Retrospective Study

The Hopeless Case? Palliative Cryoablation and Cementoplasty Procedures for Palliation of Large Pelvic Bone Metastases

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Background: Metastases to the bone are common in cancer patients, and it has been estimated that up to 50% of patients with pelvic bone metastases will not achieve adequate pain control with medications alone. This has led to a paradigm shift over recent years towards the use and development of minimally invasive image-guided treatment options for palliation of bony metastases. Despite these developments, large metastatic lesions are still often considered to be "hopeless cases" that would garner little to no benefit from image-guided intervention. This study is the first large series to describe the novel use of combination percutaneous cryoablation and cementoplasty for palliation of such large metastases to the pelvis.

Objectives: We aim to evaluate the efficacy and safety of image-guided percutaneous cryoablation and cementoplasty for palliation of large pelvic bone metastases.

Study Design: This retrospective analysis was approved by our institutional review board. This study was conducted from January 2013 to December 2016, where consecutive patients referred for pain management of large pelvic bone metastases underwent combination percutaneous cryoablation and cementoplasty.

Setting: This study took place at a tertiary care center after patients were referred following formal review from a multidisciplinary conference, which was comprised of interventional radiologists, pain management and palliative care physicians, radiation and medical oncologists, and when available, anesthesiologists.

Methods: Forty-eight patients (36 men and 12 women) with a mean cohort age of 77.5 years (range: 52 – 89 years) were referred from the multidisciplinary conference for palliation of pelvic bone metastases. The inclusion criteria included patients with metastases greater or equal to 5.0 cm and significant pain refractory to conventional pain management regimens. All of the patients were deemed not to be surgical candidates. Mean pain scores were collected at numerous time-points along with procedural technical success rates and complication rates.

Results: Combination cryoablation and cementoplasty was performed on 48 consecutively referred patients with a 100% technical success rate and no immediate complications. The pain levels demonstrated a significant decrease ($P < 0.001$) following intervention, with mean pain scores of 7.9 (range: 5 – 10) and 1.2 (range: 0 – 7) throughout the week prior to intervention and at 24 hours post-intervention, respectively. The post-intervention pain scores remained stable at 1 to 9 weeks follow-up (mean: 4.1 weeks). Three patents (6.3%) reported no change in pain following the intervention; however, no patients reported worsened pain.

Limitations: The limitations of this study include its retrospective nature and the length of follow-up, which was often restricted given the life expectancy of our patient cohort.

Conclusion: Combination cryoablation and cementoplasty is a novel and efficacious treatment option for palliation of large pelvic bone metastases. Marked improvements in pain, as well as mobility and quality of life, are often attainable.

Key words: Pain, palliative care, palliation, percutaneous, cryoablation, cementoplasty, metastases, pelvis, interventional radiology, thermal ablation

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Metastases to the bone occur in 20 – 80% of cancer patients, with lung, breast, and prostate being the most frequent primary lesions (1-3). Moreover, bony involvement in the setting of multiple myeloma is a commonly encountered clinical scenario (1,2). It has been estimated that throughout the course of malignant disease, up to 50% of patients will not achieve adequate pain control, particularly in cases of pelvic bone metastases (4-7). These patients present clinically with intractable pain, limited mobility, and dramatic deterioration in quality of life (2,8-12). While surgical reconstruction to improve skeletal instability is sometimes a viable option, this is often impractical in a frail patient with a short life expectancy (13). The current mainstay of non-surgical management for palliation of pelvic bone metastases includes: analgesics, radiotherapy, and chemotherapy. Given the fact that these treatments are often unable to achieve adequate pain control (4-7,14-21), there has been a recent shift towards the increased use and development of novel minimally invasive image-guided treatment options. These include: radiofrequency ablation (RFA), microwave ablation (MWA), high-intensity focused ultrasound (HIFU), and cementoplasty and cryoablation (alone or in combination) (22-31).

