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TECHNICAL NOTE

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Stereotactic cryoablation of large tumors of the sellar region with intraoperative CT scans—technical note

Arun Angelo Patil

Abstract

Background: Cryoablation has been used by neurosurgeons in the past and is currently being used by other disciplines to treat kidney cancer, skin lesions, and cardiac conduction defects. Because the currently available cryogenic probes can safely create large lesions and the lesion generation (in the form of ice-ball) can be monitored on intraoperative CT images, cryoablation was used to treat large tumors in and around the sella. In this paper, the author describes a technique to perform this procedure.

Main body: Three large tumors in 3 patients were treated with this method. Age of the patients was 26–58 years with a male/female ratio of 2/1. Patient 1 had a non-secreting pituitary adenoma (measuring 8 × 8 cm) and presented with long-standing total visual loss in both eyes, severe headache, and seizures. She had previous resection and radiation therapy. Patient 2 had prolactinomas (measuring 5.1 × 4.6 cm) and presented with progressive loss of vision and diplopia. Patient 3 had recurrent craniopharyngioma (measuring 7.2 × 5 cm) with prior treatment with resection radiation and frequent drainage of the cyst. He presented with headache and progressive worsening of his vision.

The procedure was done on the CT table with intraoperative scans, using Patil stereotactic frame and argon cryoablation probe (Healthtronics). 3-D images were used to plan targets and trajectories. The probe was placed at the target via a trans-nasal trans-sphenoidal route. One to 3 lesions measuring 2.5–3 cm in diameter were made to ablate the tumor. Ice-ball formation was monitored live on CT images.

There is no complication. One patient had near-complete resolution of the tumor, two had partial resolution of their tumors, and all had resolution of their presenting symptoms at follow-up of 3–24 months (median 6 months). In one patient, symptoms reoccurred due to the formation of new tumor masses.

Short conclusion: Cryoablation of intracranial tumors and can be done safely and effectively. Live monitoring of lesion generation using CT imaging is a major advantage of this technique.

Keywords: Stereotactic, Intraoperative CT scan, Cryoablation, Large tumors

Correspondence: aapatil@cox.net
E-poster presentation at the American Association of neurological surgeon, in San Diego CA, USA, in April 2019.
Department of Surgery, Creighton University School of Medicine, 7710 Mercy Road, Suite 501, Omaha, NE 68124, USA

Background

Management of massive suprasellar tumor tumors is challenging, because these tumors are surrounded by several critical structures. The challenge becomes even more difficult when the tumors are recurrent and have received radiation. The current treatment options for these tumors include medical treatment with dopamine agonist, trans-sphenoidal and/or transcranial resection, frequent drainage of the cyst, intra-cavitary chemotherapy, and radiation therapy.

Aim

The aim of the paper is to describe a technique to perform cryoablation of abovementioned pathology.

Existing literature

Cryoablation is well known to neurosurgeons [1, 2]. It was popularized by Cooper in the treatment of movement disorder using a nitrogen freezing system. Though its use by neurosurgeons tapered off, other disciplines continue to use it. Presently, it is used to treat kidney tumors, cardiac conduction dysfunctions, skin lesions, and lesions of the eye.

The issue under discussion

The currently available cryogenic probes using argon are much smaller in outer diameter (1.7 mm) compared to those using nitrogen (3.5 mm) and can safely create well-circumscribed large lesions (in the form of ice-ball) (Fig. 1), which can be monitored on intraoperative CT images. It is, therefore, a method worth considering in the treatment of intracranial tumors. In this paper, the author presents a technique to cryoablate large tumors in and around the sella.

Main text

Materials and method

Three patients were treated with this method over the last 3 years. Thye age of the patients was 26–58 years with a male/female ratio of 2/1. Patient 1 had a non-secreting pituitary adenoma (measuring 8 × 8 cm) (Fig. 2a, b) with long-standing total visual loss in both eyes and seizures. She had previous resection and radiation therapy. She presented with severe headache. Patient 2 had prolactinomas (measuring 5.1 × 4.6 cm) with a prolactin level of 366 ng/mL (Fig. 3a, b) and progressive loss of vision and diplopia. The patient was treated with bromocriptine after surgery. Patient 3 had recurrent craniopharyngioma (measuring 7.2 × 5 cm) (Fig. 4a–d). Prior treatment at another facility included resection, radiation, and frequent drainage of the cyst. He presented to us with headache and progressive worsening of his vision. Opened decompression was discussed with the patient but he opted for cryoablation.

