Evaluation of plan quality based on a novel plan difficulty index and its preliminary application in radiotherapy

Qicheng Li, Huanli Luo, Xianfeng Liu, Mingsong Zhong, Han Yang, Dan Tao and Fu Jin
Chongqing Key Laboratory of Translational Research for Cancer Metastasis and Individualized Treatment, Chongqing University Cancer Hospital, Chongqing, China

ABSTRACT
To propose a novel plan difficulty index (PDI) and scoring model and evaluate its application in intensity-modulated radiation therapy (IMRT) plans for lung cancer. Thirty-four optimal IMRT plans of lung cancer were retrospectively analyzed. These plans have been clinically implemented to treat patient. Four scoring models, segmented uniform (SU), segmented non-uniform (SNU), non-segmented uniform (NSU) and non-segmented non-uniform (NSNU), containing 12 metrics, were designed for plan evaluation. A novel PDI was defined to quantify how easy or difficult a treatment plan is to make and verify the rationality of scoring models, followed by the evaluation of the relationship between PDI and scoring value of plan. Significant differences were found between different scoring models. These scores were 72.34 ± 10.10, 69.40 ± 12.06, 53.11 ± 10.44 and 50.30 ± 11.67 for SU, SNU, NSU and NSNU models, respectively. The pass rate (64.7%) of plans with scores of ≥70 was superior in the SU model compared to that of other models (SNU: 38.2%, NSU: 5.9%, and NSNU: 2.9%). The mean PDI of 34 plans was 4.20 for the uniform scoring model and 4.47 for the non-uniform scoring model. Negative correlations were shown between PDI and scores [SU: −0.52 (P < 0.05), SNU: −0.49 (P < 0.05), NSU: −0.59 (P < 0.05), and NSNU: −0.53 (P < 0.05)]. PDI is feasible for IMRT plan evaluation for lung cancer, and the SU scoring model was superior to NSU, SNU, and NSNU models in clinical practice.

1. Introduction
Precision radiotherapy has certain challenges because of changes on location, size, and shape of tumors, plus the sparing of organs at risk (OARs) and the remaining volume at risk (RVR) around them. Thus, an effective treatment plan and its accurate delivery are required (AI AAE: ICRU, 1999; Gregoire et al., 2010). With the improvement of computer software and dose calculation algorithms, we can obtain a plan with high quality by inverse planning techniques, such as intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) (Oderinde & Du Plessis, 2019; Rehman et al., 2018). However, there are still many differences in plan quality (Li et al., 2009; Nelms, Tome et al., 2012; Yamamoto et al., 1999). Even with the same structure sets and the same dose constraints within identical computed tomography (CT) images, the quality of plans designed by different planners can differ (Nelms, Robinson et al., 2012).

The level of plan quality directly affects the clinical outcome (Clark et al., 2015; Peters et al., 2010). The conventional process of plan evaluations in clinical contexts is that isodose curves (such as 95% of the prescribed dose) are reviewed layer by layer in CT images and dose volume histograms (DVHs) are used to check the planning target coverage [such as V95% (the target volume receiving at least 95% of the prescribed dose), D98% and D2% (dose covering the 98% and 2% of the volume of target), and so on] and its conformity index and homogeneity index (CI, HI), and then some dose metrics of OARs and remaining healthy tissue [such as Dmax<40 Gy for spinal cord, V20 (the volume of lung receiving a dose of 20 Gy) <30% and V30 < 20% for lung, V30 < 40% and V40 < 30% for heart] are also checked. However, for the complex targets and OARs, this process takes more time, even for the experienced evaluator. On the other hand, for highly similar tentative plans that involve many OARs sparing, the decision is made based on qualitative impressions informed by subjective prior experience (Stavreva et al., 2010), but sometimes it’s hard to look for some differences among plans by the naked eye. Also, numerous study document that such decision-making is often quite variable (Moore et al., 2012). Then, the question is posed to the evaluator: how does one know that they are looking at the best achievable plan for their patient?

