Monte Carlo simulation of radiation interaction with biological system at cellular level: an introduction to Geant4-DNA package

Maynard E. Limbaco[1]*, and Salasa A. Nawang[1]

[1]Mindanao Radiation Physics Center, Department of Physics, Mindanao State University - Iligan Institute of Technology, A. Bonifacio Avenue, Iligan City, 9200, Philippines

*email address: maynard.limbaco@g.msuiit.edu.ph

ABSTRACT

In recent years, radiobiology is an actual concern when ionizing radiation is increasingly widely used in many fields from nuclear center, agriculture, technology, aviation to medicine. Experts desire to understand the detailed action of ionizing radiation on living tissues at cellular, chromatin fiber, nucleosome and DNA levels. Monte Carlo track structure (MCTS) simulation has become a pivotal tool and developed to satisfy the estimation of the radiobiological effects induced by ionizing radiation on living beings. As of to date, several Monte Carlo codes, with different level of complexity, are already available and are commonly used in research fields such as nanodosimetry, radiotherapy, radiation protection, and space radiation for the simulation of track structures at energies that ranges from several eV to MeV at the molecular scale in biological medium. However, most of these codes were designed for very specific applications and not always easily accessible.

This work presents an enhancement of an existing model for radiobiological purposes, in order to account for the indirect and mixed DNA damage induced by ionizing particles. The GATE/GEANT4-DNA simulation toolkit was used to simulate physical, pre-chemical and chemical stages of the early DNA damage induced by photons and secondary electron particles. This was designed to be developed and delivered in a FREE software spirit under Geant4 license, which can be easily upgraded and improved. Liquid water was used as the medium for simulations. To the best of our knowledge, this is the first time the GEANT4-DNA code is used in conjunction at the DNA atomic scale resolution.

INTRODUCTION

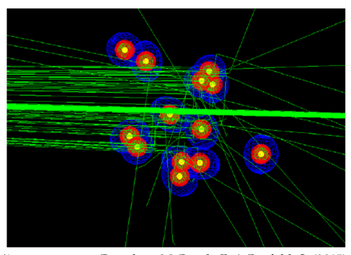

*image courtesy: Douglass, M.,Bezak, E. & Penfold, S. (2015)

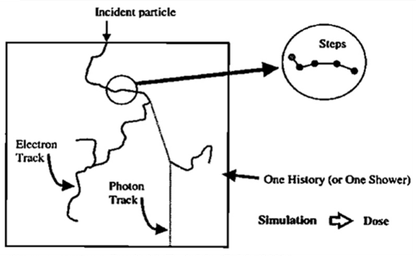

*image courtesy: Pawlicki, T., & Ma, C. M. (2001).

In recent years, radiobiology is an actual concern when ionizing radiation is increasingly widely used in many fields from nuclear center, agriculture, technology, aviation to medicine

The development of the Monte Carlo track structure (MCTS) simulation has become a key tool for estimating the detailed impact of ionizing radiation on living tissues at the cellular, chromatin fiber, nucleosome, and DNA levels. Although, a number of Monte Carlo codes are currently available and frequently used in research fields, the majority of these codes were extremely designed for very specific applications, were not easily accessible and have limited user-extensibility and capability.

The Geant4-DNA project was then designed to be developed and delivered in a FREE software spirit under the Geant4 license that is easily upgradeable. This package extends the general purpose Geant4 Monte Carlo toolkit for the simulation of radiation interaction with biological systems at the cellular including the physical, pre-chemical, and chemical steps and then predict early DNA damage.

http://geant4-dna.in2p3.fr/

Therefore, the objective of this work is to evaluate the Geant4-DNA package in the physical stage and compare it with the existing Geant4 - Electromagnetic Standard Physics Model by simulating a conventional clinical treatment of water volume using medical linear accelerator.

METHODOLOGY

In this work, GATE (GEANT4 Application for Tomographic Emission) v.9.2 coupled with Geant4-DNA (*Geant4 v.11.0.3*) was used to simulate radiotherapy treatment in this study. It encapsulates the GEANT4-DNA libraries and its other dependencies in order to achieve a modular, versatile, scripted simulation toolkit adapted to the field of nuclear medicine. The use of GATE does not require C++ programming but is capable to perform and to control Monte Carlo simulations of realistic setups.

http://www.opengatecollaboration.org/

Virtual Linac

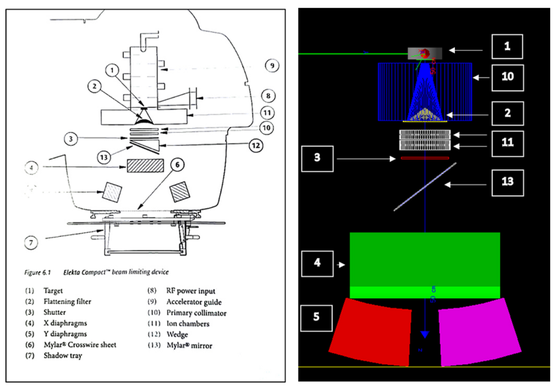

Figure 2.1. The Schematic Diagram of Elekta Compact™ Linac according to the manufacturer's manual (left) and virtual Linac model created in GATE (right).

