Multiple energy extraction delivery technique in synchrotron-based intensity-modulated proton therapy (IMPT) may exacerbate motion interplay effects for lung cancer treatment

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INTRODUCTION

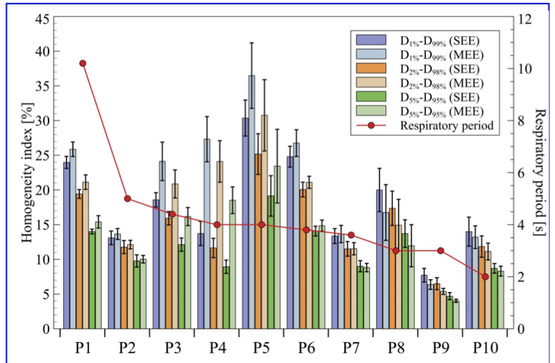
Multiple energy extraction (MEE) is a delivery technique for synchrotron-based proton delivery systems that can reduce treatment delivery time by ~35% compared to single energy extraction (SEE) by extracting protons of multiple energies, rather than single energy, from the accelerator during each accelerator spill. However, the effect on motion-induced dose degradation (*i.e.*, interplay effects) is not well-understood. The aim of this study was to test the null hypothesis that SEE and MEE are indistinguishable according to dose-volume histogram (DVH)-based metrics of the delivered target dose homogeneity, target dose coverage, and dose to organs-at-risk (OARs).

METHOD

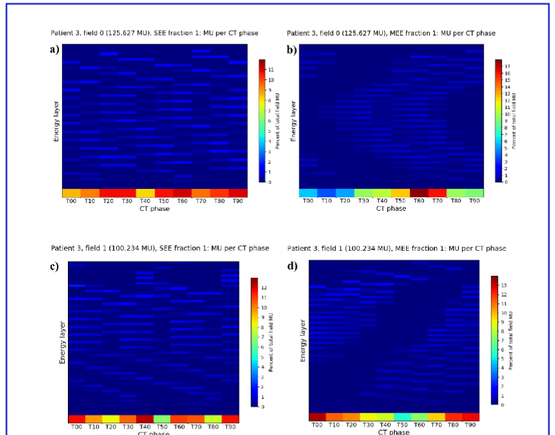
A patient cohort of ten lung cancer patients representing a broad range of respiratory periods and motion amplitudes was non-randomly selected. Interplay effects were evaluated using 4D dynamic dose. The Wilcoxon rank-sum test was used to get statistical significance. The following procedures were used to compare dose distributions delivered using the SEE and MEE techniques:

- We calculated DVH indices to measure target dose homogeneity, coverage, and sparing of OARs from ten pairs of single-fraction dose distributions delivered using the SEE and MEE techniques with identical random initial phases for each patient in the cohort.
- We plotted the distribution of machine units (MUs) to each 4D CT phase within every energy layer in order to identify differences between the SEE and MEE spot delivery sequences for each patient in the cohort.
- We compared single-fraction dose distributions in color wash with the SEE and MEE techniques.
- For the patient that had the worst interplay effects with MEE, the corresponding plan was delivered with multiple fractions to determine whether target dose homogeneity and coverage could improve to reach the clinically-acceptable levels.
- We compared the multiple-fractionated 4D dynamic doses calculated using ten and two CT phases for the patient having the worst interplay effects with MEE to determine whether the 4D dynamic dose calculated using two phases was a good approximation of the 4D dynamic dose calculated using ten phases.

