International Journal of Radiation Oncology biology • physics

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Physics Contribution

Statistical Assessment of Proton Treatment Plans Under Setup and Range Uncertainties

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Received Nov 26, 2012, and in revised form Mar 25, 2013. Accepted for publication Apr 5, 2013

Summary

Assessing proton treatment plan under uncertainties is important to avoid unexpected deviations from the original design. In this study, a statistical approach based on comprehensive simulation of setup and range uncertainties is used to evaluate the integrity of proton therapy plans of various clinical sites.

Purpose: To evaluate a method for quantifying the effect of setup errors and range uncertainties on dose distribution and dose–volume histogram using statistical parameters; and to assess existing planning practice in selected treatment sites under setup and range uncertainties.

Methods and Materials: Twenty passively scattered proton lung cancer plans, 10 prostate, and 1 brain cancer scanning-beam proton plan(s) were analyzed. To account for the dose under uncertainties, we performed a comprehensive simulation in which the dose was recalculated 600 times per given plan under the influence of random and systematic setup errors and proton range errors. On the basis of simulation results, we determined the probability of dose variations and calculated the expected values and standard deviations of dose–volume histograms. The uncertainties in dose were spatially visualized on the planning CT as a probability map of failure to target coverage or overdose of critical structures.

Results: The expected value of target coverage under the uncertainties was consistently lower than that of the nominal value determined from the clinical target volume coverage without setup error or range uncertainty, with a mean difference of −1.1% (−0.9% for breath-hold), −0.3%, and −2.2% for lung, prostate, and a brain cases, respectively. The organs with most sensitive dose under uncertainties were esophagus and spinal cord for lung, rectum for prostate, and brain stem for brain cancer.

Conclusions: A clinically feasible robustness plan analysis tool based on direct dose calculation and statistical simulation has been developed. Both the expectation value and standard deviation are useful to evaluate the impact of uncertainties. The existing proton beam planning method used in this institution seems to be adequate in terms of target coverage. However, structures that are small in volume or located near the target area showed greater sensitivity to uncertainties.

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This project is supported by grant P01CA021239 from the National Cancer Institute.

Conflict of interest: none.

Int J Radiation Oncol Biol Phys, Vol. 86, No. 5, pp. 1007–1013, 2013
0360-3016/$ - see front matter
http://dx.doi.org/10.1016/j.ijrobp.2013.04.009

Introduction

Conventional plan assessment includes checking dose distribution quality (eg, conformity, homogeneity, and cold or hot spots) by overlaying the 3-dimensional dose distribution on patient anatomic images. In addition, volume-specific metrics, such as the mean dose of a volume of interest (VOI), dose−volume histogram (DVH), or other similarly derived quantities (eg,V_D, the volume receiving at least dose D), are also used. However, the dose distribution and DVHs in traditional plan review only represent a nominal setting that does not contain uncertainties caused by stopping power uncertainties in CT images, daily patient setup errors, and interfractional and intrafractional anatomy changes. These uncertainties make it difficult to assess plan robustness, especially for proton therapy. Traditionally a geometrically expanded volume, such as the planning target volume (PTV) or the planning risk volume, is used for treatment design and evaluation. For example, under the assumption that dose distribution is static in space and the extent of motion of the clinical target volume (CTV) is contained within the margin of the PTV, PTV coverage can be considered the worst case of CTV coverage. For this reason, PTV is often used in prescribing and reporting rather than the CTV itself. The assumption that dose distribution is static in space is crucial for such interpretation. However, previous studies revealed that this assumption does not apply to protons because of their sensitivity to the density variation in the beam path (1). Therefore, the paradigm of using PTV as a surrogate for CTV under uncertainty does not translate well to proton therapy.

