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Biomedical applications of acoustic radiation force based on somatosensory reception

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We have previously shown that short pulses of focused ultrasound may be used to stimulate locally receptor neural structures and thereby induce all of the sensations that humans can perceive through the skin (for example tactile, warmth and cold, tickling, pain, etc.). Furthermore, ultrasound modulated by sound signals (tone, speech, music, etc.) can induce sound sensations corresponding to the nature of the modulation in people with normal hearing. It was shown that the radiation force associated with ultrasound was the mechanism underlying these effects that have been used for diagnosis in clinical practice. We also showed recently that the phenomenon of the radiation force could be used possibly in robotic systems, sensors, and automated control systems, based on the use of tactile sensations in the human-machine interface, as well as in devices that may allow blind and visually impaired persons to perceive textual information presented on a tactile display.

1 Early investigations

The radiation pressure of ultrasound may be used to stimulate receptor neural structures. It has been demonstrated during the 1970s that pulses of 1-3 MHz focused ultrasound of duration ranging usually from fractions to tens of milliseconds can induce a variety of somatic sensations in humans [1-3]. It was shown that by means of ultrasound stimulation it is possible to reproduce all of the sensations experienced by a human through the skin in everyday life, i.e., tactile, thermal (warmth and cold), tickling, itching, and also various kinds of pain sensations, including deep ones [1-7]. Fig. 1 illustrates the method of investigation of somatic sensations in a human hand. A focused transducer and the volunteer's hand were placed in a bath containing distilled water and the arm was fixed in a special mould [3]. A removable focus pointer was mounted to the transducer to locate the center of the focal region. Stimuli of focused ultrasound with frequencies of 0.48, 0.88, 1.95 and 2.67 MHz and with durations of 1, 10 and 100 ms were generally used. The intensity of the stimuli was increased until a sensation was reported by the volunteer. After that the person was asked to describe its character.

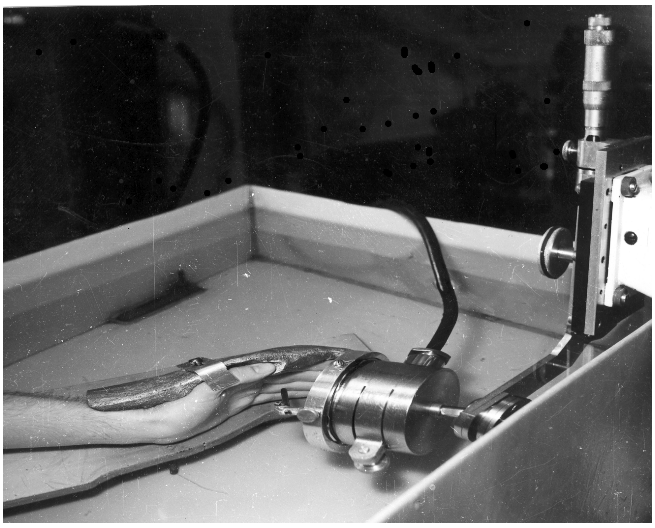

Fig. 1. Stimulation of skin receptors on the volunteer's hand by pulses of focused ultrasound.

It was shown also that ultrasound modulated by sound signals (tone, speech, music, etc.) can induce in humans sound sensations corresponding to the character of modulation in persons with normal hearing [3-5, 7].

2 Mechanisms. Role of the radiation pressure

To use the stimulating effect of ultrasound efficiently in practice, it is important to understand its mechanism. Investigations showed that the most likely factor responsible for inducing auditory sensations in humans is the effect of sonic oscillations arising from the variable components of the radiation pressure acting on the receptors in the labyrinth [3-4, 7]. Dalecki et al. [8] in their experiments with unfocused ultrasound transducer and a piece of plastic placed on the skin surface to exclude propagation of ultrasound inside the tissue, suggested that the radiation force was the main acting factor responsible for the inducing of tactile sensations. The essential difference between this approach and the one described above was that, in our studies, focused ultrasound was used for a direct stimulating action on neural structures, including deep ones.

