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Physical and Radiobiological Evaluation of Radiotherapy Treatment Plan

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Abstract

Radiation treatment planning plays an important role in modern radiation therapy; it could simulate to plan the geometric, radiobiological, and dosimetric aspects of the therapy using radiation transport simulations and optimization. In this chapter, we have reviewed several quantitative methods used for evaluating radiation treatment plans and discussed some important considering points. For the purpose of quantitative plan evaluation, we reviewed dosimetrical indexes like PITV, CI, TCI, HI, MHI, CN, COSI, and QF. Furthermore, radiobiological indexes like Niemierko’s EUD-based TCP and NTCP were included for the purpose of radiobiological outcome modeling. Additionally, we have reviewed dose tolerance for critical organs including RTOG clinical trial results, QUENTEC data, Emami data, and Milano clinical trial results. For the purpose of clinical evaluation of radiation-induced organ toxicity, we have reviewed RTOG and EORTC toxicity criteria. Several programs could help for the easy calculation and analysis of dosimetrical plan indexes and biological results. We have reviewed the recent trend in this field and proposed further clinical use of such programs. Along this line, we have proposed clinically optimized plan comparison protocols and indicated further directions of such studies.

Keywords: Treatment plan evaluation, Dosimetrical indices, Radiobiological indices, Tolerance doses, Radiation toxicity

1. Introduction

We have reviewed the methods used for quantitative comparison of different radiation treatment plans, the process of treatment plan comparison protocol, and the further direction of treatment plan evaluation programs. For the purpose of quantitative plan evaluation, we reviewed dosimetical indexes like prescription isodose to target volume (PITV) ratio,
homogeneity index (HI), conformity index (CI), target coverage index (TCI), modified dose homogeneity index (MHI), conformity number (CN), critical organ scoring index (COSI), and quality factor (QF). Furthermore, radiobiological indexes like Niemierko’s EUD-based tumor control probability (TCP) and normal tissue complication probability (NTCP) were included for the purpose of radiobiological outcome modeling. Additionally, we have reviewed dose tolerance for critical organs including RTOG clinical trial results, QUENTEC data, Emami data, and Milano clinical trial results. For the purpose of clinical evaluation of radiation-induced organ toxicity, we have reviewed RTOG and EORTC toxicity criteria. Several programs could help for the easy calculation and analysis of dosimetric plan indexes and biological results. We have reviewed the recent trend in this field and proposed further clinical use of such programs. It is well known that plan comparison study still remain many controversies. The major issue is that plan evaluation methods are used in plan comparison and plan optimization. We have reviewed well-known dosimetric and biological plan indexes and several commercial and non-commercial plan evaluation programs. Along this line, we have proposed clinically optimized plan comparison protocols and indicated the further directions of such studies.

2. Background: Radiotherapy, radiation treatment planning, and planning decision support program

2.1. Radiotherapy

Over the past few decades, radiation treatment has become a technologically advanced field in modern medicine, especially with the advent of intensity-modulated radiation therapy (IMRT) [1]. Traditional radiation therapy planning is a manual, iterative, and simple process in which treatment fields are placed and beam modifiers are inserted.

Modifications are then made after manual inspection of the dose distribution calculated after each iteration [2]. In IMRT, the dose calculation engine specified dose distribution over the target volume and surrounding normal structures. Furthermore, dose calculation engine displayed a 2D dose intensity map by using its optimization algorithms [3]. Moreover, the inverse planning algorithm required users to set a dose/volume criteria for the specific organ/structure, and the computer calculated to find out a final solution to satisfy the criteria. [4]. Another breakthrough of modern radiation treatment is image-guided radiotherapy (IGRT). With the adoption and integration of imaging information in treatment designs, IGRT is the most innovative area in advanced radiotherapy [5]. IGRT has increased knowledge of exact tumor targets and their movements during the treatment process [6]. Despite improvements in target coverage and normal tissue sparing, the implementation of IMRT and IGRT remains a labor-intensive trial and error process. The creation of optimized treatment plans for personalized therapy still requires significant time and effort. Radiation treatment includes CT simulation, organ contouring, treatment planning, quality assurance, and dose delivery (Figure 1) [7].
2.2. Radiation treatment planning

For radiation treatment, a team of radiation oncologists, radiation therapists, medical physicists, and medical dosimetrists plan the appropriate external beam radiotherapy treatment
technique for a patient with cancer [8]. There are generally two different types of planning algorithms, forward planning and inverse planning. The forward planning technique is mostly used in external-beam radiotherapy treatment planning process. For example, a medical physicist determines the beam angles in the treatment planning systems to maximize tumor dose when sparing the healthy tissues. This type of planning is used for the majority of external-beam radiotherapy treatments, but is only useful for relatively uncomplicated cases in which the tumor has a simple shape and is not near any critical organs. Inverse planning is a technique used to inversely design radiotherapy treatment plans (Figure 2). The radiation oncologist defines a patient’s critical organs and tumor. Then, the dosimetrist provides target doses for each. An optimization program is then run to find the treatment plan that best matches all input criteria. This type of trial-and-error planning process is time and labor intensive.

There are several commercial treatment planning systems (TPS) available nowadays. Table 1 summarizes information about commercial TPS [9].

2.3. Planning decision support program

Dose volume histogram (DVH) provides dose volume coverage information. However, it fails to provide more information like hot spot and dose homogeneity. Dosimetrical indices were widely used for plan evaluation for a specific purpose. For example, a homogeneity index refers to the intensity of dose distributions in target volume, those plans with both “hot” spot...
and “cold” spot could be distinguished by this index. Additionally, some indices consider dose conformity in the target volume. Conformity index was an example of such indices. Another method to review and evaluate treatment plan quality was biological index. A tumor control probability could indirectly estimate a tumor could be controlled by a certain dose. Furthermore, normal tissue complication probability could estimate the probability of a surrounding critical structure becomes some radiation-induced complications. Many programs have been designed and developed to calculate both dosimetrical and biological indices since the 2000s [10-29]. This is shown in Figure 3.

| Treatment planning system | Company | Website |
|---------------------------|---------|---------|
| ScandiPlan                | Scanditronix | http://www.scanditronix-magnet.se |
| Pinnacle3                 | Philips Healthcare | http://www.healthcare.philips.com |
| ISOgray                   | DOSIsoft | http://www.dosisoft.com |
| iPlan                     | Brainlab | https://www.brainlab.com |
| XiO                       | Electa | http://www.elekta.com |
| Monaco                    | Electa | http://www.elekta.com |
| Theraplan Plus            | Electa | http://www.elekta.com |
| Oncentra MasterPlan       | Electa | http://www.elekta.com |
| Oncentra Prostate         | Electa | http://www.elekta.com |
| Oncentra GYN              | Electa | http://www.elekta.com |
| Pinnacle                  | Philips Healthcare | http://www.healthcare.philips.com |
| Plato RTS                 | Electa | http://www.elekta.com |
| Plato BPS                 | Electa | http://www.elekta.com |
| Cad Plan                  | Varian Medical Systems | http://www.varian.com |
| Corvus                    | nomos | http://www.nomos.com |
| KL-Medical Electron Linear Accelerator treatment system | KLZ Healthcare | http://klz.comedb.com |
| Prowess 3-D               | Prowess | http://www.prowess.com/ |
| Brachyvision              | Varian | http://www.varian.com |
| Leksell GammaPlan®        | Electa | http://www.elekta.com |
| Eclipse                   | Varian Medical Systems | http://www.varian.com |
| VariSeed                  | Varian Medical Systems | http://www.varian.com |
| RayStation                | RaySearch Laboratories | http://www.raysearchlabs.com |

Table 1. Commercial RTP lists
3. Plan evaluation

3.1. Plan evaluation methods

3.1.1. Qualitative analysis

In conventional radiation therapy, an isodose distribution is used for plan analysis and evaluation. Figure 4 shows the typical isodose distribution of 3D conformal treatment plans and IMRT plans.

3.1.2. Quantitative analysis

DVH is the relationship between the dose distribution of a certain organ and 100% normalized volume of such organ. It was calculated and generated based on 3D reconstructed images in the treatment planning systems [9]. DVH could simplify 3D information of dose distribution.
into a 2D graph or quantitative values [30-34]. Figure 5 shows a typical DVH for helical tomotherapy (HT) and intensity modulated proton therapy (IMPT) plans for prostate cancer.

Figure 4. Typical isodose distribution of (a) 3D conformal treatment plan and (b) IMRT plan.

