Dose monitoring for adaptive radiotherapy: estimation and measurement of cumulated dose in deformable structures

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1. **The CAMI context**

Medical Interventions (surgery, interventional radiology, radiotherapy) can benefit from a significant boost for progress in terms of patient-specific optimal planning and performance. To fulfil the patient’s demands for quality, senior operators demand to see beyond the immediately visible, to be assisted in their real-time vital decisions and to provide access to enhanced dexterity, while junior operators need to “learn to fly” before being left alone, and public health authorities and companies require demonstrations of the medical benefit of innovations.

The Computer Assisted Medical Interventions LABEX (CAMI LABEX) strategic vision is that an integrated approach of medical interventions will result in breakthroughs in terms of quality of medical interventions, demonstrated in terms of medical benefits and degree of penetration of CAMI technology in routine clinical practice.

Among the different actions that will be undertaken in the scope of the CAMI LABEX, 6 to 10 doctoral works starting yearly are to be financed. Subjects dealing with topics within LABEXs scientific field and resulting from collaboration between different CAMI partners will be favoured. The following thesis proposal falls within this framework.

2. **Context and objectives**

Radiotherapy is one of the reference cancer treatments, mainly in prostate cancer. Major innovations have been recently developed in radiation techniques. Intensity Modulation Radiation
Therapy (IMRT) has first greatly enhanced the ability to deliver highly conformal dose distributions in complex anatomical configurations, such as in concave shape tumor (like the prostate or pelvic lymph nodes) with surrounding convex organ at risk (like the rectum and the bladder). However, such accurate delivery is a non-trivial task due to the fact that all the treatment is classically defined in only one planning CT. Indeed, several intra- and inter-fractional anatomical variations (e.g., organ movement and deformation) may potentially occur during the 7 to 8 weeks of treatment, leading to discordance between the very well optimized IMRT planned dose and the actual delivered dose (1). Imaging devices, such as cone beam computed tomography (CBCT), have been therefore integrated to the linear accelerators. They allow the visualization of the soft tissues, and if needed, to reposition the patient according to the tumor altered position (2-3). Deformations (such as rectal volume variations) are however more complex to correct and re-planning may be necessary, even if their frequency are not well defined.

The calculation of cumulative dose distribution, session after session, in the different deformable anatomical structures is indeed crucial to trigger re-planning at the right time, leading to the concept of Dose Guided Radiotherapy (DGRT) (4), strongly associated with the adaptive radiotherapy concept (5). However, this calculation is very complex and present several uncertainties. The cumulative dose can be estimated based on the use of new image acquisition during treatment (e.g., weekly CT or daily CBCT), and through deformable registration methods. After calculation of the dose distribution on the newly acquired images, the deformation can be estimated by applying deformable registration between the two images, corresponding to a deformation field that maps each voxel of the planning image to a corresponding point in the image acquired during treatment (Figure 1). A large number of registration algorithms, can however give different deformation fields for the same visual result and each proposed algorithm must be validated (6-7). Similarly, several methods for estimating the cumulative dose have been historically proposed. The most widely used is a trilinear interpolation of the dose by direct application of the deformation field on the map of dose (8). This interpolation can be however inaccurate in heterogeneous density areas (9). To improve the estimate of cumulative dose, several methods have been proposed. One possibility is to calculate the dose directly in the deformed geometry in order to overcome the interpolation errors (10). Another approach is to apply the resulting registration vectors not on the dose but on the energy and mass (9, 11). The contribution of energy and mass of each image tracking voxel is calculated.

The evaluation of all these approaches requires the use of a reference. To access such a reference, digital phantoms incorporating a biomechanical model of organs’ deformation can be used. They allow a full understanding of deformation and thus, could be used to develop a cumulative dose of ground truth. Another possibility is the use of physical deformable phantoms (12). Dose measurements at different points could be therefore performed and compared to the cumulative dose obtained by registration. However, accurate measurements of the impact of the deformation in physical phantoms are particularly complex, with very few data concerning patient "in vivo" measurements in the context of IGRT. Adapted technologies, such as miniaturized dosimeter, should be used for such in vivo dosimetry (13). Moreover, beyond the measures that will show differences, a statistical tool to make an objective decision of the need of adaptation or not is necessary. Such tools are available and have been already tested in the case of modification of calculation algorithms in dosimetry (14).
The objective of this PhD research project is to develop image processing and validation tools for cumulating the dose in irradiated deformable structures. The scientific objectives will focus therefore on the issues of dose monitoring for fully exploiting the benefit of IGRT (Image Guided RadioTherapy). The application will concern mainly the rectum in case of prostate cancer IGRT.

