Complications of Percutaneous Bone Tumor Cryoablation: A 10-year Experience

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Conflicts of interest are listed at the end of this article.

See also the editorial by Jennings in this issue.

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Background: Percutaneous cryoablation has been shown to be effective in the management of painful bone tumors. However, knowledge of the complication rate and risk factors for complication is currently lacking.

Purpose: To report the complication rate and associated risk factors for bone tumor cryoablation.

Materials and Methods: This retrospective study reviewed complications in 239 consecutive patients (131 men and 108 women; median age, 64 years; age range, 6–86 years) who underwent cryoablation of 320 primary or metastatic bone tumors between January 2008 and November 2017. Common Terminology Criteria for Adverse Events was used to categorize complications as major (grade 3–4) or minor (grade 1–2). Multivariable analysis was performed for variables with *P* values less than .20, including age, tumor location, adjacent critical structures, number of cryoprobes, and Eastern Cooperative Oncology Group performance status (ECOG-PS).

Results: Among the 320 tumors, the total complication rate was 9.1% (29 of 320; 95% confidence interval [CI]: 6%, 12.2%). The major complication rate was 2.5% (eight of 320; 95% CI: 0.8%, 4.2%), with secondary fracture the most frequent complication (1.2% [four of 320]; mean delay, 71 days); cryoablation site infection, tumor seeding, bleeding, and severe hypotension were each observed in 0.3% (one of 320) of procedures. Minor complications included postprocedural pain (2.2% [seven of 320]), peripheral neuropathy (0.9% [three of 320]), and temporary paresthesia (0.9% [three of 320]). For all complications, associated risk factors included ECOG-PS greater than 2 (odds ratio [OR], 3.1 [95% CI: 3, 7.6]; $P = .01$), long-bone cryoablation (OR, 17.8 [95% CI: 2.3, 136.3]; $P = .01$), and use of more than three cryoprobes (OR, 2.5 [95% CI: 1.0, 6.0]; $P = .04$); for major complications, associated risk factors included age greater than 70 years (OR, 7.1 [95% CI: 1.6, 31.7]; $P = .01$) and use of more than three cryoprobes (OR, 23.6 [95% CI: 2.8, 199.0]; $P = .01$).

Conclusion: Bone tumor cryoablation is safe, with a 2.5% rate of major complications, most commonly secondary fracture (1.2%). Major complications are associated with age greater than 70 years and use of more than three cryoprobes.

Online supplemental material is available for this article.

Percutaneous image-guided cryoablation is a well-established technique that uses cold thermal energy to treat tumors in various organs, including the breast, lung, liver, kidney, prostate, bone, and soft tissues (1).

Cryoablation has been shown to be effective in the management of painful bone tumors (1,2) and has been used successfully to treat bone metastases in patients with oligometastases (3,4). In contrast to radiation therapy, the technique is repeatable, effectiveness is independent of tumor histology (3), and osseous consolidation may be performed concurrently to mitigate subsequent fracture risk.

Cryoablation of bone tumors performed with palliative or curative intent is generally considered safe, with a reported complication rate of 6.4%–24% (5,6). Complications may occur due to unintended thermal damage to nontarget anatomic structures in close proximity to the ice ball. For this reason, a wide range of thermoprotective techniques have been described and used in conjunction with cryoablation (7). However, few studies (5,6) have specifically evaluated the complication rate of bone tumor cryoablation; therefore, there is currently a substantial lack of knowledge regarding factors associated with development of adverse events.

The purpose of this study was to retrospectively evaluate the complication rate and determine risk factors associated with complications following percutaneous image-guided cryoablation of bone tumors.

Materials and Methods

A.G. and J.G. are advisors to BTG International. No funding was received for this analysis. All authors have control of the data and information submitted for publication.

Abbreviations

CI = confidence interval, CTCAE = Common Terminology Criteria for Adverse Events, ECOG-PS = Eastern Cooperative Oncology Group performance status, IQR = interquartile range, OR = odds ratio

Summary

Bone tumor cryoablation is safe, with a 2.5% rate of major complications, most commonly secondary fracture (1.2%).

Key Points

- Bone tumor cryoablation was associated with a 2.5% rate of major complications.
- The most frequent major complication of bone tumor cryoablation is secondary fracture, occurring in approximately 1.2% of patients.
- Major complications are seven times more likely to occur in older patients (> 70 years) and over 20 times more likely when more than three cryoprobes are used.

