Percutaneous Image-Guided Cryoablation of Head and Neck Tumors for Local Control, Preservation of Functional Status, and Pain Relief.

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Percutaneous Image-Guided Cryoablation of Head and Neck Tumors for Local Control, Preservation of Functional Status, and Pain Relief

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OBJECTIVE. We report nine consecutive percutaneous image-guided cryoablation procedures of head and neck tumors in seven patients (four men and three women; mean age, 68 years; age range, 50–78 years). Ablation of the entire tumor for local control or ablation of a region of tumor for pain relief or preservation of function was achieved in eight of nine procedures. One patient experienced intraprocedural bradycardia, and another developed a neopharyngeal abscess. There were no deaths, permanent neurologic or functional deficits, vascular complications, or adverse cosmetic sequelae due to the procedures.

CONCLUSION. Percutaneous image-guided cryoablation offers a potentially less morbid minimally invasive treatment option than salvage head and neck surgery. The complications that we encountered may be avoidable with increased experience. Further work is needed to continue improving the safety and efficacy of cryoablation of head and neck tumors and to continue expanding the use of cryoablation in patients with head and neck tumors that cannot be treated surgically.

Salvage head and neck surgery has been reported to result in complications in 13–40% of cases and in major complications in 16% of cases (2.7% mortality) in a relatively typical sample [1]. Because of these complication rates, there has been recent active research into new alternative, less invasive potential treatment options for patients with recurrent and metastatic head and neck cancer including superselective intraarterial chemotherapy infusion [2–4]; reirradiation with protons [5, 6], carbon ions [6], and charged particle beams [7]; and stereotactic body radiotherapy [8]. Superselective intraarterial chemotherapy has not been shown to be superior to standard IV chemotherapy [4]. Long-term follow-up is needed for the radiation studies to evaluate for associated late toxicities, which lead to speech and swallowing impairment in 43% of patients receiving traditional radiation therapy [9].

Percutaneous image-guided thermal ablation also offers a potentially less morbid minimally invasive treatment option. Although CT- and MRI-guided percutaneous aspiration of head and neck tumors is well documented [10, 11], the studies in the literature of head and neck ablation are sparse and are limited primarily to case reports and to CT- and ultrasound-guided radiofrequency ablations (e.g., [12–15]). A few studies have reported successful CT-guided cryoablation and MRI-guided laser-induced thermotherapy procedures [16, 17]. None of these techniques depict the precise margins of ablation. We have adopted a technique of percutaneous cryoablation using CT, PET, or MRI guidance to treat head and neck tumors. This technique allows precise positioning of the cryoprobe and near–real-time monitoring of the margins of the cryoablation ice ball to ensure adequate coverage of the target while avoiding injury to adjacent structures.

Materials and Methods

We retrospectively reviewed nine consecutive percutaneous image-guided cryoablation procedures of head and neck tumors performed at Brigham and Women's Hospital by a single interventional neuroradiologist between May 2013 and July 2015. These procedures were performed on seven patients (four men and three women) with a mean age of 68 years (age range, 50–78 years). Patient demographics and tumor information are presented in Table 1. All patients were evaluated by a surgeon, and each patient either was a poor surgical candidate or had declined surgery. Standard procedural informed consent was obtained from each patient before each procedure and in-

Keywords: cryoablation, cryosurgery, head and neck neoplasms, interventional oncology

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TABLE 1: Patient Demographic Characteristics and Tumor Characteristics for Nine Consecutive Percutaneous Image-Guided Cryoablation Procedures of Head and Neck Tumors

