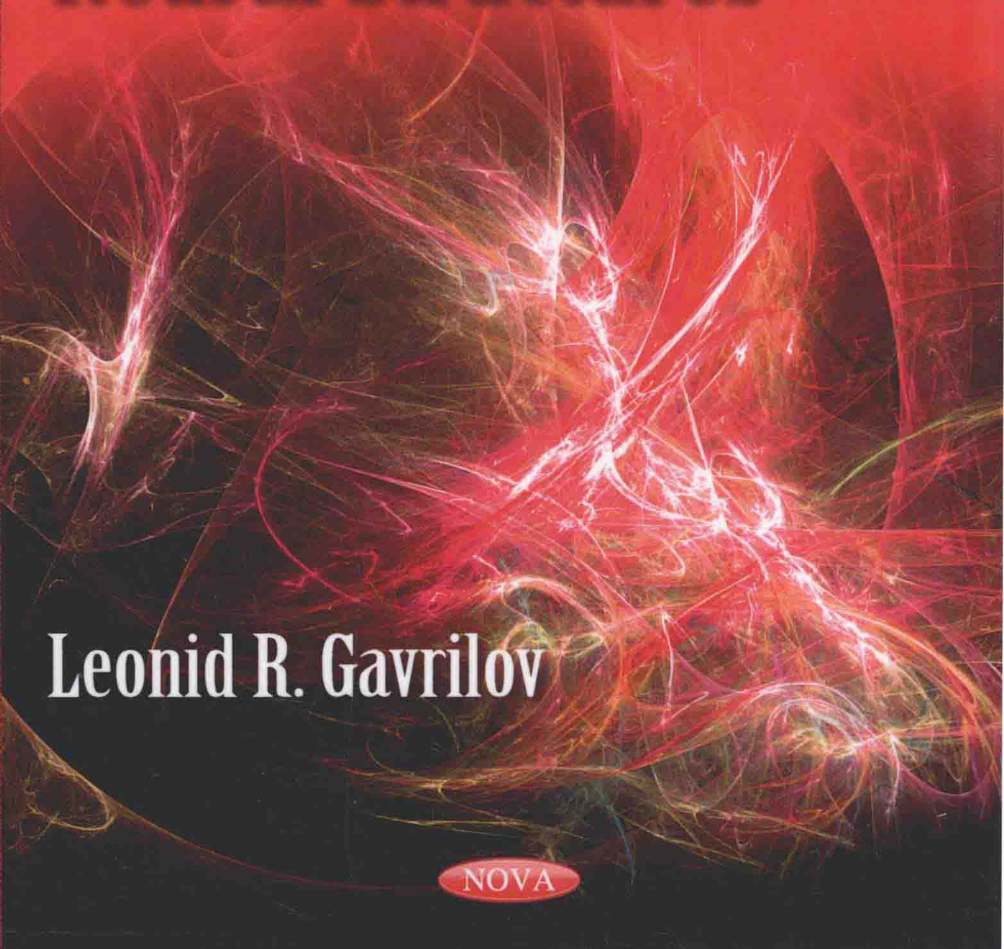
Acoustics Research and Technology

Use of Focused Ultrasound for Stimulation of Various Neural Structures



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Introduction

An important task of physiology and medicine was and is searching for artificial stimuli that can activate neural structures noninvasively and locally and induce different sensations. A wide-spread and classical means for stimulation of neural structures is an electric current. However, sometimes it is impossible to use this method for local stimulation of single receptors or other neural structures without affecting the neighboring ones. If it is necessary to activate a deep located structure, such the method couldn't be considered as a noninvasive one because the electrodes need to be in a direct contact with an activated structure. The subject of this book is the description and analysis of research on application of focused ultrasound for stimulation of somatosensory, hearing and other neural structures.

It is well-known that over the past several decades, focused ultrasound has become one of the most popular, safe and effective method for application in medicine amongst existing physical technologies. In fact, high-intensity focused ultrasound, or HIFU, is used widely for local ablation of diseased or damaged tissues. When for guidance of ultrasound treatment the magnetic resonance imaging (or MRI) is used, the method is called Magnetic Resonance-guided Focused Ultrasound (MRgFUS or MRgHIFU). When for such guidance an ultrasound diagnostic technique is preferable, the method is called Ultrasound-guided Focused Ultrasound (USgFUS or USgHIFU). MRgHIFU is approved for the treatment of uterine fibroids in the USA, Canada, Europe, Israel, Asia, etc. The devices based on the application of focused ultrasound are used in dozens of medical centers for minimally invasive treatment of prostate. In several countries, first of all in China, tens of thousands clinical trials were carried out for the treatment of cancers of the liver and kidney, breast, pancreas, bone, etc. Wide experiments were carried out to investigate possibilities of applications of focused ultrasound for control bleeding, targeted drug delivery to specific sites of the body, liposuction (removal of unwanted fat), for neurosurgery, including brain therapy through an intact skull, for destruction of tissues located behind the rib cage, for cardiology, etc. All these possibilities of focused ultrasound have been described in details in numerous books and reviews.

