

## Physics Contribution

# Assessing the Clinical Impact of Approximations in Analytical Dose Calculations for Proton Therapy

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Received Dec 24, 2014, and in revised form Mar 13, 2015. Accepted for publication Apr 2, 2015.

## Summary

The clinical impact of uncertainties in analytical dose calculations was investigated by comparing dose-volume histogram—based properties,  $\gamma$ -index, and tumor control probability for 50 patients from 5 treatment sites (liver, prostate, breast, head and neck, and lung). Significant differences in tumor control probability were found for lung (11%), head and neck (6.5%), and prostate (6%). Liver and breast patients showed good agreement (<2.5% discrepancy) between the 2 algorithms. Predictions of normal

**Purpose:** To assess the impact of approximations in current analytical dose calculation methods (ADCs) on tumor control probability (TCP) in proton therapy.

**Methods:** Dose distributions planned with ADC were compared with delivered dose distributions as determined by Monte Carlo simulations. A total of 50 patients were investigated in this analysis with 10 patients per site for 5 treatment sites (head and neck, lung, breast, prostate, liver). Differences were evaluated using dosimetric indices based on a dose-volume histogram analysis, a  $\gamma$ -index analysis, and estimations of TCP.

**Results:** We found that ADC overestimated the target doses on average by 1% to 2% for all patients considered. The mean dose, D95, D50, and D02 (the dose value covering 95%, 50% and 2% of the target volume, respectively) were predicted within 5% of the delivered dose. The  $\gamma$ -index passing rate for target volumes was above 96% for a 3%/3 mm criterion. Differences in TCP were up to 2%, 2.5%, 6%, 6.5%, and 11% for liver and breast, prostate, head and neck, and lung patients, respectively. Differences in normal tissue complication probabilities for bladder and anterior rectum of prostate patients were less than 3%.

**Conclusion:** Our results indicate that current dose calculation algorithms lead to underdosage of the target by as much as 5%, resulting in differences in TCP of up to 11%. To ensure full target coverage, advanced dose calculation methods like Monte Carlo simulations may be necessary in proton therapy. Monte Carlo simulations may also be required to avoid biases resulting from systematic discrepancies in calculated dose

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Conflict of interest: none.

*Acknowledgments*—This work was supported by NIH/NCI under CA U19 21239. We would like to thank the MGH Monte Carlo group for many fruitful discussions. We also thank Jonathan Jackson and Tao Song of the Enterprise Research Infrastructure and Services (ERIS) group at Partners Healthcare for their in-depth support and smooth computing cluster operations, upgrades, and fixes.

tissue complication probability for prostate patients agreed within 3%.

distributions for clinical trials comparing proton therapy with conventional radiation therapy. © 2015 Elsevier Inc. All rights reserved.

## Introduction

With an increasing number of proton therapy centers currently being built around the world, the number of patients receiving full or partial treatment with proton therapy is steadily increasing. The standard method to calculate and optimize dose distributions for a patient treatment plan is based on fast analytical dose calculation (ADC) algorithms. These algorithms calculate dose along narrow-width beams (pencils) with a certain spread. Although more accurate dose calculations are available, they are not yet standard in clinical practice. The Monte Carlo (MC) simulation method is considered the gold standard to describe particle interactions and to calculate the resulting dose (1). Several studies comparing proton dose distributions calculated with MC and ADC algorithms have demonstrated the shortcomings of the latter, in particular when delivering fields to heterogeneous patient geometries (2, 3). Soukup et al (4) have reported the shortcomings of ADCs on the target coverage based on dose-volume histograms (DVHs) of 6 example patients; however, a systematic analysis of the effects has not yet been conducted.

In a recent study, we assessed the clinical impact of range uncertainty margins in proton therapy (5). The range of protons is subject to uncertainties arising from various sources such as inaccuracies in patient setup, computed tomographic (CT) imaging, conversion of CT Hounsfield units to material composition, and limitations of the dose calculation engine. The impact of the latter has been assessed with respect to coverage of clinical target volumes (CTVs) (6, 7). So-called range margins are added around the CTV to ensure full coverage of the target despite these uncertainties and are generally a function of the range of the proton field, neglecting dependencies on the patient geometry. We have shown that margins can be reduced for homogeneous treatment sites such as prostate, liver, and whole brain. By contrast, for heterogeneous sites such as head and neck, breast, and lung, the currently applied generic range margins are insufficient to cover range fluctuations for each individual treatment field (5). Although this previous study quantified range uncertainties resulting from dose calculations in proton therapy, it did not address target coverage. Approximations in dose calculation can affect target coverage 2-fold, either leading to a geometric miss from overestimating the range or predicting unrealistic dose homogeneity caused by underestimation or overestimation of scattering effects in tissue. In this study we investigate the clinical significance of approximations in ADCs.

## Methods

### Patient cohort

Fifty patients from 5 treatment sites (10 patients per site) were selected from our clinical database, covering the full range from relatively homogeneous patient geometries (liver) to patients with high geometric complexity (air cavities and density heterogeneities in head and neck, lung, and breast patients) and from shallow targets (breast) to deep-seated tumors (prostate). Table 1 lists the ranges of parameters of the patient cohort.

### Analytical dose calculation and Monte Carlo simulations

Dose distributions for patient treatment plans for double-scattered proton therapy at the Francis H. Burr Proton Therapy Center at the Massachusetts General Hospital are calculated using an ADC algorithm implemented on the XiO treatment planning system (by Computerized Medical Systems Inc, now by ELEKTA). This ADC algorithm is based on a parameterized beam model propagating protons through the patient-specific compensator and patient geometry. The lateral spread is estimated based on a physics model developed by Hong et al (8), which separates the beam into a central axis part (kernel) and a Gaussian fluence map to account for the lateral beam spread. The width of this Gaussian distribution is determined by the scattering angle distribution of the incident beams within the patient and patient-specific treatment head components.

The dose distributions predicted by the planning system were recalculated using TOPAS (TOOl for PArTicle Simulations, version beta8) (9), which is layered on top of Geant4 (version 9.6.p02) (10). TOPAS has been extensively validated for proton therapy showing agreement with measurements well within the clinical requirements for quality assurance purposes (11). In addition, for each field investigated here, the initial proton energy was adjusted by as much as 1 MeV to ensure the same range (within 0.3 mm) for each SOBP, as calculated inside a water phantom for both algorithms. Field flatness and modulation width between measurements and MC agree within clinical specifications.

TOPAS determines the material composition for each voxel in the patient geometry based on its CT Hounsfield unit following the approach by Schneider et al (12) as described in detail elsewhere (9, 13, 14). Following previous approaches (5), the density of each material was adjusted to ensure that the stopping power to Hounsfield unit curve of the MC and ADC system were identical. MC

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