Figure 5. Typical DVH for helical tomotherapy (HT) treatment plan and intensity modulated arc therapy (IMAT) plan of prostate cancer: (a) axial slice, (b) sagittal slice. Planning target volume (PTV), critical structures, and four different isodose lines shown. (c) Dose-volume histogram comparison for prostate case. Solid lines, tomotherapy plan; dashed lines, intensity modulated arc therapy (IMAT) plan (International Journal of Radiation Oncology Biology Physics, 69(1), 2007).
4. Plan analysis

Isodose distribution and DVH analysis were insufficient compared to complicated and advanced planning techniques. As the femoral head DVHs in Figure 4 show, it was difficult to distinguish whether IMPT (continuous red line) or HT (dashed red line) plans were superior. For low dose volume ($V_0$ to $V_{20}$), IMPT was more favorable than HT. However, this relationship reversed for high dose volume ($V_{20}$ to $V_{50}$). As a result, there are several indexes that may represent target conformity and dose homogeneity [31, 35-38].

4.1. Dosimetric analysis

4.1.1. Index

Several quantitative evaluation tools were reviewed in this paper. These included the prescription isodose to target volume (PITV) ratio, homogeneity index (HI), conformity index (CI), target coverage index (TCI), modified dose homogeneity index (MHI), conformity number (CN), quality factor (QF) for PTV, maximum dose, mean dose, dose volume histogram (DVH), and critical organ scoring index (COSI) for the OAR (Figure 6).

4.1.2. PTV index

The PITV ratio, obtained by dividing prescription isodose surface volume by target volume, is expressed as:

$$\text{PITV} = \frac{\text{PIV}}{\text{TV}}$$  \hspace{1cm} (1)

In the above equation, PIV represents prescription isodose surface volume and TV refers to target volume [39]. The PITV ratio is a conformity measure, and a value of 1.0 indicates that the volume of the prescription isodose surface equals that of the PTV. A PITV ratio of 1.0 does not necessarily imply that both volumes are similar. To ensure adequate PTV coverage, this measure should always be used in conjunction with a PTV-DVH [39]. The CI and HI indices for targets were computed to assess the quality of IMRT plans. CI is defined as the ratio of target volume and the volume inside the isodose surface that corresponds to the prescription dose. CI is generally used to indicate the portion of a prescription dose that is delivered inside the PTV [40].

CI is expressed as:

$$\text{CI} = \frac{\text{PTV}_{PD}}{\text{PIV}}$$  \hspace{1cm} (2)
In the above equation, $PIV$ represents prescription isodose surface volume and $PTV_{PD}$ represents PTV coverage at the prescription dose. CI of 1 indicates that 100% of a prescription dose is delivered to the PTV, and no dose is delivered to any adjacent tissue [40]. The CI is less than 1 for most clinical cases. Higher CI values indicate poorer dose conformity to the PTV. HI is defined as the ratio of maximum dose delivered to the PTV divided by the prescription dose delivered to the PTV [41].

HI is expressed as:

$$HI = \frac{D_{\text{max}}}{PD}$$

(3)

In the above equation, $D_{\text{max}}$ represents PTV maximum dose. An HI of 1 represents the ideal uniform dose within a target. Higher HI values indicate greater dose heterogeneity in the PTV [39].

TCI refers to the exact coverage of PTV in a treatment plan for a given prescription dose. TCI is expressed as:

$$TCI = \frac{PTV_{PD}}{PTV}$$

(4)

In the above equation, $PTV_{PD}$ represents PTV coverage at the prescription dose.

MHI is similar to HI, and is expressed as [41]:

$$MHI = \frac{D_{95}}{D_5}$$

(5)

In the above equation, $D_{95}$ and $D_5$ represent doses received at 95% and 5% of the volume coverage, respectively.

Conformity number (CN) is a relative measurement of dosimetric target coverage and sparing of normal tissues in a treatment plan [42]. The CN is expressed as:

$$CN = TCI \times CI = \frac{PTV_{PD}}{PTV} \times \frac{PTV_{PD}}{PIV}$$

(6)

In the above equation, $PTV_{PD}$ refers to PTV coverage at the prescription dose and $PIV$ represents prescription isodose surface volume [42].
### Figure 6. Comparison of the various dosimetric indices in various clinical cases.

| Index                  | Formula                        | Concept | Value = 1 | Value <1 or value >1 |
|------------------------|-------------------------------|---------|-----------|----------------------|
| PTV (prescription isodose to target volume) | $PTV = \frac{PIV}{TV}$       | ![](image) | ![](image) | ![](image) |
| CI (conformity index)  | $CI = \frac{PTV_{PD}}{PIV}$   | ![](image) | ![](image) | ![](image) |
| TCI (target coverage index) | $TCI = \frac{PTV_{PD}}{PTV}$ | ![](image) | ![](image) | ![](image) |
| CN (conformity number) | $CN = \frac{PTV_{PD}}{PTV}$   | ![](image) | ![](image) | ![](image) |

- **HI (homogeneity index)**
  - $HI = \frac{D_{max}}{PD}$

- **MHI (modified homogeneity index)**
  - $MHI = \frac{D_{ref}}{D_h}$

- **COSI (critical organ scoring index)**
  - $COSI = 1 - \sum\frac{TV(organ_{PD})}{TC}$

- **Legend**:
  - PTV (planning target volume)
  - OAR (organ at risk)
  - TV (target volume)
4.2 Biological analysis

4.2.1. Overview of biological models

For radiobiological model-based plan evaluation, Niemierko’s equivalent uniform dose (EUD)-based NTCP and TCP model were reviewed [12, 19]. First, the DVHs from each plan were exported from the appropriate treatment planning system (TPS) for each modality. The DVHs were then imported into MATLAB version R2012a (The Math Works, Inc., Natick, MA, USA) for TCP and NTCP modeling analysis. According to Neimierko’s phenomenological model, EUD is defined as:

\[
EUD = \left( \sum_{i} V_i \text{EUD}_i \right)^{1/2}
\]  

(7)

where \(a\) is a unitless model parameter that is specific to the nominal tumor structure of interest, and \(V_i\) is a unitless parameter that represents the \(i^{th}\) partial volume receiving dose \(D_i\) in Gy [12].

Since the relative volume of the whole structure of interest corresponds to 1, the sum of all partial volumes \(V_i\) will equal 1. In equation [5], the EQD is a biologically equivalent physical dose of 2 Gy defined as:

\[
EQD = D \times \left( \frac{\alpha + D}{\beta \cdot n_f} \right)^{1/2}
\]  

(8)

where \(n_f\) and \(d_f = D/n_f\) are the number of fractions and the dose per fraction size of the treatment course, respectively. In this equation, \(\alpha/\beta\) is the tissue-specific linear quadratic (LQ) parameter of the organ being exposed. Niemierko’s TCP [12] is defined as:

\[
TCP = \frac{1}{1 + \left( \frac{TCD_{50}}{EUD} \right)^{\gamma_{50}}}
\]  

(9)

where \(TCD_{50}\) is the tumor dose required to control 50% of cancer cells when a tumor is homogeneously irradiated and \(\gamma_{50}\) is a unitless model parameter that is specific to the tumor of interest. The slope of the dose response curve is described by \(\gamma_{50}\). Niemierko’s NTCP [19] is defined as:

\[
TCP = \frac{1}{1 + \left( \frac{TCD_{50}}{EUD} \right)^{\gamma_{50}}}
\]  

(10)
where $TD_{50}$ is the tolerance dose of a 50% complication rate at a specific time (e.g. 5 years in the Emami et al. normal tissue tolerance data [43]) for an entire organ of interest. This parameter also describes the slope of the dose response curve.

### 4.3. Overall plan index

#### 4.3.1. Overall plan index

A comprehensive quality index (CQI) including surrounding OARs were introduced to evaluate the individual difference between OARs and PTV and the small volume of critical structures. CQI is expressed as [44]:

$$CQI = \frac{1}{N} \sum_{i=1}^{N} QI_{i} = \frac{1}{N} \sum_{i=1}^{N} \left( \frac{P_{\text{max}}^{\text{plan}}}{P_{\text{max}}^{\text{tol}}} \right)$$

(11)

In this equation, $I$ is the index of the critical organs, which are several critical structures in certain plan. CQI was designed to compare the ability of avoiding these organs around the PTV given the same weighting to all organs. Although CQI may overweight certain organs that are below tolerance, we chose this index as it represents a global measure of the capability of avoiding sensitive structures. Individual QIs are shown for direct comparison of each OAR. A CQI less than one indicates that HT provides a better plan for the surrounding OARs, and vice versa.

