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Ideal Tumor Contouring for Radiotherapy in lung cancer - Enduring Myth

Introduction:

Lung cancer is the leading cause of cancer related mortality worldwide. Approximately one third of patients presents at a curable stage of the disease. Radiotherapy plays a very important role in curative management of lung cancer. In stage I NSCLC, stereotactic body radiation therapy is the treatment of choice in medically inoperable patients and those who refused surgery. In stage III, concurrent chemoradiation is the standard treatment. Indications for radiation therapy to primary lung tumor has expanded with the recent evidence in oligometastatic non-small cell lung cancer. SBRT is also routinely employed for pulmonary metastases from other primary tumors.

Target delineation is a very critical step and is a common source of error in lung cancer radiotherapy. Tumor delineation is subjective, physician dependent and requires expertise. Intra and inter observer variability is a common feature in contouring of lung cancer. Positron emission tomography (PET) with computed tomography (CT) reduces interobserver variability but does not completely eliminate. Objective methods like PET-CT guided auto delineation of tumor depends on the segmentation method and threshold can be used for tumor volume generation.

Another significant challenge in target contouring is respiratory tumor motion. Motion encompassing techniques like four dimensional computed tomography (4DCT) is used to generate individual internal target volume (ITV). Post processing tools like maximum intensity projection (MIP) is the most common and time efficient technique for ITV generation. However, its utility is not proven in locally advanced lung cancer patients. Other techniques like tumor contouring in all 10 phases of respiration is laborious and time expensive technique. In this synopsis, we aimed to review 1) PET-CT based auto contouring using various thresholds and its comparison with pathological tumor size in early lung cancer and 2) ITV generation using MIP and contouring in all phases of respiration in locally advanced lung cancer.

Material and Methods:

In theseIRB approved studies, ideal contouring of tumor volume was assessed using two different methods in early and locally advanced lung cancer datasets. First, we assessed the PETCT based primary tumor delineation using various percentage thresholds of maximum standardized uptake value (SUVmax). From January 2013 to July 2014, 37 surgically resected early stage NSCLC who underwent PET CT at our institute were retrospectively enrolled. Here, we did auto delineation of primary tumor using various percentage threshold of SUVmax as objective criteria and compared the largest tumor diameter in any dimension with largest pathological tumor diameter. Optimal SUV threshold was obtained using linear regression analysis and Bland Altman plot. In second dataset, we compared primary tumorcontouring using MIP datasetand contouring in all 10 phases of respiration. From January 2014 till March 2017, 30 consecutive patients of locally advanced NSCLC who underwent 4DCT were retrospectively enrolled. Both the contoured volumes were compared using matching index (MI). It is the ratio of the intersection of two volumes to the union of two volumes. Results:In early lung cancer, the mean optimal percentage threshold of SUVmax that correlated with pathological tumor size was $36\% \pm 18\%$. Using Bland-Altman plots, auto-contouring of primary tumor with 40%SUVmax was in greater agreement with thepathological tumor size. In the locally advanced lung cancer, tumorvolume delineation using MIP is significantly smaller than tumor delineation in all 10 phases of respi-

ration. Themean MI was 0.75 (range 0.57-0.88). The mean tumor volume delineated using all 10 phases on tespiration. Themean MI was 0.75 (range 0.57-0.88). The mean tumor volume delineated using all 10 phases not covered by MIP based tumor delineation was 23.5%, compared to vice versa of 6%. Mean MI reduced to 0.73 for tumor adjacent to high density structures like mediastinum, chest wall and diaphragm. MI was not different between smaller and larger tumors. However, the average time required for ITV delineation was considerably less with MIP (9 vs 96 minutes).

Conclusion:Precise and accurate tumor delineation in lung cancer is a complex process. Auto-contouring using percentage threshold of 40% SUVmax might be a good objective criteria for accurate tumor delineation and requires further validation in a larger cohort of all stage patients. MIP based primary tumor delineation is a simple time-efficient technique however, can miss the tumor edges. Continued use of MIP should proceed with caution especially in tumor adjacent to high density structures like mediastinum, chest wall and diaphragm. It is advisable to see for completeness of tumor contours on CT slice in various respiratory phases.

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