Proton therapy of cancer offers potential clinical advantages compared with photon radiation therapy for many cancer sites. However, the treatment cost with proton is much higher than with conventional radiation. The objective of this study is to explore a decision method based on four analyses: dosimetric, global with gamma index, radiobiologic and statistic to compare proton versus photon treatments plans and select the best treatment for each patient.

For each case, 2 treatment plans should be generated, the dose in Plan 1 can be calculated with photons, and in Plan 2 with protons. Then the following steps can be carried out to check the benefit of treatment and to orient the patient to protons or photons, as shown in figure 1:

**Dosimetric analysis:** the dosimetric data derived from DVH metrics for each plan can be compared. This includes quality indices and dosimetric data for target and dose constraints for OAR.

**2D gamma (γ):** the γ-maps with cumulative Pixels-γ-Histograms can be used to evaluate the under/overestimation dose [1].

**Statistical analysis:** the bootstrap method using N random iterations can be used to assess the significance of differences, and to estimate the 95% confidence intervals. Wilcoxon and Spearman’s rank tests were used to calculate p-values and correlation coefficients.

**Clinical evaluation:** the balance TCP/NTCP can be calculated using a radio biological model, such as Uniform Equivalent Dose (EUD) and Lyman models [2,3]. Then Uncomplicated Tumor Control Probability (UTCP) can be calculated as: $\text{UTCP} = \sum_{i} \text{TCP}_{i}(1-\text{NTCP}_{i})$, where “$i$” includes the organs at risks that should be considered for each cancer site.

**QALYs:** in order to quantify the benefit in terms of QALYs (quality-adjusted life-years), the physical NTCP predicted from DVHs should be calibrated and multiplied with the “Utility value”, calculated as:

$$\text{NTCP}_{\text{QALY}} = \text{NTCP} \times U \times \gamma$$

where U varied from zero to 1, including age, the number of years that survivors would be expected to gain because of the radiotherapy, grade, … etc., as shown in figure 2.

The cost utility ratio: can be calculated as

**Conclusion**

**Discussion and Conclusion**

The comparison of DVH metrics should be carried out using the most accurate dose calculation algorithms, and after a major effort to optimize the plans. Then, for PTV and OARs, the dosimetric data can be fairly compared, as shown in figure 3. The predicted TCP/NTCP also depends on the performance of dose calculation methods [4,5]. Using TCP/NTCP data will significantly influence the predictive QALY, justifying the use of more accurate algorithms. Otherwise, it would be difficult to justify a treatment using photons vs protons with lower predicted toxicity. Using, as an example, AAA showed significant difference compared to pencil beam density correction methods (PB-MB or EPL). The relevant lung TCP/NTCP data showed lower TCP and higher NTCP with AAA is compared to PB-MB, as shown in figure 4.

We propose here, a realistic method to approach a clinical decision to choose protons vs photons. The decision analysis methods were applied to the concept of UTCP. The analysis tools to rank treatment plans are based on expected QALY. Among other considerations, this should attract attention about the choice of “clinical parameters” to estimate TCP/NTCP, otherwise important uncertainties can be expected. The matching between γ-maps with CT-Scan visualize the anatomical location of dose differences confirming if the benefit is located on PTV or OAR. The better plan should show more predicted dose for target and/or less dose to the OAR. The introduction of QALY for medical decision should be carefully done and take very accurately account of the consequences of the treatments by the best possible NTCP prediction for all irradiated healthy tissues.

References:


