GATE activities @ LPC

January 22 2020

University of Wuppertal, Germany

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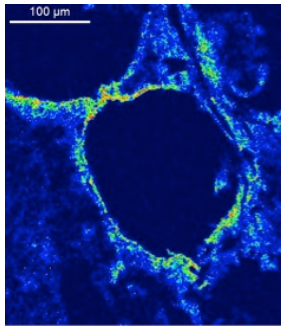
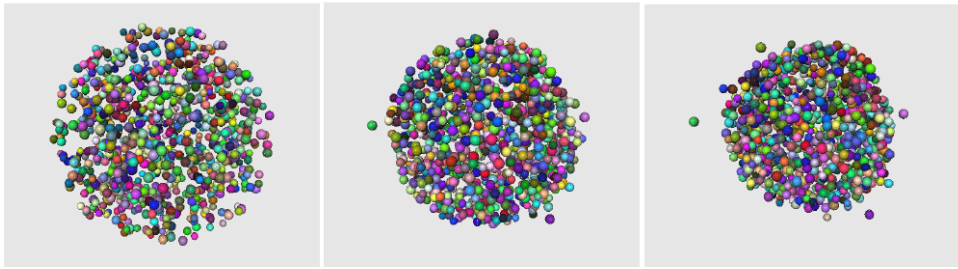
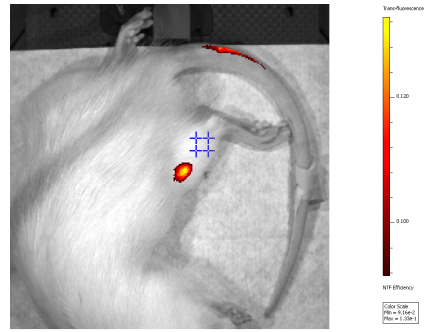
Health team @ LPC

- 16 faculty members
- 4 technical staff
- 4 PhD students
- 3 postDocs



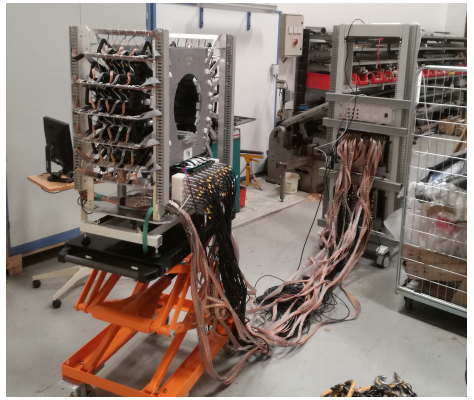


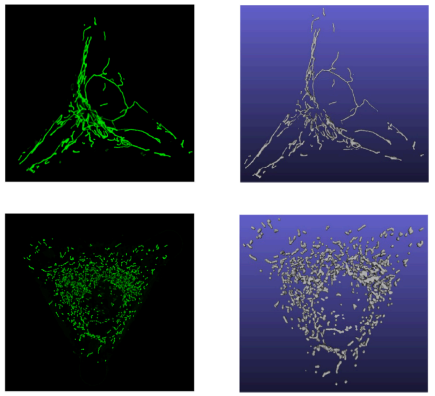


***In vivo* imaging (IVIS spectrum)**
Au@AF647
(Wollongong university collaboration)

Research areas:

- Biomaterials
- On line dose control in hadrontherapy
- Simulation/Modeling (GATE & Geant4-DNA)
- Radiation biology (NP)/Mitochondrial DNA