Patient			Head and Neck Tumor			
No.	Age (y)	Sex	Location	Size (mm)	Pathology	Goal of Procedure
1	76	M	Right neck, level III lymph node	19	Metastasis, squamous cell carcinoma	Complete ablation
1	78	M	Right neck, level II and III lymph nodes	20, 17	Metastasis, squamous cell carcinoma	Complete ablation
2	73	F	Right neck, retropharyngeal lymph node	18	Metastasis, squamous cell carcinoma	Partial ablation for local control
3	75	M	Neopharynx	37	Recurrent tumor, squamous cell carcinoma	Partial ablation to prevent airway occlusion
4	59	M	Left neck, extensive and ill-defined tumor with focal area encasing and narrowing the carotid and vertebral arteries	26	Metastasis, squamous cell carcinoma	Partial ablation to minimize mass effect
5	50	M	Left parapharyngeal lymph node	19	Metastasis, adenoid cystic carcinoma	Complete ablation
2	74	F	Right neck, retropharyngeal lymph node	14	Metastasis, squamous cell carcinoma	Partial ablation for local control
6	65	F	Right foramen ovale	27	Metastasis, adenoid cystic carcinoma	Partial ablation for pain relief
7	61	F	Right trigeminal nerve, right foramen ovale, right pterygoid muscles	37	Metastasis, squamous cell carcinoma	Partial ablation for pain relief

cluded a thorough explanation of the procedure, the potential risks and benefits of the procedure, and alternatives to the procedure. This retrospective review was approved by our institutional review board and was performed in compliance with HIPAA. Informed patient consent for participation in the retrospective review was waived.

The imaging guidance modality, imaging techniques, and reasons for choosing the guidance modality were recorded for each procedure. Similarly, cryoablation technical parameters were reviewed and recorded for each procedure.

The initial technical objective of each procedure was either cryoablation of an entire tumor for local control or cryoablation of a predetermined partial tumor region for pain relief or preservation of function. Because this study is not a prospective study, no formal measures were obtained to determine the level of pain relief or level of functional status. Pain relief was reported subjectively by patients in follow-up clinical encounters. Functional status deficits were reported subjectively by patients and were evaluated with physical neurologic examination in follow-up clinical encounters. For the purposes of this study, a procedure was considered technically successful if the ablation zone included the tumor volume targeted on intraprocedural imaging.

All follow-up imaging examinations and clinic notes were reviewed to establish outcomes to the time of writing this article.

Results

All cryoablation procedures were performed in a dedicated image-guided operating room or interventional suite using a 3-T MRI system (Magnetom Verio, Siemens Healthcare), a PET/CT system (Biograph mCT 64 PET/CT, Siemens Healthcare), or a 64-MDCT system (Somatom Sensation 64 Fluoroscopy CT, Siemens Healthcare). The rationale for the choice of guidance modality is outlined for each procedure in Table 2.

All CT examinations were performed in the axial plane. Sagittal, coronal, or oblique reconstructions were generated at the scanner when necessary to optimize visualization of the cryoprobe or ice ball. All MRI examinations were performed with a turbo spin-echo T2-weighted sequence (TR/TE, 5820/103; slice thickness, 2 mm; slice spacing, 2 mm). The MRI plane of imaging was chosen to op-