This study describes our institution's experience using the combination of cryoablation and cementoplasty as a novel treatment option for palliation of large pelvic bone metastatic lesions. We sought to assess the value of these procedures in improving pain management, mobility, and quality of life for palliative patients with metastatic disease. These patients had failed to achieve adequate pain control using conventional therapeutic regimens or had been rejected as unsuitable candidates for treatment, and it is our hope to demonstrate this technique as a viable treatment option to be considered by all clinicians involved in palliative care.

Methods

Patient Population

This single-center retrospective analysis was approved by our institutional review board. This study was conducted from January 2013 to December 2016, where consecutive patients referred to our tertiary care center for pain management of large pelvic bone metastases underwent a combination of percutaneous cryoablation and cementoplasty. The patients were referred after formal review from a multidisciplinary conference, which was comprised of interventional radiologists, pain management and palliative care physicians, radiation and medical oncologists, and when available, anesthesiologists. The patient demographics were collected at the time of patient referral.

Patient Selection

At the multidisciplinary conference, the clinical condition of the patient was reviewed in conjunction with up-to-date imaging. Based on a clinical and radiological assessment, individual patient management plans were formulated to treat the patient's most symptomatic lesion. This conference is centered around the use of minimally invasive image-guided procedures.

For the purpose of this study, the inclusion criteria included: patients with large pelvic bone metastases (greater or equal to 5.0 cm in maximal diameter) and significant pain refractory to conventional pain management regimens. All of the patients were deemed not to be surgical candidates. The exclusion criteria included: intractable coagulopathy, systemic infection at the time of intervention, or lesions being inaccessible from a safe percutaneous tract.

Procedure

Patients who were deemed suitable for an interventional procedure were then reviewed by the Department of Anesthesiology. The decision to use conscious sedation or general anesthetic was made by the attending anesthesiologist on the day of the procedure.

Following anesthetic review, the patient's pre-procedural imaging was reviewed and the percutaneous access sites were selected. Fluoroscopically-guided procedures were performed with the assistance of cone beam computed tomography (cone beam CT) using either a Philips AlluraClarity (Philips Healthcare Canada, Markham, Ontario) bi-plane fluoroscopy unit or a Siemens Artis Zee single-plane fluoroscopy unit (Siemens Canada, Oakville, Ontario). Local anesthetic (10 – 15 mL of 1% lidocaine hydrochloride solution) was used at the skin entry sites. Two grams of Ancef (Sandoz Canada, Boucherville, Quebec) was administered intravenously prior to skin puncture. Cone beam CT facilitated targeting for bone access. Either 11-gauge or 13-gauge Confidence Spinal Cement System™ introducer needles with a beveled tip (DePuy Synthes Spine, Inc., Raynham, MA) were used. Appropriately sized cryoablation probes (Galil Medical Ltd., Yokneam, Israel) were placed either co-axially through the needles or directly into the metastatic deposit being treated (Fig. 1a). The cryoablation probes were chosen based on the lesion

size, the volume of the tumor to be treated, and the lesion's relationship to adjacent critical anatomic structures, such as neurovascular bundles. Once appropriate positioning was confirmed, 2 cryoablation cycles of 8 minutes of freezing time followed by 6 minutes of active thawing time was utilized. The appropriate probes were repositioned and the ablation cycle was repeated if larger volume deposits required treatment.

The cryoablation probes were subsequently removed and bone access needles were positioned within the new ablation site in order to optimize cement injection (Fig. 1b and 1c). The volume of cement used was tailored to the individual case. At the conclusion of the procedure, all of the patients received 32.5 mg of intravenous ketorolac tromethamine (Roche Canada, Mississauga, Ontario).

Following the intervention, all of the patients were hospitalized for 24 hours of monitoring. Activity after 2 hours of bed rest was as tolerated. The follow-up pain scores were recorded on a numeric scale from 0 to 10 at 3 separate time points (worst pain in the week prior to intervention, 24 hours post-intervention, and at 1 to 9 weeks post-intervention by phone). Analgesics were administered as required throughout the admission.

