Comparison of Tissue Injury from Focused Ultrasonic Propulsion of Kidney Stones Versus Extracorporeal Shock Wave Lithotripsy

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Purpose: Focused ultrasonic propulsion is a new noninvasive technique designed to move kidney stones and stone fragments out of the urinary collecting system. However, to our knowledge the extent of tissue injury associated with this technique is not known. We quantitated the amount of tissue injury produced by focused ultrasonic propulsion under simulated clinical treatment conditions and under conditions of higher power or continuous duty cycles. We compared those results to extracorporeal shock wave lithotripsy injury.

Materials and Methods: A human calcium oxalate monohydrate stone and/or nickel beads were implanted by ureteroscopy in 3 kidneys of live pigs weighing 45 to 55 kg and repositioned using focused ultrasonic propulsion. Additional pig kidneys were exposed to extracorporeal shock wave lithotripsy level pulse intensity or continuous ultrasound exposure 10 minutes in duration using an ultrasound probe transcutaneously or on the kidney. These kidneys were compared to 6 treated with an unmodified Dornier HM3 lithotripter (Dornier Medical Systems, Kennesaw, Georgia) using 2,400 shocks at 120 shock waves per minute and 24 kV. Histological analysis was performed to assess the volume of hemorrhagic tissue injury created by each technique according to the percent of functional renal volume.

Results: Extracorporeal shock wave lithotripsy produced a mean ± SEM lesion of 1.56% ± 0.45% of functional renal volume. Ultrasonic propulsion produced no detectable lesion with simulated clinical treatment. A lesion of 0.46% ± 0.37% or 1.15% ± 0.49% of functional renal volume was produced when excessive treatment parameters were used with the ultrasound probe placed on the kidney.

Conclusions: Focused ultrasonic propulsion produced no detectable morphological injury to the renal parenchyma when using clinical treatment parameters but produced injury comparable in size to that of extracorporeal shock wave lithotripsy when using excessive treatment parameters.

Key Words: kidney, nephrolithiasis, high-intensity focused ultrasound ablation, lithotripsy, iatrogenic disease

Abbreviations and Acronyms

p+ = peak positive pressure

SPPA = spatial peak pulse average

SW = shock wave

SWL = extracorporeal SW lithotripsy

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A recent analysis of NHANES (National Health and Nutrition Examination Survey) data indicated that the prevalence of stone disease in the United States increased markedly in the last 20 years from 5.2% of the population in the early 1990s to 8.8% in 2010.[1] Unfortunately, this trend will presumably be sustained into the future, placing an increasing burden on health care services because of limited resources and urologist availability. Knowing that the strain of caring for patients with stones is increasing highlights the need to make stone removal technology as effective and efficient as possible.

Successful removal of renal stones often requires 2 separate steps, including fracturing the calculus into small pieces and subsequently removing those stone fragments. The primary modality for fragmenting kidney stones is currently SWL. Many patients choose SWL because it is noninvasive and can be performed on an outpatient basis. While the overall success of this technique is impressive, SWL leaves residual fragments in many patients. As an added concern, several groups have suggested that the effectiveness of SWL has decreased among newer generation machines,[2–5] raising the fear that residual fragments will become more common. Having residual fragments after treatment is not confined only to SWL since recent reports showed that as many as 38% of patients retained detectible fragments after ureteroscopic stone removal[6] and up to 79% retained fragments after percutaneous nephrolithotomy.[7]

Residual stone fragments in the urinary collecting system are a clinical problem that represents a challenge to rendering patients truly stone free. The main concern with fragmented calculi in the urinary tract is that these residual fragments increase the risk of future stone growth and recurrent symptoms.[8–11] Because of this concern, several studies have focused on the optimal management of stones prone to produce difficult to displace fragments, such as fragments from calculi in lower pole calyces.[12–14] While procedures such as diuresis, percussion and inversion therapy are helpful for displacing fragments, measureable amounts of fragments remain resistant to removal.[15,16]

Focused ultrasonic propulsion is a new, noninvasive technique designed to move kidney stones and residual fragments out of the urinary collecting system using focused ultrasound energy. Preliminary in vitro and in vivo studies of this technology showed significant success at lifting and maneuvering implanted artificial stones and human urinary calculi out of the renal calyces.[17,18] This technique could be used in conjunction with any stone removal procedure to help expel residual fragments. However, since ultrasonic propulsion is a noninvasive procedure, it would be particularly attractive when coupled with SWL. While this technique shows promise, little is known about the potential for tissue damage using focused ultrasound under these conditions.

Ultrasonic propulsion has similarities to SWL, in that each is transcutaneous with focused acoustic energy originating from an extracorporeal source. However, for an estimated 20 to 40-minute treatment ultrasonic propulsion generates pulses with substantially lower pressure (12 vs 35 to 110 MPa) and lower total energy (25 vs 100 to 200 J) delivered to a kidney than SWL. Because the amount of energy delivered to a kidney by ultrasonic propulsion is considerably less than that produced by SWL, injury from ultrasonic propulsion would be expected to be less than that from SWL. We compared the volume of tissue injury produced by focused ultrasonic propulsion vs that produced by SWL under situations mimicking clinical treatment conditions.

MATERIALS AND METHODS

Ultrasonic Propulsion Machines

Two prototype focused ultrasonic propulsion machines were described previously.[17–19] The original system, referred to as the research system, which was developed for high intensity focused ultrasound applications, was used to initially test and refine the ultrasonic propulsion concept. This system consisted of an 8 cm diameter, water filled source head that included an annular therapy transducer and a diagnostic imaging probe. Separate systems drove the therapy probe and performed imaging, and only focal length could be adjusted electronically.[17,18] A newer, more advanced treatment system was developed and termed the clinical prototype system.[19] It consists of an ultrasound engine (Verasonics®), an HDI C5-2 or P4-1 ultrasound imaging probe (Philips Healthcare, Andover, Massachusetts), a computer processor and a monitor display. The user can target, push and observe stone movement on the touchscreen in real time. The duration of each push attempt is 1 to 2 seconds, as selected by the user. A 1-second push delivers a 100-μsecond pulse, which is repeated every 3 millisecond for 1 second or in other words a 3.3% duty cycle for 1 second. When working at a depth of 7 cm, this clinical prototype produces 12 MPa peak pressure and an average peak pulse intensity of 2,400 W/cm^2 in situ.

Animal Studies

The surgical and animal treatment protocols used to assess renal injury in this study were done in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and were approved by the University of Washington and Indiana University School of Medicine institutional animal care and use committees.

Experiments

Ultrasonic propulsion. Ureteroscopic surgery was performed on 3 kidneys in 3 female farm pigs (Hardin Farms, Danville, Indiana) weighing 45 to 55 kg while under