# Implementation of the biological dose in hadrontherapy using Gate : application with MMKM and NanOx models

Yasmine Ali

# PhD subject

Implementation of the biological dose in hadrontherapy using Gate : application with MMKM and NanOx models

## A pluridisciplinary subject

**Hadrontherapy** | **Radiobiology** | **Dosimetry** | **Modeling**

## A collaboration between laboratories

PhD supervisors : Michael Beuve (ip2i), Lydia Maigne (LPC),
Etienne Testa (ip2i), Jean Michel Letang (CREATIS)

# Overview

**Problematics in hadrontherapy**

**MMKM and NanOx cell survival predictions**

**Biodose actor implementation in Monte Carlo platform GATE**

**Biological dose and RBE calculation for clinical beams**

**Conclusion**

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# Radiotherapy

Radiation therapy technique using X rays to kill tumoral cells.

**Dose deposition in depth**

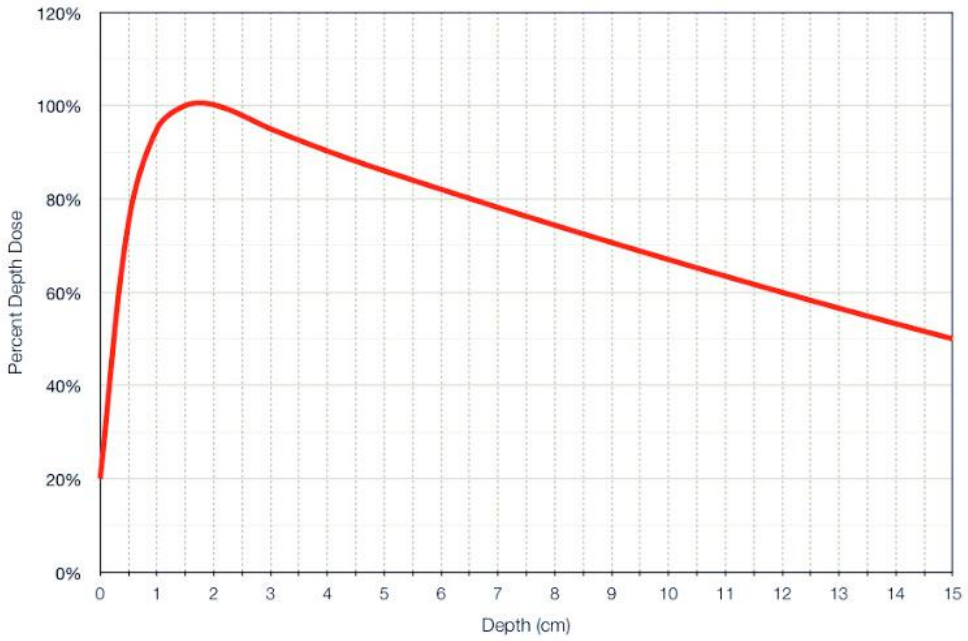


Figure – Dose distribution in function of the depth for X rays beams

**The quantity used for treatment planification is the energy imparted to the irradiated cells : the dose.**

**Treatment planification**

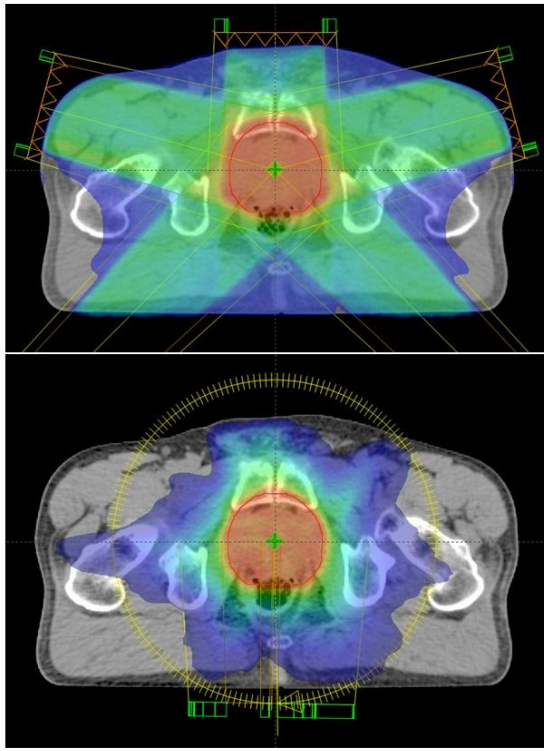

Figure – Example of treatment optimization for prostate cancer

**The beams are arranged as several irradiation fields with different angles in order to reduce the dose imparted to healthy tissues**

# Hadrontherapy

Radiation therapy technique using heavy ions to kill tumoral cells.

## Dose deposition in depth

**Spread out Bragg peak (SOBP)**

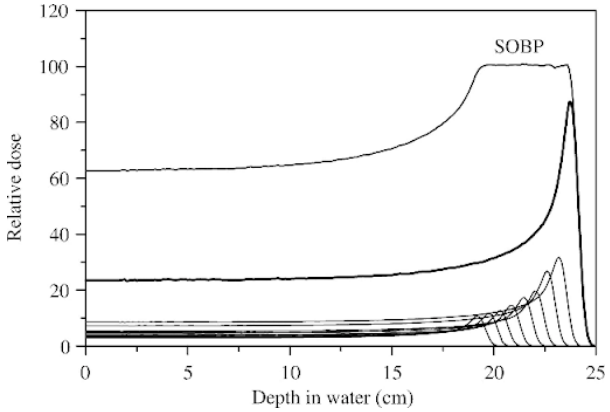


Figure – Dose distribution in function of the depth for a SOBP

**The dose deposition profiles are inverted. Pristine Bragg peaks are stacked into a SOBP. The biological consequences must be taken into account.**

## Biological dose in Hadrontherapy

**RBE x Physical Dose = Biological dose**

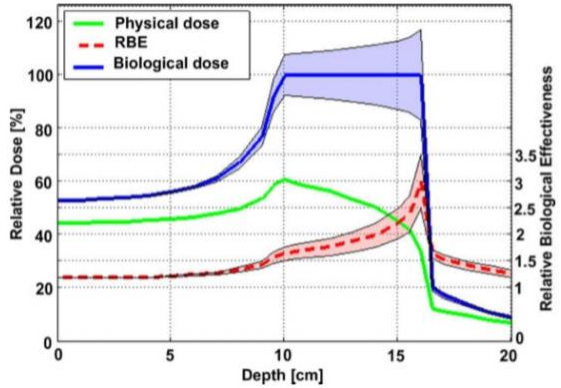


Figure – Physical dose, biological dose and RBE in function of the depth

$$RBE = \frac{D_X}{D_R}$$

**$D_X$ is a reference absorbed dose of radiation of a standard type X**
**$D_R$ is the absorbed dose of radiation of type R that causes the same amount of biological damage**

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# Multiscale approach in Hadrontherapy

**Micrometric and nanometric scale**

**MMKM and NanOx**

Kase et al. (2008) Cunha et al. (2017)