The procedures were performed on the CT table using the Patil stereotactic frame with intraoperative CT imaging. Argon cryoablation system (Healthtronics, Austin TX) was used to create lesions. 3-D images were used to plan targets and trajectories. The probe was placed to the target via a trans-nasal trans-sphenoidal route. A 12 G Steinman was used to drill the bone along the trajectory through the anterior wall of the sphenoid sinus and

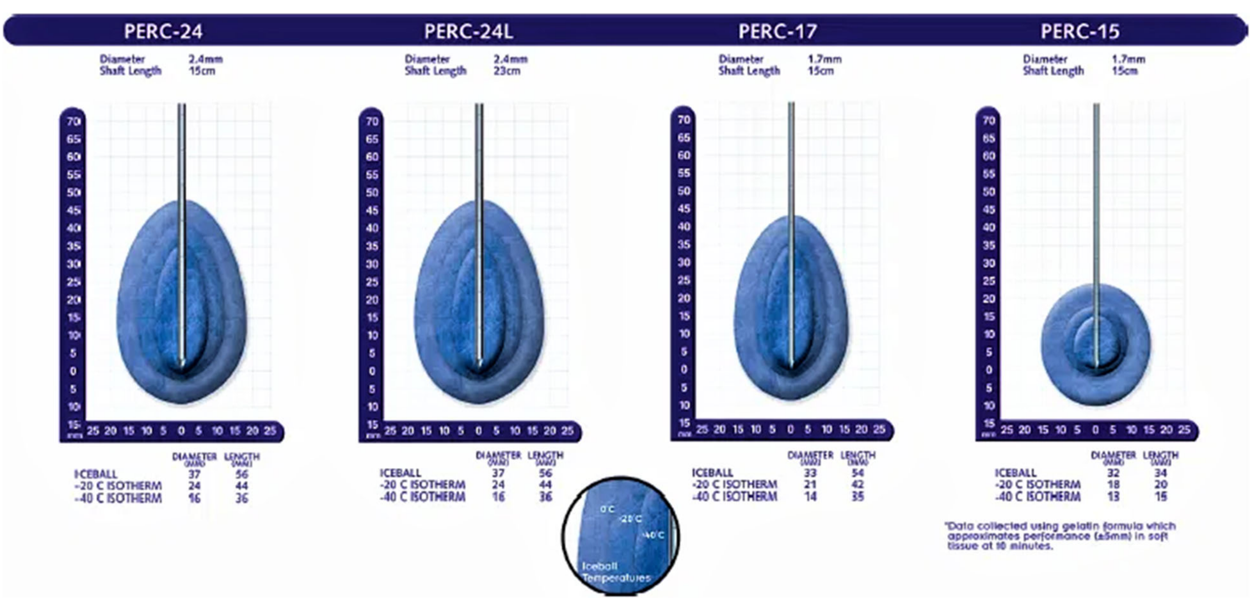

Fig. 1 Shows the configuration of ice-ball formation based on the length and diameter of the shafts (from the manufacturer's brochure, Healthtronics, Austin TX, with permission from the vendor)

