

# PERCUTANEOUS CRYOABLATION OF PORCINE KIDNEYS WITH MAGNETIC RESONANCE IMAGING MONITORING

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## ABSTRACT

**Purpose:** We determined the feasibility of a percutaneous approach using magnetic resonance imaging (MRI) for creating cryoablation lesions in the porcine kidney.

**Materials and Methods:** Three domestic swine underwent renal cryoablation under MRI guidance with a total of 6 cryoablation lesions created in 5 kidneys. A 3 mm. cryoprobe was placed under MRI guidance using an interventional MRI unit. With a pressurized argon gas cooling unit the cryoablation lesion was created and monitored by MRI. Gross and histological examination of the kidneys was performed 1 week after the procedure.

**Results:** All animals survived the procedure without difficulty. A total of 6 cryoablation lesions were produced in 5 kidneys. The lesions were  $1.9 \times 1.3$  to  $3.9 \times 1.9$  cm. on MRI. Histological examination 1 week after treatment showed that the lesions were  $1.7 \times 1.0$  to  $3.2 \times 1.2$  cm. There was an area of coagulation necrosis surrounded by a transition zone of inflammatory reaction a mean of 0.5 cm. in diameter with each lesion.

**Conclusions:** Percutaneous renal cryoablation using MRI imaging proved to be a successful technique for guiding probe placement and monitoring ice ball formation. Because MRI allows imaging in 3 planes, it may be useful for cryoablation of intraparenchymatous tumors.

**KEY WORDS:** kidney, magnetic resonance imaging, swine, cryosurgery

The National Cancer Institute estimates that approximately 30,000 new cases of renal cell carcinoma are diagnosed yearly. Surgical therapy is the gold standard for treatment. Recently interest has developed in nephron sparing surgery for this disease.<sup>1,2</sup> Further evolution in treatment has occurred with the use of cryotherapy for freezing small tumors.<sup>3</sup> This procedure has been performed via the laparoscopic or open approach.<sup>3,4</sup> There have been a few case reports of the use of renal ultrasonography to achieve percutaneous approach with some success.<sup>5</sup> We evaluated percutaneous cryoablation using an interventional magnetic resonance imaging unit for guiding probe placement and ice ball formation.

## MATERIALS AND METHODS

**Animals and surgery.** Approval for this protocol was obtained from the Institutional Animal Care and Use Committee, and met the requirements of the National Institutes of Health, Public Health Service Policy on Humane Care and Use of Laboratory Animals. Castrated male Yorkshire-cross pigs weighing 30 kg. were obtained from a local commercial farm. Animals were anesthetized with 0.025 mg./kg. atropine sulfate (The Butler Co., Columbus, Ohio), 0.08 mg./kg. medetomidine hydrochloride (Pfizer Animal Health, Exton, Pennsylvania), 0.2 mg./kg. butorphanol tartrate (Fort Dodge Animal Health, Fort Dodge, Iowa) and 10 mg./kg. ketamine hydrochloride (Fort Dodge Animal Health) given intramuscularly. At sacrifice the animals were placed on 4% to 5% isoflurane USP (Abbott Laboratories, North Chicago, Illinois) administered by facemask to induce a deep plane of anesthesia and the kidneys were then harvested. Intraoperative imaging was performed using the Signa SP 0.5 Tesla open MRI unit (General Electric, Milwaukee, Wisconsin).

**Cryosurgery equipment.** A Cryohit cryoablation unit (Galil, Ltd., Tel Aviv, Israel) using pressured argon gas at 4,000 psi created the ice ball lesion at  $-80^{\circ}\text{C}$  and heated helium gas at  $70^{\circ}\text{C}$  was used to melt the lesion. A single 3 mm. diameter probe constructed of MRI compatible metal was placed into the kidney for lesion creation and temperature monitoring was performed using the temperature sensor at the probe tip.

**Cryoablation technique.** After anesthesia administration each pig was placed prone in the interventional MRI unit and scanning was performed through the abdomen to localize the kidneys. The skin overlying each kidney was marked, prepared and draped in normal sterile fashion. The puncture site was anesthetized with 1% to 2% lidocaine. A 3 to 4 mm. incision was made at the site of local anesthesia. Under MRI guidance the cryoprobe was inserted after placing a 10Fr standard Meditech vascular sheath (Boston Scientific Corp., Watertown, Massachusetts).

Initial localization with fast multiplanar gradient images was obtained as well as spoiled gradient images. This method provided initial axial and coronal localization of the kidneys and the overlying skin. After probe insertion began spin echo or T1-weighted images were obtained for optimal spatial imaging and anatomy characterization. A single shot fast spin echo was used as a substitute for a T2-weighted image with the benefit of 3-second image acquisition versus the 16-second image acquisition of traditional T2-weighted imaging. The T2-weighted images were used to evaluate the cystic or other fluid components of the kidney.

After the probe position was optimized and confirmed T1-weighted fast spin echos with a prolonged echo train of 4 were used to monitor the developing ice ball and cryoablation process. These images were obtained in the axial, coronal and sagittal planes. Other multiplanar slices were obtained perpendicular and parallel to the cryoablation probe access tract as needed.<sup>6</sup> At the completion of the freeze cycle the probe

was thawed and removed. The contralateral kidney was then prepared and treated in the same fashion.

Each incision was closed with a subcutaneous suture. The pig was removed from the interventional MRI unit, awakened and transported to the laboratory facilities. Each probe was tested immediately before insertion for leaks. The probe was placed in a water bath and examined visually during the freezing and thawing cycles to access its integrity. The process was repeated after treatment was completed.

#### RESULTS

All animals survived the procedure without morbidity. They were sacrificed 1 week after the procedure and the kidneys were harvested. A total of 6 lesions were produced in 5 kidneys with 2 lesions in 1 kidney. The table shows the total freeze time and lesion size in the specimen and MRI image. Freeze time was 2 to 8 minutes with a resulting lesion of  $1.9 \times 1.3$  to  $3.9 \times 1.9$  cm. Figure 1 shows probe placement in the kidney under MRI monitoring. Figure 2 shows an MRI image of ice ball formation in the kidney.

**Histology.** Gross examination of the kidneys revealed a small perinephric hematoma surrounding the probe entry site into the kidney. Figure 3 shows the cryoablation lesion created in 1 kidney. The histological sections of the areas of cryoablation had 4 distinct zones (fig. 4). In the center was a large area of complete necrosis. Outside of the area of complete necrosis was a zone approximately 1 mm. wide consisting of an infiltrate of neutrophils and then a rim of hemorrhage. Peripheral to the hemorrhage was a region of regeneration and fibrosis 1 to 4 mm. thick. The area of complete necrosis demonstrated coagulative necrosis of all tissue structures, including the interstitium and blood vessels as well as the glomeruli and tubules. The tubules and glomeruli were also necrotic within the hemorrhagic zone. Small blood vessels were growing inward from the region of regeneration and fibrosis was present within the hemorrhagic zone.

Thrombosed glomeruli and fresh fibrin thrombi were found in the arteries and veins in the inner part of the region of regeneration and fibrosis. Other arteries showed a proliferation of loose intimal connective tissue occluding the vessel lumens that was often associated with fibrinoid necrosis of the arterial media. There was marked proliferation of fibroblasts within this region that surrounded regenerating small tubules, and calcified tubules and glomeruli. Beyond the region of regeneration and fibrosis was an abrupt transition to histologically normal kidney. The cryoprobe injury extending outside of the renal capsule resulted in complete necrosis of the capsule and adjacent adipose tissue. The zone of inflammation was wider than in the kidney and there was a large accumulation of serous fluid and blood, producing small perinephric hematomas. The blood within the hematoma was contained within a thick rim of fibroblastic tissue.

#### DISCUSSION

This study demonstrates the feasibility of using of MRI as a monitoring system for percutaneous probe placement and ice ball formation in the swine kidney. This system has

*Cryoablation time and renal lesion size*

Kidney Cryolesion No.	Total Freeze Time (mins.)	MRI Lesion (cm.)	Pathological Lesion (cm.)
1	2	$2.4 \times 1.5$	$1.7 \times 1.0$
2	2	$1.9 \times 1.3$	$2.0 \times 1.4$
3	5	$3.1 \times 1.4$	$3.5 \times 1.2$
4	8	$2.9 \times 1.8$	$2.4 \times 1.8$
5	5	$1.8 \times 1.6$	$1.6 \times 1.2$
6	7	$3.9 \times 1.9$	$3.2 \times 1.2$



FIG. 1. MRI of cryoprobe (arrow) in porcine kidney



FIG. 2. MRI of ice ball (arrow) being created by cryoprobe

multiple advantages over ultrasound. MRI allows imaging in 3 dimensions, while ultrasound is 2-dimensional. In addition, the quality of MRI images is superior to that of ultrasound images and the problem of shadowing after the ice ball formation in ultrasound is completely avoided with MRI. Computerized tomography exposes the physician and patient to ionizing radiation, which is not the case with MRI or ultrasound. Ultrasound has poor soft tissue resolution and only 2-dimensional imaging capability compared with MRI. Laparoscopy is a much more invasive procedure than the percutaneous approach. An additional drawback is the necessity of using ultrasound as the imaging modality during laparoscopy with all of the aforementioned limitations. In regard to direct visualization of the ice ball during its formation Chosy et al reported difficulty in determining the distal aspect of the ice ball.<sup>7</sup> MRI monitoring avoids this problem due to its ability to image in 3 dimensions.

