Proton therapy offers new treatment possibility for recurrent lung cancer

Advanced form of image-guided radiation therapy is an option for patients who previously had none

SAN FRANCISCO, March 16, 2017—A new study offers hope for patients with recurrent lung cancer, who historically have been considered ineligible for curative treatment. In the largest analysis to date of reirradiation using intensity-modulated proton therapy (IMPT) for lung and other thoracic tumors, more than three-fourths of patients were free from local recurrence at one year following retreatment, and fewer than one in ten patients experienced severe side effects. The study will be presented today at the 2017 Multidisciplinary Thoracic Cancers Symposium.

Lung cancer causes more deaths in the United States than any other type of cancer, due in part to its aggressive nature and likelihood of recurrence. Historically, recurrences have been challenging to treat, because many of these patients are not candidates for surgery. Moreover, concerns about cumulative radiation doses to essential organs near thoracic tumors (e.g., heart, lungs, esophagus) may limit the use of curative radiation therapy (RT) for patients who received thoracic RT in the past. Accordingly, patients whose lung cancer recurs are generally offered only palliative options to manage pain and other symptoms.

Proton therapy, an advanced type of RT, allows radiation oncologists to spare critical normal tissues while delivering escalated, curative doses of radiation to nearby tumors. In particular, IMPT is able to exactly target a tumor, even if the tumor wraps around a critical normal tissue structure, such as a lung.
“Treating patients who have already received a prior course of thoracic radiation is a common clinical scenario, and it is particularly challenging to subsequently provide strong enough radiation doses to eliminate the new tumor without causing significant harm to normal tissues,” said Jennifer Ho, MD, lead author of the study and a resident in radiation oncology at the University of Texas MD Anderson Cancer Center in Houston. “Our study is the first to show that IMPT can be safe and effective for these patients—and that it offers these patients a chance for lasting cancer control without adding significant toxicity.”

Researchers retrospectively examined the records of 27 patients who received reirradiation for thoracic tumors using the IMPT technique through prospective clinical trials at a single institution between 2011 and 2016. Twenty-two patients (81%) had non-small cell lung cancer (NSCLC). All patients had previously received curative thoracic RT.

Time to reirradiation ranged from 0.1 months to 212 months, with a median of 29.5 months. The median radiation dose was 66 Gray (Gy), with a range of 43.2 to 84 Gy, and it was delivered in 2 Gy fractions. The median follow-up for all patients in the study was 11.2 months.

The median overall survival (OS) for patients in this study was 18 months following IMPT reirradiation. At one year following retreatment, the majority of patients were free from local and regional relapse (freedom from local failure = 78%; local-regional relapse = 61%). Just over half of the patients were free from disease progression (progression-free survival, PFS = 51%), and the one-year OS rate was 54 percent. Four of the patients (15%) experienced a local recurrence within one year of retreatment.

Patients who were prescribed a higher dose of IMPT reirradiation were even less likely to experience recurrence or progression. At one-year follow-up, patients who received IMPT reirradiation doses at or above the population median were twice as likely to be free from local failure (100% vs. 49%, p = 0.01) and nearly four times as likely to be free from local-regional failure (84% vs. 23%, p = 0.035). The one-year PFS rate was five times higher for these patients, as well (76% vs. 14%, p = 0.05). Several disease characteristics, namely higher T stage at diagnosis, squamous histology and higher recurrent tumor volume, were associated with worse OS rates.

Reirradiation with IMPT was well-tolerated among the patients. Only two patients (7%) experienced moderate to severe long-term lung toxicity (i.e., grade 3 or higher side effects). There were no severe long-term esophageal side effects nor any life-threatening toxicities among these patients.
“Historically, 20 to 30 percent of patients have experienced moderate or severe side effects, and even fatal side effects, following reirradiation. We knew that IMPT would allow us to generate much more precise radiation treatment plans that spared normal tissue, but we weren’t sure if this would translate into excellent clinical outcomes,” said Joe Y. Chang, MD, senior author of the study and a professor of radiation oncology at MD Anderson. “Our findings demonstrate that the use of IMPT resulted in better local control and survival, with very minimal toxicity, compared to other radiation types, suggesting that IMPT is the optimal treatment modality for re-treatment of thoracic cancers.”

The abstract, “Reirradiation of thoracic cancers with intensity modulated proton therapy,” will be presented in detail during the plenary session at the 2017 Multidisciplinary Thoracic Cancers Symposium in San Francisco (full details below). To schedule an interview with Dr. Ho, Dr. Chang or an outside expert, contact the ASTRO media relations team at press@astro.org or 703-286-1600.

ATTRIBUTION TO THE 2017 MULTIDISCIPLINARY THORACIC CANCERS SYMPOSIUM REQUESTED IN ALL NEWS COVERAGE.