#### 4.3.2. COSI

The COSI index accounts for both target coverage and critical organ irradiation [45]. The main advantage of this index is its ability to distinguish between different critical organs. COSI is expressed as:

$$\text{COSI} = 1 - \sum_{i} w_{i} \frac{V_{i}(\text{OAR})_{\text{ad}}}{TCV}$$

(12)

where $V_{i}(\text{OAR})_{\text{ad}}$ is the volume fraction of OAR that receives more than a predefined tolerance dose. TCV is the volumetric target coverage, which is defined as the fractional volume of PTV covered by the prescribed isodose. Modified COSI is expressed as:

$$m\text{COSI} = \sum_{i=1}^{8} W_{i} \left( \frac{\text{COSI}_{10} + \text{COSI}_{20} + \cdots + \text{COSI}_{80}}{8} \right)$$

(13)

Although the COSI index focuses only on OARs that receive high dose region volumes, the modified COSI considers both high dose and low dose regions.
4.3.3. Quality factor

The quality factor (QF) introduced in this study is a dosimetric index that can evaluate the quality of an entire plan [23]. The QF of a plan is analytically expressed as:

\[
QF = \left[ 2.718 \exp \left( -\sum_{i=1}^{N} W_i X_i \right) \right]^{1/10}
\]  

(14)

In the above equation, \( X_i \) represents all PTV indices, including PITV, CI, HI, TCI, MHI, CN, and COSI. The weighting factor (\( W_i \)) values can be adjusted between 0 and 1 for all relatively weighted indices for a user-defined number of indices (N). A weighting factor of 1 was used for all separate indices. Thus, the QF was mainly used to compare the conformity of plans throughout various trials of a treatment.

5. Radiation tolerance dose and toxicity

The dose to critical structures plays an important role in treatment plan evaluation and is a challenging parameter in radiotherapy treatment planning. Here, Emami data [43], QUENTEC data [46], RTOG data, and the Milano study were reviewed. Doses based on tumor location in the body related to critical organs are as follows (Table 2-4).

5.1. Radiation toxicities

The assessment and reporting of toxicity plays a central role in oncology [47-50]. The foundation of toxicity reporting is the toxicity criteria system. Multiple systems have been developed in the last 30 years, and they have evolved substantially since their first introduction. The wide adoption of standardized criteria will facilitate comparison between institutions and clinical trials.

The Radiation Therapy Oncology Group (RTOG) acute radiation morbidity scoring criteria developed in 1984 consists of 13 scales that cover most body regions [51]. This system was used by the RTOG and in other clinical trials for over 30 years. The inclusion of acute radiation criteria into a multimodality grading system facilitated toxicity grading in all oncologic disciplines. This system also allows radiation oncologists to recognize and grade toxicities that were not available in the previous RTOG system. Tables 5 and 6 summarize acute toxicity categorized by body region.

The RTOG/EORTC (European Organization for Research and Treatment of Cancer) system for scoring late effects was developed in 1984 alongside the RTOG acute criteria. It contains 16 organ categories (Tables 7, 8) and has been used widely. However, its shortcomings have prompted the development of other systems.
| Critical Structure | Dose/ fx | Vol. | Dose | Max. Dose | Protocol | Treated organ | Critical Structure | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | TD 60/5 | TD 90/5 | Organ | Dose Tolerance | Endpoint |
|-------------------|---------|------|------|----------|----------|---------------|-------------------|-------------|----------|---------------|------------------|--------|--------|--------|--------|--------|--------|-----------|----------|
| Brachial Plexus | 2 Gy    | 5%   | 60 Gy| 619      | Postop H&N| Brain         | QUANTEC data      | <60 Gy      | <3%      | Symptomatic necrosis | Whole             | 2/3    | 1/3    | 1/3    |        |       |         |          |
|                   | 2 Gy    | 60 Gy| 522  | Definitive H&N | Brain     | 72 Gy        | Symptomatic necrosis | 4500    | 5000    | 6000         | Brain             | 6500   | 7500   |       |        |       |         |          |
|                   | 2 Gy    | 66 Gy| 0619 | Postop H&N, lung, nasopharynx | 90 Gy    | 10%     | Symptomatic necrosis | 6000    | 6100    | 6200         | Brachial plexus   | 7700   |       |       |        |       |         |          |
|                   | 3 Gy    | 36 Gy| 937  | Lung     |           |               |                  | <60 Gy      | <3%      | Neuropathy or necrosis | Brain stem         | 5000   | 6000   | 6500   | –      | –    | –     | Brain stem |
|                   | 4 Gy    | 30 Gy| 937  | Lung     |           |               |                  | <54 Gy      | <5%      | Neuropathy or necrosis | Brain stem         | 5000   | 6000   | 6500   | –      | –    | –     | Brain stem |
| Brainstem         | 1.8-2Gy | 0.03 cc | 55 Gy| 0.03 cc | Intermediate risk meningioma | 539     | –        | –         | –         | –             | –                          | –      | –      | –      | –      | –      | –      | –         |
|                   | 33 fx   | 54 Gy| 615  | Nasopharynx | Brain stem | <64 Gy      | –         | –         | –         | –             | –                          | –      | –      | –      | –      | –      | –      | –         |
|                   | 1.8-2Gy | 0.03 cc | 539 | 0.03 cc | High risk meningioma, glioblastoma | 0539, 083 | –       | –         | –         | –             | –                          | –      | –      | –      | –      | –      | –      | –         |
|                   | 2 Gy    | 52 Gy| 1016 | Oropharynx |           |               |                  | <54 Gy      | <5%      | Neuropathy or necrosis | –                          | –      | –      | –      | –      | –      | –      | –         |
| Cochlea           | 33 fx   | 5%   | 55 Gy| 615      | Nasopharynx | Mean        | <=45 Gy       | <30%      | Sensory neural hearing loss | Ear                    | 5500   | 5500   | 5500   | 6500   | 6500   | 6500   | 6500     |
|                   | Mean    | 20 Gy| 1016 | Oropharynx |          | Cochlea      | Mean          | <=45 Gy       | <30%      | Sensory neural hearing loss | Larynx (necrosis) | 7000   | 7000   | 7900   | 8000   | 8000   | 9000   | 9000     |
| Larynx, glottis  | 2 Gy    | 45 Gy| 0619 | Postop H&N, definitive H&N, nasopharynx | Larynx   | <66 Gy      | Vocal dysfunction | 4500    | 4500    | 8000         | –                          | –      | –      | –      | –      | –      | –      | –         |
|                   | Mean    | <44 Gy| <20% | Edema    | Larynx (edema) | Mean <50 Gy | <30%      | Aspiration    | 7000    | 7900    | 8000         | –                          | –      | –      | –      | –      | –      | –      | –         |
|                   | Mean    | <44 Gy| <20% | Edema    | –                  | Mean <50 Gy | <27%      | –           | 4500    | 4500    | –             | –                          | –      | –      | –      | –      | –      | –      | –         |
| Critical Structure | Dose / Vol. | Treated organ | Critical Structure | Dose / Vol. | Toxicity Rate | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | Organ Dose Tolerance | Endpoint |
|-------------------|-------------|---------------|-------------------|-------------|---------------|-----------------|-------|-------|--------|----------------------|----------|
| Lens              | 5 Gy (0.03 cc) | Intermediate risk meningioma | Lens | 539 | - | - | 1800 | - | - |
| Lips              | 1.8-2 Gy | 2 Gy | Mean | >20 Gy | 1016 | Oropharynx | 66 Gy | 1016 | Oropharynx | - | - |
| Mandible / TM joint | 33 fxs | 2 Gy | Mean | 1 cc | 75 Gy | Nasopharynx | 6000 | 6000 | 6500 | 6500 | 7200 | 7200 | 7700 | Nasopharynx | - | - |
| Optic nerve       | 54 Gy (0.03 cc) | Intermediate risk meningioma | Optic nerve / chiasm | 539 | <55 Gy | <5% | Optic neuropathy | 5000 | - | - | 6500 | - | - |
| Optic nerve       | 56 Gy (0.03 cc) | High risk meningioma, glioblastoma | Optic nerve / chiasm | 0319 | 55-60 Gy | 3-7% | Optic neuropathy | 5000 | - | - | 6500 | - | - |
| Oral cavity       | 1.8-2 Gy | 50 Gy (0.03 cc) | Intermediate risk meningioma, nasopharynx | 0319 | >60 Gy | >7-20% | Optic neuropathy | 5000 | - | - | 6500 | - | - |
| Oral cavity       | 1.8-2 Gy | 55 Gy (0.03 cc) | High risk meningioma, glioblastoma | Optic nerve | 0319 | 5000 | - | - | - | 6500 | - | - |