For each procedure, technical success and immediate complications were recorded. Post-procedural complications were assessed utilizing current guidelines from the International Working Group on Image-Guided Tumor Ablation (32).

Results

A total of 48 consecutive patients (36 men and 12 women) with a mean cohort age of 77.5 years (range: 52 – 89 years) were referred for treatment of large painful pelvic bone metastases. No patients were excluded from this study. The tumor types were: lung carcinoma (n = 15), prostate carcinoma (n = 10), renal cell carcinoma (n = 6), colorectal carcinoma (n = 6), breast carcinoma (n = 4), cholangiocarcinoma (n = 2), multiple myeloma (n = 2), lymphoma (n = 2), and squamous cell carcinoma of the head and neck (n = 1).

Eighty-five percent (n = 41) of patients underwent general anesthesia while 15% (n = 7) underwent conscious sedation. The volume of injected cement varied significantly depending on the size and location of the lesions being treated (range: 3 – 34 mL; mean: 15 mL). One to 8 cryoprobes (mean: 2 probes) were utilized per case. The procedure time ranged from 70 to 190 minutes (mean: 125 minutes).

Combination cryoablation and cementoplasty was performed on all of the patients, with a 100% technical success rate and no immediate complications. No post-procedural complications were encountered apart from mild pain and bruising at the percutaneous puncture

