High-dose radiotherapy with chemotherapy found to be effective in treating people with non-small cell lung cancer

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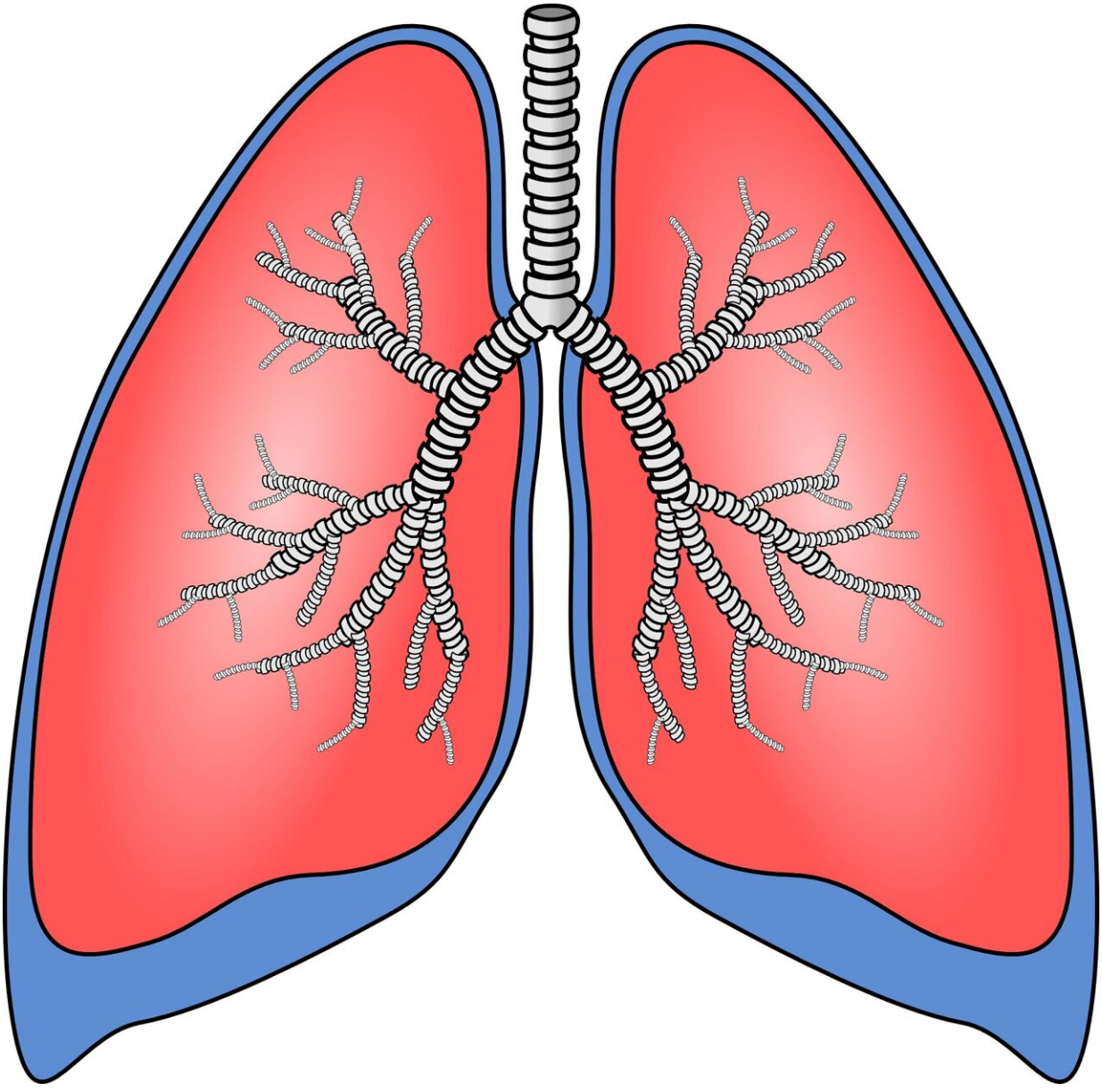

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A new study led by researchers from the UCLA Health Jonsson Comprehensive Cancer Center shows that using high doses of radiation while integrating an ablative radiotherapy technique called stereotactic ablative radiotherapy (SABR) concurrently with chemotherapy is safe and effective in treating people with locally advanced non-small cell lung cancer that is not suitable for surgery.

Based on mid-treatment response, researchers found the combination treatment, which involves a second radiation plan to personalize a boost for the last third of radiation treatments, is a viable and promising option that helps reduce the risk of toxic side effects and having the cancer return within the chest.

