Cryoablation of Benign Thyroid Nodules: Preliminary Experience in 3 Cases

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Editor:

Heat-based (laser, radiofrequency, or microwave) ablation has become a common procedure for the treatment of patients with cosmetic complaints and/or compressive symptoms secondary to benign thyroid nodules (1,2). Recently, small cervical metastatic lymph nodes from thyroid cancer have been successfully treated by ultrasound (US)-guided cryoablation (3,4), but this technique has not yet been described for treatment of benign thyroid nodules. This report describes the preliminary results of US-guided cryoablation of benign thyroid nodules.

The pilot study protocol was approved by the ethics committee of the Hospital of Clinics of the University of São Paulo (approval number 5.712.194). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patients provided informed consent before inclusion in the study.

Three female patients presenting a benign thyroid nodule in the right lobe reported pressure symptoms and cosmetic complaints (**Table 1**). Two consecutive fine-needle aspiration biopsies of each nodule confirmed benignity. Serum calcitonin levels were normal. Color Doppler showed nodule peripheral vascularization and homogeneous centripetal enhancement on contrast-enhanced US (**Fig E1a-c**, available online on the article's Supplemental Material page at *www.jvir.org*). The surrounding thyroid parenchyma had normal texture by US in all cases.

The patients underwent intravenous moderate sedation at the discretion of the anesthesiology team. Sterile skin preparation and local anesthesia of the skin to the thyroid capsule with 1% lidocaine were carried out. Hydrodissection of the planes between the right thyroid lobe and the trachea required 90-mL sterile saline with the aid of a 22-gauge needle. The cryoablation protocol included multiple overlapping ablations within the nodule with a 2.4-mm V-tip argon-based cryoprobe (Varian, Irvine, California) opened from 1.5 to 3.0 cm wide. Double freeze-thaw cycles of 1–3 minutes freezing cycles were interspersed with 1-minute thawing (**Table 2**). The posterior margin of the ice ball was estimated by measurement of the radius from the needle to the ice ball surface (**Fig 1a, b**). The ice ball planning avoided the posterior thyroid margins, and an additional 120-mL perithyroid hydrodissection was performed to ensure safety.

US of the ablated areas showed a clear change from a hyperechoic to a hypoechoic pattern a few minutes after ablation, which helped to plan the overlapping sessions. After cryoablation, no pain complaints were recorded, and the patients were discharged from the hospital after 3 hours. The patients reported transient neck swelling and mild pain within the first 3 days after ablation. Continuous improvement was observed after a 5-day course of nonsteroidal anti-inflammatory drugs. No moderate or severe adverse events were observed.

The standard clinical, laboratory, and imaging protocol included baseline; 1-week; and 1-, 3-, 6-, and 12-month posttreatment assessments. Laboratory tests were performed by electrochemiluminescence immunoassay methods with commercially available kits (Roche Diagnostics, Rotkreuz, Switzerland; and Beckman Coulter, Brea, California). Imaging comprised B-mode, color Doppler, and contrast-enhanced US (**Table 1**). The patients reported complete improvement of compressive symptoms at the 3-month follow-up. Patient 1 presented with a clearly visible volume reduction of the cervical lump with no scars at the 1-month follow-up (**Fig 2a, b**). The US follow-up showed significant volume reduction ratio and heterogeneous texture of the treated nodules (**Table 1**; **Fig 3a, b**), with peripheral blood flow on color Doppler and contrast-enhanced US in all cases (**Fig E1**, available online at *www.jvir.org*).

Benign thyroid nodules have been treated with heat-based energy in the past 2 decades, but the use of cryoablation in this context was not yet explored. Therefore, medical decision making for selection of cryoablation versus other ablative technologies or procedures is still a matter of research. Several preliminary observations were noted based on this initial experience. First, no artifacts within the thyroid nodule were observed after complete thawing of the ice ball. On the contrary, the thawed area became clearly hypoechoic and, thus, was easily depicted under US just a few minutes after cryoablation. Conversely, heat-based ablation techniques generate gas during energy deposition, which results in imaging artifacts that remain for a few minutes. Second, a mean 62.9% nodule volume reduction ratio after 3 months of follow-up is promising; although the 3-month preliminary data are not conclusive,

Figure E1 can be found by accessing the online version of this article on *www.jvir.org* and selecting the Supplemental Material tab.

https://doi.org/10.1016/j.jvir.2023.08.030

Table 1. Patient Demographics, Nodule Pattern at Ultrasound Examination, and Laboratory Features before and after Treatment

