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Technical Note: GATE-RTion: a GATE/Geant4 release for clinical applications in scanned ion beam therapy

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1 **Technical Note:** GATE-RTion: a GATE/Geant4 release for clinical applications in Scanned Ion Beam Therapy.

2
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24
25 **Abstract:**

26 **Purpose:**

27 GATE-RTion is a validated version of GATE for clinical use in the field of Light Ion Beam Therapy. This
28 paper describes the GATE-RTion project and illustrates its potential through clinical applications developed
29 in three European centers delivering scanned proton and carbon ion treatments.

30 **Methods:**

31 GATE-RTion is a collaborative framework provided by the OpenGATE collaboration. It contains a validated
32 GATE release based on a specific Geant4 version, a set of tools to integrate GATE into a clinical environment
33 and a network for clinical users.

34 **Results:**

35 Three applications are presented: Proton radiography applications at the Centre Antoine Lacassagne (Nice,
36 France); Independent dose calculation for proton therapy at the Christie NHS Foundation Trust (Manchester,
37 UK); Independent dose calculation system for protons and carbon ions at the MedAustron Ion Therapy center
38 (Wiener Neustadt, Austria).

39 **Conclusions:**

40 GATE-RTion builds the bridge between researchers and clinical users from the OpenGATE collaboration in the
41 field of Light Ion Beam Therapy. The applications presented in three European facilities using three completely
42 different machines (three different vendors, cyclotron and synchrotron-based systems, protons and carbon ions)
43 demonstrate the relevance and versatility of this project.

44
45 **1. Introduction**

46 The OpenGATE collaboration has been created in 2002 with the initial purpose to provide a Geant4-based Monte
47 Carlo (MC) research toolkit for PET and SPECT simulations¹. In the very first paper¹, the extension of GATE for
48 dosimetry application was discussed, together with the potential of GATE to simulate in-line tomography in
49 hadrontherapy. A few years later, the GATE toolkit was indeed extended to CT and radiotherapy modeling^{2,3}. The
50 developments provided new features, such as the modeling of moving sources and motion, thus allowing for IMRT
51 and arc therapy applications. A carbon ion therapy application combining radiation therapy modeling and emission
52 tomography was presented as a proof of concept of the combined imaging and dosimetric, time-resolved,
53 capabilities of the GATE platform^{2,4}. In this paper, the terminology Light Ion Beam Therapy (LIBT) is used⁵. Light
54 ions are defined as those nuclei with an atomic number lower or equal to 10, i.e. including all ions from protons to
55 neons⁶. The terminology Scanned Ion Beam Delivery (SIBD, often called pencil beam scanning)⁷ is used in
56 contrast with passive beam delivery techniques⁶. More detailed PET-based dose delivery verification for LIBT
57 were presented elsewhere^{8,9}. The overall capabilities of GATE for radiation therapy and dosimetry applications
58 were reviewed¹⁰. In parallel of the GATE developments, the Geant4 MC toolkit was extensively used for passive
59 scattering proton delivery system and TPS evaluation^{11,12} and the FLUKA MC code was proven to be a useful tool
60 for in-vivo beam delivery and range verification^{13,14}. These pioneer works demonstrated the usefulness of
61 integrating general purpose MC codes into LIBT clinics to support medical physics activities¹⁵. Several other

