

**Purposes:** This study aimed to assess the changes of lung ventilation (V) and perfusion (Q) function by single photon emission tomography (V/Q SPECT) at 45 Gy during radiation therapy (RT), and determine if V/Q SPECT during-RT can be used to decrease dose to the functioning lung.

**Methods:** V/Q SPECT-CT and FDG-PET-CT were performed prior and during-RT (@45Gy) for patients enrolled in prospective clinical trials for stage I-III NSCLC. The V and Q functions were assessed using a semi-quantitative system. An adaptive plan was generated after RT of 45 Gy to the target based on the during-RT FDG-PET-CT. The during-RT SPECT was used to optimize the plan to minimize dose to the functioning lung.

**Results:** Of 45 patients analyzed, 100% had lung functional defects at or around the primary tumor and the majority of them have defects in the remaining lung. The V/Q defects were mismatched in 40% and 50% patients for pre- and during-RT SPECT, respectively. After 45 Gy, the global and local lung function improved in one third patients. Specifically, there was a significant improvement in V scores in ipsilateral lung ( $P=0.002$ ), while there was no significant changes in V scores of the contralateral lung and Q scores of the ipsilateral lung at or around the tumor at 45 Gy during-RT. Using V/Q SPECT at 45 Gy for voxel based optimization, the mean dose to the functioning lung decreased remarkably while maintaining the physical dose to the target and the physical dose based lung normal tissue complication probability.

**Conclusion:** V/Q SPECT-CT acquired during the course of treatment has a potential to escalate the tumor dose and or decrease the dose to the functioning lung. Clinical trials are ongoing to assess if the therapeutic ratio (long-term survival over lung toxicity) will improve in patients with NSCLC.