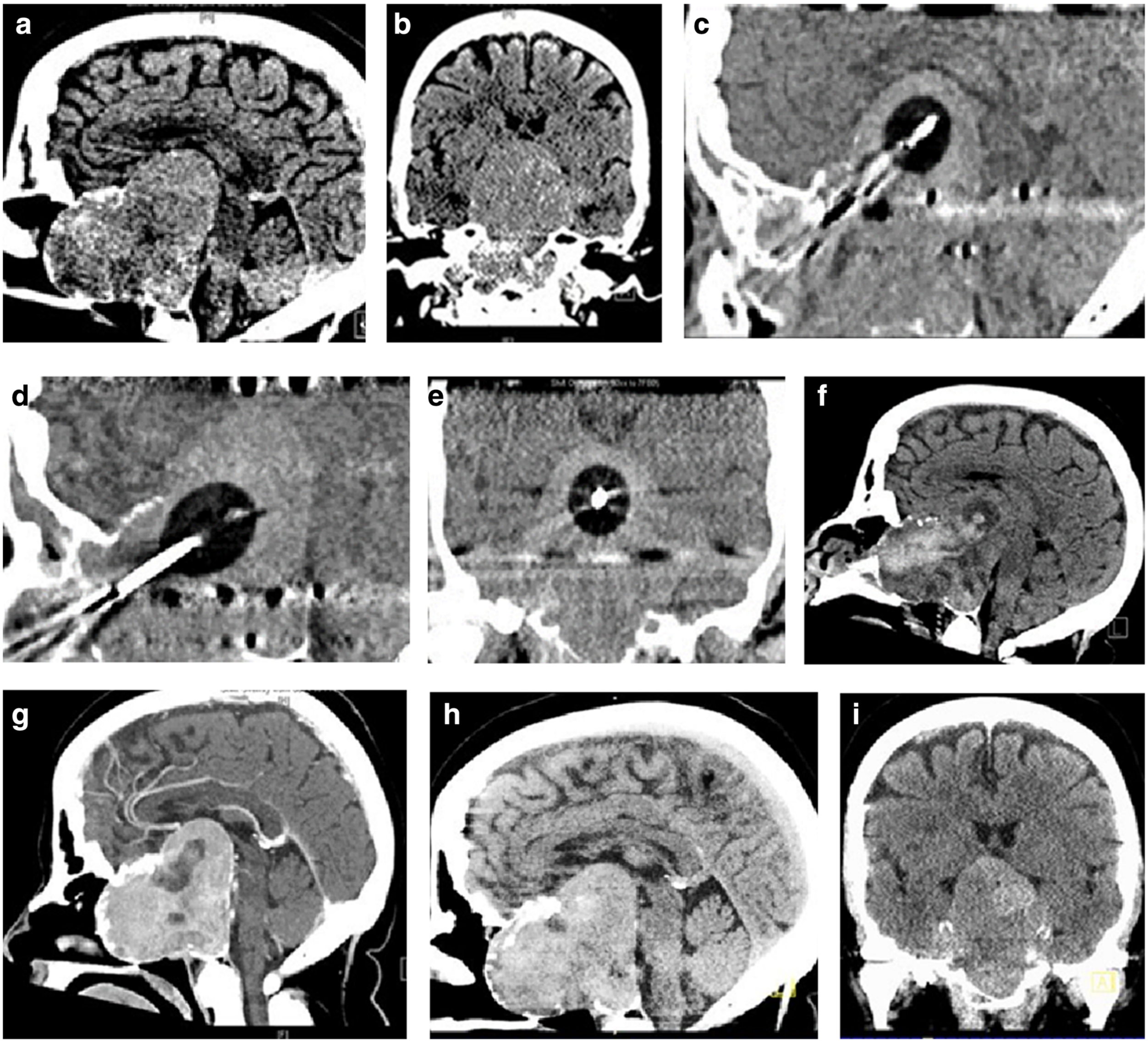

Fig. 2 **a**, **b** MRI shows a massive pituitary tumor (8 × 8 cm) with large suprasellar extension. **c**–**e** Intraoperative CT images show ice-ball formation (seen as black void) around the probe. **f**, **g** CT images show the evolution of the tumor 1 and 2 weeks respectively after treatment. **h**, **i** CT images show a reduction of tumor size from 6.7 to 5.1 cm. 2 years after treatment

the floor of the sella. The cryoprobe was then inserted through this opening into the target. The exposed tip length was chosen based on the chart provided by the manufacturer (Fig. 1). Intraoperative CT images were obtained to confirm accurate probe placement and to monitor ice-ball formation. The temperature was lowered down to − 40 °C. One to 3 ice-balls measuring 1–3 cm in diameter were created. CT scans were obtained every 3 min during the freezing. To reduce the radiation dose to the patient, scans were obtained only in the CT planes in which the tumor was seen. When the desired size of ice-ball was formed, freezing was stopped. Freezing time was between 5 and 9 min for each ice-ball formation. The probe was then thawed with helium prior to its removal. To decrease the risk of complications, the ice ball was never allowed to reach the tumor periphery.