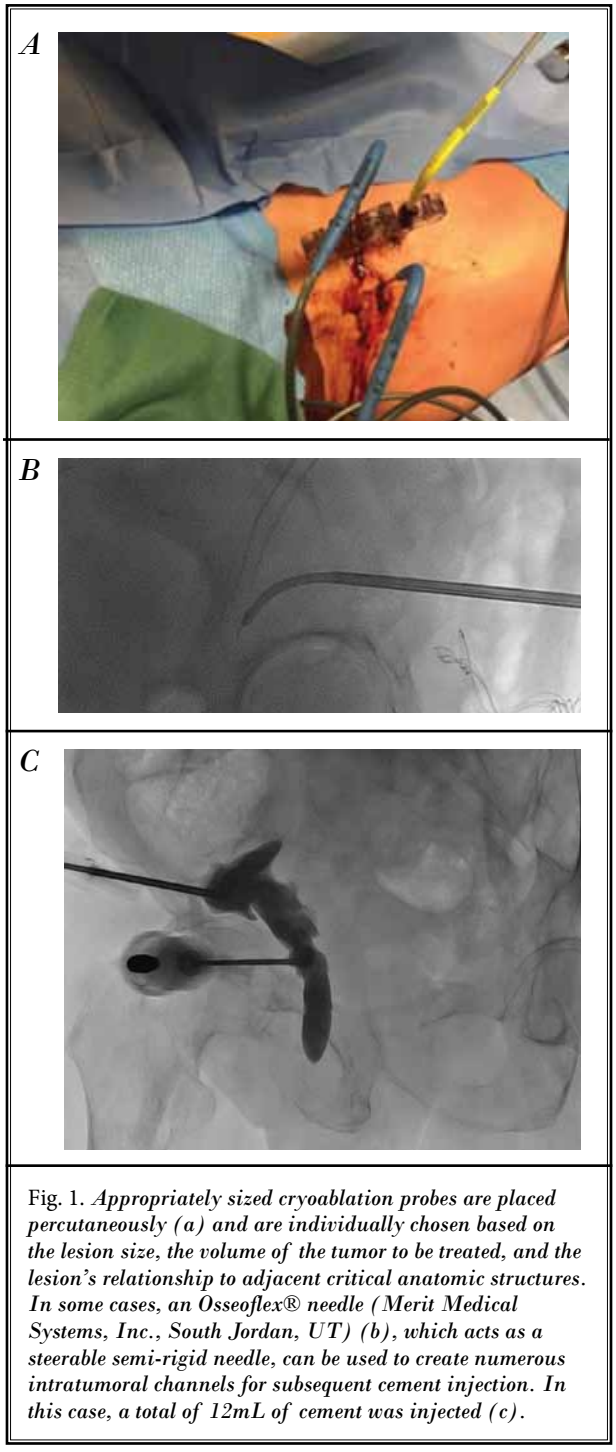


Fig. 1. *Appropriately sized cryoablation probes are placed percutaneously (a) and are individually chosen based on the lesion size, the volume of the tumor to be treated, and the lesion's relationship to adjacent critical anatomic structures. In some cases, an Osseoflex® needle (Merit Medical Systems, Inc., South Jordan, UT) (b), which acts as a steerable semi-rigid needle, can be used to create numerous intratumoral channels for subsequent cement injection. In this case, a total of 12mL of cement was injected (c).*

sites. Pain scores were collected from all of the patients. The pain levels demonstrated a significant decrease ($P < 0.001$) following the intervention, with pain scores of 7.9 (range: 5 – 10) and 1.2 (range: 0 – 7) throughout the week prior to intervention and at 24 hours post-intervention, respectively. The post-intervention pain scores remained stable at 1 to 9 weeks follow-up (mean: 4.1 weeks). Three patients (6.3%) reported no change in pain following the intervention; however, no patients reported worsened pain.

Discussion

The use of thermal ablation techniques as minimally invasive treatment options for tumor deposits has been well described, with RFA and cryoablation being the most widely studied techniques to date. RFA has been shown to be highly effective in pain management (26,33), but has a number of limitations which have led to a recent shift towards the use of cryoablation. Unless MRI guidance is used, direct visualization of the RFA ablation zone is not readily achieved, unlike with cryoablation where the ice ball (ablation zone) can be easily visualized with peri-procedural CT imaging (Fig. 2). Cryoablation also produces highly predictable and reproducible ablation zones (Fig. 2); this allows for customizable and very large thermal ablation zones to be created (Fig. 2), which is particularly useful in the setting of large metastatic lesions (Fig. 3 and Fig. 4). RFA ablation is also generally more painful than cryoablation, such that patients undergoing cryoablation require significantly less analgesic administration (34).

The treatment of metastatic lesions with cryoablation does not, however, improve bony stability, and in some cases it can potentially weaken the bone and predispose it to fracture (35,36). Augmentation with cementoplasty can provide reinforcement of the bone, particularly in weight-bearing areas such as the acetabulum. At present, only limited literature is available describing the use of combination cryoablation and cementoplasty for patients with bony metastases (37-39).

Patients with bony metastases most commonly present with pain due to a combination of mechanisms including: the release of cytokines which results in nerve stimulation, periosteal stretching, direct compression of adjacent soft tissues and nerves, and in some cases, pathologic fractures (40-42). As such, the primary goal of therapy should be to destroy the lesions for palliation while also reducing the likelihood of subsequent osseous fractures. Neoplastic tissue is destroyed through thermal ablative techniques that increase (RFA; MWA; HIFU) or decrease (cryoablation) intra-tumoral temperatures (43), whereas consolidative treatments (percutaneous cementoplasty) provide skeletal stability. A number of studies have described the use of RFA in conjunction with cementoplasty (31,44-51), but to our knowledge, very few reports of combination cryoablation and cementoplasty have been made in the current literature (37-39). Previous reports have also tended to focus more on the treatment of small lesions, with larger lesions (greater than 5.0 cm) being viewed as exclusion criteria in many cases. In the past, these patients have generally been viewed as poor interventional candidates and unlikely to benefit from treatment. Nevertheless, our findings demonstrate that combination cryoablation and cementoplasty is a safe and highly efficacious procedure for palliation of patients with large bony metastases.