Histological examination of the cryoablation lesion demonstrated a relatively close correlation of image size on MRI

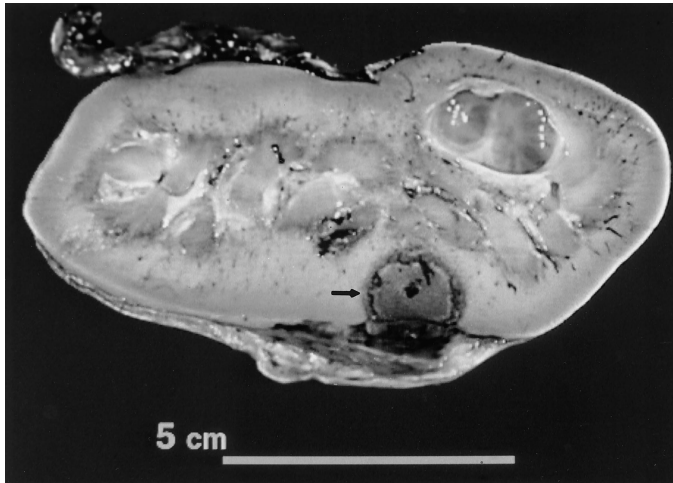


FIG. 3. Gross longitudinal section of kidney with visible cryoablation lesion (arrow).

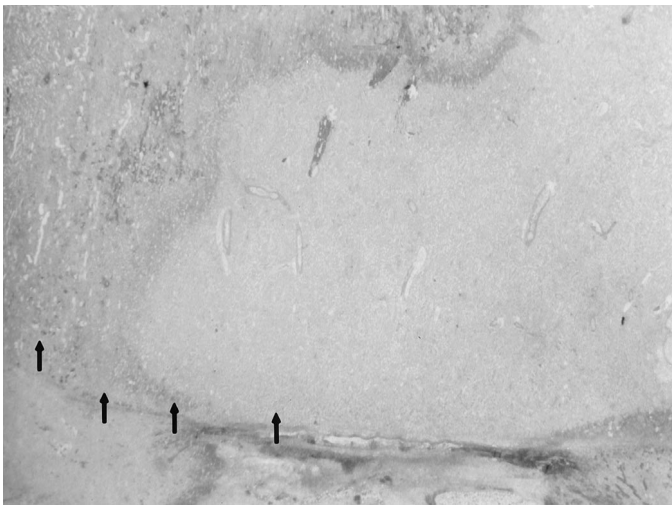


FIG. 4. Photomicrograph of cryoablation lesion with complete necrosis, inflammatory zone with hemorrhage, zone of regeneration and fibrosis, and normal renal parenchyma (arrows). Reduced from  $\times 40$ .

with pathological size. The discrepancy that existed may have been due to slight shrinkage in the lesion in the interval between generation of the cryoablation lesion and pathological examination. To err on the safe side the ice ball front was

commonly extended 0.5 to 1.0 cm. beyond the tumor border. Two lesions were slightly smaller on MRI than on pathological examination. An explanation may be inaccurate measurement of the MRI cryoablation lesion. The problem of hemorrhage due to ice ball cracking, as noted by Chosy et al,<sup>7</sup> was not a problem in our study. Gross examination of the kidneys demonstrated only a small amount of perinephric hemorrhage at the probe insertion site.

An issue that was not addressed in this study was the use of thermal sensors for temperature monitoring within the ice ball. We have performed experiments measuring the temperature within the ice ball using temperature sensors in non-living tissue.<sup>8</sup> The temperature in the ice ball is not uniform but the cryoablation lesion achieves a sufficient freezing temperature for cell destruction. We are developing a temperature monitoring system to determine better the temperature during the in vivo procedure.

#### CONCLUSIONS

MRI guidance of percutaneous probe placement and ice ball formation monitoring was technically successful in an animal model. Histological examination results correlated relatively well with the size of the ice ball on MRI. Percutaneous renal cryoablation with MRI monitoring may prove to be an option as minimally invasive treatment of renal cell carcinoma.

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