**Biological data**

Reference α, β values, cell nucleus and radius of the sensitive volume

**Physical data**

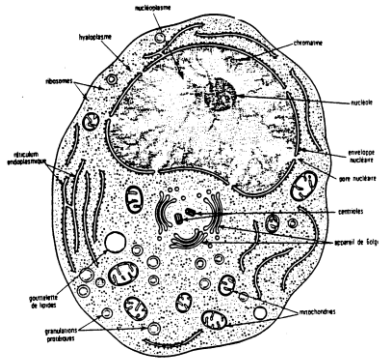
Specific energy deposited in the cell sensitive volume on a micro and nanometric scale

**Chemical data**

Yield of OH· radiolytic species in the sensitive volume

**Cell scale**

**Cell survival fraction**



**The cell survival fraction depicts the relationship between the fraction of cells surviving and the absorbed dose of radiation.**

**Patient scale**

**Treatment planification**

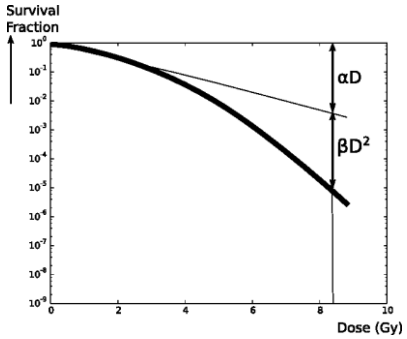
**An appropriate treatment optimization based on patient images imported in a TPS must be provided.**

# Kanai approximation

**The pre calculated α and β tables will be used with the Kanai approximation.**

## CELL SURVIVAL FRACTION DATABASES

**Survival Fraction= $e^{-(\alpha D+\beta D^2)}$**




**α, β: coefficients of the linear-quadratic model**

**For each type i of particle we estimate $\alpha_i$ and $\beta_i$**

## CALCULATION OF α MIX AND β MIX

**For a SOBP**

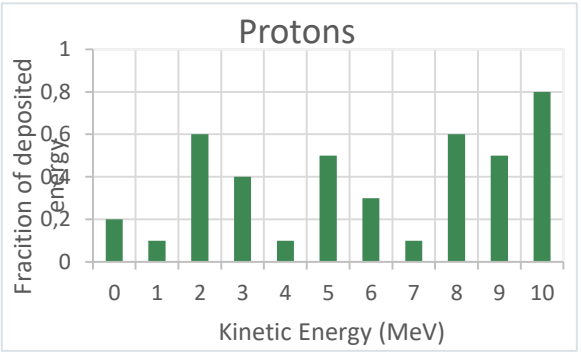
$$\alpha_{mix} = \sum f_i \alpha_i ;$$
$$\sqrt{\beta_{mix}} = \sum f_i \sqrt{\beta_i} ;$$

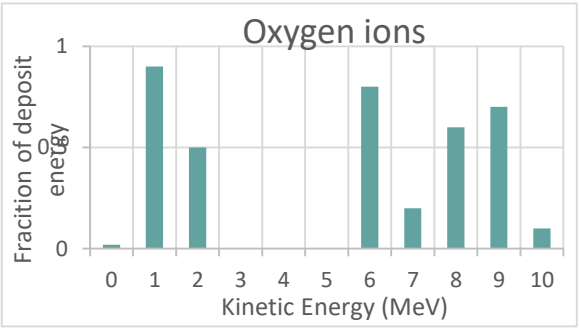
**(Kanai et al., 1997)**

**The α values are combined in a linear way while the square root β values are combined.**

## FRACTION OF DOSES

**The field contains primary ions and nuclear fragments of different kinetic energies.**




**We estimate the fractions of dose $f_k$.**

# Alpha beta tables

## Biophysics models predictions database

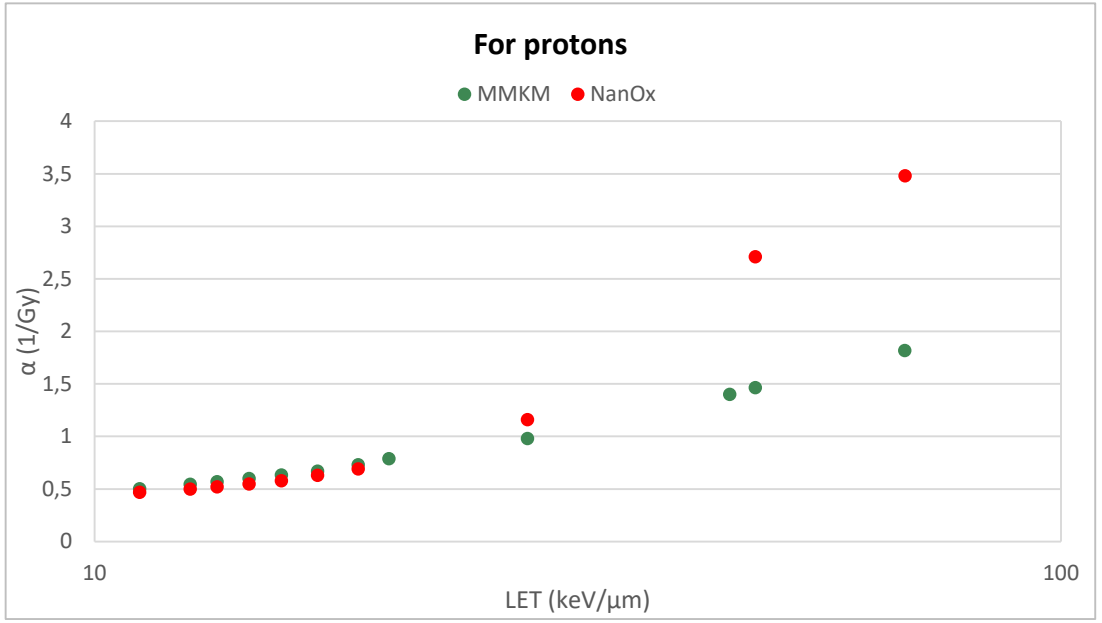
```
helium,2;0;0.646;0.00618733;
helium,2:2;1.01;0.00743869;
helium,2:6;1.268;0.00997782;
```

