Cloud Computing in Preclinical Radiation Treatment Planning

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Abstract- **Preclinical radiation treatment planning using cloud computing is proposed to improve the efficiency of dose calculation generated by Monte Carlo simulation. In the translational research process, preclinical small-animal research is a crucial component, as it can inspire and guide clinical research pursuits of novel technological applications and new anti-cancer agents. In order for meaningful translation of preclinical research to clinical application, the disparity between the small-animal treatment and clinical treatment should be minimized. This is particularly true for investigation of local therapies such as radiation therapy for which tumour response and treatment-related toxicity is highly dependent on the dose and delivery technique of radiation. For dose calculation in preclinical radiation treatment planning, Monte Carlo simulation has widely been recognized as a benchmark to provide the accurate photon and electron transports in a heterogeneous medium (e.g. small-animal anatomy). For the huge number of voxels (~ 1000 million) based on the high-resolution mouse computed tomography (CT) with voxel size in the range of 0.1 – 0.5 mm, the time-consuming Monte Carlo method takes a long time (~ day) to calculate the dose making preclinical treatment planning not practical in routine application. In this paper, cloud computing is utilized to improve the speed of Monte Carlo simulation in preclinical radiation treatment planning. By uploading the small-animal CT anatomy and radiation beam data to the cloud through a graphical user interface (GUI), dose distribution can be calculated with high speed depending on the number of compute nodes selected. Since there is no concern on the patient privacy and security in using small-animal anatomy, preclinical treatment planning becomes straightforward, comprehensive and speedy using cloud computing.**

Keywords- Cloud Computing; Graphical User Interface; Radiation Dose Calculation; Monte Carlo Simulation; Preclinical Model; Treatment Planning

I. INTRODUCTION

The investigation of novel agents, technologies, and processes for the treatment of cancer involves preclinical small-animal studies, which comprise a crucial component in the translational research process. To maximize the benefit of recent technological advances aimed at targeted radiation therapy delivery, preclinical irradiation takes a significant role in collecting small-animal experimental data for radiobiological modelling. To fulfil this task, preclinical radiation treatment planning using Monte Carlo simulation is currently used by different groups [1-3].

Clinical radiation therapy has made dramatic advances over the past decade with incorporation of 3D imaging for radiation planning, accurate dose calculations, intensity modulated radiation therapy (IMRT), and image-guided radiation therapy [4, 5]. For estimation of the dose distribution in patients using clinical radiation therapy systems, there has been significant work using the accurate but time consuming Monte Carlo methods [6, 7]. To parallel these advances, radiation delivery systems have been developed to deliver conformal radiation to very small targets in small animals [8-11]. Imaging capabilities have also advanced in the preclinical setting to facilitate accurate imaging and radiation targeting of small tumours with sub-millimeter (mm) accuracy and accurate treatment setup [12-14]. However, the estimated dosimetry in small-animal irradiation experiments is limited and the high-resolution mouse computed tomography (CT) images (Fig. 1) are under-utilized with regards to calculating accurate dose. One of the limitations in estimating dose delivered at this resolution (voxel size in the range of 0.1 – 0.5 mm) is the lack of an accurate and fast dose calculation method. Hence, cloud computing is used to perform preclinical treatment planning using Monte Carlo simulation as a dose calculation engine.

In Section II of this paper, the rationale of preclinical treatment planning and heterogeneous correction in dose calculation using Monte Carlo simulation are explained. Section III introduces a treatment planning graphical user interface (GUI) using Monte Carlo simulation. Section IV is about the basic concept of cloud computing and how to implement cloud computing on preclinical treatment planning. In addition, Section IV discusses some computing issues such as the selection of number of compute nodes and image data privacy/security.

