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The OpenGATE ecosystem for Monte Carlo simulation in medical physics

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Abstract

This paper reviews the ecosystem of GATE, an open-source Monte Carlo toolkit for medical physics. Based on the shoulders of Geant4, the principal modules (geometry, physics, scorers) are described with brief descriptions of some key concepts (Volume, Actors, Digitizer). The main source code repositories are detailed together with the automated compilation and tests processes (Continuous Integration). We then described how the OpenGATE collaboration managed the collaborative development of about one hundred developers during almost 20 years. The impact of GATE on medical physics and cancer research is then summarized, and examples of a few key applications are given. Finally, future development perspectives are indicated.

1. Motivation and significance

Monte Carlo (MC) simulations are a group of computational methods that can be used for approximating real phenomena by sampling the known physical laws of nature encoded in a computer by models. MC simulations are an indispensable tool for performing virtual experiments involving ionizing irradiation and radiation transport phenomena. As such, these tools have been widely used for investigating radiation processes in medical imaging technologies and radiotherapy, assessing the efficiency and accuracy of imaging and treatment devices used in medicine. This is particularly true for the diagnosis and management of cancer where some of the most often used imaging (e.g. computer tomography (CT), single photon emission computer tomography (SPECT) and positron emission tomography (PET)) and therapy modalities (e.g. external beam radiation therapy (EBRT), Radiopharmaceutical therapy (RPT), trans-arterial radioembolization (TARE) and brachytherapy) use radiation for cancer characterization and management. In this paper, we describe the ecosystem and general structure of the GATE Monte Carlo toolkit (GEANT4 Application for Tomographic Emission) which was originally developed as a tool for simulating emission tomography applications, but was later expanded to simulate a large range of imaging and therapy approaches for cancer management. The GATE toolkit has been in the research landscape for almost 20 years [62].

This open-source software is designed to help researchers and engineers to perform a large range of Monte Carlo simulations in the medical physics field. Typical applications are generally split into two sub-domains: imaging and dosimetry. The first one includes simulation of radiation-based imaging systems such as: PET, SPECT, Compton Camera, CT, CBCT (Cone-Beam CT), etc. Such types of simulation represents a keystone to design or improve imaging systems, to optimize acquisition parameters, and to develop advanced image processing algorithms (reconstruction, segmentation, denoising, image corrections etc). The second domain refers to several types of radiation therapies such as external beam radiotherapy (including proton and carbon ion therapy). This also concerns absorbed dose assessment and energy deposition in imaging, such as CT or interventional radiology. Among numerous other applications, the most prominent examples contain beam characterization of various beam delivery systems or dosimetry studies.

Several review articles have already been published, accompanying the major evolution of the code. From a historical perspective, we can mention: the first publication on PET and SPECT developments in 2004 [62], the evolution towards radiation therapy in 2011 [63], some extensions to other dosimetry applications in 2014 [131] and, more recently in 2021, a specific topic for emission tomography imaging [132]. Even if the major novelties and applications have been already described, no description of the architecture and/or about the organization of the collaborative source code development have been published. Moreover, in addition to the core software, satellite projects have been conducted and are currently used by the community while having never been presented. The goal of this paper is thus to describe the GATE ecosystem and the technical organization of the whole project. In the conclusion, we describe the work in progress and the projects aiming to reshape the future of GATE.

2. GATE ecosystem

2.1. On the shoulders of Geant4

The underlying pillar of GATE is the Geant4 toolkit [1; 6; 7], developed at CERN about 25 years ago (first release in 1998). This open-source toolkit offers C++ classes and functions allowing users to build complex Monte Carlo simulations tracking particles through matter. A large number of experiments in high energy physics, astrophysics, space science, medical physics, and radiation protection are using Geant4, having more than 34k citations on google scholar.

GATE is a regular Geant4 application, written in C++, focused on the medical physics and radiation protection field, like other Geant4 applications such as (among others): Gamos [11], Topas [107] or PTSIM [14]. Consequently, the core Monte Carlo particle tracking engine, all physics databases and models are originating from Geant4. The main principle of GATE is to facilitate the modeling of complex medical physics simulations such that the end-user only needs to write simple text files containing high-level commands in a so-called “macro” language. Advanced users and GATE developers collaboratively contribute to the same C++ source code, which is open (see next section), providing brick classes and specific algorithms that are accessible through macros. Once installed, GATE provides one command line executable taking as input a file of macro commands describing the simulation to run. In addition to user-friendly access to Geant4 simulations, GATE also offers the user a large number of tools, to both speed-up simulations (variance reduction techniques, parallel execution with split and merge tools, source geometries and moving volumes, interface to medical imaging standards like DICOM, etc) and to facilitate the extraction of input data and exploitation of simulation results. In this regard, GATE provides built-in support of additional toolkits (ROOT, ITK-RTK, and PyTorch).

2.2. Regular releases

Because Geant4 regularly evolves, with about one major version per year (often in December), GATE follows the same pace. It has been decided to provide a new GATE version per year, compatible with the latest Geant4 release. Every GATE version is thus associated and tested with one single Geant4 version. In practice, however, an advanced user may compile GATE against some older versions of Geant4, although this is not officially supported. Latest versions of GATE are presented in table 1.

In addition to the source code, GATE can be installed from Virtual Machine system (the so-called vGATE) or with a Docker version that can easily be deployed for example on clusters.

Openness and users contributions.—The philosophy of GATE is that everyone can contribute to the source code, from simple typo corrections in the documentation up to the addition of new features. Indeed, when users want to propose additional code, they contact the collaboration. They can either directly propose their own code on the platform or discuss with the developers about its integration. In practice, all developers' contributions are managed via the GitHub PullRequest (PR) mechanism. Once the new source code is proposed, it is discussed and integrated in the main source code by maintainers. Thanks to the GitHub Actions mechanism, every time a modification is proposed in any part of the source code, the whole code is recompiled and tested on several architectures (Linux, MacOS), with different options. In principle, any new contribution should be proposed via PR with 1) source code, 2) documentation and 3) test case (or benchmark). Once a year, all changes are integrated into the new release.

2.3. The GATE ecosystem and open organisation

Through the years, the GATE ecosystem evolved a lot and is now - in 2022 - the following. All source files are stored in Git repositories, currently hosted on the GitHub platform, in one single organization named OpenGATE. The Git system is the cornerstone of the GATE software development as it allows to host the source code, to manage all user proposed modifications (enhancement or bug correction), as well as the documentation, benchmarks, software tests, example simulations, and related tools. Note that, even if everything is currently hosted on the GitHub platform, the intrinsic decentralized nature of Git would allow to easily move to alternative hosting systems. Four main repositories are included under OpenGATE organization name: the main source code is in `Gate`, the benchmarks are gathered in `GateBenchmarks, GateContrib` regroups some user contributions and `GateTools` propose additional convenient Python tools. They are detailed below.