RTOG data | QUANTEC data | Emami Data | Milano Data

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http://dx.doi.org/10.5772/60846
| Critical Structure | RTOG data | QUANTEC data | Emami Data | Milano Data |
|-------------------|-----------|--------------|------------|-------------|
| Dose/ Vol. | Mean Dose | Max. Dose | Protocol | Critical Structure | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | Organ | Dose | Endpoint |
| Parotid Glands | 2 Gy | Mean one gland | 0.0619, 0.0522, 1016 | Postop H&N, definitive H&N, oropharynx | Mean | <=25 Gy | <20% | Long-term salivary function | <25% | Parotid | | Mean dose 26 Gy | Postop H&N, definitive H&N, oropharynx | Late Grade 2 xerostomia, <75% of long-term salivary function loss |
| Pharynx, posterior wall | 2 Gy | 33% 50 Gy | 0156 | Oropharynx | Mean | <=50 Gy | <20% | Symptomatic dysphagia and aspiration |
| Retina | 1.8-2 Gy | 45 Gy (0.03 cc) | 0159 | Intermediate risk meningioma | Retina | 4500 | – | – |
| Spinal Cord | 1.8 Gy | 45 Gy | 0623, 0615 | Lung, Nasopharynx | 50 Gy | <=20% | Myelopathy | Spinal cord | EUD < 52 Gy, Max < 55 Gy | <=5% grade 3 toxicity |
| Submandibular Gland | 2 Gy | Mean <39 Gy | 1016 | Oropharynx | 69 Gy | 50% | Myelopathy | Spinal cord | EUD < 52 Gy, Max < 55 Gy | <=5% grade 3 toxicity |
| Critical Structure | Dose/ fx | Vol. Dose | Max. Dose | Treated organ | Critical Structure | Dose/Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | Dose Tolerance | Endpoint |
|-------------------|---------|-----------|-----------|----------------|-------------------|-----------|-----------|--------------|----------------|--------|--------|--------|---------------|----------|
| Esophagus         | 1.8 Gy  | Mean     | 34 Gy     | 0625, 0617    | Lung              | Mean      | <34 Gy    | 5-20%        | Grade 3- esophagitis | Whole | 2/3    | 1/3    | <30%          | V30 and <550 <30% |
|                   | 1.8 Gy  | 10 cm    | 60 Gy     | 623           | Lung              | V35       | <50%      | <30%         | Grade 2- esophagitis | Esophagus | 5500   | 5800   | 6000          | 6800   | 7000   | 7200 |
|                   | 2 Gy    | Mean     | 30 Gy     | 1104          | Esophagus         | V50       | <40%      | <30%         | Grade 2- esophagitis | (striaclitis, perforation) |
|                   | 3 Gy    | 47 Gy    | 937       | Lung           | Lung              | V70       | <20%      | <30%         | Grade 2- esophagitis | Thyroid   | 4500   | 8000   | -              | -        |
| Heart             | 1.8 Gy  | 33%      | 60 Gy     | 0625, 0617    | Lung              | Mean      | <26 Gy    | <15%         | Pericarditis        | Heart   | 4000   | 4900   | 6000          | 5000   | 5500   | 7000 |
|                   | 1.8 Gy  | 33%      | 50 Gy     | 436           | Eosphagus         | V30       | <46%      | <15%         | Pericarditis        | (periactitis) |
|                   | 1.8 Gy  | 87%      | 45 Gy     | 0623, 0617, 0436 | Lung, esophagus   | V25       | <10%      | <1%          | Long term cardiac mortality |
|                   | 1.8 Gy  | 100%     | 40 Gy     | 0623, 0617, 0436 | Lung, esophagus   |
|                   | 3 Gy    | 47 Gy    | 937       | Lung           |
|                   | 3 Gy    | V48      | <30%      | 937            | Lung              |
| Critical Structure          | Protocol | Treated organ | Dose/ fx | Vol. | Dose | Max. Dose | Toxicity | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | TD 95/5 | Late grade 2 in | Late grade 3 in | Late grade 3 in | mLd <10-20 Gy | Late grade 3 in | V30 <10-15% | V30 <25% 30% | Late grade 3 in | mLd <6-10% |
|---------------------------|----------|---------------|----------|------|------|-----------|----------|------------------|-------|-------|--------|--------|----------------|----------------|----------------|----------------|----------------|--------------|--------------|----------------|---------|
| Lung, single              | 2 Gy     | 3 cm CWS to field | 413      | Breast | V20  | <=30%     | <20%     | Symptomatic pneumonitis | Lung  | 1750  | 3000   | 4500   | 2400           | 6000           | 6000           | 6000           | 6000           | 6000         | 6000         | 6000           | 6000       |
| Lungs, total              | 2 Gy     | V20 20%       | 630      | Sarcoma | Mean | 7 Gy      | 5%       | Symptomatic pneumonitis | Lung  | –     | 5000   | –     | –             | 6000           | –              | –              | –              | –            | 6000         | –            | –              |
|                           | 2 Gy     | V20 37%       | 0617, 0623 | Lung   | Mean | 13 Gy     | 10%      | Symptomatic pneumonitis | Lung  | –     | –     | –     | –             | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 2 Gy     | Mean 20 Gy    | 617      | Lung   | Mean | 20 Gy     | 20%      | Symptomatic pneumonitis | Lung  | –     | –     | –     | –             | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 3 Gy     | Mean 20 Gy    | 937      | Lung   | Mean | 24 Gy     | 30%      | Symptomatic pneumonitis | Lung  | –     | –     | –     | –             | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 3 Gy     | V20 < 30%     | 937      | Lung   | Mean | 27 Gy     | 40%      | Symptomatic pneumonitis | Lung  | –     | –     | –     | –             | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 3 Gy     | 150 cc 30 Gy  | 937      | Lung   | Small bowel (individual loops) | V15 | <320 cc | <10%     | Grade 3+ toxicity | Small intestine | 4000 | 5000   | 5000   | 6000   | –              | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 3 Gy     | 100 cc 35 Gy  | 937      | Lung   | Small bowel (peritoneal cavity) | V45 | <195 cc | <10%     | Grade 3+ toxicity | (obstruction, perforation) | 5000 | 5000   | 5000   | 6000   | –              | –              | –              | –              | –              | –            | –            | –              | –          |
|                           | 3 Gy     | 50 cc 40 Gy   | 937      | Lung   | –     | –     | –     | –     | –              | –              | –              | –              | –              | –              | –              | –          |
| Small Bowel               | 3 Gy     | 1 cc 45 Gy    | 937      | Lung   | –     | –     | –     | –     | –              | –              | –              | –              | –              | –              | –              | –          |
|                           | 4 Gy     | 100 cc 30 Gy  | 937      | Lung   | –     | –     | –     | –     | –              | –              | –              | –              | –              | –              | –              | –          |
|                           | 4 Gy     | 50 cc 35 Gy   | 937      | Lung   | –     | –     | –     | –     | –              | –              | –              | –              | –              | –              | –              | –          |
|                           | 4 Gy     | 1 cc 40 Gy    | 937      | Stomach | D100  | <45 Gy | <7%     | Ulceration | (ulceration, perforation) | 5000 | 5500   | 6000   | 6300   | 6700           | 7000           | –              | –              | –              | –            | –            | –              | –          |
| Critical Structure | Dose/fx | Vol. | Dose | Max. Dose | Protocol | Treated organ | RTSG data | QUANTIC data | Enami Data | Milano Data | Organs | Dose tolerance | Endpoint |
|-------------------|---------|------|-------|----------|----------|----------------|------------|--------------|------------|-------------|---------|----------------|----------|
| Lung, Nasopharynx | 1.8 Gy  | 45 Gy | 0623, 0615 | 50 Gy | 0.20% | Myelopathy | (20 cm) (10 cm) (5 cm) | (10 cm) (5 cm) | Spinal cord | - | Max < 50 Gy | <5% grade >= 3 toxicity |
| Spinal cord       | 2 Gy    | 50.5 | 617   | 60 Gy   | 6%     | Myelopathy | 4700 5000 5000 | 7000 7000 | Cervical spinal cord | - | EUD < 32 Gy | <9% grade >= Max < 50 Gy |
| Spinal cord       | 1.8 Gy  | 10 cm | 50 Gy | 69 Gy | 50% | Myelopathy | Mean <15-18 Gy | <5% | Clinical dysfunction | Kidney | 2300 3000 5000 2800 4000 | - | Anemia, azotemia, HTN, edema |
| Kidney            | 3 Gy    | 36 Gy | 937   |       |        |                | Mean <28 Gy | <50% | Clinical dysfunction | Kidney | V12 <55% | <5% Clinical dysfunction |
