Ultrasonics 91 (2019) 10–18

Contents lists available at ScienceDirect

Ultrasonics

journal homepage: www.elsevier.com/locate/ultras

Kriging model to study the dynamics of a bubble subjected to tandem shock waves as used in biomedical applications

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ARTICLE INFO

Keywords:
Tandem shock waves
Biomedical applications
Cavitation
Numerical simulation
Metamodel
Kriging

ABSTRACT

The purpose of this work was to develop a metamodel (Kriging model) to identify the most important input parameters of shock wave pressure profiles as used in biomedical applications without solving a large number of differential equations. Shock wave-induced cavitation is involved in several biological effects. During bubble collapse, secondary shock waves and microjets are formed. For some applications, it is desirable to enhance this phenomenon by applying a second shock wave before bubble collapse; however, the delay between the leading shock wave and the second pressure pulse has yet to be optimized. This optimization can be done using numerical analysis. A metamodel that predicts the most convenient ranges for the input variables and provides information on the joint effects between the input variables was tested. Because the metamodel is an analytical expression, running it fifty thousand times and analyzing variables, such as the pressure amplitude, delay between pulses, and pressure rise time, was fast and easy. Furthermore, this method can be a helpful tool to study the joint effect between the input variables and reduce the computation time. The metamodel can also be adapted to analyze simulations based on equations different from the Gilmore-Akulichev formulation, which was used in this study.

1. Introduction

The high efficacy of shock waves in treating patients with urinary calculi, a technique referred to as extracorporeal shock wave lithotripsy (SWL), motivated the use of such shock waves as an alternative treatment for stones in the gallbladder, the common bile duct, the pancreatic duct and the salivary gland ducts. There is a large variety of devices (lithotripters) to perform SWL, which all consist of a shock wave generator, a coupling device, a patient treatment table, and imaging systems (ultrasound and/or fluoroscopy). Extracorporeally generated shock waves enter the body through a fluid-filled cushion and are focused on the calculus by means of lenses, reflectors or spherically curved shock wave sources. From several hundred to a few thousand shock waves may be required to pulverize a stone. In urological SWL, stone debris passes through the urinary tract and is eliminated during the days following the treatment. Research has been focused on designing shock wave sources to emit pressure profiles that enhance stone comminution without increasing tissue damage [1]. Remarkably, shock waves are currently also used in a variety of clinical applications different from SWL, such as the treatment of the nonunion of long bones, plantar fasciitis, calcaneal spurs, tendinopathy of the shoulder, Achilles tendinopathy, epicondylitis of the elbow, heart diseases, erectile dysfunction, and chronic pelvic pain syndrome. Other promising uses are the shock wave-mediated transformation of bacteria and fungi, as well as human cell transfection [1]. The typical pressure waveforms used in biomedical applications consist of a 10–150 MPa compression pulse with a duration t^{+} of approximately 0.5–3 µs and a rise time between a few nanoseconds and approximately 500 ns, followed by a decompression pulse of up to -25 MPa with a duration of approximately 2–20 µs. The duration t^{+} is defined as the time from the instant when the pressure exceeds 50% of the peak positive pressure for the first time to the instant when the pressure drops again to this value. Energy flux densities vary between 0.2 and 2.0 mJ/mm^2 [1–3].

One of the most important stone comminution mechanisms during SWL is acoustic cavitation, i.e., the growth and collapse of bubbles in liquids resulting after a sudden pressure change, which plays a crucial role in obtaining small fragments. Microbubbles existing in the fluid close to the focal zone of a lithotripter suffer a forced collapse after the passage of the positive peak of each shock wave. An instant later, the high pressure inside the compressed bubbles and the trailing tensile

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https://doi.org/10.1016/j.ultras.2018.07.005
Received 26 May 2018; Received in revised form 12 July 2018; Accepted 12 July 2018

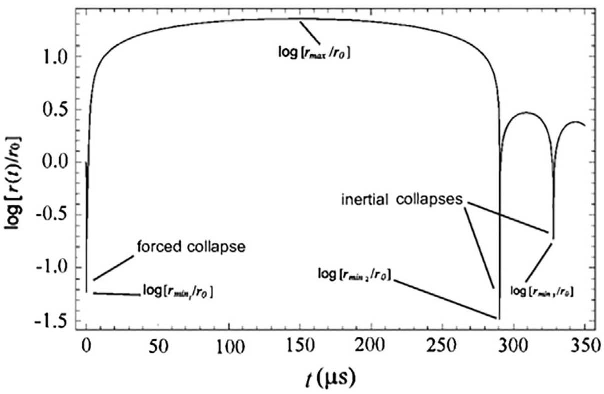

Fig. 1. Base 10 logarithm of the bubble radius $r(t)$ normalized by the initial bubble radius (r_o = 70 μm) plotted as a function of time after the passage of a typical lithotripter shock wave (positive pressure amplitude = 100 MPa). The second bubble collapse occurred at approximately 290 μs.

phase of the shock wave trigger their fast growth. As the volume of the bubbles increases, the pressure inside them decreases until they suffer a violent inertial collapse after hundreds of microseconds (Fig. 1). Bubble collapse is affected by the surrounding fluid and is generally asymmetrical. As a consequence, the pressure difference outside the bubble creates a high-speed fluid microjet that burrows through the bubble [4]. Secondary shock waves may be produced by the collision between the microjet and the inward-moving wall of each bubble. These secondary shock waves have a short range. Nevertheless, this phenomenon is considered to be an additional mechanism for increasing the efficacy of calculi disintegration. Even at positive pressure amplitudes of only 10 MPa, liquid microjets are emitted in the direction of the incoming shock wave [5]. The larger a bubble grows, the more violent its collapse will be. Shock wave-induced microjets are also useful to introduce large-sized molecules into cells for therapeutic applications and the genetic transformation of bacteria and fungi [1,5].