`Gate` repository.—This repository contains all the C++ source files of the main executable. It is composed of approximately 600 classes, in 3200 files and 780,000 lines of code. The source code is divided into folders grouping classes of related functionalities. Figure 1 shows a description of the main classes in GATE. The main folders are:

- `geometry`. Contains classes related to volume definition, shape, material, position etc, including management of voxelized volumes;

- `physics`. Contains classes related to physics lists, cuts management and all types of particle sources (such as voxelized source or source dedicated to pencil beam scanning in hadrontherapy);
- `digits_hits`. Contains classes related to all scoring methods (see section 2.4), including all actors and management of digitization process of detectors (such as coincidence sorter for PET systems);
- `general`. Contains generic tools and classes used to manage a complete simulation;
- `externals`. Contains external open source code developed by other organizations, such as some ITK methods used to read and write image.

In this repository, several Git branches are used. The main ones are the following: 1) the `develop` branch containing the last work in progress version of the source code. 2) the branch `GateRTIon` containing the specific version for GATE-RTion (see section 2.6). Every released version has its own tag (v9.1, v9.0, etc.) making it easy to retrieve previous stable versions.

`GateBenchmarks` repository.—This repository contains a set of test cases. They are used to check and evaluate every new change in the source code. Every time a modification is proposed in the source code, the whole list of tests is executed and analyzed. Every test is composed of a (ideally simple and short) GATE simulation, described by macro files and is associated with a Python script comparing the simulation output with a reference output. If differences exceed a given test-specific threshold, a flag is raised requiring further investigation. There are currently more than 20 different benchmarks, each of them evaluating a specific feature, such as energy deposition or dose scoring in voxelized geometries or quantification of NECR (Noise Equivalent Count Rate) in PET systems.

`GateContrib` repository.—Examples of GATE simulations provided by users that can be used as reference or template, are provided in this repository. Note that these simulations are not evaluated and remain at the responsibility of the users to be tested. These simulations mainly serve as examples and show-how for the different applications of GATE.

`GateTools` repository.—This repository contains a companion project aiming at providing Python functions and command-line tools to help create or analyse outputs from GATE simulations. Provided functions deal with various tasks such as images' management (conversion from and to DICOM format, resampling, etc), DVH (Dose Volume Histogram), gamma index, phase-space analysis, etc. It heavily relies on the ITK toolkit‡.

2.4. Focus on three key concepts: Volumes, Actors, Digitizer

In this section, three key concepts of the GATE architecture are highlighted: "Volumes" the handling of the geometry, "Actors" that serve several scoring purposes, and the "Digitizer" specific for imaging systems.

‡ https://www.itk.org

Volumes.—In Geant4, all geometrical elements that compose a simulation are described with three concepts. `LogicalVolumes` represent the properties (e.g. material composition), `PhysicalVolumes` manage the spatial positioning, and `Solids` define the shape of a geometrical element. In GATE, the three concepts are encapsulated into a single `GateVolume` that abstracts those notions. The user only manipulates *Volumes* without the burden to manage the three different concepts. This allows to simplify the simulation description, but some advanced Geant4 capabilities are not available within GATE (e.g. "parallel world").

Actors.—The Actors are scorers that encapsulate several Geant4 concepts. They are used as a callback from the Geant4 engine to score information or modify the default behavior of particles during a simulation. An Actor combines the Geant4 `SensitiveDetector` and `Actions` callbacks within a single class that can perform tasks each time a Run, Event, Track or Step starts or ends in a given volume. Actors are mainly used to record parameters or information of interest calculated during the simulation, but they can also be used to act on the current particle, for example to stop tracking it. About 30 Actors are currently available. Among the most used are:

- the `GateDoseActor`: recording of the absorbed dose (or energy deposited) in a volume according to a 3D matrix whose dimensions are defined by the user. The Actor also records the uncertainty on the calculated dose value in each voxel;
- the `GatePhaseSpaceActor`: recording of the characteristics of the radiation (type of particles, energy, direction, creation process, etc.) passing through a volume;
- the `GateKillActor`: stop tracking a particle if it reaches the volume, in order to save computation time. It is the responsibility of the user to ensure that the physics is correct (it is always recommended to the users, to validate their results to justify the appropriate use of the Actors).

It is also possible to associate each Actor with one or more filters allowing to select a type of particle, an energy or even a specific direction. Figure 2 depicts the structure of the Scorers and Actors in GATE.

Digitizer.—The response of the photodetection components, for example in PET, SPECT or Compton Camera detectors modeling, is managed by a suite of analytical models that form a *Digitizer* (Figure 3). This module is based on Geant4 virtual methods dedicated for such functionality. It takes as input a list of interaction events, the *Hits* gathered in a *HitsCollection*, within a crystal or detector element (*Sensitive Detector*), and generates digital pulses, called *Digits*, with associated information (energy, position, time, etc) gathered in *DigiCollection*. In a digitization, a digit represents a detector output, such as an ADC/TDC count or a trigger signal. The first step of the Digitizer is to construct *Single* digits, each of them mimics one specific hardware response with their associated uncertainty. Currently, there are 37 signal processing modules available in GATE that can be enabled by users to represent hardware output (see examples in Figure 3 and in [62], [37]). In the case of PET imaging, a specific Digitizer part for constructing coincidences exists.

It passes, firstly, by a `CoincidenceSorter` where coincidence candidates are pre-selected. Then, they can be processed by one of the 5 dedicated *Coincidence Digitizer Modules*. A Digitizer chain may also be separated from the main Monte Carlo simulation (*offline*): the simulation stores hits and/or singles in a large root file, and the digitization can then be performed with this file as input, allowing to compare several digitization chains with the same hits.

2.5. Collaboration with other toolkits

In addition to Geant4 which GATE is built on, several toolkits cooperate with GATE. The ROOT [25] data analysis framework is heavily used throughout the hits analysis to store and organize all physical information during a simulation. Note that, since version 9.0, an alternative NumPy [55] output can also be used. The Python module UpRoot is used within the GateTool to efficiently process ROOT files [110]. Also in GateTools, all 2D and 3D images are managed with ITK [89]. SpekCalc [112] can also be used to define the X-ray beam source characteristics for X-ray based imaging devices. Image reconstruction from simulated list-mode or projections may be performed with other open-source toolkits such as STIR [141], CASToR [94] or RTK [117]. Indeed, STIR implement analytical and iterative reconstruction methods for PET [71] and SPECT [67] imaging devices using GATE's output as input. CASToR also proposed iterative PET reconstruction algorithms and can conveniently read GATE generated ROOT output [64]. RTK [117] performs tomographic reconstructions from GATE generated projection images. While initially designed for CBCT images, it can now also be used for SPECT reconstruction (OSEM, with attenuation, scatter and PSF corrections) [120; 121] and contains specific features for motion compensated reconstruction. It is also used internally within the GATE code to perform variance reduction algorithms (see section 3.1). All those toolkits helped GATE to build this ecosystem on medical physics.

