IMPACT PROFILE

Bone Cell-Nerve Signaling and Its Role in Chest Wall Pain After Thoracic Radiosurgery

Translational Science Benefits Model

translationalsciencebenefits.wustl.edu

Determining if risedronate, an osteoporosis prevention medication, can help prevent bone loss and chest pain caused by radiation treatment.

The Challenge

Nearly half of all cancer patients undergo radiation therapy, with many receiving effective, high dose per fraction stereotactic body radiation therapy (SBRT). However, SBRT can lead to significant chest wall pain (CWP) and rib fractures, particularly when treating lung tumors close to the chest wall. This can severely impact breathing and overall quality of life. The **Osteoclast-Neuron Crosstalk Project** is the first study to examine whether CWP after radiation is caused by radiation-triggered activation of bone resorbing cells called osteoclasts. The project also tests whether blocking osteoclast activity can help prevent pain and reduce bone loss.

The Approach

The **Osteoclast-Neuron Crosstalk Project** tested whether risedronate can help prevent CWP and rib fractures after lung cancer radiation by:

1. Testing whether risedronate can protect bones from radiation damage by looking at bone structure and cell activity.
2. Testing whether risedronate can block pain signals caused by radiation in bone and nerve cells.
3. Measuring how much pain radiation causes and whether risedronate can reduce it using movement and touch tests.

The Impact

This pilot generated data indicating that signals between bone and nerve cells after radiation could contribute to debilitating CWP. These data are included in our application for the "Risedronate Intervention Before SBRT (RIBS)" Trial, in which we propose to use a higher dose of risedronate to prevent CWP and bone loss/fractures after radiation. The study also identified a putative molecular signal called Transforming Growth Factor-beta (TGFβ). We then tested with an inhibitor that has previously been shown to be well-tolerated in clinical trials. These data serve as robust indicators that inhibiting osteoclast-neuronal crosstalk with bisphosphonates is a strategy for preventing CWP clinically.

RESEARCH HIGHLIGHTS

The **Osteoclast-Neuron Crosstalk Project** resulted in

- **Identification of several potential signal pathways** that cause CWP from SRBT for targeted therapy.
- **Suppressing TGFβ signaling with the well-tolerated TGFβ receptor-inhibitor Galunisertib,** preventing pain responses in neurons caused by crosstalk with SBRT-activated osteoclasts.
- **Risedronate may reduce CWP and bone degradation** after SBRT delivery.

Key Benefits

The Osteoclast-Neuron Crosstalk Project resulted in ***Community*** and ***Clinical*** benefits.

Community

Life Expectancy & Quality of Life: Prevent debilitating chest wall pain and rib fractures in lung cancer patients. (*Potential*)

Clinical

Biomedical Technology: Use risedronate to prevent rib fractures and chest wall pain. (*Potential*)

Clinical

Therapeutic Procedures: Inform whether risedronate with/without TGFβ signaling inhibition is/are effective therapeutic approach(s). (*Potential*)

Clinical

Therapeutic Procedures: Identified crosstalk signals between radiation-activated osteoclasts and neurons. (*Demonstrated*)

The team:

Sun Park, Radiation Oncology
Michael Farris, Radiation Oncology

Contact:

Jeffrey Willey, PhD, Wake Forest University School of Medicine, Radiation Oncology

Find out more:

Contact Dr. Willey at Jeffrey.Willey@advocatehealth.org to learn more about this project!

View this and other Impact Profiles