Canadian Cancer Trials Group | Groupe canadien des essais sur le cancer

A RANDOMIZED PHASE III STUDY COMPARING STEREOTACTIC BODY RADIOTHERAPY (SBRT) VERSUS CONVENTIONAL PALLIATIVE RADIOTHERAPY (CRT) FOR PARTICIPANTS WITH PAINFUL NON-SPINE BONE METASTASES (NCT06391242)

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RATIONALE

- Approximately 1 in 5 patients with metastatic cancer will suffer from bone metastases, and the incidence varies according to tumour type occurring most commonly in patients with prostate, lung, renal and breast cancer.
- The goals of SBRT in this population are to target tumour tissue with higher and more conformal doses of RT compared to conventional palliative external beam RT (CRT), thus enabling greater tumour cell kill and symptom relief.

HYPOTHESIS

SBRT will provide palliation that is superior to CRT for patients with painful bone metastases based on a strong radiobiologic rationale and level 1 data demonstrating efficacy of SBRT to treat painful spinal metastases (Sahgal 2021).

THE NEED FOR A STUDY

- SBRT is a complex and costly technique and there are important risks and incompletely understood implications associated with its adoption to treat bone metastases.
- A properly designed and conducted randomized controlled trial will provide important data regarding efficacy, toxicity and patient reported outcomes.

SCHEMA

Solid tumour malignancy with painful non-spine bone metastasis eligible for CRT or SBRT

Minimal ESAS score 2 at Target (dominant site)

→ RANDOMIZATION →

ARM 1
Conventional EBRT (CRT)
20 Gy/5

ARM 2
Stereotactic Body Radiotherapy (SBRT)
30 Gy/5*
35 Gy/5

*>4 cm target diameter to limit toxicity, or PTV overlaps with the femoroacetabular or gleno-humeral joint space, or OAR constraints cannot be met for 35Gy/5

STRATIFICATION

- Presence of extraosseous vs. no extraosseous disease extension at the dominant non-spine bone metastasis
- Radiosensitivity: breast, hormone sensitive prostate cancer vs. other histology
- Pelvic vs non-pelvic dominant non-spine bone metastasis location

ELIGIBILITY CRITERIA

- Histologic confirmation of a solid tumour
- Patient with a dominant painful non-spine bone metastasis and a worst minimum pain score of 2 using the ESAS attributed to that dominant site
- Expected overall survival of greater than 6 months as determined by the treating physician
- Suitable for protocol defined SBRT and CRT
- Stable pain with no immediate plan to alter analgesic regimen
- ECOG performance status of 0-2
- Age of 18 years or older
- Able and willing to complete the pain and analgesic diary and PRO questionnaires in either English or French
- Signed consent

INELIGIBILITY CRITERIA

- Metastases of the hands, feet, cranium and spine (including sacrum) as index lesion
- Bone metastasis arising from a small cell or germ cell carcinoma, or haematological malignancy including lymphoma and myeloma
- Radionuclide therapy within 30 days of randomization
- Patient treated with prior palliative RT to the dominant painful bone metastasis site (prior radiation exposure is permitted if prior to development of the dominant metastasis and would not influence the applicability of either treatment arm of the current study)
- Received systemic chemotherapy within 1 week of the protocol RT, or who are expected/planned to receive chemotherapy within one week of completing protocol RT
- Participants with an unstable pathologic fracture at the dominant painful non-spine bone metastasis, or for whom surgical fixation would be the preferred intervention if possible
- Pregnant or lactating individuals

OBJECTIVES

Primary:

To compare the 3-month complete pain response rate (CPR) of conventional EBRT versus SBRT administered to a dominant site of painful non-spine bone metastasis and analgesic intake with response assessment according to ICPRE (Chow 2012)

Secondary:

To compare treatment arms with respect to:

- Early (1 month post RT) and late (6 months post RT) CPR and response patterns (partial, and progressive pain)
- Re-irradiation rate within the 6-month follow-up period
- Incidence of fracture at the radiation target site
- Incidence of treatment related AE rates > Grade 2
- Imaging-based local control rates at 3 and 6 months post treatment (investigator reported and centrally reviewed)
- Other patient reported outcomes (EORTC QLQ-C30 and QLQ-BM22)

SAMPLE SIZE

- Estimated complete response rates: CRT Arm 17%, SBRT 34%
- Error rates: 2 sided $\alpha=0.05$ $\beta=0.2$
- Drop out rate: 15%
- N=230

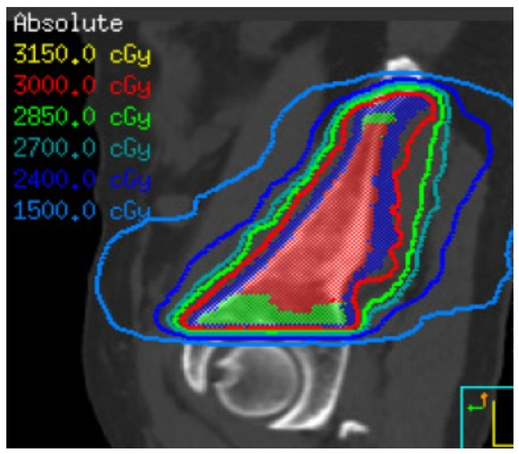
RADIOTHERAPY

CRT:

- Standard linear accelerator with beam energies ranging from 6 MV to 18 MV photons
- For field-based planning, the beam arrangement can be a parallel-opposed pair, or a conformal beam arrangement with no more than 4 beams. The choice of beam arrangement is at the discretion of the treating radiation oncologist as long as target coverage objectives are met. For IMRT, more than 4 beams is allowed and for VMAT arcs will be used

SBRT:

- Photons and an energy ranging from 6 MV to 10 MV
- MLC are permitted for LINACs
- For Cyberknife, its own collimation system is used



Isodose Curves
Example of sagittal slice showing single dose distribution.

QUALITY OF LIFE/PAIN ASSESSMENT

- Function and symptom domains of EORTC QLQ-C30 and QLQ-BM22
- QoL data collected electronically (iPads or web-based) using the Canadian Cancer Trials Group on-line SPROUT system
- Pain / Analgesics Patient Diary: pain score at dominant painful site and use of analgesic medications (opioid and non-opioid)
- Pain Response evaluated by International Bone Metastases Consensus Endpoint definitions (composite pain scores and analgesia use)

CORRELATIVE STUDIES

- Optional Plasma and Serum collection
- Collected:
  - After randomization but prior to start of treatment
  - Immediately after the 5th fraction of protocol radiotherapy
- Goal: assess biomarkers which may prove predictive of response to radiotherapy

PROGRESS TO DATE

Status: Open to Accrual

Activation Date: June 06, 2024

Accrual as of April 27, 2026: 44

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