Diagn Interv Radiol 2017; 23:381–384

INTERVENTIONAL RADIOLOGY

TECHNICAL NOTE

Fibrillar collagen injection for organ protection during thermal ablation of hepatic malignancies

Bill S. Majdalany
Jonathan Willatt
Jeffrey Forris Beecham Chick
Ravi N. Srinivasa
Wael A. Saad

ABSTRACT

Percutaneous image-guided ablation is performed throughout many areas of the body for various pathologies including hepatic malignancies. Heat and cold-based ablative technologies are effective and well-tolerated with an acceptable safety profile. However, ablative therapies may be technically more challenging and cause collateral thermal injury if the targeted lesion is adjacent to critical organs. Previously, techniques including artificial ascites and pneumoperitoneum have been utilized to displace or insulate critical structures from the ablation zone. This technical innovation describes (10–30 mL) fibrillar collagen dissolved in fluid as a focal thermal insulation technique. Small volume fibrillar collagen instillation, and thermal ablation were technically successful in three cases without complication. Clinical follow-up and 3-month imaging confirmed complete ablation of all hepatic malignancies without collateral injury.

Image-guided percutaneous ablation is accepted in the treatment paradigm of hepatocellular carcinoma (HCC) (1–3). Regarded as safe, major complications occur in less than 4% of cases (1–3). In an effort to minimize inadvertent injury during thermal ablation, several authors suggest at least a 1 cm margin between the target lesion and adjacent structures (1, 2). Radiofrequency ablation of HCC in a multicenter study revealed that 0.7% of procedures were complicated by bowel wall perforation, with two resulting fatalities (3). Similar findings were noted in a multicenter study utilizing microwave ablation for HCC (2).

Microwave ablation, which creates larger ablation zones more quickly than radiofrequency ablation, potentially increases the risk of collateral thermal injury to adjacent structures (1, 3). Strategies to protect adjacent structures have included artificial ascites and pneumoperitoneum, balloon interposition, thermometry, and torqueing with probes (4, 5). However, each approach has limitations which decrease the precision and durability of organ separation.

Fibrillar collagen has been used as a hemostatic agent during surgical resections and injected percutaneously (6). When mixed with fluid, including contrast and saline, fibrillar collagen forms a slurry, which may be focally delivered to create safe organ separation during ablation (Fig. 1). Moreover, fibrillar collagen is not absorbed as rapidly as fluid or gas and has the potential to aid in hemostasis or healing if injury occurs. Herein, fibrillar collagen mixed with contrast and saline was focally interposed between the liver and adjacent structures prior to hepatic microwave ablation (Fig. 1).

Technique

Small case series are exempted from institutional review board approval at our institution. This study complied with the Health Insurance and Portability and Accountability Act. Informed consent was obtained from all individual participants included in the study. All patients undergoing thermal ablation using fibrillar collagen injection (Helitene; Integra Life Sciences) for organ protection in 2015 were identified (n=3) using retrospective review of a prospectively collected database (Excel 2016, Microsoft Corporation) and other medical and imaging records.

Multidisciplinary tumor board review reached a consensus to proceed with percutaneous tumor ablation in all patients. All patients were seen in the interventional radiology clinic

From the Division of Vascular and Interventional Radiology (B.S.M. ✉ *bmajdala@med.umich.edu*), Department of Radiology, University of Michigan Health System, MI, USA.

Received 3 April 2017; revision requested 11 May 2017; revision received 12 May 2017; accepted 31 May 2017.

Published online 24 August 2017.
DOI 10.5152/dir.2017.17120

You may cite this article as: Majdalany BS, Willat J, Beecham Chick JF, Srinivasa RN, Saad WA. Fibrillar collagen injection for organ protection during thermal ablation of hepatic malignancies. Diagn Interv Radiol 2017; 23:381–384.

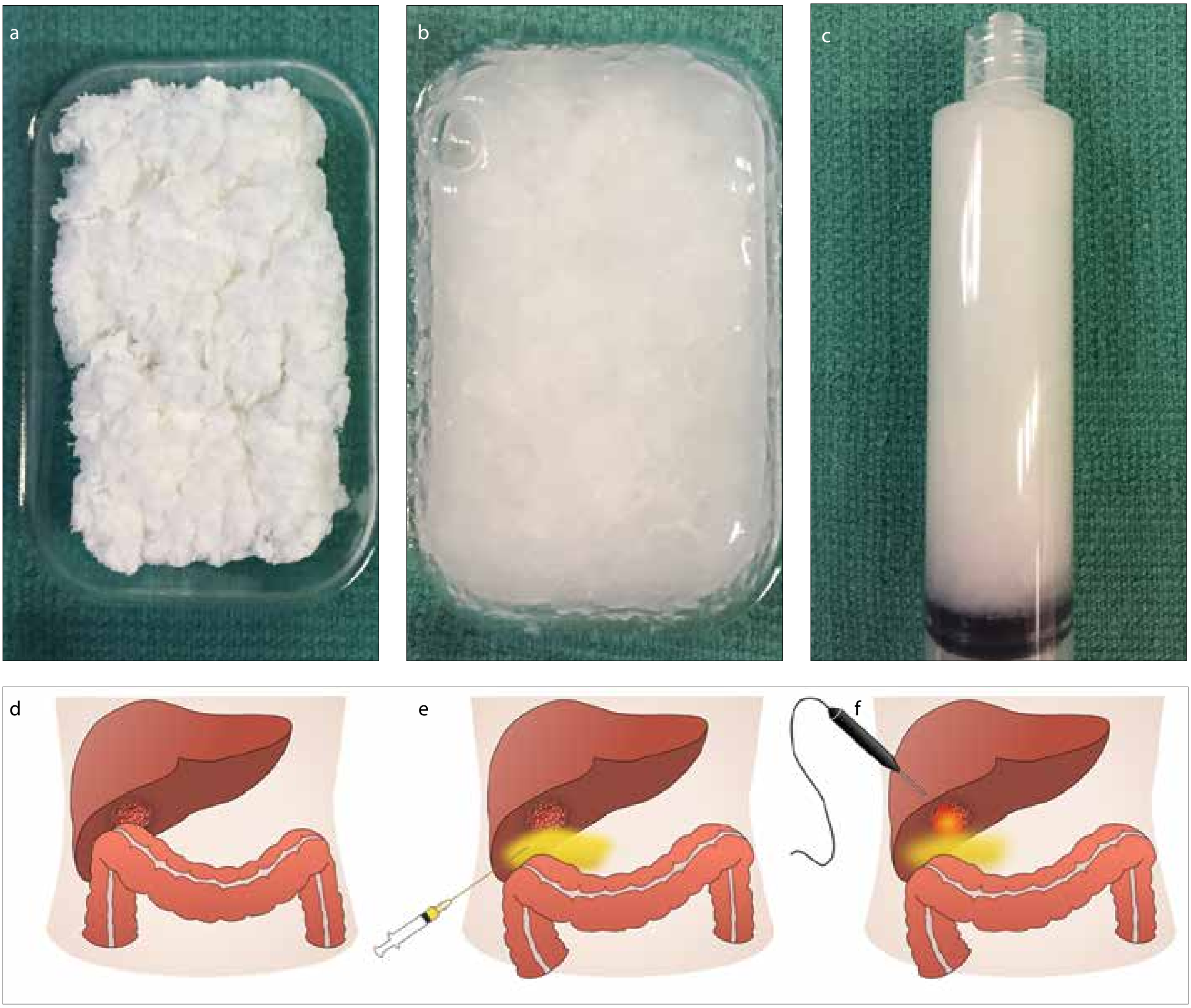

Figure 1. a–f. Fibrillar collagen **(a–c)** and schematic representations of the fibrillar collagen injection technique **(d–f)**. Fibrillar collagen is shown before **(a)** and after **(b)** dissolution with contrast and saline. After removing the back end of a 10 mL syringe the fibrillar collagen was then poured into the syringe and the plunger was replaced **(c)**. Panel **(d)** shows an intrahepatic mass in close proximity to the hepatic flexure of the colon. Due to its higher viscosity, longer dwell time, and better ability to displace structures, fibrillar collagen is percutaneously injected **(e)** in order to displace the colon away from the mass. A microwave probe is inserted into the mass **(f)** in order to perform tumor ablation.

