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Percutaneous thermal ablation of sacral metastases: assessment of pain relief and local tumor control

Short title:

Percutaneous thermal ablation of sacral metastases

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Abstract

Purpose. To retrospectively report on safety, pain relief and local tumor control achieved with percutaneous ablation of sacral bone metastases.

Materials and Methods. From February 2009 to June 2020, 23 consecutive patients (12 women and 11 men; mean age, 60 ± 8 [SD] years; median, 60; range: 48-80) with 23 sacral metastases underwent radiofrequency (RFA) or cryo-ablation (CA), with palliative or curative intent at our institution. Patients' demographics and data pertaining to treated metastases, procedure-related variables, safety, and clinical evolution following ablation were collected and analyzed. Pain was assessed with numerical pain rating scale (NPRS).

Results. Sixteen (70%) patients were treated with palliative and 7 (30%) with curative intent. Mean tumor diameter was 38 ± 19 (SD) mm (median, 36; range: 11-76). External radiation therapy had been performed on five metastases (5/23; 22%) prior to ablation. RFA was used in 9 (39%) metastases and CA in the remaining 14 (61%). Thermo-protective measures and adjuvant bone consolidation were used whilst treating 20 (87%) and 8 (35%) metastases, respectively. Five (22%) minor complications were recorded. At mean 31 ± 21 (SD) (median, 32; range: 2-70) months follow-up mean NPRS was 2 ± 2 (SD) (median, 1; range: 0–6) vs. 5 ± 1 (median, 5; range: 4–8; P < 0.001) at the baseline. Three metastases out of 7 (43%) undergoing curative ablation showed local progression at mean 4 ± 4 (SD) (median, 2; range: 1-8) months follow-up.

Conclusion. Percutaneous ablation of sacral metastases is safe and results in significant longlasting pain relief. Local tumor control seems sub-optimal; however, further investigations are needed to confirm these findings due to paucity of data.

Keywords: Bone neoplasms; Neoplasm metastasis; Pain management; Radiofrequency ablation; Sacrum.

Abbreviations

CA: Cryoablation

CTCAE: Common terminology criteria for adverse events

ECOG-PS: Eastern Cooperative Oncology Group Performance Status

ERT: External radiation therapy IQR: Interquartile range MWA: Microwave ablation NPRS: Numerical pain rating scale RFA: Radiofrequency ablation SD: standard deviation

Introduction

Spine is the most common site of skeletal metastasis, with lumbar, thoracic and cervical segments being the most affected areas [1–3]. Accordingly, the sacrum is the spinal segment with the lowest incidence of metastatic spread [4].

Surgery and external radiation therapy (ERT) have traditionally represented the two most common first-line treatments proposed to patients presenting with primary or metastatic sacral tumors. Nevertheless, these treatments, and especially surgery, often result in high rates of complications [5–10].

During the last decades, percutaneous ablation has rapidly integrated the armamentarium of treatments available for the management of bone metastases [11,12]. Ablation has proven to be safe [13,14] and highly effective in providing fast and long-lasting pain relief [15,16], as well as high rates of local tumor control in selected patients [17,18]. Therefore, percutaneous ablation currently represents a valuable alternative to surgery/ERT; or an additional therapeutic option to be proposed in combination with these more established treatments, with the final aim of improving pain relief or local tumor control [19–22]. Despite increased application of percutaneous ablation for the treatment of spinal tumors [23–25], there is a paucity of data on ablation provided for the treatment of sacral metastases [26].

The purpose of this study was to retrospectively report our experience with percutaneous ablation of sacral metastases with the intent of adding to the limited existing literature in terms of safety, pain relief and local tumor control.

2. Materials and methods

This single center retrospective study was approved by the institutional review board with permission to perform chart review and a waiver of written informed consent was obtained at both centers.

2.1 Patient selection

All consecutive patients with metastatic tumors of the sacrum who underwent radiofrequency ablation (RFA) or cryoablation (CA) from February 2009 and June 2020 were identified by searches performed from our institutional radiological information system (Xplore[®]; EDL). Four keywords ("RFA", "CA", "sacrum", "malignancy") were entered simultaneously. A total of 28 patients were identified. Two patients were excluded since they presented with primary malignant bone tumors. Three other patients were also excluded since no follow-up data were available after discharge from hospital. Consequently, 23 patients (11 [48%] men; 12 [52%] women; mean age, 60 ± 8 (standard deviation [SD] years; median, 60; range: 48-80; interquartile ranges [IQR]: 55–66) who had received percutaneous ablation of 23 sacral metastases were finally included (**Fig. 1**).

