Percutaneous computed tomography fluoroscopy–guided conformal ultrasonic ablation of vertebral tumors in a rabbit tumor model

Laboratory investigation

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Object. Radiofrequency ablation (RFA) has proven to be effective for treatment of malignant and benign tumors in numerous anatomical sites outside the spine. The major challenge of using RFA for spinal tumors is difficulty protecting the spinal cord and nerves from damage. However, conforming ultrasound energy to match the exact anatomy of the tumor may provide successful ablation in such sensitive locations. In a rabbit model of vertebral body tumor, the authors have successfully ablated tumors using an acoustic ablator placed percutaneously via computed tomography fluoroscopic (CTF) guidance.

Methods. Using CTF guidance, 12 adult male New Zealand White rabbits were injected with VX2 carcinoma cells in the lowest lumbar vertebral body. At 21 days, a bone biopsy needle was placed into the geographical center of the lesion, down which an acoustic ablator was inserted. Three multisensor thermocouple arrays were placed around the lesion to provide measurement of tissue temperature during ablation, at thermal doses ranging from 100 to 1,000,000 TEM (thermal equivalent minutes at 43°C), and tumor volumes were given a tumoricidal dose of acoustic energy. Animals were monitored for 24 hours and then sacrificed. Pathological specimens were obtained to determine the extent of tumor death and surrounding tissue damage. Measured temperature distributions were used to reconstruct volumetric doses of energy delivered to tumor tissue, and such data were correlated with pathological findings.

Results. All rabbits were successfully implanted with VX2 cells, leading to a grossly apparent spinal and paraspinal tissue mass. The CTF guidance provided accurate placement of the acoustic ablator in all tumors, as corroborated through gross and microscopic histology. Significant tumor death was noted in all specimens without collateral damage to nearby nerve tissue. Tissue destruction just beyond the margin of the tumor was noted in some but not all specimens. No neurological deficits occurred in response to ablation. Reconstruction of measured temperature data allowed accurate assessment of volumetric dose delivered to tissues.

Conclusions. Using a rabbit intravertebral tumor model, the authors have successfully delivered tumoricidal doses of acoustic energy via a therapeutic ultrasound ablation probe placed percutaneously with CTF guidance. The authors have thus established the first technical and preclinical feasibility study of controlled ultrasound ablation of spinal tumors in vivo. (DOI: 10.3171/2010.5.SPINE09266)

Key Words • tumor • spine • ultrasonic ablation • high-intensity ultrasound

Abbreviations used in this paper: CTF = CT fluoroscopic; HIFU = high-intensity focused ultrasound; HIITU = high-intensity interstitial ultrasound; RFA = radiofrequency ablation.
Amenable to surgical treatment. Unfortunately, for patients with tumoral spine disease, there is currently no adequate alternative to the immediate pain relief that may occur with minimally invasive percutaneous vertebroplasty. However, such vertebroplasty, at best, only affects pain symptoms and has not been designed to eradicate the cancer. Radiofrequency ablation has proven to be an effective method for the treatment of malignant and benign tumors. It works through the application of a current that generates thermal energy and causes localized cellular damage, coagulation, and necrosis at temperatures above 60°C. This technique has been used in several organs and is receiving increasing attention for the treatment of musculoskeletal diseases, such as osteoid osteomas, chondroblastomas, epithelioid hemangioendotheliomas, and bone metastasis, including spinal lesions in rare reports. High-intensity interstitial ultrasound is a more recently developed thermal ablation technology that allows for the delivery of ultrasound treatment to deeply seated tumors that are not accessible to the more commonly used extracorporeal HIFU. In addition, HIIU provides advantages over conventional RFA in terms of its penetration depth, coagulation speed, directionality, and accuracy of thermal lesion size.

The major challenge of using thermal ablation for spinal tumors, however, is the difficulty of protecting the spinal cord and nerves from damage if energy is applied close to the posterior vertebral body wall or in epidural tissue. Conforming ultrasound energy to the exact anatomy of the tumor may provide successful ablation in such sensitive locations, but it first requires accurate image guidance. Computed tomography fluoroscopy may offer a viable solution by providing real-time visualization of the needle or catheter throughout the procedure. In the present experiment we postulated that thermal HIIU ablation can be safe and efficacious in the management of metastatic spine cancer. Toward proving this hypothesis, we outline our mechanism and approach by which conformal ultrasound ablation is safely delivered in a minimally invasive manner under CTF guidance in a rabbit spinal tumor model.