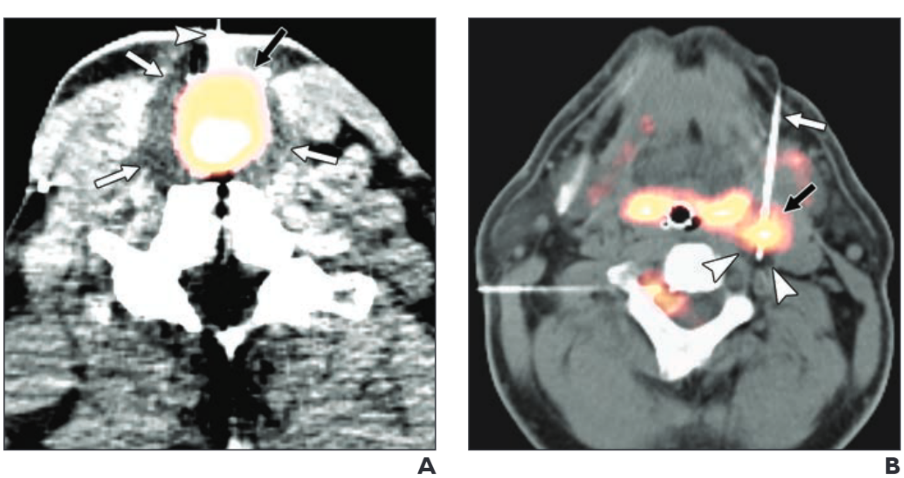

Fig. 1—PET/CT images obtained during cryoablation of head and neck lesions.
A, 75-year-old man (patient 3 in Table 1) with recurrent squamous cell carcinoma of neopharynx. Intraprocedural axial fused PET/CT image shows cryoprobe (*arrowhead*) within FDG-avid lesion (*black arrow*) and ice ball (*white arrows*) encompassing FDG-avid lesion and entire neopharynx.
B, 50-year-old man (patient 5 in Table 1) with adenoid cystic carcinoma metastases. Intraprocedural axial fused PET/CT image shows cryoprobe (*white arrow*) within hypermetabolic lesion (*black arrow*) with faintly visible ice ball (*arrowheads*) encompassing lesion. Second cryoprobe is shown in right vertebral foramen metastasis, which was simultaneously ablated.

TABLE 2: Methods of Nine Consecutive Percutaneous Image-Guided Cryoablation Procedures of Head and Neck Tumors

Patient No.	Guidance Modality	Reasons for Choice of Guidance Modality	Cryoprobe Type[a] (Cryoprobe Position) [No. of Cryoprobes]	Ablation and Thaw Times (min) and Cryoprobe Flow Rates	Major Structures Within 1 mm of Tumor Being Ablated
1	CT	CT was chosen because PET/CT was not yet being used as guidance modality at our institution	IceSphere (middle aspect of mass)	15 Freeze, 10 thaw, 10 freeze at –20%, 0%, 20%, respectively	Carotid artery, jugular vein, vagus nerve
			IceSphere (inferior aspect of mass)	15 Freeze, 10 thaw, 10 freeze at –20%, 0%, 20%	
			IceSeed (superior aspect of mass)	15 Freeze, 10 thaw, 10 freeze at –50%, 0%, 100%	
1	PET/CT	PET/CT was best modality to use to confirm small target and to ensure ice ball covered metabolically active region	IceSphere [2]	15 Freeze, 10 thaw, 10 freeze at –100%, 0%, 100%	Carotid artery, jugular vein, vagus nerve
2	MRI	MRI was best modality to use because deep location of tumor and many major structures surrounding tumor required precise placement of cryoprobe	IceSeed [2]	15 Freeze, 10 thaw, 15 freeze at –100%, 0%, 100%	Carotid artery, jugular vein, vagus nerve
3	PET/CT	PET/CT was best modality to use to confirm small target and to ensure ice ball covered metabolically active region	IceSphere [4]	15 Freeze, 10 thaw, 15 freeze at –100%, 0%, 100%	Airway stoma, neopharyngeal mucosa
			IceSphere (left aspect not in ice ball)	15 Freeze, 10 thaw, 15 freeze at –100%, 0%, 100%	
4	PET/CT	PET/CT was best modality to use to confirm small target and to ensure ice ball covered metabolically active region	IceSeed (hypermetabolic region adjacent to vasculature) [2]	11 Freeze, 4 freeze, 10 thaw, 11 freeze, 4 freeze at –100%, 40%, 0%, 100%, 40%	Vertebral artery, carotid artery, jugular vein, vagus nerve
5	PET/CT	PET/CT was best modality to use to confirm small target and to ensure ice ball covered metabolically active region	IceSphere (center of mass)	15 Freeze, 10 thaw, 15 freeze at –100%, 0%, 100%	Carotid artery, facial artery, esophagus
2	PET/CT	PET/CT was best modality to use because deep location of tumor and many major structures surrounding tumor required precise placement of cryoprobe	IceSeed (center of hypermetabolic region)	Procedure discontinued	Carotid artery, jugular vein, vagus nerve
6	MRI	MRI was best modality to use because deep location of tumor and many major structures surrounding tumor required precise placement of cryoprobe	IceRod (center of mass)	15 Freeze, 10 thaw, 15 freeze at –100%, 0%, 100%	Right temporal lobe, cavernous carotid artery
7	MRI	MRI was best modality to use because deep location of tumor and many major structures surrounding tumor required precise placement of cryoprobe	IceSeed (center of mass, submandibular approach)	15 Freeze, 10 thaw, 6 freeze, 4 freeze, 5 freeze at –60%, 0%, 60%, 80%, 100%	Right temporal lobe, cavernous carotid artery

[a]IceSphere, IceSeed, and IceRod are manufactured by Galil Medical.

timize visualization of the tumor, cryoprobe, and ice ball relative to the adjacent vascular and neural structures and mucosa. Intraprocedural monitoring MRI or CT was performed at approximately 3-minute intervals.