Patients were referred for ablation by a multidisciplinary tumor board, including oncologists, radiation oncologists, orthopedic surgeons, anesthesiologists, and interventional radiologists. Curative treatment (i.e., complete tumor ablation) was proposed for patients with an oligometastatic (less than three metastases; < 3 cm) or oligo-progressing (1–2 metastases not responding to systemic therapy) oncological disease. Palliative treatment was reserved for patients with painful bone metastases refractory to or with recurring pain after standard palliative therapies, including analgesics and ERT. Patients with life expectancy < 1 month, irreversible coagulopathies, active sepsis, focal neurological deficits, mechanical instability (assessed with the Spinal Instability Neoplastic Score [27]) for which the tumor board indicated surgical rather than percutaneous bone consolidation, and significant risk from anesthesia, were not offered percutaneous ablation.

2.2 Percutaneous ablation

All procedures were performed on an inpatient basis under general anesthesia and strict surgical asepsis. Combination of systemic and local analgesics was used to manage peri-operative pain [28,29].

Using computed tomography guidance, procedures were performed by six physician authors experienced in performing bone ablation procedures (P.D.M. and P.A. with 1 year of experience; R.L.C. and G.K. with 6 years of experience; J.G. with 13 years of experience; and A.G. with 20 years of experience).

Different straight 17-gauge mono- (Cool-tip[®], Medtronic) or bi-polar (Osteocool[®], Medtronic) electrodes with different active tip sizes (1-3 cm for the monopolar system; 0.7-2 cm for the bipolar system) were used to perform RFA. CA was performed with straight 17-gauge cryoprobes (Ice-Seed[®], Ice-Sphere[®], Ice-Rod[®], Boston Scientific). The number and type of electrodes or cryoprobes were selected based on preoperative assessment of the size and morphology of the target metastasis on baseline imaging, along with evaluation of the therapeutic intent (i.e., palliative or curative). Among the ablation techniques available in our institution during the study period (i.e., RFA, CA, microwave ablation [MWA]), operators systematically opted for RFA or CA due to the relatively limited experience available so far with bone tumors MWA [30]. Moreover, aside from general wide-accepted rules (e.g., avoiding RFA for mixed/osteoblastic tumors), the choice between RFA or CA was completely operator-driven.

Curative procedures were performed in order to result in an ablation area that expanded 5–10 mm beyond the borders of the target metastasis (**Fig. 2**). For palliative procedures, treatment aimed to ablate the bone-tumor interface to control pain; and whenever technically and clinically feasible, ablation was carried out with the intent of destroying the entire metastasis with the largest achievable safety margin (**Fig. 3**). When the target tumor had already destroyed the cortical bone, ablation devices were placed directly into the target metastasis without any coaxial needles; otherwise 10-13-gauge bone trocars were used to penetrate the cortex prior to coaxial placement of the ablation devices.

RFA ablation protocols were as follows: i), ablation time 8–15 minutes and target temperature \geq 65 °C for metastases treated with mono-polar RFA; and ii), ablation times 6.5–30 minutes and target temperature \geq 70°C for metastases treated with bi-polar RFA. With CA simultaneous

activation of all the deployed probes was performed to allow a double 10-minute freezing cycle interspaced by a single 10-minute passive thawing.

In patients with large hyper vascular metastases for which a massive "sink-effect" was anticipated, percutaneous embolization was performed within the same interventional ablation session in order to maximize the chances to reach the desired curative or palliative goal (**Fig. 3**).

When non-target structures such as nerves or skin were 1 cm within the expected ablation zone, one or more ancillary thermo-protective measures, including carbon dioxide gas/hydrodissection, thermocouples, and active nerve monitoring through electrostimulation or somatosensory evoked potentials were used [31,32].

Patients were followed-up clinically at one month by the treating interventional radiologist, and thereafter at variable intervals (every few weeks to every six months) at the discretion of the referring oncologist. Follow-up imaging was performed at 3- to 6-month intervals or according to oncologists' discretion. Patients being treated with a palliative intent underwent clinical follow-up only, and imaging was obtained exclusively with post-ablation recurring pain or complications being suspected in the treated area.