**Methods**

The animal model of spinal tumor in New Zealand White rabbits and rabbit VX2 cells has been previously described. Using CTF guidance, we injected 12 adult male rabbits with a 20-μl suspension containing 400,000 cells of VX2 carcinoma in the lowest lumbar vertebral body. Lower-extremity motor function was assessed daily, using the neurological grading system for rabbits described by Fowl et al. (Grade 0, complete paralysis; Grade 1, partial deficit; and Grade 2, no deficit). At 21 days, the rabbits underwent CT scanning to corroborate the growth of the tumor. Following radiographic assessment of the anatomy of the lesions, each rabbit underwent ultrasonic ablation. Specifically, for each lesion, a bone biopsy needle was placed into the geographical center of the lesion or at the edge of the lesion adjacent to vertebrae. This needle served as the working channel for the acoustic ablator (Fig. 1). The ablator energy pattern was either 360° circumferential or 180° directional. Following corroboration of ideal needle position with CTF guidance, 3 multisensor thermocouple...
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arrays were placed around the lesion to provide measurements of tissue temperature during ablation. Computed tomography scanning was again conducted to determine the spatial relationship of the implanted hardware with respect to the location and anatomy of the tumor (Fig. 2).

A single 360° or 180° radial acoustic ablator was then inserted down the working channel of the biopsy needle. Using temperature measurements from the implanted thermocouples, the tumor volumes were given an average of 10 minutes of treatment at temperatures of 50°–70°C, a necrosing tumoricidal dose. All animals were monitored for 24 hours to determine immediate and acute procedure-related morbidity and then were killed using an intravenous euthanasia solution in accordance with our institutional Animal Welfare and Safety Committee guidelines. Tissue samples containing tumor and peritumoral bone and soft tissue were harvested, sectioned, and stained to determine extent of tumor death and surrounding tissue damage. Temperature distribution data were used to reconstruct volumetric thermal dose delivered to tumor tissue, and the findings were spatially correlated with pathological findings.

Results

In all 12 rabbits, VX2 cells were successfully implanted, leading to grossly apparent spinal and paraspinal tissue masses. One rabbit was paraplegic on Day 21 prior to ablation (Fowl neurological Grade 0) due to tumor impingement on the spinal cord and was killed immediately following the ablative procedure. All other animals underwent ablation with no immediate or acute complications, all could walk immediately following the procedure, and all were assigned pre- and postoperative Fowl neurological grades of 2. Computed tomography fluoroscopic guidance provided accurate placement of the acoustic ablator in all tumors, as corroborated on gross and microscopic histological inspection (Fig. 3). To further define the anatomical relationship of the ablator, acoustic energy field, and tumor volume, 3D reconstructions were created using data from the temperature probes and histological and radiographic information. Furthermore, significant tumor death (> 90% assessed cross sectionally) was noted in all specimens without collateral damage to nearby nerve tissue. Marginal death—that is, tissue destruction just beyond the margin of the tumor—was noted in some, but not all, specimens. Reconstruction of temperature distribution data allowed accurate assessment of volumetric thermal dose delivered to tissues (Fig. 4).

Discussion

Current methods of surgical treatment for spinal...
Column neoplastic disease consist of highly invasive procedures, such as vertebrectomy or corpectomy with complex spinal reconstruction, which aim to achieve substantial tumor removal and spinal column stabilization but carry inherent risks due to their duration, complexity, and associated surgical and neurological morbidities. Percutaneous vertebroplasty provides a minimally invasive alternative that can swiftly and adequately treat symptoms, but has high rates of tumor persistence. Radiofrequency ablation has been used successfully to treat a variety of solid tumors in other organs and has the potential to provide tumor control while still remaining minimally invasive. The spinal column, however, presents the challenge of adequately ablating tumors while preserving closely adjacent neural structures. We hope to overcome such a treatment barrier by combining HIU applicators with CTF guidance for accurate placement of the directional ultrasound therapy probe and, therefore, more spatially precise and targeted delivery of the HIU to the tumor. In this study, we used an animal model to test the feasibility of CTF-guided HIU for vertebral neoplasms.

In this current study, rabbit VX2 carcinoma cells were implanted under CTF guidance into the lowest lumbar vertebral body in each of 12 adult male New Zealand White rabbits. This led to the successful growth of a vertebral mass involving paravertebral tissue in all rabbits, as confirmed by CT scanning on Day 21. After imaging on Day 21, each of the rabbits underwent ultrasound ablation procedures, after which there were no acute adverse events, and no paraplegia was noted. Histological analysis of tumor and peritumoral tissue demonstrated significant tumor death in all of the specimens as well as no significant damage to adjacent neural structures. Furthermore, temperature distribution measurements allowed for the spatial reconstruction of thermal dose delivery to each tumor volume.