Recently researchers reported evaluation methods that account for both setup and range uncertainties in an effort to assess robustness directly. Lomax (2) and Albertini et al (3) proposed the use of worst-case dose distribution and error−volume histogram that are derived from dose distributions calculated under extreme conditions. Trofimov et al (4) proposed to use the DVH bands to visualize the range of DVH variation under uncertainties. However, these methods rely on dose distributions calculated under a handful of (often extreme) conditions (ie, 6 calculations for setup errors and 2 calculations for under- and overestimated range errors). Although these methods are fast and convenient, the metrics used are generally too conservative and sometimes unrealistic. In other words, these approaches lack the assessment of a large number of scenarios and statistical interpretations. Maleike et al (5) and Henriquez et al (6) proposed methods that fully characterize the probability density function (PDF) of individual point dose distributions to quantify expected value and sttandard deviation of point dose, and similar approaches can be done for DVHs. However, their studies were limited to dose variations caused by predefined organ motion models (5) and dose calculation inaccuracies (6). The influence of setup and range uncertainties was not addressed. Using statistical methods to characterize proton dose uncertainties is difficult because the PDF of a point dose distribution under such uncertainties is not known in advance. Multiple-instance sampling of DVH is necessary because point dose distribution may be spatially correlated. To our knowledge, no studies have been performed to quantify such statistical parameters to assess the effects of setup and range uncertainties on proton plans. In addition, the validity of conventional proton therapy treatment planning methods for various cancer sites needs to be investigated under such rigorous robust analysis. In this study we established a method of estimating PDF of dose distribution under the uncertainties based on a large number of simulations (ie, 600 dose calculations per plan). We compared the nominal DVH with its expected value for several clinical sites.

Methods and Materials

Patient selection and treatment planning

We retrospectively evaluated the clinically approved proton plans of 20 patients with locally advanced non-small cell lung cancer who were randomly selected from the clinical trial protocol, and 10 previously treated prostate cancer cases and 1 brain cancer case. Of the 20 lung cancer patients, 5 were treated with breath-hold technique. Seventeen patients were prescribed to 74 Gy and 3 patients to 60 Gy. LungV_{20Gy}, mean lung dose, esophagus V_{65Gy} and V_{45Gy}, heart V_{60Gy} andV_{30Gy}, and maximum spinal cord dose were considered critical planning parameters. For all prostate cases, dose was prescribed to 78 Gy while rectum V_{45Gy} and V_{70Gy} and bladder V_{45Gy} andV_{70Gy} were recorded. For the brain case, 60 Gy was prescribed to the CTV with maximum dose to brainstem and optical nerves considered as dose-limiting factors.

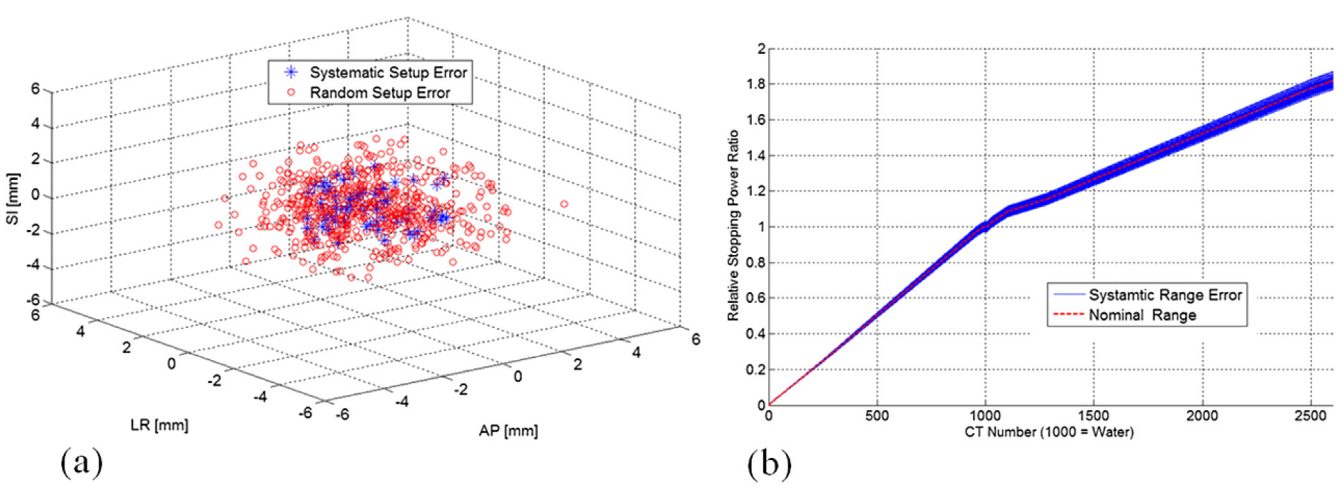

Fig. 1. (a) Randomly selected systematic and random setup error coordinates for a selected patient; (b) CT number-to-relative stopping power curve for nominal and with systematic range error.