Adjuvant bone consolidation was performed using percutaneous osteoplasty, osteosynthesis, or both [33] according to the indication of the tumor board. Osteoplasty was performed with polymethyl methacrylate (Osteopal V[®], Heraeus Medical); osteosynthesis with cannulated self-tapping self-drilling screws (Asnis III Cannulated Screw System[®]; Stryker) being coaxially deployed over a 1.8–3.2 mm Kirshner guidewire.

2.3 Data collection

For each patient and ablation procedure, demographic, tumor characteristics, procedure characteristics, procedure safety and outcome were collected when available. Patients' demographics included sex and age, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), and goal of treatment (i.e., curative vs. palliative). Tumor characteristics included size (i.e., major diameter assessed on multiplanar preoperative imaging), histopathologic features, radiographic features (i.e., osteolytic vs. osteoblastic, cortical bone disruption) of the target metastasis and previous ERT at the treated site. Procedure-related variables included prior embolization, number of electrodes or cryoprobes used, use of thermo-protective measures and/or

adjuvant bone consolidation. Procedure safety was evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE v5.0) scale; furthermore, complications were graded as minor (grade ≤ 2) or major (grade > 2) as usually reported in large bone ablation series [13,14]. Clinical evolution was evaluated according to the goal of the procedure. Therefore, pain drop was assessed in patients undergoing palliative treatments according to a 0–10 numerical pain rating scale (NPRS). Local tumor progression was evaluated in patients undergoing curative treatments, and was accorded when tumoral enhancing foci were noted at the treated site at contrast-enhanced imaging follow-up performed with magnetic resonance imaging, computed tomography or positron emission tomography.

2.4 Statistical analysis

Categorical variables were expressed as absolute numbers, proportions and percentages. Continuous variables were expressed as means \pm SD and ranges or medians with IQR. Wilcoxon and Fisher exact tests were used to compare continuous and binary variables, respectively. A *P*value < 0.05 was considered statistically significant. Statistical analysis was performed by using R v3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Baseline characteristics

Patient and tumor characteristics are summarized in **Table 1**. Twenty (20/23; 87%) patients had an ECOG-PS ≤ 2 . Sixteen patients (16/23; 70%) were treated with palliative intent and 7 (7/23; 30%) with curative intent.

Twenty-one (21/23; 91%) metastases were osteolytic and eighteen (18/23; 78%) presented with cortical bone disruption. The mean diameter of the target metastasis was 38 ± 19 (SD) mm (median, 36; range: 11–76; IQR: 22–53). Metastases mainly originated from breast (8/23; 35%), lung (4/23; 17%), colorectal (4/23; 17%), and kidney (2/23; 9%) cancers. ERT had been performed on five metastases (5/23; 22%) prior to ablation.

RFA was used to treat nine metastases (8/23 [35%] with bipolar and 1/23 [4%] with monopolar systems) and CA to treat the remaining 14 (14/23; 61%). The mean number of ablation probes

applied per tumor was 2 ± 1 (SD) (median, 2; range: 1–4; IQR: 2–3). Embolization was used before ablation in three metastases (3/23; 13%). Additional thermo-protective measures were used whilst treating 20 metastases (87%); and adjuvant bone consolidation was used in the form of osteoplasty (6/23; 26%) or osteosynthesis (2/23; 9%) to consolidate the treated bone immediately after ablation. Procedural data are summarized in **Table 2**.

3.2 Safety

Complications developed in 5 patients (5/23; 22%). These adverse events were consistent with (grade 2) peripheral neuropathies in four patients (4/23; 17%), and (grade 1) post-operative pain in one patient (1/23; 4%). Among these five procedure-related complications, three were consistent with a direct thermal-mediated injury to nearby non-target structures, notably nerve roots (**Table 3**).

Although complications were more common in patients receiving palliative treatments (4/16; 25%) compared to those receiving curative ones (1/7; 14%), the difference was not significant (P > 0.99). In one metastatic site being treated with ablation and ERT (1/5; 20%) a post-ablation complication was noted vs four sites (4/5; 80%) that did not receive previous ERT (P > 0.99).