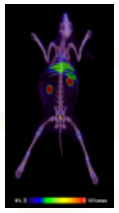
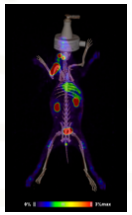
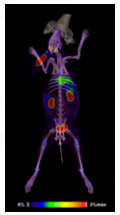
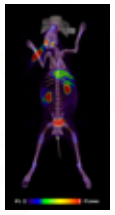
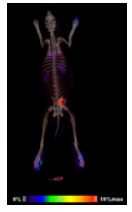
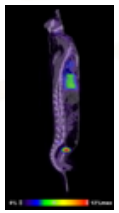
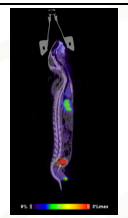
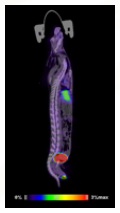
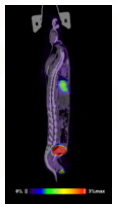
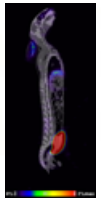
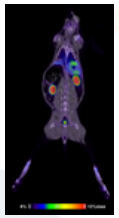
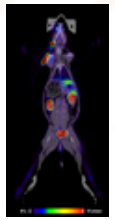
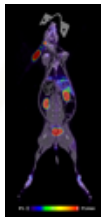
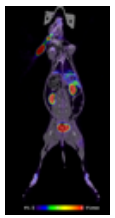
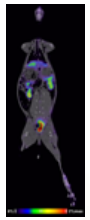
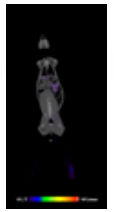
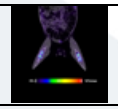
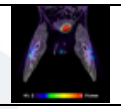
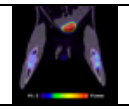
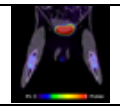
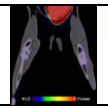
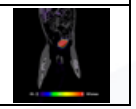


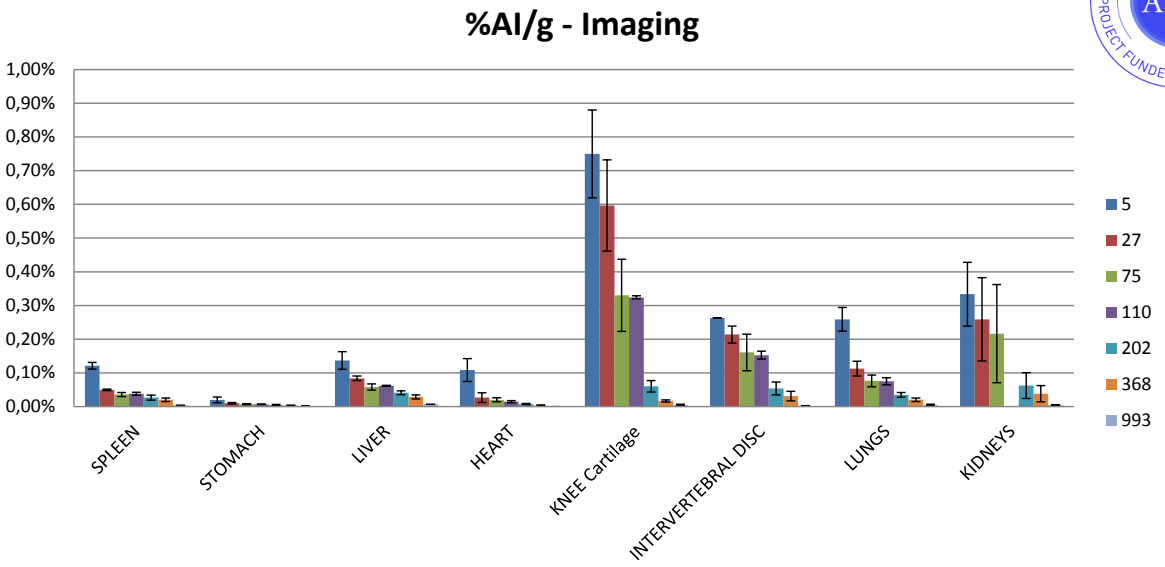


PROJECT 1: Internal dosimetry of [99mTc]NTP15-5 radiotracer for cartilage imaging in preclinical and clinical models (1/2)

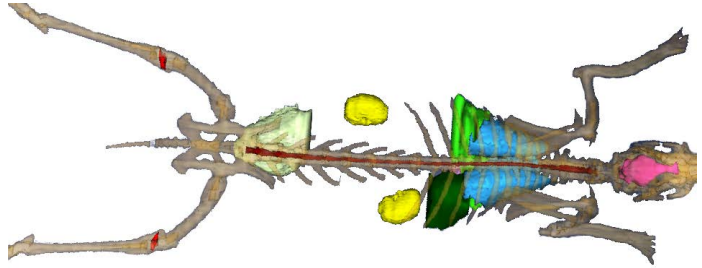
Collaboration LPC- Jean Perrin Cancer centre

dual-head SPECT/CT device (Symbia® T2, Siemens) with a Low Energy High Resolution (LEHR) collimator.