In patient 1, the goal was to reduce the headache by decreasing the size. Three separate cryolesions were made within the tumor. The ice-ball were oblong and measured 4.5 cm in length and 3 cm in the largest diameter. Two freezing cycles were used for each ice ball. Figure 2c–e shows ice-ball formation around the probe.

In patient 2, one oblong ice-ball formation measures 2.5 × 3 cm (Fig. 3c). One freezing cycle was done.

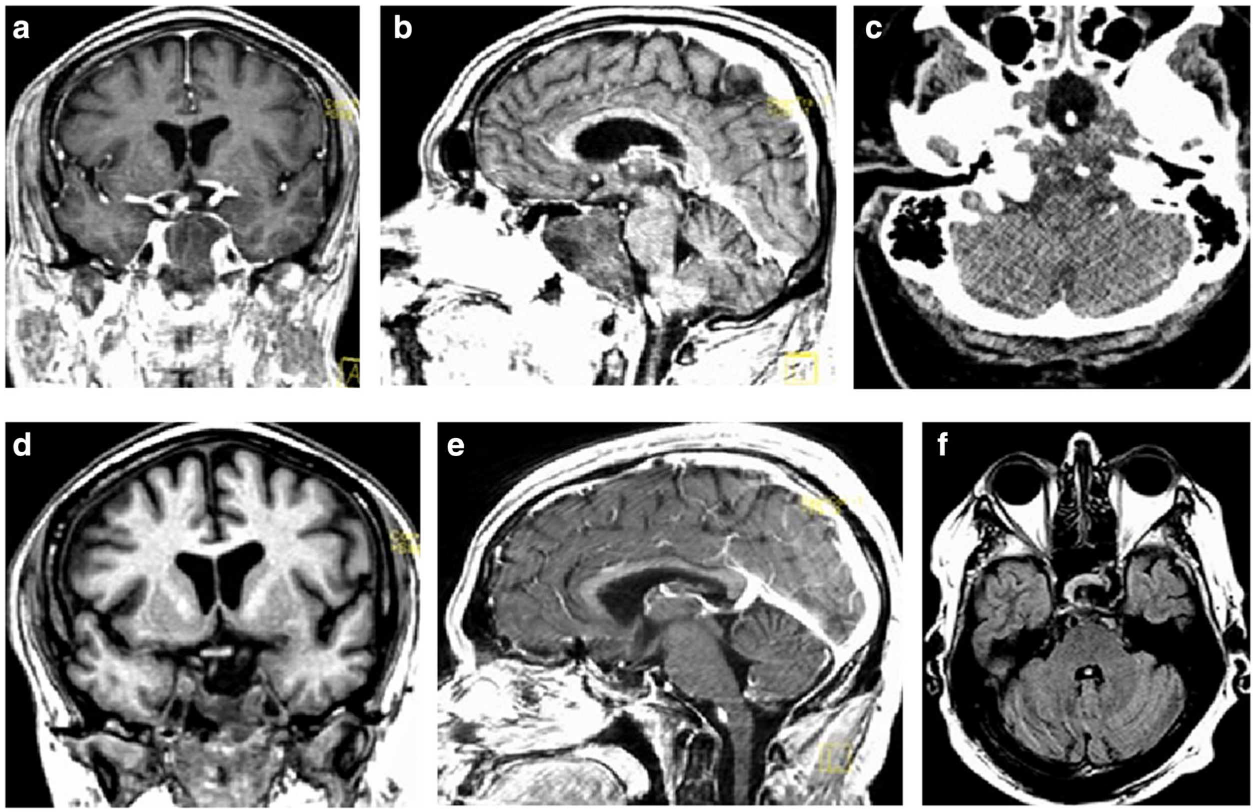

Fig. 3 **a**, **b** MRI shows a large pituitary tumor. **c** CT shows the probe in the tumor with surrounding ice-ball formation (seen as black void). **d**–**f** Shows MRI in coronal, sagittal, and axial view with a significant decrease in size of the tumor

In patient 3, enhancing mass on the posterior wall of the cyst (Fig. 4d) was cyroablated with an ice-ball of 1.5 × 1 cm (Fig. 4e).

