Abstract

Background: The use of hypofractionated intensity-modulated radiation therapy (IMRT) ensured the safe application of internal mammary lymph node area (IMN) in the treatment field as well as protect organs at risk such as the heart and lungs in cases of left breast cancer; however, little is known about the effect of respiratory motion on regional node irradiation IMRT for advanced breast cancer. We analyzed the effect of intra-fractional and inter-fractional motion during IMRT of left-side breast and regional lymphatics by calculating dose distribution based on four-dimensional computed tomography (4D-CT).

Materials and Methods: Twenty patients diagnosed with left breast cancer were enrolled. Three-dimensional (3D)-CT along with ten phases of 4D-CT were collected for each patient, with target volumes independently delineated on both 3D-CT and all phases of 4D-CT. IMRT plans were generated based on 3D-CT (43.2Gy in 16 fractions). The plan parameters for each segment were split into phases based on time duration estimates for each respiratory phase, with phase-specific dose distributions calculated and summated (4D-calculated dose). The procedure is repeated for 16 fractionations by randomly allocating starting phase using random-number generation to simulate inter-fractional discrepancy caused by different starting phase. Comparisons of plan quality between the original and 4D-calculated doses were analyzed.

Results: There was a significant distortion in 4D-calculated dose induced by respiratory motion in terms of conformity and homogeneity index compared to those of the original 3D plan. Mean doses of the heart and the ipsilateral lung were significantly higher in the 4D-calculated doses compared to those of the original 3D plan (0.34Gy, p=0.010 and 0.59Gy, p<0.001), respectively). The mean IMN dose was significantly greater in the 4D-calculated plan, compared to the original 3D plan (1.42Gy, p<0.001).

Conclusions: DIBH may help in reducing dose increment caused by free-breathing motion in heart and lung. IMN doses should be optimized during the dose-calculation for the free-breathing left breast IMRT.

References

1. Poortmans PM, Collette S, Kirkove C, Van Limbergen E, Budach V, Struikmans H, et al. Int ernal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. N Engl J Med. 2015;373(4):3 17-27.

2. Whelan TJ, Olivotto IA, Levine MN. Regional Nodal Irradiation in Early-Stage Breast Cancer. N Engl J Med. 2015;373(19):1878-9.

3. Lu HM, Cash E, Chen MH, Chin L, Manning WJ, Harris J, et al. Reduction of cardiac volu me in left-breast treatment fields by respiratory maneuvers: a CT study. Int J Radiat Oncol Biol Phys. 2000;47(4):895-904.

4. Pedersen AN, Korreman S, Nystrom H, Specht L. Breathing adapted radiotherapy of breast ca ncer: reduction of cardiac and pulmonary doses using voluntary inspiration breath-hold. Radiother Onco 1. 2004;72(1):53-60.

5. Latty D, Stuart KE, Wang W, Ahern V. Review of deep inspiration breath-hold techniques for the treatment of breast cancer. J Med Radiat Sci. 2015;62(1):74-81.

6. Bergom C, Currey A, Desai N, Tai A, Strauss JB. Deep Inspiration Breath Hold: Techniques and Advantages for Cardiac Sparing During Breast Cancer Irradiation. Front Oncol. 2018;8:87.

7. Qi XS, White J, Rabinovitch R, Merrell K, Sood A, Bauer A, et al. Respiratory organ motio n and dosimetric impact on breast and nodal irradiation. International Journal of Radiation Oncology Bi ology Physics. 2010;78:609-17.

8. Qi XS, Hu A, Wang K, Newman F, Crosby M, Hu B, et al. Respiration induced heart motio n and indications of gated delivery for left-sided breast irradiation. International Journal of Radiation O ncology Biology Physics. 2012;82:1605-11.

9. Yue NJ, Li X, Beriwal S, Heron DE, Sontag MR, Huq MS. The intrafraction motion induced dosimetric impacts in breast 3D radiation treatment: A 4DCT based study. Medical Physics. 2007;34:2 789.

10. Wang W, Bin Li J, Hu HG, Sun T, Xu M, Fan TY, et al. Evaluation of dosimetric variance in whole breast forward-planned intensity-modulated radiotherapy based on 4DCT and 3DCT. Journal of radiation research. 2013;54:755-61.

11. Frazier RC, Vicini FA, Sharpe MB, Yan D, Fayad J, Baglan KL, et al. Impact of breathing motion on whole breast radiotherapy: A dosimetric analysis using active breathing control. International Journal of Radiation Oncology Biology Physics. 2004;58:1041-7.