Acquisition time (min)	10	29	74	110	193	381
Rabbit N°	Rabbit 1 (34344)	Rabbit 2 (34317_t1)	Rabbit 2 (34317_t2)	Rabbit 2 (34317_t3)	Rabbit 3 (36303_t2)	Rabbit 3 (36303_t3)
Maximum Intensity Projection (MIP)						
Sagittal view						
Frontal view						
Zoom on knees						



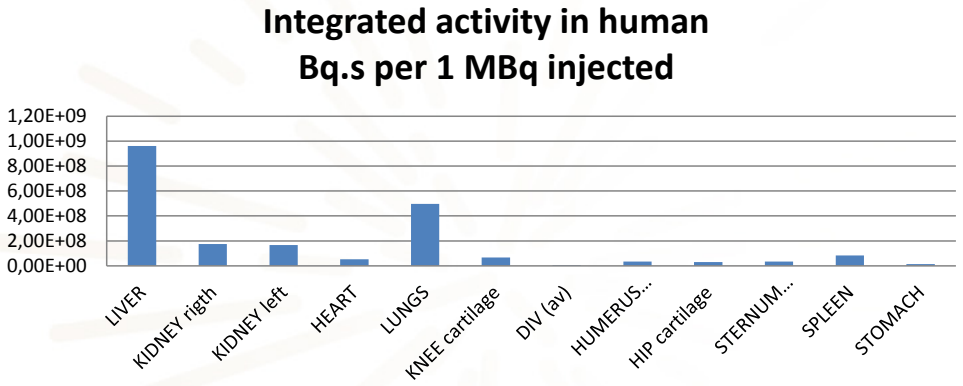
DOSE µGY/MBq inj	
KIDNEY	33,7 ± 13,8
HEART	7,6 ± 1,6
LIVER	21,9 ± 2,9
SPLEEN	13,8 ± 2,8
SPINAL CORD	2,5 ± 0,6
LUNGS	8,0 ± 1,5
KNEE CARTILAGE	5,0 ± 0,7
LUMBAR DISC (av)	4,3 ± 1,3
THORACIC DISC (av)	11,7 ± 2,7

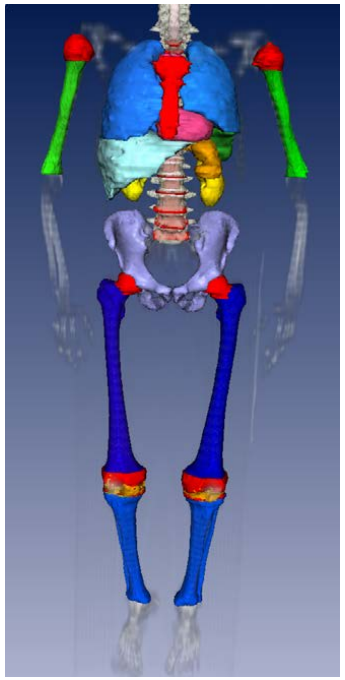


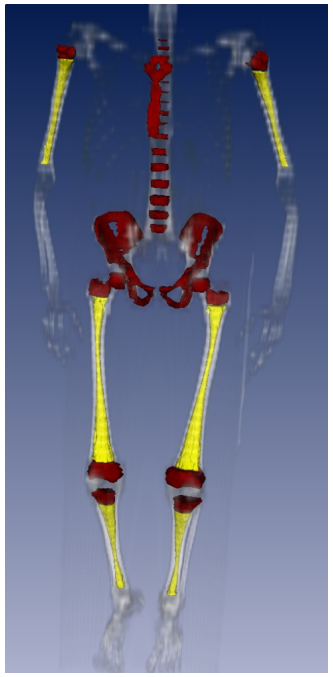
seTLE methodology (Smekens et al.)

PROJECT 1: Internal dosimetry of [99mTc]NTP15-5 radiotracer for cartilage imaging in preclinical and clinical models (2/2)

$$\tilde{A}[human] = \tilde{A}[rabbit] \cdot \bar{m}[rabbit] \cdot \frac{\%Di/organ(human)}{\%Di/g(rabbit)}$$







Dose (µGy/MBq)		Imaging
ORGANS	Liver	3,1 ± 0,5
	Kidney R	4,6 ± 1,6
	Kidney L	4,0 ± 1,6
	Spleen	1,8 ± 0,4
	Stomach	1,0 ± 0,3
	Lung R	1,8 ± 0,4
	Lung L	1,6 ± 0,4
	Heart	1,5 ± 0,3
	Brain	0,02 ± 0,004
	Bladder	0,09 ± 0,02
	Spinal cord	0,7 ± 0,2

