Implementation and validation of a biological dose actor in GATE 10

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Biological dose

Objective of the biological dose

effects of the physical dose on biological tissues

$$D_B = RBE \times D_\varphi = \frac{-\alpha_{ref} + \sqrt{\overline{\alpha}\, D_\varphi + (\overline{\sqrt{\beta}}\, D_\varphi)^2}}{2\,\beta_{ref}}$$

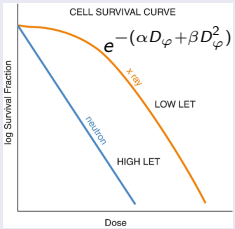
- D_B: biological dose
- D_φ: physical dose
- RBE: Relative Biological Effectiveness
- α_{ref}/β_{ref}: reference X-ray beam values (0.313/0.0615)
- $\overline{\alpha}/\overline{\sqrt{\beta}}$: mean $\alpha/\sqrt{\beta}$ values

Biological dose

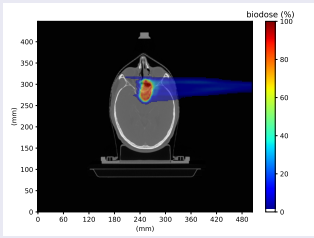
nano/micro scale

- mMKM
  (Kase et al., 2006)
- NanOx
  (Cunha et al., 2017)

cellular scale



macro scale



Biophysical model databases

Cell line Human Salivary Glands (HSG): `HSG_mMKM.db` or `HSG_NanOx.db`
$\Longrightarrow$ easy to provide new cell lines or biophysical models

Example:

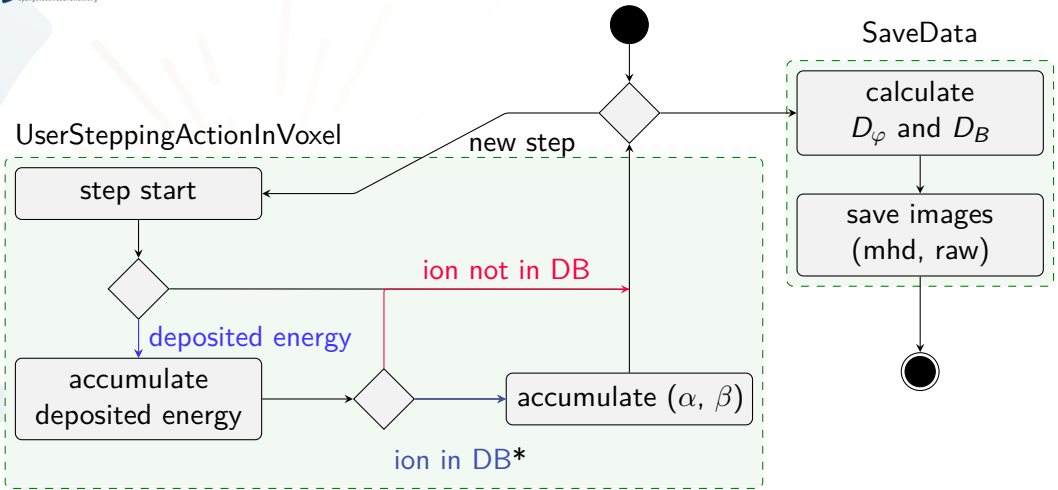
α, β: from Geant4-DNA/LPCHEM simulations

```
// Ion type

H
...
He
...
C
...
O
...
Li
...
```

// energy (MeV)	alpha (Gy^{-1})	beta (Gy^{-2})
H		
0.1	3.528	0.059
0.125	3.584	0.022
0.15	3.642	0.098
...		
1	0.932	0.059
...		
10	0.376	0.063
...		
300	0.339	0.109

BioDoseActor process diagram



* our database (DB) contains values for {H, He, C, O, Li}

User interface

GATE 9.4 (macros):

```
/gate/actor/addActor                    BioDoseActor Bio

/gate/actor/Bio/attachTo                volume
/gate/actor/Bio/setVoxelSize            1 60 60 mm
/gate/actor/Bio/setPosition             0 0 0

/gate/actor/Bio/setCellLine             HSG
/gate/actor/Bio/setBioPhysicalModel NanOx
/gate/actor/Bio/setAlphaRef             0.313
/gate/actor/Bio/setSqrtBetaRef          0.0615
/gate/actor/Bio/enableDose              true
/gate/actor/Bio/enableUncertainty       true
/gate/actor/Bio/save                    output/biodose.mhd
```