| Kidney, bilateral | 1.8 Gy  | 67% | 30 Gy | 436 | 436 | Esopehagus | Kidney, bilateral, V12 <55% | <5% | Clinical dysfunction |
| Kidney            | 2 Gy    | 50% | 14 Gy | 630 | 630 | Sarcoma       | V20 <32% | <5% | Clinical dysfunction |
| Kidney            | 3 Gy    | V18 | < 25% | 937 | 937 | Lung          | V20 <30% | <5% | Clinical dysfunction |
| Critical Structure | RT0G data | QUANTEC data | Emami Data | Milano Data |
|--------------------|-----------|--------------|------------|-------------|
|                    | Dose/ Vol. | Dose Max. Dose | Protocol Treated organ | Dose/ Vol. | Dose Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 3/5 | TD 50/5 | Organ | Dose tolerance | Endpoint |
|                    | 1.8 Gy | 50% 35 Gy | 436 Esophagus | Mean <30-32 Gy | <5% RILD (in normal liver function) | Liver | 3000 3500 5000 4000 4500 5500 | Liver | 1/3: 40-80 Gy | Late 2/3: 50-60 Gy | 3/3: 25-35% |
| Liver              | 3 Gy | >700 cc | <35 Gy | 937 Lung | Mean <42 Gy | <50% RILD (in normal liver function) | Liver | | | |
| Mean <28 Gy | <5% RILD (in Child-Pugh A or HCC) | Liver | | | |
| Mean <36 Gy | <50% RILD (in Child-Pugh A or HCC) | Liver | | | |
| Critical Structure | Dose | Protocol | Treated organ | Partial Organ | Percentage | Volume (±10% late) | Critical Structure | Dose | Percentage | Volume (±10% late) | Toxicity Rate | Toxicity Endpoint | Organ | TD 5/5 | TD 50/5 | Specialization | Dose | End Point |
|-------------------|------|----------|---------------|---------------|------------|-------------------|-------------------|------|------------|-------------------|---------------|----------------|--------|--------|--------|----------------|------|-----------|
| Bladder           | 1.8 Gy | 60% | 50/Gy | 621 | Prostate | Whole | Bladder (bladder cancer) | Partial Organ | 30 Gy | (9-10% late) | V60 | <50% | Grade 3+ toxicity | Whole | 2/3 | 1/3 | Whole | 2/3 | 1/3 |
| Bladder           | 1.8 Gy | 60% | 45/Gy | 534 | Postop prostatic | Whole | Bladder (prostate cancer) | Partial Organ | 10 Gy | (10-40% late) | V50 | <50% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 55% | 50/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (5-10% late) | V30 | <50% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 50% | 35/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 50 Gy | (20% late) | V70 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 50% | 65/Gy | 534 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 70 Gy | (20% late) | V50 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 50% | 65/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 70 Gy | (20% late) | V50 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 45% | 65/Gy | 534 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 60 Gy | (35% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 44.6 Gy | 621 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 60 Gy | (35% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 40% | 45/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (35% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 40% | 45/Gy | 415 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 35% | 45/Gy | 415 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 50 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 35% | 70/Gy | 415 | Prostate | Whole | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| Bladder           | 1.8 Gy | 30% | 70/Gy | 529 | Anus | Urethra | Bladder (prostate cancer) | Partial Organ | 60 Gy | (20% late) | V30 | <25% | Grade 3+ toxicity | Bladder | <900 | 8000 | N/A | 8000 | N/A |
| External genitalia | RTOG data | Handbook | QUANTEC data | Emami Data | Milano Data |
|-------------------|-----------|----------|--------------|------------|-------------|
| Critical Structure | Dose/| Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy 90% 20 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 35% 30 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 5% 40 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 50% 30 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 13% 30 Gy | 416 | Endometrium | | | | | | | | | | | | | | |
| 1.8 Gy 40% 40 Gy | 522 | Rectum | Anorectal necrosis | | | | | | | | | | | | | | |
| 1.8 Gy 35% 40 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 25% 45 Gy | 522 | Rectum | | | | | | | | | | | | | | |
| 1.8 Gy 10% 50 Gy | 534 | Prostate | | | | | | | | | | | | | | |
| 1.8 Gy 5% 44 Gy | 529 | Anus | | | | | | | | | | | | | | |
| Femoral Head | | | | | | | | | | | | | | | | |
| Critical Structure | Dose/ | Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy 5% 50 Gy | | | | | | | | | | | | | | | | |
| 1.8 Gy 5 Gy | PMED Prostate Group Consor | | | | | | | | | | | | | | |
| 1.8 Gy 3 Gy | 50 Gy | 530 | Sarcoma | | | | | | | | | | | | | | |
| 1.8 Gy 50 Gy | 522 | Rectum | | | | | | | | | | | | | | |
| 1.8 Gy 35 Gy | 712 | Bladder | | | | | | | | | | | | | | |
| Bladder | | | | | | | | | | | | | | | | |
| Critical Structure | Dose/ | Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy 35% 30 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 35% 40 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 5% 50 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 50% 55 Gy | 529 | Anus | | | | | | | | | | | | | | |
| Large Bowel | | | | | | | | | | | | | | | | |
| Critical Structure | Dose/ | Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy 35% 40 Gy | 529 | Anus | | | | | | | | | | | | | | |
| 1.8 Gy 5% 50 Gy | 529 | Anus | | | | | | | | | | | | | | |
| Penile Bulb | | | | | | | | | | | | | | | | |
| Critical Structure | Dose/ | Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy Mean 52.5 Gy | 415 | Prostate | | | | | | | | | | | | | | |
| Penile Bulb | | | | | | | | | | | | | | | | |
| Critical Structure | Dose/ | Vol. | Dose | Max. Dose | Partial | Organ | Tolerance (< 2 Gy Gy/ft) | Critical Structure | Vol. | Dose/ Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 5% | TD 50% | Organ | Dose tolerance | Endpoint |
| 1.8 Gy Mean 52.5 Gy | 415 | Prostate | | | | | | | | | | | | | | |
| Critical Structure | RTOG data | Handbook | QUANTEC data | Enami Data | Milano Data |
|-------------------|-----------|----------|--------------|------------|-------------|
|   | Dose/Ex  | Vol.   | Dose  | Max. Dose | Protocol | Treated organ | Dose | Max. Dose | Tolerance (1.8–2.0 Gy/fx) | Critical Structure | Vol. | Dose/Vol. | Max. Dose | Toxicity Rate | Toxicity Endpoint | Organ | TD 50 | TD 50% | Organ | Dose tolerance | End point |
| 1.8 Gy 60% | 30 Gy | 418 | Endometrial | Whole | 60 Gy | Rectum | GYN HDR | V50 | <8% | <10% | Grade 3+ toxicity | Rectum | V80 | <10% | <10% | Grade 3+ toxicity | Rectum | V50 = 3 Gy | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8-2 Gy 80% | 35 Gy | 712 | Bladder | Rectum | GYN HDR | Point A | Rectum | V60 | <10% | <10% | Grade 3+ toxicity | Rectum | V70 | <15% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 80% | 30 Gy | 415 | Prostate | Rectum | GYN HDR | Point A | Rectum | V65 | <10% | <10% | Grade 3+ toxicity | Rectum | V75 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 80% | 60 Gy | 415 | Prostate | Rectum | GYN HDR | Point A | Rectum | V75 | <10% | <10% | Grade 3+ toxicity | Rectum | V70 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 66.6 Gy | 61 | Prostate | Rectum | GYN HDR | Point A | Rectum | V80 | <10% | <10% | Grade 3+ toxicity | Rectum | V75 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 20% | 35 Gy | 415 | Prostate | Rectum | GYN HDR | Point A | Rectum | V85 | <10% | <10% | Grade 3+ toxicity | Rectum | V75 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 20% | 70 Gy | 415 | Prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 25% | 65 Gy | 415 | Prostate | Rectum | GYN HDR | Point A | Rectum | V85 | <10% | <10% | Grade 3+ toxicity | Rectum | V75 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 25% | 40 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 20% | 45 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 20% | 70 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 25% | 60 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 25% | 40 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |
| 1.8 Gy 20% | 45 Gy | 534 | Postop prostate | Rectum | GYN HDR | Point A | Rectum | V90 | <10% | <10% | Grade 3+ toxicity | Rectum | V80 | <20% | <10% | Grade 3+ toxicity | Rectum | V50 = 2 in < 20-25% | Late grade | V70 = 2 in < 20-25% | 5.10% |

