Generator of focused shock waves in water for biomedical applications

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Résumé

Generator of focused two successive (tandem) shock waves in water (FTSW) based on the production of two pressure waves generated by underwater multichannel electrical discharges has been developed. In this work principles of generation of FTSW in water and the results on biological effects of focused tandem shock waves will be presented on *in vitro* and *in vivo* experiments.

Introduction

The generation of focused shock waves by a high-current spark discharge in water has been studied for many years in connection with extracorporeal lithotripsy of kidney stones. Early experiments showed that the rarefaction part of the generated shock waves is weak at the focus [1]. This weak rarefaction wave is due to the fact that the high-current spark discharge generates in water a spherical shock wave. Because the shock wave is situated in the focus of a metallic semi-ellipsoidal reflector, through the secondary focus is propagated without a change in the waveform. Cavitation bubbles created by the rarefaction wave and by the collapse of the discharge bubble relax near the discharge channel, and thus, the rarefaction wave is strongly dampened at the secondary focus. The great success of lithotripsy has stimulated research on the application of focused shock waves in other branches of medicine. Most of this attention has been focused on the possible treatments of some types of cancers. However, unlike kidney stones, cancer tissues are acoustically the same as the surrounding healthy tissues, and shock waves of the type used in lithotripters barely interact with cancer tissues. To achieve localized action of shock waves in an acoustically homogeneous medium such as soft tissue, the utilization of two subsequent (tandem) shock waves seems to be a possible option assuming that the first shock creates at the focal region an acoustic non-homogeneity (rarefaction wave) in water on which the second shock will dissipate.

For this purpose we have recently developed a generator of focused two successive (tandem) shock waves in water (FTSW), which is based on the production of two cylindrical pressure waves generated by underwater multichannel electrical discharges at two porous ceramic-coated cylindrical metallic electrodes of different diameter [2,3]. The primary cylindrical pressure waves generated at each electrode are generated with a set time delay between them, focused by a metallic parabolic reflector to a common focal point and only close to focus are transformed into a strong shock wave. We have found that at time interval of 10-15 μs between the two shocks the second, originally pressure wave, is strongly attenuated at the focal region and reaches the focus as a rarefaction wave. Amplitude of the pressure wave is up to 100 MPa, while the amplitude of the rarefaction wave falls down up to -80 MPa, producing thus at the focus a large number of cavitation bubbles. The collapsing cavitation bubbles produce secondary, short-wavelength shock waves and fast microjets that may be able to interact with cell-scale structures. In this work principles of generation of FTSW in water and the results on biological effects of focused tandem shock waves will be presented.

Experimental

Fig. 1 shows scheme of generator of focused two successive (tandem) shock waves in water. The generator is divided by acoustically transparent membrane into two parts. The first part, which is filled with highly conducting saline solution (with the conductivity of the order of tens of mS/cm), consists of two metallic cylindrical high-voltage electrodes of different diameter covered by a thin porous ceramic layer (composite anode) placed along the axis of the outer metallic parabolic reflector (cathode). The pulsed high voltage applied to the composite electrodes is provided by a pulse power supply that consists of two 0.4 μF capacitors charged up to 30 kV and two triggered spark gaps (SG). The focal point of the reflector is situated in the second part of the generator, which is filled with a tap water. Design of the composite electrode allows simultaneous generation of a large number of filamentary discharge channels in water, which are distributed almost homogeneously along the whole surface of the electrode at a moderated applied voltage (20-30 kV) [4]. Every discharge channel creates a semi-spherical pressure wave, and by superposition of all of the waves a cylindrical pressure wave propagating from the anode is formed. The primary cylindrical pressure wave is focused by a reflector and near the focus it is transformed into a strong shock wave.

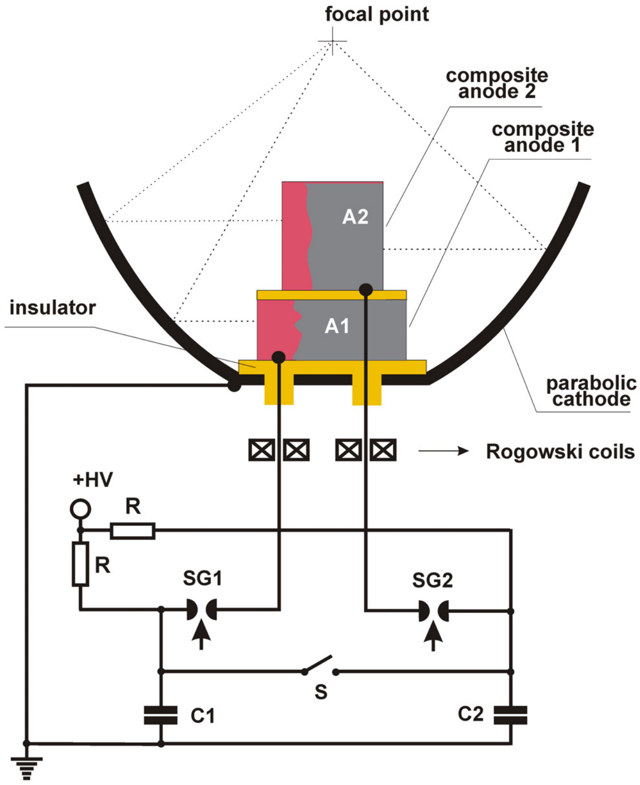

Fig. 1: Scheme of FTSW generator.

Results

Presented FTSW generator is used for investigation of biological effects of focused tandem shock waves. We have recently demonstrated *in vivo* using laboratory rabbits that such tandem shocks are capable of causing localized lesions at a predictable location deep inside soft animal tissue. In subsequent *in vitro* experiments, we have demonstrated that exposure of carcinomas cells to the tandem shocks results in cells membrane perforation and, at a higher dose, damage to the cells. Because healthy and cancerous tissues do not differ acoustically, the localized action of the shock waves in such an acoustically homogeneous medium (soft tissue) is generally due to cavitation bubbles produced by the rarefaction wave. Local (micrometer dimensions) thermal effects accompanying the collapse of cavitation bubbles (sonoluminescence) and production of chemical radicals may also play roles in cell damage. *Ex vivo* experiments on laboratory mice revealed that the tumors from the exposed cells grow much slowly than in controls. Currently, *in vivo* experiments on synergistic effects of the tandem shocks in combination with cytostatic and photo-/sono-sensitive anticancer drugs on the growth rate of tumors are preformed on laboratory rats. Preliminary results of these experiments and prospects of FTSW to enhance cytotoxic efficiency of anticancer drugs will be discussed.

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