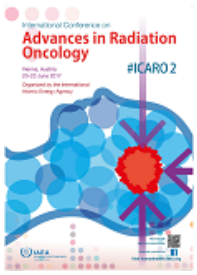

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Normal tissue complication probability calculation in normal and hypo-fractionated radiotherapy of head & neck tumors

Thursday, June 22, 2017 10:35 AM (5 minutes)

Although radiobiological modeling has a lot of promise in clinical applications it is still an investigational tool. The linear-quadratic (LQ) formalism is the tool most commonly used for quantitative predictions of dose/fractionation. Hypo-fractionation requires consistent iso-effect dose calculations and the LQ formalism is appropriate for treatments with this dosing scheme. Nevertheless various Normal Tissue Complication Probability (NTCP) models have been used the most commonly applied models is the Lyman, Kutcher, Burman (LKB) model. Others like Källman relative seriality model have been also used. Dose magnitudes with "biological sense" like Equivalent Uniform Dose (either physical EUD or biologically effective EUBED) will improve the predictions made with these response models. Other authors have recommended some corrections to alpha/beta values (*effective* alpha/beta) which take into account both the dose heterogeneity and the volume effect for the late-responding normal-tissue. Nowadays it is running in our center the HYPNO project granted by IAEA which is directed to establish an optimal radiotherapy hypo-fractionation schedule for head and neck cancer (HNC) treatment that permit to take a better advantage of own equipment availability by means of an enhanced quality assurance program for 3D-CRT and IMRT modalities. The goal of the present work is to evaluate the differences in the estimation of NTCP using the LKB and Källman models for hypo-fractionated treatment in radiotherapy of HNC and the comparison with the normo-fractionation schedule. Different sources of variations: radiobiological parameters variability and heterogeneity of spatial dose distributions as well as the evaluation of adequate choice of dose magnitudes (EUD, uniform UBED or mean BED) were considered.

The dose data used in this work were obtained from the IMRT plans of patients bearing H&N tumors those included in the IAEA - HYPNO study at INOR. The data belong to two branches: Branch A: normo-fractionated schedule: 66Gy in 33 fractions 1.6Gy/fraction both given in 5 fractions per week and Branch B: hypo-fractionated schedule: 55Gy (higher dose) in 20 fractions giving 2.75Gy per fraction in 5 fractions per week. The DICOM RT files were exported from the TPS as anonymous and the DVHs for the spinal cord, brainstem, right and left parotids, pharynx and esophagus was built.

The mean BED, EUD (Nimierko generalized model) were calculated from the DVHs. The dose delivered for a particular treatment scheme was expressed in terms of the Equivalent Dose at 2Gy fractions (EQD2Gy) using either mean BED or UBED. The NTCP was calculated for both branches using the LKB and Källman models adapting its formulation by inclusion of LQ model parameters through the estimation of EQD2Gy calculated from mean BED or UBED. The maximum likelihood method was used to fit the NTCP models to the data. An average dose-volume histogram was estimated by averaging the volume fractions which receives EQD2Gy in the same dose interval for a given OAR. The NTCPs values for both models were also estimated using this average EQD2Gy-volume histogram. The feasibility of this approach was compared with the results using the individual information of each patient.

The ranking of the models was based on Akaike's information criterion (AIC). The effect of alpha/beta variability on NTCP was studied generating normal-distributed sequences in the interval like mean value +/- standard deviation. A sequence (2000-3000) of alpha/beta values was generated and the NTCP for each one was calculated. The set of alpha/beta was generated using the Box-Müller polar method. The mean NTCP for the OAR was then calculated by averaging overall NTCP values.

Conclusion

The variability of alpha/beta in the calculation of NTCP produces curves less steep than those when a fixed alpha/bta value is used. The effect increases as alpha/beta is diminished and it was also observed for both branches. Similar effects have been described for tumor control curves which must be included in the algorithm for biological evaluation of radiotherapy plans. There was no significant difference between the calculations done with the NTCP models used considering the AIC calculation. The mean BED produced a similar description than those made with EUD or UBED even considering the differences in the consideration of volume effects. Nevertheless the *effective* alpha/beta correction will be useful for the biological evaluation of treatment plan that includes the tumor DVH.

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