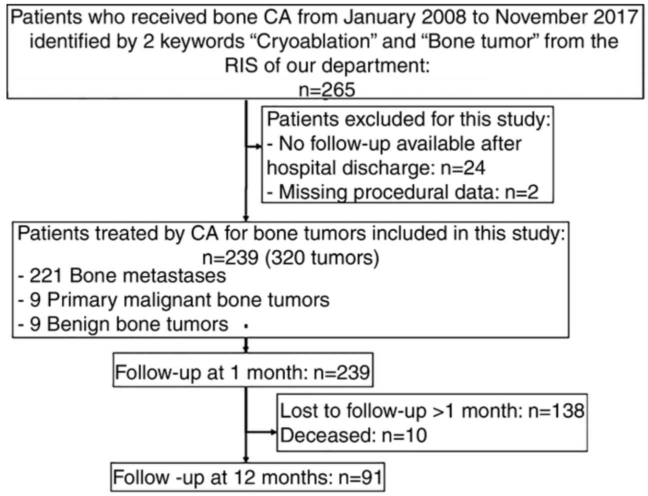


Figure 1: Flowchart illustrates number of patients treated with bone tumor cryoablation (CA), excluded patients, study population, and follow-up. RIS = radiological information system.

This retrospective study was approved by the institutional review board with permission to perform chart review and a waiver of written informed consent. All consecutive patients with primary (benign or malignant) and metastatic bone tumors who underwent cryoablation from January 2008 to November 2017 were identified by research performed in our institutional radiological information system (Xplore; EDL, la Seyne-sur-Mer, France); two keywords (“cryoablation” and “bone tumor”) were entered simultaneously. A total of 265 patients were identified. Two patients were excluded due to missing procedural data about the applied cryoablation protocol on the radiologic reports, and 24 were excluded since no follow-up data were available after their discharge from the hospital. Consequently, 239 patients (with a total of 320 bone tumors) were included in the study (Fig 1).

Patients were referred for cryoablation by a multidisciplinary tumor board including oncologists, orthopedic surgeons, anesthesiologists, and interventional radiologists. Curative treatment (complete tumor ablation) was proposed for patients with painful benign tumors (eg, osteoid osteoma) and with oligometastatic (less than three metastases; < 3 cm) or oligoprogressing (1–2 metastases not responding to systemic therapy) cancer. Palliative treatment (ablation of bone-tumor interface and tumor debulking) was reserved for patients with painful bone metastases that were refractory to or recurrent following standard palliative therapy (eg, analgesia and radiation therapy). Additional cementoplasty and/or osteosynthesis was planned and performed for bone metastases at risk for pathologic fracture (Mirels’ score > 8, > 50% cortical involvement, or according to orthopedic advice) in patients unwilling or unfit to undergo surgery. Patients with life expectancy less than 1 month, irreversible coagulopathy or active sepsis, spinal tumors causing neurologic impairment or instability, risks from anesthesia, and damage to adjacent (< 1 cm) critical structures (nerves, vessels, organs [solid or hollow], cartilage, or skin) were deemed unacceptable candidates and were generally not referred for cryoablation.

Bone Tumor Cryoablation

All procedures were performed on an inpatient basis under moderate sedation or general anesthesia and strict surgical asepsis. For antibiotic prophylaxis, 2 g cefazoline was administered intravenously before the procedure. Using CT guidance, procedures were performed by five physician authors experienced in performing cryoablation procedures (R.L.C., with 5 years of experience; G.K. and J.C., each with 6 years of experience; and J.G. and A.G., each with 11 years of experience).

Different 17-gauge cryoprobes producing unique ice-ball sizes and shapes were used with a commercially available cryoablation system (IceSphere or IceRod probes with the SeedNet cryoablation system; Galil Medical, Yokneam, Israel). The number and type of cryoprobes were selected based on preoperative CT assessment of tumor size and morphology and therapeutic intent (palliative or curative). When several probes were used (mean, 2.6 ± 1.6 per session), they were spaced 1–2 cm apart to allow a synergistic effect with a fusion of the ice ball generated by each cryoprobe (8). Probes were inserted via their access cannulae. Where intraosseous placement was required, a 13-gauge bone trocar (Gangi Special Vertebroplasty Needle; Optimed, Ettlingen, Germany) was used to penetrate the cortex prior to probe placement.