Main points

- Thermal ablation of hepatocellular cancer has proven to be highly effective, but can be challenging when adjacent to thermally sensitive structures. Several techniques have been described to decrease the potential for collateral thermal injury, though each has limitations.
- Fibrillar collagen has been used as a hemostatic agent and can be dissolved to form a consistent slurry that can be focally delivered. In this case series, fibrillar collagen was delivered and successfully created a barrier between the ablation zone and thermally sensitive tissue.
- Advantages of using fibrillar collagen to displace thermally sensitive tissue is the durability of displacement, the small volume that is needed, and the presence of collagen to facilitate hemostasis and healing.

before the procedure by an attending interventional radiologist. Injury to adjacent critical organs and potential maneuvers to mitigate such risks were specifically discussed in each case. All procedures were performed under general anesthesia administered by an attending anesthesiologist. All interventional procedures were performed by an attending interventional radiologist.

All procedures were performed in a single hybrid angiography suite using EPIQ ultrasound (Philips Medical), Artis Zee interventional angiography system (Siemens Medical), and SOMATOM Definition AS computed tomography (CT) (Siemens Medical). All ablations were formed with a microwave ablation system (HS Amica). Fibrillar collagen injection and percutaneous ablation were performed, in standard clinical fashion, based on operator preference. Targeted ultrasound of the liver was performed to identify the hepatic malignancy and determine a safe path for percutaneous placement of a 14-gauge × 15 cm microwave antenna. The antenna was placed centrally within each lesion under ultrasound-guid-