RED BONE MARROW	Lumbar vertebrae (av)	0,8 ± 0,3
	Thoracic vertebrae (av)	1,2 ± 0,1
	Femur top	0,8 ± 0,1
	Femur bottom	0,6 ± 0,1
	Tibia (av)	0,6 ± 0,1
	Pelvis	0,5 ± 0,1
	Humerus (av)	0,6 ± 0,1
	Sternum	0,6 ± 0,1

To be published in Medical Physics journal

PROJECT 2: Clinical transfer of 131I-ICF01012 to treat melanoma (1/2)

Collaboration LPC- Jean Perrin Cancer centre

1 patient/month to be treated with 131I-ICF01012; duration of the clinical transfer 6 months
LPC in charge of S values calculation with GATE & Jean Perrin Cancer Centre in charge of imaging acquisitions

2 phases:

Phase 1 diagnostic: 1 full body CT scan + SPECT @ 1, 3, 24, 96, 168 hours post injection
Phase 2 therapeutic: SPECT @ 264 hours post injection
Doses to calculate: Brain, Liver, Kidneys, Lung, retina, metastasis
Escalation of injected activity along the project: 800 MBq/m2 to 4000 MBq/m2

Maximum Dose allowed (Gy)	
Liver	26
Kidneys	16.2
Lung	15
Retina	40

S-values in Gy/Mbq.s		
GATE	OLINDA	
2.54E-08	2.69E-08	BRAIN
1.58E-07	1.85E-07	KIDNEYL
1.78E-07	1.85E-07	KIDNEYR
1.62E-08	2.04E-08	LIVER
1.17E-07		LUNGL
1.12E-07		LUNGR
1.00E-07	1.08E-07	META1
1.42E-06	1.47E-06	META2
4.04E-06	4.04E-06	META3
3.46E-08	3.62E-08	META4
1.01E-06	1.01E-06	META5
1.20E-05	1.28E-05	RETINE
8.77E-08	9.23E-08	SPLEEN

GATE and OLINDA provide comparable values except when organ are very specific

½ day to provide S-values calculation to Cancer centre

PROJECT 2: Clinical transfer of 131I-ICF01012 to treat melanoma (2/2)

Collaboration LPC- Jean Perrin Cancer centre

For therapeutic injected activity of 1240 MBq

	Bq.s/MBq	Facteurs S personnalisés GATE 8.2 (en Gy/(MBq.s)													
		Organes	Rétine G	Rétine D	Poumon G	Poumon D	Foie	Rate	Rein G	Rein D	Métastase 1	Métastase 2	Métastase 3	Métastase 4	Métastase 5	Cerveau
Retine G	9.29E+01	Rétine G	1.20E-05	0.00E+00	1.47E-10	1.38E-10	1.89E-11	6.21E-12	5.68E-12	5.43E-12	5.88E-11	4.92E-12	2.69E-12	1.33E-12	2.13E-12	4.34E-10
Retine D	0.00E+00	Rétine D	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Poumon G	6.57E+03	Poumon G	2.59E-11	0.00E+00	1.17E-07	1.61E-09	2.52E-10	5.62E-10	2.90E-10	1.06E-10	3.61E-10	7.07E-11	1.28E-10	3.31E-11	2.11E-11	1.16E-11
Poumon D	3.65E+03	Poumon D	2.14E-11	0.00E+00	4.32E-10	1.12E-07	1.30E-09	1.53E-10	1.96E-10	2.96E-10	2.50E-09	1.66E-10	7.16E-11	2.49E-11	1.43E-11	2.34E-11
Foie	4.48E+04	Foie	1.73E-12	0.00E+00	2.71E-11	1.71E-10	1.62E-08	2.25E-11	4.18E-11	1.64E-10	4.15E-11	7.31E-11	1.61E-11	6.64E-12	4.52E-12	8.45E-13
Rate	1.60E+03	Rate	4.28E-12	0.00E+00	2.25E-09	6.76E-10	2.53E-10	8.77E-08	3.16E-09	2.69E-10	6.89E-11	2.20E-10	1.92E-09	2.50E-10	6.89E-11	1.64E-12
Rein G	1.11E+03	Rein G	3.85E-12	0.00E+00	1.15E-09	9.30E-10	4.73E-10	3.16E-09	1.58E-07	7.64E-10	7.72E-11	6.45E-10	6.34E-09	5.88E-10	1.74E-10	1.16E-12
Rein D	1.64E+03	Rein D	6.57E-12	0.00E+00	4.18E-10	1.07E-09	1.48E-09	2.64E-10	7.59E-10	1.78E-07	8.08E-11	8.25E-09	3.93E-10	2.61E-10	4.74E-10	7.85E-13
Meta 1	4.06E+04	Métastase 1	5.01E-11	0.00E+00	1.44E-09	8.94E-09	3.03E-10	6.83E-11	7.83E-11	8.13E-11	1.00E-07	4.98E-11	3.00E-11	1.24E-11	1.59E-11	1.84E-11
Thyroïde	0.00E+00	Métastase 2	4.52E-12	0.00E+00	2.83E-10	6.08E-10	7.21E-10	2.16E-10	6.54E-10	8.24E-09	5.03E-11	1.42E-06	3.93E-10	3.65E-10	7.63E-10	5.75E-13
Meta 3	1.21E+03	Métastase 3	3.48E-12	0.00E+00	5.11E-10	3.83E-10	1.90E-10	1.90E-09	6.39E-09	4.03E-10	3.58E-11	4.19E-10	4.04E-06	1.24E-09	1.69E-10	5.57E-13
Meta 4	1.71E+05	Métastase 4	1.35E-12	0.00E+00	1.35E-10	1.36E-10	8.62E-11	2.53E-10	5.92E-10	2.68E-10	1.25E-11	3.70E-10	1.25E-09	3.46E-08	3.61E-10	2.03E-13
Meta 5	1.42E+03	Métastase 5	1.06E-12	0.00E+00	3.06E-11	6.19E-11	5.59E-11	2.69E-11	6.97E-11	1.99E-10	6.70E-12	3.22E-10	6.74E-11	1.46E-10	1.01E-06	1.15E-13
Cerveau	5.05E+03	Cerveau	1.56E-09	0.00E+00	3.88E-11	2.36E-11	9.39E-12	8.48E-12	4.77E-12	2.77E-12	5.48E-11	2.03E-12	1.51E-12	7.89E-13	2.87E-13	2.54E-08
			Rétine G	Rétine D	Poumon G	Poumon D	Foie	Rate	Rein G	Rein D	Métastase 1	Métastase 2	Métastase 3	Métastase 4	Métastase 5	Cerveau
	Dose GATE (Gy)		1.395	0.000	1.066	1.015	0.947	0.246	0.371	0.436	5.069	0.106	6.354	7.338	1.865	0.161

PROJECT 3: Development and optimization of cell survivals using biophysical models MKM and NanOx for ion beam therapy

Multidisciplinary project

Hadrontherapy | **Radiation biology** | **Dosimetry** | **Modeling**

Collaboration between 3 laboratories within LabEx PRIMES

Supervisors: Michael Beuve (ip2i), Lydia Maigne (LPC), Etienne Testa (ip2i), Jean Michel Letang (CREATIS), David Sarrut (CREATIS)

PhD student: Yasmine Ali

PROJECT 3: Development and optimization of cell survivals using biophysical models MKM and NanOx for ion beam therapy

Microkinetic model

Cell survival fraction

$$S = e^{-\langle L_n \rangle}$$

Number of damages in the nucleus

$$\langle L_n \rangle = (\alpha + \beta z)D + \beta D^2$$

Inaniwa T. et al. (2010)

NanOx

Cell survival fraction

$$S = S_{local\ events} \cdot S_{non\ local\ events}$$

LOCAL EVENTS

Effective lethal function

$$F(z) = -N \ln(1-f(z))$$

NON LOCAL EVENTS

Oxidative stress

$$F(Y) = e^{(-\langle \alpha Y + \beta Y^2 \rangle)}$$

C. Monini et al. (2017)

Trainee student in computing science

The biophysics models requires several types of data to lead to the relative biological effectiveness

Biological data

α, β : constants of the linear and quadratic components of cell killing

Physical data

z: specific energy deposited in a target
N : targets distributed in sensitive volume

Chemical data

Y : yield of OH· the sensitive volume

PROJECT 3: Development and optimization of cell survivals using biophysical models MKM and NanOx for ion beam therapy

Methodology

Biological data

The survival fraction constants α and β are extracted from the cell survival fraction estimations.

GEANT4 LPCHEM GEANT4-DNA

Data tables

Biological, physical and chemical data are stored under data tables.