In many instances, only a minority of the volume of these large lesions were treated. In spite of a significant portion of the tumor being unablated or uncemented (Fig. 3 and Fig. 4), marked pain relief was still achieved. We choose to limit treatment, while ensuring the following goals are achieved: 1) to cement fractures, 2) to ablate, wherever possible, the interface between the tumor and normal bone to prevent further invasion or destruction, 3) to debulk soft tissue extension, thus impeding further invasion and compression of adjacent structures, and 4) to reinforce weight- and stress-bearing bone via cementoplasty. It is possible that more aggressive tumor ablation could have resulted in further improvement in palliation, however, we choose instead to balance this against the added risk of complications and increased procedure time. Some authors have also advocated for the use of image-guided percutaneous screw placement to further reinforce skeletal reconstruction (52). This may certainly provide further benefit; however, our institution does not have experience with these techniques at the present time.

Our study showed no immediate symptomatic post-procedural complications apart from bruising and tenderness at the percutaneous puncture sites. A small amount of cement extravasation into the surrounding soft tissues was experienced, and in 4 instances, leakage of cement into adjacent joints (hip joint, n = 2; sacroiliac joint, n = 2) was noted without symptoms or complications otherwise.

The pain relief from cryoablation and cementoplasty also demonstrates a lasting effect, as our patients' pain scores remained stable at the time of follow-up. There were, however, 3 patients who reported no pain

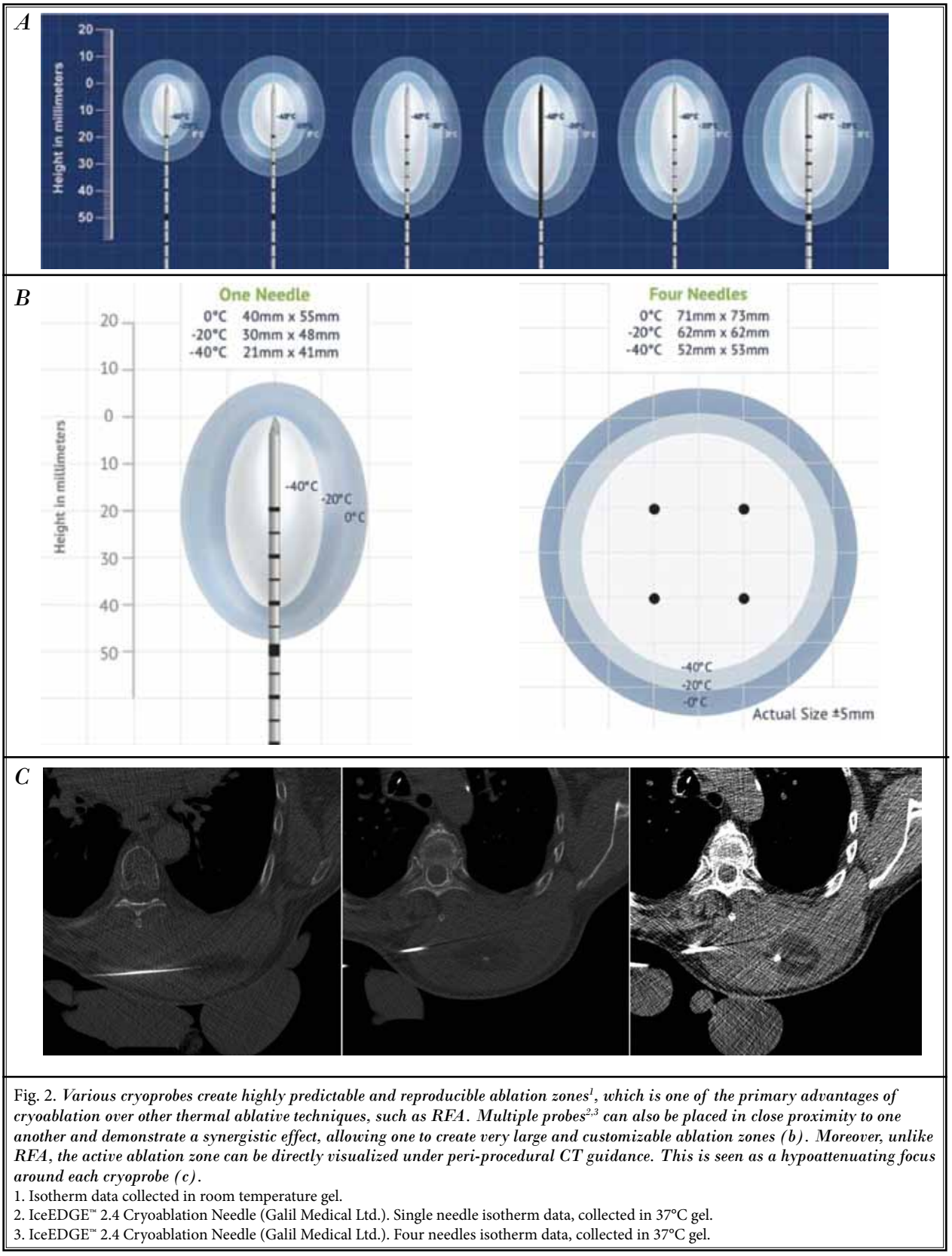
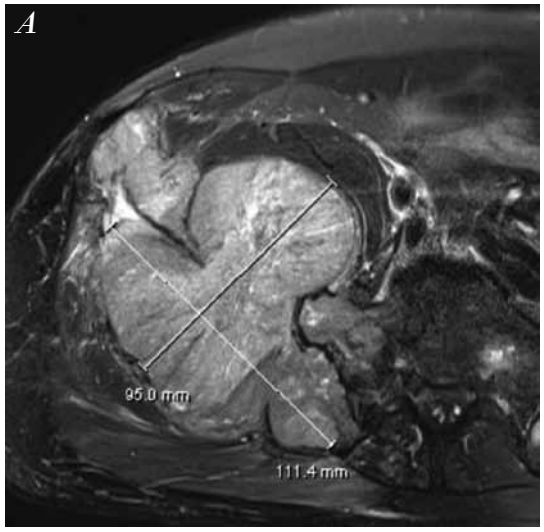
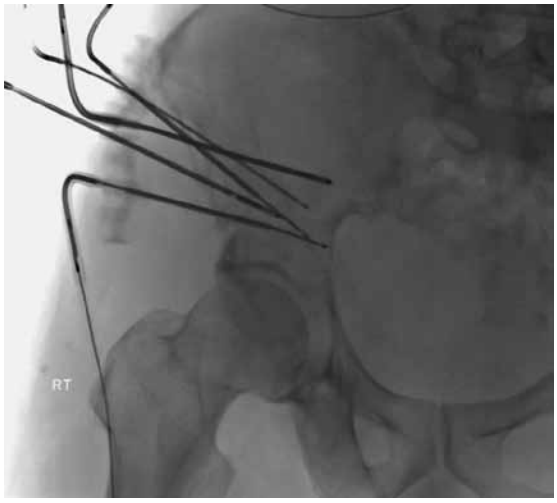
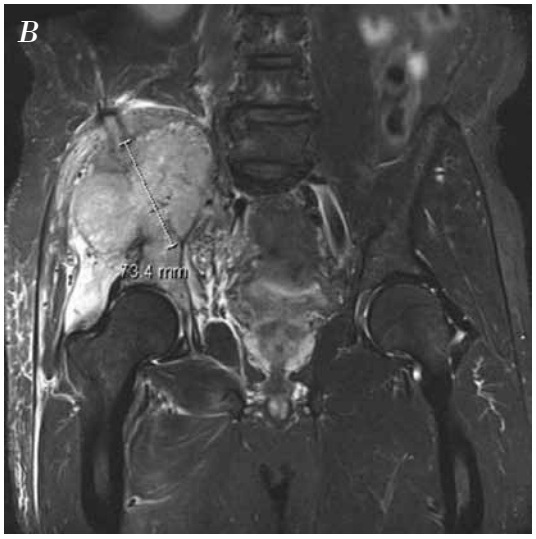