62 general purpose Monte Carlo codes are used in the field of medical physics and LIBT, such as MCNP¹⁶, Shield-
63 HIT¹⁷ and PHITS¹⁸. Due to the complexity of Geant4, several Geant4 applications have been developed over the
64 years to simplify the user interactions with Geant4, such as GATE¹⁰, GAMOS¹⁹, PTSim²⁰ and TOPAS²¹. To our
65 best knowledge, GATE is historically the first Geant4-based application developed for medical physics purposes
66 and it is currently the reference platform for imaging in nuclear medicine. In addition, following the clinical trend
67 towards SIBD systems, the first modeling of a commercial IBA dedicated nozzle for scanned proton beams was
68 also developed in GATE^{22,23} and used as Independent Dose Calculation (IDC) system for validating the XiO TPS
69 from Elekta (Stockholm, Sweden)²⁴. These results demonstrated the potential of the GATE platform and generated
70 logically a lot of interest from other LIBT Facilities and TPS vendors. In particular, GATE was used to model
71 complex beam optics variations from the Skandion proton beam lines²⁵, to support the MedAustron facility start-
72 up and beam line design for proton and carbon ion beams²⁶⁻²⁸ and to evaluate the RayStation TPS proton pencil
73 beam algorithm (RaySearch Americas Inc. (NY))²⁹. In addition, extensive validation tests were performed at
74 MedAustron for scanned proton beams³⁰⁻³² and carbon ion beams (not yet published). Off-line PET-based
75 treatment monitoring was also considered³³. With the increased interest of GATE for clinical purposes, a GATE
76 satellite workshop was organized in March 2017 by David Sarrut, David Boersma and Loïc Grevillot at the
77 Skandion proton therapy center during the Swedish DOTSKAN meeting. The purpose was to define actions to
78 ease the implementation of GATE in clinical centers. The GATE-RTion project has been developed specifically
79 for this reason. It is a project of the OpenGATE collaboration aiming at building the bridge between researchers
80 and clinical users. The GATE-RTion project has been officially approved by the OpenGATE collaboration in May
81 2017 and presented at the first ESTRO physics for health workshop in November 2017 (Glasgow, UK). GATE is
82 free, open-source and benefits of a collaborative development model. Indeed, users do not need C++ to run
83 simulations as GATE can be fully configured and controlled via simple macros. However, experienced users can
84 access the code and, therefore, participate in the development of GATE. In the following sections, the GATE-
85 RTion concept is presented together with some validation tests. The result section focuses on clinical applications
86 performed in three different European LIBT facilities.

87 88 2. Materials and Methods

89 a. The GATE-RTion concept

90 The GATE releases follow every new Geant4 release in order to stay compatible with the latest Geant4 versions
91 and to provide additional features specific to GATE. In contrast, the implementation of a general-purpose MC
92 code in clinical centers requires extensive validation before clinical use, which is not compatible with an annual
93 release cycle. To support the implementation of GATE in clinical centers, three key milestones have been
94 identified: 1) Providing a stable and “long-term” GATE release (See Discussion section 4 for more details), called
95 GATE-RTion, having all necessary features for dosimetric applications in LIBT facilities equipped with SIBD
96 systems. 2) Providing a collection of tools to the clinical users for integrating GATE into the clinics. 3) Developing
97 a clinical user network and establish guidelines. GATE-RTionV1.0* based on GATE version 8.1 and
98 Geant4.10.03p03 was released in May 2018. A collection of open source python tools is available in the *GateTools*
99 repository released since December 2019 and contains in particular the functionalities related to beam modeling,
100 DICOM (image, structure, plan, dose, 3D gamma index computation) management and cluster management.
101 Meanwhile, several clinical centers started collaborating on the use of GATE-RTion, thus fostering the
102 development of clinical applications and guidelines for the use of GATE-RTion in LIBT facilities.

103 104 b. GATE-RTion key features and validation tests

105 An overview of the GATE features are presented in references^{2,10}. The GATE-RTion clinical users share validation
106 tests under the GATE-RTion folder from the *GateContrib* repository. These validation tests focus on the key
107 features of GATE-RTion necessary for dosimetric applications in LIBT facilities equipped with SIBD systems.
108 Currently two validation tests are available. The first one focuses on the features of the source used for simulating
109 SIBD systems (*TPS Pencil Beam Source*). The second one focuses on the features allowing scoring energy and
110 dose distributions (*Dose Actor*[†]). From a medical physics view point, these validation tests can be considered as
111 acceptance testing. When performing these tests, the user verifies that GATE-RTion delivers scanned beams
112 according to the treatment plan, multiple gantry angles and particle types can be delivered according to the
113 prescription, the nozzle geometry can be explicitly simulated or not, the user can change the beam model and
114 source properties, the dose can be computed in voxelized geometries (such as CT) or non-voxelized phantoms. We
115 rely on Geant4 for the validation of physics processes (Geant4 Medical Physics Benchmarking group[‡] and
116 validation testing[§]). In addition, a list of GATE publications have been presented in Introduction to validate the
accuracy of the Geant4 proton physics based on independent data sets and medical physics commissioning data³⁰⁻