Fig. 1 Computed tomography slice of a mouse showing the lungs. The voxel size is 0.3 ×0.3 ×0.3 mm^3. One division of the ruler scale represents 2.5 mm

II. SMALL-ANIMAL DOSE CALCULATION USING MONTE CARLO SIMULATION

Preclinical studies employing radiation are concerned with testing the effect of radiation, usually in combination with additional therapy, but the exact radiation dose is not crucial. In addition, many of these studies have historically employed sub-cutaneous tumor models, in which the tumor could be easily localized and dose to surrounding tissues is not a confounding factor. In these situations, exact knowledge of

the dose delivered to the tumor and the rest of the animal may not be important for the overall outcome of these studies [15, 16]. However, for recent radiation therapy studies using orthotropic tumor models, or radiosensitizers such as gold nanoparticles acting as contrast and dose enhancer, delivered dose is highly concentrated in the tumour [17, 18]. Since the goal of such studies is to enhance the tumour dose but spare the surrounding critical tissues, an accurate 3D conformal irradiation is necessary to enable analysis not only of the dose to the tumour but the dose to the surrounding organs-at-risk.

Monte Carlo calculations are the gold standard for accurate calculations. In particular, Monte Carlo simulations can handle backscatter from bone or scatter perturbations by small and irregular air cavities more accurately than any other current models [19]. Moreover, Monte Carlo simulations can accurately model radiation fields from a small-animal irradiator in presence of complex anatomy, treatment aids and beam geometries [9, 20]. Monte Carlo simulation therefore can potentially be the backbone of our proposed small-animal treatment planning system using cloud computing.

A. Tissue Heterogeneities

Zhou et al [21] proposed a bone composition model using an analytical formulation for Monte Carlo computations. Elemental compositions and densities of adult human bones from literature were used as references. Different discrete bones were generated from the proposed model and tested by Monte Carlo simulations using the DOSXYZnrc code [22]. The total energy released per unit mass of primary photons (TERMA) were calculated and compared. They found that the results of TERMA agreed well with the published data with deviation within 2.2% and 1.2% for the kilovoltage (kV) and megavoltage (MV) spectra studied. This new bone model for Monte Carlo simulation is important for the kV beam dosimetry for small animal whose bone composition may differ substantially from that of adult human bones.

B. Resolution of Dose Calculation Grid

For the Monte Carlo calculation at sub-mm voxel resolution, Bazalova et al [23] evaluated the efficiency of simulation using a homogeneous solid water phantom with voxel sizes of $0.2 \times 0.2 \times 0.2$ mm^3. Photon beams of 120 kVp were used with field sizes equal to 2 – 30 mm diameter. The EGSnrc-based BEAMnrc and DOSXYZnrc codes [22] were used with the variance reduction techniques studied for an efficient and accurate calculation. For two calculation approaches involving or not involving the phase-space file, they found that to achieve a 1% statistical uncertainty, the optimum bremsstrahlung splitting number (NBRSPL) is about 1×10^6. Moreover, for the photon beams with field sizes of 2 and 30 mm diameter, dose calculations using the phase-space file are more efficient than not using by factors of 54 and 1.6, respectively. This study provides valuable information in Monte Carlo simulation using heterogeneous mouse anatomy from high-resolution (sub-mm) CT image set.

C. Radiation Treatment Planning

For the treatment planning in small-animal radiotherapy, Motomura et al [3] investigated the dose distribution of the target under different plans using various beam fields and configurations. A cylindrical solid water phantom and photon beams of 120 kVp with field sizes of 1 – 10 mm diameter were used. The dose distributions were calculated using Monte Carlo simulations based on the DOSXYZnrc code. They found that for a central and symmetric target, the number of beams required to achieve an acceptable dose distribution decreased with increased size of target. However, for a non-central and symmetric target, no significant loss of conformality was found with increasing offset from the isocenter. Motomura et al [3] also studied the dose distribution in the irradiation of a mouse lung tumour using the DOSXYZnrc. However, it should be noted that the DOSXYZnrc does not contain the mouse but only human tissue dataset for Monte Carlo simulation. To determine dose distribution accurately in small animal, a small-animal tissue dataset should be acquired for Monte Carlo method.

