Applications of the Biologically Effective Uniform Dose to Adaptive Tomotherapy and Four-dimensional Treatment Planning

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Abstract

The ultimate goal of radiation therapy is to efficiently deliver radiation in order to eradicate tumors, while adequately sparing nearby normal tissues. With the emergence of advanced technologies in radiation delivery, more and more conformal radiation delivery has been achieved in order to overcome challenges such as motion management between treatment fractions as well as during radiation delivery. Adaptive tomotherapy, which takes account of the inter-fractional organ motion, systematically manage treatment feedback and allows the user to respond to the temporal variations occurring between treatment fractions. Four-dimensional radiation therapy, which corrects the intra-fractional organ motion, is believed to achieve high conformality through additional consideration in time axis during delivery of intensity modulated radiotherapy. However, the clinical benefit versus to the cost of extra time and effort of complex treatment planning for these advanced technologies remains mostly unproven. The biologically effective uniform dose is able to comprehensively evaluate treatment plans both physically and biologically. For a comprehensive assessment of clinical outcomes in adaptive tomotherapy and four-dimensional treatment planning, the biologically effective uniform dose is applied together with the complication-free tumor control rate. The calculation of the biologically effective uniform dose is based on the linear-quadratic-Poisson model with the consideration of dose-response characteristics of various organs. Adaptive tomotherapy was implemented using the Hi-Art TomoTherapy system in conjunction with the Planned Adaptive software. Four lung cancer patients who underwent helical tomotherapy were selected retrospectively. The delivered dose and dose distributions were evaluated using the Planned Adaptive software together with the biologically effective uniform dose. For radiobiological evaluation of the four-dimensional treatment planning, nine lung cancer patients were randomly selected. For each of the nine patients, ten multileaf collimator-based intensity modulated radiation therapy plans were developed for different respiratory phases. The four-dimensional treatment plans were, then, developed based on the deformable registration between each of different respiratory phases and the reference phase. Results of radiobiological assessment of the adaptive tomotherapy show a significant increase of 13.2% in the complication-free tumor control rate of treatment plans for lung cancer patients, indicating the clinical benefit of adaptive tomotherapy. When comparing four-dimensional treatment plans with intensity modulated radiation therapy plans of different respiratory phases, similar but not identical curves of dose volume histogram were found with slightly different mean doses in tumor (up to 1.5%) and normal tissue in all cases based on the examined lung cancer patients and the margin set around the planned target volume. When it comes to biological evaluations, there was no definitively planned target volume size-dependence observed in complication-free tumor control rate among these nine lung cancer patients with various sizes of planned target volumes. Moreover, it is not necessary that four-dimensional plans would have better target coverage or higher complication-free tumor control rate as compared to a fixed phase intensity modulated radiation therapy plan. However, on the contrary to significant deviations in complication-free tumor control rate (up to 14.7%) observed if delivering the intensity modulated radiation therapy plan made at end-inhalation incorrectly at end-exhalation phase, we estimated the overall tumor control probability without fatal complications for four-dimensional composite plans which have accounted for intra-fractional respiratory motion. In summary, the biologically effective uniform dose effectively estimates the biological efficacy regarding the management of internal organ motion both inter-fractionally for adaptive planning of tomotherapy and intra-fractionally for four-dimensional treatment planning. The scope of this thesis is mainly focused on the assessment of the unknown advancement in biological effectiveness regarding the adaptive tomotherapy and four-dimensional radiation therapy. The application of the biologically effective uniform dose evaluation, however, can be expanded continuously to other novel technologies of radiation therapy.

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