FKPPL Project application (2012)

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

List of participants

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	Dae Yeon Kim	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

Requested LIA specific funding from France

Description	Euro/unit	Nb of units	Total (euros)	Requested to: *
LPC Clermont participation to PTCOG and 2 weeks visit to NCC	8000	1	8000	IN2P3
CENBG participation to PTCOG and 2 weeks visit to NCC	4000	1	4000	IN2P3
Visit of Mr J. I. Shin to LPC Clermont for one month	3000	1	3000	IN2P3
Visit of Mr J. I. Shin to CENBG for one month	4000	1	4000	IN2P3
Total	19000	4	19000	

Requested funding from Korea

Description	Won/Unit	Nb of units	Total (Won)	Requested to: **
NCC participation to FKPPL2012 Meeting in France for one week	4,000,000	1	4,000,000	NCC
NCC participation to G4DNA Collaboration Meeting for one week	4,000,000	1	4,000,000	NCC
KBSI participation to FKPPL2012 Meeting in France for one week	4,000,000	1	4,000,000	KBSI
Geant4/GATE/GRID workshop	2,000,000	1	2,000,000	NCC
Total	14,000,000	4	14,000,000	

Additional funding

Additional funding from France			Additional funding from Korea		
Provided by or requested to * **	**Type**	**Euro**	**Provided by or requested to**	**Type**	**Won**

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* For example: IN2P3, CEA. ** Korean University or Institute. *** French Embassy, CNRS Egide,……

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Summary of Project

We propose to focus our 2012 activities both on simulation activities using GATE/Geant4/Geant4-DNA and on experimental radiobiology activities using the NCC protontherapy facility:

1. **Monte Carlo modeling activities using GATE/Geant4**

a) Modeling of the NCC proton beam line using GATE

The NCC team has recently upgraded their Geant4-based NCC protontherapy beam line application to the 9.4 release of the Geant4 toolkit. This application will be upgraded to Geant4 9.5 and ported to GATE in 2012. As the first step, NCC will provide a simple model of Proton beam nozzle with passive mode and it will be designed for Geant4-DNA simulations of radiobiology experiments.

b) Experimental validation of Geant4 physics models for protontherapy through GATE using recommended Geant4 physics lists and experimental dose profile measurements performed at NCC

Using the GATE-ported NCC protontherapy application, it will be possible to further validate Geant4 recommended physics configurations for the modeling of protontherapy setups (electromagnetic physics standard options 2 & 3, reference Physic lists such as QGSP_BIC, QGSP_BERT, …). For this purpose, experimental measurements of Bragg curves will be performed at NCC. A special dosimetry will be tried for micro-beam measurement with film and emulsion

c) Modeling of direct biological damages using the Geant4-DNA extension

The Geant4-DNA extension of the Geant4 toolkit allows Geant4 users to model ionizing track structures in 3D geometries of cell nuclei, including description of genetic material in biological cells, such as chromatin fiber elements, nucleosomes, histones, DNA loops and bases. A first geometrical model of a nucleus has been developed in combination with Geant4-DNA physics processes and models, in order to estimate non-complex single and double strand breaks resulting from direct interaction of ionizing radiation with DNA bases. This geometrical model is built from a voxellized realistic cellular phantom (HaCat keratinocyte cell), which includes a mathematical description of the DNA conformation. This Geant4-DNA physics-geometry combination enables the testing of several hypothesis that needs to be made in order to quantify such direct biological damages: dimensions and conformation of the DNA geometry, probability to induce single strand breaks, cross section models describing elementary interactions of particles in liquid water… In this context, we propose to test the influence of several DNA geometrical conformations (A-, B-, Z-DNA) as well as the influence of the probability of break induction, on estimated direct single and double strand breaks. Comparison to other Monte Carlo codes (such as PARTRAC) will be performed.

d) Combination of GATE and Geant4-DNA

Geant4-DNA physics processes will be made available in GATE either through the usage of the recommended Geant4 Physics constructor "G4EmDNAPhysics" or by adding each individual Physics process into GATE. In combination with several realistic DNA geometries, it would become possible to simulate direct effects using GATE at the DNA scale. Besides, the combination of Geant4-DNA Physics models with other Geant4 electromagnetic processes and models ("standard" and "low energy") allows the simulation of multi-scale setups, where the usage of Geant4-DNA processes can be restricted to small size biological targets (such as DNA) and where the other Geant4 electromagnetic processes are applied to larger "container" volumes, such as tissues and organs. This multi-scale combination will be tested with GATE and could be applied to a geometrical model of a mouse (for eg. phantom).

e) Modeling of non-direct biological damages using the Geant4-DNA extension

Since December 2011 (Geant4 release 9.5), Geant4-DNA can simulate water radiolysis, including diffusion and mutual interaction of oxidative radicals. It is known that non-direct effects induce more DNA damages than direct effects. If time permits, we will investigate the possibility to estimate non-direct effects using a geometrical model of a cell nucleus. For this, it will be necessary to evaluate the feasibility of combination of physico-chemistry processes with geometrical models of DNA, including a description of DNA nucleotides not only represented by geometrical volumes but as molecular entities able to react chemically with oxidative radicals. This R&D activity will be part of the development of the Geant4-DNA extension in the Geant4 toolkit.

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2. Radiobiology experiments

a) E. coli

We select some genes related to the evolution or industrial bioengineering and investigate their variation by the irradiation (for eg. The glutathione S-transferase (GST) gene which, related to detoxification) By classifying E. coli's by phenotype difference, we analyze the DNA fragmentation, gene expression profiles.

b) Mouse

We plan to irradiate a mouse with a photon beam (at the Korea Atomic Energy Research Institute) and take tissues from the irradiated and non-irradiated positions. We compare their contents, such as DNA, proteins, metabolites. Using GATE simulation, these radiation effects will be interpreted, possibly using the combination of Geant4 electromagnetic processes and Geant4-DNA processes (directly in GATE) in combination with a geometrical description of the mouse (phantom based).

3. Outreach

Moreover, the next Particle Therapy Co-Operative Group (PTCOG) will meet at NCC on May 14-19, 2012 (http://ptcog.web.psi.ch/). For the first time, we wish to present our activities and developments (GATE/Geant4-DNA simulations, irradiation experiments at NCC, quantification of biological damages) to the PTCOG community. An abstract and talk will be proposed and presented.

Finally, we are enthusiastic for the organization of a GATE/Geant4/Grid tutorial in Korea.