Cryoablation was performed with the following equipment: 17-gauge cryoprobes (IceSphere, IceSeed, or IceRod; Galil Medical) with a cryoablation system (SeedNet, Galil Medical). The specific cryoprobe types, position, and power settings used for each cryoablation procedure are outlined in Table 2. An anesthesiologist administered general endotracheal anesthesia to patients for all procedures. Prophylactic antibiotics were not administered. The skin at the entry site was typically kept warm using warm saline–soaked gauze or sponges. The guidance modalities and major structures located within 1 mm are outlined in Table 2 for each procedure.

TABLE 3: Results of Image-Guided Cryoablations of Head and Neck Tumors in Chronologic Order

Patient No.	Complications	Technical Success[a]	Imaging Follow-Up (mo)	Follow-Up Imaging Modality	Clinical Follow-Up	Outcomes	
						Imaging	Clinical
1	Minimal hoarseness and dysphagia; resolved over several weeks	Yes	18	CT	18 mo	Involuted tissue at the ablation site; increasing size of right level II and III lymph nodes	No symptoms
1	None	Yes	4	CT	5 mo	Involution of both lesions	Death[b]
2	None	Yes	3	PET/CT	3 mo	Enlarging residual or recurrent tumor	No symptoms; second ablation planned
3	Postprocedure abscess requiring surgical débridement	Yes	NA	NA	1 wk	Follow-up imaging was not available	No residual viable tumor was in the ablation bed according to a surgical report from an outside hospital
4	None	Yes	3	CT	5 mo	Necrosis in ablation bed with patent vessels; increased bulk of residual tumor peripheral to the ablation zone	Death[c]
5	None	Yes	1	CT[d]	3 mo	New nasopharyngeal lesion, no mention of ablation areas	Completed additional radiation therapy, no symptoms
2	Bradycardia with severe hypotension; resolved with discontinuation of the procedure	No	NA	NA	6 mo	Follow-up imaging was not performed	No neck pain and no neck or neurologic symptoms[e]
6	None	Yes	3	MRI	3 mo	Residual 1.1-cm tumor lobulation along lateral edge of ablation zone	Complete subjective pain relief reported; ablation of residual tumor planned
7	None	Yes	1	CT	2 mo	Regions of necrosis in ablation zone but increased leftward extent of nonablated portion of mass	Reported partial subjective pain relief with slow subsequent return to baseline pain over approximately 2 mo

Note—NA = not applicable.
[a]Technical success determined by whether the ablation zone included the targeted tumor volume on intraprocedural imaging. All outcomes do not correlate with technical success of the procedure.
[b]Cause of death reported as "natural causes."
[c]Patient died in hospice.
[d]Only CT report was available.
[e]Patient is in home hospice.

Complications, technical success, and outcomes are outlined in Table 3. Patient 1 experienced minimal hoarseness and dysphagia, likely due to vagus nerve stunning, after cryoablation of a 19-mm level III lymph node metastasis that was immediately adjacent to the vagus nerve; these complications resolved over several weeks. Patient 2 experienced transient bradycardia—from 80 to 40 beats/min—when the cryoprobe was placed into a right retropharyngeal lymph node metastasis and subsequently experienced immediate bradycardia to 40 beats/min and severe hypotension when cryoablation began. The procedure was discontinued, and the patient's heart rate and blood pressure immediately returned to normal. Patient 3 developed an abscess in the region of ablation that required surgical débridement approximately 1 week after cryoablation of a 37-mm recurrent neopharyngeal tumor. The tumor had been causing increased mass effect on an airway stoma and involved neopharyngeal mucosa. No residual tumor was found in the ablation bed according to a surgical report from an outside hospital.