The studies analyzed in this book are related mainly with research into application of focused ultrasound for activation of peripheral receptor structures. Pulses (stimuli) of focused ultrasound in the frequency range from 0.5 up to 3.5 MHz and with the duration ranging from parts of milliseconds to hundreds milliseconds were used in these studies. The advantages of the proposed method of stimulating of neural structures are the following: (1) the method is noninvasive, since it doesn't require a destruction of tissues to access deep structures; (2) the size of a stimulated region can be controlled and varied by changes in ultrasound frequencies and parameters of a transducer, which provides selectivity and locality of the effect on neural structures; (3) it is possible to control precisely the parameters of an ultrasound stimulus, such as the intensity, duration, volume and area of action, and repetition frequency of stimuli; and (4) it is possible to affect not only the superficial structures (e.g., located in the skin), but also tissues deeply located in the body. It was shown that the use of amplitude-modulated ultrasound for inducing of hearing sensations has become a separate and important field of research useful for application in diagnostics of different hearing disorders as well as for prosthetics of hearing function of the deaf people. An important part of the book is investigations of the main affecting factors of focused ultrasound and mechanisms of its stimulating effects. The possibilities of the practical use of these effects including their applications in clinical medicine for diagnostics of different neurological, dermatological and hearing diseases are also presented in this book.

The results of all these studies, carried out in Russia from the beginning of 1970s and lasting up to nowadays, were published in several books and in dozens of articles and naturally, first of all, in Russian. So, at the moment, these publications are practically unknown to investigators in other countries and some of them have become a bibliographic rarity even in Russia. This book allows to present at least a part of the obtained results and to acquaint with them the colleagues and other readers interested in this field of the science. One of the aims of this book was also to submit a review and analysis of numerous works carried out in many countries and, first of all, in the USA, regarding the use of focused ultrasound for reversible effects on different neural structures, including the brain structures. Such well-known effects as so called ultrasound neurostimulation and neuromodulation of the brain structures will be discussed, as well as advantages and limitations of focused ultrasound as a tool for neuromodulation of the central nervous system.

An essential part of Chapters 2-5 of this book is based on the results obtained with many colleagues and, first of all, with a long-term co-author Dr. Efim M. Tsirulnikov, Leading Research Scientist at the Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences. Author expresses his sincere appreciation and gratitude to him.

The book is intended, first of all, for specialists in medical ultrasound and physiology, particularly in research of somatosensory, hearing and other neural structures, in clinical and experimental medicine, and also in biophysics, medical physics, and ultrasound applications. In the modern scientific literature there was no book, especially devoted to applications of focused ultrasound for stimulation of neural structures.

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Contents

Chapter I

Biological Effects of Focused Ultrasound

The content of this chapter is a discussion of biological effects of focused ultrasound and their mechanisms. These effects include heating, cavitation, and mechanical interactions of the acoustic field with the tissue due to the radiation force and acoustic streaming. Knowledge of basic mechanisms for the production of biological effects with ultrasound is critically important to the development of new ultrasonic methods for medical applications and for their safe and effective implementation in clinical practice. The reversible effects on brain and other neural structures, as well as effects of neurostimulation and neuromodulation of brain tissues will be discussed. In conclusion, advantages and limitation of focused ultrasound as an artificial stimulus will be considered.

1.1. Main Physical Factors of Focused Ultrasound

Effects of focusing of sound waves due to reflection from concave surfaces were known from immemorial times. Focusing of sound and ultrasound is similar to focusing light. In both cases effects of focusing can be implemented, for example, by means of collecting lenses, systems of mirrors or reflectors. However the most convenient, at least, for the purposes of medical ultrasound, appeared to be so called spherical focusing radiators (Rosenberg 1969) with a concave spherical surface. Other example of a device for focusing of ultrasound is the use of phased arrays allowing not only to steer electronically the focus over the space, but also to create several foci simultaneously.

The size of the focus is comparable with the wavelength of ultrasound. That means that if the size of a focal spot should be of the order of millimeter, it is necessary to use MHz-range ultrasound. Using of spherical focusing radiators allows focusing the ultrasonic energy near the center of curvature of the radiating surface. In this case, a wave front converging in the focus has a spherical form. Thus the intensity on the surface of the converging front increases in inverse proportion to a decreasing a surface of the front, i.e., according to the law $1/r^2$, where r is the radial coordinate counted from the center of the focal region. However because the geometric approach near the focus is inapplicable (Rosenberg 1969), the intensity in the center of the focal region does not achieve an infinity, and has a quite certain size.

