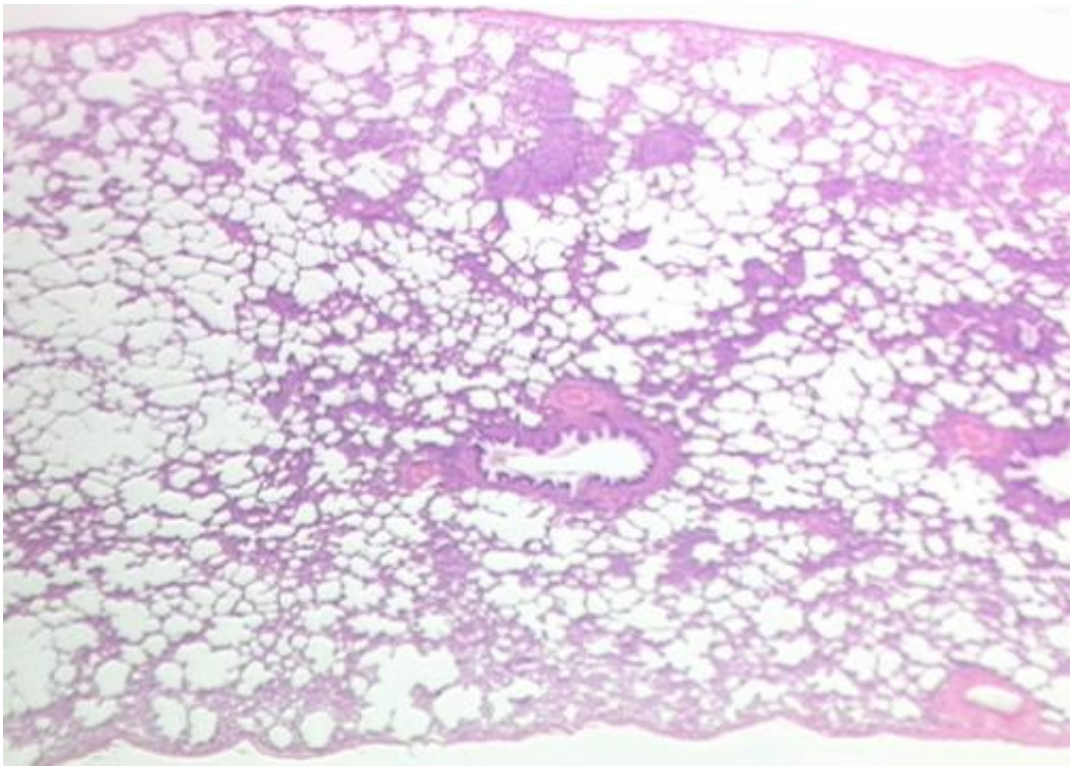
Study shows safety of adaptive radiotherapy in non small cell lung cancer patients

January 29 2021



Lung tissue. Credit: Rutgers University

The NRG Oncology and the American College of Radiology Network (ACRIN) multicenter, phase II trial, NRG-RTOG 1106/ACRIN 6697, is the first randomized trial to demonstrate the feasibility and safety of performing adaptive radiotherapy (RT) escalation in patients with locally advanced non-small cell lung cancer (NSCLC). The improvement of in-

field tumor control appeared similar to the level (1% improvement with 1Gy dose escalation) of the single institutional study of adaptive radiotherapy performed at University of Michigan, and different from that of RTOG617 with non-adaptive high dose radiation in stage III NSCLC. The results were presented at the virtual edition of the International Association for the Study of Lung Cancer 2020 World Conference on Lung Cancer, Singapore.

The NRG Oncology randomized phase III trial NRG-RTOG 0617 offered the insight that a higher dose of radiotherapy delivered with chemoradiotherapy actually worsened tumor control and survival for this patient population. NRG-RTOG 1106/ACRIN 6697 was designed to bridge this treatment gap by testing adaptive radiotherapy dose escalation with chemotherapy to see if this treatment could enhance two-year local-regional tumor control compared to the 60 Gy standard dose of radiotherapy this patient population typically receives. The use of fluorodeoxyglucose-positron emission tomography (FDG-PET/CT) imaging would help identify resistant aggressive tumor identified mid-treatment and adapt personalized treatment plans per each individual's tolerance.

Patients with Stage III NSCLC were randomly assigned in a 2:1 ratio to receive either the standard radiotherapy at 60 Gy (Standard Arm) or the adaptive radiotherapy treatment that resulted in a median dose escalation of 11 Gy (Adaptive Arm). Patients on both treatment arms received FDG-PET/CT imaging at mid-treatment for radiation. The Standard Arm included 43 eligible patients whereas the Adaptive Arm included 84 eligible patients. The Standard Arm had a median follow up of 3.7 years for surviving patients with acceptable overall radiotherapy compliance rates (92.9% and 50% per protocol). The 2-year overall local-regional progression free rate was 59.5% (95% CI: 37.9, 75.7). Median local-regional progression free time was 27.5 months (95% CI: 14.3, not reached) in the Standard Arm. The Adaptive Arm had a median follow

up of 3.4 years for surviving patients with acceptable overall radiotherapy compliance rates (95.8% for the initial course of treatment and 32.4% for adaptive course per protocol) and 2-year overall local-regional progression free rates were 54.6% (95% CI: 39.9, 67.0). Median local-regional progression free time was 28.4 months (95% CI: 19.1, not reached) in the Adaptive Arm. There were no significant differences in grade 3 or worse toxicity of lung, esophagus, and heart or overall survival, progression-free survival, and lung cancer specific survival between treatment arms. Adaptive radiotherapy did increase in-field local-regional tumor control by 11% and in-field primary tumor control by 17% during the trial.

"Not all patients respond the radiation dose escalation in the same way. We have already learned from a genotypic study of RTOG617 (which was recently presented in ASTRO 2020) that only one third of stage III patients with radiation resistant genotype on DNA repair pathway genes will benefit from dose escalation. Future trial designs should be focused on individualizing radiotherapy dose prescriptions according to patient's intrinsic sensitivity in order to improve survival. Additionally, further research should investigate if adaptive radiotherapy could increase normal tissue sparing factor (Sp) to improve survival on top of dose optimization in each individual," said Feng-Ming (Spring) Kong, MD, Ph.D., FACR, FASTRO of the Clinical Oncology Center, the University of Hong Kong—Shenzhen Hospital; and Li Ka Shing Faculty of Medicine, The University of Hong Kong; Department of Radiation Oncology, Case Western Reserve University, and the lead author of the NRG-RTOG 1106/ACRIN 6697 abstract.

More information: Kong FM, Hu C, Machtay M, Haken RT, Xiao Y, Matuszak M, Hirsh V, Pryma D, Siegel BA, Gelblum D, Hayman J, Robinson C, Loo, Jr. BW, Videtic GMM, Faria SL, Ferguson C, Dunlap N, Kundapu V, Paulus R, Bradley J. Results of RTOG1106/ACRIN9969: A Randomized Phase II Trial of

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Provided by NRG Oncology