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A Delta TCP tool, based on biological parameters of tumor voxels, to quantify effectiveness of different dose distributions in tumor control

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Introduction

Tumor control is the principal aim of curative radiotherapy. For the last decades great advances have been achieved on radiotherapy for delivering highly conformal dose distributions allowing for dose escalation to the most resistant areas. In order to adequately develop strategies for the redistribution of dose (or dose boosting), the predicted effectiveness of the created dose distribution should be quantified in terms of tumor control.

In 1999 Sánchez-Nieto and Nahum introduced the concept of the Δ TCP DVH-bin-based model. The aim of their work was to provide a tool to quantitatively evaluate the influence of delivering non-uniform dose to a tumor and evaluate how this affects the probability of controlling that tumor.

In this work, we propose a Δ TCP voxel-based model using the patient information and the computational tools available nowadays. The developed tool evaluates the impact on the TCP of different dose distributions with the possibility of incorporating information about the oxygen distribution and number of clonogens within a voxel in the target.

Methods

The software was developed on C++ language using ITK.

As input data, the following information is uploaded into the program: anatomical information of the patient (Planning CT), tumour contour (CTV), possible sub volumes within the tumour (BTV) and dose distribution of either 1 or 2 different plans, one used as a reference and the other one as a tested dose distribution.

If previous information on the tumour sub volumes is available (i.e. PET-defined hypoxic area), oxygenation levels are assigned to the tumour, being expressed as oxygen histograms associated to different regions of the tumour. Oxygen-corrected radiosensitivity parameters, $\alpha(p)$, are calculated using literature equations and parameters for all the possible oxygen pressures within the histograms.

Using this information, the probability of controlling all the cells in every voxel, or Voxel Control Probability (VCPs), is calculated using the linear-quadratic model. This is done for both, the tested dose distribution (D_t) and for the reference dose distribution (D_r) taking into account the local $\alpha(p)$ and, if available, the specific clonogenic cell density.

If there is only one dose distribution and the oxygenation levels available, VCPs are calculated considering one dose distribution, but making the difference if the oxygen levels are taken into account or not.

It was shown by Sánchez-Nieto and Nahum that the VCP distribution by itself was not a useful indicator due to the lack of sensibility to changes on the dose .

Because of this, using the VCPs calculated on the previous step, a Δ TCP is defined for every (ijk) voxel as the impact on the final TCP of having the tested dose ($D_{t_{ijk}}$) instead of the reference one ($D_{r_{ijk}}$).

This Δ TCP is computed according to equation (1), where $TCP((p)_x)$

is calculated as the multiplication of all the VCPs for $(p)_x$. Patient-to-patient variabilities are considered using $\alpha_x = 0.35 Gy^{-1}$, $\beta = 0.06 Gy$ and constant λ . Homogenous number of clonogenic cells in assumed across the tumour if further information is not available.

$$\Delta TCP_{ijk} = \sum_{x=1}^n (g_x) TCP(\alpha(p)_x) \left[1 - \frac{VCP_{ijk}(\alpha(p)_x, D_r)}{VCP_{ijk}(\alpha(p)_x, D_t)} \right] \quad (1)$$

As voxel influences are sometimes too small, volume based calculations were also evaluated. In this case the (ijk) on the equation, will be changed to the identification of the different sub volumes.

Results ---

For testing the tool two different HN cases were used. The first cases is a treatment delivered with homogeneous dose through the tumor without considering oxygenation levels. Based on FDG PET images three differently oxygenated regions were identified. The tool was used to compute the Δ TCP distribution considering as D_r a uniform dose and oxygen distributions and as D_t the effect of the same dose distribution considering the information about the oxygenation inhomogeneity. Voxel wise, and volume wise calculations were computed.

For second case included on this study 2 different dose distributions are available, a homogeneous dose and a boosted dose distribution. The tool in this case was tested to compare the impact of the boost, in both cases considering the inhomogeneity on the oxygen distribution.

Results of the examples can be found on the attached table

Conclusions

A functional useful tool was created and tested; It I possible to identify the impact on the TCP of delivering inhomogeneous dose to inhomogeneously oxygenated tumors. Further improvements will be done to the tool allowing to create “megavoxel” considering regions with similar oxygenation level and delivered dose.

Country

Chile

Institution

Pontificia Universidad Católica de Chile

Primary author: FABRI, Daniella (Pontificia Universidad Católica de Chile)

Co-authors: LÓPEZ-MEDINA, Antonio (Galaria-Hospital do Meixoeiro-Complexo Hospitalario Universitario de Vigo); GAGO-ARIAS, Araceli (Pontificia Universidad Católica de Chile); SÁNCHEZ-NIETO, Beatriz (Pontificia Universidad Católica); GUERRER-URBANO, Teresa (Guy’s and St Thomas’ Hospital)

Presenter: FABRI, Daniella (Pontificia Universidad Católica de Chile)

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