GATE 10 (Python):

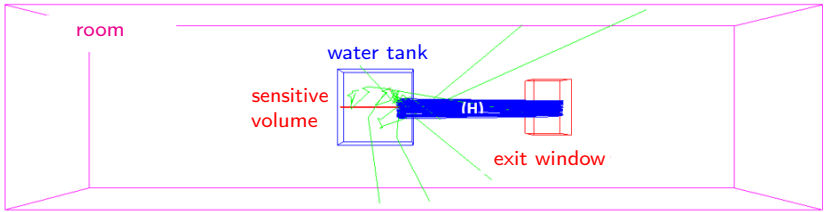
```
biodose = sim.add_actor("BioDoseActor", "biodose")

biodose.attached_to        = volume
biodose.spacing            = [1 * mm, 60 * mm, 60 * mm]
biodose.translation        = [0, 0, 0]
biodose.size               = [400, 1, 1]
biodose.cell_line          = "HSG"
biodose.biophysical_model  = "NanOx"
biodose.alpha_ref          = 0.313
biodose.sqrt_beta_ref      = 0.0615
biodose.dose               = True
biodose.uncertainty        = True
biodose.output             = "output/biodose.mhd"
```

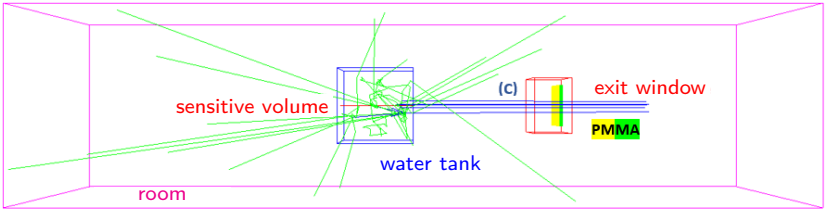
H/C-ion SOBP clinical PBS beams in water

- Human Salivary Glands
- Pencil Beam Scanning:
  - H: 95.9 – 113 MeV
  - C: 120 – 402 MeV/u
- Water box: $400 \times 400 \times 400$ mm^3
- Sensitive volume: $400 \times 60 \times 60$ mm^3
- Voxel size: $1 \times 60 \times 60$ mm^3
- PhysicsList:
  - H: `QGSP_BIC_EMZ`
  - C: `Shielding_EMZ`
- multiple stepfunctions
- multiple steplimiters

H-ion:



C-ion:



Results – dose profiles

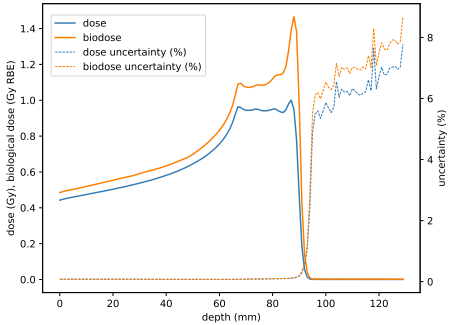


Figure: H-ion in water with 1×10^7 primaries, production cut 100 m, step limiter 10 µm (HSG, NanOx)

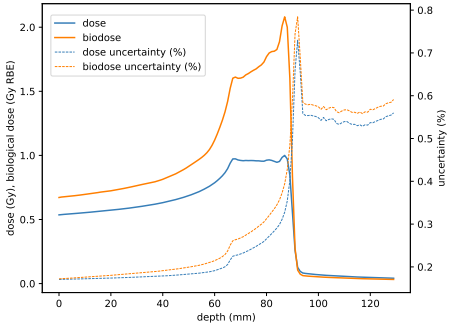
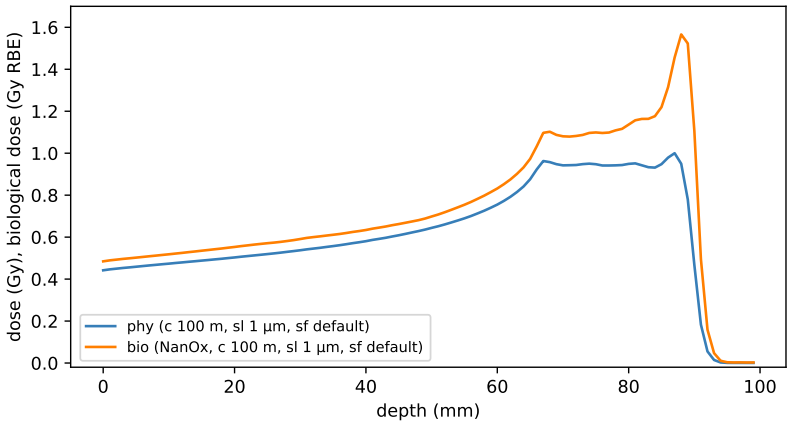