3.3 Clinical evolution

In the group of patients undergoing palliative ablation, mean follow-up was 31 ± 21 years (median, 32; range: 2–70; IQR: 11–42). At that time point, mean NPRS was 2 ± 2 (SD) (median, 1; range: 0-6; IQR: 0–3) vs. 5 ± 1 (SD) (median 5; range: 4-8; IQR: 4–6) at baseline (P < 0.001). The rate of patients reporting a NPRS drop of at least 3 points was similar (P > 0.99) following RFA (4/5; 80%) or CA (9/11; 82%). Analogously, the rate of patients reporting a NPRS drop of at least 3 points was similar (P > 0.99) following at least 3 points was similar (P > 0.99) following at least 3 points was similar (P > 0.99) following ablation (10/13; 77%) or ablation and ERT (3/3; 100%).

In the group of patients undergoing curative ablation, mean follow-up was 21 ± 21 (SD) months (median, 17; range: 1-65; IQR: 10–22). During such time interval, 3 metastases out of 7 (43%) showed local progression at variable time points ranging between 1 and 8 months (mean, 4 ± 4 [SD]; median, 2; IQR: 2–5). Local tumor progression occurred in 3 patients out of five (3/5;

60%) receiving ablation alone vs no local tumor recurrence noted among the two patients receiving ablation and ERT (P=1).

4. Discussion

In the present study, we have retrospectively summarized our single-center experience with percutaneous RFA or CA applied to treat sacral metastases with a palliative or curative intent spanning over 11 years. Despite more than 300 bone metastases having undergone percutaneous ablation in our center during this lengthy study period, the search conducted in our radiological information system revealed only 23 sacral metastases receiving such a treatment. This further confirms the relatively rarity of metastatic spread to the sacrum, which is in line with previous interventional and non-interventional experiences reporting on the management of metastatic sacral disease [5,7,9,10,26,34]. In addition to the rarity of the sacral metastatic disease, there were no sacral metastases being treated with ablation in the last period of our study (January-June 2020), which was probably the result of the COVID-19 pandemic obliging our interventional oncology service to dramatically shut down its activity during the first period of the pandemic due to shortage of anesthesiology services, which is in line with other similar experiences [35].

In our series, we noticed a relatively low rate of minor procedure-related complications (22%), with only 3 (3/23; 13%) being related to direct thermal-mediated injury to the nearby non-target structure. In fact, we have noticed 3 occurrences of post-ablation neural deficit; with one of them (bladder dysfunction) being expected since it was evident that reaching complete local tumor control would have compromised nearby nerve roots. This patient had been exhaustively informed of such risk during the pre-ablation consultation and consented to the procedure. Thankfully, a complete recovery occurred within six months. Other complications were consistent with one patient experiencing an intense post-RFA pain, which is a well-known common outcome after bone tumors RFA [14,36], warranting the adoption of adequate post-ablation analgesic protocols [29]; and one brachial plexus syndrome, which is another known although rare complication, often occurring in patients undergoing prolonged interventional procedures or surgery in the prone position [37]. Interestingly, there were no skin burns, which may be a common occurrence whilst ablating superficial tumors [38].

Concerning our clinical outcomes, palliative treatments were more common than curative ones (70% vs. 30%); and pain relief was overall relevant (median NPRS reduction of 5 points) and long-lasting (median follow-up 32 months). On the other hand, in patients receiving curative ablation (n = 7), local tumor progression occurred at 3 (43%) treated sites at a median follow-up of 17 months.

Madaelil et al. reported their experience with sacral metastases in 11 patients undergoing RFA for pain relief (11/11), or for pain relief and local tumor control (4/11) [26]. With a median clinical follow-up of 4.7 months, they reported no procedure-related complications, extensive long-lasting pain relief (pain NPRS trend: pre-procedure, 6; 1 month, 3; 3 months, 4; 6 months, 2), and a high rate of local tumor control (3/4 patients [75%] at a median follow-up of 7.6 months) [26]. Our results regarding pain relief are in line with Madaelil et al. [26]. However, compared to the aforementioned study, we reported a lower rate of local tumor control, which may be explained by the fact that all recurring tumors were sized > 2 cm, presented with cortical bone disruption, and were very close to nerve roots, all of which have been associated to poor post-ablation local tumor control [17,18,23].