Some scholars have done much work and issued some plan quality evaluation methods, such as plan quality metric (PQM) (Nelms, Robinson et al., 2012),...
dose distribution index (DDI) (Alfonso et al., 2015) and radiation planning index (RPI) (Ślosarek et al., 2008). The PQM with 14 submetrics can remove any ambiguity of the plan objectives and provide a fair platform to compare plan results; but, it is important to note that the PQM algorithm employed does not purport to describe the best clinical plan (Nelms, Robinson et al., 2012). The DDI is proposed to assist in the choice of radiotherapy treatment plans for any given cancer patient and defined as a weighted sum of three components (the dose coverage, conformity, and homogeneity on the planning target; OARs; RVR); but there is a need to discuss the priority of target coverage versus the sparing of OAR and RVR, and also the positional relationship between the targets and organs is not considered (Alfonso et al., 2015). The study on RPI formula was focused on the relative comparison between alternative plans for the same patient rather than establishing absolute scoring levels, and also treatment plan comparison among different patients is inefficient when using RPI values (Ślosarek et al., 2008). So far, these evaluation methods have not been widely applied in the clinic.

The evaluations of plan quality in clinic involve the radiation oncologists (ROs) requirements, as well as technical feasibilities of the plans. There are situations where the ROs have to consider tradeoffs between coverage of the planned target volume (PTV) and OARs dose that have exceeded set tolerance. Some ROs would consider prioritizing the PTV coverage over the OARs depending on whether they are serial or parallel in nature or considered ‘quality of life goals,’ e.g. the parotid gland. Thus, how can one find a more effective plan evaluation method that can be used in clinical contexts. The aim of this study is to establish a scoring model for plan quality, based on quality metrics, which are derived from the DVHs generated in the treatment planning systems (TPS), as well as physical metrics (such as the conformation number (CN) (Gintz et al., 2016, Riet et al., 1997) CI (Shaw et al., 1993), and HI (Feuvret et al., 2006). Another aim is to propose the novel concept of plan difficulty index (PDI) taking the positional relationship between the targets and organs into account, followed by analysis of the correlation between PDI index and scoring value of plan.

2. Methods

2.1. Patient case

Thirty-four patients diagnosed with lung cancer were selected by a sampling method. Their treatment plans and standard structures contoured at the time of RT treatment planning were recovered and retrospectively analyzed in this study. These patients had already undergone treatment in the supine position by using a fixation of a thermoplastic mask with their arms elevated and free-breathing (FB). The characteristics of patient, tumor, treatment, etc. were shown in Table 1.

2.2. CT images and anatomy contours

All simulation images were obtained by the Brilliance Big Bore CT 16-slice scanner (Philips Medical Systems, Cleveland, OH, USA) and had the scanning range from the cricoid cartilage to the second lumbar vertebra including the whole lung.

On all of the patients’ images, the gross target volume (GTV), clinical target volume (CTV) and PTV were contoured according to the definition of international commission on radiation units and measurements (ICRU) reports No.62 (Al AAE: ICRU, 1999). A margin of 6 mm (for squamous cancers) or 8 mm (adenocarcinomas) around GTV and CTV in the anterior–posterior and right–left directions was used to determine the CTV and PTV; in the superior–inferior direction, to copy GTV regarded as CTV according to the actual situation and 10 mm margin to CTV generated PTV. The OARs (such lung, heart, spinal cord, etc.) were outlined by ROs according to RTOG1106. The volumes, equivalent circular radius, distances among the geometric centers and minimum edge distances were recorded and measured for targets and OARs, showed in Table 1.

2.3. Plan information and its reevaluate

All plans have been clinically implemented to treat patient. These plans were optimized by the experienced planner using Varian treatment planning software Eclipse version 11 (Varian Medical Systems, Inc., Palo Alto, CA) and sliding-window technology was employed, and reviewed by two experienced ROs before treatment. The prescription dose was 60 Gy in 30 fractions to the PTV. A 95% of the prescription dose covering 100% of the PTV was required. The doses to OARs were distributed according to the RTOG1106.