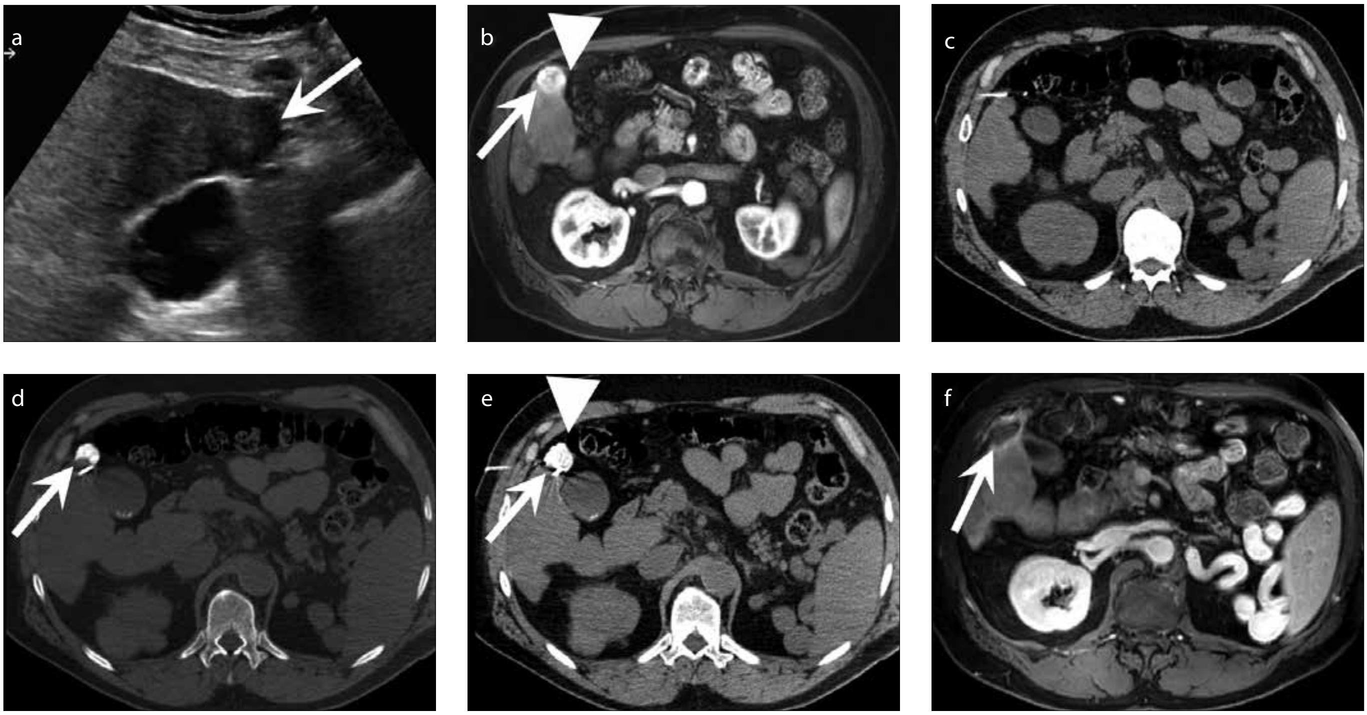

Figure 2. a–f. Ultrasound image **(a)** demonstrates a hypoechoic mass *(arrow)* within segment 5 of the liver. Contrast-enhanced MRI **(b)** shows an avidly enhancing mass within segment 5 of the liver anteriorly *(arrow)*. The transverse colon is noted to abut the liver mass with essentially no free interface between the colon and the liver *(arrowhead)*. Panels **(c–e)** show a needle inserted just anterior to the liver mass in order to inject contrast-loaded fibrillar collagen and displace the colon away from the mass *(arrow)*. There is a much wider interface between the mass (**e,** *arrow*) and the colon (**e,** *arrowhead*). Follow-up contrast-enhanced MRI **(f)** of the mass after ablation *(arrow)* demonstrates complete devascularization of the mass without injury to adjacent structure.

ance with subsequent CT confirmation. In all cases, adjacent critical organ collateral damage was inevitable and a protection strategy was undertaken. A 21-gauge × 15 cm Chiba needle was interposed between the liver and the adjacent critical organ. Over a 0.018-inch wire, the needle was exchanged for a 4 F dilator. Fibrillar collagen, dissolved in a solution of 9 mL normal saline and 1 mL of iodinated contrast (Isovue 300; Bracco Diagnostics), was loaded in a 10 mL syringe and subsequently injected in small aliquots to displace the at-risk organ. Intraprocedural CT imaging was performed to confirm that all at-risk organs were safely displaced from the prospective ablation zone. Injected volumes ranged from 10–30 mL. In each case, microwave ablation was performed using 40–60 watts for 12–15 minutes to cover the entire lesion with a margin of 5–10 mm.

All patients were discharged within 24-hours and clinical evaluation in the interventional radiology clinic occurred within 2-weeks, which consisted of an interval history and physical examination with laboratory evaluation. No minor or major complications occurred. Three-month clinical follow-up included a clinic visit and interval imaging which showed completely ablated malignancy without collateral organ injury in all cases.

Patient #1:

A 65-year-old male, Eastern Cooperative Oncology Group (ECOG) 0 and Childs-Pugh (CP) Class A, with history of Hepatitis C cirrhosis and no prior locoregional therapy, developed a 2.6 cm HCC along the anteroinferior capsular margin of hepatic segment 5, abutting the gallbladder fundus and hepatic flexure of the colon (Fig. 2).

Patient #2:

A 78-year-old female, ECOG 0 and CP Class A, with history of alcoholic cirrhosis and no prior locoregional therapy, developed a 1.9 cm HCC in the posteroinferior margin of hepatic segment 6, abutting the gallbladder body and hepatic flexure of the colon (Fig. 3).

Patient #3:

A 66-year-old male, ECOG 1 and CP Class B, with a history of Hepatitis C cirrhosis and HCC previously underwent transarterial chemoembolization to 2 lesions and microwave ablation to 2 further lesions, developed a new 10 mm HCC in segment 3 abutting the stomach.

Discussion

Percutaneous tumor ablation is performed throughout the body to address malignancies with high success and low complication rates. However, despite refinements in ablation technology, a limitation in liver ablation is adjacent thermal injury when the target lesion is along the surface of the liver as demonstrated in these patients. Strategies have emerged to protect the surrounding tissues including fluid or gas displacement, balloon interposition, thermometry, and torqueing of tissue (4, 5).