2.6. Slow pace development: GATE-RTion

GATE was historically the first Geant4-based application for medical physics. Over the past 15 years, its usage and interest in the field of light ion beam therapy has been growing considerably, with the first modeling of an IBA pencil beam scanning system [50] and several subsequent applications related to beam modeling [8; 35; 45], dosimetry [22; 44; 51; 52; 114; 128] and associated imaging applications [93; 122; 123]. The idea of the Gate-RTion project was initiated in 2017, with the purpose of easing the implementation of GATE in clinical centers [53]. The first Gate-RTion version was released in 2018. It provides a stable and long term GATE release, including validation tests (available in the GateContrib repository) for dosimetric applications in light ion beam therapy (mainly scanned proton and carbon ion beams). It provides a collection of tools necessary for the clinical users to interface GATE with the clinical environment (available in the GateTools repository). Gate-RTion establishes a bridge between researchers and clinical users, to facilitate the transfer of research applications into the clinics and allows users to establish more standardized guidelines [152]. The next version of Gate-RTion is currently planned for 2023.

2.7. The OpenGATE collaboration

The OpenGATE scientific collaboration currently brings together 25 public and private institutions (list of partners available on www.opengatecollaboration.org) committed to develop, maintain, and promote the GATE software by respecting the rules set by the steering committee. The collaboration is based on a *Gentleman agreement* and is open to every group willing to contribute. The collaboration is represented by a spokesperson and its developments are supervised by a scientific coordinator. Twice a year, the collaboration organizes a scientific workshop during which current developments and the latest validations are presented. During these workshops, the limits and priorities for each development are identified. In addition, a group of developers meets regularly with the scientific coordinator to solve technical challenges. The group is open to everyone who wants to contribute. The current GATE mailing list contains more than 2000 registered people, it may give an indication on the number of users.

Twice a year, the collaboration organizes training for beginners as well as training to help advanced users in their analyzes of simulation data with the Python language. These courses are open to researchers from the academic and private sectors. The collaboration supports any initiative to use the platform in the university environment for teaching. As an example, all medical physics students that are following the DQPRM diploma in France (required to be certified as medical physicist) follow a GATE initiation course. In addition, several schools are set up internationally to train master's level students. These training courses are organized mainly remotely, participants can practice exercises under the supervision of expert collaborators by accessing a complete IT environment on a dedicated remote server. For example, the OpenGATE collaboration in association with IEEE Nuclear and Plasma Sciences society are organizing two schools per year in different parts of the world by adapting the scientific content to the needs of the students in collaboration with the academics of each country (schools have been organized in Asia and Africa, and will be extended to North and South America).

2.8. Limitations

The collaboration does not manage money (except from a small amount dedicated to the organisation of one-time events or to pay GitHub servers) and the collaboration does not employ engineers and developers directly. All contributions are performed by researchers according to their own projects and budgets, inherently limited in duration. It is indeed a very flexible organisation but depends on the success of the members to grant applications. Hence, the long-term management and maintenance of the software is challenging as authors of some specific features may leave. The number of active developers is also relatively small: around 20 people contributed to the source code in the last 3 years.

3. Impact on cancer research and medical physics

This section briefly reviews the impact of GATE regarding cancer-related medical physics applications. A representative part of the available applications is presented here focusing to the most recent developments. For clarity, the section is split into two main parts dedicated to imaging and dosimetry. Previous papers are referred, wherever appropriate, for illustration of the ecosystem's applications. Figure 4 depicts an estimation of the number of publications throughout the lifetime of GATE, covering all the available applications in medical physics (with almost 900 publications from 2004 until 2021). The graph is provided by the Scopus platform (www.scopus.com) and incorporates the different publications in the fields of medical imaging, dosimetry and radiotherapy. Figure 5 summarizes the main applications of GATE that can be found in the literature, also separated into two main fields, imaging and dosimetry.

3.1. Imaging-related applications

Nuclear medicine imaging.—In the last few decades there has been a dramatic evolution of nuclear medicine imaging, which provided methods for earlier and more accurate cancer diagnosis, therapy and therapy response assessment. This period coincided with the development of GATE, which since its first release in 2004, has been used to advance nuclear imaging capabilities and accuracy, particularly in PET and SPECT imaging [16; 146]. GATE has been extensively used and is a well-validated tool for: i) the design and the development of new imaging systems , ii) the evaluation and the optimization of image processing algorithms, iii) the development of new radiotracers. Recent developments of GATE MC simulations for emission tomography were presented in a topical review [132].

For more than 20 years, imaging systems like CT, PET and SPECT modalities have become essential tools in cancer diagnosis and for therapeutic efficiency evaluation. GATE is widely used to characterize and investigate/optimize image quality of scanners produced by most main manufacturers (e.g. Siemens [4], General Electric [134] or Philips [147]) as well as to design, optimize and validate new systems that will be put on the market. GATE is for example used to optimize the choice of the detection medium (crystal or liquid scintillator, semi-conductor, etc.), the light collection system (PMT, APD, PSPMT, SiPM, etc.), the geometry of the scanner (dead zone reducing, packing fraction optimization, etc.), to improve the spatial and temporal resolution, the sensitivity and the image contrast recovery. All these parameters are critical in image quantification for oncology applications. GATE is also widely used for prototype detector developments and the next imaging system generations integrating concepts like heterostructured scintillators for ultra-fast TOF-PET scanners [76], total body acquisition [98; 146], or Compton Camera systems [40; 41; 43; 101; 102] with a dedicated module [37]. GATE has been also used to optimize PET detector design for proton therapy range monitoring that is particularly challenged by low signal-to-noise ratio with respect to the diagnostic PET scanners (see section 3.1). In addition, GATE is also used in the field of data correction and tomographic reconstruction where the production of simulated data is crucial to validate the interest of new algorithms to improve quantitative analysis.

Optical imaging—Optical imaging techniques such as bioluminescence imaging [116], fluorescence imaging [82], and Cerenkov luminescence imaging [124] are essential for translational cancer research. GATE can simulate optical imaging techniques by modeling the optical photon transport inside biological tissues [32] as validated against MCML optical simulation software [150]. The optical properties of biological tissues such as refractive index, absorption and scattering coefficients can be defined as a function of wavelength thereby allowing realistic simulations optical imaging and near-infrared thermal therapy [33]. In addition, an optical lens was implemented into GATE for more realistic optical imaging simulations of bioluminescence and near infrared fluorescence (NIRF) imaging [66]. Moreover, GATE also allows the Cerenkov luminescence simulations (see examples in Figure 6) that can be used as a basic research tool for both nuclear medicine [30] and radiotherapy [68; 140].

