEU buffer, cells discharge their DNA in this process.
In this lysate, we could extract plasmid DNA using DNA extraction kits called by "nucleobond xtra midi"
Using TE buffer and UV Spectrophotometry, we can make samples, which have concentration "0.1ug/ul".
We irradiate 25, 50, 100, 200 Gy dose to those samples at LET region using proton beam facility at NCC
After irradiation, we dyed samples using glycerol, bromophenol, xylene cyanol, EtBr for marking DNA.
Then we used CFGE(Constant Field Gel Electrophoresis) which filled with samples, agarose gel and TE buffer.
We measure the absorbance by EtBr from gel imaging in dark room and analyze the light intensity from the contrast of each sample.
Figure1. is a result of gel imaging. In this figure, we could see correlation between movement of DNA following electric field and irradiation dose.
If irradiated sample move longer distance then non-irradiated sample, we can think that DNA breaks caused by irradiation happen in this sample.
Figure2. and **Table1.** is the result of light intensity analysis. In this figure, we could see correlation between density of DNA breakage and irradiation dose.
If gel imaging of high dose-exposed sample has higher intensity then a low dose-exposed sample, we can think that DNA breaks depends on irradiation dose.

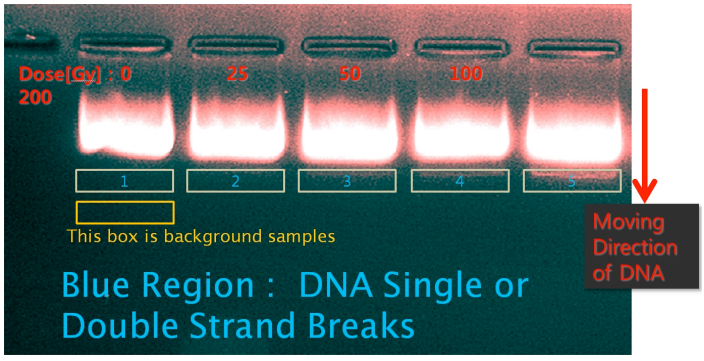
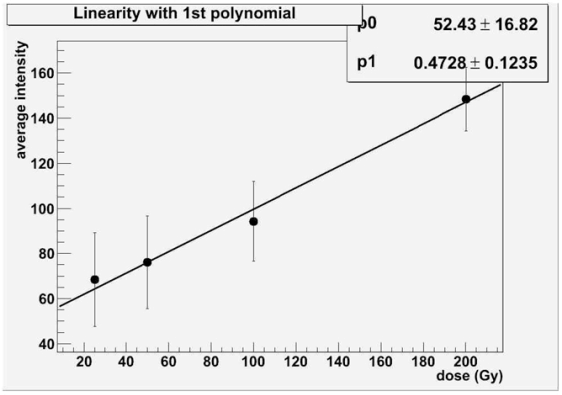


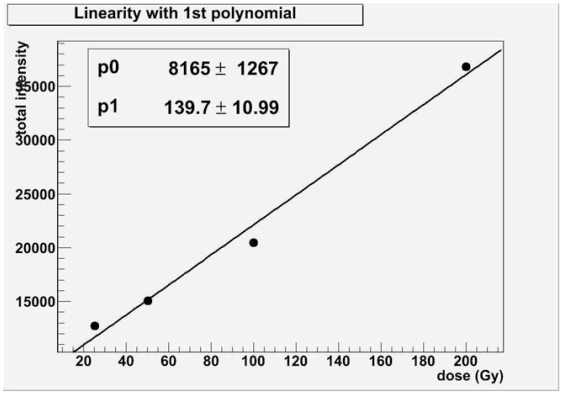
Figure1. Gel imaging results

FKPPL Project report (2011)

Red info should be replaced by the appropriate text in black

Summary of 2011 activities





Average Intensity

Total Intensity

Figure2. Light Intensity and Linear Fitting

Monitor Unit(MU) / Proton Dose (Gy)	Light Intensity (average)	RMS	Total Light Intensity (Total)
0 / 0	24.42	16.25	632.35
1676 / 25.14	68.47	20.73	12717.7
3341 / 50.12	76.18	20.57	15047.7
6668 / 100.02	94.2	17.71	20485.7
13339 / 200.09	148.5	14.17	36830.7

Table1. Data sheet about Light Intensity

FKPPL Project report (2011)

Red info should be replaced by the appropriate text in black

Summary of 2011 activities

2) Impact of proton radiations on the bacteria model Escherichia Coli.

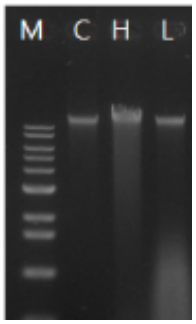
Description:

The purpose of this joint experience between the French laboratories (LPC, CENBG) and the Korean institutes (NCC and KBSI) is to evaluate the damages occurred to the E. Coli bacteria after a proton irradiation. The goal was to quantify the bacterial survival and the DNA breakages occurred after irradiation in order to validate the Monte Carlo simulation software GEANT4-DNA for which, the very low energy electromagnetic processes have been modeled as well as the non-direct processes occurred by the water radiolysis. An other issue is to obtain valuable results on the impact of ionizing radiation on the cellular growth to develop an in silico platform being able to model the bacteria evolution.

To fill those requirements, the LPC and the NCC medical physics staff irradiated E. Coli bacteria samples at different doses (10, 20, 30, 40 and 50 Gy) using two different LET values (0.3 keV/nm and 2 keV/nm). The samples were prepared in the microbiology lab hosted at NCC by the french group. Bacteria colonies introduced in a liquid medium (NaCl) were also irradiated at 50 Gy using two different LET in order to analyze the DNA breakages and the potential modifications occurred on the proteome of the bacteria. The biological analysis has been taken in charge by the KBSI and Hannam Univ; the purpose was to evaluate in a first approach the DNA damages using agarose gel electrophoresis and then a Real Time Polymerase Chain Reaction (RT-PCR) analysis concerning the two frequently mutating genes involved in the DNA conformation (topA and fis genes). Six genes of E.Coli (topA, fis, ompF, sopT, pykF and rpsM) were analyzed by RT-PCR. rpsM is the gene that was known as rarely mutating gene. We included rpsM gene as a control in order to compare difference.

Results:

- Survival rates: as expected, high LET irradiation caused a lower survival rate for the E.Coli bacteria comparing to a radiation therapy beam using 15 MV photons. Low LET proton irradiation didn't show significant modifications on the survival rate comparing to the photon irradiation.
- DNA analysis: The 2D electrophoresis shows many fragments of DNA after irradiation. Low LET irradiation produced much more small DNA fragmentations compared to high LET irradiation. From RT-PCR, we could not find the noticeable difference in the mutation frequency between rpsM and the other genes



M : Marker
C : control
H : High LET
L : Low LET

Figure 3: 2D electrophoresis after irradiation at 50 Gy

3) Monte Carlo simulation of the proton beam line.

The third activity took place thanks to the Geant4/GATE tutorial that was organized at KISTI in October-November 2011. During this tutorial, the new features of the Geant4 toolkit (release 9.4) were introduced, including the recommended usage of electromagnetic physics builders (G4EmStandard_option3) and the recommended physics lists for protontherapy applications (for eg. QGSP_BIC), including selected hadronic processes. J. I. Shin and S. Incerti could collaborate together in order to upgrade the Geant4 Monte Carlo code developed at NCC a few years ago for the modeling of the proton beam line.

FKPPL Project report (2011)

Red info should be replaced by the appropriate text in black

Publications since 2007	No publication yet.