The most commonly employed strategies involve introduction of fluid or gas as a barrier, predominantly normal saline, 5% dextrose in water, or CO_2 gas. However, both fluid and gas have low viscosity, distribute freely throughout the abdomen, and may be absorbed by the peritoneum, decreasing the durability of separation. Not uncommonly, large volumes or continuous infusions are required, which may increase intra-abdominal pressure, may be problematic in patients susceptible to fluid overload, and may result in patient discomfort. Additionally, CO_2 gas may preclude the use of ultrasonography for lesional targeting or adjustment of probes. Studies have shown

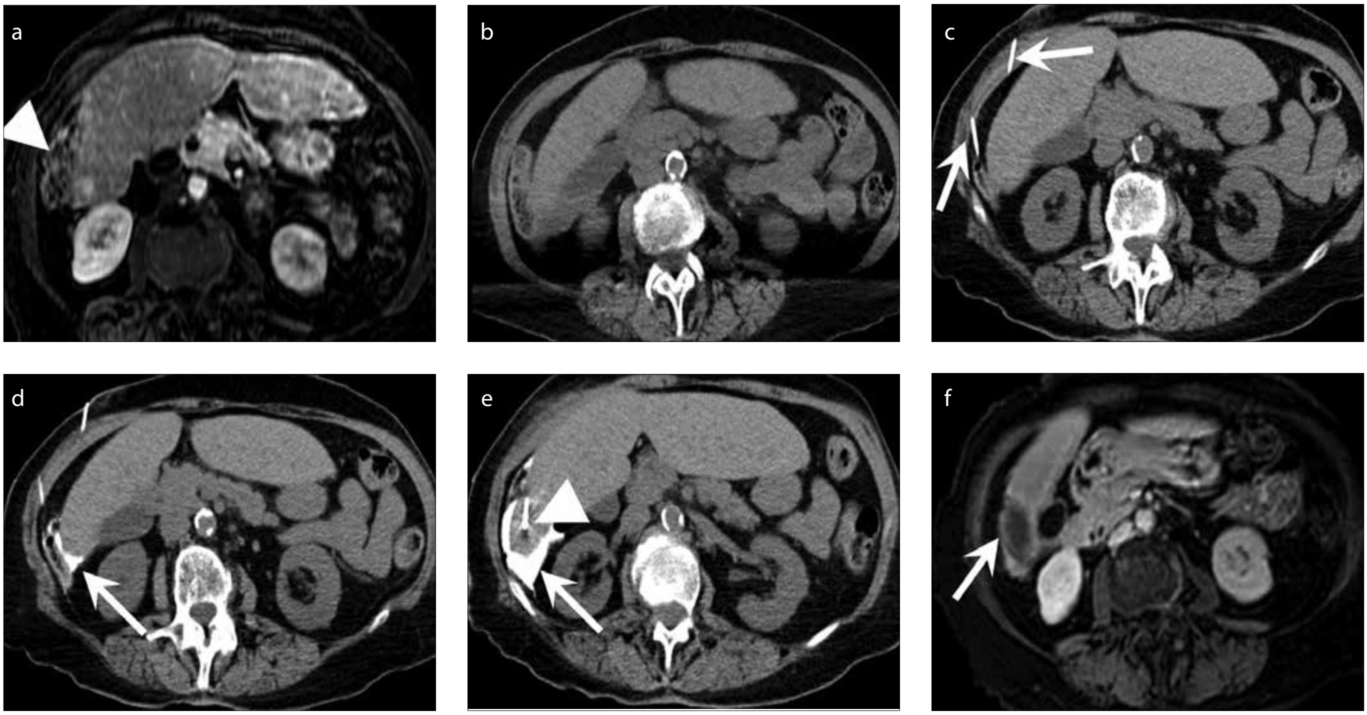

Figure 3. a–f. Contrast-enhanced MRI **(a)** shows a hypervascular mass within segment 6 of the liver. The colon *(arrowhead)* is noted to abut this area of the liver with no window for safe ablation. Unenhanced CT images prior to ablation **(b, c)** demonstrate the narrow window between the liver and colon. Two needles are positioned in the peri-hepatic space under CT-guidance (**c,** *arrows*). CT images **(d, e)** show injection of contrast-loaded fibrillar collagen in order to displace the colon. Early injection **(d)** demonstrates the needles to be in adequate position with fibrillar collagen filling the space between the colon and the liver *(arrow)*. Continued injection of fibrillar collagen **(e)** adequately displaces the colon away from the mass and a microwave ablation probe is seen positioned into the segment 6 mass prior to ablation *(arrowhead)*. Contrast-enhanced MRI post-ablation **(f)** demonstrates no residual enhancement of the mass *(arrow)* and no injury to adjacent structure.

that the instillation of fluid separated the liver from the gastrointestinal tract in 78% of cases (4, 5). Most recently, reports have emerged using a hyaluronic acid gel in humans and thermoprotective gels in an animal model (7, 8).

Fibrillar collagen is an absorbable bovine collagen hemostatic agent, which is available in fibrillar and pad forms. The fibrillar form dissolves in solution and is used as a hemostatic agent (6). Dilution of fibrillar collagen in 10 mL of fluid creates a slurry, which is easily injected through a 3 F or 4 F dilator. In these cases, utilizing between 10 and 30 mL of fibrillar collagen slurry created 15–21 mm of durable separation between the liver and adjacent structures which persisted throughout the remainder of the ablation procedure without reapplication. Although the package insert for fibrillar collagen states that complete intraperitoneal absorption may not occur at 56 days, follow-up imaging at 8–12 weeks revealed resorption of the collagen in these 3 patients.