Fig. 2. *Various cryoprobes create highly predictable and reproducible ablation zones*[1], *which is one of the primary advantages of cryoablation over other thermal ablative techniques, such as RFA. Multiple probes*[2,3] *can also be placed in close proximity to one another and demonstrate a synergistic effect, allowing one to create very large and customizable ablation zones (b). Moreover, unlike RFA, the active ablation zone can be directly visualized under peri-procedural CT guidance. This is seen as a hypoattenuating focus around each cryoprobe (c).*

1. Isotherm data collected in room temperature gel.
2. IceEDGE™ 2.4 Cryoablation Needle (Galil Medical Ltd.). Single needle isotherm data, collected in 37°C gel.
3. IceEDGE™ 2.4 Cryoablation Needle (Galil Medical Ltd.). Four needles isotherm data, collected in 37°C gel.







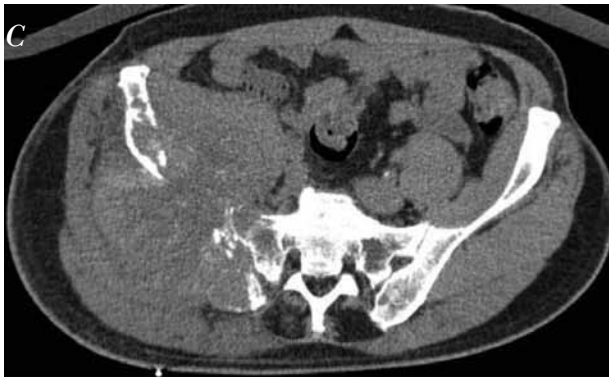


Fig. 3. *This 72-year-old man presented with metastatic lung adenocarcinoma, as shown on his pre-intervention MRI (a,b) and CT imaging (c). The large (11.1 x 9.5 x 7.3 cm) metastatic lesion is centered at the junction of the right iliac wing and body with extension into the acetabular roof and medial wall. The latter was the target of skeletal reinforcement. Five cryoablation probes were placed under bi-planar fluoroscopic guidance and cone beam CT (d). Subsequently, two 13-gauge cementoplasty needles were used to inject 27 mL of cement into the recently created ablation site (e). The pre-procedural pain score for this patient was 8/10, which then decreased to 1/10 post-intervention. Moreover, this patient was immobile prior to intervention, but could mobilize short distances at home and required decreased analgesic dosing following combination cryoablation and cementoplasty.*

