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Original paper

A support vector machine tool for adaptive tomotherapy treatments: Prediction of head and neck patients criticalities

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ABSTRACT

Purpose: Adaptive radiation therapy (ART) is an advanced field of radiation oncology. Image-guided radiation therapy (IGRT) methods can support daily setup and assess anatomical variations during therapy, which could prevent incorrect dose distribution and unexpected toxicities. A re-planning to correct these anatomical variations should be done daily/weekly, but to be applicable to a large number of patients, still require time consumption and resources. Using unsupervised machine learning on retrospective data, we have developed a predictive network, to identify patients that would benefit of a re-planning.
Methods: 1200 MVCT of 40 head and neck (H&N) cases were re-contoured, automatically, using deformable hybrid registration and structures mapping. Deformable algorithm and MATLAB® homemade machine learning process, developed, allow prediction of criticalities for Tomotherapy treatments.
Results: Using retrospective analysis of H&N treatments, we have investigated and predicted tumor shrinkage and organ at risk (OAR) deformations. Support vector machine (SVM) and cluster analysis have identified cases or treatment sessions with potential criticalities, based on dose and volume discrepancies between fractions. During 1st weeks of treatment, 84% of patients shown an output comparable to average standard radiation treatment behavior. Starting from the 4th week, significant morpho-dosimetric changes affect 77% of patients, suggesting need for re-planning. The comparison of treatment delivered and ART simulation was carried out with receiver operating characteristic (ROC) curves, showing monotonous increase of ROC area.
Conclusions: Warping methods, supported by daily image analysis and predictive tools, can improve personalization and monitoring of each treatment, thereby minimizing anatomic and dosimetric divergences from initial constraints.

Introduction

In modern radiation therapy (RT), kilo-voltage Cone Beam computed tomography (kV-CBCT) or megavoltage computed tomography (MVCT) devices integrated with an inline linear accelerator (LINAC) allow to keep under control patient daily anatomic variations and mismatch positioning during treatment sessions [1–3]. Rigid co-registrations (RR), through global translation and rotations, can correct macroscopic anatomical changes of the body and can detect setup errors by the registration of bony-soft tissue structures [4].

Beyond these checks, in Adaptive Radiation Therapy (ART) deformable transformation models should be taken into account to follow the organ motion and warping [5]. A daily contouring of organ at risk (OAR) and tumor might allow distributing the dose to the observed deformations [6]. By using a hybrid deformable image registration (HDIR) algorithms during treatments, a quantitative

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evaluation of warping become possible for each single fraction, enabling proper modifications of treatment plan related to the observed variations [7–9].

In ART approach, after RR, an automatic contour, a structure deformation and a re-plan should be done in clinical practice. However, taking into account time consumption and costs of human resources, all this workflow would be unfeasible for all patient cohorts [10,11]. Statistic outcome prediction is possible, but it remains very hard to consider multiple correlations simultaneously within clinical cases [12].

Machine learning methods, for early cancer diagnosis, prediction of clinical complications and biological outcomes, could improve the effectiveness of RT with the aim to develop a daily personalized plan based on automatic validated processes [13–15].

The unsupervised machine learning developed in this research allows quantitatively analysis of volumetric and/or dosimetric variations that may occur during radiation treatment weeks, to evaluate possible treatment failure causes or increasing in toxicity [16,17]. The aim of our study is to combine variables into a predictive model, to identify criticalities of specific fractions and to restrict re-planning to selected patients, thereby allowing ART techniques to be sustainable in terms of clinical practice for properly selected patients [7].

Materials and methods

Clinical data

Statistical sample is composed of 40 head and neck (H&N) patients (11 females and 29 males with 64 years of mean age), treated between 2013 and 2014 with same simultaneous integrated boost protocols delivered in 33 fractions. A total dose of 54 Gray (Gy), to the T + N regions and 66 Gy in the T area, defined using CT and PET, is being delivered. Based on QUANTEC constraints, for parotid glands a recommended mean dose limit <20 Gy was planned to avoid xerostomia [18,19]. A mean treatment period of 6 weeks is being considered (Table 1). The analysis of spinal cord, mandible, clinical target volume at the low dose (CTV54) and parotid glands (right and left) are being considered for the study reported.

