**Recent Questions and Answers**

**Q:** *Is the pig an appropriate animal model for SWL research?*

**A:** The pig is regarded as the best animal model for the study of the effects of SWL on renal structure and function, and the scientific community that is studying the bioeffects of SWL on the kidney concur. (A PubMed search shows that the number of SWL studies performed in the swine are more than double that of any other species.) Porcine kidneys resemble human kidneys in size, weight, architecture and overall function.\(^1\)\(^-\)\(^3\) These similarities permit us to apply SWL to pig kidneys in the same setting as clinical lithotripters used for SWL in patients. This is not feasible with smaller animals.


**Q:** *Will shock wave lithotripsy at higher (but safer) doses result in improved stone comminution and clinical outcomes?*

**A:** SWL is rarely 100% effective in a single treatment session. Indeed, the stone-free rate for treatment in one session is typically only ~50%.\(^1\) As such, to be rendered stone-free the majority of patients require retreatment by SWL or subsequent intervention using an ancillary invasive procedure such as ureteroscopy.

In vitro tests have shown conclusively that the overall efficiency of stone breakage by SWs is dependent on the dose of SWs applied.\(^2\) That is, the comminution of stone mineral increases with the number of SWs delivered. However, most lithotripters cannot be used to deliver more than ~2500 SWs, an FDA imposed limit on treatment dose. This dose limit differs only slightly for different lithotripters and is determined from animal testing conducted by the manufacturers. Importantly, such animal testing has never employed procedures for SW delivery shown to be protective. That is, existing limits for SW dose set by the FDA are based on studies that did not employ an injury-protective strategy such as slow SW rate or stepwise ramping of SW voltage. As such, a principal factor that limits the effectiveness of SWL during a single session is the FDA imposed limit on treatment dose.

We propose that current limits on SW number in a single session can be exceeded provided the treatment protocol is refined utilizing the principles of tissue-protective-treatment-strategies in concert with other procedural steps, such as unobstructed acoustic coupling, know to improve efficient delivery of SW energy to the stone. This will undoubtedly result in more complete stone breakage and improved outcomes.

1. Cui et al., Urolithiasis 41:231, 2013

Q: Are tissue-protective strategies for SWL transferable among lithotripter devices?

A: All lithotripters produce a pressure pulse that has fundamentally the same waveform. The distinguishing feature is the acoustic output, which is described primarily by the magnitude of the acoustic pressures produced and the dimensions of the focal zone. Much of the research work on tissue-protective strategies for SWL has been performed on pigs using the Dornier electrohydraulic HM3 lithotripter. We have begun to examine the effects of a SW voltage ramping strategy for tissue protection in pigs using the Compact S electromagnetic lithotripter. Our preliminary findings show that delivery of 2500 SWs at power level (PL) 6 caused an average lesion size of 7.5% FRV (Functional Renal Volume), whereas treatment with SWs at PL1 followed by 2500 SWs at PL 6 caused an average lesion size of only 2.8% FRV—a 62% reduction in lesion size. Such tissue-protective strategies are beginning to be incorporated into clinical practice with reports of reduced tissue injury, as measured by urinary biomarkers of kidney injury and inflammation, in stone patients treated with the Doli 50 electromagnetic lithotripter, Compact S electromagnetic lithotripter, or Sonolith Vision electroconductive lithotripter. Although some optimization will undoubtedly be needed to achieve maximal tissue protective benefits, both animal and clinical data would suggest that tissue-protective strategies are transferable among lithotripter devices.


Q: What is the primary mechanism for the success of tissue-protective strategies?

A: SWs can injure renal tissue. The primary acute lesion is vascular trauma with breakage of blood vessels and pooling of blood within and/or surrounding the kidney. The mechanism(s) involved in the success of tissue-protective strategies in SWL is unknown, but we have shown that such a SWL strategy enhances renal vasoconstriction—using Doppler measurements of resistive index in renal arterioles—at a time when tissue injury would normally be expected to occur. We propose that a constricted blood vessel would be stiffer and less susceptible to rupture by SWs forces and there would be less bleeding within the renal tissue to support SW-induced cavitation activity. Such factors could contribute to protecting the kidney from the damaging effects of SWs.

Q: How will you test the renal vasoconstriction hypothesis?

A. We will monitor renal blood flow in real time with implanted flow probe transducers on the renal artery and titrate renal blood flow to levels that should either express or suppress the tissue protection phenomena if our working hypothesis is correct.

Q: How do you alter renal blood flow and will such a change in flow affect arterial blood pressure?
A: We and others have reported in small animal models that infusing vasoactive agents directly into the renal artery can alter blood flow without influencing arterial blood pressure.\textsuperscript{2-4} Based on our data from five pigs, renal blood flow decreased \(~30\%\) during intrarenal infusion of methoxamine (a stable norepinephrine analog given at a dose of 20 \(\mu g/min/kg\)) and increased \(~35\%\) during intrarenal infusion of acetylcholine (vasodilator agent given at a dose of 10 ng/min/kg). Neither infusion significantly altered arterial blood pressure.

1. Handa et al., BJUI 103:1270, 2009
2. Parekh, AJP 268:F967, 1995
3. Leong et al., AJP 292:F1726, 2007

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