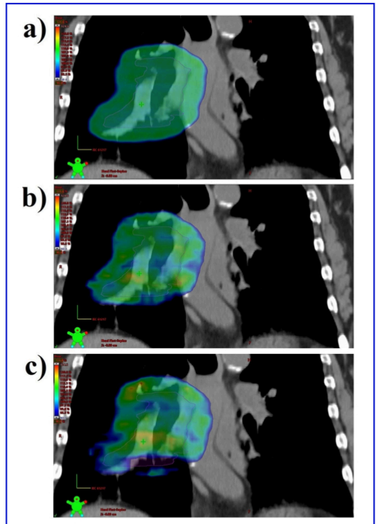
RESULTS



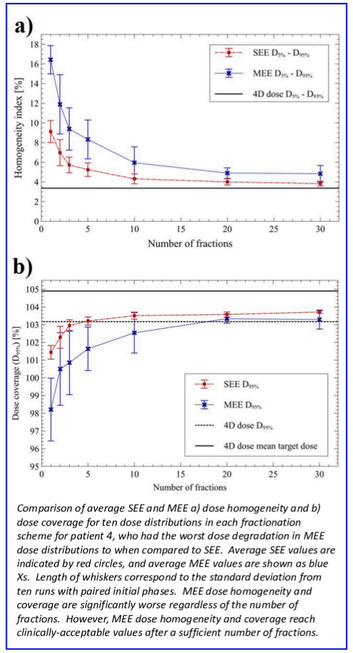
Homogeneity indices for ten single-fraction dose distributions for each patient in the cohort. The height of each bar and the length of the whiskers indicate the average and standard deviation, respectively. Initial respiratory phases were randomly selected for each paired SEE and MEE single-fraction delivery. The red circles on the overlaid plot correspond to the patient respiratory period measured during CT simulation. Statistically significant differences in dose homogeneity were measured for patients 1, 3, 4, 5, and 9. For patients 3, 4, and 5 with the largest differences in dose homogeneity, MEE performed significantly worse than SEE and the respiratory period was approximately four seconds.



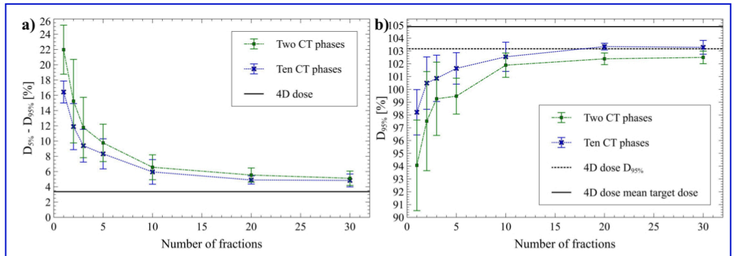
Total MU of all spots delivered to each CT phase on each energy layer (with total field MU delivered to each CT phase at the bottom of the plot) for one delivery of patient 3 fields using SEE (a and c) and MEE (b and d) delivery techniques. Energy layers are ordered from highest energy at the top to lowest energy at the bottom. Synchronization between treatment delivery and patient respiration was observed in MEE (b and d). For this patient, the MEE delivery technique resulted in significantly worse dose homogeneity.



Color wash images of a) plan dose, b) single-fraction SEE dose, and c) single-fraction MEE dose for patient 4, which had the largest reduction in dose homogeneity when switching from the SEE delivery technique to the MEE delivery technique. Hot and cold spots were observed in the SEE and MEE dose distributions (b and c) that are characteristic of the interplay effect. For this patient, the MEE delivery technique led to significantly worse dose homogeneity and dose coverage in the single-fraction dose distributions.



Comparison of average SEE and MEE a) dose homogeneity and b) dose coverage for ten dose distributions in each fractionation scheme for patient 4, who had the worst dose degradation in MEE dose distributions to when compared to SEE. Average SEE values are indicated by red circles, and average MEE values are shown as blue Xs. Length of whiskers correspond to the standard deviation from ten runs with paired initial phases. MEE dose homogeneity and coverage are significantly worse regardless of the number of fractions. However, MEE dose homogeneity and coverage reach clinically-acceptable values after a sufficient number of fractions.



Comparison of a) average dose homogeneity and b) average dose coverage calculated from ten paired 4D dynamic dose distributions using the MEE delivery technique with two CT phases and ten CT phases for worst-case patient 4. Current PTCOG guidelines suggest that 4D dynamic dose calculations with two CT phases (corresponding to maximum inhalation and exhalation) can be used as an upper bound on dose degradation to reduce required calculation time in the clinical workflow. Average dose homogeneity and coverage with two CT phases (green circles) indicated worse dose degradation than average values from ten CT phases (blue Xs) regardless of the number of fractions.

CONCLUSIONS

- No significant difference between clinically-relevant OAR DVH indices from dose distributions delivered with the SEE and MEE techniques.
- MEE can significantly reduce target dose homogeneity for some patients.
- Patients with the worst interplay effects with MEE had respiratory periods of approximately four seconds.
- Dose distribution quality degradation may be related to the synchronization between patients' respiration periods and accelerator spill durations in the MEE delivery technique.
- Dose distribution quality degradation was reduced by multiple fractionation, however, the degradation in target dose homogeneity with MEE compared to SEE persisted even after thirty fractions.
- With sufficiently high target mean dose, acceptable target dose coverage can still be achieved with the MEE delivery technique
- 4D dynamic dose calculated with two phases can be used to obtain a good estimate of the interplay effects for the dose distributions with MEE.
- Irregular respiratory motion is likely to mitigate the interplay effects.

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