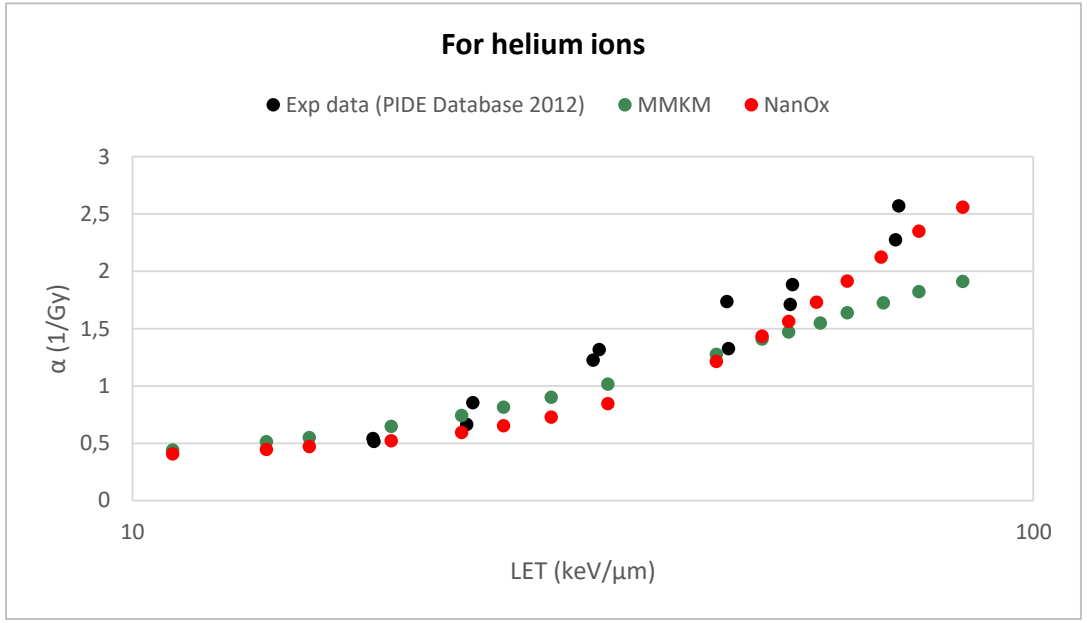
example : HSG data table

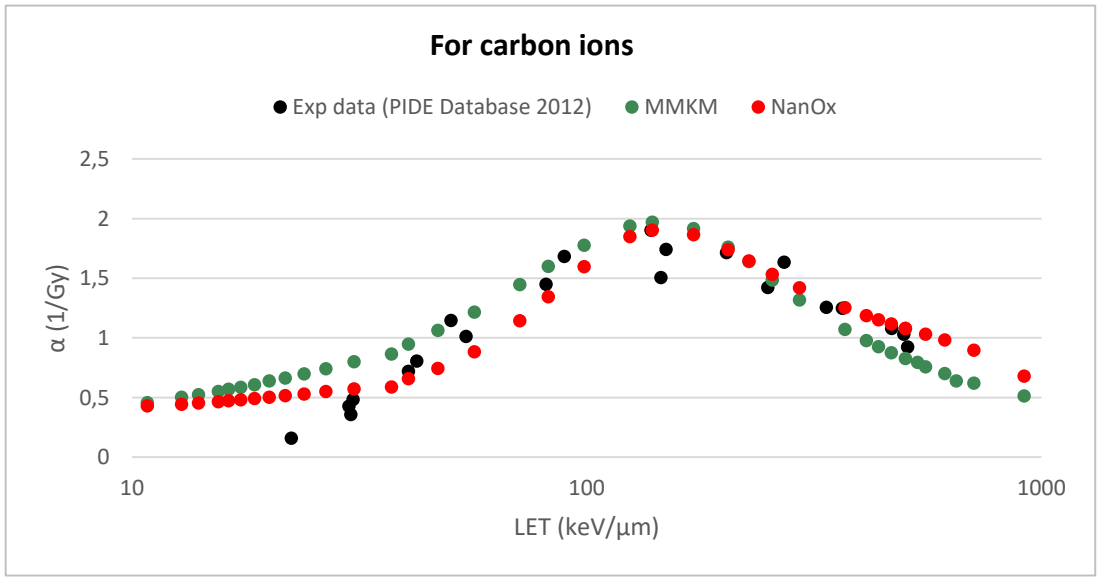
- The name of the ion
- The charge of the ion
- The kinetic energy
- The α value
- The β value

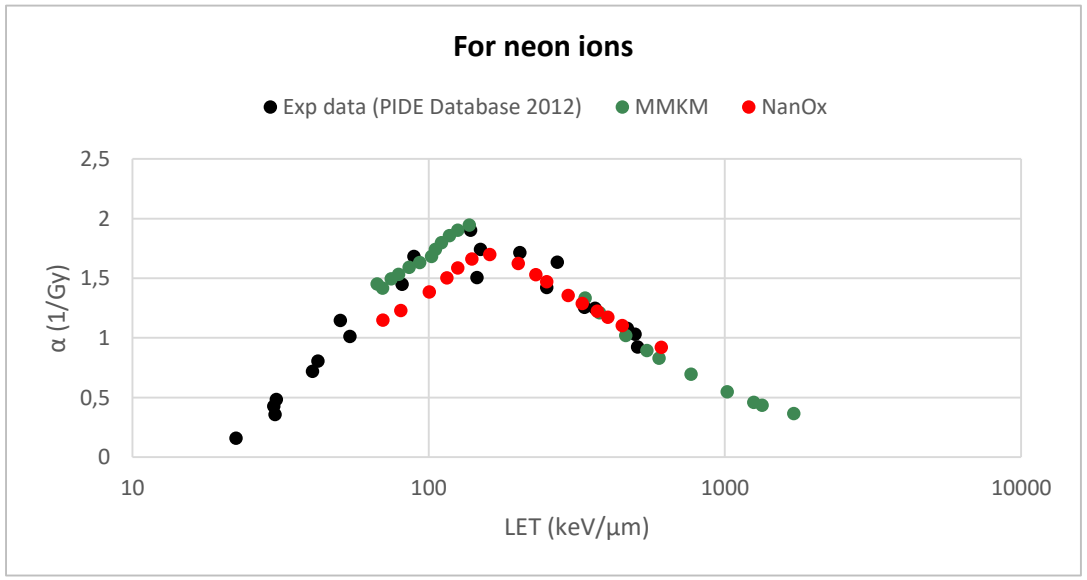
| IONS | HSG | CHO-K1 | V79 | SQ20B |
|---|---|---|---|---|
| PROTON ( 0 to 400MeV ) | ✓ | ✓ | ✓ | ✓ |
| HELIUM ( 0 to 400MeV/n ) | ✓ | ✓ | ✓ | ✓ |
| CARBON ( 0 to 400MeV/n ) | ✓ | ✓ | ✓ | |
| OXYGEN ( 0 to 400MeV/n ) | ✓ | ✓ | ✓ | |
| NEON ( 0 to 100MeV/n ) | ✓ | ✓ | ✓ | |

# α values in function of the LET for HSG cells



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# GATE

**Geant4 platform**

Gate is a Geant4 platform that offers ease and accessibility to simulations using the monte carlo code.

**Medical applications**

Its use has been validated for various medical applications as well as hadronic processes simulation.

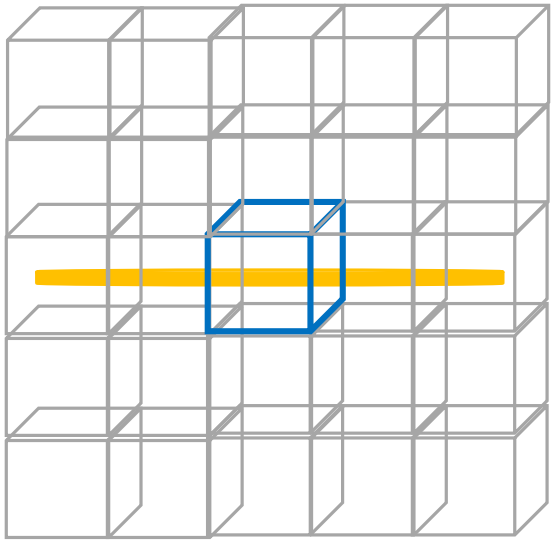
**Biodoseactor implementation**

We develop a tool in Gate named the Biodose Actor that will use the pre calculated predictions of the models to estimate the biological dose and RBE.