Feasibility DVH in PlaniQ™ (Sun Nuclear Corp., Melbourne, FL) (Fried et al., 2017, Nelms et al., 2015) were employed to audit whether further optimization was possible for each desired metric in 34 plans. The feasibility DVH has four zones: probable (green), challenging (yellow), difficult (orange), and impossible (red), as shown in Figure 1. In post-plan analysis, when an actual plan exported from TPS is achieved and loaded, that plan’s resulting DVH will be plotted over the Feasibility DVH (black line in Figure 1), showing which zones it achieved and highlighting OARs that were preferentially spared (perhaps even to the point of removing dose coverage from the target volumes) (Jiang et al., 2016).
Table 1. Characteristic of patient, tumor, treatment, position, and so on.

| Cohort                | Value               | Cohort                | Value               |
|-----------------------|---------------------|-----------------------|---------------------|
| Number of patients    | 34                  | PTV volume, cm³       |                     |
| Age, years            | Mean ± SD 61.41 ± 9.24 | volume of Lung structure, cm³ | Mean ± SD 114.60–1142.00 |
| Range                 | 40–79               | Range                 |                     |
| Sex                   | Male 28             | Mean ± SD 3354.82 ± 1124.16 | Range 1433.90–5532.90 |
| Female                | 6                   | Mean ± SD 607.47 ± 19.00 | Range 383.60–809.00 |
| Histology             | Squamous cell carcinoma 14 | Equivalent circular radius of PTV, cm | Mean ± SD 9.15 ± 1.63 |
|                       | Adenocarcinoma 10    | Equivalent circular radius of Lung, cm | Mean ± SD 18.34 ± 2.10 |
|                       | Small cell carcinoma 7 | Equivalent circular radius of Heart, cm | Mean ± SD 10.46 ± 0.72 |
|                       | non-Small cell carcinoma 3 | Distances between GC of PTVs and lungs, cm | Mean ± SD 6.64 ± 2.01 |
|                       | FIGO stage, n II    | Distances between GC of PTVs and hearts, cm | Mean ± SD 9.90 ± 2.23 |
|                       | Ill 15              | MED between PTVs and spinal cords, cm | Mean ± SD 6.76–16.98 |
|                       | IV 15               |                      |                     |
|                       | Unknown 2           |                      |                     |
| CT slice thickness, mm| 5                   |                      |                     |
| Tumor location        | Central location 26 |                      |                     |
|                       | Peripheral location 8 |                      |                     |
| Tumor Laterality      | Right 16            |                      |                     |
|                       | Left 18             |                      |                     |
| EBRT dose             | 60 Gy/30 F          |                      |                     |
| Beam energy           | 6 MV                |                      |                     |
| Number of beams       | 5 to 8              |                      |                     |

Abbreviations: SD, standard deviation; FIGO, International Federation of Gynecology and Obstetrics; CT, computerized tomography; EBRT, external beam radiotherapy; PTV, planned target volume; GC, geometric center; MED, Minimum edge distances; Lung structure or Heart structure: the volume of the normal lung or heart minus GTV (Gross tumor volume).

Figure 1. An example for Lung structure in feasibility DVH™, comparing of the DVH in TPS with the feasibility DVH in PlanIQ. The black curve represents the DVH exported from an actual plan in TPS. The Lung structure was generated by the whole lung subtracting GTV.

2.4. Plan scoring model

To create a plan scoring model, a plan quality algorithm need to be defined. The plan quality algorithm is a collection of components and each component consists of two parts: the metric and the metric score function. The metric is the result to generate from the plan, structure set, and dose data. PlanIQ™ system has a library of metric options that includes simple metrics [such as region-of-interest (ROI) min, ROI mean, and ROI max dose, global max dose], DVH metrics (dose-at-volume, volume-at-dose, etc.), published metrics (conformation number, homogeneity index, inhomogeneity index), and other useful metrics (serial slice OAR evaluation, global max location). Considering conventional treatment guidelines in our institution, 12 metrics were defined in this study, as shown in Table 2. In Table 2, the Conformation Number (CN) was defined in Eq.(1), as following:

\[ CN = \frac{V_T \cdot ref^2}{V_T \times V_{ref}} \]
Table 2. Two score distributions for 12 metrics, maximum sum of values = 100.