* <http://www.opengatecollaboration.org/GateRTion>

† In GATE terminology, an „Actor“ is a kind of scorer that will output simulation results.

‡ <https://twiki.cern.ch/twiki/bin/view/Geant4/G4MSBG>

§ https://geant4.web.cern.ch/publications_validations/testing_and_validation

32. Similar work will be performed with carbon ions (and other light ions) in the future. Once accepted at the user facility, the level of accuracy of GATE-RTion must be evaluated as part of the medical commissioning process for each user, as it will depend on user specific input parameters (e.g. the beam model, the CT calibration curves, physics models and settings used, etc.). The definition of tolerances and actions levels used for clinical application must be defined during the medical commissioning process of GATE-RTion for each facility. Of course, establishing GATE-RTion in several clinics will support the users in sharing experience and establishing commissioning guidelines.

c. Applications of GATE-RTion in clinical centers

Usually the first step of the clinical implementation consists in developing and validating a beam model, which is out of scope of this note. Instead, this technical note focuses on the clinical applications performed once the beam model is available. An overview of the three different LIBT centers and SIBD systems available is provided in Table 1.

Table 1: SIBD system properties

LIBT facility	Manufacturer	Machine type	Ion Species	SIBD technique ⁶	Gantry angles	Energy range
Centre Antoine Lacassagne (Nice, France)	IBA PT (Louvain-la-Neuve, Belgium)	Synchro-Cyclotron (S2C2) ^{34,35}	Protons	Discrete scanning	from 320° to 180°	70-230 MeV
Christie NHS Foundation Trust (Manchester, UK)	Varian (Palo Alto, California, US)	ProBeam (Cylcotron)	Protons	Discrete scanning	from 0° to 360°	70-245 MeV
MedAustron (Wiener Neustadt, Austria)	MedAustron	MAPTA ⁷ (Synchrotron)	Protons Carbon ions	Quasi-discrete scanning	0° and 90° 0° and 90°	60-250 MeV 120-400 MeV/n

The different centers agreed in using similar physics settings. Physics settings were selected using Geant4 recommendations for medical physics applications^{**}, personal communications with Geant4 developers and independent validation tests using GATE. For protons, the physics-builder QGSP_BIC (containing Binary Cascade for nuclear processes) is used³¹, while for carbon ions the SHIELDING physics-builder (containing the Quantum Molecular Dynamics model for nuclear processes) is used^{36,37}. For both particle types, the electromagnetic option EMZ (also called electromagnetic option 4, which is the most accurate) is selected³⁰. For more details, the reader is referred to the Physics Reference Manual^{††} of Geant4. Additional parameters may be set, such as the maximum step size for ions, a range cut and a tracking cut for secondary electrons, positrons and photons, which are usually comprised between 0.1 and 1 mm (compromise between speed and accuracy)³⁸.