In our research we also tried to identify the mechanism responsible for the stimulation of skin and tissue receptor structures [2–5, 7]. The purpose of these studies was to determine which ultrasonic parameter was least dependent on ultrasonic frequency, which was varied from 0.5 to 2.7 MHz. Although that parameter appeared to be the amplitude of displacement (i.e. an alternating-sign factor), it seemed logical that such a factor should be related to the unidirectional mechanical effect of ultrasound caused by the demodulation of high-frequency ultrasonic oscillations [3–5, 7]. It was evident that such a parameter could be the radiation force which is proportional to the acoustic power. Investigations of tactile sensations showed that with an almost 6-fold change of the frequency, and therefore with approximately a 30-fold change in the area of the focal region (i.e. the area of stimulation of neural structures), the product of the threshold intensity to the area of the focal region was approximately constant. However, it was not completely clear why, in the case of high frequencies, we never observed the small values for threshold intensity seen at low frequencies, even though in the case of the highest frequency the dimensions of the focal region were always much larger than the dimensions of the sonicated receptor structures.

The next step in the investigation of the mechanism underlying the stimulating effect of ultrasound was described in [9]. One purpose of this study was to determine why the threshold value of the radiation force necessary to stimulate tactile sensations does not depend on the area of its action. The mechanism based on generation of shear waves with relatively large values of displacement amplitude under the effect of the radiation force has been suggested. For example, it was demonstrated by previous investigators [10] that focused amplitude-modulated ultrasound with parameters similar to those necessary for stimulation of neural structures could generate displacements in a tissue of approximately 30–40 μm. In [11], an expression was obtained for the maximum displacement amplitude $u_{\max}$ in a medium associated with relatively short pulses of focused ultrasound whose duration did not exceed the propagation time of the pulse through the focal region. In our paper [9] this expression has been modified for longer pulses, whose duration is larger than the propagation time through the focal region, corresponding to the case of stimulation of neural structures. In this case, the maximum value of the displacement amplitude is

$$u_{\max} = \frac{\alpha_0}{\rho c_l c_t^2} a^2 I = \frac{\alpha_0}{c_t \mu} a^2 I = const * W$$

$$\text{for long pulses } \ (t_0 >> a / c_t), \qquad (1)$$

where a is the radius of the focal region, α_0 is the ultrasonic absorption coefficient in the medium, t_o is the duration of the pulse, ρ is the density of the medium, $c_t = \sqrt{\mu / \rho}$ is the propagation velocity of shear waves, μ is the shear modulus of the medium, c_l is the velocity of longitudinal waves, and I and W are the intensity and acoustic power averaged over the pulse duration. Thus, the maximum value of the displacement amplitude is proportional to the acoustic power and, therefore, to the radiation force. Figure 2 illustrates the shape of an acoustic signal, the acoustic power, and the shear displacement of the medium during the action of ultrasound on it.

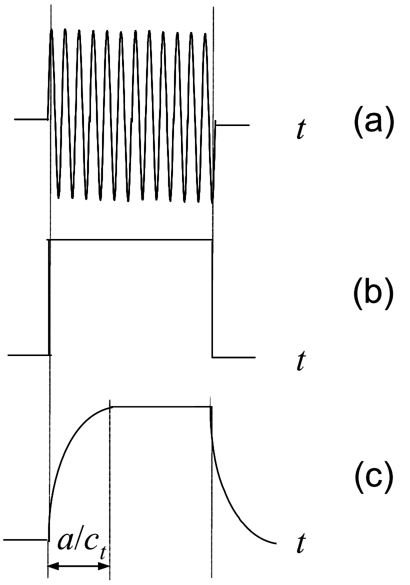

Fig. 2. Diagram illustrating the shape of (a) an acoustic signal, (b) acoustic power, and (c) shear displacement of the medium.

One can see that the displacement of the medium (Fig. 2c) does not reproduce the shape of the acoustic signal (Fig. 2a) or the acoustic power (Fig. 2b). The displacement achieves its maximum value $u_{\max}$ after a time lag equal to the propagation time of a shear wave through the focal region ($t_0 = a/c_t$). This time is relatively small; for example, for a = 1 mm and c_t = 3 m/s, t_0= 0.3 ms, which is much shorter than the length of an ultrasonic stimulus (commonly, from 1 to 100 ms). After this time, the value of the shear displacement remains constant up to the pulse end. This agrees well with our observations that pulses of ~5–10 ms to 500 ms duration cause tactile sensations as a response to the start and end of a stimulus, or that a person cannot distinguish a long pulse of duration, for example, 400 ms, from two short pulses separated by the same time interval [3, 4]. These data provide evidence in favor of the fact that stimulation of a neural structure is connected precisely with the gradient of the stimulating factor (the unidirectional displacement of the medium in this case).