1. emstandard_opt3_mixed_emdna (DNA physics at detector slab); and
2. emstandard_opt3 was employed.

Simulation Setup

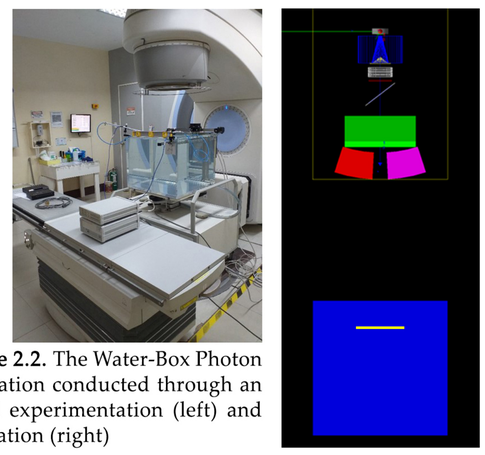

Figure 2.2. The Water-Box Photon Irradiation conducted through an actual experimentation (left) and simulation (right)

Parameters

Source:	Electron (6 MeV)
Source-to-Surface Distance:	100 cm
Field Size:	10 cm x 10 cm
Detector Volume (yellow):	10 cm x 10 cm x 100 μm

CONCLUSION AND RECOMMENDATION

The simulation set-up of this work was shown to be in good conformance with the actual clinical treatment with at least 95% confidence using 3%/3m gamma criterion. This work has successfully reconstructed an Elekta Compact™ Linac on GATE MC tool. Additionally clear evidence was observed with regards to discrepancy using MixedDNA physics and EMstandard physics particularly at low-energy. This is to be expected as this physics was created with the intent to establish a model for bilogical application at cellular and DNA level.

The researchers recommends further analysis particularly on the use of the newest version of Geant4 and Gate to establish more concrete conclusion. Additionally, the researcher recommends to use and explore MixedDNA on GATE for the pre-chemical, chemical and biological stages of radiation interaction with matter. And finally to implement cellular targets based on actual data to evaluate the capability of MCTS DNA physics.

RESULTS AND DISCUSSION

ELEKTA-GATE Linac Validation

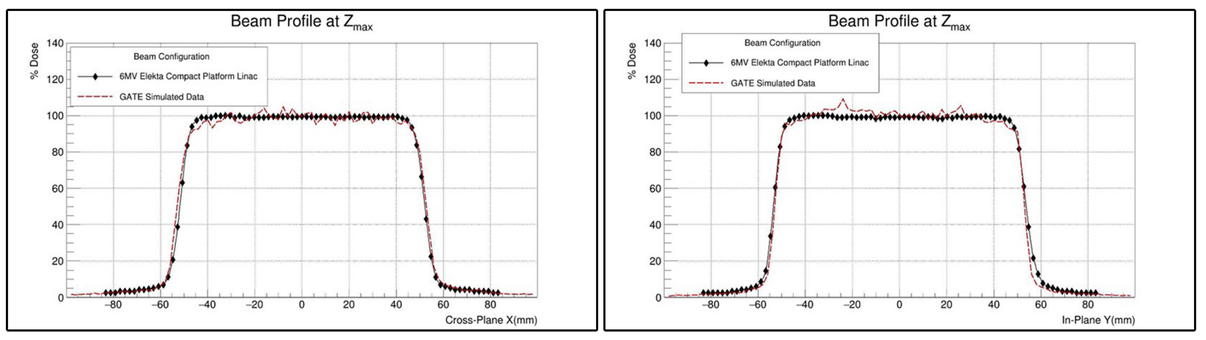

Figure 3.1. Lateral Beam Profile graph along the crossplane (x-axis; left) and in-plane (y-axis; right) between the measured and simulated data with number of events (N) = 10^9 events measured at Z=D_{max}

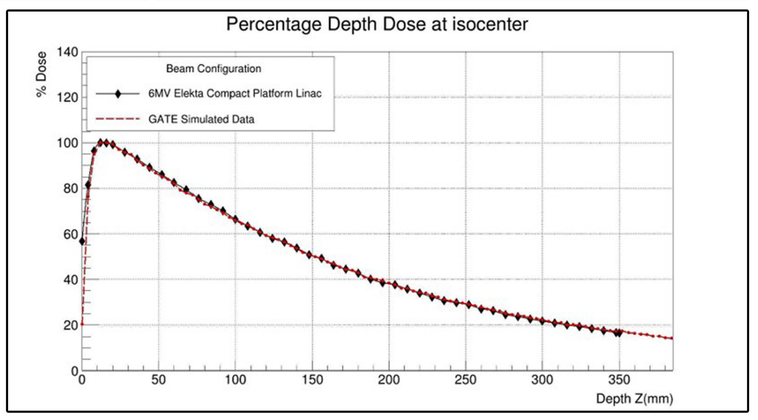

Figure 3.2. Percentage Depth Dose (PDD) graph between the measured and simulated data with number of events (N) = 10^9 events and field size of 10 cm x 10 cm located at the central axis.