Cryoablation was generally performed using a double 10-minute freeze protocol (two 10-minute freeze cycles separated by an 8-minute passive thaw) (9,10). Intermittent CT images were obtained to monitor extension of the ice ball during freezing. For curative procedures, the ice ball was required to completely expand beyond tumor borders with an additional minimum margin of 5–10 mm (malignant tumors) or 2–3 mm (benign tumors). For palliative procedures, treatment aimed to ablate the bone-tumor interface to control pain. Freezing cycles were terminated prematurely or reduced in power (at the operator’s discretion) if the ice ball extended within 1 cm of adjacent critical structures, and if ancillary thermoprotective measures were deemed insufficient for a safe procedure. Additional freezing cycles and additional probe placement or repositioning were performed if ice-ball extension was less than anticipated.

Adjunctive consolidation was performed using percutaneous osteoplasty, osteosynthesis, or both (11). In bones under predominantly compressive stress (eg, vertebrae), osteoplasty alone was performed by using polymethyl methacrylate (PMMA; Osteopal V, Heraeus Medical, Wehrheim, Germany) injection through a 10-gauge bone trocar. In the pelvic ring, where shear and torsional forces also occur (12,13), screw-mediated osteosynthesis was generally performed using threaded guidewires and cannulated self-tapping screws (Asnis III Cannulated Screw System; Stryker, Kalamazoo, Mich). Osteosynthesis was occasionally combined with cementoplasty to improve screw anchorage in osteolytic bone.

When necessary, one or more ancillary thermoprotective measures (Fig 2, Movie E1 [online]), including gas dissection (carbon dioxide gas) and/or hydrodissection, thermocouples, and nerve root electrostimulation, were used to protect nearby (< 1 cm) nontarget structures (7,14), including the skin in patients with superficial tumors. Gas dissection and hydrodissection were used to displace and/or insulate vulnerable organs by injecting carbon dioxide or saline through 21-gauge needles positioned between the planned ice-ball margin and adjacent vulnerable structure. Hydrodissection was performed using 3%–5% diluted contrast medium to optimize CT visualization of injected fluid. Thermocouples were placed at appropriate locations to monitor temperature around at-risk structures. Electrostimulation was used to monitor nerve root conductivity by positioning a stimulating electrode in contact with the nerve proximal to the region of ablation (15).

