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RESEARCH ARTICLE

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Image-guided percutaneous cryoablation of unresectable sacrococcygeal chordoma: Feasibility and outcome in a selected group of patients with long term follow-up

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Abstract

Background: Chordoma is a rare malignant tumor of the axial skeleton. Percutaneous cryoablation (PCA) is a minimally invasive technique that allows freezing of tumors under imaging control. The purpose of our retrospective study was to investigate the outcome of PCA in a selected cohort of patients with sacrococcygeal chordoma, with a minimum of 5 years follow-up.

Materials and Methods: Four patients were treated in 10 sessions. The mean follow-up was 57.3 months. We evaluated the feasibility, the procedure-related complications, the impact on pain control and oncological outcomes.

Results: Freezing of 100% of the tumor volume was possible in 60%. Pain control was not reliably evaluable. Local recurrence occurred in 90% of the treated lesions; the mean time to progression was 8.1 months (range 1.5–16). At last follow-up, one patient had died of the disease, one of another cause and one was receiving the best supportive care. The only patient alive without the disease had received additional carbon-ion radiotherapy. The 5-year survival rate after index PCA was 50%.

Conclusion: Complete freezing of the tumor was technically challenging, mainly due to the complex local anatomy. Recurrence occurred in 90% of the lesions treated. PCA should be considered with caution in the curative management of sacrococcygeal chordoma.

KEYWORDS

percutaneous cryoablation, sacrococcygeal chordoma

1 | INTRODUCTION

Chordoma is an uncommon malignant, but slowly growing tumor of the axial skeleton of notochordal origin. The most common location is the sacrococcygeal region (40%–50%), followed by the skull base (35%–40%) and the vertebral body (15%–20%). The incidence of the disease is 0.84/1,000,000/year, with a median age of about 60 years old. Elderly people have a six times higher risk than young adults. The risk of distant spread is minimal (5%), but can reach up to 65% in the late stage of the disease.[1-3]

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Whenever feasible, wide "en-bloc" excision is still the mainstay of sacral chordoma management, with expected 5%–17% local recurrence rate in clear surgical margins.[4,5] Local recurrence may be managed with additional surgical interventions.[6] Wide resection is often associated with significant morbidity, including bladder, bowel, and sexual impairment. Lower extremity motor or sensitive deficits are expected with higher sacral levels.[7] Finally, chronic pain often develops, causing anxiety, and depression.[8-10]

Recently introduced therapies, especially proton- and carbon-ion beam radiation therapy, have increased the rate of conservative treatment.[11,12] Medical treatments, including targeted therapies and immunotherapy, are still under evaluation and the Chordoma Global Consensus Group stressed in 2017 the urgent need for efficient medical therapies for unresectable chordomas.[13,14]

Image-guided percutaneous cryoablation (PCA) is a minimally invasive technique to treat tumors: extreme cold (−40°C) is applied with the use of cryoprobes placed into the lesion. Cold leads to the rupture of the cell's membrane through osmotic changes, ice crystal formation, and protein denaturation. Ice formation leads to cell death in a perimeter of up to 2 cm around the tip of the probe.[15,16]

PCA has become an established treatment option in the management of a number of tumors, like renal or hepatocellular carcinomas, and for tumors of limited size, it can be considered as an alternative to surgery.[17,18] PCA is also frequently used for pain control, especially in the setting of advanced cancer.[19,20]

This retrospective analysis evaluated the outcome in all patients treated by PCA in our sarcoma center for unresectable sacral primary- or loco-regionally recurrent chordoma, with a minimal 5 years follow-up.

2 | MATERIALS AND METHODS

This study was approved by our local ethics committee (CER-VD, protocol number 114/15, 08.02.2016).

We retrospectively reviewed our institutional database and identified four patients treated with PCA for sacral chordoma between 2010 and 2014, to warrant a minimum of 5 years' follow-up. The medical records of all patients were reviewed, including the prior treatments, technical data of PCA procedures, and follow-up.

The characteristics of the patients and technical data are summarized in Table 1.

The mean follow-up was 57.3 months (range 18–96). Three patients have been followed up until their death or to the time of best supportive care (54, 57, 96 months) and one patient is still alive at 87 months.

One patient was female, three male. The mean age was 56.8 years old (range 34–77) at diagnosis and 58.5 years old (range 36–78) at index PCA. Two patients had a primary tumor and two a locally recurrent sacrococcygeal chordoma. The two recurring patients, aged 34 and 40 at initial diagnosis, had undergone multiple prior treatments, including wide "en bloc" resection of the primary tumor in our institution, both with clear margins. The two older patients, aged 76 and 77 at initial diagnosis, had refused potentially mutilating surgery of their primary tumor.

Workup included a thoraco-abdominal computed tomography (CT) scan and magnetic resonance imaging (MRI) of the tumor. All the treatment steps were discussed in a sarcoma board.

Three patients had a single lesion, i.e. primary tumor or local recurrence in the sacral bone stump. The fourth patient had a bi-focal tumor, that is, a local recurrence in the sacral bone stump and regional bone metastasis (in the acetabulum).

Two patients had a single session of PCA, that is, a primary tumor and a local recurrence in the sacral bone stump. One patient had two sessions, that is, one for the primary tumor and a second after 7 months for local progression. The last patient was treated four times for a local recurrence in the sacral bone stump and two additional regional metastases in the anterior acetabular wall and the internal obturator muscle.

A total of six lesions were treated in eight sessions: three lesions were treated one time (a primary tumor, a local recurrence in the sacral bone stump, and regional bone metastasis), two lesions had a second PCA after progression (a primary tumor and a regional metastasis in the obturator muscle), and one local recurrence in the sacral bone stump was treated three times.

The mean tumor volume was 44.4 cm^3 (median 10.5, range 0.5–146.6). We measured it using the mathematical formula of ellipsoid volume $V = \frac{4}{3}\pi abc$, where a, b, and c are the greatest dimensions on pretreatment MRI. Five lesions were smaller than 2 cm, and four reached at least 5 cm in the greatest dimension.

All the procedures were performed in general anesthesia, under CT scan guidance, by a single experienced interventional radiologist of our sarcoma center (50–60 PCA yearly). A maximum of 11 cryoprobes were used (mean 4.2 (range 1–11). Two freezing cycles of a mean of 9.3 min (range 6–12) were applied to the tumors. The iceball formation was monitored under a CT scan. In five cases (50%), we insufflated CO2 to insulate adjacent anatomic structures at risk (sacral nerve roots, rectum, bladder, skin, femoral vessels). In one case, neuromonitoring was performed on an S2 root.

We analyzed the completeness of the treatment (ie, complete or partial freezing of the tumor), as estimated by the interventional radiologist, and by reviewing the procedural imaging by the first author. We looked for early and late complications, hospital stay, pain relief, oncological outcomes (time to recurrence and survival), and subsequent treatments. Chordoma progression was evaluated by MRI approximately every 3 months.

Due to the small number of patients and procedures, no specific statistical analysis of our data was performed.

3 | RESULTS

The results and outcomes are summarized in Table 2.

In all the cases, PCA was technically feasible, whatever the location of the tumor. Freezing was deemed complete in 60% of the procedures.

TABLE 1 Epidemiology and technical data

Patients	Sex	Age at index PCA	Location of primary tumor	Prior treatments	Number of lesions	Location	Volume in cm^3	Number of needles	CO_2 insulation	Freezing time in minutes	Number of cycles
1	Male	76	S1-S3	None	1	S1-S3	146.6	6	No	8 + 6	2
2	Male	36	S4-coccyx	Surgery Radiation therapy Chemotherapy	1	S2 bone stump and soft tissues	113.1	7	Yes	12 + 12	2
3	Male	44	S5-coccyx	Surgery	3	Acetabulum	0.5	1	Yes	Unknown	2
				Pre- and post-op radiation therapy		S3 bone stump	0.8	1	Yes	8 + 8	2
				Radiogrequency ablation		S3 bone stump *progression*	0.5	2	No	Unknown	2
						Internal obturatorius muscle	1.1	1	No	Unknown	2
						S3 bone stump *progression*	16.8	4	No	8 + 10	2
						Internal obturatorius muscle *progression*	4.2	1	No	8 + 10	2
4	Female	78	S3-S5	None	1	S3-S5	72	8	Yes	Unknown	2
						S3-S5 *progression*	88	11	Yes	12 + 10	2
Median (range)		58.5 (26–78)			1.5 (1–3)		44.4 (0.5–146.6)	4.2 (1–11)	50%	9.3 (6–12)	2

TABLE 2 Results and outcomes

Patients	Location	Complete versus incomplete freezing	Pain relief	Time to progression in months	Additional treatments	Status at last follow up	Follow up from index PCA in months	Overal survival (from first treatment)
1	S1-S3	Incomplete	Yes	16	Proton therapy	No evidence of disease	78	78
2	S2 bone stump and soft tissues	Complete	Yes	13	Radiation therapy Chemotherapy	Dead of the disease	18	48
3	Acetabulum	Complete	Yes	No progression	Chemotherapy Immunotherapy	Alive with the disease	96	132
	S3 bone stump	Complete	Partial	9				
	S3 bone stump *progression*	Incomplete	Unknown	7				
	Internal obturatorius muscle	Complete	Unknown	7				
	S3 bone stump *progression*	Complete	Unknown	8				
	Internal obturatorius muscle *progression*	Complete	Unknown	4				
4	S3-S5	Incomplete	No pain before PCA	7	None	Dead of unrelated cause	37	37
	S3-S5 *progression*	Incomplete	No pain before PCA	1.5				
Median (range)		60% complete		8.1 (1.5–16)			57.3 (18–96)	73.8 37-132)

Abbreviation: PCA, percutaneous cryoablation.

Two complications resolved spontaneously: transient subcutaneous emphysema and an increase in local pain of the treated area. One patient presented a major complication, that is, definitive unilateral perianal anesthesia after freezing of metastasis in the internal obturator muscle.

Pain relief could not be reliably evaluated in our study, because in half of the cases, the patient had no significant pain before PCA. Moreover, no systematic visual, numeric, or any other scoring system was used in the follow-up visits. Hence, the pain was mentioned after three PCA, with two cases of significant relief, and one case of significant but short-lived pain increase.

All four patients developed local recurrence (recurrence rate 100%) after a mean of 10.5 months (range 7–16). Altogether, 9 of the 10 lesions recurred (six lesions in four patients, some treated several times [see above]), yielding a progression rate of 90%. The mean time to progression after PCA for the 10 procedures was 8.1 months (range 1.5–16). The only lesion that did not recur was a 0.5 cm^3 (1 × 1 × 1 cm) regional bone metastasis in the acetabulum.

The two primary tumors progressed after 7 and 15 months, respectively: the first patient accepted a second PCA, but progressed again after 1.5 months. She suffered from severe dementia and died a few months later of an unrelated cause. The second patient refused another session, as he was asymptomatic, but also because PCA would have caused severe neurological damage as the tumor filled the entire body and bilateral wings of S1 to S3, with anterior extraosseous protrusion. He refused conventional radiation therapy as well. When he became symptomatic, 3.5 years after the PCA, he received curative proton-ion beam radiation therapy. He was still progression-free at the last follow-up visit, almost 7 years after the PCA and 3.5 years after the radiation therapy.

Two patients had received PCA for local recurrence: they progressed after 13 and 9 months, respectively: the first patient had concomitant distant metastases and progressed despite chemotherapy and radiation therapy treatments. He died of the disease 5 months later, that is, 18 months after the PCA and 4 years after the initial diagnosis. The second patient presented local and multifocal regional recurrences and received another two PCA therapies before distant metastases appeared and chemo- and immunotherapy were started. At the time of data collection, he was in the end-stage of the disease, 8 years after the first PCA, and 11 years after the initial diagnosis.

For the whole series, the 5-year survival rate after the index PCA was 50%. Mean survival was 57.3 months (range 18–96).

4 | DISCUSSION

Surgery remains the cornerstone of the management of chordoma.[21] In a large literature review, Denaro et al. analyzed the results of 1347 surgically treated sacrococcygeal chordomas: they confirmed that clear margins allow for the favorable oncological outcome, with 5%–17% local recurrence rates, as compared to 71%–81% with marginal or intralesional resections. They also found that adjuvant radiation therapy increases local control in close margins, but not in wide contaminated surgical fields.[4] In a recent international survey on the management of newly diagnosed chordomas performed in 31 surgical centers, 79% of the participants favor wide "en bloc" excision if feasible, without adjuvant treatment. If not feasible without significant morbidity, they still favor surgery, but with the adjunction of radiation therapy in case of unclear margins.[22]

In recurrent chordoma, whenever possible, some authors still favor surgical treatment: Yang et al.[6] reported on 34 recurrent sacral chordomas that were re-operated on and found a 53.9% 10-year survival rate and 62.5% disease-free survival rate at last follow-up after 50 months. We share the opinion that whenever possible, surgical treatment of sacrococcygeal chordoma should be favored.

To date, there is no consensus on the role of the photon-, proton- and carbon-ion beam radiation therapy in the treatment of chordoma.[11,12,23] In their recent review on the role of adjuvant radiation therapy in 282 vertebral and sacral chordomas, Yolcu et al.[24] concluded that the adjunction of radiation therapy after gross total resection (R0 resection) added no benefit in terms of local control, at the price of higher complications rate. On contrary, Pennicooke et al.[25] concluded from a review of 40 papers that either form of radiation therapy should be considered as an adjunct to surgery, as it may improve local control. Moreover, Imai et al.[23] reported encouraging outcomes in 188 patients treated with carbon-ion beam radiation therapy alone for unresectable sacral chordoma, with 77% local control after 5 years. Their optimistic conclusions are not shared by Williams et al.[26] from the Canadian Agency for Drugs and Technologies in Health, who concluded from a large literature review in 2018 that there is no evidence for more effectiveness of carbon-ion beam radiation therapy over other treatment modalities for chordomas.[26]

Conventional chemotherapy confirmed to be of minimal efficacy in the management of chordoma.[27] More recently, targeted- or immunotherapies have gained interest and show some potential for the future. Nonetheless, there is to date little evidence for an long-lasting efficient medical treatment for advanced chordoma in the literature.[28-31] The medical treatment of chordoma is beyond the scope of the present paper, but we can conclude with the Chordoma Global Consensus Group who stated in 2017 that efficient drugs are urgently needed for advanced chordoma.[14]

To our knowledge, this is the first case series on long-term results of PCA in the treatment of recurrent or unresectable chordoma: Inaba et al. reported on a single patient managed with PCA for a bulky recurrent sacral chordoma, which remained stable after 4 years.[32] Kurup et al. published a series of six sacrococcygeal tumors, including five chordomas (three primary and two recurrent tumors), with promising results regarding pain and local control, but with an extremely short follow-up (15 months).[33] As chordomas tend to grow slowly, no definitive conclusions on tumor recurrence can be drawn from these data.

Finally, Susa et al.[34] published in 2016 a series of 11 PCA for bone and soft tissue tumors in nine patients, including one chordoma, without providing any details. Again, the mean follow-up was short (24.1 months), and no conclusion can be drawn.

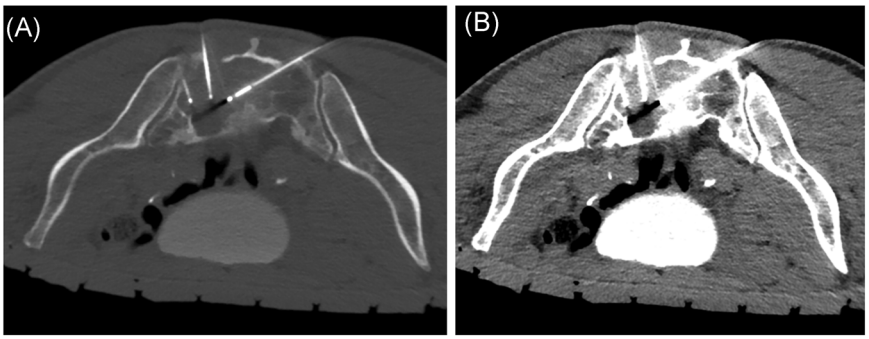

FIGURE 1 PCA of a sacral chordoma under CT scan guidance: (A) Monitoring of cryoprobe positioning. (B) Control of iceball progression during the procedure. Note the limited accuracy of CT-scan due to metal artefacts. CT, computed tomography; PCA, percutaneous cryoablation

Our series demonstrates that PCA in advanced sacrococcygeal chordoma is technically feasible since all the procedures were performed as planned. Freezing was deemed complete, i.e. the whole tumoral volume was included in the iceball, in 60% of the PCA. The ability to evaluate the completeness of the treatment is limited by the poor accuracy of CT scan to monitor the extension of the tumor and iceball. Moreover, the use of up to 11 needles in our series induced metal artifacts, increasing the difficulty to evaluate the iceball outer dimension (Figure 1). Cazzato et al.[35] published in 2018 a review on PCA under MRI guidance and concluded that it may indeed show several advantages as compared to CT or US. Finally, the complex local anatomy makes it difficult to treat the tumor in its entirety, because of the risk of severe damage to the surrounding structures (bowel, bladder, nerve roots, dural sac, and vessels). Warm liquid instillation, CO2 insufflation, and neuromonitoring are used to prevent local damages (Figure 2). Nonetheless, the use of CO_2 is inefficient to mobilize fixed structures like the dural sac and the nerve roots inside the sacrum or at their emergence in the sacral foramina. In our series, PCA was incomplete whenever the tumor was abutting the stump of the dural sac and the nerve roots near the sacral foramina.