12. Rao M, Wu J, Cao D, Wong T, Mehta V, Shepard D, et al. Dosimetric impact of breathing motion in lung stereotactic body radiotherapy treatment using image-modulated radiotherapy and volume tric modulated arc therapy. International Journal of Radiation Oncology Biology Physics. 2012;83:e251-e 6.

13. Radiation Therapy Oncology Group. Breast Cancer Atlas for Radiation Therapy Planning: Con sensus Definitions.Available at:http://www.rtog.org/LinkClick.aspx?fileticket=vzJFhPaBipE%3d&tabid=236; Accessed June 7, 2019.

14. Feng M, Moran JM, Koelling T, Chughtai A, Chan JL, Freedman L, et al. Development and validation of a heart atlas to study cardiac exposure to radiation following treatment for breast cancer. Int J Radiat Oncol Biol Phys. 2011;79(1):10-8.

15. Weiss E, Wijesooriya K, Dill SV, Keall PJ. Tumor and normal tissue motion in the thorax d uring respiration: Analysis of volumetric and positional variations using 4D CT. Int J Radiat Oncol Bio 1 Phys. 2007;67(1):296-307.

16. Oechsner M, Odersky L, Berndt J, Combs SE, Wilkens JJ, Duma MN. Dosimetric impact of different CT datasets for stereotactic treatment planning using 3D conformal radiotherapy or volumetric modulated arc therapy. Radiation Oncology. 2015;10:249.

17. Darby SC, McGale P, Taylor CW, Peto R. Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300,000 women in US SEER cancer registries. Lancet Oncol. 2005;6(8):557-65.

18. Darby SC, Ewertz M, McGale P, Bennet AM, Blom-Goldman U, Bronnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med. 2013;368(11):987-98.

19. Marks LB, Yorke ED, Jackson A, Ten Haken RK, Constine LS, Eisbruch A, et al. Use of N ormal Tissue Complication Probability Models in the Clinic. International Journal of Radiation Oncolog y Biology Physics. 2010;76.

20. Seppenwoolde Y, Lebesque JV, de Jaeger K, Belderbos JS, Boersma LJ, Schilstra C, et al. C omparing different NTCP models that predict the incidence of radiation pneumonitis. Normal tissue co mplication probability. Int J Radiat Oncol Biol Phys. 2003;55(3):724-35.

21. Sterpin E, Tomsej M, De Smedt B, Reynaert N, Vynckier S. Monte carlo evaluation of the AAA treatment planning algorithm in a heterogeneous multilayer phantom and IMRT clinical treatments for an Elekta SL25 linear accelerator. Med Phys. 2007;34(5):1665-77.

22. Kroon PS, Hol S, Essers M. Dosimetric accuracy and clinical quality of Acuros XB and AA A dose calculation algorithm for stereotactic and conventional lung volumetric modulated arc therapy pl ans. Radiat Oncol. 2013;8:149.

Luo J, Jin K, Chen X, Wang X, Yang Z, Zhang L, et al. Internal Mammary Node Irradiation (IMNI) Improves Survival Outcome for Patients With Clinical Stage II-III Breast Cancer After Preoper ative Systemic Therapy. International Journal of Radiation Oncology Biology Physics. 2019;103:895-904.
Ramadaan IS, Peick K, Hamilton DA, Evans J, Iupati D, Nicholson A, et al. Validation of V arian's SmartAdapt(R) deformable image registration algorithm for clinical application. Radiat Oncol. 20 15;10:73.

25. Nelli FE, Harwood JR. A method for assessing the dosimetric consistency of single phase 4D CT dose accumulation based on deforming image registration. Physica Medica. 2016;32:275.

26. Camilleri J, Mazurier J, Franck D, Dudouet P, Latorzeff I, Franceries X. 2D EPID dose calib ration for pretreatment quality control of conformal and IMRT fields: A simple and fast convolution ap proach. Phys Med. 2016;32(1):133-40.

27. Han T, Mikell JK, Salehpour M, Mourtada F. Dosimetric comparison of Acuros XB determini stic radiation transport method with Monte Carlo and model-based convolution methods in heterogeneou s media. Med Phys. 2011;38(5):2651-64.

28. Fogliata A, Nicolini G, Clivio A, Vanetti E, Cozzi L. Dosimetric evaluation of Acuros XB A dvanced Dose Calculation algorithm in heterogeneous media. Radiat Oncol. 2011;6:82.

29. Bush K, Gagne IM, Zavgorodni S, Ansbacher W, Beckham W. Dosimetric validation of Acur os XB with Monte Carlo methods for photon dose calculations. Med Phys. 2011;38(4):2208-21.