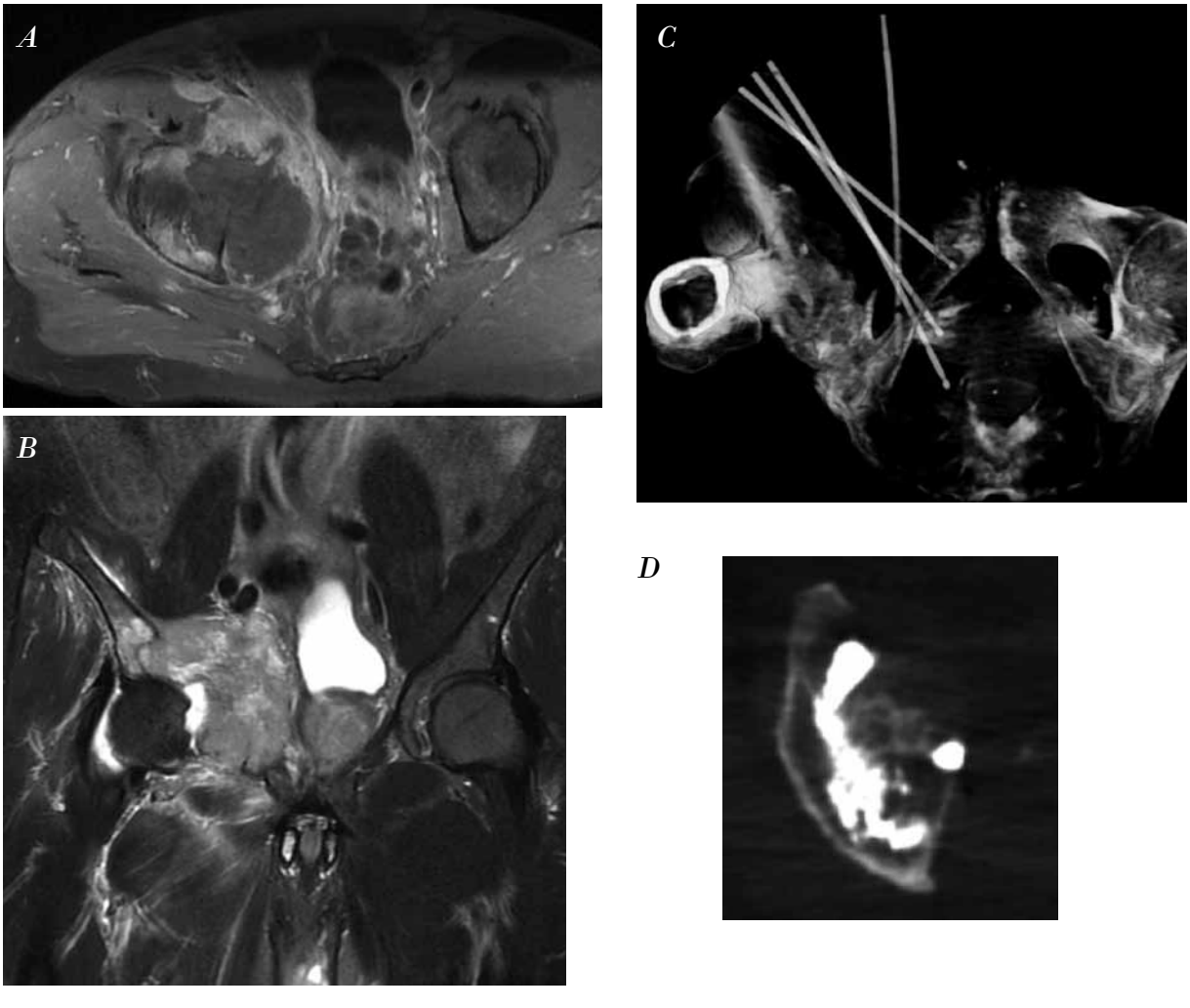


Fig. 4. *Another case demonstrates a 74-year-old man with metastatic renal cell carcinoma and a large metastatic lesion involving the right hemi-pelvis, as shown on pre-intervention MRI (a,b). Four cryoablation probes were placed under bi-planar fluoroscopic guidance and cone beam CT (c), and four 13-gauge cementoplasty needles were used to inject 22mL of cement into the recently created ablation site (d). The pre-procedural pain score for this patient was 9/10, which then decreased to 1/10 post-intervention. This patient was previously hospitalized for 62 days for pain control prior to the intervention and was discharged home 36 hours following combination cryoablation and cementoplasty.*

relief following the intervention, comprising 6.3% of our study cohort.

The limitations of this study include its retrospective nature, which limited the acquisition of ancillary data for all of the patients, such as: pre- and post-procedural opiate requirements, improvement in mobility, and formal quality of life measures. While we have numerous qualitative measures demonstrating profound improvements in mobility and quality of life, prospective studies are warranted and are required in the future literature. Another limitation of this study was the length of follow-up, which was restricted in many cases given the life expectancy of our study cohort.

Conclusion

Combination cryoablation and cementoplasty is a novel intervention that has been shown to be a safe and viable option for palliation of large bony metastases. While prior literature has often excluded large metastases, this data supports the notion that these are no longer to be considered "hopeless cases." As such, these procedures can play a significant role in the multidisciplinary care of palliative patient populations.

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