Rectum

References:

- Physical and Radiobiological Evaluation of Radiotherapy Treatment Plan. 2009. PubMed: 18947938

For more information, visit: [Physical and Radiobiological Evaluation of Radiotherapy Treatment Plan](http://dx.doi.org/10.5772/60846)
## Table 4. Radiation tolerance dose in pelvis

| Critical Structure | Organs | RTOG data | Handbook | QUANTEC data | Emami Data | Milano Data |
|--------------------|--------|------------|-----------|--------------|------------|-------------|
| Small Bowel | | | | | | |
| Dose | Vol. | Dose | Max. | Dose | Partial | Critical | Dose/ Vol. | Max. | Dose | Toxicity | Toxicity | Organ | TD 5/5 | TD 50/5 | Organ | Dose | tolerance | End point |
| 1.8 Gy | 200 cc | 30 Gy | 529 | Anus | Small bowel | Small volume | 50 Gy | V15 | <120 cc | <10% | Grade 3+ toxicity | Small intestine | 4000 | 5000 | 5000 | 6000 |
| 1.8 Gy | 130 cc | 35 Gy | 529 | Anus | Small bowel | Whole | >40 Gy | V45 | <195 cc | <10% | Grade 3+ obstruction, perforation | | |
| 1.8 Gy | 30 cc | 40 Gy | 822 | Rectum | | | | | | | | | |
| 1.8 Gy | 30 cc | 40 Gy | 822 | Rectum | | | | | | | | | |
| Skin, longitudinal | | | | | | | | | | | | | |
| Dose | 3 Gy | 20 Gy | 630 | Sarcoma | | | | | | | | | |
| Testis | | | | | | | | | | | | | |
| Dose | 3 Gy | 30 Gy | 630 | Sarcoma | | | | | | | | | |
| Vulva | | | | | | | | | | | | | |
| Dose | 3 Gy | 30 Gy | 630 | Sarcoma | | | | | | | | | |
| Anus | | | | | | | | | | | | | |
| Bone, weight-bearing | 2 Gy | 30 Gy | 630 | Sarcoma | | | | | | | | | |
| Joints | 2 Gy | 30 Gy | 630 | Sarcoma | | | | | | | | | |
| Tissue                      | Grade 0                                      | Grade 1                                      | Grade 2                                      | Grade 3                                      | Grade 4                                      |
|-----------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
| Skin                        | No change over baseline                      | Follicular, faint, or dull erythema/epilation/dry desquamation/decreased sweating | Tender or bright erythema, patchy moist desquamation/moderate edema | Confluent, moist desquamation other than skin folds, pitting edema | Ulceration, hemorrhage, necrosis            |
| Mucosal membrane            | No change over baseline                      | Injection/may experience mild pain not requiring analgesic | Patchy mucositis which may produce an inflammatory aseptic or erosive reaction/desquamation/may experience moderate pain requiring analgesia | Confluent fibrous mucositis/may include severe pain requiring narcotic | Ulceration, hemorrhage, necrosis            |
| Eye                         | No change over baseline                      | Mild conjunctivitis with or without scleral injection/increased tearing | Moderate conjunctivitis with or without keratitis requiring steroids and/or antibiotics/dry eye requiring artificial tears/relieves with photophobia | Severe keratitis with corneal ulceration/objective decrease in visual acuity or in visual fields/acute glaucoma/painful/ulcers | Loss of vision (unilateral or bilateral)     |
| Ear                         | No change over baseline                      | Mild external otitis with erythema, pruritus, secondary to dry desquamation not requiring medication. Audiogram unchanged from baseline | Moderate external otitis requiring topical medication/serious otitis medius/hypoausia on testing only | Severe external otitis with discharge or moist desquamation/symptomatic hypoacusia/limitus, not drug related | Deafness                                      |
| Salivary gland              | No change over baseline                      | Mild mouth dryness/slightly thickened saliva/may have slightly altered taste such as metallic taste/changes not reflected in alteration in baseline feeding behavior, such as increased use of liquids with meals | Moderate to complete dryness/thick, sticky saliva/markedly altered taste | Severe dysphagia or odynophagia with dehydration or weight loss (>15% from pre-treatment baseline) requiring N-G feeding tube, I.V. fluids, or hyperalimentation | Acute salivary gland necrosis                |
| Pharynx and esophagus       | No change over baseline                      | Mild dysphagia or odynophagia/may require topical anesthetic or non-narcotic analgesics/may require soft diet | Moderate dysphagia or odynophagia/may require narcotic analgesics/may require puree or liquid diet | Persistent hoarseness but able to vocalize/referred ear pain, sore throat, patchy fibrous exudate or mild arytenoid edema not requiring narcotic/cough requiring antibiotics | Complete obstruction, ulceration, perforation, fistula |
| Larynx                      | No change over baseline                      | Mild or intermittent hoarseness/cough not requiring antihistamine or erythema of mucosa | Persistent hoarseness but able to vocalize/referred ear pain, sore throat, patchy fibrous exudate or mild arytenoid edema not requiring narcotic/cough requiring antibiotics | Neurologic findings present sufficient to require home care/nursing assistance may be required/medications including steroids/anti-seizure agents may be required | Marked dyspnea, stridor, or hemoptysis with tracheostomy or intubation necessary |
| CNS                         | No change over baseline                      | Fully functional status (i.e., able to work) with minor neurologic findings, no medication needed | Neurologic findings requiring hospitalization for initial management | Neurologic findings requiring hospitalization for initial management | Serious neurologic impairment which includes paralysis, coma, or seizure >3 per week despite medication/hospitalization required |
| Organ/Tissue | Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|-------------|--------|--------|--------|--------|--------|
| Upper G.I   | No change | Anorexia with <=5% weight loss from pretreatment baseline/nausea not requiring antiemetics/abdominal discomfort not requiring parasympatholytic drugs or analgesics | Anorexia with <=15% weight loss from pretreatment baseline/nausea and/or vomiting requiring antiemetics/abdominal pain requiring analgesics | Anorexia with >15% weight loss from pretreatment baseline or requiring N-G tube or parenteral support. Nausea and/or vomiting requiring tube or parenteral support/abdominal pain, severe despite medication/hematemeses or melena/abdominal distention (flat plate radiograph demonstrates distended bowel loops) | Ileus, subacute or acute obstruction, perforation, GI bleeding requiring tube decompression or bowel diversion |
| Lower G.I   | No change | Increased frequency or change in quality of bowel habits not requiring medication/rectal discomfort not requiring analgesics | Diarrhea requiring parasympatholytic drugs (e.g., Lomotil)/mucous discharge not necessitating sanitary pads/rectal or abdominal pain requiring analgesics | Diarrhea requiring parenteral support/severe mucous or blood discharge necessitating sanitary pads/abdominal distention (flat plate radiograph demonstrates distended bowel loops) | Acute or subacute obstruction, fistula or perforation; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion |
| Lung        | No change | Mild symptoms of dry cough or dyspnea on exertion | Persistent cough requiring narcotic, antitussive agents/dyspnea with minimal effort but not at rest | Severe cough unresponsive to narcotic antitussive agent or dyspnea at rest or diffuse pulmonary/intermittent oxygen or steroids may be required | Severe respiratory insufficiency/continuous oxygen or assisted ventilation |
| Genitourinary | No change | Frequency of urination or nocturia twice pretreatment habit/dysuria, urgency not requiring medication | Frequency of urination or nocturia that is less frequent than every hour. Dysuria, urgency, bladder spasm requiring local anesthetic (e.g., Pyridium) | Frequency with urgency and nocturia hourly or more frequently/dysuria, pelvis pain, or bladder spasm requiring regular, frequent narcotic/gross hematuria with/without clot passage | Hematuria requiring transfusion/acute bladder obstruction not secondary to clot passage, ulceration, or necrosis |
| Heart       | No change over baseline | Asymptomatic but objective evidence of EKG changes or pericardial abnormalities without evidence of other heart disease | Symptomatic with EKG changes and radiologic findings of congestive heart failure or pericardial disease/no specific treatment required | Congestive heart failure, angina pectoris, pericardial disease responding to therapy | Congestive heart failure, angina pectoris, pericardial disease, arrhythmias not responsive to nonsurgical measures |
| Organ/Tissue       | Grade 0 | Grade 1                                      | Grade 2                                      | Grade 3                                      | Grade 4 | Organ/Tissue       |
|-------------------|---------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------|-------------------|
| Subcutaneous tissue | None    | Slight atrophy; pigmentation change; some hair loss | Patch atrophy; moderate telangiectasia; total hair loss | Marked atrophy; gross telangiectasia | Ulceration | Death related to radiation effects |
| Mucosa membrane    | None    | slight induration (fibrosis), and loss of subcutaneous fat | Moderate fibrosis but asymptomatic; slight field contraction; <10% linear reduction | Severe induration and loss of subcutaneous tissue; field contraction; >10% linear measurement | Necrosis | Death related to radiation effects |
| Mucosa membrane    | None    | Slight atrophy and dryness                 | Moderate atrophy and telangiectasia; little mucous | Marked atrophy with complete dryness; severe telangiectasia | Ulceration | Death related to radiation effects |
| Salivary gland     | None    | Slight dryness of mouth; good response on stimulation | Moderate dryness of mouth; poor response on stimulation | Complete dryness of mouth; no response on stimulation | Fibrosis | Death related to radiation effects |
| Spinal cord        | None    | Mild L'Hermitte's syndrome                 | Severe L'Hermitte's syndrome               | Objective neurological findings at or below cord level treated | Mono, para quadriplegia | Death related to radiation effects |
| Brain              | None    | Mild headache; slight lethargy             | Moderate headache; great lethargy          | Severe headaches; severe CNS dysfunction (partial loss of power or dyckinesia) | Seizures or paralysis; coma | Death related to radiation effects |
| Eye                | None    | Asymptomatic cataract; minor corneal ulceration or keratitis | Symptomatic cataract; moderate corneal ulceration; minor retinopathy or glaucoma | Severe keratitis; severe retinopathy or detachment severe glaucoma | Panophthalmitis/blindness | Death related to radiation effects |
| Larynx             | None    | Hoarseness; slight arytenoid edema         | Moderate arytenoid edema; chondritis        | Severe edema; severe chondritis             | Necrosis | Death related to radiation effects |
| Organ/Tissue          | Grade 0                                                                 | Grade 1                                                                 | Grade 2                                                                 | Grade 3                                                                 | Grade 4                                                                 | Grade 5                                                                 |
|----------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Lung                 | None                                                                    | Asymptomatic or mild symptoms (dry cough); slight radiographic appearances | Moderate symptomatic fibrosis or pneumonitis (severe cough); low grade fever; patchy radiographic appearances | Severe symptomatic fibrosis or pneumonitis; dense radiographic changes | Severe respiratory insufficiency/continuous O2assisted ventilation       | Death related to radiation effects                                      |
| Heart                | None                                                                    | Asymptomatic or mild symptoms; transient 7 wave inversion and ST changes; sinus tachycardia (>100) | Moderate angina on effort; mild pericarditis; normal heart size; persistent abnormal 7 wave and ST changes; low ORS | Severe angina; pericardial effusion; constrictive pericarditis; moderate heart failure; cardiac enlargement; EKG abnormalities | Tamponade/severe heart failure/severe constrictive pericarditis         | Death related to radiation effects                                      |
| Esophagus            | None                                                                    | Mild fibrosis; slight difficulty in swallowing solids; no pain on swallowing | Unable to take solid food normally; swallowing semi-solid food; dilation may be indicated | Severe fibrosis; ability to swallow only liquids; may have pain on swallowing; dilation required | Necrosis/perforation fistula                                           | Death related to radiation effects                                      |
| Small/large intestine | None                                                                    | Mild diarrhea; mild cramping; bowel movement 5 times daily; slight rectal discharge or bleeding | Moderate diarrhea and colic; bowel movement >5 times daily; excessive rectal mucosa or intermittent bleeding | Obstruction or bleeding, requiring surgery | Necrosis/perforation fistula                                           | Death related to radiation effects                                      |
| Liver                | None                                                                    | Mild lassitude; nausea, dyspepsia; slightly abnormal liver function       | Moderate symptoms; some abnormal liver function tests; serum albumin normal | Disabling epatitis insufficiency; liver function tests grossly abnormal; low albumin; edema or ascites | Necrosis/hepatic coma or encephalopathy                                | Death related to radiation effects                                      |
| Kidney               | None                                                                    | Transient albuminuria; no hypertension; mild impairment of renal function; urine 25–35 mg%; creatinine 1.5–2.0 mg%; creatinine clearance > 75% | Persistent moderate albuminuria (2+); mild hypertension; no related anemia; moderate impairment of renal function; urine > 36–60 mg%; creatinine clearance (50–74%) | Severe albuminuria; severe hypertension; persistent anemia (>10%); severe renal failure; urine > 40 mg%; creatinine > 4.0 mg%; creatinine clearance < 50% | Malignant hypertension; uric acid coma/uric > 100%                        | Death related to radiation effects                                      |
| Bladder              | None                                                                    | Slight epithelial atrophy; minor telangiectasia (microscopic hematuria)    | Moderate frequency; generalized telangiectasia; intermittent macroscopic hematuria | Severe frequency and dysuria; severe generalized telangiectasia (often with proteinuria); frequent hematuria; reduction in bladder capacity (<150 cc) | Necrosis/contracted bladder (capacity < 100 cc); severe hemorraghic cystitis | Death related to radiation effects                                      |
| Bone                 | Asymptomatic; no growth retardation; reduced bone density              | Moderate pain or tenderness; growth retardation; irregular bone sclerosis | Moderate stiffness; intermittent or moderate joint pain; moderate limitation of movement | Severe pain or tenderness; complete arrest of bone growth; dense bone sclerosis | Necrosis/spontaneous fracture                                           | Death related to radiation effects                                      |
| Joint                | None                                                                    | Mild joint stiffness; slight limitation of movement                       | Serous joint stiffness; pain with severe limitation of movement         | Severe joint stiffness; pain with severe limitation of movement         | Necrosis/complete fixation                                              | Death related to radiation effects                                      |
6. Radiation treatment plan analysis programs