Technical success was achieved in eight of nine procedures. The only procedure in which technical success was not achieved was in the second ablation of patient 2, which was discontinued because of bradycardia and hypotension.

Patient 5 was lost to follow-up. Good imaging and clinical outcomes were achieved in five of the seven other technically successful procedures. Patient 2 had increasing disease after the first ablation. Patient 7 experienced only partial pain relief after partial cryoablation of a 37-mm lobulated mass focused over the foramen ovale and slow subsequent return to the baseline level of pain, which was likely because of tumor infiltrating superior to the foramen ovale into Meckel cave, beyond the zone of ablation.

Discussion

Percutaneous image-guided cryoablation offers a potentially less morbid minimally invasive treatment option than salvage head and neck surgery, which has complication rates of 13–40% [1]; potentially fewer long-term side

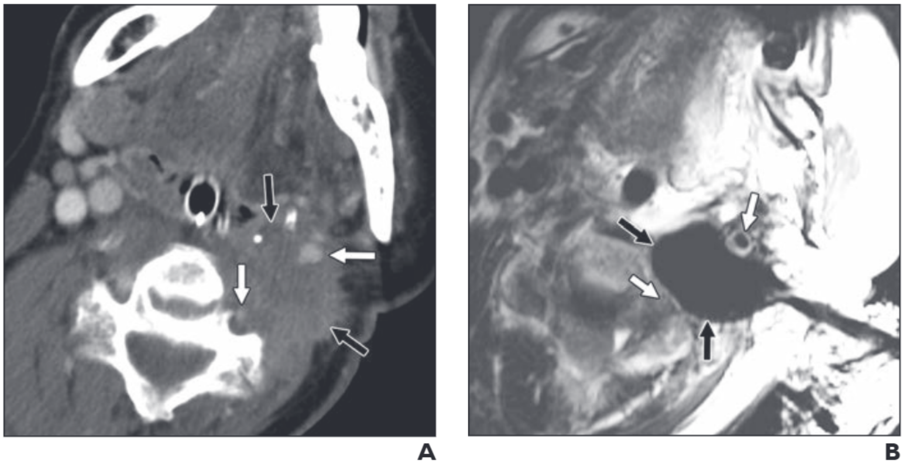

Fig. 2—59-year-old man (patient 4 in Table 1) with squamous cell carcinoma metastasis.
A, Preprocedure axial contrast-enhanced CT image shows ill-defined lesion (*black arrows*) involving carotid and vertebral arteries (*white arrows*). After cryoprobe placement with PET/CT guidance, patient was moved to MRI for cryoablation monitoring.
B, Intraprocedural axial turbo spin-echo T2-weighted MR image shows ice ball (*black arrows*) adjacent to carotid and vertebral arteries (*white arrows*) with deformed ice ball contour due to flow-related heat sink effect, preserved flow voids, and mild surrounding edema; warm saline–soaked gauze overlies skin.

effects than radiation therapy, which results in a 43% rate of impaired speech and swallowing [9]; and potentially fewer severe complications, including carotid blowout, stroke, and death, than heat-based ablative techniques [18, 19]. The advantages of percutaneous image-guided cryoablation are superior visualization of the region of ablation using the ice ball as an ablation zone proxy and the inherent protection of vascular structures and the spinal cord by the warm flow of blood and CSF. For these reasons, at our institution we are currently using cryoablation as the exclusive thermal ablation modality to treat head, neck, and spine tumors, which are typically adjacent or close to critical CNS and vascular structures.

There were two complications in this study cohort. First, a patient with a right retropharyngeal mass encasing the carotid sheath developed bradycardia and hypotension that resulted in the discontinuation of the procedure. Multiple other tumors adjacent to the vagus nerve were ablated without a similar complication, likely because of the protective heat sink effects of carotid and jugular flow. In this symptomatic patient, the jugular vein was thrombosed. Second, a patient with a recurrent tumor of the neopharynx developed an abscess approximately 1 week after ablation that required surgical débridement. The neomucosa involved by the recurrent tumor was likely devascularized during the ablation, and the patient was asymptomatic in the first postoperative week because the neopharynx was not innervated. Postablation infection in the head and neck has previously been reported [20].