| Type       | Metric       | Definition                                      | Uniform score | Non-uniform score |
|------------|--------------|-------------------------------------------------|---------------|-------------------|
| For PTV    | V₃₇          | Percent of PTV volume ≥ 57 Gy                   | 8.33          | 15                |
|            | V₆₃          | Percent of PTV volume ≥ 60 Gy                   | 8.33          | 10                |
|            | V₆₆          | Percent of PTV volume ≥ 66 Gy                   | 8.33          | 10                |
|            | CN₉₅         | CN under the reference dose of 57 Gy            | 8.33          | 10                |
|            | D₀,₀₃        | Maximum dose of PTV                            | 8.33          | 5                 |
| For OARs   | Lung         | V₅           | Percent of Lung volume ≥ 5 Gy                    | 8.33          | 6                 |
|            | V₂₀         | Percent of Lung volume ≥ 20 Gy                  | 8.33          | 10                |
|            | V₃₀         | Percent of Lung volume ≥ 30 Gy                  | 8.33          | 6                 |
|            | V₄₀         | Percent of Heart volume ≥ 40 Gy                 | 8.33          | 6                 |
| Heart      | V₅₀         | Percent of Heart volume ≥ 30 Gy                 | 8.33          | 6                 |
|            | D₀,₀₃        | Maximum dose of Spinal Cord                     | 8.33          | 10                |
| Spinal Cord| D₀,₀₃        | Anatomic location of global maximum             | 8.37          | 6                 |

Table 3. Description of the notation used in the formula of plan difficulty index (PDI).

| Symbol | Description |
|--------|-------------|
| r₅₀₇₆ | Equivalant spherical radius of PTV. |
| r₅₀₇₆ | Equivalant spherical radius of lung. |
| V₅₀₇₆ | Geometric center between PTV and lung. |
| V₅₀₇₆ | Overlap area between PTV and lung. |
| V₅₀₇₆ | Volume of PTV. |
| V₅₀₇₆ | Volume of lung. |
| r₅₀₇₆ | Equivalant spherical radius of heart. |
| d₅₀₇₆ | Geometric center between PTV and heart. |
| d₅₀₇₆ | Overlap area between PTV and heart. |
| d₅₀₇₆ | Volume of heart. |
| d₅₀₇₆ | The shortest surface distance between PTV and spinal cord. |
| d₅₀₇₆ | Weight factor. |

\[
PDI = K_{\text{lung}} \left( \frac{d_{\text{PTV-lung}}}{d_{\text{PTV-lung}}} + \frac{V_{\text{PTV-lung}}}{V_{\text{lung}}} + \frac{V_{\text{PTV-lung}}}{V_{\text{PTV}}} \right) \\
+ K_{\text{heart}} \left( \frac{d_{\text{PTV-heart}}}{d_{\text{PTV-heart}}} + \frac{V_{\text{PTV-heart}}}{V_{\text{heart}}} + \frac{V_{\text{PTV-heart}}}{V_{\text{PTV}}} \right) \\
+ K_{\text{spinal}} \left( \frac{d_{\text{PTV-spinal}}}{d_{\text{PTV-spinal}}} \right)
\]

(2)

3. Results

3.1. Plan evaluation by feasibility DVH

Analysis of whether further optimization was possible for 34 plans showed that most DVHs for the lungs and hearts fell in the challenging (76.47%; 38.26%) and difficult zones (20.59%; 14.71%), listed in Table 4. Most DVHs for spinal cords fell in the probably zone (79.41%) since the limitation (45 Gy) of the maximum dose to spinal cord was easy to achieve with the prescription dose of 60 Gy to the PTV. In consideration of

Table 4. Distributions of actual DVHs in the regions of feasibility DVH for some OARs in 34 plans.

| OARs     | Probable (green) | Challenging (yellow) | Difficult (orange) | Impossible (red) |
|----------|------------------|----------------------|--------------------|-------------------|
| Lung     | 1                | 26                   | 7                  | 0                 |
| Heart    | 12               | 13                   | 5                  | 4                 |
| Spinal cord | 27             | 7                    | 0                  | 0                 |
the unicity of feasibility DVH evaluation and the comprehensiveness of actual plans, these plans were determined to have reached their optimal states.

