A breakthrough in medical acoustics

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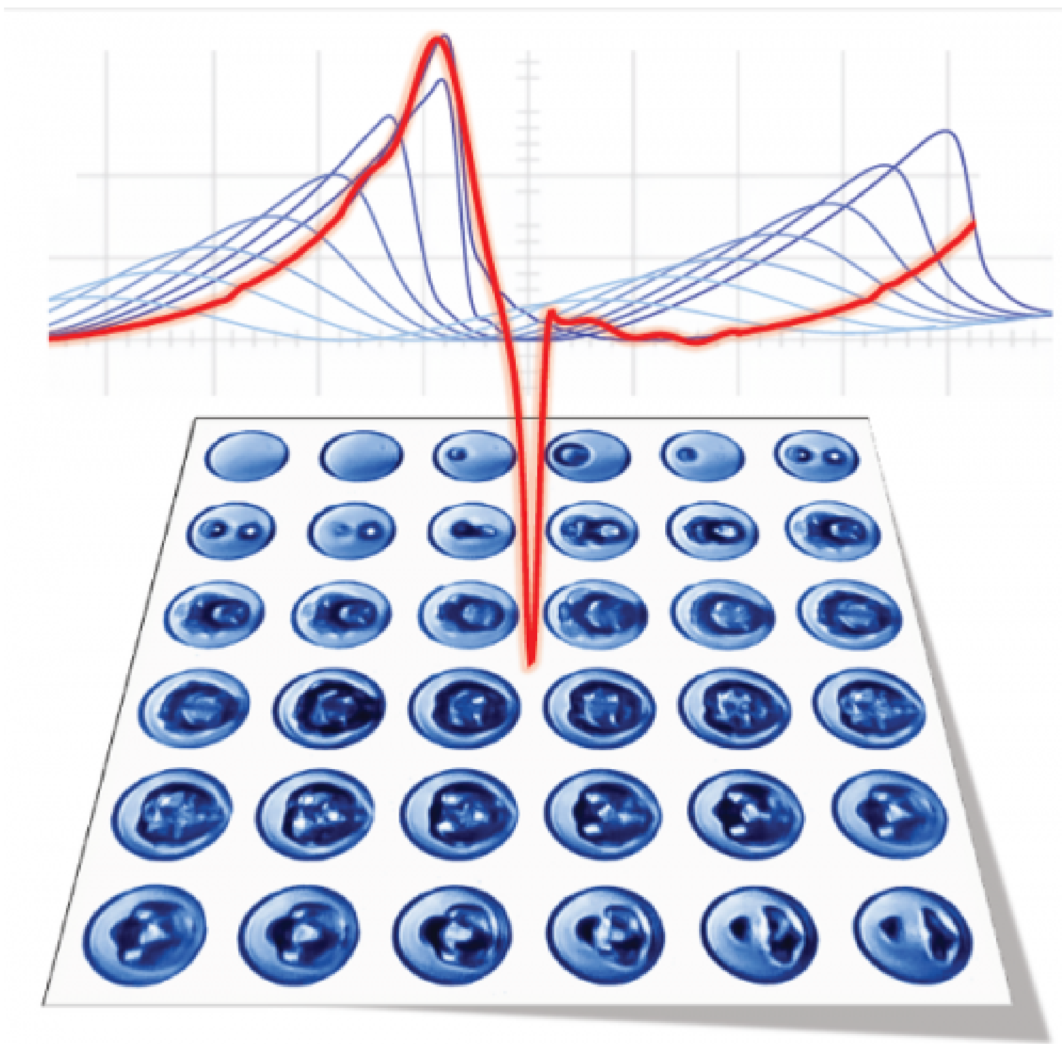

The ultrasound wave distorts to form a shock wave that is then focused within the drop. The highly focused ultrasound results in the vaporization of the drop, made visible here by Brandaris 128 high-speed imaging at a rate of 20 million frames per second (50 nanoseconds between each frame). Credit: PNAS

Researchers at the University of Twente, Delft University of Technology (TU Delft) and Erasmus MC (University Medical Center Rotterdam) have achieved a breakthrough in the field of medical ultrasound. Ultrasound irradiation has recently made it possible to activate minuscule nanodrops for diagnostic (tumour detection) and therapeutic (local administration of medicine) purposes. This breakthrough in medical acoustics was published in the leading scientific magazine *PNAS* last week.

Nanodrops with a boiling point below body temperature become overheated when injected, but do not spontaneously vaporize due to a thin shell applied around the drop. Once in the body, the drops are able to exit the bloodstream and enter the leaking circulatory system of tumours, for example, due to their small size. Through the administration of an intense pulse of ultrasound, the drops vaporize and form small bubbles of gas. Ultrasonographic equipment is then used to obtain an efficient image of the bubbles. Toxic medicines carried along in drops can also be delivered to tumours using this method, without any harmful side effects on healthy tissue in the rest of the body. The result is a local, controlled form of chemotherapy.

Mystery solved

For many years, exactly how ultrasound vaporizes drops remained a mystery. The required pressures were too high and the relationship with frequency was the exact opposite of what existing theory stated. Using images captured with the fastest camera in the world (the Brandaris 128), researchers noticed that the ultrasound was focused on one single point in the drops. Strangely enough, the wavelength of the ultrasound transmitted is many times greater than the drop and, just as with light, there can then be no lens effect.

Shock wave

The explanation can be found in a unique phenomenon that occurs during ultrasound propagation. Sound is a wave movement consisting of high and low pressure that is propelled forward according to the speed of the sound. But inside bodies, high pressure propagates faster than low pressure, which causes the wave to distort. This results in a shock wave. In effect, a whole series of harmonics result from the original sound. The wavelength of those harmonics is now much smaller, being the size of the drops. Combinations of various harmonics are able to interfere in the drops. This leads to a localized focus of sound with sufficient energy to cause the drop to vaporize.

"It was a real puzzle," says Michel Versluis, Professor of physical and medical acoustics at the University of Twente. "Fundamental physics theory, experiments at nanometre and nanosecond scale and advanced numerical simulations carried out in Delft and Rotterdam were combined to produce an elegant scientific explanation."

Safer and broader clinical application

"These new insights will allow us to develop a new class of nanodrops and to build new ultrasound sources, within which we can make clever use of those particular harmonics," adds Oleksandr Shpak, doctoral degree candidate at the Fundamenteel Onderzoek der Materie (FOM) foundation. This will enable us to reduce the pressures. This will lead to a safer and broader clinical application of this promising technique."

More information: Oleksandr Shpak, Martin Verweij, Hendrik J. Vos, Nico de Jong, Detlef Lohse, and Michel Versluis. "Acoustic droplet vaporization is initiated by superharmonic focusing." *PNAS* 2014 ; published ahead of print January 21, 2014, DOI:

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