Results

In patient 1, Fig. 2f, g shows the evolution of the tumor 1 and 2 weeks respectively after treatment with hemorrhage within the tumor and cavity formation. The patient was on high-dose steroids for 3 weeks after lesion generation as a prophylaxis against swelling. None of the postoperative scans showed peritumoral swelling. At 2 years, her headaches were gone, and tumor size reduced to 6.7 × to 5.1 cm (Fig. 2h, i). There was no improvement in vision. There was no complication from the procedure.

In patient 2, the diplopia and visual loss improved within 24 h after the procedure. At 7 months after the operation, the scans showed large shrinkage of the tumor to 2.1 × 1.3 cm (Fig. 3d–f), and his neurological examination, including eye examination, was normal. There was no complication from the procedure.

In patient 3, at 4 months after cryoablation, he was free of headache and vision was almost back to normal. The cyst had completely collapsed (Fig. 4f), and there was no need to tap the reservoir. There was no complication from the procedure. After he was free of all symptoms for 8 months, his headache and visual symptoms recurred due to formation of several new enhancing masses on the cyst wall. He then transferred care to another facility because his insurance did not cover his care at our facility.

Discussion

James Arnott [3] was the first to try cryosurgery using salted ice at − 18 °C to − 24 °C to freeze tumors to decrease their size in 1850. In 1948, Hass and Taylor [4] produced well-circumscribed necrotic lesions 2 to 3 cm in diameter in the brain using pressurized carbon dioxide. In 1959, Fay [5] used local and generalized refrigeration to treat brain tumor.

In 1960, Cooper and Lee [1, 2] invented an automated cryosurgical device using liquid nitrogen. This system rapidly and continually extracted heat to drop the tissue to temperature − 196 °C. It was used to produce cryogenic lesions in the brain to treat Parkinson’s disease. A heating element was also attached to the probe to warm it after the lesion was generated.