# BioDose Actor

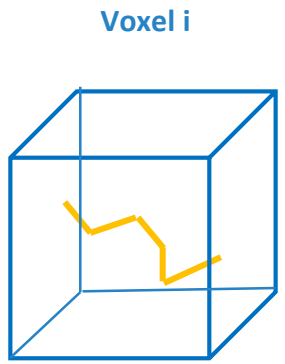
## The actor methodology

**VOXELIZED TARGET VOLUME**



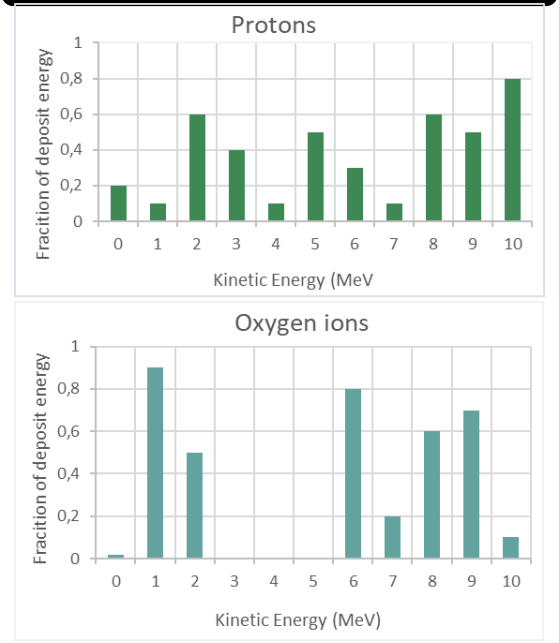
The resolution of the matrix, the size of the voxels, the position of the matrix are initialized via to the user's settings.

**ENERGY DEPOSITION**




Is retrieved from each step :
- The particle type
- The kinetic energy
- The energy deposition

**PER PARTICLE & PER KINETIC ENERGY**




An histogram of the cumulative deposited energy is created for each type of particle as a function of the kinetic energy.

**α and β MIX CALCULATION**

$$\alpha_{mix} = \sum_{k=1}^{N} f_k \alpha_k$$

$$\beta_{mix} = \sum_{k=1}^{N} f_k \sqrt{\beta_k}$$

We weight each α and β values with the deposit energy fraction according to obtain the α mix and β mix values.

# BioDose Actor

## Input parameters

```
/gate/actor/addActor                    BioDoseActor myBioDose
/gate/actor/myBioDose/attachTo          Phantom

/gate/actor/myBioDose/setSize           200 300 1000 mm

/gate/actor/myBioDose/setResolution     1 1 1000
```

The matrix volume

The matrix resolution or the voxel size

```
/gate/actor/myBioDose/setCellLine       HSG
/gate/actor/myBioDose/setModel          NanOx
```

We select the cell line and the biophysics model we want to use the pre calculated α and β tables.

```
/gate/actor/myBioDose/save              output/output.txt
```

The name and the format of the desired output
txt, root, mhd or py

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# Beam line modeling in Gate

We reproduce the geometry of clinical beams in order to simulate the energy deposition with a SOBP

**Beam line geometry**

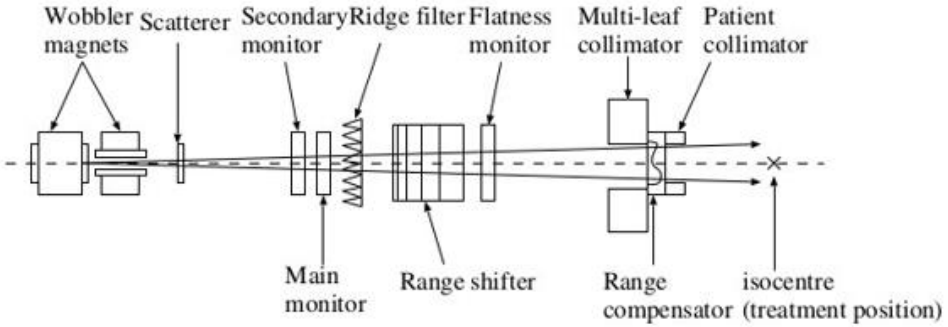



Figure - Geometry of HIMAC at the NIRS (Inaniwa et al. 2010)

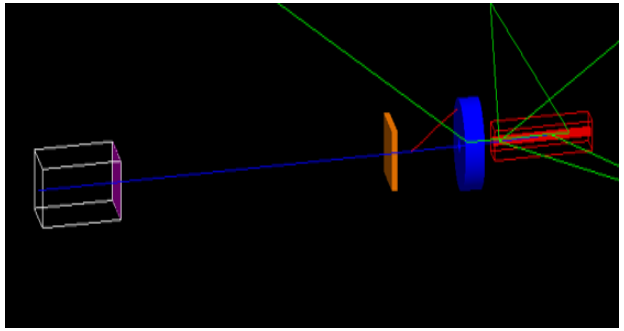


Figure - Geometry of HIMAC simulated in Gate

**SOBP simulation**

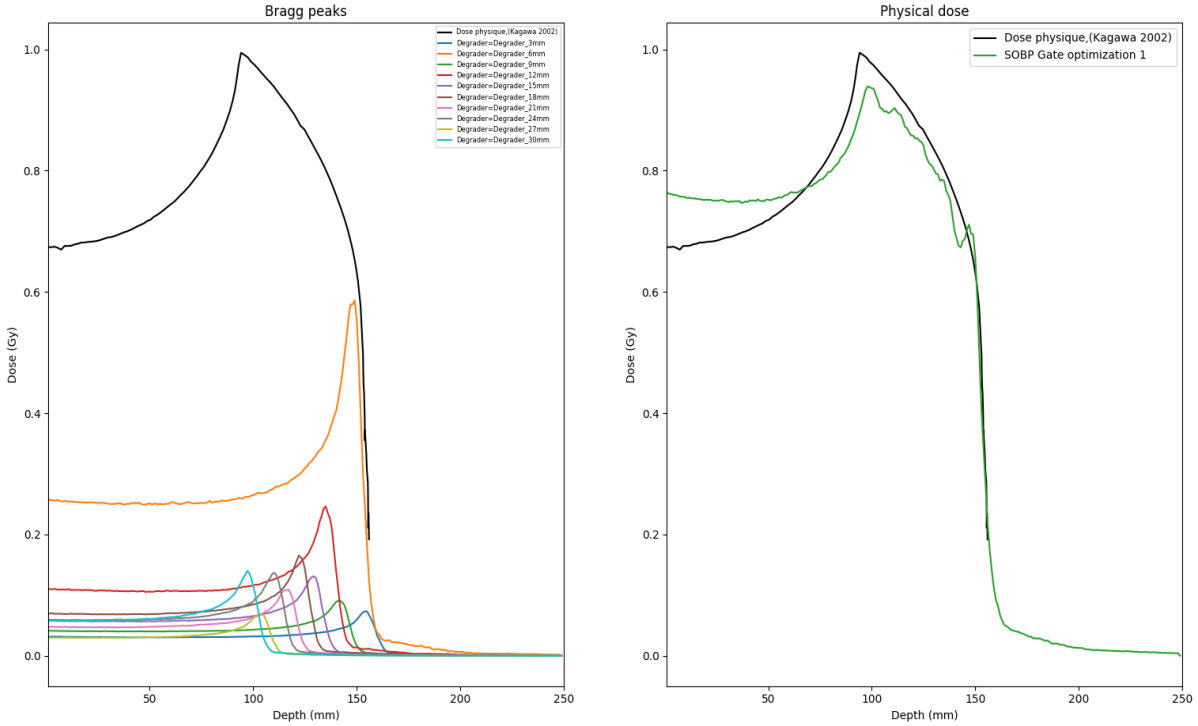
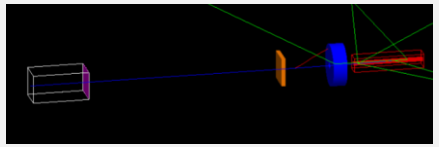