3. Possible applications

We now discuss possible applications of methods associated with the use of the acoustic radiation force and based on the stimulation of neural structures, in particular, skin and tissue receptor structures, some of which have already been realized. For example, stimulation of neural structures by means of focused ultrasound has been used to diagnose various diseases associated with abnormal perception. A number of neurological, dermatological, hearing and other diseases are accompanied by considerable changes in some sensations (e.g., tactile or pain for skin sensations) in comparison with normal perception. By measuring and comparing the thresholds of different sensations induced by stimuli of focused ultrasound in normal and pathological states, it was possible to diagnose the diseases and evaluate the extent of the pathological processes [3, 6-7]. These diagnostic techniques are especially valuable when existing "traditional" methods fail to provide a definitive diagnosis.

Recently, the stimulating effect of ultrasound attracted a special interest (especially in Japan) in connection with the development of promising robotic techniques and systems, sensors, automated control systems, and also "human–machine" interfaces based on the use of tactile sensations. In this area of research, one of the most promising directions of work is the development of tactile displays for transmission of information to humans by an acoustic method based on the effect of radiation pressure [12–14]. In these studies, a cap made of a foamy silicon rubber was put on a human finger and irradiated by focused ultrasound generated by a combination of eight linear phased arrays [14]. However, the quality of focusing provided by this system was inappropriate and the level of grating lobes was too high for a practical application. This system was intended for generation and steering only one focus over the display area which is another basic disadvantage of the design described in [14].

One of the main aims of the current work was to propose and study using numerical modeling experiments an alternative way of developing such tactile displays based on the use of a two-dimensional array with elements randomly distributed on its surface (so called random array). Similar arrays were studied in detail in a series of previous papers [15–20], and it was demonstrated that such arrays have significant advantages over more common and very popular regular arrays with equidistant location of elements [21–24]. We have demonstrated [16–20] that irregularity in the element distribution over the array surface improves the quality of the acoustic and thermal fields generated by such arrays by reducing the level of secondary intensity maxima caused by the regular discrete structure of an array, and by increasing the capability to steer sets containing a relatively large number of foci along and off the array axis. The ability of the arrays to generate simultaneously and move in space a large number of foci is the major advantage of two dimensional phased arrays [21, 23, 24], which, as shown, is implemented most effectively with the use of random arrays [16, 18–20].

The calculation of the spatial distributions of acoustic fields was performed for arrays shaped as a part of a spherical shell with diameter of 65 mm and radius of curvature of 60 mm. The ultrasonic frequency was 3.0 MHz. The arrays consisted of 256 flat disk elements of 2.5 mm in diameter (i.e., 5 λ at this frequency of ultrasound). Arrays of two types were investigated in this work: (i) an array of 256 elements distributed regularly on the surface in a square pattern (a typical distribution of elements for the majority of existing two-dimensional arrays, - see, e.g., [22-24]); the minimum distance between the element centers was 3 mm; (ii) an array of 256 elements randomly distributed on the surface; in this case, the distance between the element centers was different and $\geq$3.0 mm. The total active area of the array elements was 12.5 cm^2. Figure 3 shows the element positioning for the random array.

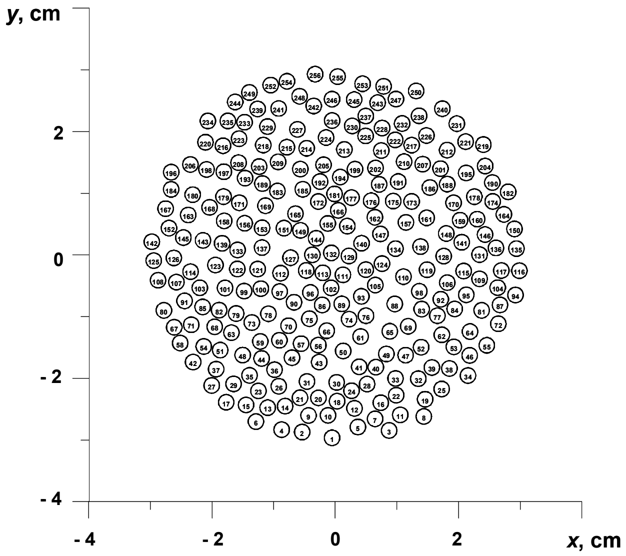

Figure 3. Positioning of elements in the random array.

