Medical Engineering & Physics 37 (2015) 126–131

Contents lists available at ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

Technical note

On feature extraction and classification in prostate cancer radiotherapy using tensor decompositions

Auréline Fargeas[a,b], Laurent Albera[a,b,*], Amar Kachenoura[a,b], Gaël Dréan[a,b], Juan-David Ospina[a,b,d], Julie Coloigner[a,b], Caroline Lafond[c], Jean-Bernard Delobel[c], Renaud De Crevoisier[a,b,c], Oscar Acosta[a,b]

[a] INSERM, U1099, Rennes F-35000, France
[b] Université de Rennes 1, LTSI, Rennes F-35000, France
[c] Département de Radiotherapie, Centre Eugène Marquis, Rennes F-35000, France
[d] Escuela de Estadística, Universidad Nacional de Colombia – Sede Medellín, Colombia

ARTICLE INFO

Article history:
Received 30 July 2013
Received in revised form 11 August 2014
Accepted 25 August 2014

Keywords:
Classification
Canonical polyadic decomposition
Deterministic multi-way analysis
DIAG
Prediction of toxicity
Radiotherapy
Prostate cancer

ABSTRACT

External beam radiotherapy is commonly prescribed for prostate cancer. Although new radiation techniques allow high doses to be delivered to the target, the surrounding healthy organs (rectum and bladder) may suffer from irradiation, which might produce undesirable side-effects. Hence, the understanding of the complex toxicity dose–volume effect relationships is crucial to adapt the treatment, thereby decreasing the risk of toxicity. In this paper, we introduce a novel method to classify patients at risk of presenting rectal bleeding based on a Deterministic Multi-way Analysis (DMA) of three-dimensional planned dose distributions across a population. After a non-rigid spatial alignment of the anatomies applied to the dose distributions, the proposed method seeks for two bases of vectors representing bleeding and non bleeding patients by using the Canonical Polyadic (CP) decomposition of two fourth order arrays of the planned doses. A patient is then classified according to its distance to the subspaces spanned by both bases. A total of 99 patients treated for prostate cancer were used to analyze and test the performance of the proposed approach, named CP-DMA, in a leave-one-out cross validation scheme. Results were compared with supervised (linear discriminant analysis, support vector machine, K-means, K-nearest neighbor) and unsupervised (recent principal component analysis-based algorithm, and multidimensional classification method) approaches based on the registered dose distribution. Moreover, CP-DMA was also compared with the Normal Tissue Complication Probability (NTCP) model. The CP-DMA method allowed rectal bleeding patients to be classified with good specificity and sensitivity values, outperforming the classical approaches.

1. Introduction and related work

External beam radiotherapy is one of the standard treatment for localized prostate cancer. The main challenge in Prostate Cancer RadioTherapy (PCRT) is to deliver the prescribed dose to the clinical target (prostate and seminal vesicles) while minimizing the dose to the neighboring Organs At Risk (OAR), namely the rectum and the bladder, and thus avoiding subsequent toxicity-related events. The precision of the radiotherapy has been recently increased by new techniques such as Intensity Modulated RT (IMRT) and Image Guided RT (IGRT) [7], which allows the dose to be increased to the target. However, the potential secondary effects due to the delivered dose to the OAR are far from being completely explained [11]. Therefore, unraveling the underlying local dose–volume effect toxicity relationships and identifying patients at higher risk, appears as a cornerstone in further definitions of constraints for personalized IMRT planning. In case of rectal toxicity, different studies have shown a correlation between dose, volume, and secondary effects [10,23]. However, most of the proposed models have been solely based on the dose–volume histograms such as the Normal Tissue Complication Probability (NTCP) model [20,26,8], thereby loosing spatial information. These methods do not perform a formal classification exploiting the spatial characteristics of the dose distributions since they considered the organs as having homogeneous radio-sensitivity. Buettner et al. [4,3] addressed the issue of spatial