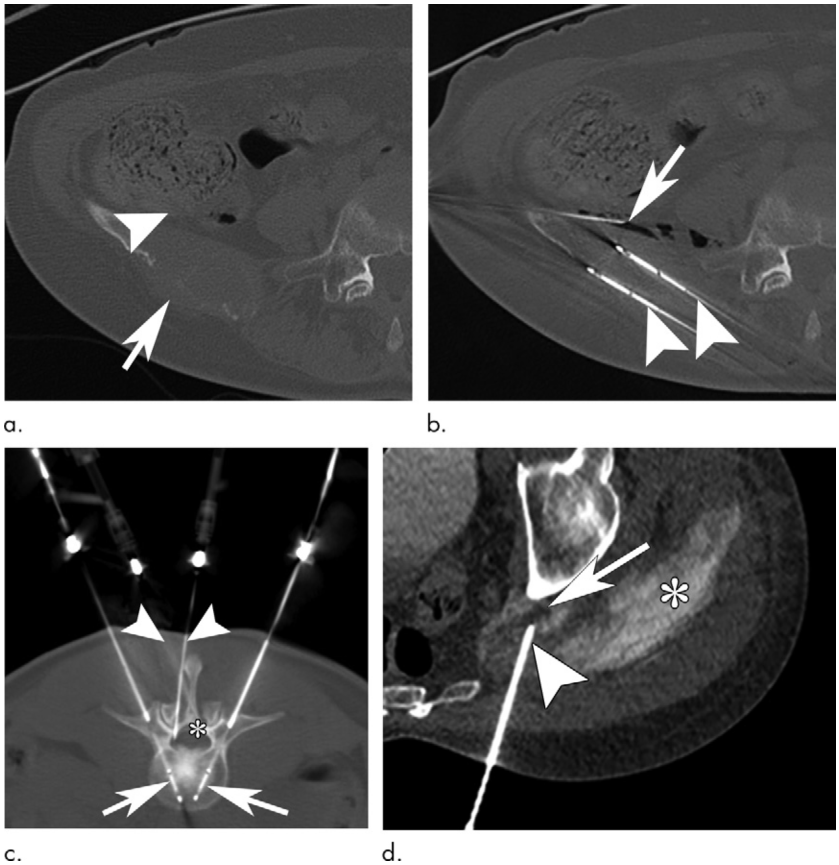


Figure 2: Protection techniques used during cryoablation. **(a, b)** Images in a 63-year-old man with a history of lung cancer. **(a)** Axial CT image shows an iliac metastasis (arrow) close to bowel (arrowhead) **(b)** displaced by gas dissection (arrow) (more suitable than hydrodissection in this case because carbon dioxide rises to dissect nondependent tissue planes). Cryoprobes were already positioned within the metastasis (arrowheads). **(c)** Axial CT image in a 60-year-old man with a history of prostate cancer shows cryoablation of vertebral metastasis close to spinal cord. Cryoprobes (arrows) were coaxially introduced within vertebral trocars and two 22-gauge needles (arrowheads) were advanced inside the spinal canal, allowing hydrodissection (asterisk) and temperature monitoring using a coaxially introduced thermosensor positioned close to the spinal cord. **(d)** Axial CT image in a 35-year-old man with a history of sacral chondrosarcoma illustrates protective measures associated with the cryoablation of the chondrosarcoma. The adjacent sciatic nerve (arrow) was protected using hydrodissection (*) and functional nerve monitoring was undertaken using an electrostimulation probe (arrowhead) placed in contact with the upstream sciatic nerve; Figure E1 (online) shows the response to electrostimulation.

Patients were followed up clinically after 1 month by the treating interventional radiologist and at variable intervals (every few weeks to every 6 months) at the discretion of the referring oncologic or orthopedic physician. Follow-up imaging was performed at 3- to 6-month intervals or according to clinician discretion for oncologic patients.

Data Collection and Analysis

The following data were collected: patient characteristics (age, sex, previous radiation therapy, Eastern Cooperative Oncology Group performance status [ECOG-PS]); goal of treatment (curative or palliative); tumor characteristics (histology, size [largest diameter on multiplanar CT]); tumor location (spine, pelvis, long bone, others [rib, scapula, sternum, talus, calcaneum]); radiographic features of the tumor (osteolytic, osteoblastic, mixed, presence of cortical disruption); presence of critical structures (nerves, vessels, solid organs, bowel, cartilage, or skin) located 1 cm or less from tumor; and procedural details (type of anesthesia, number of cryoprobes and freeze cycles, and additional consolidation procedures).

Patients were categorized as greater than 70 years of age or less than 70 years of age, based on commonly used oncological age cutoffs (16). Chart review was performed by P.A. and R.L.C. (interventional radiologists with 3 and 5 years of experience, respectively), who were blinded to procedural, clinical, and tumor details during data collection. Chart review was performed by single authors in each case. Intraobserver variability was not specifically assessed.

Complications

The complication rate was reported as the number of complications divided by the number of tumors treated. Complications were classified according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Major complications were defined as CTCAE grade 3 or 4, and minor complications as CTCAE grade 1 or 2 (17). Complications were further classified as immediate (< 24 hours), periprocedural (< 30 days), or delayed (≥ 30 days) (18).

Statistical Analysis

Categorical variables are provided as absolute numbers and percentages. Continuous variables are provided as medians with interquartile ranges (IQRs) and were compared by using the Wilcoxon rank sum test. The following data were analyzed by using univariable mixed effects logistic regression to identify potential factors associated with development of complications: patient age, sex, prior radiation therapy, and ECOG status; goal of treatment; tumor histology, size, location, radiographic characteristics, and cortical disruption; presence of adjacent critical structures; use of ancillary thermoprotective techniques; number of cryoprobes and freeze cycles; type of anesthesia; and use of adjunctive consolidation. All complications and major complications were analyzed as subgroups, and variables with a P value less than .20 were tested in a multivariable model. P values less than .05 were considered to indicate a statistically significant difference. Statistical analysis was performed by using SAS version 9.4 (SAS, Cary, NC).

Results

Baseline Characteristics

Patient and tumor characteristics are summarized in Table 1. Among the 239 patients, there were 131 (54.8%) men and 108 (45.2%) women. Median patient age was 64 years (range, 6–86 years [IQR, 54–69 years]; median age for men, 65 years [IQR, 57–70 years]; median age for women, 61 years [IQR, 49–67 years]; P = .10), and the majority (178 of 239 [74.5%]) had ECOG-PS of 2 or less. Two hundred twenty-one (92.5%) patients were treated for bone metastases and 18 (7.5%) for primary bone tumors (nine benign, nine malignant). Fifty-one patients (21.3%) were treated for two or more tumors in the same or a separate session. The majority of tumors were treated with palliative intent (262 of 320 [81.9%]); located in the pelvis (145 of 320 [45.3%]) and spine (68 of 320 [21.2%]); and osteolytic (206 of 320 [64.4%]) with cortical disruption (205 of 320 [64.1%]). Sixty-seven (20.9%) tumors had undergone prior radiation therapy. Median tumor diameter was 4.4 cm (range, 0.3–14.0 cm; IQR, 2.7–6 cm). Adjunctive consolidation was performed for 20.6% of treated tumors (66 of 320). One or more adjacent critical structures were present near 67.2% of tumors (215 of 320); median minimum distance to adjacent critical structures before hydro/gas-displacement was 5 mm (range, 2–14 mm; IQR, 4–7.5 mm); and ancillary thermoprotection was performed in 47.5% of procedures.

