FLASH radiation therapy shows promise in first-in-human trial

October 23 2022

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FLASH radiation treatment—which delivers therapeutic doses of radiation in a fraction of a second—may hold promise as a potential treatment for tough-to-kill tumors, a first-in-human study in a small

number of people with bone cancer suggests. The technology, previously tested in animals, was shown to be as safe and appeared to be as effective as conventional radiation without causing unexpected side effects. Findings of the FAST-01 trial (NCT04592887) will be presented today at the American Society for Radiation Oncology (ASTRO) Annual Meeting.

"Our study shows FLASH radiotherapy with protons is a practical modality to reduce pain," said Emily C. Daugherty, MD, lead author of the study and an assistant professor of clinical radiation oncology at the University of Cincinnati Cancer Center. "It deserves further exploration because of its potential to decrease the side effects associated with conventional radiation treatments."

FLASH radiotherapy (RT) delivers radiation at dose rates that are more than 300 times higher than those used in conventional radiation treatments. This induces a phenomenon known as the FLASH effect, which reduces the harm that may occur to normal tissue surrounding a tumor during conventional radiation therapy, while still killing the cancer cells at the tumor site.

"Because FLASH radiotherapy is given at ultra-high dose-rates, it appears to cause less normal tissue injury. This offers the possibility of delivering larger doses of radiation—which could result in higher cure rates for patients with resistant tumors—without increasing side effects," said John Breneman, MD, FASTRO, principal investigator on the trial and a professor of radiation oncology and neurosurgery at the University of Cincinnati Cancer Center.

Most early research on FLASH RT used electron beams to deliver the radiation, but these beams don't penetrate very deep into tissue, limiting its applicability for this treatment approach. Using proton beams for ultra-high dose-rate radiation allows for penetration sufficient to reach

tumor locations in most people. While pre-clinical trials with animals suggested FLASH-RT could safely deliver high doses of radiation with fewer harmful side effects, prior to the FAST-01 trial, the treatment had never been tested under a clinical trial in humans.

In this study, ultra-high-dose rate radiation was delivered to 10 patients, ages 27-81 years, each with one to three painful bone metastases in their extremities. Treatments were delivered to a cumulative 12 metastatic sites in patients' arms and legs. Patients were given 8 Gy of radiation in a single fraction, delivered at ≥40 Gy per second via a FLASH-enabled proton therapy system. Pain, use of pain medications and adverse events were measured on the day of treatment, 15 days following treatment, and at one, two and three months following treatment. Researchers continued measuring these results every two months for up to 13 months. The median follow-up was 4.8 months.

Researchers chose patients who would have received conventional radiation therapy at the same dose as they were given with FLASH RT. "We used the exact same regimen, but with FLASH dose-rate radiation. The patient experience is the same as it would have been receiving conventional radiation, only the treatment delivery process is shorter," said Dr. Daugherty.

Following FLASH RT, seven of the 10 patients experienced complete or partial pain relief. Of the 12 treated sites, pain was relieved completely for six sites and partially for two additional sites. Temporary pain flares occurred in four of the 12 sites treated.

Side effects from treatment were mild. Four patients experienced mild skin hyperpigmentation (darkening skin tone), one experienced skin discoloration, two experienced mild limb edema (swelling or puffiness), two experienced pruritis (itchy skin), one experienced fatigue, one experienced erythema (reddening of the skin) and one experienced

extremity pain.

Each FLASH treatment takes about 3/10 of a second, Dr. Daugherty explained. Following treatment, "both pain relief and side effects were in-line with what might have happened with conventional radiation. We did not see any unexpected additional toxicity with the substantially shorter treatment."

FLASH RT would potentially be most useful in treating hard-to-kill cancers in the brain, lungs or gastrointestinal area, where healthy tissue surrounding tumors is particularly vulnerable to radiation exposure, said Dr. Breneman. However, clinical trials in these sites cannot be authorized until studies show ultra-high dose-rate radiation is safe and effective in other, less-sensitive areas. The FDA limited its approval for this study to adults with bone metastases in their arms and legs, areas at much lower risk should complications arise.

"From a practical standpoint, this is not the type of cancer that FLASH is designed to treat, but we need human data to see if there are any unexpected side effects. Treating arms and legs is not as risky as treating someone's brain or lungs," said Dr. Breneman, who he also serves as medical director of the Cincinnati Children's/UC Medical Center Proton Therapy Center.

Ultimately, FLASH RT could also be useful in treating pediatric cancers, since children are more sensitive to the side effects of radiation therapy, he said. But much more research needs to be done before that can occur.

Researchers don't fully understand why FLASH RT kills tumors with fewer side effects than conventional radiation and further research is needed to determine the biological mechanisms driving the FLASH effect, said Dr. Daugherty.

Next, the research team will test the safety and efficacy of FLASH RT with patients who have metastases closer to the lungs and heart. The FAST-02 trial (NCT05524064) is currently enrolling adult patients with thoracic bone metastases.

More information: plan.core-apps.com/myastroapp2 … ff-ab92-6981a8e2fe81

Provided by American Society for Radiation Oncology

Citation: FLASH radiation therapy shows promise in first-in-human trial (2022, October 23) retrieved 25 April 2024 from https://medicalxpress.com/news/2022-10-therapy-first-in-human-trial.html