In the future, we plan to administer antibiotics covering oral flora to patients with mucosal involvement. Hydrodissection of adjacent but uninvolved mucosa or mucosal protection with a saline-filled balloon may also be helpful in future studies. We postulate that the use of cryoablation, particularly with intraprocedural MRI monitoring, should make severe complications such as carotid blowout and stroke less likely because structures such as the carotid artery and CSF-filled thecal sac have warm flow that provides protection from freezing and because the ice ball margins can be precisely visualized in near real time.

The choice of imaging modality is based largely on three factors: the visibility of the tumor, depth of the tumor, and presence of complex critical adjacent anatomy along the planned cryoprobe trajectory. In our experience, PET/CT is a valuable tool to identify small or ill-defined target tumors that are not visible in postoperative regions on MRI but that are distinctly hypermetabolic on PET/CT (Fig. 1). When the lesion is visible on MRI and the patient has no contraindication to MRI, MRI is preferred because it more clearly shows the ice ball as a black zone as opposed to a subtle gray zone on PET/CT. MRI is also superior for depicting the adjacent nerves and vessel flow voids without the need for contrast administration (Figs. 2 and 3).

The primary limitations of this study are the small number of treated patients and short-term follow-up. Larger studies and more operator experience will be required to establish complication rates and a safety profile.

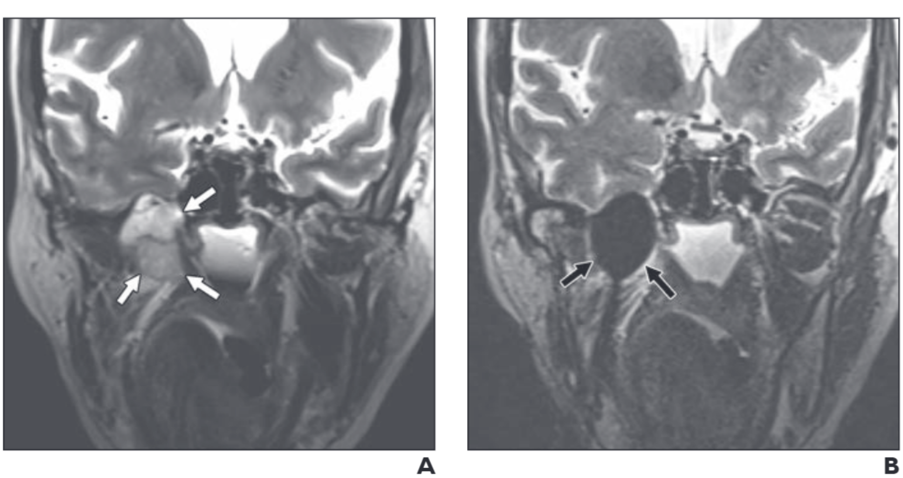

Fig. 3—65-year-old woman (patient 6 in Table 1) with metastatic adenoid cystic carcinoma metastasis causing severe right-sided facial pain.
A, Preprocedure (**A**) and intraprocedural (**B**) coronal turbo spin-echo T2-weighted MR images show mass (*arrows*, **A**) and cryoprobe with ice ball (*arrows*, **B**) covering entire mass and extending to right temporal lobe. Ice ball was also adjacent to right cavernous carotid artery several millimeters posterior to this plane.

In summary, this article describes the technical success, complications, and outcomes of nine consecutive percutaneous image-guided cryoablation procedures of head and neck tumors. Guidance and monitoring modalities were chosen on a case-by-case basis depending on tumor visibility and location. The technical objective was either cryoablation of the entire tumor for local control or cryoablation of a predetermined partial tumor region for pain relief or preservation of functional status. Technical success was achieved in eight of nine procedures. There were no deaths, permanent neurologic or functional deficits, vascular complications, or adverse cosmetic sequelae due to the procedures. The complications that we encountered may be avoidable with increased experience. Further work is needed to continue improving the safety and efficacy of cryoablation of head and neck tumors and to continue expanding the use of cryoablation in patients with head and neck tumors that cannot be treated surgically.

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