Median clinical follow-up was 6 months (range, 1–112 months; IQR, 1–24 months) and 91 patients had at least 1-year follow-up.

Table 1: Patient and Tumor Characteristics

Parameter	Value
Patient characteristics (n = 239)	
No. of men	131 (54.8)
No. of women	108 (45.2)
Median age (y)*	
Entire group	64 (54–69)
Women	61 (49–67)
Men	65 (57–70)
ECOG performance status	
≤2	178 (74.5)
>2	61 (25.5)
Tumor	
Metastasis	221 (92.5)
Benign	9 (3.8)
Primary malignant tumor	9 (3.8)
Tumor characteristics (n = 320)	
Goal of treatment	
Palliative	262 (81.9)
Curative	58 (18.1)
Tumor location	
Spine	68 (21.2)
Pelvis	145 (45.3)
Long bone	7 (2.2)
Others	100 (31.3)
Radiographic features	
Lytic	206 (64.4)
Blastic	68 (21.2)
Mixed	46 (14.4)
Cortical interruption	205 (64.1)
Previous radiation therapy	67 (20.9)
Tumor diameter (cm)*	4.4 (2.7-6)
Presence of adjacent critical structure	215 (67.2)
Distance between tumor and critical structure (mm)*	5 (4–7.5)
No. of cryoprobes > 3	78 (24.4)
Consolidation	66 (20.6)
Thermoprotective measure†	152 (47.5)

Note:—Unless stated otherwise, data in parentheses are percentages. ECOG = Eastern Cooperative Oncologic Group.

* Data are medians. Data in parentheses are interquartile ranges.

† Gas or hydrodissection, thermocouple, electrostimulation, or combination of these protective measures.

Complications

Among the 320 bone tumors treated with cryoablation, complications developed for 29 (9.1%; 95% confidence interval [CI]: 6%, 12.2%); there were major complications for eight tumors (2.5%; 95% CI: 0.8%, 4.2%) and minor complications for 21 tumors (6.6%; 95% CI: 3.9%, 9.3%).

Half of the major complications were fractures (four of 320; mean time to fracture, 71.5 days ± 40.5; Fig 3). Two fractures occurred in the supra-acetabular region after 103 and 120 days despite adjunctive osteoplasty. Subsequent percutaneous osteosynthesis was performed in both cases without further complications at 30- and 27-month follow-up, respectively. We observed no complications directly attributable to consolidation