In modern radiation therapy, physical dose indices, such as mean doses, dose-volume histograms (DVHs), and isodose distribution charts, are often used for treatment plan evaluation. DVHs provide dose volume coverage information. However, they fail to provide information regarding hot spots and dose homogeneity. When reviewing physical dose indices, the resulting biological objectives, such as tumor control rate and normal tissue complication probability, must be indirectly estimated based on clinical experience and knowledge. In some competing plans, it is possible that a similar mean dose, maximum dose, or minimum dose might have significantly different radiobiological outcomes. To facilitate the direct and accurate comparison and ranking of treatment plans, radiobiological models for treatment plan evaluation have been introduced. These radiobiological models are based on the idea that the radio-sensitivity of different organs should be taken into account. As a result, the physical dose delivered to an organ is directly associated with the dose–response probability of inducing complications in normal tissues. Many programs have been designed and developed to calculate both dosimetrical and biological indices, as shown in Table 9 [10-29].

7. Multidisciplinary strategies: Planning decision support concept

7.1. Methods could be used for planning a decision support system

In this section, we highlight dosimetrical and biological models in radiation oncology treatment planning, with focus on the methodological aspects of prediction model development. In radiation treatment planning analysis, dose volume histograms were the most widely used quantitative results. To comprehensively evaluate a certain DVH, we proposed several dosimetrical and biological models in the earlier sections. For dosimetrical models, there were PTTV, CI, and TCI for target coverage index, and MHI, HI for homogeneity index and COSI, QF, and CQI for overall index. For radiobiological models, there were TCP and NTCP for tumor or critical structures, representatively. There were still other factors like treatment time, planning time, or overall monitor units irradiated in patients could be helpful for making more reasonable decision. Some characteristic prognostic and predictive factors like radiation-induced organ toxicities were discussed in earlier sections. We also enumerate the normal tissue tolerance criteria including QUENTEC and EMAMI database.