Positronium imaging.—The GATE platform can be used as a tool to develop novel PET imaging methods beyond the conventional two-photons tomography. In particular, GATE/Geant4 is capable to simulate *positronium* decay, a bound atomic state of an electron and a positron, that is formed before annihilation occurs. The measurement of positronium properties, e.g. its mean lifetime, can provide supplementary information about the metabolic processes in the patient's body [99]. In tissues, the positronium properties are influenced by the size of inter- and intramolecular voids and the concentration of molecules such as molecular oxygen in them, and the extraction of this information may provide insight into disease progression [98]. This approach opens a new field of applications in cancer diagnosis [97; 135]. The positronium tomography technique is especially suitable for large field-of-view high-sensitivity scanners. Positronium imaging performance studies for several large-field-of-view plastic-based scanner prototypes has been described in [100].

X-ray imaging.—GATE is also used for X-ray medical applications, either for imaging or/and dosimetry, as in CT [18; 56; 73; 103], dual energy CT (DECT) [77], Cone-Beam CT (CBCT) with kV beams [13; 26; 57; 86; 149; 153; 154] and MV beams [19; 20], or mammography [38; 38; 39]. Imaging systems were simulated either to assist image improvement methods (such as scatter estimation), or to estimate the dose to the patient (such as organ dose calculations). SpekCalc [112] can be used to define the X-ray beam source characteristics. GATE also proposes various variance reduction techniques dedicated to X-ray imaging, like the Fixed-Forced Detection (FFD) that makes use of the fast ray-tracing capabilities of the RTK library [27; 154]. More recently, a module was added to GATE in order to perform X-ray phase-contrast imaging [36], as well as processes for the refraction and total reflection of X-rays and an analytical wave optics algorithm for generating Fresnel diffraction patterns. All these tools specific to X-ray imaging techniques were successfully validated against data.

Ion imaging.—Patient imaging using particles like protons or ions is also a promising research field and several studies have been done with GATE for simulating ion beams in complex configurations (voxelized volumes, detectors, etc.). Using GATE capabilities for both imaging and dosimetry, these works mainly investigate potential benefits of proton radiography and tomography techniques while optimizing reconstruction algorithms [9; 72; 75; 113; 118; 137]. Imaging with uncommon beams such as with muon [2] or with Helium [108] was also proposed.

Proton range monitoring.—Among the applications of GATE for radiation therapy, a newly implemented multi-stage GATE framework, `ProTheRaMon` [23], joins and extends GATE capability to simulate proton therapy treatments, secondary radiation induction

(Sec. 3.2), and PET imaging including reconstruction with CASTOR package (see Sec. 3.1). `ProTheRaMon` was developed to be executed on a computational cluster with the aim to simplify multi-parameter simulation studies exploiting large number of patient CT images and treatment plans, all needed to design, test and compare PET detector designs and precision of proton therapy range monitoring in clinical environment [74; 85]. `ProTheRaMon` was developed in the frame of a research project aiming at designing and optimizing a range monitoring detector based on J-PET technology [96–98; 100] at CCB Krakow proton therapy centre (Poland) [61; 127]. It is an open-source GATE repository available on ProTheRaMon. Currently, `ProTheRaMon` is also used by researchers from Paul Scherrer Institute (PSI, Switzerland) within the scope of the PETITION project (Swiss National Science Foundation, Grant CRSII5_189969), a collaboration between ETH Zurich, Le Centre hospitalier universitaire vaudois (CHUV, Lausanne) and PSI [119], which aims to develop a dedicated proton therapy PET scanner for brain and head-and-neck tumours, aiming at hypoxia guided proton therapy [84] and proton therapy range monitoring [92]. Others online proton range monitoring methods are also studied with GATE, such as line-cone reconstruction with Compton Camera [80].

3.2. Dose-related applications

External beam radiation therapy.—GATE has been used to provide answers to complex issues that cannot be resolved with clinical software available for photon radiotherapy. These are, for example, dose calculations with large heterogeneities [17], skin dose for breast cancer treatments [10], or double calculation of radiotherapy treatment plans [79]. However, GATE is less used for external photon beam therapy than, for example, EGSnrc [70]. GATE has a stronger impact in light ion beam therapy centers supporting research and development, as well as clinical applications derived from the Gate-RTion release in particular. AUTOMC was the first Gate-RTion-based proton Independent Dose Calculation (IDC) system. It has been set-up in clinical operation since the start of the Christie NHS Foundation Trust, a proton therapy facility that opened in December 2018 in Manchester (UK) [3]. It is used to support the Patient Specific Quality Assurance (PSQA) Process. AUTOMC/Gate-RTion was successfully validated against more than 730 clinical plans, for which physical QA measurements were performed with a 2D detector array and a thimble ionization chamber. AUTOMC is a stand-alone software directly providing the IDC output in terms of gamma pass rate [81]. IDEAL (Independent DosE cAlculation for Light ion beam therapy) is an alternative Gate-RTion-based IDC system for light ions. IDEAL was designed in a DICOM-in/DICOM-out fashion, in order to be compatible with standard DICOM interfaces available at light ion beam therapy centers. IDEAL is a proton and carbon ion IDC system and the first version was released in March 2021 [54] (available on the Git repository of OpenGATE). It is being used at the MedAustron ion therapy center in Austria, mainly for carbon ion IDC. Current hot topics in the field of proton and carbon ion therapy, such as variable proton Relative Biological Effectiveness (RBE) depending on Linear Energy Transfer (LET) [136] (see next sections), the influence of fragmentation spectra on carbon ion RBE [115], influence of new stopping power tables (e.g. ICRU90) for 3D dosimetric applications with protons and carbon ions [22] are fully supported by the Gate-RTion release.

Radionuclide therapy.—The impact of GATE on cancer research significantly increased after the addition of radiation therapy and dosimetry applications in 2014 [33; 54; 131], MC simulations serve as gold standard for dosimetry calculations and can now be conveniently used for combined imaging and therapy applications in GATE, which is of high importance for theranostics [95; 145]. Emulated by Geant4 to model the energy deposition in biological media, GATE allows dosimetry through full Monte Carlo, dose point kernels (DPKs), or more recently deep learning (DL) for fast dose computation [42; 47; 48; 78; 106]. GATE has been used for image-based dosimetry in research and clinical practice [10; 20; 24; 34; 125]. Specific to nuclear medicine, high-precision dosimetry becomes an essential tool for targeted radionuclide therapy with ^{177}Lu or ^{90}Y [111; 125], and is poised to continue growing in importance with the development of short range alpha emitters [143]. In Targeted Alpha Therapy (TAT), the understanding of the dose deposition in tissue such as the bone marrow close to bony metastases is essential to develop efficient and safe therapeutics. Very recently, GATE was extensively validated for brachytherapy applications incorporating both high dose rate (HDR) and low dose rate (LDR) sources with ^{192}Ir and ^{125}I respectively [29]. The GATE platform combining high precision dosimetry and well-validated image modeling has the potential to become a tool of choice for investigating and developing novel approaches using a plethora of radionuclides.