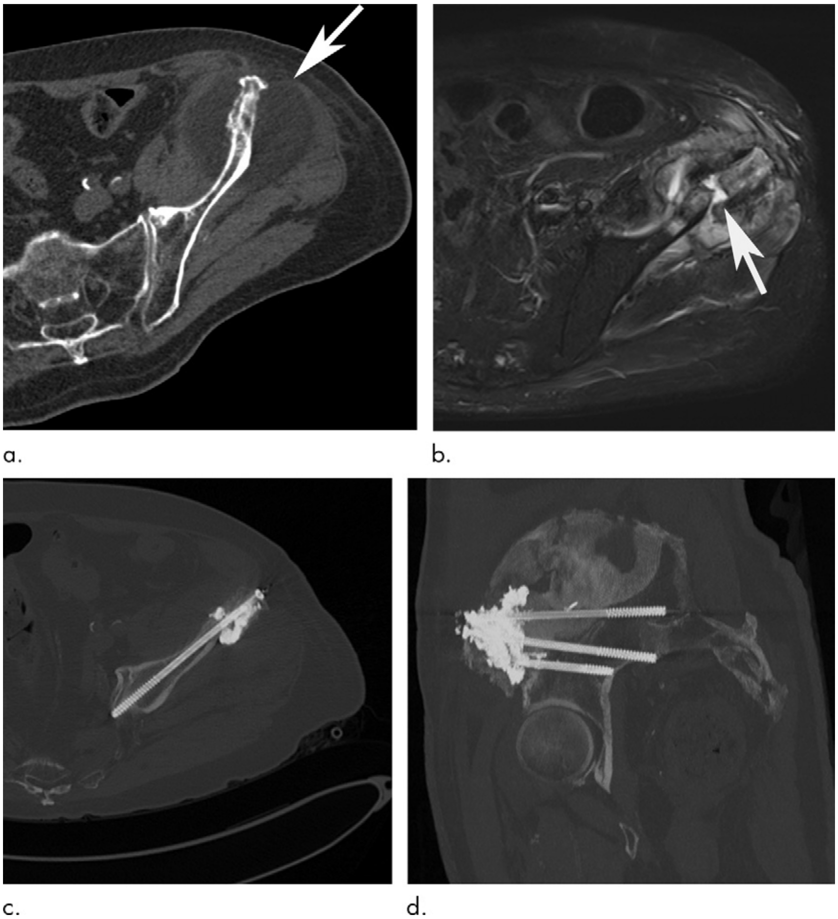


Figure 3: Images in a 76-year-old man with a history of esophageal cancer show cryoablation of an iliac wing metastasis complicated by secondary fracture 30 days after cryoablation. **(a)** Axial CT image during cryoablation of left iliac wing metastasis; the tumor is completely covered by the ice ball (arrow). **(b)** Axial short inversion time inversion recovery MR image demonstrates a fracture (arrow) at the cryoablation site, with high signal intensity of adjacent bone and muscle. **(c)** Axial CT and **(d)** multiplanar reconstructed CT images following percutaneous fracture consolidation with screws and polymethyl methacrylate cement.

procedures. The remaining major complications were tumor seeding (one of 320), cryoablation site infection (one of 320), severe hypotension (one of 320), and arterial bleeding through the bone trocar (one of 320).

Minor complications included pain (seven of 320), peripheral sensory or motor neuropathy (three of 320) (Fig 4), paresthesia (three of 320), skin burn (one of 320), arthropathy (one of 320), asymptomatic fracture (two of 320), acute urinary retention (one of 320), infection of cutaneous puncture site (one of 320), venous skin bleeding (one of 320), and fixation of a 13-gauge bone trocar (used as a coaxial needle for cryoprobe insertion) within a heavily osteoblastic tumor (one of 320). All patients presenting with sensory or motor neuropathy or paraesthesia recovered completely and uneventfully within 5.2 months ± 3.7. Symptoms were generally moderate and categorized as CTCAE grade 2. We did not observe complete and definitive nerve damage.

Twenty-one (19 minor and two major) complications (72.4%) were immediate; one minor complication (3.4%) was periprocedural; and seven complications (six major and one minor; 24.1%) were delayed (Fig E1 [online]). Complications were randomly distributed throughout the study period, with no evidence of a "learning curve" effect, noting that higher-risk cases were undertaken more frequently with increasing institutional experience.

Risk Factors Associated with Development of Complications

For all complications, there were several associated factors in the univariable model (Table E1 [online]). After applying the multivariable model, only three factors remained statistically significant: ECOG-PS greater than 2 (odds ratio [OR], 3.1 [95% CI: 1.3, 7.6]; $P = .01$); more than three cryoprobes used (OR, 2.5 [95% CI: 1.0, 6.0]; $P = .04$); and cryoablation performed in long bones (OR, 17.8 [95% CI: 2.3, 136.3]; $P = .01$) (Table 2).

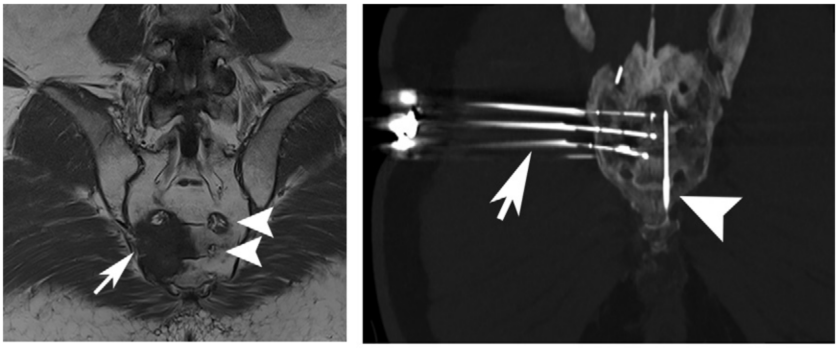
For major complications, there were two associated factors found on univariable analysis: patient age greater than 70 years (OR, 7.1 [95% CI: 1.6, 31.7]; $P = .01$) and application of more than three cryoprobes (OR, 23.6 [95% CI: 2.8, 199.0]; $P = .01$) (Table E2 [online]). Multivariable analysis was not performed given the paucity of events in this group.

Major and minor complications and their management are summarized in Table 3 and Table 4, respectively.