* Corresponding author at: Université de Rennes 1, LTSI, Rennes F-35000, France. Tel.: +33 223235058.
E-mail address: laurent.albera@univ-rennes1.fr (L. Albera).

http://dx.doi.org/10.1016/j.medengphy.2014.08.009
1350-4533/

information loss. In [3], a classification approach based on locally connected neural network using a two-dimensional dose-surface maps was performed. In [4], they proposed a parameterized representation of the dose to describe its geometrical properties, such as the eccentricity, and its lateral and longitudinal extent which still remains approximative in terms of spatial location. New methods aimed at jointly taking advantage of the Three-Dimensional (3D) dose distributions, unraveling the subtle correlation between local dose and toxicity at a voxel level to classify patients at risk, are still to be devised.

Performing classification by simultaneously exploiting the 3D signal across a population is challenging because the inter-individual anatomical variability leading to a misalignment of information. To cope with this issue, non-rigid registration methods have been employed in order to map all the data to a common coordinate system where voxel analysis may be meaningful in terms of spatial localization [1,31]. Following this idea, previous classification approaches exploiting the 3D signal across a given population have been proposed. For instance, Principal Component Analysis (PCA) was used by Fripp et al. [12] to discriminate Alzheimer's disease and normal elderly control participants based on non-rigidly registered 3D Positron Emission Tomography (PET) images. With the same objective, Higdon et al. [15] performed a comparison of different classification methods (logistic regression, Linear Discriminant Analysis (LDA) and quadratic discriminant analysis) which were used after a data reduction algorithm (PCA and Partial Least-Squares (PLS)) using FDG-PET images. A leave-one-out cross validation showed that better results could be obtained when PLS and LDA are used for data reduction and classification, respectively. Nevertheless, it appears that methods based on PLS slightly outperform PCA-based methods on diagnostic accuracy. In the context of rectal bleeding in PCRT, authors proposed in [9] to use PCA to analyze non-rigidly registered dose distributions. The authors identified one basis of orthogonal vectors from 3D dose distributions of the whole database (patients with and without rectal bleeding) allowing for classification. More precisely, the new patient to be classified is projected on subspace spanned by the more discriminant features (eigenvectors selected in the training step) that better divide the two classes. Another paper, proposed by Phan et al. [25], has considered the problem of feature extraction and classification based on orthogonal or nonnegative tensor (multi-way) decompositions and higher order (multilinear) discriminant analysis using TUCKER decompositions, whereby input data are considered as tensors instead of more conventional vector or matrix representations. The algorithms are verified on three different datasets (images of objects, handwritten digits and EEG). Hunyadi et al. [16] proposed to detect seizure using the nuclear norm regularization, that allows the conveying of the structural information of the multichannel EEG matrix. More recently, Signoretto et al. [28] developed a learning framework and extends regularization via nuclear norm to the case of higher order arrays.

We introduce, in this paper, a novel method based on a Deterministic Multi-way Analysis (DMA) of 3D planned dose distributions across a population. The proposed technique aims at finding two bases of vectors from 3D non-rigidly registered dose distributions of patients with and without rectal bleeding, respectively, from a Canonical Polyadic (CP) decomposition [29,6,18] of two appropriate Fourth Order (FO) arrays. Unlike [4], it takes advantage of complete 3D information when performing decomposition without any parametrization, so that each voxel is independently considered. The uniqueness of the subspaces spanned by both computed bases is ensured by looking for rank-1 basis vectors. The orthogonality constraint imposed by PCA is then relaxed. A new patient is thus classified according to its distance to the subspaces spanned by both bases. Tests on real clinical data demonstrate an improved sensitivity and reliability for group analysis. The novel method, named CP-DMA, opens the way for potential applications in IMRT planning.