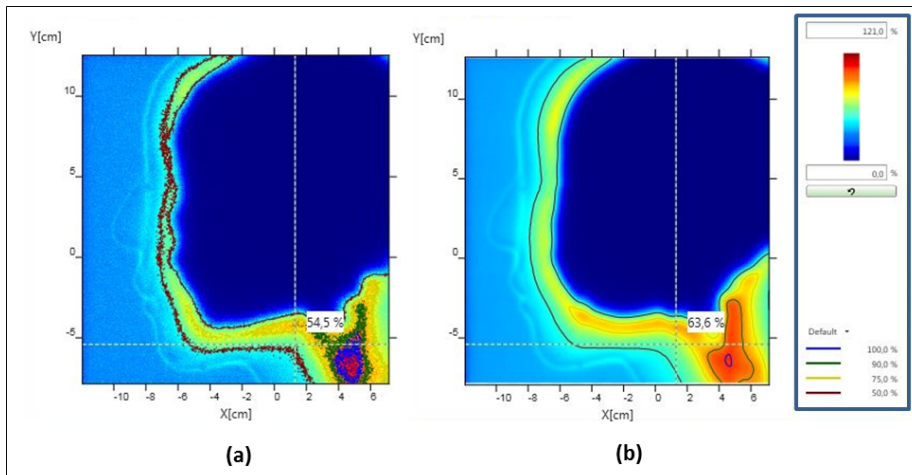
3. Results

i. Proton Radiography at Centre Antoine Lacassagne

The goal of the project consists in evaluating the potential of proton radiography images for patient positioning using GATE-RTion. An anthropomorphic human head phantom (PBU-50, Supertech, USA) was scanned in a CT. Treatment plans used to generate the proton radiography images of the anthropomorphic phantom were prepared with the RayStation 6.0 TPS, using beam ranges larger than the phantom largest dimensions and a Monte Carlo algorithm. Dose distributions were scored downstream the phantom in a plan perpendicular to the beam direction, resulting in 2D proton radiography images. Proton radiography images were then simulated using GATE-RTion at the same positions. In addition, proton radiography images were acquired using the Lynx 2D scintillator (IBA Dosimetry, Schwarzenbrück, Germany) having a spatial resolution of 0.5 mm. The images were all imported into the MyQA software (IBA Dosimetry, Schwarzenbrück, Germany) for comparisons. Isodoses contours were first compared qualitatively, and then γ -index analyses were performed. A good qualitative agreement was found for patient contours between Monte Carlo simulations and measurements (Figure 1). Using a γ -index analysis (2%, 2mm) between GATE-RTion simulations and TPS, more than 95% of the pixels are passing the test. This study demonstrates the feasibility of using GATE-RTion to predict proton radiography images.

** https://geant4.web.cern.ch/support/user_documentation

†† <http://geant4-userdoc.web.cern.ch/geant4-userdoc/UsersGuides/PhysicsReferenceManual/fo/PhysicsReferenceManual.pdf>



