

Non-invasive cardiac pacing with image-guided focused ultrasound.

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SUPPLEMENTARY DATA

Passive Cavitation Detection (PCD)

A single-element PCD (Y133_MR, 10kHz – 20 MHz bandwidth, 5 mm active diameter, unfocused MR-compatible hydrophone, Sonic Concepts, WA, USA) was connected to a digitizer (Oscar, 12-bit, 100MHz sampling frequency, Gage Applied Technologies, DynamicSignal LLC, IL, USA) through a 20 dB preamplifier (PA133_MR, 100 kHz to 15 MHz operating band down to -3dB from max amplification, MR-compatible, Sonic Concepts, WA, USA) and used to passively acquire acoustic emissions during sonication. For *ex vivo* experiments, the device was positioned horizontally into the tank, at the vicinity of the heart, and oriented toward the sonicated region. *In vivo*, the device was positioned on the skin of the animal, using vertical and horizontal positions measured from MR images acquired prior to sonication. Time-frequency maps were derived from the backscattered temporal signal using a customized spectrogram function (Hamming window, 98% overlap, 1024-point Fast Fourier Transform in MATLAB® 2015b, Mathworks, MA, USA). Harmonics of the HIFU frequency were filtered out in order to account only for broadband noise. Total broadband energy within the 1.2-25 MHz frequency band was computed as a metric of inertial cavitation^{24,25} and compared to the same computation performed in the absence of sonication to determine noise level. An unpaired two-tailed Student's t-test was used to determine if the broadband energy measured was significantly higher ($p < 0.05$) than the noise for each

pressure. Results obtained from 2189 sonications *ex vivo* and 240 sonications *in vivo* targeting the left ventricle in both cases can be seen in figure 7.

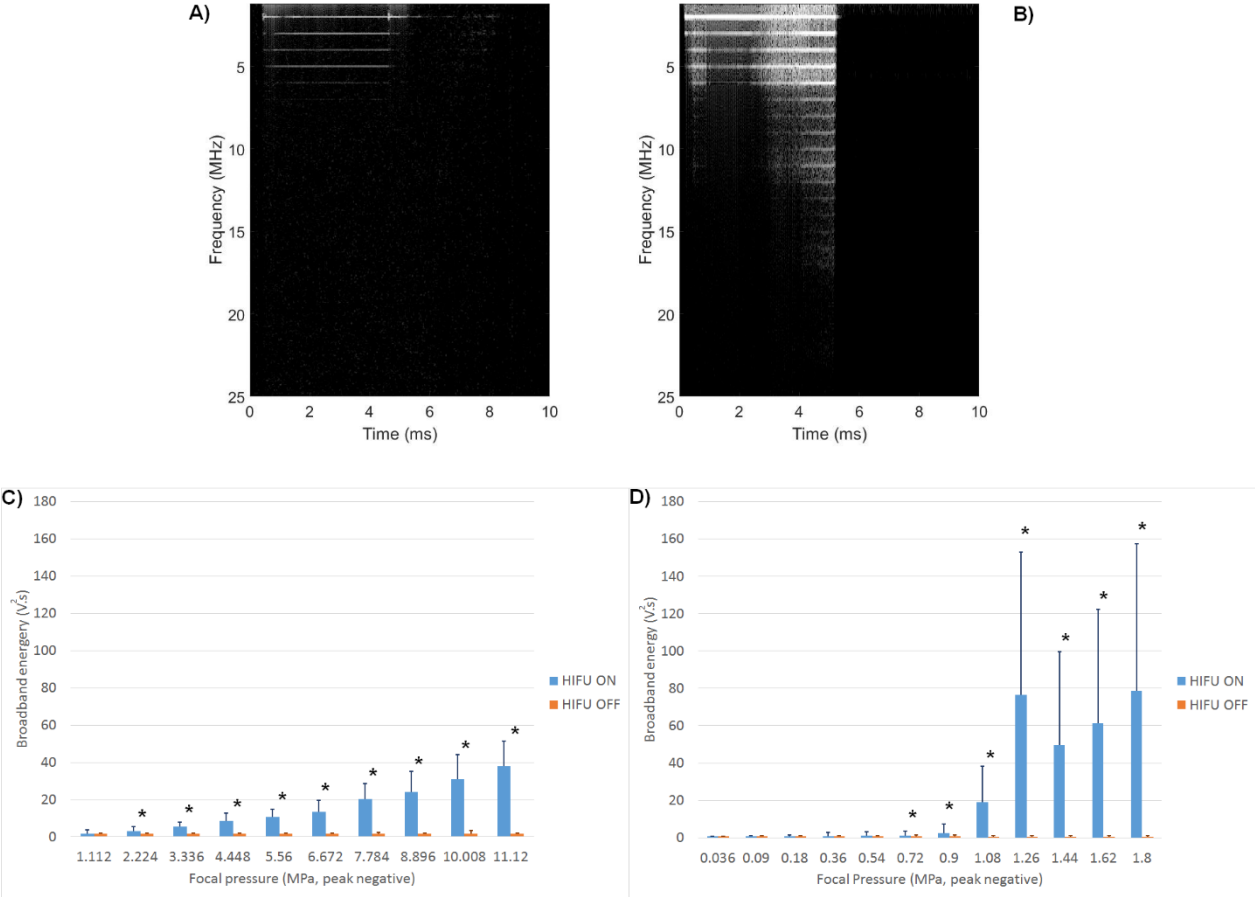


Figure 7. Examples of spectrograms in the 1.2MHz-25MHz frequency range obtained in vivo with no significant inertial cavitation (A) and with significant inertial cavitation (B). Histograms show values of broadband backscattered acoustic energy measured during both *ex vivo* (C, N=2189) and *in vivo* (D, N=240) experiments. * denotes a p-value < 0.05 (unpaired two-tailed Student's t-test) between acoustic sonication and noise level and therefore significant detection of inertial cavitation.