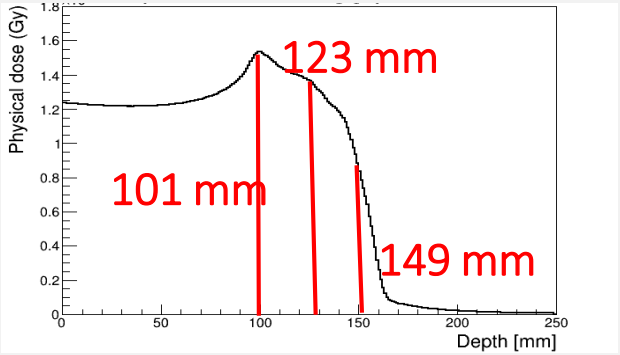

Figure – HIMAC dose deposition simulated with Gate

# HIMAC LINE
## Chiba, Japan

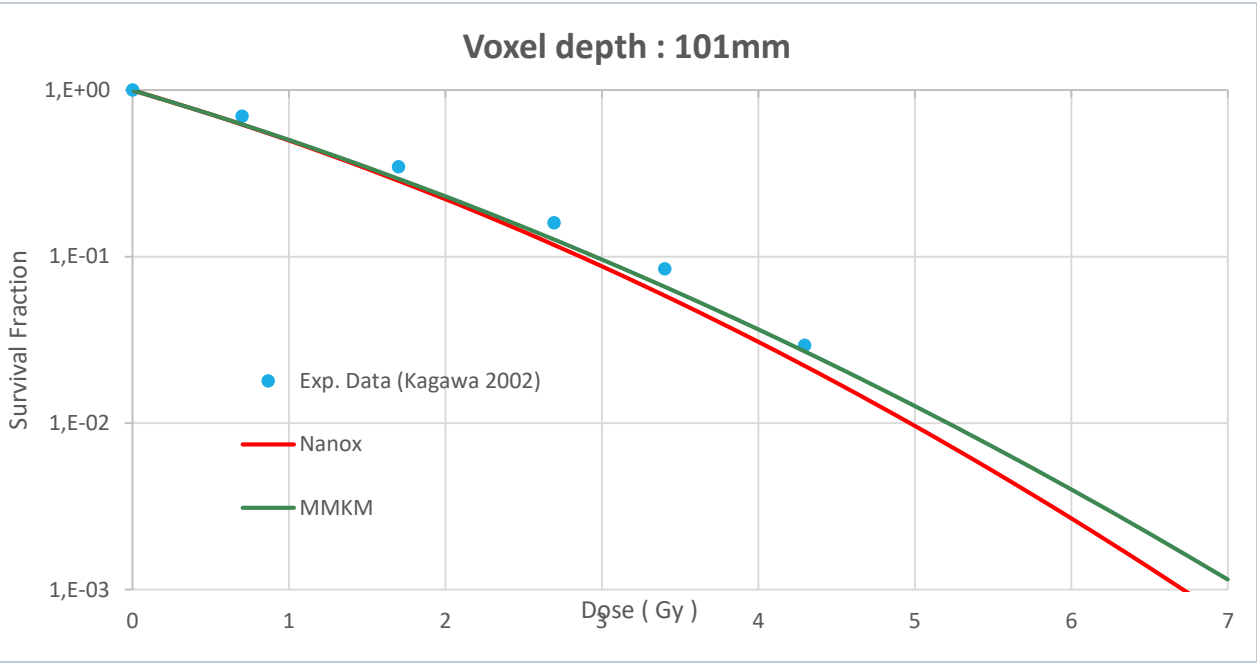
HSG cells irradiated at 3 positions of the SOBP, in 2002.