III. THE DOSCTP GUI

The goal of radiation treatment planning is to deliver a highly conformal absorbed dose to a prescribed target volume and at the same time to spare surrounding healthy tissue as much as possible. Accurate dose calculation in planning is important especially when the target is associated with heterogeneous medium such as lung. It is well-known that Monte Carlo dose calculation method, such as the EGSnrc-based DOSXYZnrc code, is a benchmark tool to calculate dose distributions in a heterogeneous medium [19]. A CT image dataset, which is typically used in commercial external treatment planning systems, is necessary for the above Monte Carlo simulations. As the DOSXYZnrc is a popular and widely used simulation code, the associated CTCREATE routine is able to convert a DICOM/RTOG/Pinnacle-formatted CT image dataset into a 3D DOSXYZnrc phantom for Monte Carlo simulation. However, the CTCREATE routine functions through a command line interface and the existing DOSXYZnrc GUI has no visualization tool to view and position the beams within a CT phantom. Furthermore, there is only limited support in the DOSXYZnrc to view and analyse the calculated doses after simulation conveniently.

The DOSCTP is a computer GUI for non-IMRT treatment plans that uses the EGSnrc as a dose calculation engine to external beam treatment planning system for comparison and evaluation [2, 24]. The current DOSCTP has the following essential features: (1) a user-friendly interface for importing CT image datasets in DICOM format and converting them into a 3D DOSXYZnrc phantom with user-defined voxel size and/or number; (2) transverse/sagittal/coronal viewing of the CT image slices to assist the user in contouring the target/critical organ, defining an isocenter, and orienting beams; (3) a user-friendly database for the user to build up a library of phase-space beams using the EGSnrc-based BEAMnrc [25]; (4) an automated link to the DOSXYZnrc for performing Monte Carlo simulation ; (5) a GUI for displaying calculated dose distributions on top of CT images for analysis. Moreover, the DOSCTP supports RTOG import and export, so that treatment plan performed by the DOSCTP can be imported easily into commercial treatment planning systems like Pinnacle[3] for further detailed analyses such as plan evaluation using dose volume histogram and calculations of radiobiological parameters.

Figure 2 shows the program flow of the DOSCTP. The user loads a DICOM image set or DOSXYZnrc phantom into the system to initiate a plan. This is followed by definition of the isocenter coordinates and beam(s) placement. If the image source is DICOM, it is converted into a DOSXYZnrc phantom based on user-selected voxel numbers or sizes. The user is then given a chance to edit the phantom. After the DOSXYZnrc phantom is set up, the GUI then performs

"Monte Carlo Simulation with the DOSXYZnrc". The user may adjust a set of the DOSXYZnrc simulation parameters found within the DOSCTP. The GUI then automatically generates the input file(s), one for each beam, and performs dose calculation with the DOSXYZnrc. When more than one beam is used in the plan, the GUI automatically merges all dose output files to obtain the total dose distributions. To view the isodose lines, "Display Dose Contour" block is executed to import and display the doses. The user has the option of selecting a normalization point, either graphically, or by manually defining a set of coordinates. Finally, in the "Export" block, information relevant to the plan can be exported in a text file as a report, while the treatment plan can be exported as RTOG. The DOSXYZnrc phantom can also be exported in DICOM format for import into commercial treatment planning systems.