3.2. Plan scoring value

The radiotherapy (RT) image, structure set, plan, and dose of each plan were exported from Eclipse system and then loaded to PlanIQ™ system. The scores of plans quality determined by four scoring models are shown in Figure 3. The scoring value of four models is $72.34 \pm 10.10$ (40.80–89.49) for SU, $69.40 \pm 12.06$ (39.00–89.46) for SNU, $53.11 \pm 10.44$ (24.24–75.22) for NSU and $50.30 \pm 11.67$ (23.41–73.42) for NSNU.

In Figure 3, the means in the segmented curves were higher than those in the non-segmented curves, and standard deviations in the uniform score distributions were lower than those in the non-uniform score distributions. In the segmented uniform scoring model, there were 22 of 34 plans (64.71%) whose
scoring value was ≥70, and in the other three scoring models, these statistics were 13 plans (38.2%) for SNU, 2 plans (5.9%) for NSU and 1 plan (2.9%) for NSNU, respectively.

3.3. Plan difficulty index (PDI)

The mean PDI of 34 plans was 4.20 ± 0.99 (range of 2.66 to 7.29) in uniform score distribution and 4.47 ± 1.17 (range of 2.89 to 7.99) in non-uniform score distribution, \( P < 0.05 \), as shown in Figure 4(a).

The correlations between the scoring values of plan quality and PDI are shown in Figure 4(b) and Figure 4(c). The relevance trends with a fixed intercept of 100 were established by the least square method. These results show that the scoring value of plan quality and PDI were significantly negatively correlated under the four scoring models. The Pearson coefficients were −0.52 (\( P < 0.05 \)), −0.49 (\( P < 0.05 \)), −0.59 (\( P < 0.05 \)) and −0.53 (\( P < 0.05 \)) for SU, SNU, NSU and NSNU models, respectively.

4. Discussion

In clinical practice, the choice of one treatment plan among many alternatives is based on clinical experience. So, different radiation oncologists might make different choices. To avoid these situations, the evaluation of plan quality on the basis of objective metrics is preferred.

Good plan evaluation criterion should include both evaluations of PTV coverage and OAR sparing. At present, there are two categories of plan assessments: one based on biological metrics and the other on physical metrics. In model of biological metrics, tumor control probability (TCP) (Webb & Nahum, 1993, Zaider & Minerbo, 2000), normal tissue complication probability (NTCP) (Jackson et al., 1993, Niemierko & Goitein, 1993) or equivalent uniform dose (EUD) (Ebert, 2001, Qi et al., 2006) are used for plan ranking and comparison. However, this model has the lack of parameter values for individual patient (Cozzi et al., 2000, Zaider & Amols, 1999). In our study, the evaluation model with extensive applicability was constructed based
on physical metrics, as an evaluation tool of the decision-making process. Unlike other models reported in literatures (Alfonso et al., 2015, Nelms, Robinson, et al., 2012; Ślosarek et al., 2008), four scoring models by combining two function curves with two score distributions were presented to evaluate 34 plans used in radiotherapy of lung cancer. The retrospective study on the quality of 34 plans by using feasibility DVH™ indicated that these plans had reached the ideal state, which was very important for this study to choose a reasonable and reliable evaluation model. In four models, the SN scoring model showed 64.71% of all plans with scoring value ≥70 (88.24%, ≥60), much higher than the other three models. The analysis on four plans with scoring value <60 in the SN scoring model found that the ratio of lung volume to target volume of these four patients (serial number of patient with the scoring value of plan from high to low: No.1, No.32, No.2, No.24) was relatively small, and the geometric center distance between lung and target was also relatively small. As a result, in the protection of the lung tissue, target volume covered by 100% and 95% of prescription dose were slightly deficient in the face of clinical requirements, and the maximum dose also fell outside PTV.