Physical data

The dose mean specific energy distribution, the restrictive specific energy are simulated for micrometric and nanometric targets.

Chemical data

The radiochemical species yields are simulated and calculated.

GATE 8.2

Data tables

Biological, physical and chemical data.

Biophysics Models

The models use the data tables data to then estimate the RBE.

Biological dose

Gate models the 3D biological dose distribution

Physical dose

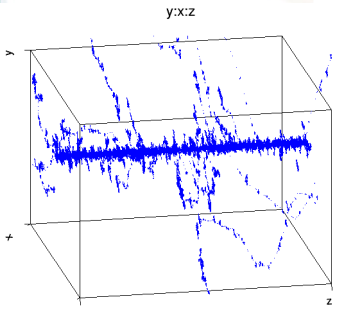
Gate models the 3D physical dose distribution

PROJECT 3: Development and optimization of cell survivals using biophysical models MKM and NanOx for ion beam therapy

Specific and lineal energy distributions in micrometric and nanometric targets with LPCHEM and G4-DNA calculated for electrons and protons

ENERGY TRANSFERT POINTS

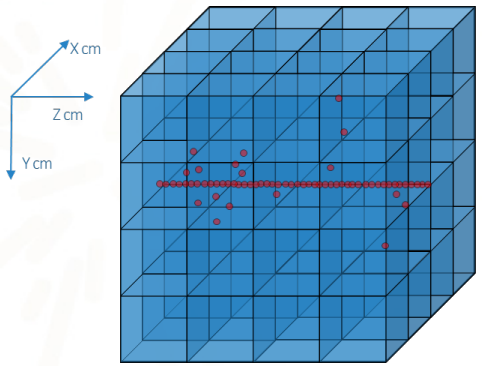
From LPCHEM or G4DNA



The LPCHEM and G4DNA physical modules simulate the energy transfer points.

THE MESH AND 3D MATRIX

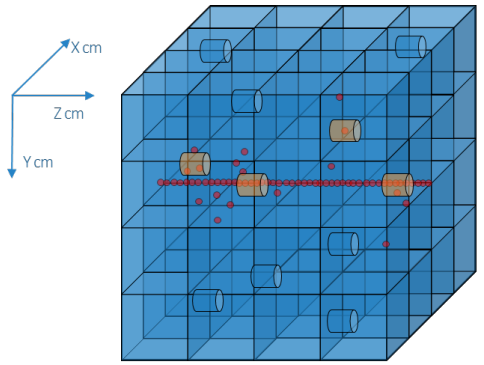
Calculation time saving biased method



TED uses the same track volume. The track volume is devided into voxels.

THE TARGETS

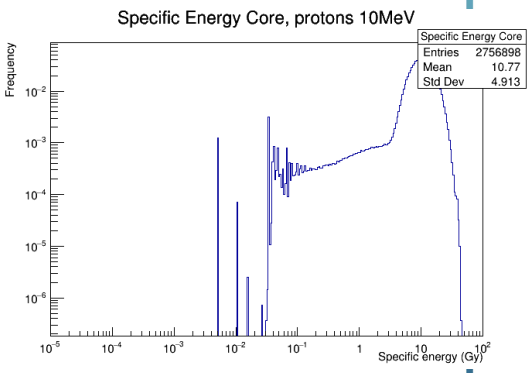
1µm micrometric and 10nm nanometric targets



Targets are generated in the voxels containing energy transfert points.