One rabbit experienced paraplegia prior to tumor ablation. It is important to note that the rabbit spinal cord traverses the entire length of its lumbar spine, in contrast to the human L1–2 conus medullaris. The variance between rabbit and human anatomy should be considered when interpreting neurological outcomes from this experimental model. To establish a context for future projects, it is also important to clarify that acoustic ablation necrotizes the tumor but does not measurably alter the tumor’s mass. Therefore, immediate improvement in neurological function would not be expected in an impaired individual, as this would require a reduction in gross tumor size. Such a scenario does not pertain to the current study, as all but one animal suffered no neurological deficits prior to ablation.

In 1960, Fry and Fry\textsuperscript{23} were the first to describe the use of high-intensity ultrasound technology for neurosurgical applications. High-intensity focused ultrasound has since gained popularity as a treatment modality for prostate cancer, with recurrence-free survival outcomes nearing those of radiation therapy.\textsuperscript{53} Lafon et al.\textsuperscript{35–38,40,41} and Diederich et al.\textsuperscript{16} have pioneered the development of interstitial ultrasound applicators, or HIU, now being investigated in animal models for use in the ablation of liver tumors, as well as for the endoscopic ablation of esophageal and other gastrointestinal tract malignancies.\textsuperscript{15,35–38,40,41,55} High-intensity interstitial ultrasound is a promising technology for the ablation of spinal tumors that are inaccessible to HIFU and are poor candidates for RFA because of their proximity to sensitive neurological structures.\textsuperscript{39,49} Because it is less invasive than percutane-
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An important component of this study was the use of CTF to guide HIIU applicator placement. Computed tomography fluoroscopic guidance improves on CT imaging by providing image acquisition and reconstruction at 6–8 frames per second or nearly real-time speed. First introduced by Katada et al.30,31 in 1993, the technology has been most commonly used for percutaneous interventional procedures such as biopsy and abscess drainage in the thorax and abdomen, as well as for various surgical procedures throughout the body, including drainage of intracranial hematomas. Some investigators have reported potential benefits such as decreased needle placement time, decreased overall procedure time, decreased patient radiation exposure, and improved diagnostic accuracy compared with conventional CT-guided procedures.5,25,32,56 Computed tomography fluoroscopic guidance has also been shown to have benefits when used in spinal procedures such as percutaneous vertebroplasty, and it has been used for various procedures including RFA treatment of bone metastases and percutaneous spinal fixation procedures.6,26,54 In this study, we demonstrated the successful use of CTF to provide real-time guidance for the accurate placement of the HIIU applicators into tumors.

Using the rabbit intravertebral tumor model developed at our institution, we have been able to successfully deliver tumoricidal doses of acoustic energy via an RFA probe that was placed percutaneously with CTF guidance. In this way, we established the technical and preclinical feasibility of controlled ultrasound ablation of spinal tumors in vivo. Data from this initial set of animals are being integrated into a rabbit-based navigation software system. The next set of animal experiments will involve additional technical developments including frameless anatomical imaging (Fig. 5), the integration of enhanced tumor imaging, and modified acoustic ablators capable of more accurate energy delivery.14,48,61

**Conclusions**

Use of an HIIU ablation probe placed via CTF guidance successfully killed tumor cells in a rabbit spine tumor model without leading to collateral neurological damage. From these initial experiments, we hope to develop a family of HIIU ablators that, according to measured physical parameters, are expected to be appropriate for conformal ultrasound ablation of primary and metastatic spinal tumors in humans.

**Disclosure**

Dr. Gokaslan owns stock in Spinal Kinetics and US Spine; receives clinical or research support from AO North America, Medtronic, DePuy, and Integra; and receives fellowship support and an honorarium from AO North America, where he is also a board member. Dr. Sciubba receives an honorarium from DePuy Spine. Dr. Diederich is the inventor and patent holder of the technology described in this study.

**Fig. 4.** Graph demonstrating temperature distribution and maximal volumetric thermal dose delivered to target tissues measured by the temperature probes.

**Fig. 5.** Illustration of interstitial ablation technique using a rabbit-based navigation system that will allow imaging of the spine without external fixation.
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