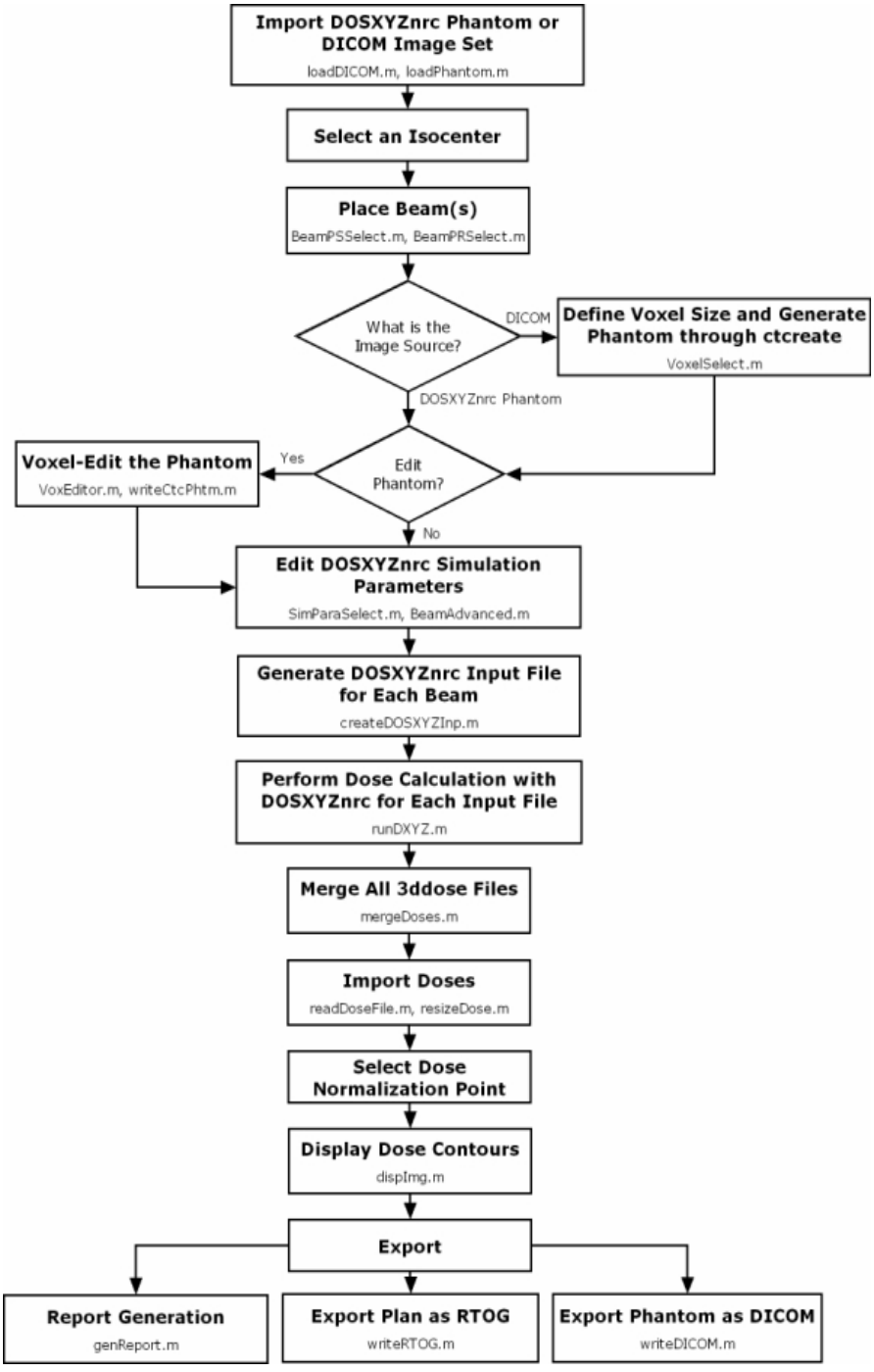

Fig. 2 Block diagram showing the flowchart with main components of the DOSCTP

Figure 3 shows the front-end window of the DOSCTP. The GUI contains some of the basic features of a treatment planning system. 2D CT images are displayed in viewing windows (see Fig. 3, in black). The standard transverse (large), sagittal (top small), and coronal (bottom small) views are available. A panel (top left) manages the beam configuration. There, phase-space beams (P.S. Beam) generated by the user in the BEAMnrc can be called from a user-built library and added to the plan. Alternatively, the user has the option to use monoenergetic parallel rectangular beams (P.R. Beam), which does not require phase-space files. The contour panel (middle left) assists the user in adding and editing contours. The