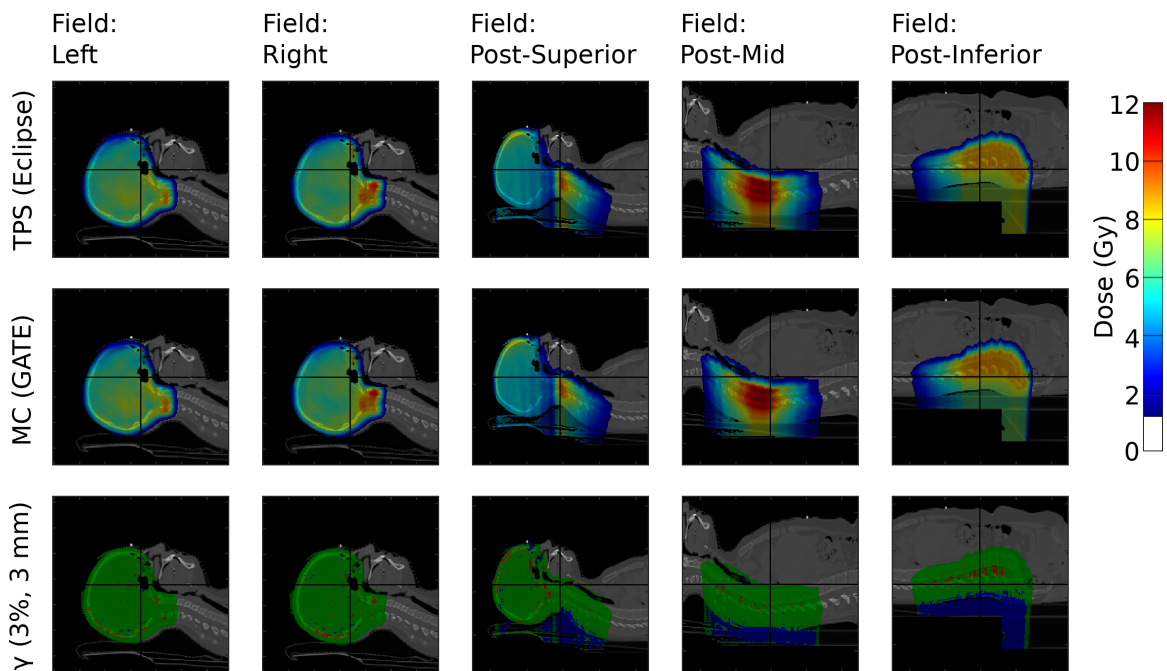
161

162 *Figure 1: Relative comparison of a GATE dose simulation (a) and a 2D Lynx measurement (b) acquired at the same downstream*
 163 *position for an anthropomorphic phantom.*

164

165 **ii. Independent Dose Calculation of proton beam therapy plans at The Christie**

166 Treatment planning is done using the Varian Eclipse (version 13.7) TPS, with Varian's proton-convolution-
 167 superposition (PCS version 13.7.16) analytical dose calculation algorithm. Prior to treatment, measurement-based
 168 Patient Specific Quality Assurance (PSQA) is performed on each plan. In addition, Independent Dose Calculation
 169 (IDC) using an in-house system called AutoMC and based on GATE-RTion is performed. AutoMC acts as a
 170 wrapper around GATE-RTion to fully automate IDC with the aim to ease the use and minimize the risk of user
 171 error when configuring simulations. It is implemented within an Octave³⁹ environment, and uses modular beam-
 172 models and CT calibrations. An example MC re-calculation in patient CT of the first phase of a 2-phase plan
 173 treating a craniospinal axis is presented in Figure 2. The prescription for this phase was 23.4 Gy in 13 fractions,
 174 delivered using 5 fields: a pair of left/right fields to the brain, and 3 fields to the spine (superior, mid and
 175 inferior). A 5 cm WET range-shifter was used for all 5 fields. The percentage of voxels in the patient having $\gamma \leq$
 176 1 was between 92.4% and 95.8% for all fields, and the GATE-RTion simulation was between 1.6% and 2.4%
 177 hotter than the TPS in terms of the median dose to the patient. Dose differences occurring outside the patient
 178 surface were excluded from the analyses.



179

180 *Figure 2: Comparison of TPS (Varian Eclipse) and MC (AutoMC / GATE-RTionV1.0) calculations of a 5-field craniospinal axis*
 181 *pencil beam scanning proton plan, planned at the Christie for delivery on a Varian ProBeam system. Top row: TPS; Middle*

182 row: GATE-RTion; Bottom row: Gamma at 3% (local), 3 mm using a 10% lower dose threshold. Voxels in green have $\gamma \leq 1$,
183 while voxels in (red/blue) have $\gamma > 1$ and are (hotter/colder) than the TPS respectively.