Figure: C-ion in water with 1×10^6 primaries, production cut 100 m, step limiter 10 µm (HSG, mMKM)

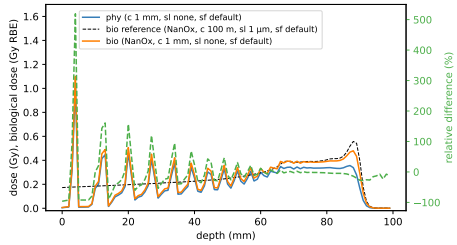
Tests on stepping parameters

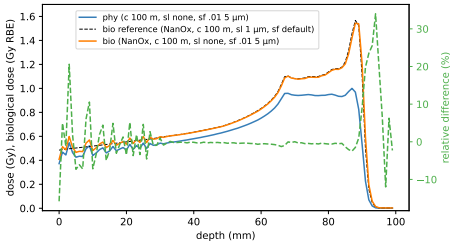
Parameter	**Value**				
Legend ID	**default**	**c 100 m sl 1 µm sf default**	**c 100 m sl 10 µm sf default**	**c 100 m sl 100 µm sf default**	**sf .01 1 µm**
Production Cut (e-, gamma, positron)	1 mm	100 m			
Step Limiter (proton, deuteron, triton, alpha, GenericIon)	-	1 µm	10 µm	100 µm	-
Step Function (proton, deuteron, triton, alpha, GenericIon)	default: $\alpha_R = 0.2$ $\rho_R = 1$ mm				$\alpha_R = 0.01$ $\rho_R = 1$ µm

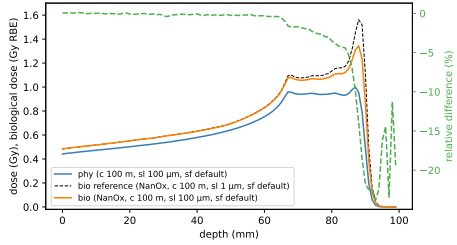
H-ion SOBP clinical beam (reference)

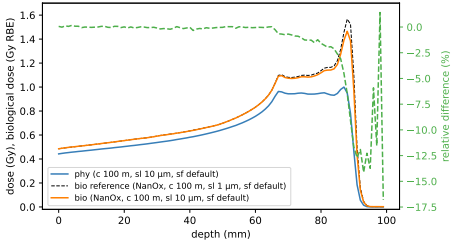


H-ion SOBP clinical beam (differences)

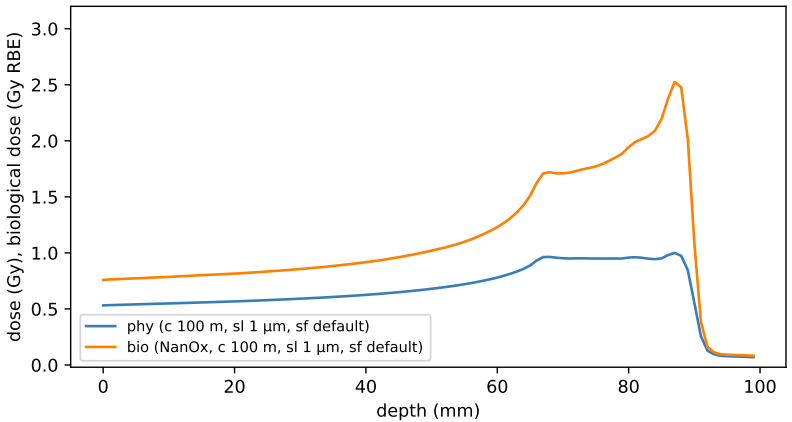




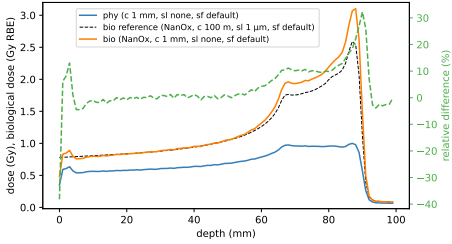


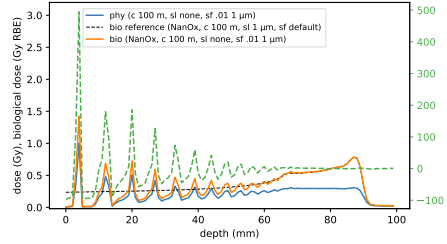


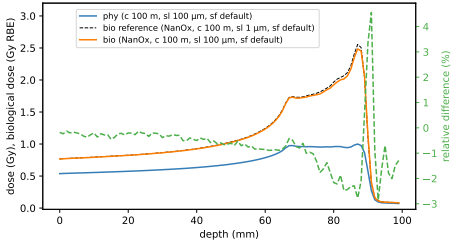
C-ion SOBP clinical beam (reference)