Discussion

The total complication rate of our study was 9.1% (29 of 320) for all tumors and 8.6% (26 of 301) for bone metastases only, without any procedure-related mortality. Of these, 2.5% (eight of 320) were major and 6.6% (21 of 302) were minor complications, suggesting that bone tumor cryoablation is a safe procedure. All complications were more likely to be observed in patients with limited functional status (ECOG-PS > 2; OR, 3.1), where multiple (> 3) cryoprobes were used (OR, 2.5), and in long bone tumors (OR, 17.8). Major complications were associated with patient age greater than 70 years (OR, 7.1) and more than three cryoprobes used (OR, 23.6).

The most common major complication was secondary fracture, occurring in four patients (1.2%) with osteolytic bone metastases, treated with curative ($n = 1$) or palliative ($n = 3$) intent. Fractures occurred in the acetabulum (two patients), iliac wing (one patient), and scapula (one patient). All fractures were related to tumors with significant cortical disruption (three with > 50%), and the two acetabular fractures were associated with local tumor progression on repeat CT. Only one patient with secondary fracture (and neuropathy) had undergone prior radiation therapy; hence, it was not possible to evaluate whether radiation therapy represented an additional



a. b.

Figure 4: Images in a 55-year-old man with a history of colorectal cancer show cryoablation of a sacral metastasis located close to neural structures. The patient developed a sensory neuropathy following the procedure (partial anesthesia of the gluteal region). **(a)** Coronal T1-weighted MR image illustrates the metastasis (arrow) prior to treatment, directly adjacent to the sacral foramen (arrowheads indicate contralateral foramen). **(b)** Coronal CT image shows three cryoprobes (arrow) close to the sacral foramen. A thermocouple (arrowhead) was positioned in the sacral hiatus to monitor local temperature; this did not prevent neural damage in this case.

Table 2: Risk Factor Analysis for Complications

Type of Complication	Odds Ratio*	*P* Value
All complications		
Univariable analysis		
Age > 70 years	2.7 (1.2, 6.3)	.02
Cryoablation performed in long bone	16.5 (2.3, 116.2)	.02
No. of cryoprobes > 3	2.8 (1.3, 6.3)	.01
ECOG-PS > 2	2.7 (1.2, 6.2)	.02
Multivariable analysis		
Cryoablation performed in long bone	17.8 (2.3, 136.3)	.01
No. of cryoprobes > 3	2.5 (1.0, 6.0)	.04
ECOG-PS > 2	3.1 (1.3, 7.6)	.01
Major complications		
Univariable analysis		
Age > 70 years	7.1 (1.6, 31.7)	.01
No. of cryoprobes > 3	23.6 (2.8, 199.0)	.01

Note.—ECOG-PS = Eastern Cooperative Oncology Group performance status.
* Data in parentheses are 95% confidence intervals.

risk factor for fracture (or nerve damage). The two acetabular fractures occurred despite adjunctive osteoplasty, raising the question of whether consolidation is of overall benefit for postablation fracture prophylaxis. Our study did not demonstrate any complications related to consolidation, nor any significant association between consolidation and development of major complications (including fracture). However, the number of fractures is small and firm conclusions cannot be drawn. The literature is similarly equivocal regarding whether consolidation increases subsequent fracture risk (19). At our institution, we typically perform consolidation in patients at risk for postablation fracture, although there is currently no robust evidence to support long-term efficacy of this approach. Other major complications (eg, tumor seeding, infection, severe hypotension, arterial bleeding from the trocar) occurred only sporadically in this study.

The most common minor complication was postprocedural pain (seven of 320; 2.2%), which generally resolved after 2–3 weeks of simple oral analgesia (including opioids). Of all ablative techniques, cryoablation is the least painful modality, probably due to the intrinsic analgesic properties of ice (20). Nerve injury occurred in 1.8% of cases (six of 320), but all deficits were transient and recovered completely within a few months, either spontaneously or following steroid therapy. We observed two other minor complications of note: fixation of a 13-gauge bone trocar within a markedly osteoblastic tumor, preventing manual retrieval (removed by advancing a larger coaxial bone trocar over the fixed distal tip (21,22), and painful ankle arthropathy following cryoablation of a periarticular calcaneal osteoid osteoma (which resolved following intraarticular corticosteroid injection).