The findings were published in the journal JAMA Oncology.

"This treatment method explores uncharted territory," said Dr. Trudy Wu, a radiation oncology resident at UCLA and first author of the study. "Our field has been moving towards hypofractionation across many disease sites; however, it is particularly challenging in locally advanced lung cancer due to the close vicinity of tumor to sensitive structures such as the airways and esophagus."

"This treatment is also typically delivered with chemotherapy which magnifies treatment-related toxicity. Using a novel adaptive boost technique personalized to an individual's treatment response after the first two-thirds of radiation treatment allows for a tighter conformal radiation boost plan and reduction of healthy tissue receiving radiation."

In the past, the prognosis for those with unresectable, locally advanced non-small cell lung cancer has been poor, with low survival rates despite treatment with a combination of chemotherapy and radiation. Current standard of care for this group of patients consists of 30 treatments spanning over six weeks, which can be logistically challenging for many patients.

While outcomes have improved with the help of modern treatment advances, like immunotherapy, a portion of patients still develop disease relapse in the chest.

One potential way to prevent cancer from returning within the chest after local therapy is to deliver radiation with a higher dose per single treatment in a more intense, or ablative, fashion.

To find the highest personalized boost dose that could be given safely in combination with chemotherapy, 28 patients at UCLA with stage II or III non-small cell lung cancer were enrolled between May 2011 and May 2018 on an early phase dose escalation trial.

All patients first received a base radiation dose of 4 Gy × 10 fractions followed by an adaptive SABR boost to target any remaining metabolically active cancer. The first 10 patients received a boost dose of 25 Gy (low, 5 Gy × 5 fractions). If this was deemed safe within a specified follow-up period, patients proceeded to receive a higher boost dose of 30 Gy (intermediate, 6 Gy × 5 fractions), followed by 35 Gy (high, 7 Gy × 5 fractions), all with concurrent weekly chemotherapy.

Along with determining the maximum tolerated dose of this novel and personalized approach, the researchers aimed to improve progression-free survival and shorten the overall duration of treatment for locally advanced non-small cell lung cancer.

The investigators observed the most promising results in the intermediate-dose cohort, where patients received a total of 70 Gy in 15 fractions, inclusive of a 30 Gy boost. This dosage showed a favorable balance between side effects while being a very effective treatment.

Rates of two-year local control, which is when the cancer does not grow back, were 74.1%, 85.7%, and 100.0% for the low-, intermediate-, and high-dose cohorts. Two-year overall survival was 30.0%, 76.2%, and 55.6% for the low-, intermediate-, and high-dose cohorts.

There were no severe toxic effects observed in the intermediate-dose boost cohort. Most patients experienced some degree of mild side effects which included fatigue, and inflammation of the esophagus or lungs resulting in sore throat or cough, respectively. The high dose regimen led to severe treatment-related side effects in two cases.

"Our data shows patients may benefit from targeted, high-dose radiation with chemotherapy if it's done thoughtfully with adaptive radiation," said Dr. Beth Neilsen, a study author and radiation oncology resident at UCLA. "For the intermediate dose regimen, the incidence of severe side effects was relatively low and showed potential for better local control of the cancer."

The authors note this approach could be explored further in future trials with the addition of consolidation immunotherapy, which is now standard of care in this setting.

"This study contributes to ongoing efforts to improve the treatment lung cancer, a leading cause of cancer-related death," said Dr. Michael Steinberg, professor and chair of radiation oncology at the David Geffen School of Medicine, director of Clinical Affairs at the UCLA Health Jonsson Comprehensive Cancer Center and one of the senior authors on the study.

"The integration of adaptive radiation with chemotherapy offers a novel approach that shows promise in terms of safety, effectiveness and improved patient outcomes, paving the way for more effective and personalized treatments."

The investigators also noted the study has limitations, including a small sample size and need for longer follow-up to assess late side effects.

The study's senior author is Dr. Percy Lee, who was a professor of radiation oncology at UCLA when the research was conducted and is now a practicing radiation oncologist at City of Hope. Other involved UCLA researchers include Dr. Jonathan Goldman, Dr. Edward Garon, Dr. Jay Lee, Carol Felix, Minsong Cao, Stephen Tenn and Daniel Low.

More information: Accelerated Hypofractionated Chemoradiation Followed by Stereotactic Ablative Radiotherapy Boost for Locally Advanced, Unresectable Non– Small Cell Lung Cancer, *JAMA Oncology* (2024). DOI: 10.1001/jamaoncol.2023.6033

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