2. Materials and methods

The different steps of the proposed CP-DMA method are summarized in Fig. 1. After a pre-processing step, where 3D doses are non-rigidly aligned, the training of the CP-DMA consists in learning from the data two vector bases, $(\boldsymbol{e}_1^{(1)}, \ldots, \boldsymbol{e}_{R^{(1)}}^{(1)})$ and $(\boldsymbol{e}_1^{(2)}, \ldots, \boldsymbol{e}_{R^{(2)}}^{(2)})$, spanning two vector subspaces, $\mathcal{E}^{(1)}$ and $\mathcal{E}^{(2)}$, characteristic of patients with and without toxicity, respectively. Then a new patient is classified by evaluating its distance to $\mathcal{E}^{(1)}$ and $\mathcal{E}^{(2)}$.

2.1. Data and pre-processing

A total of 99 patients treated for localized prostate cancer with IMRT were included in the study. The used treatment planning system was Pinnacle V7.4 (Philips Medical System, Madison, WI). The total prescribed dose was 46 Gy to the seminal vesicles delivered in 4.6 weeks, and 80 Gy to the prostate delivered in 8 weeks, with a standard fractionation of 2 Gy per fraction. The patient positioning, CT acquisition, volume delineations and dose constraints complied with GETUG 06 recommendations as described in [5]. For the rectal, the constraints were the maximal dose had to be lower than 76 Gy (measured within at least 1.8 cm^3) and a V72 Gy[1] lower than 25%. The size of the planning CT images in the axial plane was 512 × 512 pixels, with 1 mm image resolution, and 2 mm slice thickness. The median follow-up was 38 months, with a minimum of 24 months for all patients. Rectal toxicity events were prospectively collected and scored according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. The events were defined as rectal bleeding (≥ Grade 1), at least one episode occurring between 6 months and 2 years after RT. Patients with a history of hemorrhoids were not allowed to be scored as Grade 1 bleeding. A total of 17 patients presented at least a Grade 1 late rectal bleeding event. Patient's planned CT and dose distributions were elastically registered with the demons algorithm [31], on a single coordinate system (template) by combining the CTs and organs delineations as explained in [1]. A representative individual was selected as a template to be used as the common coordinate system. This typical individual maximized a similarity criterion which is the sum of squared differences computed after rigid registration. In this paper, we focused on rectal bleeding and the dose received by the rectum.

2.2. Subspace identification

Multi-dimensional arrays are those with more than two entries. The CP-DMA method uses two particular FO arrays in order to identify both vector subspaces $\mathcal{E}^{(1)}$ and $\mathcal{E}^{(2)}$. The first $(N_1 \times N_2 \times N_3 \times P^{(1)})$ array, denoted by $\mathcal{T}^{(1)}$, is built by concatenating, in the fourth dimension, the 3D dose distributions of the patients with rectal bleeding. Similarly, the second $(N_1 \times N_2 \times N_3 \times P^{(2)})$ array, denoted by $\mathcal{T}^{(2)}$, is obtained by concatenating the 3D dose distributions of the patients without rectal bleeding. Let $\mathcal{S}^{(i)}$ be the $F^{(i)}$-dimensional subspace spanned by the $P^{(i)}$ 3D dose distributions $\mathcal{T}^{(i)}_{:,:,:,p}$ concatenated in the FO array $\mathcal{T}^{(i)}$. The dimension $F^{(i)}$ of $\mathcal{S}^{(i)}$ is necessarily lower than $P^{(i)}$. We obviously assume that the $R^{(i)}$-dimensional subspace $\mathcal{E}^{(i)}$ is included in (and not necessarily equal to) $\mathcal{S}^{(i)}$. Consequently, a vector basis of $\mathcal{S}^{(i)}$ can be obtained by completing the vector basis $(\boldsymbol{e}_1^{(i)}, \ldots, \boldsymbol{e}_{R^{(i)}}^{(i)})$ of $\mathcal{E}^{(i)}$: let $(\boldsymbol{e}_1^{(i)}, \ldots, \boldsymbol{e}_{R^{(i)}}^{(i)}, \boldsymbol{e}_{R^{(i)}+1}^{(i)}, \ldots, \boldsymbol{e}_{F^{(i)}}^{(i)})$

[1] (volume receiving at least 72 Gy)