Lithotripsy
Histotripsy
Extracorporeal Shock Wave Lithotripsy for Kidney Stones

- Kidney/Gall Bladder stones (minerals)
- affect 10% of the population
- 5-20 mm diameter
- Pain/bleeding in urine
Extracorporeal Shock Wave Lithotripsy

- 1980s – first introduced
- ~1m patients are treated with ESWL, but decreasing more recently

Water-bath Lithotriptors  Dry Lithotriptors
High Pressure Shock

- Shock Wave characterized by an abrupt, nearly discontinuous change in the characteristics of the medium.
- Over 1000 shock waves are required to progressively fragment the stones.

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$f \sim 15\text{MHz}$
Courtesy of Larry Crum, Ph.D. University of Washington
Lithotripsy Pulse

- short-duration (<10 ms)
- a compressive phase (peak pressure: 30–100 MPa)
- a tensile phase (negative pressure).
Mechanism of Shockwave Action

- Spall: distall
- Cavitation: proximal
- Squeezing: equator
- Superfocusing: internal caustic

Incident SW
If the length of the pulse is smaller than the stone, then because of the geometry of the stone surface and its internal structure, the compressive phase of the shock wave will generate pressure gradients, which can result in shear and tensile stresses in the stone. These stresses can produce tearing and shearing to fragment that stone.

The shock wave reflection at the stone–water interface, with pressure inversion and splitting off of stone material by the tensile stress of the reflected wave, is emphasized.
Spallation

1) Spallation:
After shock wave enters the stone and reflects from the back wall of the stone. Stone/urine interface inverts the large positive pressure, resulting in a large tensile stress. It is added to the stress of incoming negative pressure. Tensile stress makes material fail.

The fluid of the distal stone surface represents an acoustically soft interface, and the leading compressive phase will be reflected as a tensile wave. The amplitude of the tensile stress depends on the difference in acoustic impedance and the geometry of the stone surface. Using high-speed shadowgraphy to image stress waves in translucent model calculi, maximum tension occurred within the distal part, resulting in a fracture about a third of the way from the distal end. This fracture mechanism is considered similar to freezing water inside a brittle material.

Rassweiler et al. EAU Update Series 3, 2005
Cavitation

In addition to direct shock wave effects, cavitation generated by the negative pressure phase of shock waves occurs in the fluid surrounding stones and within microcracks or cleavage interfaces. For initial fragmentation, cavitation is less relevant but becomes important as stone fragments become smaller. Cavitation-induced erosion is especially observed at the anterior surface of stones. Suppression of cavitation using highly viscous media, hyperpressure, or overpressure significantly reduces disintegrative shock wave efficacy. Recognition of the role of cavitation in stone comminution has led to efforts to enhance the action of cavitation bubbles, such as tandem shock waves generated using a piezoelectric source fitted to an electrohydraulic system, with an additional discharge circuit to produce the second pulse. However, cavitation can be detrimental to fragmentation, as it results in production of gas bubbles lasting for many seconds, therefore attenuating subsequent impulses.

Rassweiler et al. EAU Update Series 3, 2005
Quasi-static squeezing

If the focal spot is broader than the stone, then pressure waves travel in the fluid along the stone’s surface. The leading compressive phase can create circumferential stress, which acts on the stone by quasi-static squeezing, inducing a binary fragmentation with the first cleavage surfaces parallel or perpendicular to the axis of shock wave propagation. This process assumes that the shock wave velocity in the surrounding fluid is much lower than the elastic velocities within the stone. The longitudinal shock wave moves through the stone, leaving the thin waves in the fluid encircling and squeezing the stone. For squeezing to be effective, the focal width of the lithotripter must be wider than the stone; thus, high fragmentation efficiency will be promoted by large focal diameters up to 20 mm, and it is not necessary for a steep shock front to exist. Data suggest that positive pressure ($P_+$) could be reduced to 10–30 MPa—sufficient to overcome fracture thresholds (2–10 MPa). This hypothesis has stimulated discussions about the importance of larger focal sizes and lower pressures compared with small focal sizes with high pressures in large-aperture sources.

Rassweiler et al. EAU Update Series 3, 2005
Dynamic squeezing

blue - compressive stress above 20MPa and show the incident shock wave coming from below.

red - tensile stress exceeding 60 MPa

green - shear stress exceeding 40 MPa.

Leighton and Cleveland
Tissue Damage

Shock wave–induced renal trauma

According to animal experiments as well as kidney perfusion models, different dose-dependent morphologic findings can be distinguished: Damage of renal parenchyma primarily occurs at vessels and tubular cells. First, venules in the medulla are damaged (grade 1 lesion), followed by rupture of cortical arterioles (grade 2/3 lesion). The mechanical genesis of the initial damage is poorly understood, but hypotheses include tear and shear forces with the microstructure of the tissue or cavitation activity in vessels.

Cavitation-mediated tissue damage

Basic research reveals a differentiation between cavitation and pressure-induced cell damage. 20–50% of cell lysis is produced by shock wave pressure, depending on intensity. Once widespread cavitation has started, it is generally accepted that it dominates the tissue-damage process. For the HM3 lithotripter, it has been reported that it takes about a thousand impulses in a pig model for widespread cavitation to develop.
Attenuation

- higher for the positive pressure portion of the wave (higher frequencies)
- lower for the negative pressure portion of the wave (lower frequencies)

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Lithotripsy Challenges

- Avoiding damage to healthy tissue
- Size of the focal zone ~ 50 mm long (90 mm first generation)
- Breathing motion
Histotripsy

- Ultrasound-induced tissue disintegration
- Tissue outgases, boiling cavitation cloud, violently explodes
- Tissue is broken up into sub micron fragments or liquified
- Fast, effective, large volume
Histotripsy Regimes

Intrinsic Threshold Histotripsy
*University of Michigan*
3-20 μs bursts
80MPa (compression)
15-25MPa (rarefraction)
• inertial cavitation

Boiling Histotripsy
*University of Washington*
2-10 ms bursts,
40MPa (compressional)
10-15MPa (rarefraction)
• heat, then boiling
Histotripsy causes tissue “liquefaction”

Ultrasound pulses
1-10 ms

0.5-2 MHz

<50 μs

>10 MPa

Cardiac tissues

Kidney

Prostate

Boiling Histotripsy

Figure 17.6
Proposed mechanism of tissue fractionation by boiling histotripsy. From Simon et al. (2012), Physics
Sharply Demarcated Lesion
Image guidance for histotripsy

Scan Pattern

B-mode Image During Treatment

38 locations, 10-μs pulses, PRF = 50 Hz, P > 20 MPa, 2000 pulses at each location
Gross cross-section (fixed)  B-mode Image After Treatment
Image Appearance Post Histotripsy

- Histotripsy lesions appear hypoechoic (dark) on ultrasound images because tissues are disrupted into small debris that cannot effectively scatter ultrasound (backscatter reduction)

![Before](image1.png)  ![After](image2.png)

![Graph](graph.png)
Histotripsy vs Lithotripsy

- Typical waveforms

**Histotripsy**

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<td></td>
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\[ p^- = 22 \text{ MPa} \]
\[ p^+ = 74 \text{ MPa} \]

**Lithotripsy**

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\[ p^- = 14 \text{ MPa} \]
\[ p^+ = 76 \text{ MPa} \]

Larger bubbles produced by the long period of negative pressure help with stone cracking.