Figure 1 (Gavrilov, Tsirulnikov 1980) presents the main geometrical characteristics of a spherical focusing radiator: R is the radius of a radiator; F is the focal length; a_m is the angle of convergence; h is the depth; r_0 is the radius and l is the length of the focal region.

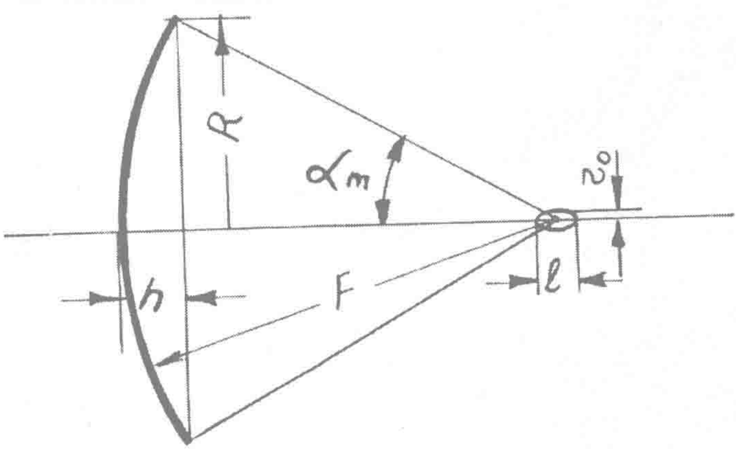

Figure 1. Main geometrical characteristics of a spherical focusing radiator (Gavrilov, Tsirulnikov 1980).

Let's presents the main relations for a single spherical focusing radiator (Rosenberg 1969). Formulae are received in the assumption that the distribution of amplitude of the particle velocity on the surface of the radiator is continuous and uniform.

Radius of the focal region is

$$r_o = 0.61\frac{\lambda F}{R}, \tag{1}$$

where $\lambda = c/f$ is the wavelength of ultrasound with the frequency f and velocity of propagation of ultrasound in the medium c.

Length of the focal region is

$$l = \frac{2\lambda}{1-\cos\alpha_m}. \tag{2}$$

For example, for a radiator with the resonant frequency of 1 MHz, with the radius and focal length equal to 42.5 and 70 mm, and the angle of convergence 36°, the diameter d and length l of the focal region are 3 and 15 mm. The maximal intensity in the center of the focal region with a not very large angle of convergence a_m (a_m <45°) is equal (Rosenberg 1969)

$$I_F = 3.7 I_o \frac{\pi R^2}{\pi r_o^{\,2}}, \tag{3}$$

where I_0 is the intensity at the surface of the radiator. The multiplier 3.7 shows that the intensity in the center of the focal region higher than the intensity averaged over its area, and also considers that through the focal spot passes only 84% of the focused energy, and 16% corresponds to the secondary maxima (Rosenberg 1969).

The pressure gain due to focusing is

$$K_p = 2\pi\frac{h}{\lambda}, \tag{4}$$

the oscillatory velocity gain is

$$K_v = K_p \cos^2\frac{\alpha_m}{2}, \tag{5}$$

the intensity gain is

$$K_I = K_p^{\,2} \cos^2 \frac{\alpha_m}{2}. \tag{6}$$

These simple relations allow defining the sizes of the focal region and values of the gain of a single focusing radiator with the accuracy applicable for practical purposes. In the majority of medical implications of focused ultrasound, when it is used for active action on a medium, the radiators with the diameter which is approximately equal to the radius of curvature of a radiating surface are applied; i.e., the angle of convergence is equal approximately 30°. In this case, the length of the focal region is approximately 5-6 times of its diameter. If the angle of convergence is smaller, the ratio of the diameter of the focal region to its length decreases. Therefore the locality of the effect on biological media and objects degrades, which, as a rule, is not appropriate for the users of this technique.

The geometry of a field of a spherical focusing radiator is shown in Figure 2 (Gavrilov, Tsirulnikov 1980).

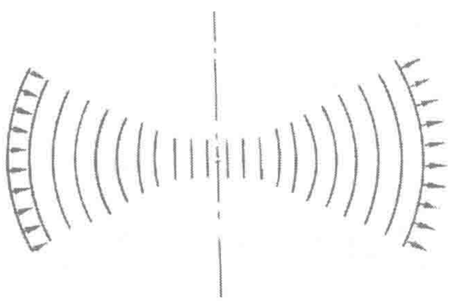

Figure 2. Geometry of a field of a spherical focusing radiator (Gavrilov, Tsirulnikov 1980)

To the left from the focal plane a converging wave is shown, on the right a divergent beam is seen. Thus, through the focal region within the limits of the main diffraction maximum a plane wave is passing. Therefore, for calculations of parameters of the sound field in the focal region, the plane wave approach is used (Bergmann 1954):

$$I = \frac{1}{2}\rho c \omega^2 A^2 = \frac{1}{2}\rho c V^2 = \frac{P^2}{2\rho c}, \tag{7}$$