Surgical series' on sacral metastases reported variable but overall significant rates of pain relief [5,7], and high rates of local recurrences (23–40%) [7,9]. Post-surgical complication rates ranged between 23% and 40% [5,7,9], with infections, cerebrospinal fluid leakages and sphincter disorders being the most common recorded events. On the other hand, ERT series' (increasingly reporting on stereotactic technique), reported significant pain relief [34], rates of local recurrence as high as 22% [10], and low post-treatment morbidity (0-14%) [10,34], with secondary bone insufficiency fractures and neural deficits being the most common adverse events [10]. These and our data essentially suggest that surgery with palliative intent should be mainly reserved for patients with an acute neurologic deficit due to nerve compression or mechanical instability untreatable with percutaneous techniques (i.e., osteoplasty, osteosynthesis) [39]. Furthermore, for patients requiring curative treatments, surgery should be ideally proposed to young patients with long life expectancy and good performance status, without extensive visceral metastatic involvement, and without primary cancers carrying a poor prognosis (i.e., any cancer other than lymphoma, breast, multiple myeloma, renal, prostate or thyroid) [40]. Accordingly, whenever possible, minimally invasive percutaneous interventional treatments or ERT, should be preferred as first-line therapies of sacral metastases, especially in patients seeking pain relief, which

definitively represents the vast majority of patients with sacral metastases. Moreover, it has been reported that combining percutaneous ablation and ERT improves pain relief and local tumor control compared to ERT alone, without significantly increasing the patients' overall morbidity [15,19–21]. Therefore, it is highly likely that in the near future an increasing number of patients will receive combined ERT and ablation for the treatment of sacral bone metastases. From a practical point of view, it seems reasonable to propose ERT following the percutaneous treatment. since this latter is often based on combination of ablation and osteoplasty/osteosynthesis, which definitively contributes to preventing one of the most common post-ERT adverse events, namely secondary fractures [6,10], particularly when the stereotactic technique granting higher rates of local tumor control and pain relief [41–43] is utilized.

Limitations of our study include the retrospective design and the relatively limited sample size, which has probably hindered achieving statistical significance whilst analyzing clinical outcomes in the cohort of patients receiving combined ablation and ERT vs. those receiving ablation only. Nevertheless, limited sample size is a common constraint among surgical, interventional and ERT series' specifically addressing sacral metastases. Moreover, given the relative rarity of sacral metastatic disease, it is not surprising that several different tumor entities were included in our and other series'. However, this element along with the very limited number of patients undergoing curative treatments, necessitates caution when evaluating results relating to local tumor control.

In conclusion, percutaneous ablation of sacral bone metastases is only sporadically used and reported in the literature, despite it being safe and resulting in significant and long-lasting pain relief. Clinical outcomes dealing with local tumor control seem sub-optimal, although the paucity of currently available data imposes cautious interpretation. Lastly, it is likely that in the near future surgical indications will narrow, thus paving the way for ERT and/ or percutaneous ablation/bone consolidation. In this perspective, given the very encouraging results already reported by previous experiences combining ablation and ERT on spinal metastases, it seems reasonable to advocate for prospective multicentric studies investigating the curative and palliative potentials of such a combined treatment also on sacral metastases.

Human rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patients. The study was approved by institutional review board with a waiver for written informed consent

Disclosure of interest

R.L.C. and J.G. are advisors to Medtronic. The authors declare that they have no competing interest in relation with this article.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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Legends for figures

Fig. 1. Flowchart summarizing the selection of the study population.

Fig 2. 53-year-old man presenting with an oligometastatic paraganglioma. (A) Axial PET-CT showing an 11 mm post-surgical sacral recurrence (arrow) of a previously resected metastasis. (B) Computed tomography guided cryoablation was performed with a single cryo-probe (arrow), which resulted in (C) complete local tumor control (arrow) demonstrated on follow-up PET-CT obtained 19 months after ablation. For cryoablation, (D, E) a 5Fr catheter (arrows) was deployed through the sacral hiatus to perform protective hydrodissection; along with (E) thermal monitoring of the right S2 nerve root (arrow).