Radiobiology.—GATE is becoming extensively used to predict the effect of radiation at micro and nano scales, from preclinical cell irradiations to advanced hadrontherapy treatments [87; 88; 105; 109; 126; 136; 138; 139; 148]. The platform is the preferred tool to simulate preclinical or clinical beam characteristics that are detailed in a phase-space file before being combined to Geant4-DNA simulations [21; 58–60] to assess radiobiological effects. To date, GATE is not able to fully handle multi-scale simulations from the calculation of dose to organs to an accurate identification and understanding of cellular and molecular damage. Upcoming developments will favor the integration of relevant features that have been tested so far through Geant4-DNA simulations. As example, we can mention the integration of various cell population models, specifically 3D cell populations, from the C++ Cell POPulation modeler (CPOP) already compliant with the Geant4 toolkit [83]. We will propose the same integration for the IDDRRA platform to score radiation induced DNA damage with a user-friendly simulation of different DNA molecules [28]. Recently, specific actors are being developed for proton and carbon ion therapy to calculate LET or biological dose-based clinical treatment planning. Linear energy transfer (LET), especially dose-averaged LET (LET_d), either as a physics component of variable RBE models [91] or alone, as a physical treatment planning parameter [90; 144], is increasingly considered in clinical practise. The recent literature indicates that the LET_d alone may not be predictive of biological effectiveness in proton radiotherapy [15; 46; 65; 104]. The GATE framework offers access to information on single particle interactions, thus, enabling calculation of single particle LET in a voxelized patient geometry. Figure 7 shows dose and LET_d distributions, as well as LET spectra for 150 MeV therapeutic proton pencil beam at the Bragg peak depth computed with GATE and measured experimentally with a TimePix detector [49]. In addition, the estimation of the biological dose will be proposed through the BioDoseActor [5]. The input data of this new actor are pre-calculated α and β cell survival parameters for Human Salivary Gland (HSG) cell line produced with mMKM [69] and NanOx [31] biophysical models for monoenergetic ions (hydrogen, carbon, helium, and oxygen) and energies ranging from 0.1 to 400 MeV/n. Some biophysical models, like the NanOx model, also consider the physicochemical and chemical consequences of radiation at nano scales by evaluating the oxidative stress undergone by cells during water radiolysis. In the future, one can expect ongoing developments concerning the simulation of chemical species reactions during water radiolysis for different dose rates [142] will be gathered in a new open-source release and could help to better estimate treatment outcomes.

3.3. General considerations

There are several advantages of GATE for medical physics research. First, GATE offers Monte Carlo simulation environments for medical physics with user-friendly macro command lines as well as interactive visualization capability thereby allowing users to conveniently develop and debug their own simulation. Second, various pre-defined medical imaging systems such as PET, SPECT, Compton camera, X-ray CT, and optical imaging are readily available thus researchers can implement new studies based on those systems. In addition, the radiotherapy and internal dosimetry simulations are available with well-validated physics models thereby allowing researchers to investigate the new cancer therapy strategies and concepts in conjunction with the radiation exposure to patients. One drawback of GATE is that Geant4 multi-threading is not available. GATE provides however job splitting tools in which the simulation tasks can be separated and assigned to multiple CPU cores thereby reducing the overall simulation time substantially. Another drawback of GATE is that the users are limited to the pre-defined imaging systems with their fixed system hierarchy.

GATE is one among several other Monte Carlo codes which have been and are in use in Medical physics applications. These codes include GEANT4 itself, EGSnrc [70], MCNP [151], TOPAS [107], GAMOS [11; 12] and each of them has its own advantages and limitations. The collaborative approach which is a feature of both GATE and GEANT4 provides both advantages (broad and powerful feature enrichment) and limitations (code coherence and efficiency). While other code systems have focused mostly on accuracy (EGSnrc, MCNP), efficiency (EGSnrc) or a particular application (TOPAS), GATE is fully open-source and would be competitive in the realms of detailed modeling of the imaging and supporting instrumentation process (e.g. signal digitization by electronic modules), obtaining results for both imaging and dosimetric interpretation in a single simulation, ease of use, original AI-based methods (see next section), and broad international support and education program.

4. Future directions

The GATE software is constantly evolving, trying to propose new features and new improvements from release to release.

Digitizer.

The aim of the first ongoing collaborative project is the restructuring of the “digitizer module”. As described in previous sections, this module simulates the response of the photodetection components in several imaging systems (PET, SPECT, Compton Camera etc). This central module has evolved a lot since the beginning of the project and has become complex and hard to maintain with multiple layers of interdependencies. The main goals of the current development are: to preserve the current functionalities, to modularize the code, to keep it as close as possible to the Geant4 framework. The main basic components of this module will be based on the notion of `HitsCollections, DigiCollections` and `DigitizerModule`. The first manages a list of “hits” corresponding to some interactions in given volumes, described by several attributes (energy, position etc.) that may be selected dynamically according to user’s needs. The second notion, `DigitizerModule` manages procedures that will take as input some `HitsCollection` and `DigiCollection` and create another ones. At the end of a complete digitization task, composed of several chained DigitizerModules, the user will get the simulation of the photodetector response.

Artificial Intelligence.

Another ongoing experimental project aims to investigate the potential interest of AI, and more specifically GANs (Generative Adversarial Networks), for the modelling of phase-space or activity sources [130; 132; 133]. The main idea is to build a neural network model of a given probability distribution of particles such that they can be quickly generated, avoiding the tracking phase. Proofs of concept have been published but there are still a lot of unknowns and uncertainties in those approaches that remain to be studied. There is, in particular, some ongoing work on conditional GANs that may allow to model a family of GANs, and to avoid time-consuming re-training [129].

Python.