184
185 **iii. Independent Dose Calculation with Scanned Ion Beams at MedAustron**
186 Treatment planning is performed using the RayStation version 8B from RaySearch Laboratories (Stockholm,
187 Sweden). For protons, the Monte Carlo algorithm version 4.2 is used. For carbon ions, the pencil beam algorithm
188 version 3.0 and the Local Effect Model (LEM) I⁴⁰ for Relative Biological Effectiveness (RBE) modeling are used.
189 The measurement-based PSQA process was set-up since the beginning of clinical operation²⁸. It is performed in
190 water only and for a limited number of measurements points²⁸ (using the 3D-block/24 PinPoint ionization
191 chambers type 31015, PTW, Freiburg). In contrary, an IDC has the advantage to evaluate patient treatments in CT
192 geometry and for the entire 3D dose distribution. A key advantage of IDC-based PSQA is to reduce beam time
193 requirements for QA and thus increase the facility treatment capacity. The Independent DosE cAlculation for LIBT
194 (IDEAL) project, including GATE-RTion as dose engine, started in 2017, in a collaboration between the
195 MedAustron ion therapy center, the Medical University of Vienna (MUW) and the Austrian Center for Medical
196 Innovation and Technology (ACMIT). A first prototype has been developed in 2018 in a research network and
197 was transferred into the clinical environment of MedAustron in October 2019. TPS plans are exported to a QA
198 database and IDEAL is run on a cluster of modular capacity (currently featured with 48 cores). A carbon ion
199 treatment recomputed using the IDEAL prototype and including a comparison to the TPS dose distribution is
200 illustrated in Figure 3. This is a curative carbon ion treatment up to 65.6 Gy RBE in 16 fractions of 4.1 Gy RBE
201 (4 fractions per week). The PTV1 is treated with 9 fractions up to 36.9 Gy RBE, using 4 beams with a horizontal
202 beam line and table rotations of 315°, 355°, 320° and 360°.

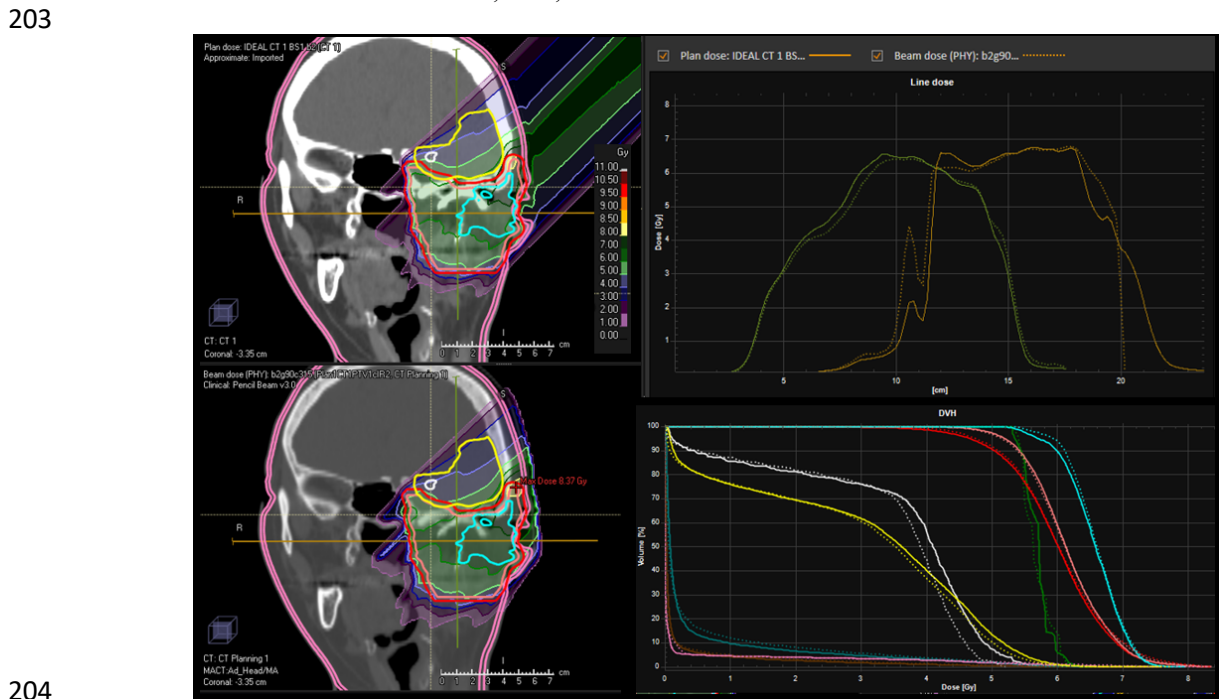


Figure 3: Comparison of the physical dose distribution for a carbon ion beam having an oblique incidence in the head region of a patient. IDEAL/GATE-RTion dose distribution (Top left) is compared to the TPS (bottom left) in terms of DVH (bottom right) and dose profiles (top right). For DVH and dose profiles, solid lines correspond to IDEAL/GATE-RTion and dotted lines to the TPS. The positions of the two orthogonal dose profiles in the patient are visible in the patient images on the left side (orange and green lines).