isocenter panel (bottom left) permits definition of the isocenter coordinates. A tools panel is located at the top of the GUI to provide additional functions when navigating the CT images, selecting a point of interest for the isocenter, orienting beams, or drawing contours. To the right of the tools panel, is a set of control used for the display of relative isodose lines and selection of a normalization point from the user. Near the bottom of the GUI, are sets of four buttons, namely "1. Export to Ctcreate", "2. Edit Phantom", "3. Export to DOSXYZ" and "4. Import Dose", which control dose calculation with the DOSXYZnrc when activated in their numbered sequence. Information regarding the imported CT images is displayed in the image information panel near the bottom right. Directly above are a set of controls to adjust the image contrast in terms of window and level.

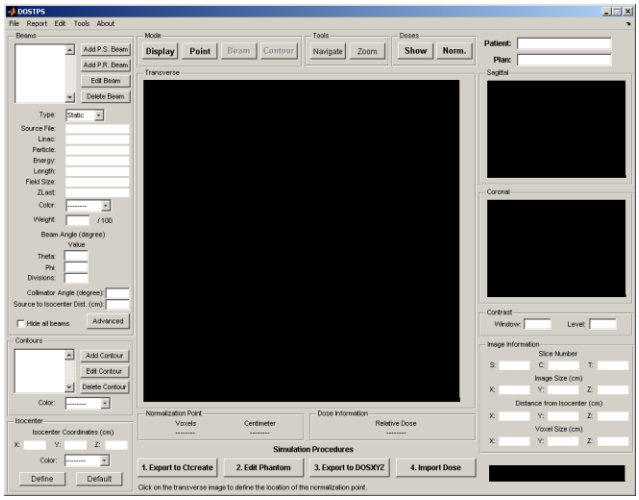

Fig. 3 The front-end window of the DOSCTP

IV. CLOUD COMPUTING

Cloud computing refers to a set of technologies (computing and storage) offered as services through the Internet [26]. The word "cloud" is inspired by the cloud symbol representing the Internet in diagrams from computer references concerning network. The "cloud" used to represent a complex network containing routers and switches that can be neglected by the user. On-demand computing infrastructure of pay-as-you-go is provided by different companies such as Amazon Inc., Google Inc., Bell Inc., and Microsoft Inc. Cloud computing has the following characteristics: (1) it is sold on demand. Users can scale their needs billed in time increments; (2) it is elastic. That is the user has freedom to order the number of virtual clusters (or number of compute nodes) in the calculation. The more the number of nodes, the higher the price but the faster the computing time; (3) it is fully managed by the provider. This is good to users as they do not need to take care of the space and maintenance cost of the server. Moreover, they do not need to worry about the system upgrade.

There are three kinds of hosted services, which can be selected by users over the Internet: (1) the infrastructure-as-a-service provides virtual server instance and operating system to the user. Example is the Amazon web services; (2) the platform-as-a-service creates applications on the provider's platform. Example is the GoogleApps; and (3) the software-as-a-service supplies software product interacting with users through a front-end portal. Example is the web-based email. In this paper concerning the preclinical treatment planning via cloud computing, the basic infrastructure-as-a-service should be used.

A. Basic Concept

The process for preclinical treatment planning using cloud computing can be seen in Fig. 4. First, the user creates a small-animal treatment plan using a treatment planning system such as the DOSCTP. The user defines all radiation beam parameters such as beam type, angle, energy and orientation. The user also needs to prepare the phase-space files for the radiation beams and defines all Monte Carlo simulation parameters related to the dose calculation. These include number of history, electron and photon cut-off energy and small-animal tissues (e.g. bone, lung and soft tissue) [22]. When all treatment planning parameters are setup, the user follows the second step to upload the plan to the cloud. In this step, the user needs to define the calculation parameters in the cloud such as the number of virtual clusters (nodes). The dose calculation is then started. When the calculation is finished, the result of calculated dose is transferred back to the treatment planning system (DOSCTP) from the cloud to display the dose distribution as the third step. In this case, the computing time depends on the selected number of nodes in the calculation. The more nodes used, the faster the calculation.