Bubble dynamics depend on several factors, such as the impinging pressure waveform, the content of dissolved gases, the viscosity, the surface tension, and the existence of cavitation nuclei. Cavitation may also be responsible for undesired effects on tissue. Fortunately, cavitation is less violent if the bubbles are constrained in soft tissue [1,6].

It is known that bubble collapse can be significantly enhanced if a second shock wave arrives just before the bubbles start to collapse [3,7]. Tandem shock waves is the name given to the production of two shock waves with a delay of approximately 10–900 μs between them; they have been generated using electrohydraulic shock wave sources with composite and confocal reflectors, as well as with two spark gaps [7–11], combined electrohydraulic and piezoelectric shock wave generators [12], and modified piezoelectric shock wave sources [13]. In vivo results have demonstrated that tandem shock waves may dramatically reduce SWL treatment times without increasing tissue damage [14,15]. Furthermore, exposing suspensions of gram-negative (*Escherichia coli*) and gram-positive (*Listeria monocytogenes*) bacteria to tandem shock waves significantly enhanced bacterial inactivation [16]. More recently, the genetic transformation of bacteria and filamentous fungi was increased by using tandem shock waves instead of conventional single-pulse shock waves [17,18]. As a further development, so-called "modified tandem shock waves", where a conventional shock wave (p_c) is followed by a relatively slow pressure pulse (p_s), were proposed [19] (see Fig. 2(a)). Because bubble collapse lasts tenths of microseconds, when using standard tandem shock waves, the negative tail of the second shock wave arrives during the inertial collapse. This effect can reduce the bubble collapse energy to a certain extent. If the second pressure pulse has a longer positive pulse duration, the positive pressure will be compressing the bubble during a longer time of its collapse, increasing the collapse energy and, as a consequence, enhancing

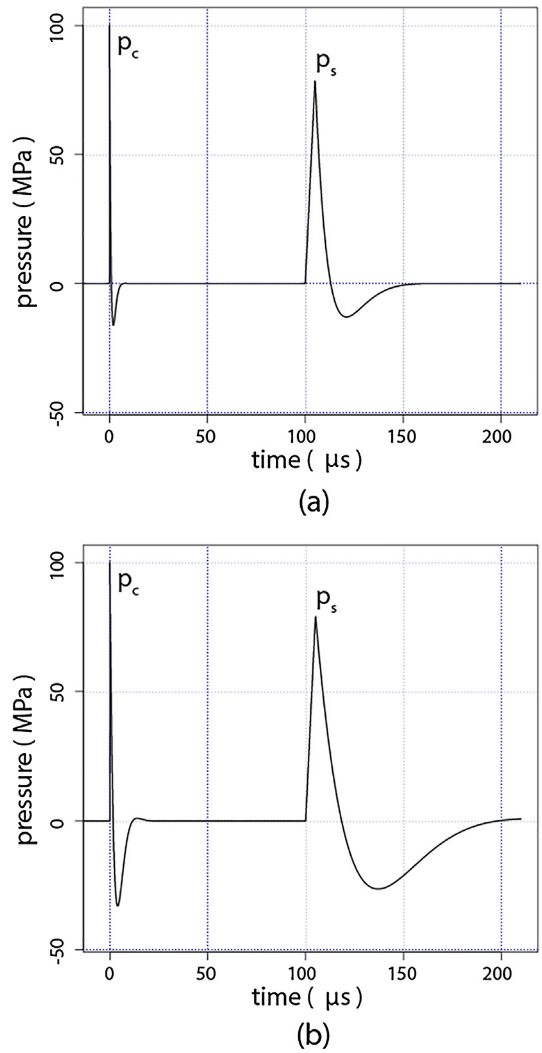

Fig. 2. Plots of two modified tandem shock waves, generated by substituting (a) α_1, ω_1 and (b) α_2, ω_2 in Eqs. (2) and (3). In both cases, t_r = 5 μs, p_1 = 100 MPa, and p_2 = 80 MPa. For clarity, Δt was chosen to be 100 μs.

microjet and secondary shock wave emissions.

The optimal delay between the leading shock wave and the second pressure wave depends on the specific application and in many cases has not been established. In vitro stone phantom fragmentation [13], dual passive cavitation detectors [20], recording of images with high-speed cameras [1], and pressure waves emitted from bubble collapses using hydrophones [1,21] may be helpful. Nevertheless, many experiments are required because the location and time of appearance of cavitation bubbles are of a statistical nature. To reduce the experimentation time, computer modeling of the dynamics of a bubble subjected to tandem shock waves at several different delays and pressure profiles has been useful [19,22]. In a previous publication, the influence of modified tandem shock waves on the collapse energy of a single bubble immersed in water was analyzed using a numerical simulation [19]. The results were compared with the dynamics of the same bubble subjected to standard tandem shock wave profiles. The main conclusion was that modified tandem shock waves could significantly improve SWL outcomes compared to those for standard tandem waves. In a second study, a numerical simulation was used to show that stress and cavitation can be enhanced using a pressure pulse with a long full width at half maximum, which reaches the urinary stone within hundreds of microseconds after two 20 μs-delayed initial shock waves [22].

Modified tandem shock waves can be generated using piezoelectric