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Abstract and Presentation Details

- Reirradiation of Thoracic Cancers with Intensity Modulated Proton Therapy
- News Briefing: Friday, March 17, 1:00 – 2:00 p.m. Pacific time, Foothill F, http://bit.do/thoracic2
- Plenary Session, Thursday, March 16, 10:30 a.m. – 12:00 p.m. Pacific time, Yerba Buena Salon 9
- This news release contains additional and/or updated information from the study author(s). Full original abstract and author disclosures available on the final page of this release.

Resources on Lung Cancer and Radiation Therapy

- Digital brochures: Radiation Therapy for Lung Cancer (Spanish version), Plain Talk about Stereotactic Radiation, Understanding Clinical Trials
- Videos: Radiation Therapy for Lung Cancer, An Introduction to Radiation Therapy
- Additional brochures, videos and information on radiation therapy from RTAnswers.org

ABOUT THE SYMPOSIUM

The 2017 Multidisciplinary Thoracic Cancers Symposium, co-sponsored by the American Society for Radiation Oncology (ASTRO), the American Society of Clinical Oncology (ASCO) and The Society of Thoracic Surgeons (STS), features the latest advances in surgery, radiation therapy, chemotherapy and novel molecular biologic therapies for thoracic malignancies such as lung cancer. The symposium will be held March 16-18, 2017, at the San Francisco Marriot Marquis. For more information about the symposium, visit www.thoracicsymposium.org. For press registration and news briefing information, visit www.astro.org/thoracicpress.
ABOUT ASTRO

The American Society for Radiation Oncology (ASTRO) is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed and maintains an extensive patient website, RT Answers (www.rtanswers.org); and created the Radiation Oncology Institute (www.roinstitute.org), a nonprofit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

ABOUT ASCO

Founded in 1964, the American Society of Clinical Oncology (ASCO) is committed to making a world of difference in cancer care. As the world’s leading organization of its kind, ASCO represents more than 40,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube.

ABOUT STS

Founded in 1964, The Society of Thoracic Surgeons is a not-for-profit organization representing approximately 7,200 cardiothoracic surgeons, researchers, and allied health care professionals worldwide who are dedicated to ensuring the best possible outcomes for surgeries of the heart, lung, and esophagus, as well as other surgical procedures within the chest. The Society’s mission is to enhance the ability of cardiothoracic surgeons to provide the highest quality patient care through education, research, and advocacy.
Abstract #5: Reirradiation of Thoracic Cancers with Intensity Modulated Proton Therapy

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**Purpose/Objective(s):** Reirradiation of thoracic malignancies is a treatment challenge, with concerns for toxicity and inability to deliver definitive doses. Given the unique physical characteristic of the Bragg-Peak, intensity modulated proton therapy (IMPT) potentially can deliver a higher radiation dose to tumor while minimizing dose to normal critical tissue, compared to photon or passive scattering proton therapy. Here, we report our reirradiation experience with the use of IMPT for thoracic malignancies.

**Materials/Methods:** Between 2011 and 2016, 27 consecutive patients who received IMPT for reirradiation of thoracic malignancies with definitive intent were enrolled in prospectively registered clinical trials, and were retrospectively analyzed. Patients were included if they received a prior thoracic radiation course, delivered with curative intent. All patients underwent 4D CT-based simulation and motion analysis and individualized tumor-motion dose-uncertainty analysis. Patients also had 4D CT re-simulation during treatment. All doses were recalculated to an equivalent dose in 2-Gy fractions (EQD2). Patients received IMPT for recurrence of thoracic cancer (93%) or sequentially after a course of thoracic stereotactic ablative radiotherapy (7%), to a median dose of 66 EQD2 Gy (range 43.2 – 84 Gy).

**Results:** Twenty-two patients (81%) were treated for non-small cell lung cancer. The median time to reirradiation was 29.5 months. At a median follow-up for all patients of 11.2 months (25.9 months for those still alive), the median overall survival (OS) was 18.0 months, with a 1-year OS of 54%. Four patients (15%) experienced an in-field local failure (LF), with 1-year and 2-year freedom from LF rates of 78%. The 1-year freedom from local-regional relapse (LRR), and 1-year progression free survival (PFS) rates were 61% and 51%, respectively. Patients who received 66 EQD2 Gy or higher had improved rates of 1-year freedom from LF (100% versus 49%, p=0.013), 1-year freedom from LRR (84% versus 23%, p=0.035), and 1-year PFS (76% vs 14%, p=0.050). Higher original T stage at diagnosis, squamous histology, and higher recurrent tumor volume were associated with worse OS. Reirradiation was well tolerated, with only 2 patients (7%) experiencing late grade 3 pulmonary toxicity, and none with grade 3 or higher esophagitis. There were no grade 4-5 toxicities.

**Conclusion:** These data represent the first and largest series of patients treated with IMPT for definitive reirradiation of thoracic cancers. They demonstrate that IMPT can provide durable local control with minimal toxicity in patients who can have extended survival, and also suggest that higher doses may improve outcomes. IMPT appears to be a safe and effective option for the reirradiation of thoracic cancers.