Cryoablation for Palliative Pain Control of Skeletal Metastases

- Metastases to bone are common and often cause pain that is difficult to alleviate.
- Cryoablation offers a potential alternative to conventional therapies for palliative pain control, such as external beam radiation or surgery.
- Cryoablation offers advantages over radiofrequency or microwave ablation because:
  - The procedure can be monitored with CT imaging.
  - Multiple cryoprobes can be placed in one treatment session.
  - It is associated with less post-procedural pain.
- Disadvantages of cryoablation include:
  - Absence of cauterization/coagulation effect.
  - Inability to treat if nearby vital structures cannot be displaced.
  - Cementoplasty can be performed with cryoablation to maintain strength of weight-bearing bone.

Skeletal metastases commonly develop in patients with cancer and can occur in up to 85% of patients with one of the three most common cancers: breast, prostate, and lung. When skeletal metastases develop, they can lead to intractable pain, fractures, and decreased mobility, all of which reduce the patient’s quality of life. While the prognosis for these patients is poor (with a median survival of three years or less), treatment is beneficial to the patient if it reduces pain and improves the quality of life.

Multiple palliative therapies are available to relieve pain and suffering, including external beam radiation or surgery, systemic therapies (including chemotherapy, hormonal therapy, radiopharmaceuticals, and bisphosphonates), and analgesics. Of these, external beam radiation therapy is the established standard of care for localized pain due to metastases. This treatment, which reaches its maximum effectiveness within 4 weeks after treatment, can result in pain relief for over 80% of patients and complete pain relief for over 50%. However, relapse occurs in a substantial proportion of patients and, because of the damaging effects of radiation, this type of therapy cannot be repeated.

Cryoablation as a Palliative Treatment

Over the past decade, cryoablation has emerged as an effective minimally invasive treatment for painful bone metastases that is an alternative to palliative surgery and a potential therapy for patients who are not candidates for radiotherapy or who have already received radiotherapy treatment. As a palliative therapy, cryoablation is not curative. Its goal is to destroy the tumor/tissue interface and debulk the tumor rather than destroy it entirely. Not all tumors cause pain, and cryoablation is only suitable for patients who experience focal pain that can be correlated with imaging findings of local metastases. It is not clear what factors mediate the perception of pain, but possible causes include cytokine-mediated osteoclast activity, inflammatory reaction, microscopic or macroscopic fractures, nerve compression, and stretching of the periosteum.

Cryoablation has several advantages over radiofrequency (RFA) or microwave ablation techniques. First, cryoablation creates an ice ball that can be visualized with CT, which allows direct monitoring of the ablation procedure. Second, cryoablation is associated with significantly less post-procedure pain than RFA. Third, multiple cryoprobes can be placed during the same procedure, which can be used to ablate zones more than 8 cm in diameter and/or treat multiple tumors simultaneously (Figure 1).
Figure 1. Cryoablation of a rib metastasis in a patient with thyroid cancer. (A) Lesion before treatment (white arrows); (B) Cryoprobes (white arrows) within lesion at 3 minutes from start of first freeze. Arrowheads indicate bag of warm saline to prevent skin freezing; (C) Fully formed ice ball (arrows).

Disadvantages of cryoablation include the lack of any cauterization or coagulation, which may result in post-procedural bleeding. In addition, the cryoablation procedure is more time consuming than RFA. Cryoablation therapy may be limited by risk of non-target injury to adjacent vital structures, such as bowel, bladder, major peripheral motor nerves, spinal cord, or the artery of Adamkiewicz. However, in many cases hydrodisplacement can be used to move vital structures out of harm’s way by instilling saline. If the tumor is superficial and skin tissue is at risk of freezing, warming pads can be placed over the treatment area. It is also possible to monitor evoked potentials to prevent damage to major motor nerves or to monitor temperatures of at-risk adjacent structures using a thermocouple.