In a preliminary numerical experiment, we investigated the possibility of synthesizing a certain symbol (for example, a square) using a large number of foci (e.g., 16 foci) produced simultaneously. Although it is feasible [19], the quality of the symbol representation (estimated using the criterion of the presence of secondary intensity maxima in the field) in this case was relatively poor. However, similar and more complex symbols can be synthesized with much better quality by using the approach described in [23, 24, 19], in which the final pattern is created by switching between several sub-sets each with a smaller number of foci, at a frequency of 10-20 Hz. Figure 4 presents the intensity distributions in the *xy* plane obtained by using the random array with the parameters described above; the pictures correspond to three different symbols: “square”, “heart” and “ring”. In this and the following figures, the contour distributions of intensity are given in the form of eight contours with the values from 0.2$I_{\max}$, where $I_{\max}$ is the peak value of intensity in the field under investigation, to 0.9$I_{\max}$ through each 0.1$I_{\max}$. The contour corresponding to 0.1$I_{\max}$ is not shown in the figures to avoid shading the field distributions and also having in mind that transmission of sensory information to a human is usually performed at intensity values slightly exceeding the threshold values. In this case, it can be assumed that the presence of sites with intensity slightly greater than 0.1$I_{\max}$ is unlikely to affect the perception of a symbol.

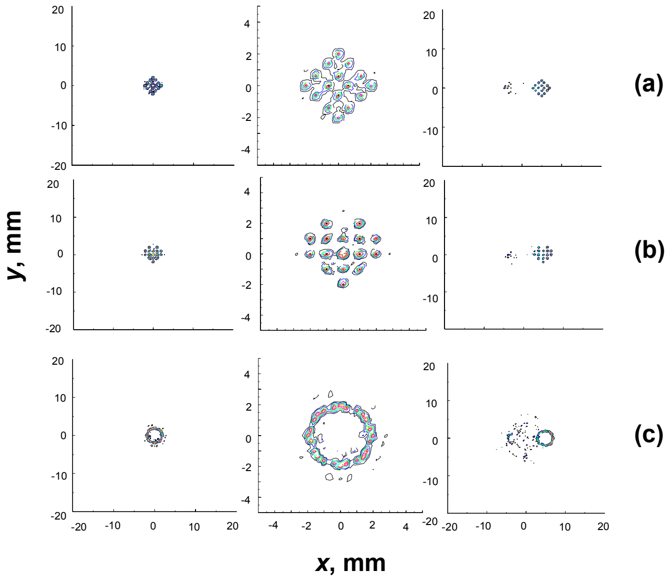

Figure 4. Generation of regions of action of focused ultrasound in the shape of various symbols with the use of the random array. The size of the investigated field is 4 x 4 cm (left and right columns) and 1 x 1 cm (central column). Left column - the absence of shift of the set of foci off the array axis, central column - the same in the enlarged scale, right column - shift of the sets of foci at 5 mm off the axis

The symbols in Figs. 4a and 4b were obtained with the use of four sub-sets of foci, with four foci in each (16 foci in total, with a spacing of 1 mm). The symbol in Fig. 4c is obtained using three sub-sets of foci with 8 foci in each (24 foci in total, located on a circle and separated by 0.52 mm from each other; this value just slightly exceeds the ultrasound wavelength). In the left- and right columns, the intensity distributions in a relatively wide field of interest (4 x 4 cm) are presented. These distributions allow one to control the presence or absence of secondary intensity maxima within the whole investigated field (an important criterion for evaluating the quality of the acoustic fields generated by an array). The distributions in the left and central columns were obtained for the case when multiple foci were located symmetrically with respect to the array axis, and the distributions in the right column for the case where the set of foci was shifted 5 mm off the array axis, which corresponds to the sizes of the tactile display. In the central column, the same distributions as in the left column are presented but in a considerably narrower field with sizes corresponding to the size of the tactile display (1 x 1 cm). Such distributions allow detailed investigation of the structure of the acoustic field in the limits of the display area.

It follows from the distributions presented in Fig. 4 that by using the random array it is possible to synthesize regions of action of focused ultrasound with complex shapes. The symbols are reproduced with adequate quality (estimated by the criterion of the intensity levels in the grating lobes and secondary maxima). Steering the sets of foci 5 mm off the array axis (the right column) does not significantly degrade the quality of the distributions (especially in the case of symbols (a) and (b)).

For comparison, in Fig. 5 the intensity distributions similar to those shown in the right column of Fig. 4 but obtained with the use of the regular array with the same parameters as for the random array are shown. In Fig. 5, the shift of the sets of foci off the array axis is equal to 5 mm in all cases. It can be seen that use of the regular array leads to occurrence of secondary sets of foci with almost the same value of peak intensity (up to 0.6-0.7 I_{max}) as that in the main set. This could cause erroneous perception of the symbols. With increasing shift of foci, the peak intensity in the secondary sets of foci can exceed that in the main sets of foci. As shown in Fig. 4 (right column), the use of a random array avoids this problem.