210
211 **4. Discussion**

212 The validated GATE-RTion release 1.0 allows clinical users to build confidence in a specific GATE/Geant4
213 version for clinical applications and share validation results. In parallel, GATE and Geant4 are evolving and may
214 provide new relevant features and improved physics models to the users in the future. For example, with respect
215 to the physics processes, uncertainties of nuclear cross-sections and models are known to be substantial, especially
216 for carbon ions⁴¹. This is where most improvements could be achieved in future. In addition, every new GATE
217 release provides new features which may be relevant for certain clinical applications, for example code
218 optimization allowing to perform simulations more efficiently or the scoring of new quantities of clinical interest.
219 Also deep learning methods started to be included during Monte Carlo simulations. In its current state, we believe
220 that the proposed GATE features and Geant4 physics models available in GATE-RTion V1.0 are sufficiently

221 accurate for most dosimetric applications in LIBT facilities. Every new GATE-RTion release will need to be
222 thoroughly re-validated and re-commissioned by each user before clinical use, which is a major effort. This can
223 only be justified by substantial improvements in the physics models or by the introduction of new features
224 clinically relevant to the users. The release cycle of GATE-RTion is therefore not planned and will depend on user
225 needs and request. However, bug fixes to GATE-RTion can be ported to the current GATE-RTion version via
226 patch mechanism. This presents the advantage of fixing software bugs (if needed), without modifying the
227 underlying Geant4 physics. GATE-RTion specific validation/acceptance could subsequently be re-run, in order to
228 validate that the patch did not affect the rest of GATE-RTion functionalities except fixing the bug. It is therefore
229 important to develop all necessary validation tests with the users, as described in section 2.b. The results provided
230 in Centre Antoine Lacassagne for proton radiography-based patient-positioning are preliminary but very
231 promising. A dedicated application wrapper would certainly help in future to integrate this innovative GATE-
232 RTion-based application into clinical environments. The IDC applications implemented at The Christie (AutoMC)
233 and MedAustron (IDEAL) are serving both the purpose of IDC, with a key difference that MedAustron extends
234 the application to carbon ions. The Christie is using GATE-RTion clinically since the start of the treatment end of
235 2018, while MedAustron is still in development and commissioning phase. The commissioning methodology and
236 dosimetric performances of GATE-RTion as implemented at The Christie and MedAustron facilities will be
237 published in order to provide reference commissioning reports to support the clinical community.
238
239

240 5. Conclusions

241 The GATE-RTion project paves the way towards the use of the GATE simulation tool in Light Ion Beam Therapy
242 facilities. GATE-RTion version 1.0 was released in May 2018 and the framework includes a validated GATE
243 release based on a specific Geant4 version, a set of tools to integrate GATE into a clinical environment and
244 a network for clinical users. Three completely different machines were modeled (three different vendors,
245 cyclotron and synchrotron-based systems, protons and carbon ions). Applications such as proton radiography and
246 Independent Dose Calculation (IDC) for scanned proton and carbon ion beam therapy were presented. This project
247 builds the bridge between clinical users and researchers using GATE, fostering the transfer of clinically relevant
248 research applications into the end-user's clinics. While applications at Centre Antoine Lacassagne and
249 MedAustron are still under development, The Christie is running GATE-RTion clinically for IDC since the start
250 of the clinical treatments end of 2018. The results presented within the first two years after the first release of
251 GATE-RTion demonstrate the versatility and relevance of this project.
252

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