Treatment planning system

ART methods and HDIR were implemented integrating a RayStation® (v.4.5.1.14, RaySearch Laboratories AB, Stockholm, Sweden) treatment planning system (TPS) in the workflow (Fig. 1), to make up the actual incapability of our Tomotherapy system (v.5.0.2) to perform deformable registration and evaluation, during the adaptive planning.

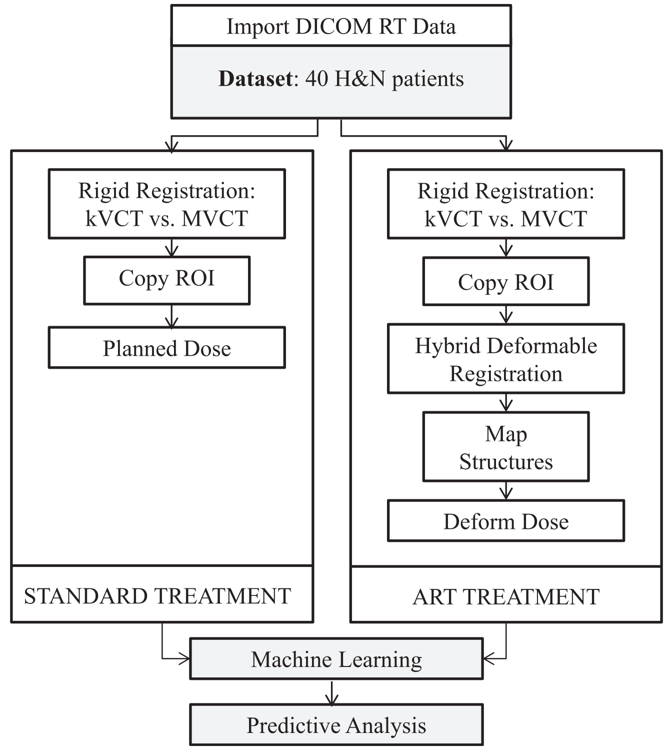

Figure 1. Standard vs. ART treatment workflow. The first phase is to import the DICOM RT file of each patient, from Tomotherapy workstation to RayStation TPS, creating a dataset of the H&N patients followed during the study. Later, for each patient, were carried out both the Tomotherapy standard treatment and the ART simulated treatment. At last, based on machine learning algorithms, a predictive analysis is available.

In the course of daily patient's setup, each MVCT study was acquired and transmitted automatically to a cloud network, via DICOM RT. To avoid and reduce the use of improper resources, we have developed dedicated python scripts that allow automating, during the night, of many manual tasks usually executed by the operators.

A RR between the reference planning CT (kVCT) and the daily MVCT was first performed to align the treatment, correcting and individuating both setup errors and patients' abnormal position due to local variations. The RR was carried out using an image registration tool of an external TPS. Based on preliminary check, the deformable registration algorithm has generated a mesh grid, for the warped regions of interest (ROIs), with a voxel-to-voxel map of the deformed vector field (DVF). A deformable grid with 0.20 cm of resolution was used to increase the image co-registration quality.

Table 1
Summary of patients' data. In the first row are reporting the total number (N) of patients with sex division. In the second row the mean value, standard deviation (STD) and range of data about patients' age (in years) and treatment duration (in days). In the third row mean value, standard deviation (STD) and range of data about H&N ROIs: volume (in cc) and dose max (in Gy) for spinal cord and mandible, volume (in cc) and dose average (in Gy) for CTV54 and parotid glands.

N Patients	40 (29 Male–11 Female)	
	Age (years)	Treatment duration (days)
Mean (±STD) Range	64 (±14) 22–90	31 (±2) 23–34

ROI	Spinal cord		Mandible		CTV54		Right parotid		Left parotid	
	Volume (cc)	Dose max (Gy)	Volume (cc)	Dose max (Gy)	Volume (cc)	Dose avg (Gy)	Volume (cc)	Dose avg (Gy)	Volume (cc)	Dose avg (Gy)
Mean (±STD) Range	28.8 (±14.2) 11.7–78.2	29.0 (±5.1) 15.8–60.0	65.9 (±14.6) 51.3–105.6	64.6 (±3.8) 52.4–71.8	503.6 (±175.5) 102.8–716.7	59.1 (±2.2) 53.6–59.4	25.1 (±8.6) 14.9–41.6	23.8 (±7.9) 3.5–50.2	24.6 (±8.7) 12.8–35.9	27.3 (±9.9) 13.3–62.3