PROBABILITY DISTRIBUTIONS

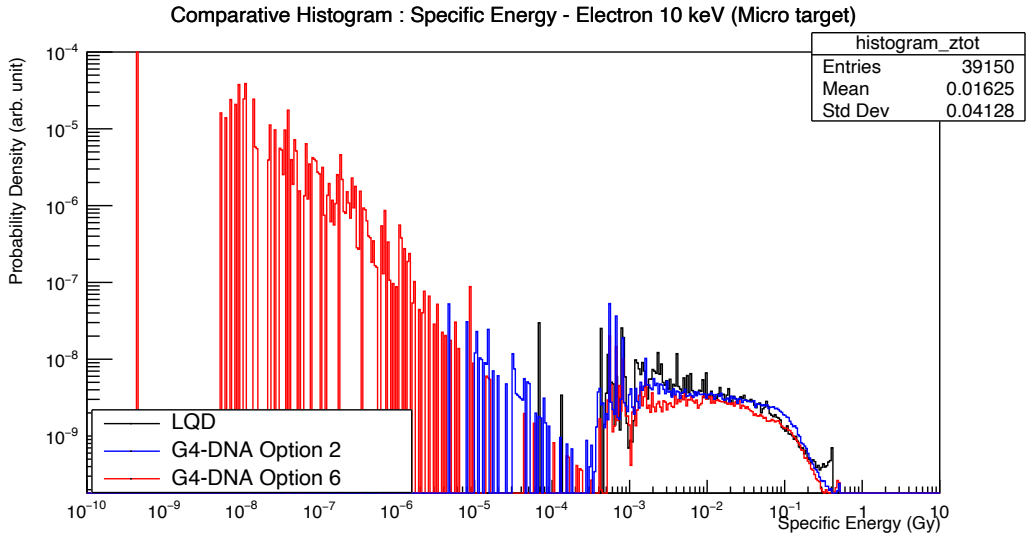
Specific energy

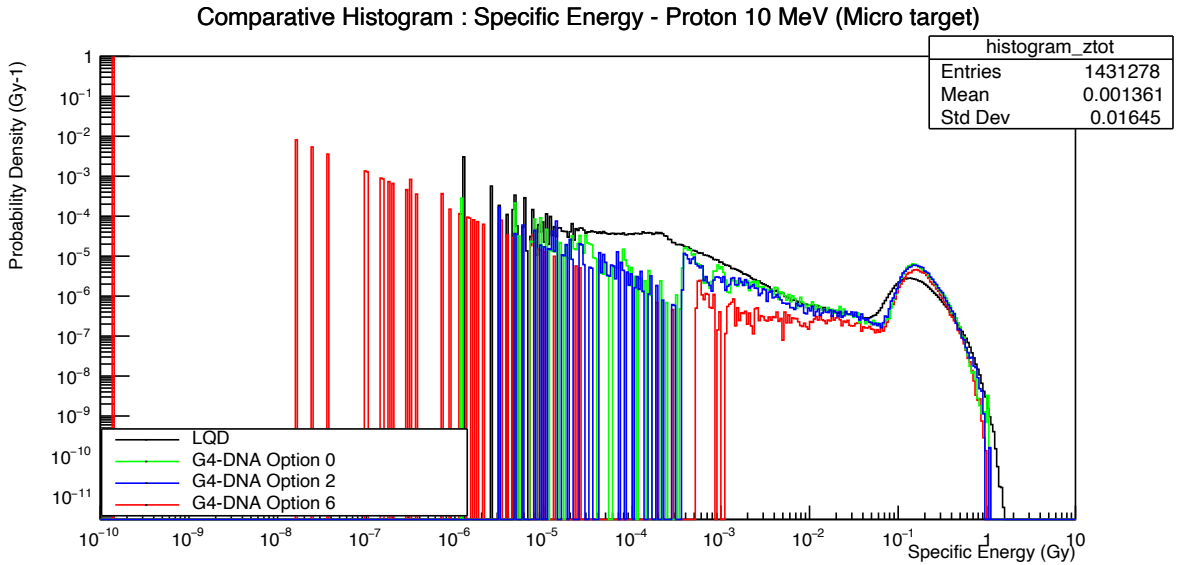


The probability distributions of specific energy are calculated.

PROJECT 3: Development and optimization of cell survivals using biophysical models MKM and NanOx for ion beam therapy

Example of results for 10 keV electrons and 10 MeV protons in micrometric targets