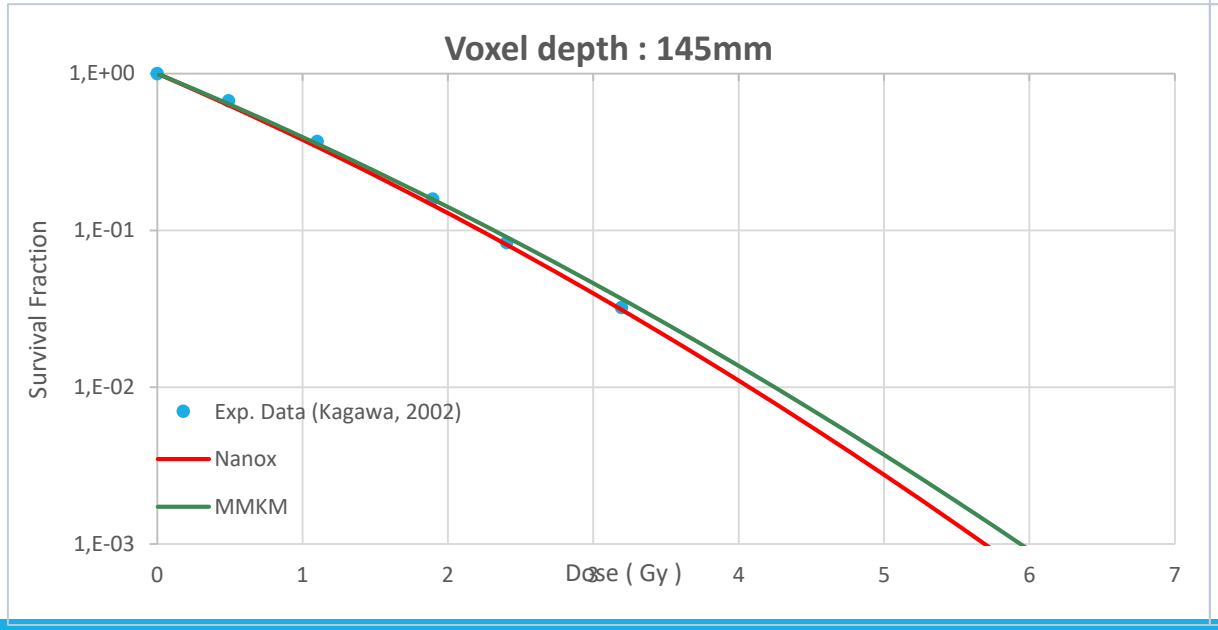


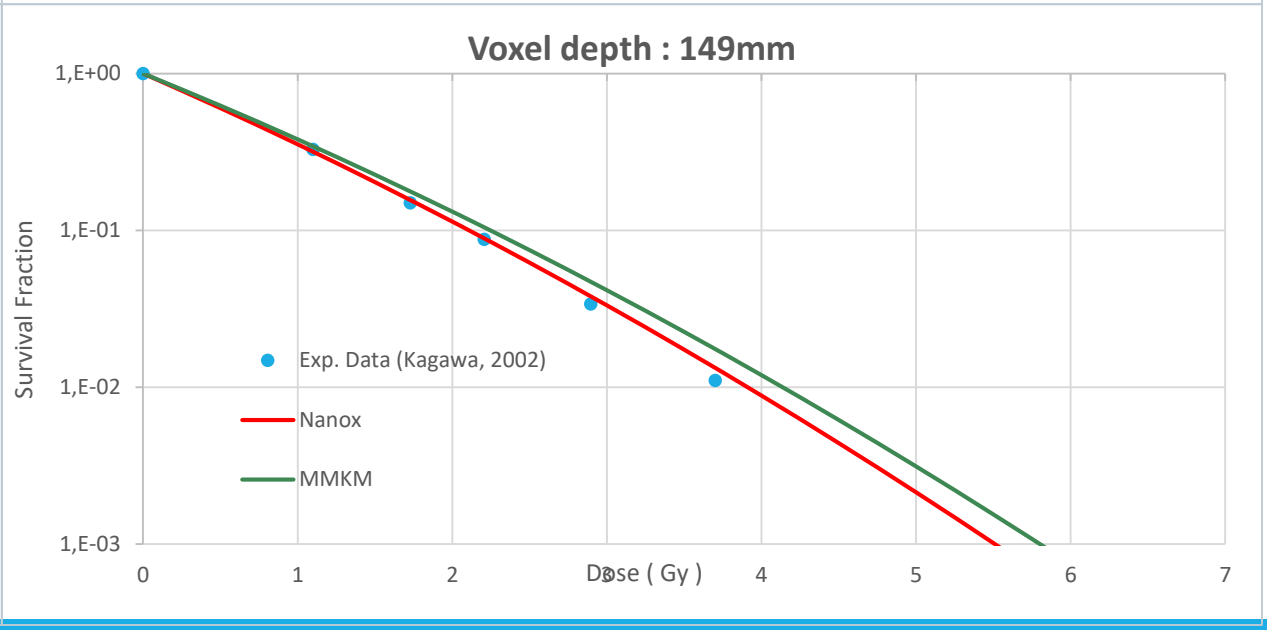
Carbon
Energy: 320 MeV/n




Kagawa et al. (2002)

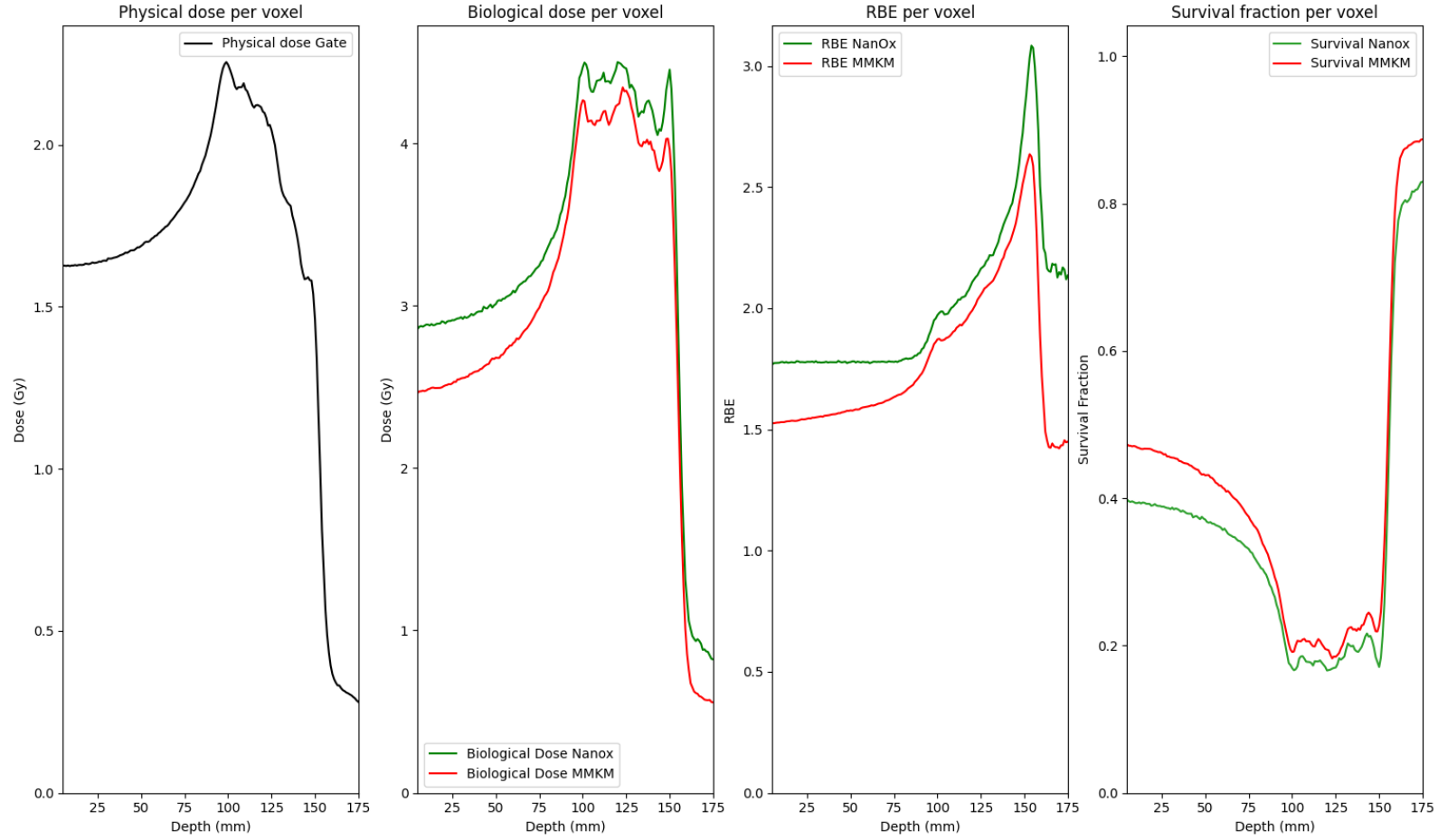


# HIMAC LINE
## Chiba, Japan

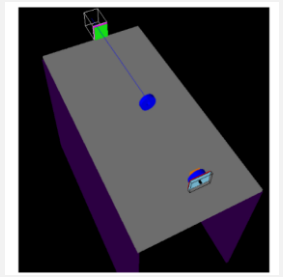
For each position of the voxelized volume, the actor delivers the physical dose, biological dose, RBE and survival fraction.