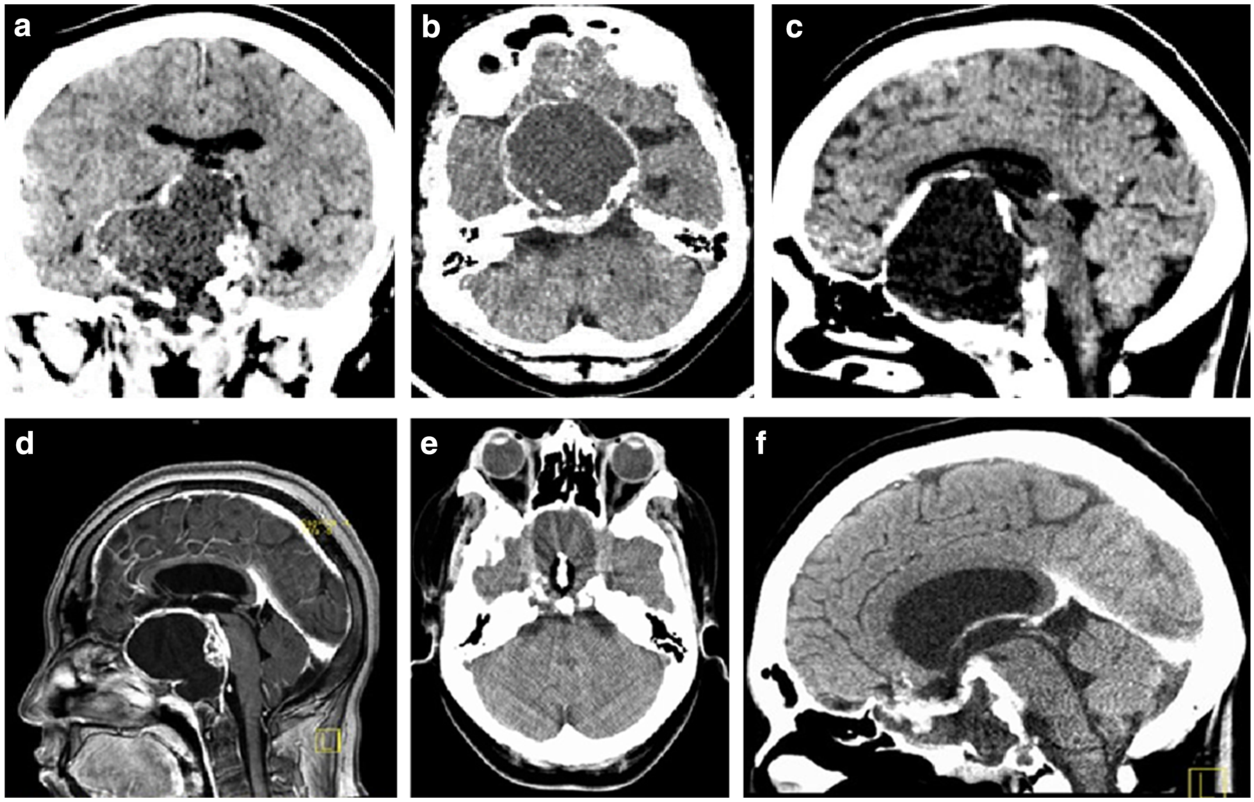

Fig. 4 a–**c** Scans show a large craniopharyngioma with a very large supra-sellar extension. **d** The cyst showed an enhancing lump on the posterior wall and **e** shows probe-tip at the posterior wall of the cyst with a black void around it. **f** CT scans 4 months after treatment shows a collapse of the cyst

In 1975, Torre [6] invented an argon gas freezing system. In this system, argon gas under a pressure of 1000 to 2500 pounds per square inch is used to drops the tissue temperature to − 185 °C, based on the Joule-Thompson effect. Helium is used to thaw the probe after the lesion is generated. Although nitrogen can reduce temperature to − 196 °C argon produces a quicker drop in temperature and requires a much smaller diameter tubing, and rapid thawing can be done using helium gas. The rapid thawing capability is critical if freezing goes beyond the required boundaries. It also helps when rapid successive cycles of freezing are needed.

Hewitt et al. [4] compared liquid nitrogen and argon probe for cryoablation. They found that although the newer nitrogen probe performed better than its older ones, they were slower than the argon gas system. However, although the argon gas is initially faster, its ice-ball formation in a warm environment is smaller than the liquid nitrogen system.

Superficial lesions can be treated by applying the freezing agent to the lesion with a swab or sprayer. For deep-seated lesions stereotactic or image guidance system is required. In the present series, stereotactic frame was used to place the probe at the target. The frame, in addition to being accurate, provides a stable probe holder. This makes the procedure very safe for intracranial pathology. Furthermore, when the procedure is done on the CT, stable accuracy of probe placement can be confirmed and progression of lesion generation can be monitored.

An effective tissue destruction depends on accurate monitoring of the process with intraoperative CT scans, quick freezing, slow thawing, and repeating the cycle. The probe should be made as cold as possible to produce the highest possible thermal gradient at the periphery [7, 8]. Extracellular ice formation begins as the temperature decreases below zero. Intracellular ice formation begins below -20^0 C. However, some tumor cells may survive at -40^0C. Therefore, temperature between − 40 and − 50 °C is needed for cell death for single freeze cycle. Ice formation within the cell is lethal to the cells. Ice formation in extracellular fluid causes cellular dehydration. In addition, ice formation bursts the cells by expansion. Cells also die when their blood supply is choked off by ice forming within small tumor blood vessels. Since clotting takes approximately 10 min, the extremely low temperature should be maintained for about 10 min. Furthermore, since there are a series of events that leads to cell death, the thaw-freeze cycle should be repeated for 2–3 cycles. In addition, repeating the treatment cycle kills the partly injured tissue.

In a canine model by Maroon et al.'s [9] cryoablation lesions' study, under the microscope, the lesions showed hemorrhagic infarcts with minimal surrounding edema and had a sharp transitional zone. The lesions were reproducible and discrete, with minimal reaction to the surrounding tissue.