	Patient	1				2				3			
Demographics	Age (y)	52				56				57			
	Sex	Female				Female				Female			
Nodule features	Composition	Solid				Solid				Solid			
	Echogenicity	Hypoechoic				Hypoechoic				Hypoechoic			
	Shape	Wider-than-tall				Wider-than-tall				Wider-than-tall			
	Margin	Smooth				Smooth				Smooth			
	Echogenic foci	None				None				Macrocalcifications			
	ACR-TIRADS	TR-4				TR-4				TR-4			
	Dimensions	Baseline	1 wk	1 mo	3 mo	Baseline	1 wk	1 mo	3 mo	Baseline	1 wk	1 mo	3 mo
	Length (cm)	4.4	4.7	3.9	4.2	5.7	4.7	4.5	4.2	3.9	3.7	3.5	3.2
	Width (cm)	3.8	4.2	3.5	2.6	3.4	3.4	2.9	2.8	1.9	1.8	1.6	1.1
	Height (cm)	3.0	3.2	2.1	1.9	4.2	2.4	2.7	2.7	1.9	1.9	1.6	1.1
	Volume (cm^3)	26.7	33.3	15.2	10.9	41.8	20.0	18.6	16.7	6.9	6.6	4.7	2.0
	Cytology*	Adenomatoid nodule* (Bethesda II to benign)				Colloid nodule* (Bethesda II to benign)				Adenomatoid nodule* (BethesdaII to benign)			
	VRR†	59.2% (3 mo)				60.0% (3 mo)				69.7% (3 mo)			
	Color Doppler	Peripheral > central	Peripheral			Peripheral > central	Peripheral			Peripheral	Peripheral		Peripheral
	Contrast-enhanced US	Homogeneous	Peripheral			Homogeneous	Peripheral			Homogeneous	Peripheral		Peripheral
Laboratory data	TSH‡	1.23	1.55	0.88	0.76	1.41	1.39	1.05	1.32	0.53	1.10	1.04	1.41
	Free T4§	0.83	1.03	1.51	0.82	0.75	1.00	0.88	0.86	0.82	0.86	0.84	0.91
	Serum Tg‖	31.2	2,611.70	37.58	29.3	363	154,761	508	290	36.9	2093	29.7	49.8

ACR-TIRADS = American College of Radiology - Thyroid Imaging Reporting Data System; T4 = thyroxine; Tg = thyroglobulin; TSH = thyroid serum hormone; TR-4 = TIRADS-4; US = ultrasound; VRR = volume reduction ratio.
*Bethesda classification for cytopathology of thyroid nodules.
†Volume reduction ratio formula = ([initial volume − final volume]/initial volume) × 100.
‡Thyroid serum hormone = 0.35–4.94 μUI/mL.
§Free thyroxine) = 0.7–1.48 ng/dL.
‖Serum thyroglobulin, <36 ng/mL.

Table 2. Cryoablation Technique Parameters for Each Patient

	Patient 1	Patient 2	Patient 3
No. of overlapping sessions*	7	14	6
Cryoprobe tip wide (cm)	1.5–3.0	1.5–3.0	1.5
Procedural time (min)	40	60	35

*Mean duration of each overlapping session: 5 minutes.

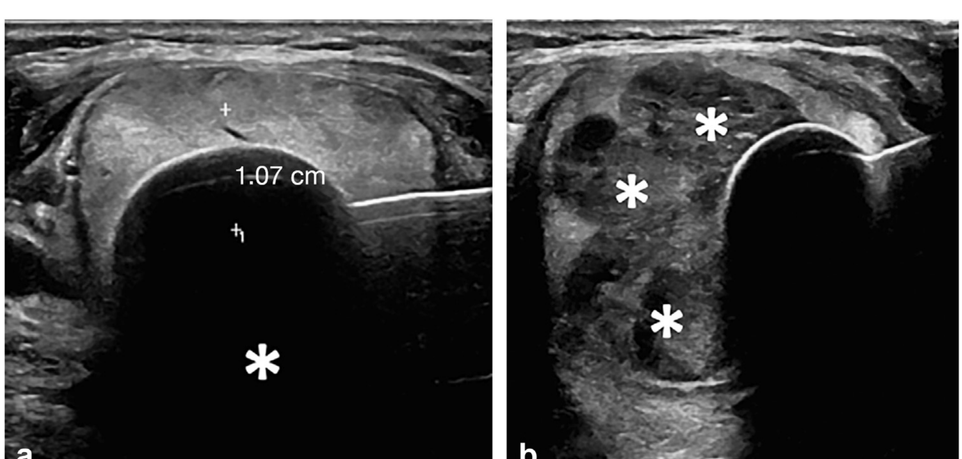

Figure 1. Ultrasound imaging of the thyroid nodule during cryoablation. **(a)** Longitudinal view of the initial ice ball formation. Measurement of the anterior radius (between calipers). Posterior acoustic shadowing from the ice ball formation (asterisk). **(b)** Final immediate hypoechoic areas of the multiple overlapping sessions (asterisks) of thyroid nodule cryoablation under ultrasound guidance.

Figure 2. Neck photograph at **(a)** 1 week and **(b)** 1 month after cryoablation showed significant goiter volume reduction and lack of surgical scaring in Patient 1, with excellent cosmetic results.