Finally, a third long-term project has started, aiming to completely rethink the way the simulations are described by the user. Indeed, the Geant4 `messenger` system, based on a text file of so-called “macro commands”, has been used for years. This is a powerful system, but has some limitations and is not always very user-friendly. For example, while feasible, it is not really convenient to create complex simulation structures involving loops, variables or computations. By acknowledging the fact that the Python language and its associated very large environment is *de-facto* a standard for data analysis, it has been decided to investigate whether simulations can be directly described in Python instead of macro files. The interests of such a mechanism are: a simulation can be described with regular Python scripts with loops or any type of variables, part of the simulation can be modularized and easily reused (with import), users do not have to learn a new language. A first prototype is currently showing the feasibility of such an approach. The mechanism is based on the Geant4 python binding thanks to pybind11§ that exposes to Python a fraction of the Geant4 API. The GATE engine is hence split into two main parts, one directly in Python that takes care of everything related to the simulation initialization part, and the second part, in C++, in charge of tasks occurring during a simulation run. Communication between Python and C++ is designed such, that only the computing-intensive parts of the simulation are still described in C++, leaving all other management to Python for simpler

§ https://github.com/pybind/pybind11

development. With this approach, there is no computation time penalty due to the use of Python, the core engine remaining Geant4. Multithreading capabilities of Geant4 are also maintained (thanks to the possibility to release the Python Global Interpreter Lock before going multi-thread). A potential drawback of this approach is the need to use two different coding languages to develop and add functionalities. However, by separating more clearly what is performed during initialization from what is done during run-time, and by moving to Python all high-level tasks, it is hoped that maintenance and development will be simplified. The first public experimental version of this approach, that may become the future GATE 10.x series, is planned in 2023.

5. Conclusion

GATE is a living open-source project run by the OpenGATE collaboration, contributing since around 20 years to medical physics cancer research. The associated community is the real strength of this initiative gathering people from different fields (radiology, nuclear medicine, radiotherapy, radiation protection, etc.) with complementary backgrounds (researchers, engineers, teachers, medical physicists, physicians, etc.).

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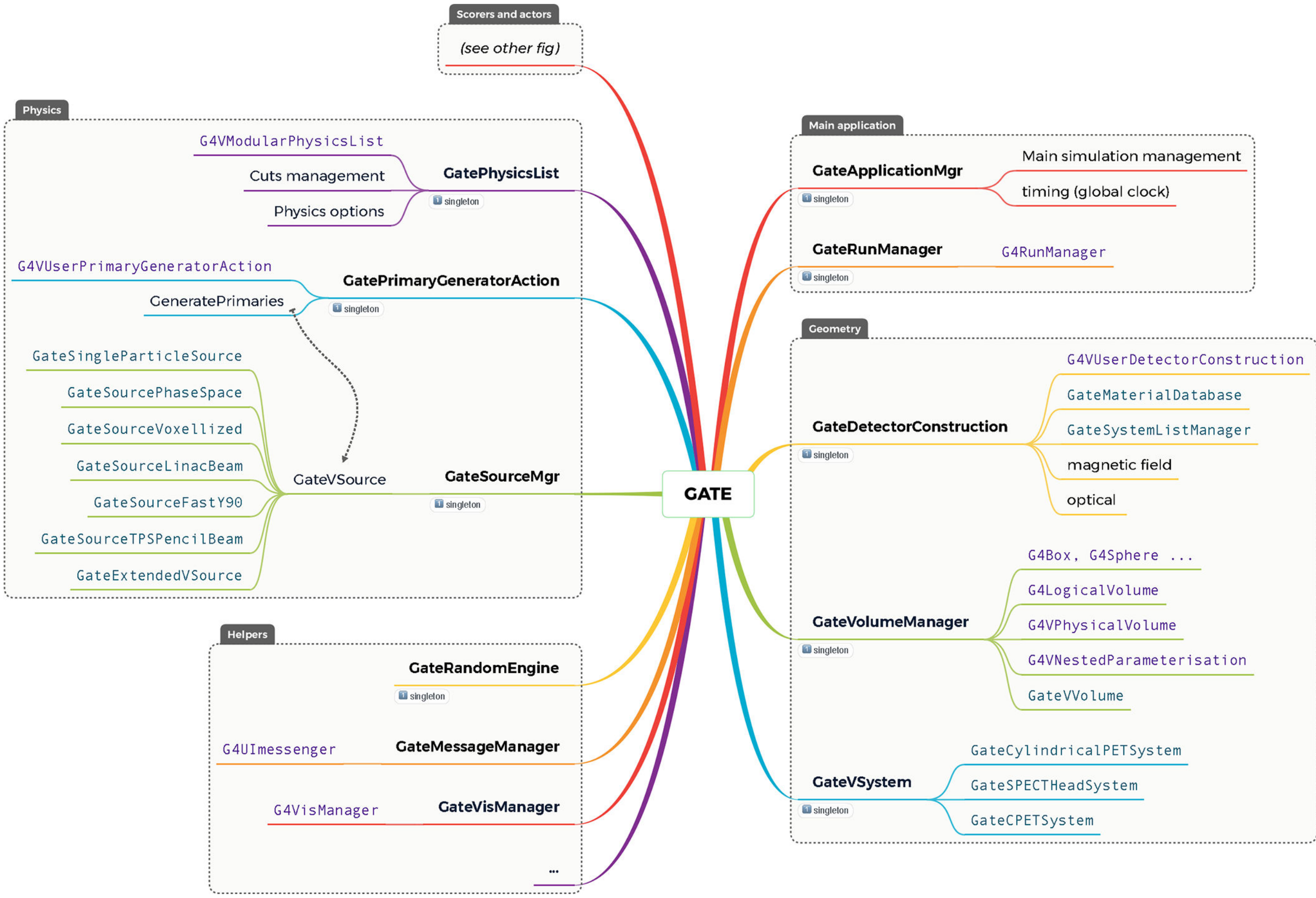

Figure 1.

Main GATE classes architecture and link with Geant4 classes. Singleton classes are depicted with a small "1" icon.