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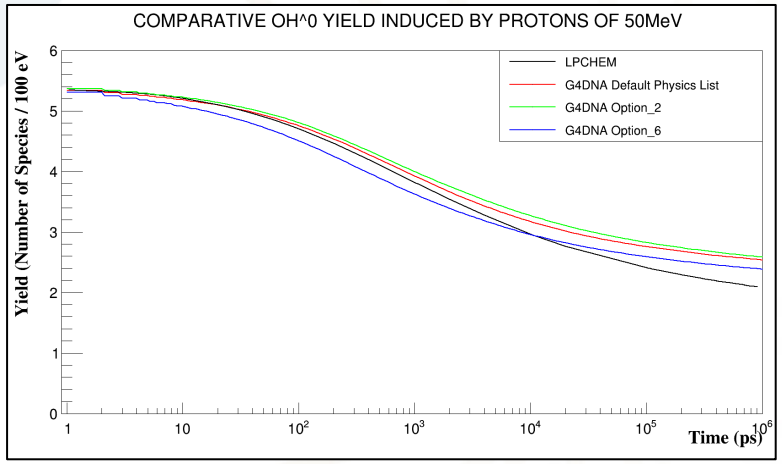
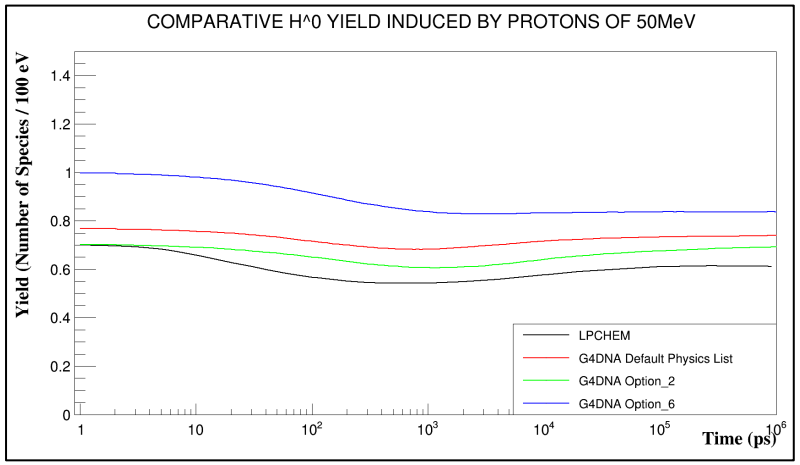
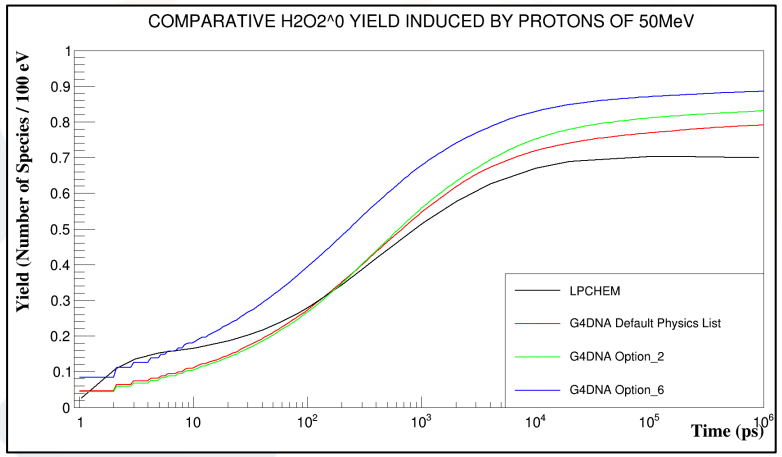
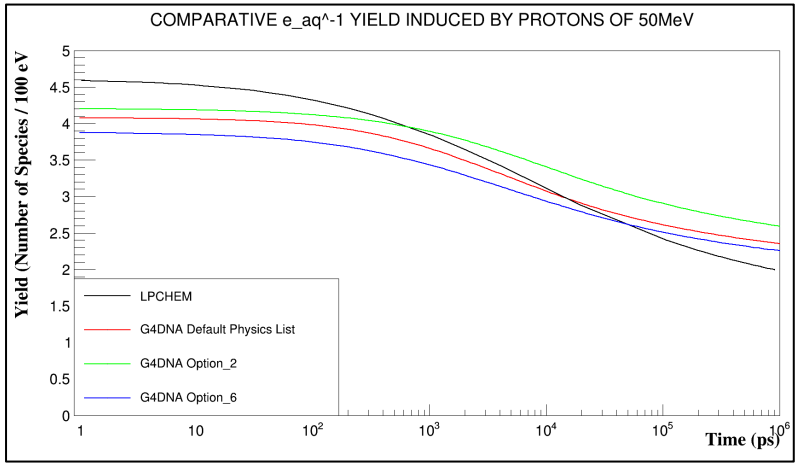
Chemical species yields generated with LPCHEM & G4-DNA









Perspectives

- Proceed collaboration with Jean Perrin cancer centre and offer a routine dosimetry in internal RT with GATE
- Partnerships with industries (improvement of detectors in molecular breast imaging)
- Implementation of MKM into GATE (by summer 2020)
- Implementation of NanOx model into GATE (by end of next year), requires the integration of specific databases for specific and chemical yields with a tuned calculation of biophysical dose