In addition to the analysis of plans between different patients or between different treatment courses in the same patient, the SN scoring model could be used to the comparison between plans in the same treatment course of the same patient. As an extension of the study, SN scoring model was applied to the clinical practice of three patients, each of whom had 2-4 IMRT plans. One of these plans was selected by radiation oncologists for clinical treatment. The results showed as follows: (1) the application of SN scoring model based on objective metrics could reduce the artificial deviation in the preliminary evaluation (in the plan preliminary assessment for Number 3 patient, the fact that the maximum dose was dropped outside the target was ignored by the planner, but the SN scoring value gave a notice); (2) there was no absolute good or bad for plan quality, and one radiation oncologist could not only depend on ‘the higher the scoring value of plan, the better the quality of plan’ to make a judgment, because in the clinical practice a variety of indicators should be taken into account [for example, for Number 1 patient receiving palliative radiotherapy with the pay attention to the life quality, the single scoring value of OARs was slightly higher, but the target had the less value than desired scoring value, which resulted in a slightly lower score for clinical treatment plans than other alternatives (difference value: 0.2)]. This result indicated that combining the total scoring value of plan with the scoring value of some interest metrics in the SN scoring model was more practical in the evaluation of plan quality for lung cancer.

A novel PDI defined in our study was used to quantificationally describe the complexity of plan design. The three weight factors used in PDI index were different between two score distributions, so the calculated PDI values were different, but the differences of mean value and standard deviation were relatively small. Therefore, although the paired T-test showed a significant difference in PDI between two score distributions, this difference had no clinical significance. As recommended above, the SN scoring model should be applied to clinical practice. Similarly, PDI formula in uniform score distribution is recommended in clinical practice. For PDI in uniform score distribution, the higher the score, the more difficult the plan design will be. For example, in this study, the highest PDI score was 7.29, which happened to be patient No. 24 with the lowest scoring value of plan quality (40.8). This was a result obtained by the radiation oncologist after comprehensive consideration of many circumstances (such as the relationship between target and OARs, individual situation and appeal of the patient, and so on). The negative correlation between the scoring value of plan quality and PDI confirmed the rationality of the SN scoring model.

The model recommended in our study has fewer tumor-based restrictions and, therefore, can be widely applied to a variety of tumor types in clinical practice. Moreover, the distribution in score was uniform, and the metric was objective, which eliminates the confounding prejudice of different evaluators and is more beneficial in clinical practice. Compared with conventional artificial methods, this evaluation method could shorten the time required for review of treatment plans and identify subtle differences among tentative plans with similar apparent value. Furthermore, the result of each metric can reveal corresponding information that influences the quality score of the plan. A future aim is to combine score data extracted from quality evaluation metrics and the physical parameters of PTV and OARs to guide further optimization of the treatment plan.

5. Conclusion

This study investigated four scoring models and defined a plan difficulty index (PDI). A negative correlation between the scoring value of plan quality and PDI demonstrated the feasibility of using PDI and evaluation criterion to plan quality assurance for external beam IMRT plans in lung cancer. The SN
scoring model is recommended to evaluate and select external beam radiotherapy plans in future clinical practice.

Acknowledgments

This study was supported by the Performance Incentive Guide Special Project of Chongqing Scientific Research Institute.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

AI AAE: ICRU Report 62. prescribing, recording and reporting photon beam therapy (supplement to icru report 50). Icru News 1999.

