



HAL
open science

Isochore Nuclear Geometry for modeling the radiation-induced DNA damage topology

Yann Thibaut, Carmen Villagrasa, Sébastien Incerti, Yann Perrot

► **To cite this version:**

Yann Thibaut, Carmen Villagrasa, Sébastien Incerti, Yann Perrot. Isochore Nuclear Geometry for modeling the radiation-induced DNA damage topology. 46th Annual Meeting of the European Radiation Research Society, ERRS 2021, Nov 2021, CAEN, France. 2021. hal-03505857

HAL Id: hal-03505857

<https://hal.science/hal-03505857>

Submitted on 31 Dec 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Copyright



ISOCHORE NUCLEAR GEOMETRY FOR MODELING THE RADIATION-INDUCED DNA DAMAGE TOPOLOGY

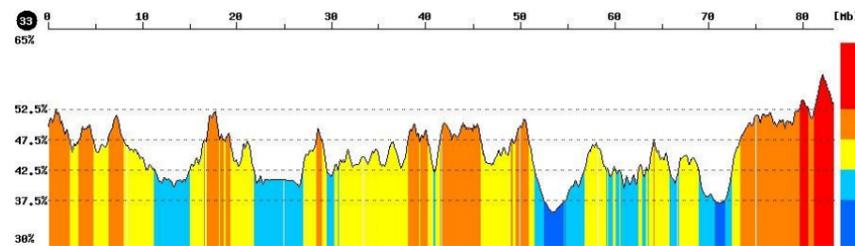
Y. THIBAUT¹, C. VILLAGRASA¹, S. INCERTI², and Y. PERROT¹
¹ IRSN/PSE-SANTE/SDOS/LDRI, ² CNRS/IN2P3/CENBG

INTRODUCTION

Large part of radiotherapy side effects results from damage to the nuclear DNA molecule of healthy cells. Thus, a better understanding of these side effects can be reached by **modeling the interactions between ionizing radiation and cell nucleus**. The more realistic the geometrical modeling of the cell nucleus, the better the calculation of the DNA damage. **DNA compaction** has an important role in the induction of early damage, that's why a new endothelial nucleus model is proposed, based on the **theory of isochores** and compared to former nucleus.

ISOCHORE GEOMETRY

- Genome is divided into 1Mbp segments which are classified in 5 families according to their **GC rate**.



Family classification for segments of the chromosome 33 according to the theory of isochores.

Families	Genomic desert			Genome core	
	L1	L2	H1	H2	H3
Heterochromatin rate	100%	70%	50%	20%	0%

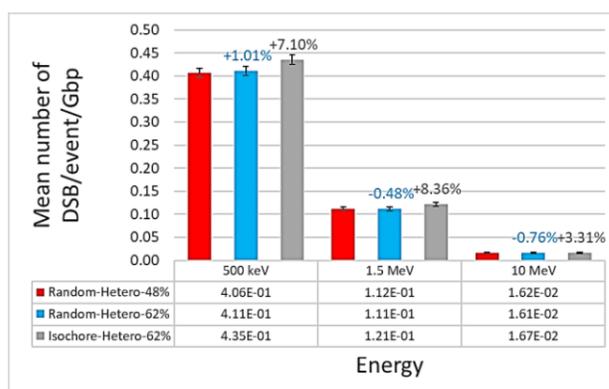
Families and their associated heterochromatin rate associated.

MATERIALS and METHODS

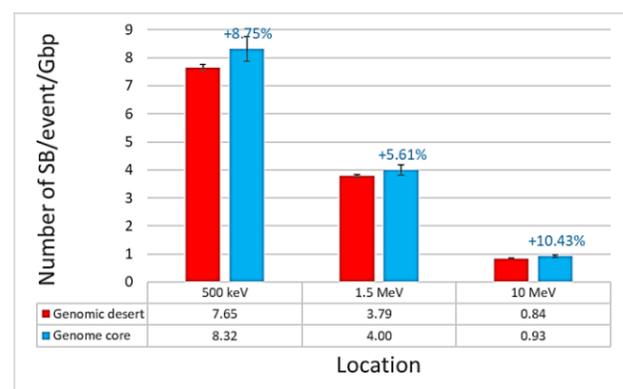
The geometrical nucleus models are integrated in a nanodosimetric calculation chain based on the **Geant4-DNA** Monte Carlo simulation toolkit (geant4-dna.org) in order to simulate the early DNA damage topology. This chain is used to benchmark the isochore nucleus with a former nucleus used in previous work, in which heterochromatin and euchromatin are randomly distributed (*Tang, Med. Phys., 2019*). As the two nuclei have a different global heterochromatin rate, so a third nucleus is included to make the results more relevant.

Simulations were performed with 1000 protons of 500 keV (43.2 keV/μm), 1500 protons of 1.5 MeV (19.5 keV/μm) and 2000 protons of 10 MeV (4.3 keV/μm).

RESULTS



Comparison of the mean number of DSB/event/Gbp for the three endothelial geometries.



Strand Break yield in the isochore nucleus with respect to their location: genomic desert or genome core.

- More DSBs with the isochore nucleus even in comparison with the nucleus with the same heterochromatin rate.
- More damage in the **genome core** than in the **genomic desert**.

DISCUSSION

Chromatin compaction distribution of DNA fiber based on the theory of the isochores **increases the mean number of DSB/event** calculated but remains in agreement with previous geometries already validated. Moreover, this model allows to simulate the **higher radiation sensitivity of the genome core**, due to a higher euchromatin concentration. This information is primordial because the genome core is transcriptionally active.

ERRS 2021, 46th Annual Meeting of the European Radiation Research Society, Caen, France