Moser et al. [10] did cryoablation studies on animals. They found that on CT imaging, the ice-ball that was formed looked like a well-demarcated radiolucent sphere that disappeared upon thawing. The post-thaw contrast-enhanced CT scan revealed a zone of blood-brain barrier breakdown extending no more than 1 mm beyond the maximum diameter that the ice-ball formation. Histological examination showed a sharp transition from a clearly necrotic brain within the ice-ball to the normal cytoarchitecture of the surrounding brain.

In open surgical procedures, Maroon et al. [11] used the cryoprobe to remove the brain, spinal cord, and orbit tumor in 71 patients without complications. They found it useful to reduce blood loss in vascular tumors. They also found it effective in ablating residual tumors when removal was incomplete in 7 cases. Intraoperative real-time ultrasonic imaging permitted precise delimitation of tumors from surrounding tissues and allowed monitoring during the production of cryosurgical lesions.

A clinical study of 74 patients aged 18–64 years with supratentorial gliomas had stereotactic cryoablation [12]. They found the method effective. The frequencies of complications in this series did not exceed those of the routine surgical interventions.

In another clinical study [13], stereotactic transsphenoidal cryohypophysectomy was performed in 70 patients with pituitary adenomas. All patients (except 2) tolerated the operation well. Vision deteriorated after operation occurred in 1 patient. Thrombosis of the left middle cerebral artery developed in another patient. All other patients noted improvement after the operations with a rapid decline of their symptoms and improvement in hormone levels. Six patients needed a second operation 1.5–6 years after the first operation. There is also a report of stereotactic cryoablation of the pituitary gland for the treatment of pain with excellent results [14].

Cryoablation is a simple and safe method to destroy tumors. Because the formation of ice-ball can be followed on serial CT images, damage to normal brain tissue can be prevented. The equipment is simple and easy to use. It is available in major hospitals in the interventional radiology department, or it can be rented out for the procedure. The CT scanner does not need any special software to see the ice-ball. Because of continuous blood flow in the vasculature surrounding the tumor, the risk of causing vascular damage is low with this method.

Although the ice-ball visible on the CT image is used as the lesion size, the actual lesion may be slightly smaller. Therefore, if the tumor is in a non-eloquent area, ice-ball, slightly bigger than the lesion, may be needed. In treating the 3 tumors in this paper, the author did not let the ice-ball reach the periphery, because critical structures surrounded the tumors. Furthermore, in patient 1, the tumor mass was extremely large. Therefore, lesioning the entire tumor could potentially cause a dangerous swelling in and around the tumor. Although 3 large ice-balls were created for this patient, the tumor size decrease was significant, but not dramatic. This is possible due to radiation fibrosis from previous radiation therapy.

Early postoperative scans on patient 1 demonstrate the evolution of the ablated tumor. The first stage is ice-ball formation. This disappears within 10–15 min. The next change is hemorrhagic transformation. Then is the stage of cavitation. Several months later, generalized shrinking of the tumor took place.

There are different methods to produce intracranial lesions. Focused radiation and ultrasound can be performed without making an opening in the skull. However, they do result in a spread to some energy to the surrounding brain. Radiofrequency probe needs an opening in the skull. It delivers a well-circumscribed energy to the tissue. However, the heating pattern may not be uniform because tissue resistance can vary. Laser ablation needs opening in the skull. It does result in tissue destruction around the primary lesion [15]. Cryoablation produces lesion, that is probably the most discrete of all the methods [16]. Furthermore, the lesion formation can be monitored real-time with intraoperative CT imaging. This makes the procedure very safe. It, however, does require making an opening in the skull. In addition to the application already discussed for this method, it might be useful in the treatment of metastatic tumors.

Conclusion

This is a simple method to treat large tumors in and around the sella with cryoablation. Based on these three cases and prior publications on this method, it is an effective and safe treatment modality. Live monitoring of lesion generation using CT imaging is a major advantage of this method. No complication resulted from the procedure. This method could also be useful for treating metastatic tumors.

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AAP is the author. He did the paper in its entirety. The author has read and approved this paper

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Declarations

Ethics approval and consent to participate
This is a technical note paper with a retrospective look at the results. There is NO case history on any of the patients. "For this type of study, formal consent is not required."
There is no identifying information about the patients in the paper.

Consent for publication
The patients agreed to the publication of the results.

Competing interests
The author certifies that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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