

## INTRODUCTORY PAPER

## GUEST EDITOR'S INTRODUCTION TO QUANTEC: A USERS GUIDE

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We are pleased to present this special issue of the *International Journal of Radiation Oncology·Biology·Physics*, dedicated to the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC). This work is the result of the diligent efforts of numerous investigators, authors, reviewers, and support personnel. We are particularly indebted to the comembers of the QUANTEC Steering Committee<sup>1</sup>, for their dedication.

This is an exciting time in the field of radiation oncology. Sophisticated treatment-planning tools and delivery systems remarkably increase our ability to steer the dose where we want it. An increased knowledge of how dose distributions affect normal tissue outcomes is critically needed to know how best to exploit these new planning/delivery tools. In 1991, Emami *et al.* (1) published a comprehensive review of the available dose/volume/outcome data, along with expert opinion where data were lacking. Since the publication of the classic paper by Emami *et al.* (1), there have been numerous additional studies providing dose/volume/outcome data. The QUANTEC reviews provide focused summaries of the dose/volume/outcome information for many organs. The reviews will be excellent resources to assist physicians and treatment planners in determining acceptable dose/volume constraints. In addition, the QUANTEC papers point out the shortcomings of current predictive models and suggest areas for future research. Despite the limitations of the data, the new information presented should be of substantial use in the treatment planning process. We are particularly pleased with the many summary tables and figures that, we hope, will adorn the walls of treatment planning areas.

This special issue is organized into three sections. There are two introductory papers: the first paper is an overview/history

with some scientific issues related to the QUANTEC effort, and the second paper contains suggestions on how to rationally incorporate the QUANTEC metrics/models into clinical practice. The latter paper includes a large summary table of dose/volume/outcome data. The bulk of this issue is 16 organ-specific clinical papers. To assist the reader, each article is organized in a consistent format that includes 10 sections (Fig. 1). The organs discussed were selected because the authors believed that there were meaningful data to review, and a clinical need to better summarize the available dose/volume data for these organs. We conclude with a series of vision papers outlining interesting issues that merit further study.

Dr. Philip Rubin, at the University of Rochester, the founding Editor of this journal, was an early leader in the field of radiation-induced normal tissue injury. He conducted many of the classic studies of normal tissue response and provided some of the earliest summaries of normal tissue dose/volume/outcome estimates. It is particularly fitting that an entire issue of the *International Journal of Radiation Oncology·Biology·Physics* be devoted to a topic so very dear to our founding editor.

QUANTEC represents an evolution from the early summary tables presented by Dr. Rubin, to the more recent reviews by investigators such as Emami *et al.* (1). All those involved in the QUANTEC effort recognize that much work remains to be done. For example, most of the available data relate to conventionally fractionated conformal irradiation, *i.e.*, not hypofractionated or intensity-modulated approaches. We anticipate regular updates of the information and believe these will help our field continue to provide quality care to our patients. We hope to be able to provide updated

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**Introductory Papers**

History/Overview/Scientific Issues

Application of QUANTEC metrics/models into clinical practice

**Organ-Specific Papers**

1. Brain
2. Optic Nerve/Chiasm
3. Brain Stem
4. Spinal Cord
5. Ear
6. Parotid
7. Larynx/Pharynx
8. Lung
9. Heart
10. Esophagus
11. Liver
12. Stomach/Small Bowel
13. Kidney
14. Bladder
15. Rectum
16. Penile Bulb

**Vision Papers**

True Dose  
Imaging  
Biomarkers  
Data Sharing  
Lessons of QUANTEC

**Each with 10 sections**

1. **Clinical Significance**- Describes the clinical situations where the organ is irradiated, and the incidence/significance of organ injury.
2. **Endpoints**- Describes the different endpoints often considered when assessing injury, the impact of endpoint-selection on the reported injury rates, the challenges/utilities of different endpoints, and the time course of organ injury.
3. **Challenges Defining Volumes**- Describes how the organ is typically defined (or segmented) on treatment planning images. Includes a discussion of uncertainties/challenges in organ definition (e.g. changes in organ volume/shape during therapy), and the associated impact on DVH's and dose/volume/outcome analyses.
4. **Review of Dose/Volume Data**- A comprehensive summary of reported 3D dose/volume data for clinically-relevant outcomes.
5. **Factors Affecting Risk**- Other clinical factors affecting the risk of injury are noted (e.g. age, combined modality therapy, dose fractionation).
6. **Mathematical/Biological Models**- Models that have been used to relate 3D dose/volume data to clinical outcomes are summarized, along with associated model parameters, limitations and uncertainties.
7. **Special Situations**- Most of the data discussed relates to conventional fractionation. This section describes situations where the presented data/models may not apply (e.g. hypofractionation).
8. **Recommended Dose/Volume Limits**- The available information is condensed into meaningful dose/volume limits, with associated risk rates, to apply clinically.
9. **Future Toxicity Studies**- Describes areas in need of future study.
10. **Toxicity Scoring**- Recommendations on how to score organ injury.

Fig. 1. Outline of the issue: the first section consists of Introductory Papers; the second section consists of Organ-Specific Papers, each containing 10 topic sections; and the third section consists of Vision Papers.

QUANTEC reviews on an ASTRO-sponsored web site, as well as perhaps on a bulletin board or blog where readers can provide comments/data for consideration for future reviews.

Attempts to limit normal tissue risks should be taken in the context of the competing need to deliver a “therapeutic dose distribution.” Target coverage may trump normal tissue sparing: recurrent tumor can be morbid/lethal, and the normal tissue risks considered in the QUANTEC reviews are often not life threatening. Furthermore, QUANTEC’s focus on three-dimensional dose/volume parameters reinforces the reliance on dose-volume histogram-based optimization systems to minimize normal tissue risk. It is important to remember that relatively simple measures (e.g., careful attention to patient positioning) can reduce normal tissue exposure and complement our newer planning/delivery/optimization tools.

It is humbling to have helped lead this QUANTEC effort, and it was a privilege to work with so many talented and dedicated people. The information presented here was inspired by our mentors and teachers and relies almost entirely on the published work of others. We hope that current and future generations of investigators—physicians, physicists, biologists, imagers, and others—will continue this area of study. Exploiting the rapidly evolving advances outlined in the vision papers (e.g., imaging, dose monitoring, genetics, and other biologic factors) will facilitate the development of better tools to understand and reduce the risks of radiation-induced normal tissue injury.

**REFERENCE**

1. Enami B, Lyman J, Brown A, *et al.* Tolerance of normal tissue to therapeutic radiation. *Int J Radiat Oncol Biol Phys* 1991;21:109–122.