Alfonso, J. C. L., Herrero, M. A., & Nunez, L. (2015). A dose-volume histogram based decision-support system for dosimetric comparison of radiotherapy treatment plans. Radiation Oncology, 10, 263. https://doi.org/10.1186/s13014-015-0569-3

Clark, C. H., Aird, E. G., Bolton, S., Miles, E. A., Nisbet, A., Snaith, J. A., Thomas, R. A., Venables, K., & Thwaites, D. I. (2015). Radiotherapy dosimetry audit: Three decades of improving standards and accuracy in UK clinical practice and trials. The British Journal of Radiology, 88, 20150251. https://doi.org/10.1259/bjr.20150251

Cozzi, L., Buffa, F. M., & Fogliata, A. (2000). Comparative analysis of dose volume histogram reduction algorithms for normal tissue complication probability calculations. Acta Oncologica, 39, 165–171. https://doi.org/10.1080/0284186004307275

Ebert, M. A. (2001). Ranking radiotherapy treatment plans: Physical or biological objectives? Radiology and Oncology, 35.

Feuvret, L., Noel, G., Mazeron, J., & Bey, P. (2006). Conformity index: A review. International Journal of Radiation Oncology, Biology, Physics, 64, 333–342. https://doi.org/10.1016/j.ijrobp.2005.09.028

Fried, D., Chera, B. S., & Das, S. (2017). Assessment of PlanIQ Feasibility DVH for head and neck treatment planning. Journal of Applied Clinical Medical Physics, 18, 245–250. https://doi.org/10.1002/acm.212165

Gintz, D., Latifi, K., Caudell, J. J., Nelms, B. E., Zhang, G., Moros, E. G., & Feygelman, V. (2016). Initial evaluation of automated treatment planning software. Journal of Applied Clinical Medical Physics, 17, 331–346. https://doi.org/10.1120/jacmp.v17i3.6167

Gigoloire, V., Mackie, T. R., & Neve, W. D. (2010). Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT):Contents. Journal of the ICRU, 10, 1–3. https://doi.org/10.1093/icru_rndq002

Jackson, A., Katcher, G. J., & Yorke, E. D. (1993). Probability of radiation-induced complications for normal tissues with parallel architecture subject to non-uniform irradiation. Medical Physics, 20, 613–625. https://doi.org/10.1118/1.597056

Jiang, W., Wang, H., & Chi, P. (2016). SU-F-T-419: evaluation of planar feasibility DVH as planning objectives for skull base SBRT patients. Medical Physics, 43, 3559. https://doi.org/10.1118/1.4956004

Li, X. A., Tai, A., Arthur, D. W., Buchholz, T. A., Macdonald, S., Marks, L. B., Moran, J. M., Pierce, L. J., Rabinovitch, R., & Taghian, A. (2009). Variability of target and normal structure delineation for breast cancer radiotherapy: An RTOG multi-institutional and multibrowser study. International Journal of Radiation Oncology, Biology, Physics, 73, 944–951. https://doi.org/10.1016/j.ijrobp.2008.10.034

Moore, K. L., Brame, R. S., Low, D., & Mutic, S. (2012). Quantitative metrics for assessing plan quality. Seminars in Radiation Oncology, 22, 62–69. https://doi.org/10.1016/j.smedonc.2011.09.005

Nelms, B. E., Robinson, G., Markham, J., Velasco, K., Boyd, S., Narayan, S., Wheeler, J., & Sobczak, M. L. (2012). Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems. Practical Radiation Oncology, 2, 296–305. https://doi.org/10.1016/j.prro.2011.11.012

Nelms, B. E., Stambaugh, C., Hunt, D. C., Tonner, B., Zhang, G., & Feygelman, V. (2015). Methods, software and datasets to verify DVH calculations against analytical values: Twenty years later(). Medical Physics, 42, 4435–4448. https://doi.org/10.1118/1.4923175

Nelms, B. E., Tome, W. A., Robinson, G., & Wheeler, J. A. (2012). Variations in the contouring of organs at Risk: Test case from a patient with oropharyngeal cancer. International Journal of Radiation Oncology, Biology, Physics, 82, 368–378. https://doi.org/10.1016/j.ijrobp.2010.10.019

Niemierko, A., & Goitein, M. (1993). MODELING OF NORMAL TISSUE RESPONSE TO RADIATION: THE CRITICAL VOLUME MODEL. International Journal of Radiation Oncology, Biology, Physics, 25, 135–145. https://doi.org/10.1016/0360-3016(93)90156-P