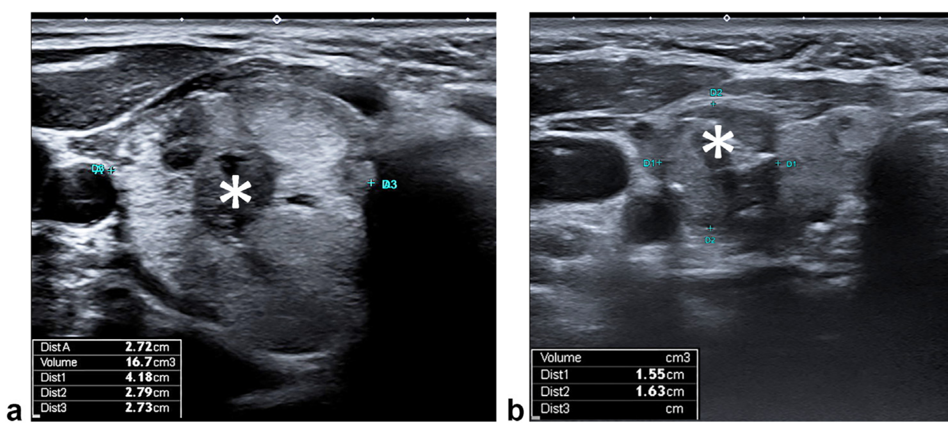

Figure 3. Ultrasound imaging of the thyroid nodules from **(a)** Patients 2 and **(b)** 3 at the 3- and 1-month follow-ups after cryoablation showed shrinkage with a volume reduction ratio of 60% and 27.9%, respectively. Central hypoechogenic areas (asterisks) represented regions of cryoablation.

the procedure reached similar results compared to heat-based ablative therapies. Third, the absence of protein denaturation secondary to cryoablation cell death may be a significant benefit, differently to the coagulation necrosis induced by heat-based ablation energies. In this context, thyroid nodule size reduction after cryoablation may hypothetically occur without calcification, a frequent cumbersome finding after heat-based ablation. Finally, although cryoablation is usually associated with less pain when compared to heat-based ablation technologies (5), potentially higher costs and logistics of the cryoablation device and gas containers are still a drawback.

In conclusion, cryoablation of benign thyroid nodules is feasible, safe, and well tolerated, with a promising nodule volume reduction within the first few months. The possibility of nodule volume reduction without scarring or calcification and a less painful procedure are potential advantages of cryoablation over heat-based techniques in the treatment of thyroid nodules but need to be confirmed with larger series and longer follow-up.

ACKNOWLEDGMENTS

The authors thank Plinio Turine Neto, MD, from the Department of Radiology; Debora Lucia Seguro Danilovic, MD, PhD, and Suemi Marui, MD, PhD, from the Department of Endocrinology; and Marcos Roberto Tavares, MD, PhD, from the Department of Head and Neck Surgery their ongoing support to this project.

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Received June 8, 2023; final revision received August 14, 2023; accepted August 20, 2023.

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None of the authors have identified a conflict of interest.

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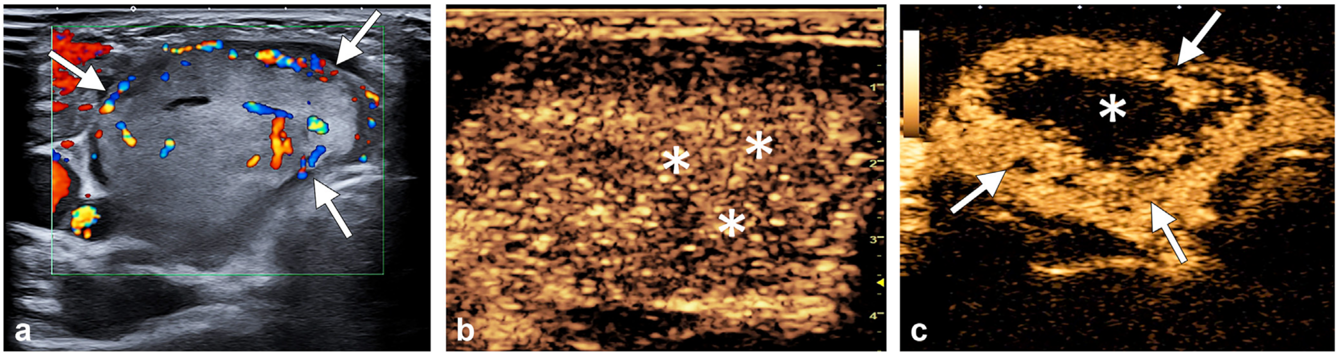

Figure E1. (a) Color Doppler showed main peripheral vascularization (arrows). **(b)** Contrast-enhanced ultrasound before cryoablation showed homogeneous centripetal enhancement (asterisks). **(c)** Contrast-enhanced ultrasound 1 week after cryoablation showed homogeneous peripheral enhancement (arrows) and no enhancement in the treated areas (asterisk).