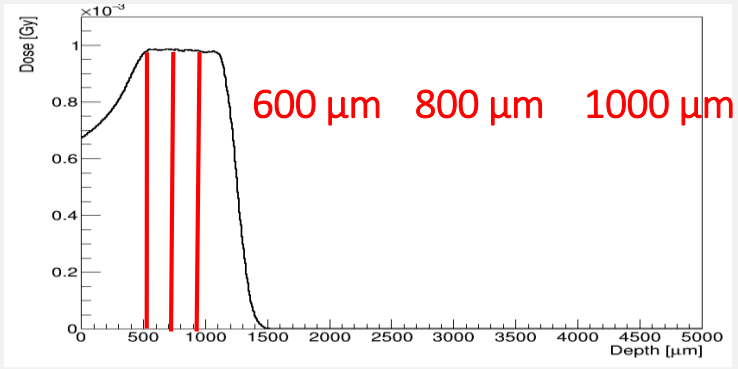
# ARRONAX BEAM LINE

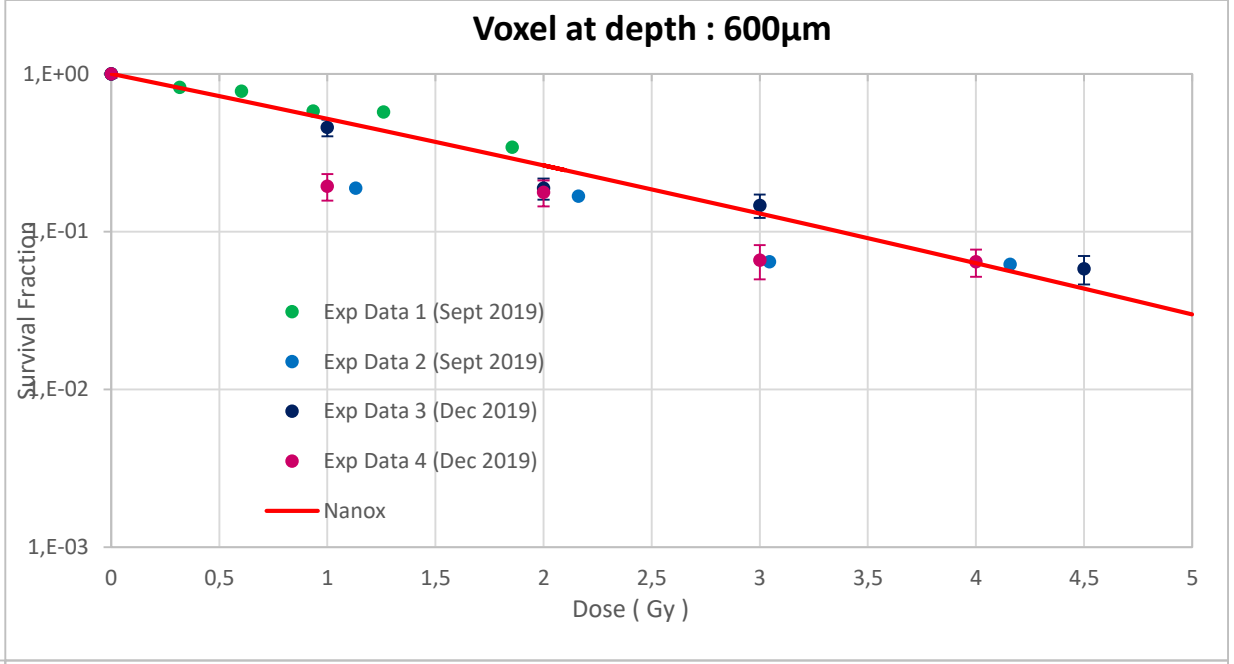
Nantes, France

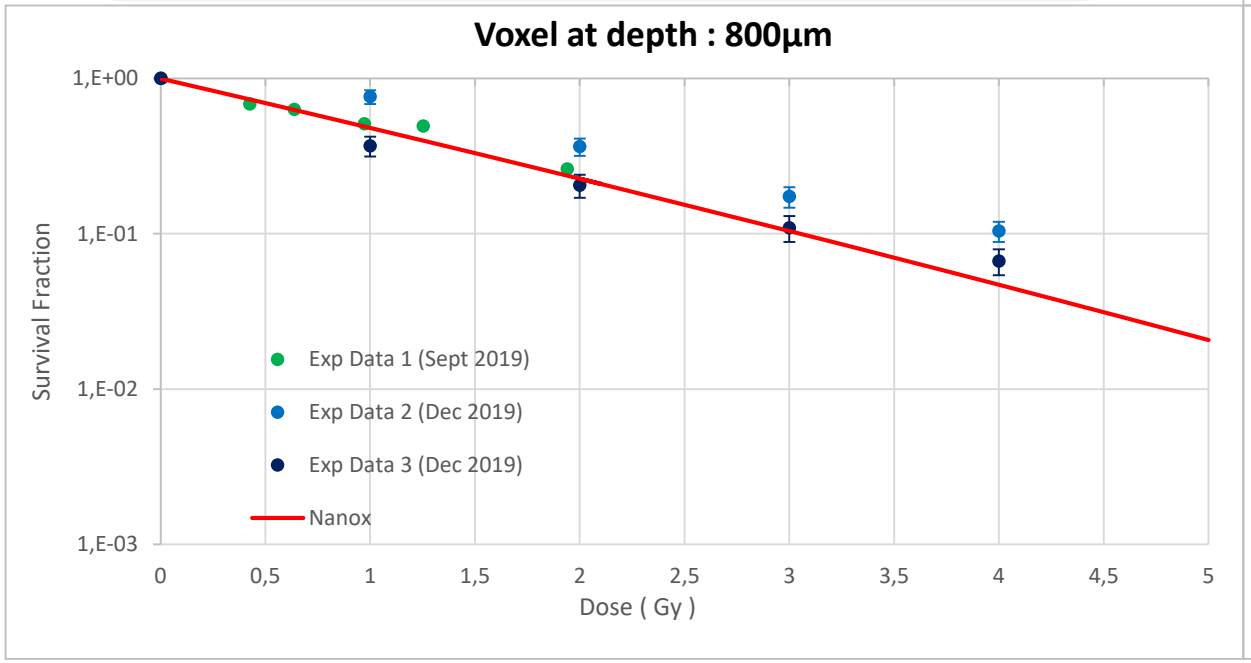
SQ20B cells irradiated at 3 positions of the SOBP, in September and December 2019.