Fibrillar collagen appears well-tolerated, safe, and is of little cost. Moreover, it does not preclude other organ separation strategies. Limitations to this study include the sample size of 3 patients and that it was performed at a single institution without comparison to other separation agents.

In conclusion, strategies and techniques have been developed to protect tissues adjacent to ablation zones. Fibrillar collagen appears to be a safe and effective addition to the armamentarium. Fibrillar collagen may have advantages in that a small volume is necessary, the separation is durable, and the presence of collagen may facilitate hemostasis and healing.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Crocetti L, de Baere T, Lencioni R. Quality improvement guidelines for radiofrequency ablation of liver. Cardiovasc Intervent Radiol 2010; 33:11–17. [CrossRef]
2. Livraghi T, Meloni F, Solbiati L, et al. Complications of microwave ablation for liver tumors: results of a multicenter study. Cardiovasc Intervent Radiol 2012; 35: 868–874. [CrossRef]
3. Livraghi T, Solbiati L, Meloni MF, et al. Treatment of focal liver tumors with percutaneous radiofrequency ablation: Complications encountered in a multicenter study. Radiology 2003; 226:441–451. [CrossRef]
4. Ginat DT, Saad WA, Davies M, Waldman D, Erturk E. Bowel displacement for ct-guided tumor radiofrequency ablation: techniques and anatomic considerations. J Endourology 2009; 23: 1259–1264. [CrossRef]
5. Bhagavatula SK, Chick JFB, Chauhan NR, Shyn PB. Artificial ascites and pneumoperitoneum to facilitate thermal ablation of liver tumors: a pictorial essay. Abdom Radiol 2017; 42:620–630. [CrossRef]
6. Izzo F, Di Giacomo R, Falco P, et al. Efficacy of a haemostatic matrix for the management of bleeding in patients undergoing liver resection: results from 237 cases. Curr Med Res Opin 2008; 24: 1011–1015. [CrossRef]
7. Hasegawa T, Takaki H, Miyagi H, et al. Hyaluronic acid gel injection to prevent thermal injury of adjacent gastrointestinal tract during percutaneous liver radiofrequency ablation. Cardiovasc Interv Radiol 2013; 36:1144–1146. [CrossRef]
8. Moreland AJ, Lubner MG, Ziemlewicz TJ, et al. Evaluation of a thermoprotective gel for hydrodissection during percutaneous microwave ablation: in vivo results. Cardiovasc Intervent Radiol 2015; 38:722–730. [CrossRef]