Fig 3. 49-year-old woman presenting with painful bone metastases from renal cell carcinoma. (A) Coronal computed tomography image of a large lytic and painful (Numerical Pain Rating Scale 8/10) metastasis (arrow) of the left sacral wing. (B) Contrast-enhanced T1-weighted magnetic resonance imaging showed the hyper-vascular aspect of this tumor (arrow). Due to tumor large size (54 mm) and hypervascularity, pre-operative embolization was conducted with the intent of increasing the effect of ablation by limiting the "heat-sink" effect: (C) intra-operative arteriography from the left internal iliac artery confirmed the hypervascularity of this tumor (arrows). (D) Intra-operative arteriography obtained from the same artery performed just after embolization (500-700micron particles), showed a nearly complete tumor devascularization (arrows). Two bipolar radiofrequency ablation electrodes (arrows) were deployed within the tumor with a (E) posterior (arrows) and (F) lateral (arrow) approaches through two different coaxial 13G bone trocars in order to perform multiple ablation cycles. At the same time, several different protective measures were deployed to protect the left L5 nerve root through thermal monitoring (not showed); the left S1 nerve root with thermal monitoring in S1 neuroforamen (not showed), and (G) with coaxial trans-osseus thermal monitoring and hydrodissection in the pelvis (arrow); sciatic nerve with hydrodissection in the retro/sub-acetabular area (not showed). Thereafter, the trans-iliac bone trocar was used to perform bone consolidation through osteoplasty. (H) A computed tomography follow-up obtained 19 months after the procedure showed increasing bone density (arrows) compared to (A), thus being in favor of good local tumor control and a drop of the Numerical Pain Rating Scale to 1/10.

Table 1. Demographics of 23 patients who underwent percutaneous thermal ablation of sacral metastases.

Table 2. Procedure details in 23 patients who underwent percutaneous thermal ablation of sacral metastases.

Table 3. Complications in five patients who underwent percutaneous thermal ablation of sacral metastases.

Patients with sacral malignancies treated with percutaneous ablation between February 2009 and June 2020 (n = 28)

Eligible patients with sacral metastases (n = 26)

Eligible patients with sacral metastases and complete data (n = 23)

Excluded patients (n = 2; 7%) Primary bone tumors

Excluded patients (n = 3; 11%) No follow-up after patient's discharge from the hospital





Men	11 (11/23; 48%)
Women	12 (12/23; 52%)
Age (years)	60 ± 8 [48-80]
ECOG-PS	
≤ 2	20 (20/23; 87%)
>2	3 (3/23; 13%)
Goal of treatment	
Palliative	16 (16/23; 70%)
Curative	7 (7/23; 30%)
Metastases	
Primary tumor	8 (8/23; 35%)
Breast	4 (4/23; 17%)
Lung Cala matal	4 (4/23; 17%)
COIO-FECUAI	2 (2/23; 9%)
Klaney	5 (5/23; 22%)
Others	
Radiographic features	
Lytic	21 (21/23; 91%)
Mixed	2 (2/23; 9%)
Cortical bone disruption	18 (18/23; 78%)
Previous radiotherapy	5 (5/23; 22%)
Tumor size (mm)	38 ± 19 [11-76]

ECOG-PS = Eastern Cooperative Oncology Group-Performance Status. Qualitative variables are expressed as raw numbers; numbers in parentheses are proportions followed by percentages. Continuous variables are expressed as means \pm standard deviations; numbers in brackets are ranges.

Sex

Ablation technique

Radiofrequency ablation	9 (9/23; 39%)
Cryoablation	14 (14/23; 61%)
Number of ablation probes	2 ± 1 (1-4)
Pre-ablation embolization	3 (3/23; 13%)
Additional thermo-protective measures	20 (20/23; 87%)
Adjuvant bone consolidation	
None	15 (15/23; 65%)
Screw	2 (2/23; 9%)
Cement	6 (6/23; 26%)

Qualitative variables are expressed as raw numbers; numbers in parentheses are proportions followed by percentages. Continuous variables are expressed as means ± standard deviations; numbers in brackets are ranges.

Patient sex & age (Primary tumor)	Procedure	Complication	Management	Final outcome
M, 68 years (Lung cancer)	Palliative cryoablation & osteoplasty	Heal hypoesthesia*	Steroids and physical therapy	Complete recovery in < 6 months
F, 65 years (Thyroid cancer)	Palliative cryoablation	Partial S1 motor deficit*	Steroids and physical therapy	Complete recovery after 18 months
F, 65 years (Colorectal cancer)	Curative cryoablation	Gluteal anesthesia and bladder disfunction*	Steroids and physical therapy	Complete recovery in < 6 months
F, 58 years (Lung cancer)	Palliative radiofrequency ablation & osteoplasty/osteosynthesis)	Post-operative pain	NSAIDs & opioids	Complete recovery in < 2 days
F, 56 years (Lung cancer)	Palliative radiofrequency ablation	Brachial plexus syndrome	Steroids	Complete recovery in < 7 days

NSAIDs: Non-steroidal anti-inflammatory drugs * Direct thermal injury