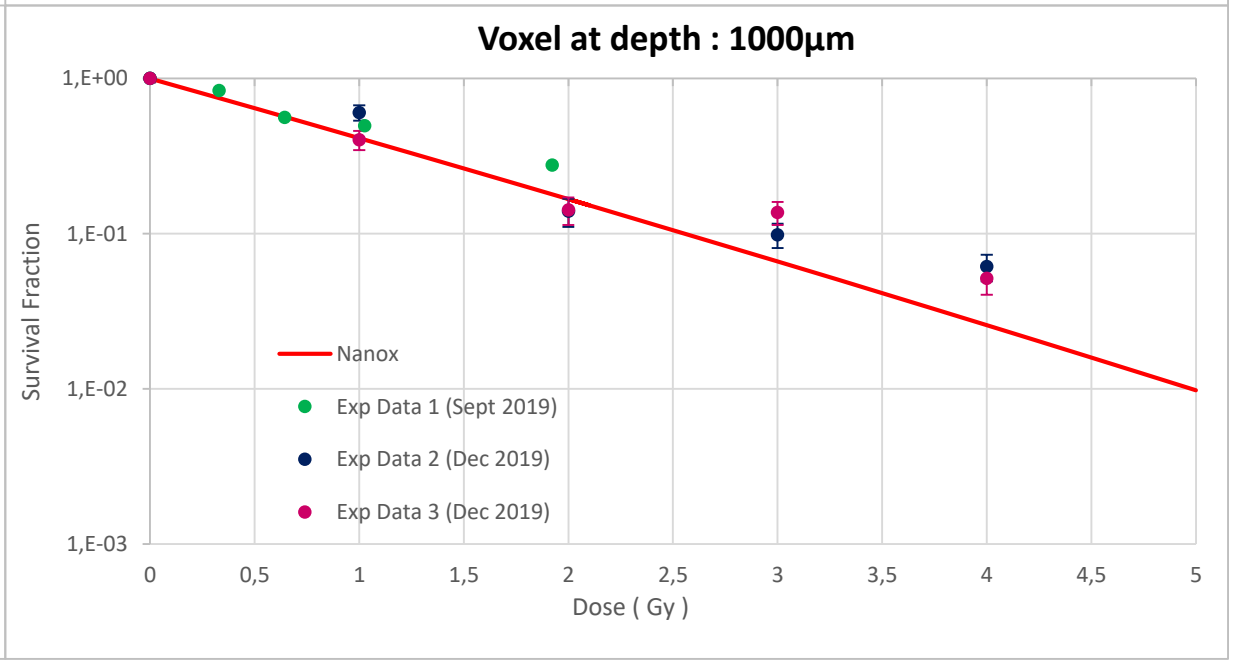


Helium
Energy: 67.4 MeV



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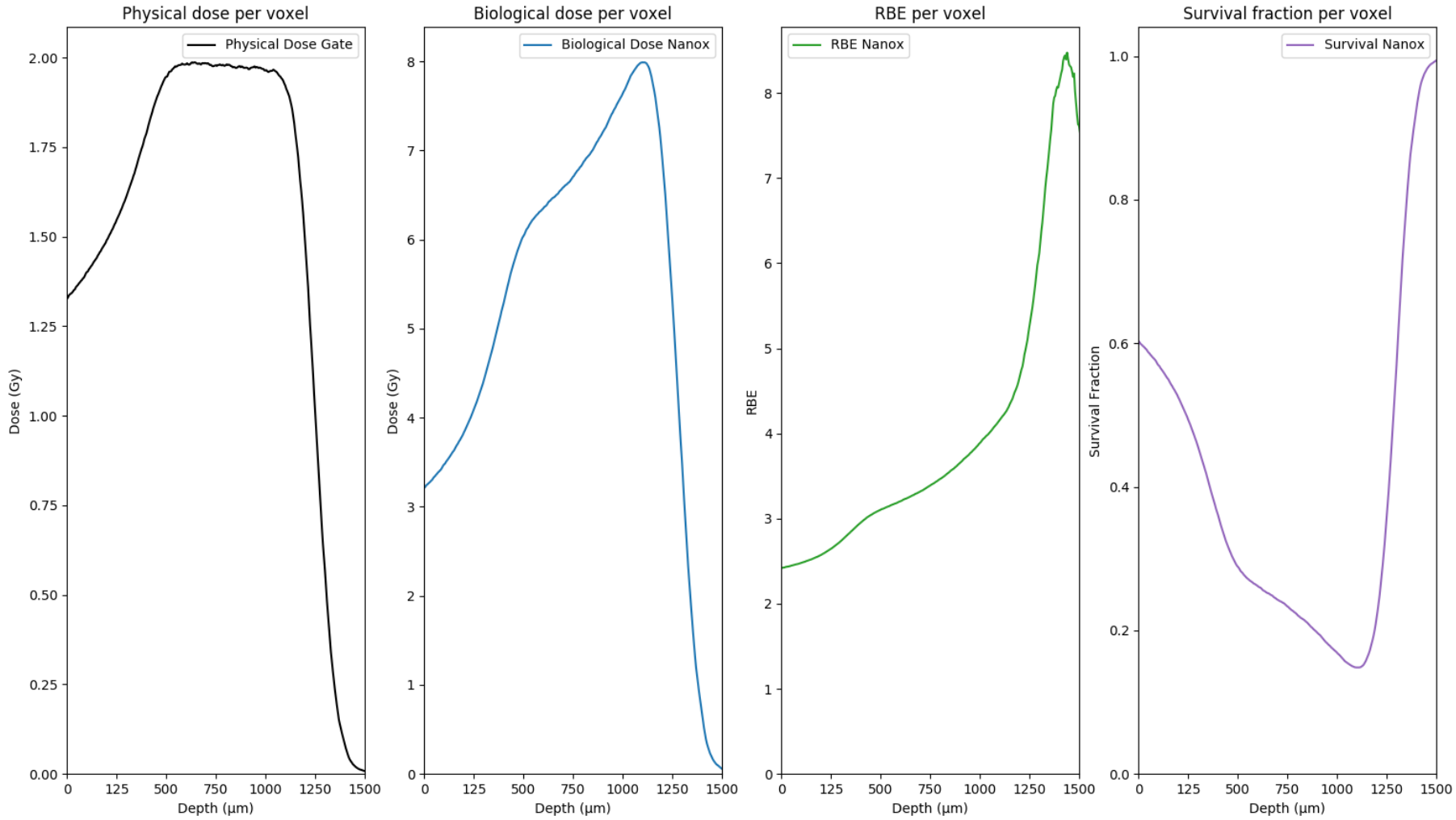

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# Conclusion and perspectives

## RESULTS

- Benchmark of the monte carlo codes G4-DNA and LPCHEM for biophysics input data
- Estimation of the cell survival coefficients with Nanox and MMKM
- Development of the first version of the Biodose actor
- First calculations of biological dose, RBE and cell survival fraction for the ARRONAX and HIMAC lines

## BIODOSE ACTOR DEVELOPMENT

### Clinical beam lines

**MediCyc, France**

**Proteus one, France**

### Biophysics models

More models to our database : LEM, LEM IV

### Cell lines

More experimental data and cell lines

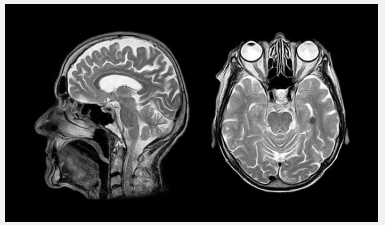
### Biodose actor optimization

An optimized version of the biodose actor

## CLINICAL PERSPECTIVES

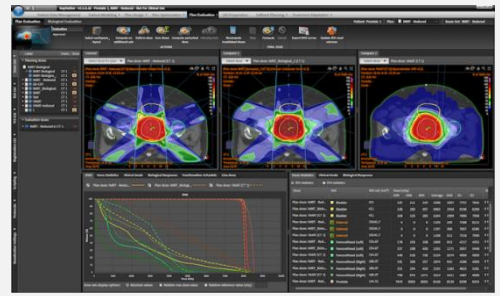
### Patient images

Patient images as input for the biodose actor



### Comparision with TPS

Benchmarking a TPS and the biodose actor for biological dose calculation



# Thank you.