Oderinde, O. M., & Du Plessis, F. (2019). Sensitivity evaluation of two commercial quality assurance systems to organ-dose variations of patient-specific VMAT plans. Journal of Radiation Research and Applied Sciences, 12, 132–139. https://doi.org/10.1016/j.jrras.2019.1618080

Peters, L. J., Ossullivan, B., Giralt, J., Fitzgerald, T. J., Trotti, A., Bernier, J., Bourhis, J., Yuen, K., Fisher, R., & Rischin, D. (2010). Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: Results from TROG 02.02. Journal of Clinical Oncology, 28, 2996–3001. https://doi.org/10.1200/JCO.2009.27.4498

Qi, S., Li, A., Kainz, K., Brammer, B., Olivera, G., Ruchala, K., Schultz, C. J., & Wilson, J. (2006). 2800: Ranking complex IMRT plans using an EUD-Based figure-of-merit index. International Journal of Radiation Oncology, Biology, Physics, 66, 5658. https://doi.org/10.1016/j.ijrobp.2006.07.1218

Rehman, J., Zahra, A. N., Khalid, M., Noor ul Huda Khan Asghar, H. M., ZA, G., Ullah, I., Nasar, G., & Mm, A. (2018). Usmani MN: Intensity modulated radiation therapy: A review of current practice and future outlooks. Journal of Radiation Research and Applied Sciences, 11, 361–367. https://doi.org/10.1016/j.jrra.2018.07.006

Riet, A. V., Mak, A. C. A., Moerland, M. A., Elders, L. H., & Der Zee, W. V. (1997). A conformation number to quantify the degree of conformity in brachytherapy and external beam irradiation: Application to the prostate. International Journal of Radiation Oncology, Biology, Physics, 37, 731–736. https://doi.org/10.1016/S0360-3016(96)00601-3

Shaw, E. G., Kline, R. W., Gillin, M., Souhami, L., Hirschfeld, A., Dinapoli, R. P., & Martin, L. (1993). Radiation therapy oncology group: Radiosurgery quality assurance guidelines. International Journal of Radiation Oncology, Biology, Physics, 27, 1231–1239. https://doi.org/10.1016/0360-3016(93)90548-A
Ślosarek, K., Grządziel, A., Szlag, M., & Bystrzycka, J. (2008). Radiation Planning Index for dose distribution evaluation in stereotactic radiotherapy. Reports of Practical Oncology & Radiotherapy, 13, 182–186. https://doi.org/10.1016/S1507-1367(10)60007-7

Stavreva, N., Nahum, A. E., Markov, K., Ruggieri, R., & Stavrev, P. (2010). Analytical investigation of the possibility of parameter invariant TCP-based radiation therapy plan ranking. Acta Oncologica, 49, 1324–1333. https://doi.org/10.3109/0284186X.2010.517782

Webb, S., & Nahum, A. E. (1993). A model for calculating tumour control probability in radiotherapy including the effects of inhomogeneous distributions of dose and clonogenic cell density. Physics in Medicine and Biology, 38, 653–666. https://doi.org/10.1088/0031-9155/38/6/001

Yamamoto, M., Nagata, Y., Okajima, K., Ishigaki, T., & Hiraoka, M. (1999). Differences in target outline delineation from CT scans of brain tumours using different methods and different observers. Radiotherapy & Oncology, 50, 151–156. https://doi.org/10.1016/S0167-8140(99)00015-8

Zaider, M., & Amols, H. (1999). PRACTICAL CONSIDERATIONS IN USING CALCULATED HEALTHY-TISSUE COMPLICATION PROBABILITIES FOR TREATMENT-PLAN OPTIMIZATION. International Journal of Radiation Oncology, Biology, Physics, 44, 439–447. https://doi.org/10.1016/S0360-3016(99)00014-0

Zaider, M., & Minerbo, G. N. (2000). Tumour control probability: A formulation applicable to any temporal protocol of dose delivery. Physics in Medicine and Biology, 45, 279–293. https://doi.org/10.1088/0031-9155/45/2/303