GAMMA (Γ INDEX) ANALYSIS

at point x_m

$$\gamma(x_m) = \min\{\Gamma(x_m, x_c)\}$$

for all x_m, where

$$\Gamma(x_m, x_c) = \sqrt{\frac{|x_m - x_c|^2}{\Delta d_M^2} + \frac{|D_c(x_c) - D_m(x_m)|^2}{\Delta D_M^2}},$$

Δd_M is the DTA,
and ΔD_M is the dosage distribution.

EXPERIMENTAL vs SIMULATED

Criteria: 3 % / 3 mm	Passing Rate
Percentage Depth Dose	97.87%
Beam Profile (Cross-plane)	98.80%
Beam Profile (In-plane)	95.18%

DISCUSSION: According to gamma index analysis, the simulated results have shown to conform the experimental output with at least 95% confidence level at 3%/3mm criterion. This result is in good agreement with the curves presented in Figures 3.1 and 3.2.

EM Standard Physics vs Mixed DNA Physics

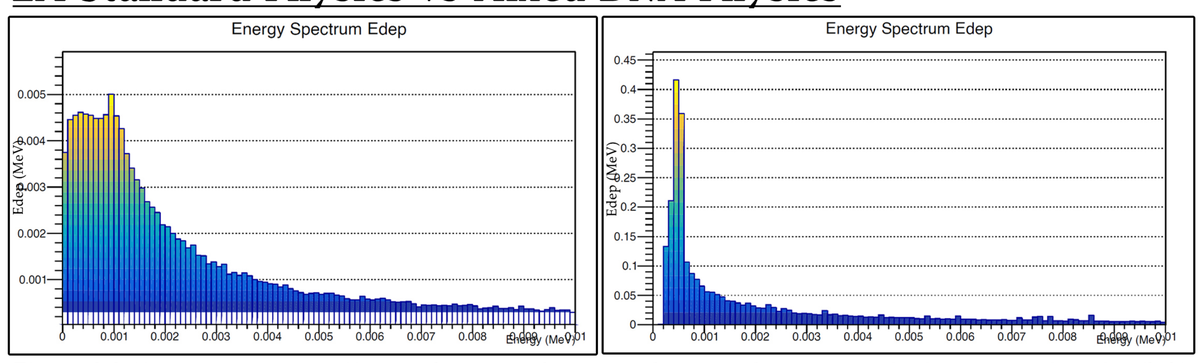

Figure 3.3. Energy spectrum vs Energy deposition histogram between the G4emstandard_opt3_mixed_emdna (left) and G4emstandard_opt3 (right) physics constructor used. Energy calculation was collected at Dose Maximum located at ~1.2 cm according to **Figure 3.1.** The white-fill histogram observed in the left figure was caused by the predetermined cut set by the user. MixedDNA has a much softer energy deposition as compared to EMstandard.

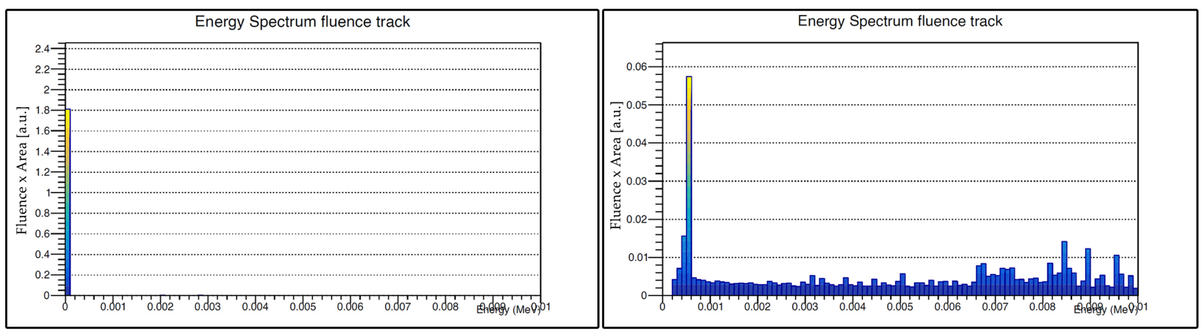

Figure 3.4. Energy spectrum vs particle count in the detector between the G4emstandard_opt3_mixed_emdna (left) and G4emstandard_opt3 (right) physics constructor used. It reveals that particle generation on MixedDNA was heavily concentrated at Low Energy (< 10 eV) as compared to EMstandard physics where it is much scattered along the energy spectrum.

ACKNOWLEDEGEMENT:

DOST-ASTHRDP

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