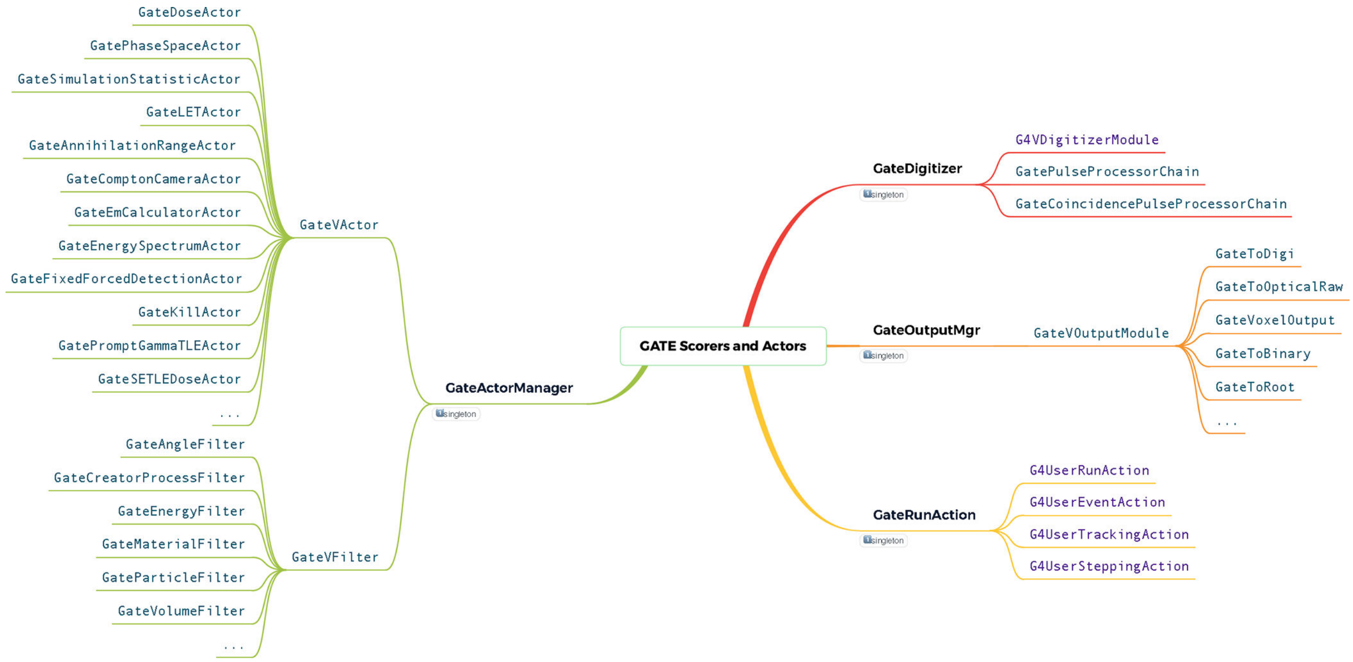

Figure 2.

Classes architecture of the GATE scorers and actors module.

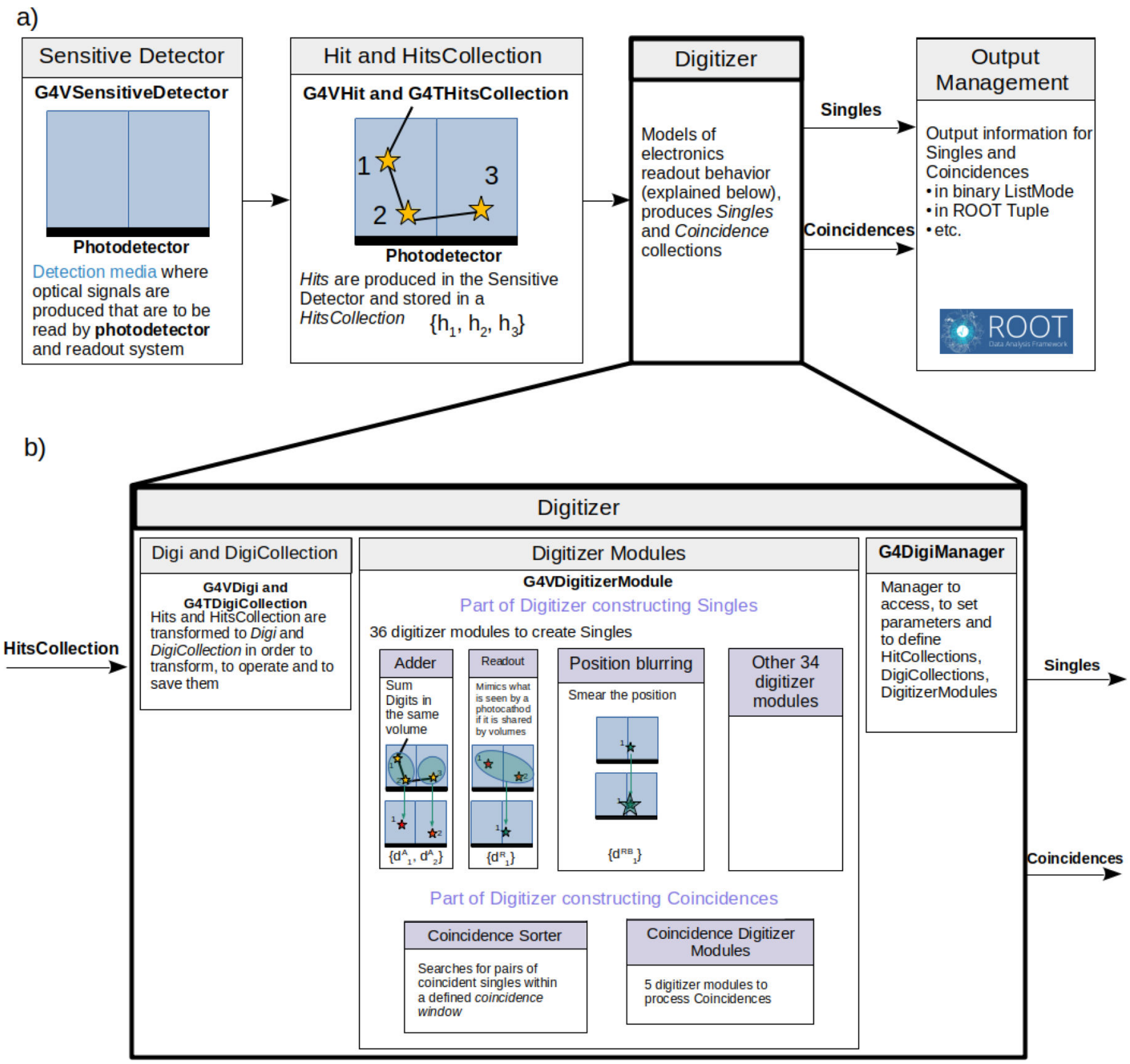

Figure 3.

A schematic of the GATE digitizer main workflow and elements: a) digitizer module within the GATE environment and its interaction with other modules; b) digitizer module. An example of a scintillation detector containing two scintillation crystals and a photocathode is illustrated.

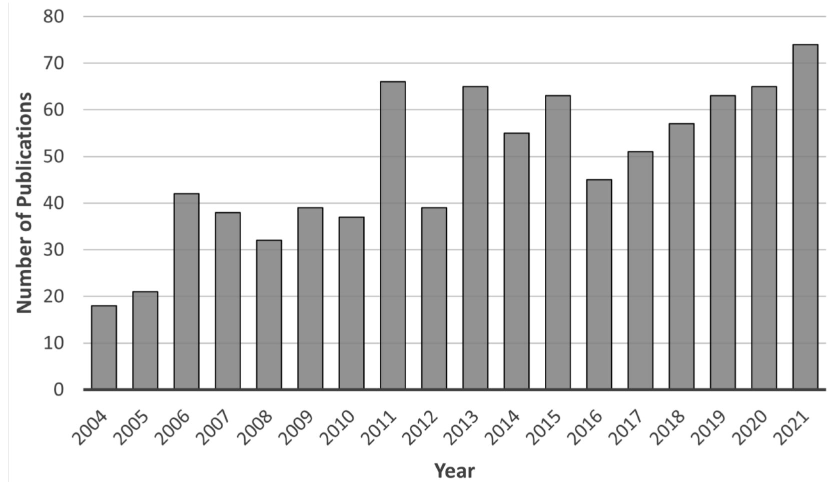

Figure 4.