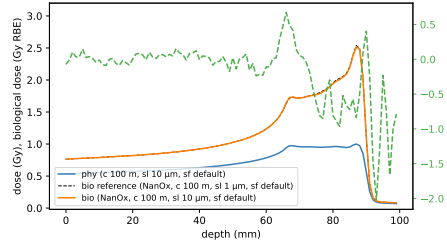


C-ion SOBP clinical beam (differences)









Runtime performances

CPU: 11th Gen Intel(R) Core i7-1165G7, 2.80 GHz
Simulation were run on a single thread

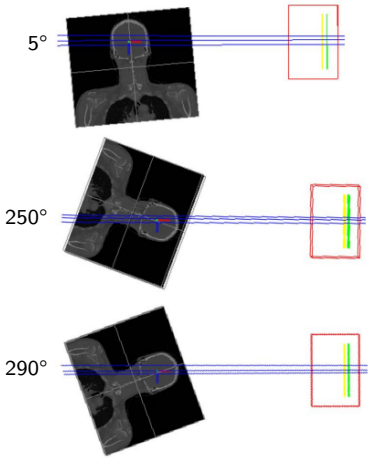
	default	**c 100 m sl 1 µm sf default**	**c 100 m sl 10 µm sf default**	**c 100 m sl 100 µm sf default**	**sf .01 5 µm**
H-ion NanOx, 1×10^6 particles	2.36 (×0.14)	0.33 (×1)	0.25 (×1.32)	0.247 (×1.34)	1.01 (×0.33)
C-ion mMKM, 1×10^5 particles	82.87 (×1.22)	100.80 (×1)	15.26 (×6.61)	6.93 (×14.55)	7.63 (×13.21)
C-ion NanOx, 1×10^5 particles	83.06 (×1.19)	99.16 (×1)	15.54 (×6.38)	6.75 (×14.69)	7.40 (×13.4)

Table: Mean simulation time per primary particule (ms)

C-ion clinical PBS beams in patient

MedAustron

- Human Salivary Glands
- Pencil Beam Scanning
- CT: $50 \times 50 \times 44$ cm^3
- Voxel size: $0.97 \times 0.97 \times 2$ mm^3
- PhysicsList: `Shielding_EMZ`
- 3 beams
- sinonasal chordoma



Results – C-ion, biological dose (NanOx)

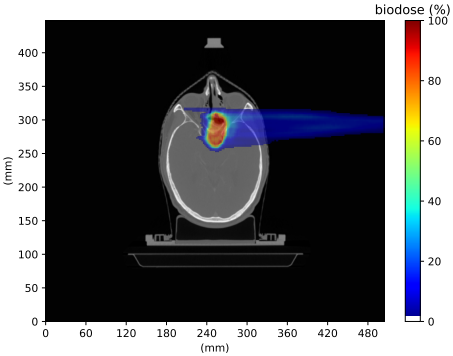


Figure: biological dose with C-ion in patient, 1×10^6 primaries per beam, production cut 100 m, step limiter 10 µm (HSG, NanOx)

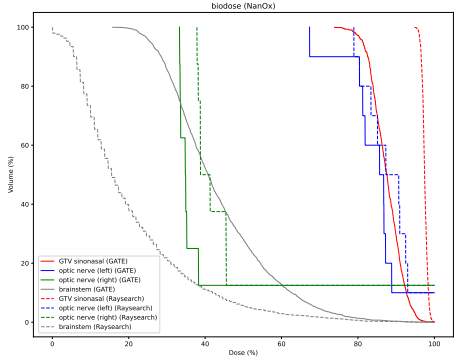


Figure: Cumulative biological DVH comparison GATE/NanOx (solid lines) and Raysearch (dashed lines)

Conclusion

BioDose actor

- validated in water and patient
- with statistical uncertainty
- execution speed similar to dose actor

Availability

- current GATE release (9.4)
- in future GATE 10 official release

to be published soon in Medical Physics journal