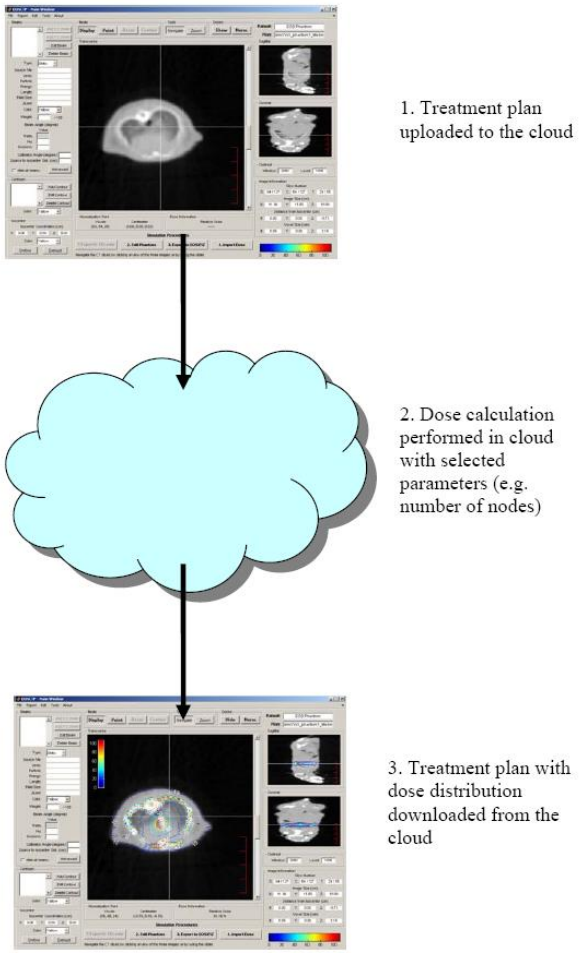

Fig. 4 Schematic of the cloud calculation process for preclinical treatment planning

B. Implementation

The implementation of cloud computing on preclinical treatment planning requires basically five steps as shown in

Fig. 5. A message passing interface which is a portable message-pass system for parallel computing should be setup to create the infrastructure for Monte Carlo simulation. This interface should contain a core of library routines with popular programming languages such as FORTRAN, C, C++ and Python for the user. In the first step, the user executes a program script (Python or C++ etc.) to allocate through the Internet one master node on the user's local computer. The user then selects the number of compute (worker) nodes in the cloud such as the Amazon Elastic Compute Cloud (EC2). The next step is to prepare the network file system. This system of disk partition is mounted to the compute nodes from the master node. In Monte Carlo simulation using the EGSnrc code, the code is uploaded to the master node from the user's local computer. The network file system provides file sharing mechanism so that the EGSnrc code only needs to be uploaded once to the master node but not every compute nodes. The third step of implementation involves in the Monte Carlo input files upload. Related input files containing parameters such as geometry of simulated CT phantom, beam and materials are uploaded from the local computer to the master node. The distribution of work is done in the forth step. The user prepares a program script containing parameters of number, type and energy of simulated particles (electron and photon). This file is embedded inside the EGSnrc code and is executed in the master node. At the same time, parameters in the file are distributed to each of the compute node. The final step is related to results of simulation. Summation of the partial dose distribution returned by individual nodes is transferred to the master node and the local computer for dose reconstruction and display.