7.2. The need of plan decision support concept in RT

With the emergence of individualized medicine and the increasing amount and complexity of available medical data, a growing need exists for the development of planning decision-support systems based on prediction models of treatment outcome [55-57]. In radiation oncology, these models combine both predictive and prognostic data factors from dosimetrical, biological, imaging, and other sources to achieve the highest accuracy to predict tumor response and follow-up event rates. The central challenge, however, is how to integrate diverse, multimodal information (imaging, dosimetrical, biological, and other data) in a quantitative manner to provide specific clinical predictions that accurately and robustly
Currently, many prediction models are being published that consider factors related to disease and treatment, but without standardized assessments of their robustness, reproducibility, or clinical utility [58]. Consequently, these prediction models might not be suitable for clinical decision-support systems for routine care.

| Program | Input system |Dicom RT platform | Plan comparison |Plan analysis | Disease features |Paper publication |
|---------|--------------|------------------|-----------------|--------------|-----------------|-----------------|
| HART    |               |                  |                 |              |                 |                 |
| CERR    |               |                  |                 |              |                 |                 |
| DREES   |               |                  |                 |              |                 |                 |
| EUD-based mathematical model |               |                  |                 |              |                 |                 |
| EUCLID  |               |                  |                 |              |                 |                 |

Estimate patient outcomes as a function of the possible decisions. Currently, many prediction models are being published that consider factors related to disease and treatment, but without standardized assessments of their robustness, reproducibility, or clinical utility [58]. Consequently, these prediction models might not be suitable for clinical decision-support systems for routine care.
| Program               | Input system | Oncent RT platform | Plan comparison | Plan analysis | Program features | Paper publication |
|-----------------------|--------------|--------------------|-----------------|--------------|------------------|------------------|
| computational platform |   √          | AAPM/√ compatibile | RTOG, DicomRT   | DicomRT      | Matlab, ARIA     | Dezhi Liu (18) 2009 |
| BIOPLAN               | √            | DVH file           | DVH file        | DVH file     | Matlab, Visual Basic | B SANCHEZ NIETO 2000 |
| Anonymous             | √            | DVH file           | DVH file        | DVH file     | Matlab           | Arun S. Oinam (21) 2011 |
| SlicerRT              | √            | DicomRT compatible | with commercial RTP | Matlab       | C++              | Csaba Pinter (22) 2012 |
| MERT                  | √            | DicomRT            | This was RTP    | Multi format(MC) | Matlab            | Murat Surnau (26) 2010 |
| DIRART                | √            | DicomRT            | use CERR import engine | Matlab       | Doshan Yang (27) 2010 |
| SABER                 | √            | DicomRT            | Eclipse         | Matlab       | Jay Burmeister (28) 2010 |
| DICOM RT tools       | √            | DicomRT            | Helas TMS       | Matlab       | Spati E (29) 2002 |
### Table 9. Review of previous programs

| Program          | Input system                  | Dicom RT platform | Plan comparison | Plan analysis | Program features | Paper publication |
|------------------|-------------------------------|-------------------|-----------------|--------------|-----------------|-------------------|
| BELDoral         | DVH file                      | DVH file          | ×               | ×            | ×               | ×                 |
| Comp Plan        | DVH file                      | DVH file in Excel | ×               | ×            | ×               | ×                 |
| CalcNTCP         | Manual input                  | Manual input      | ×               | ×            | ×               | ×                 |
| RADBIOMID        | DVH file                      | Manual input      | ×               | ×            | ×               | ×                 |
| BioSuite         | DVH file                      | Pinnacle, Eclipse | ×               | ×            | ×               | ×                 |
| RTToolbox        | √ Dicom RT                    | ×                 | ×               | ×            | ×               | ×                 |
|                 |                               |                   |                 |              | MatLab          | Su FC             |
|                 |                               |                   |                 |              | MuLab           | Holloway LC       |
|                 |                               |                   |                 |              | Visual Basic    | Khan HA           |
|                 |                               |                   |                 |              | Microsoft Excel | Chang JH           |
|                 |                               |                   |                 |              | BioSuite        | JUzan             |
|                 |                               |                   |                 |              | Virtus, our    | Lanlan, Zhang     |
|                 |                               |                   |                 |              | in-house        |                   |
|                 |                               |                   |                 |              | developed       |                   |
|                 |                               |                   |                 |              | planning        |                   |
|                 |                               |                   |                 |              | system          |                   |

**Depicts statistical analysis**
- Normal statistic
- Survival statistic

**Indicates independence from GUI**
- ×
- √
Decision making in radiotherapy is mainly based on clinical features, such as the patient performance status, organ function, and grade and extent of the tumor (e.g., as defined by the TNM system). In almost all studies, such features have been found to be prognostic for survival and development of toxicity [59, 60]. Consequently, these features should be evaluated in building robust and clinically acceptable radiotherapy prognostic and predictive models. Moreover, measurement of some clinical variables, such as performance status, can be captured with minimal effort.

Toxicity measurements and scoring should also build on validated scoring systems, such as the Common Terminology Criteria for Adverse Events (CTCAE), which can be scored by the physician or patient [50, 61]. Indeed, a meta-analysis showed that high-quality toxicity assessments from observational trials are similar to those of randomized trials. [45, 46] However, a prospective protocol must clarify which scoring system was used and how changes in toxicity score were dealt with over time with respect to treatment. Finally, to ensure a standardized interpretation, the reporting of clinical and toxicity data and their analyses should be performed in line with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies and genetic-association studies, which is represented as checklists of items that should be addressed in reports to facilitate the critical appraisal and interpretation of these types of studies (Figure 7).

Figure 7. Design of planning decision support concept in radiotherapy treatment planning.
Despite the challenges that remain, the vision of predictive models leading to plan decision support concept that are continuously updated via rapid learning on large datasets is clear, and numerous steps have already been taken. These include universal data-quality assurance programs and semantic interoperability issues. However, we believe that this truly innovative journey will lead to necessary improvement of healthcare effectiveness and efficiency. Indeed, investments are being made in research and innovation for health-informatics systems, with an emphasis on interoperability and standards for secured data transfer, which shows that “eHealth” will be among the largest health-care innovations of the coming decade. Accurate, externally validated prediction models are being rapidly developed, whereby multiple features related to the patient’s disease are combined into an integrated prediction. The key, however, is standardization—mainly in data acquisition across all areas, including dosimetric-based and biological-based models, patient preferences, and possible treatments. These crucial features are the basis of validating a plan decision support system, which, in turn, will stimulate developments in rapid-learning health care and will enable the next major advances in shared decision making.

8. Conclusion

Plan comparison studies still remain controversial. The main reason for this is because plan parameters, optimization methods, and OAR constraints are difficult to clearly define. Many researchers have focused on the influence of planning parameters on the results of treatment plans [62-64]. For instance, Gutiérrez et al. [65] reported that the use of a field width of 1 cm resulted in dosimetrically superior plans for brain irradiation compared to plans that use a field width of 2.5 cm. More recently, Skorska and Piotrowski studied the influence of treatment-planning parameters on plan qualities for prostate cancer patients using helical tomotherapy [66]. This study revealed that using a field width of 1 cm, instead of 5 cm, leads to decreases in the D20%, D40%, D60%, and D80% of the small intestine by 2.45%, 8.48%, 6.36%, and 5%. This results in a 1.22Gy, 4.24Gy, 3.18Gy, and 2.50Gy, respectively, for the prescribed dose of 50 Gy. Another bias of plan comparison studies is that the quality of a planner’s abilities and planning techniques may vary. Performing repeat planning processes and using multiple planners to cross check would minimize such bias. The use of OAR dose tolerance guidelines, such as RTOG or QUENTEC protocols, would minimize human error.

Other major issues among plan comparison studies are the method of plan analysis and evaluation. Many studies have focused on developing a simple index that represents the overall quality of plans [14, 19, 41, 42, 67]. However, none of these plans are easily used in a clinic. There is a need for programs that can easily calculate dosimetrical and biological indices [10, 12, 13, 15, 16, 22-25, 28, 68, 78-82].

There is a growing trend of studying the relationships between treatment plan results and clinical outcomes, such as toxicities, survival, and patterns of failure [69-77]. Such studies may help physicians and physicists learn more about the influence of plan results and plan quality on patient treatment.
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