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Therapeutic ultrasound and sonoporation

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Introduction

Focussed ultrasound surgery can heat tissue to a temperature that causes protein denaturation and coagulative necrosis. For high-resolution focussed ultrasound microsurgery, high working frequencies are necessary. The manufacture of such equipment is technically challenging. Low acoustic amplitudes have been associated with increased cellular drug and gene uptake.

We studied tissue, microbubbles and cells, using commercial and self-built transducers operating at various frequencies, using very low or very high acoustic amplitudes.

Methods

We manufactured a high-frequency, high-intensity focussed ultrasound transducer, using lithium niobate as the active element.

To study acoustic cavitation, we designed and built a scientific instrument combining a pulsed laser and a high-intensity focussed ultrasound transducer, capable of nucleating at precise locations. The cavitation dynamics were recorded using high-speed cameras. At high acoustic intensities, interacting cavitation clouds were formed.

Results

Clusters formed at a quarter wavelength apart owing to radiation forces. We observed cluster coalescence and translation towards the capillary wall.

Microbubbles under sonication have been observed to create transient pores in adjacent cell membranes, also known as sonoporation. We observed lipid-shelled microbubbles near cancer cells under quasi-continuous low-amplitude sonication. Typically within a second of sonication, microbubbles were seen to enter the cells and dissolve. This new explanation of sonoporation was verified using high-speed photography and confocal fluorescence microscopy.

Our custom-built transducer was capable of creating $2.5 \times 3.4\ (\mathrm{mm})^2$ lesions without affecting surrounding tissue.

Such disruptive effects of ultrasound also have applications outside medicine. Since cyanobacteria contain gas vesicles, we hypothesised that these can be disrupted with the aid of ultrasound. During 1-hour sonication in the clinical diagnostic range, we forced blue-green algae to sink, thus promoting natural decay.

Conclusion

If drug and genes can be successfully coupled to acoustically active vehicles, sonoporation might revolutionise non-invasive therapy as we know it.