In the largest clinical trial to date, a significant decrease in pain (p<0.001, n=57) was observed within one week of cryoablation, with 49% of patients reporting at least a 2-point decrease in their worst pain score; 75% of patients reported a 90% or higher degree of pain relief at some time during the study period. Pain relief was durable until

Figure 2. Cryoablation procedure, performed under CT guidance, showing a two cryoprobes inserted into a tumor. Inset shows developing ice ball in water.
Figure 3. Cryoablation and cementoplasty in a patient with renal cell carcinoma. (A) Coronal CT shows untreated lytic lesion in femur; (B) cryoablation probe (white arrowheads) placed into lesion (white arrows) and developing ice ball (black arrow); (C) Cementoplasty introducer (white arrowheads) placed after completion of cryoablation; (D) Cement (arrows) after the completion of the procedure.

At the end of the study at 24 weeks after treatment, with only 14% (5 of 35 patients) reporting recurrent pain that was equal to or greater than that reported prior to cryoablation. A decreased use of opioid analgesics was also observed in 83% of the study population, and 40% reported no opioid medication at some time following the cryoablation procedure.

Pre-procedure Planning and Cryoablation Therapy

Patients who are considering treatment with cryoablation must first undergo a physical examination in which their pain is assessed and the sites of focal pain are identified. Only those patients who report a pain score of ≥4 (on a scale of 1–10) localized to one or two sites that correlate with imaging findings are suitable for cryoablation therapy. Contraindications to cryoablation include acute spinal cord compression, systemic infection, and uncorrectable coagulopathy as well as the inability to achieve a margin of ≥1 cm from critical structures.

The procedure is carried out under general anesthesia to allow precise positioning of the cryoprobes and provide pain control. CT guidance is used to place up to eight probes in a single tumor (Figure 2). Protective measures, as described above, are used to prevent damage to vital structures. Rapid cooling is achieved through the expansion of argon gas (Joule-Thompson effect) delivered to the tip of the probe, which can achieve temperatures as low as -100°C within a few seconds. Each probe can freeze a volume that is 3-5 cm long and 1.5-3 cm wide within about eight minutes. Cell death occurs at -20°C, which is typically 3 mm inside the margin of the ice ball. The extent of freezing is monitored by CT imaging of the developing ice ball to maximize ablation while maintaining ≥1 cm clearance from critical structures. Adequate treatment of the bone/tissue interface is essential for pain relief to be
effective, which is more critical than debulking the center of the tumor. To ensure maximal ablation, the tissue is allowed to thaw over a period of about 10 minutes, and the freezing procedure is repeated. After the second period of freezing, helium gas is used to thaw the probe tip and allow its withdrawal. A final CT scan after the tissue is thawed is used to check for bleeding.

**Cementoplasty as an Adjunct Therapy**

Cementoplasty can be employed as an adjunct therapy to cryoablation in patients who are at risk of fractures in the axial skeleton, particularly in vertebrae or the periacetabular region. In this procedure, polymethylmethacrylate cement is injected into the lesion under CT or fluoroscopic guidance (Figure 3). In addition to stabilizing microfractures and strengthening bone, cementoplasty has the added advantage that the hot cement used in the procedure ablates nerves and therefore controls pain.

Cementoplasty can be performed one hour after completion of cryoablation, while the patient remains in the procedure room under general anesthesia.

**Scheduling**

Appointments for pre-planning and assessment for cryoablation of skeletal metastases can be made by calling 671-726-8396. The procedure is performed in the Interventional Radiology facilities on the main campus of Massachusetts General Hospital.

**Further Information**

For more information regarding cryoablation, please contact Ashraf Thabet, MD, Peter M. Mueller, MD, or Raul N. Uppot, MD, Interventional Radiology, Massachusetts General Hospital at 617-726-8396; or Joseph F. Simone Jr., MD, or Connie Y. Chang, MD, Musculoskeletal Radiology, Massachusetts General Hospital at 617-726-7717.

We would like to thank Ashraf Thabet, MD and Mihir Kamdar, MD, Director, Mass General Pain Clinic, for their assistance and advice for this issue.

**References**


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