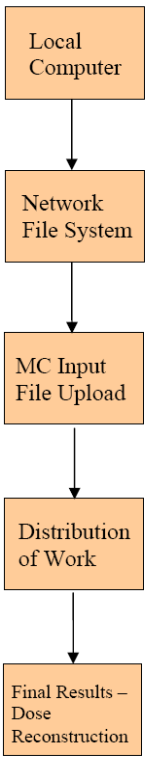

Fig. 5 Flow charts showing the implementation of cloud computing on preclinical treatment planning

C. Computing Time vs. Number of Compute Nodes

One important issue in cloud computing is to select the optimized number of compute nodes in order to perform the calculation in highest efficiency. In general, the more the number of nodes assigned, the faster the calculation. However, there is no need to select too many nodes in a calculation. Apart from the concern of cost efficiency (money paid for each node), dose reconstruction to integrate all partial dose depositions calculated from all nodes is needed to carry out. The time of dose reconstruction for the final dose distribution in the anatomy depends on how many dose deposition components are returned from compute nodes to the master node. The more number of nodes is selected, the more complex is the dose reconstruction, and the longer time will be taken to produce the final dose distribution. Wang et al estimated the relationship between the computing time and number of nodes as follows [27]:

$$y = \frac{b}{x^a} \quad (1)$$

In Eq. (1), y and x are computing time and number of nodes, respectively, while a and b are constant. Figure 6 shows the plot based on Eq. (1) using a = 1 and b = 30 [27]. It is seen in the figure that the computing time is greatly reduced when the number of nodes is firstly increased up to 10. When the number of nodes is increased further from 20, the decrease of computing time is less significant per number of nodes. The intersection point of the two straight lines in Fig. 6 is about 3.5. It means that when the number of nodes is selected between 3 and 4, the computing efficiency per node is high.

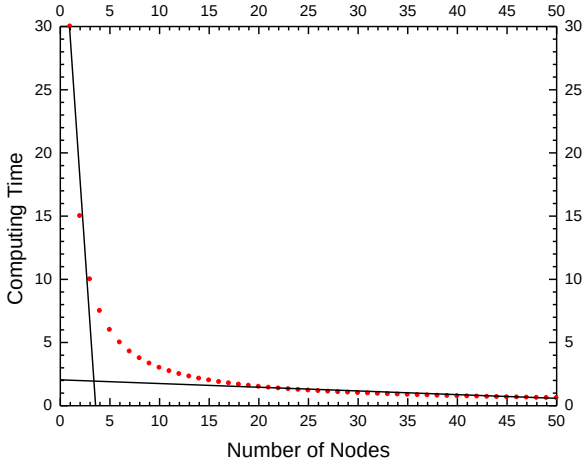

Fig. 6 Computing time vs. number of nodes based on Eq. (1), where a and b = 1 and 30, respectively

D. Clinical Concerns

Patient treatment planning using cloud computing is proposed [27, 28]. However, there are security and privacy concerns of transferring and storing personal or patient data such as patient's anatomy on networked hardware. Although there are laws related to the patient's privacy issue such as the Health Insurance Portability and Accountability Act in the USA and Personal Information Protection and Electronic Documents Act in Canada, implementation of patient radiation treatment planning would take time due to adaptation of the above laws and setup of the related policy in the hospital. Although cloud computing provider such as Amazon has guidelines to assist cloud developers for compliance with the American HIPPA regulations covering patient data privacy, related guidelines are still await in Canada. For preclinical treatment planning using cloud computing, since there is no small-animal privacy law, and dose calculation in fact does not require much personally

identifiable information over network, it can be implemented straightforwardly without any privacy and security concern.

V. CONCLUSIONS

The emerging cloud computing paradigm provides us a new option of radiation dose supercomputing. In this paper, I suggest using cloud computing in preclinical treatment planning employing Monte Carlo simulation for small animal. Future work includes developing a user-friendly web-based preclinical treatment planning system linked to the cloud for Monte Carlo dose calculation, where the user can freely select the number of compute nodes in the calculation.

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