Risk factors associated with development of major complications included age greater than 70 years (OR, 7.1) and more than three cryoprobes used (OR, 23.6); for all complications, risk factors were ECOG-PS greater than 2 (OR, 3.1), more than three cryoprobes used (OR 2.5), and long bone cryoablation (OR, 17.8). Older patients with poorer performance status (ECOG-PS of grade 3–4) are known to be at increased risk of mortality and postoperative complications (23). Multiple cryoprobes synergistically increase ice-ball size (8), probably resulting in greater extension of the ablation zone toward adjacent critical structures and increased risk of complications. The association of long bone tumor cryoablation with all complications is probably due to more frequent minor complications secondary to proximity of skin and neurovascular structures, since no association was observed with major complications.

The results of our study are in line with previously reported total complication rates of 6.4% and 24% and major complication rates of 0%–16% (2,4–6,24–27) (Table E3 [online]). In particular, secondary fracture is a well-known complication of bone tumor ablation (28,29) resulting from loss of structural integrity secondary to tumor necrosis. Nerve injury is a potentially serious complication, predominantly reported following cryoablation of spinal tumors, and local anatomy should be carefully evaluated to identify adjacent nerves and facilitate adequate thermoprotective measures (7,14). Cartilage damage has been reported in conjunction with femoral head osteonecrosis following cryoablation of a periacetabular lesion complicated by transarticular ice-ball extension; probe position less than 5 mm from the articular surface appears to be a risk factor (30). Tumor seeding has not been previously reported following bone tumor

Table 3: Major Complications of Bone Tumor Cryoablation

Complication	CTCAE Grade	No. of Occurrences (*n* =320)	Delay (d)	Management
Fracture	3	4 (1.2)		
Acetabulum		1 (0.3)	120	Screw
Acetabulum		1 (0.3)	103	Screw
Iliac wing		1 (0.3)	33	Cement + screw
Scapula		1 (0.3)	30	Screw
Tumor seeding	3	1 (0.3)	150	Surgery
Infection of cryoablation site	3	1 (0.3)	60	Surveillance
Arterial bleeding via trocars	3	1 (0.3)	0	Hemostasis by cementoplasty
Hypotension	4	1 (0.3)	0	Vasoactive drugs and intravenous fluid

Note.—Unless otherwise stated, data in parentheses are percentages. CTCAE = Common Terminology Criteria for Adverse Events.

Table 4: Minor Complications of Bone Tumor Cryoablation

Complication	CTCAE Grade	No. of Occurrences (*n* = 320)	Delay (d)	Management
Pain	2	7 (2.2)	0	Oral or parenteral analgesic drugs
Peripheral sensory or motor neuropathy	2	3 (0.9)	0	None or corticosteroid therapy
Paresthesia	1	3 (0.9)	0	None
Skin burn	2	1 (0.3)	0	Paraffin gauze dressing
Arthropathy	2	1 (0.3)	180	Articular corticosteroid injection
Asymptomatic fracture	1	2 (0.6)	0	None
Acute urinary retention	2	1 (0.3)	0	Urinary catheterization
Infection of puncture site	2	1 (0.3)	2	Antibiotics
Fixed trocar	1	1 (0.3)	0	Coaxial method with larger needle
Venous skin bleeding	2	1 (0.3)	0	Stitches

Note.—Unless otherwise stated, data in parentheses are percentages. CTCAE = Common Terminology Criteria for Adverse Events.

cryoablation but is well described following lung, liver, and renal ablation (31–33); has been reported following percutaneous consolidation of spinal tumors and osteosynthesis of trochanteric metastases; and represents both a theoretical and practical risk (34,35). Infection at the cryoablation site has been reported following bone tumor cryoablation, but there is currently no consensus regarding use of prophylactic antibiotics. Our institutional practice is to routinely administer 2 g cefazoline intravenously prior to procedures.

Our study has several limitations. First, the study population was heterogeneous, including different tumor types, sizes, and locations, as well as heterogeneous procedures with variable adjunctive consolidation, potentially conflating distinct entities and limiting generalizability. Second, due to the retrospective study protocol, the presence of osteoporosis was inconsistently recorded and could not be usefully analyzed. This confounds interpretation of postprocedural fracture prevalence, although it is noted that all fractures occurred in substantially osteolytic tumors with local tumor progression, and the contribution of osteoporosis is likely to be limited. Third, due to the small number of fractures, the relative contributions of radiation therapy and consolidation to subsequent fracture risk could not be evaluated. Finally, more than half of patients (148 of 239 [62%]) were lost to follow-up or deceased at 12 months, potentially resulting in underestimation of complications (eg, permanent nerve damage).

In conclusion, bone tumor cryoablation is a safe procedure with a very low rate (2.5%) of major complications. The majority of complications are secondary fractures, which are associated with patient age greater than 70 years and use of more than three cryoprobes.

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