Two minor and one major complication were reported in our series (30%). In their review on the use of PCA in cancer related pain (22 articles), Ferrer-Mileo et al. found highly variable rates of side effects and complications, ranging from very low to 89%. Comparatively, the complications rate of surgical treatment is known to be high, as illustrated by Baratti et al.[36] with 53% of wound healing problems in a series of 28 patients.[36] The collection of complications and pain control is difficult, especially in retrospective studies, because it essentially depends on the nurse's and residents' notes. In our series, for example, it was not possible to reliably evaluate pain, which is one of the major shortcomings of our study. The systematic use of visual or numeric scales should be a standard practice in the follow-up of patients, immediately after the procedure, and in long term follow-up as well.

Ninety percent of the treated lesions recurred in our series. There is no other study to compare our results with, but we know from large surgical series that local recurrence is higher with close or contaminated margins, as confirmed by Kayani et al. in their review

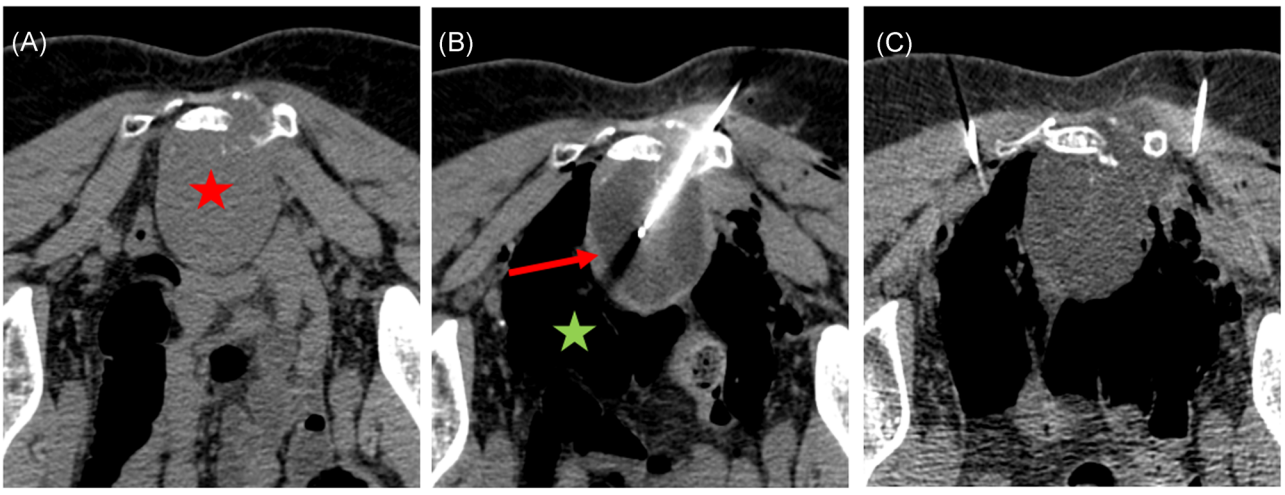

FIGURE 2 CT scan before (A), during (B) and at the end (C) of PCA: (A) Anterior bulging of a chordoma (red star) into the pelvis. (B) Insulation of the tumor by CO_2 insufflation (green star) during the PCA. Note that the iceball outer limit is well apparent (red arrow). (C) Complete freezing of the extra-osseous component of the tumor. PCA, percutaneous cryoablation [Color figure can be viewed at wileyonlinelibrary.com]

of 100 articles on the surgical treatment of chordoma.[5] Local pelvic and sacral anatomy is complex, making it virtually impossible to obtain an equivalent of wide surgical margins in PCA without sacrificing some adjacent structures. In sacral chordoma, we conclude from our experience that regarding local control, in most of the cases, PCA is only an equivalent of surgery with close or contaminated margins. We therefore only recommend its use in the palliative treatment of painful tumors or to slow down loco-regional progression in selected cases.

5 | CONCLUSION

Percutaneous cryoablation can be used in addition to other treatment modalities in the palliative management of recurrent or locally advanced sacral chordoma. It can slow down the local progression of the disease but should be considered with caution in the curative treatment options. Larger prospective studies are needed to evaluate the potential of PCA in the treatment of chordoma. Whenever feasible, wide surgical resection remains the best curative option. If surgery is deemed too mutilating, proton- and carbon-ion beam radiation therapy today seems to be the best option for local control of sacrococcygeal chordoma.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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