Estimated number of publications of GATE from 2004 to 2021 regarding imaging, dosimetry and radiotherapy applications.

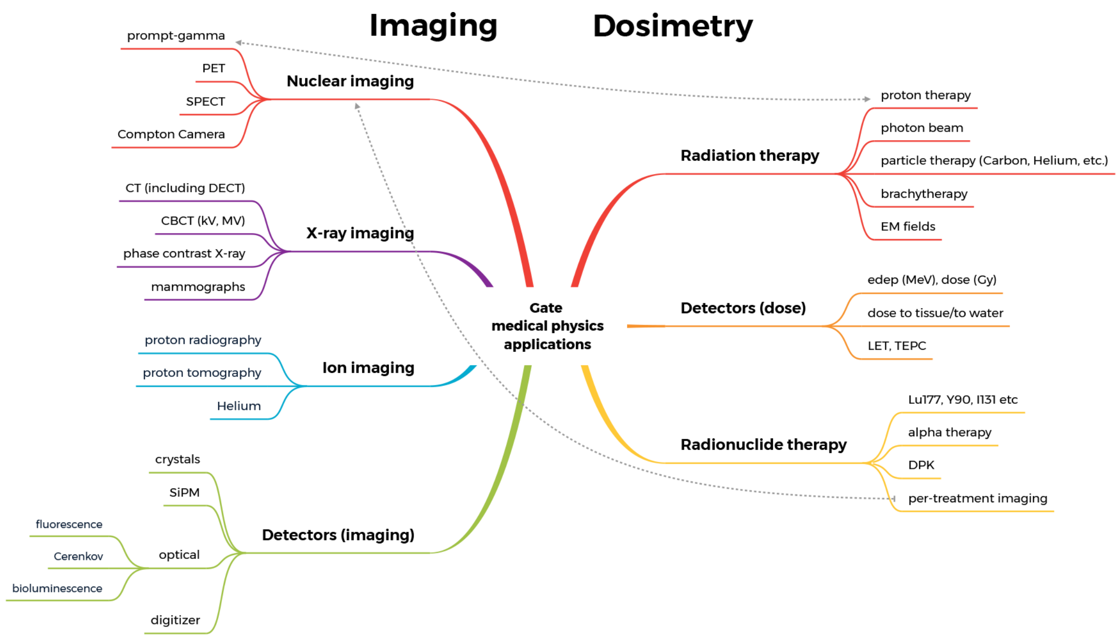

Figure 5.

Main applications of GATE in medical physics.

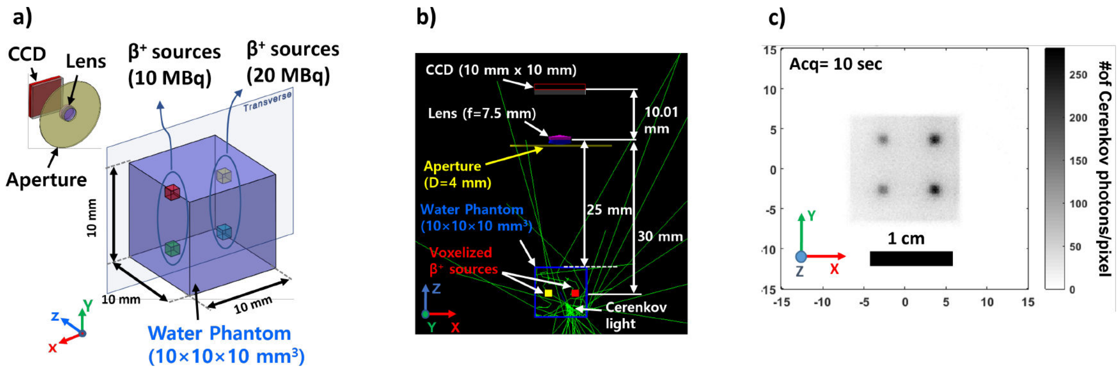

Figure 6.

a) GATE Cerenkov luminescence imaging setup with optical imaging system and positron sources inside a water phantom, b) GATE Cerenkov luminescence imaging simulation geometry, c) the CCD image that collected Cerenkov luminescence light for 10 seconds.

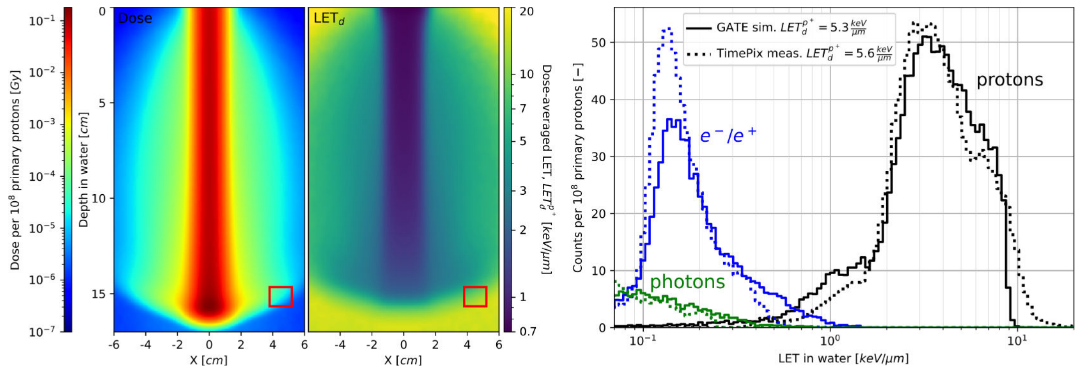

Figure 7.

2D dose (left panel) and LET_d of protons (middle panel) distributions in water for therapeutic pencil proton beam at 150 MeV and the corresponding LET spectrum (right panel) for the measurement point at the Bragg peak depth, 45 mm from the beam axis, indicated with red squares on left and middle panels. Proton, electron and photon contributions to the LET spectrum are calculated with GATE and compared to the measurement with a TimePix detector. Wide range of proton LET values is approximated by the averaged LET_d given in the legend.

Table 1.

Latest GATE releases and their corresponding Geant4 version.

GATE	Geant4	Year
9.2	11.0	2022
9.1	10.7	2021
9.0	10.6	2020
8.2	10.5	2019
8.1	10.4	2018
8.0	10.3	2017
7.2	10.2	2016