3. **Detailed subject**

The methodology developed in this project will aim to monitor the cumulative delivered dose in order to optimize the use of adaptive radiotherapy. The main issue appears therefore not only of applying the treatment based on the planning, but also of fitting the models and actions to observations accomplished in the course of the treatment, in order to take into account deformation or movement of the target and organs at risks.

The work will be more particularly focused on the four following steps:

1. To propose reliable methods for calculating the spatial distribution of cumulative dose over time, combining estimation of the 3D deformation map and local restoration of the dose, in order to develop a process of optimal readjustment of a reduced set of parameters during treatment. The elastic registration methods will allow reporting the cumulative dose in the different anatomical structures in the initial planning CT, from each daily CBCT. First, the anatomic deformations will be computed between the daily CBCT scans and the reference planning CT images. Then, using the deformations, the dose will be warped from the CBCT scans to the common pretreatment reference CT scan coordinate system, thus allowing cumulating the dose on the planning CT. This “cumulative” dose will be compared to the planned dose (Figure 1).

![DOSE WARPING Diagram](image-url)

*Figure 1: Process of cumulative dose calculation in a patient receiving radiotherapy in prostate cancer*
II. To evaluate the accuracy and the reliability of the proposed dose accumulation method by elaborating a reference numerical phantom models. These phantom models will be constructed by integrating simulation of organs’ anatomical deformations. Different metrics will be used to evaluate the proposed methods. A method for statistical assessment will be adapted for decision making (14).

III. Measurement of the "in vivo" rectal cumulative dose in case of prostate cancer radiotherapy by using the original SECURIDOSE real time in vivo dosimetric probe (15) placed within a physical deformable phantom. The phantom will be implemented either with simple object reproducing the geometry and deformations considered in the simulation (numerical phantom) or with controlled probe path reproducing the path of deformed anatomical points. The technical use of the probe is presented figure 2. The probe consists of a small volume of radioluminescent gallium nitride (GaN) as scintillator coupled with an optical fiber which ensures the transmission of the radioluminescence signal. The CT scan of the phantom with the probe will allow calculating the cumulative dose in the rectum thanks to the elastic registration method. The cumulated dose measurements and calculation will be compared.

Figure 2 : Principle of the SECURIDOSE system developed by the universities of Grenoble (UJF) and Lyon (UCBL) and Dosilab Co.

IV. Measurement of the real "in vivo" rectal cumulative dose in case of prostate cancer radiotherapy in real patients (figure 3). The SECURIDOSE probe (15) will be placed within the rectum during treatment fractions and the measurement of the dose will be performed. CBCT realized at the same treatment time will allow calculating the cumulative dose in the rectum.
using the elastic registration method. The cumulated dose measurements and calculation will be also compared.

![Figure 3: Example of possible in vivo measure with SECURIDOSE system](image)

4. Proposed course and method of collaboration within CAMI

This research project will bring together the expertise of teams involved in CAMI LABEX in Rennes and Grenoble. The LTSI Inserm U1099 (P.Haigron, A. Simon, Université de Rennes 1) will mainly deal with part I and part II with the collaboration of Inserm U836/E6 (Université Joseph Fourier, Grenoble) for this second part; part III will be mainly carried out by Inserm U836/E6 (J. Balosso, JY. Giraud and A. Chaikh, Université Joseph Fourier, Grenoble); and part IV will be developed associating Radiotherapy departments of CRLCC Eugène Marquis (R de Crevoisier, Rennes) and CHU A Michallon (C. Verry and A Chaikh, Grenoble).

Resources are specifically available in Grenoble for the development of the use of SECURIDOSE.

Parts I, III and IV can somehow start as parallel researches. However frequent exchanges will be necessary to help to build a comprehensive approach and to converge on the same concepts and practices.

The link between the different teams will be made by monthly web-conf or telephone conference and the doctoral student will spend some time along the three years alternatively in Rennes and Grenoble. One yearly meeting will also take place to deepen the exchanges and to pilot the researches of the doctoral student. These meetings could take advantage of similar meetings for the steering of the CAMI LABEX.
References


15. Ismail A. Etude et développement d'un système de dosimétrie in vivo implantable basé sur la radioluminescence du nitrure du gallium GaN. *Doctorat d'université Université Joseph Fourier, Grenoble 1*; 2009.