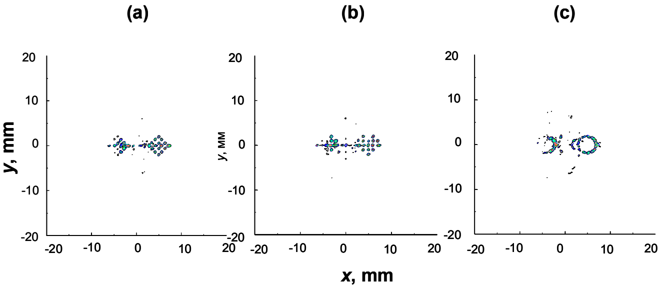

Figure 5. – Distributions of intensity distributions similar to those shown in Fig. 4 but obtained using the regular array. All sets of foci are shifted 5 mm off the array axis. High amplitude secondary maxima are seen in all cases.

Fig. 6 illustrates the possibility of using a random array "to draw" more complex symbols or figures such as, for example, the letters of the Latin alphabet. Intensity distributions in the focal plane simulating the letters S and W synthesized using a total of 24 and 25 foci produced with the use of 3 and 5 sub-sets of foci, respectively, are presented. The sizes of the field of interest are 4 x 4 cm (a) and 1 x 1 cm (b). Absence of secondary maxima in the limits of the investigated fields confirms the appropriate quality of the presented intensity distributions.

In connection with the images presented in Fig. 6, it is worthwhile to discuss briefly another possible application of the approach investigated in this work. There are tactile displays that allow blind and visually impaired persons, using tactile sensations, to read a text presented on the display as a relief-dot font with the use of raised or embossed dots. For representation of letters or numbers, Braille type is used which allows with the use of 6 (sometimes 8) dots to create an analog of planographic letters or numbers. Usually, Braille's dots are arranged in two vertical columns with 3 dots in each. Representation of Braille's symbols on a display is much easier than the letters, for example, of the Latin alphabet or Cyrillic. However, existing tactile displays have disadvantages and limitations. For example, the displays in which pins move mechanically are noisy, the direct contact of the skin of a person with the pins is required, and the velocity of moving of an "image" on the display or renewing of a "frame" is low. Ultrasonic tactile displays have several potential advantages, for example they are noiseless, contactless and can rapidly renew the information on the display screen. Although the expedience of practical application of ultrasonic displays for representation of planar typed symbols and not their Braille equivalents is an object for a separate study, the technological possibility of the development of such devices can be considered to be proved, as it is demonstrated in this report.

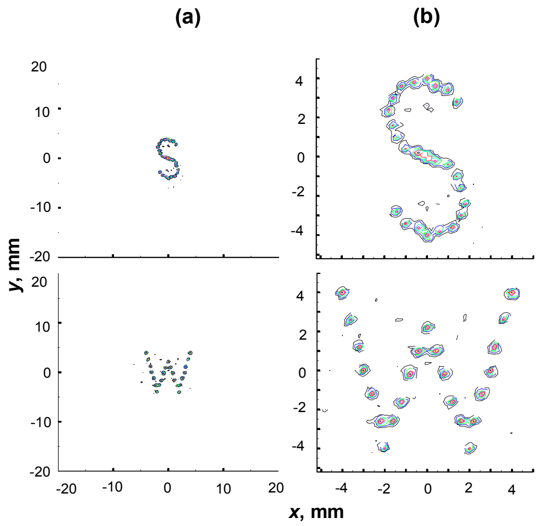

Figure 6. Synthesis of more complicated symbols, for example, letters of the Latin alphabet with the use of the random array. The sizes of the investigated field are 4 x 4 cm (a) and 1 x 1 cm (b)

4 Conclusion

The results obtained show that methods and devices based on the use of the acoustic radiation force could be used for stimulation of peripheral neural structures. It has been shown that with the use of ultrasound stimulation it is possible to reproduce all the sensations experienced by a human through the skin in everyday life. Furthermore, ultrasound modulated by sound signals (tone, speech, music, etc.) can induce sound sensations corresponding to the nature of the modulation in people with normal hearing. Ultrasound stimulation of neural structures has been used for the diagnosis of various diseases (neurological, dermatological, hearing and others) that are associated with changes from normal perception. These diagnostic techniques are especially valuable when existing "traditional" methods do not present an unequivocal diagnosis. The phenomenon of the radiation force could be used in future robotic systems, sensors, and automated control systems, based on the use of tactile sensations in the human-machine interface, as well as in devices that may allow blind and visually impaired persons to perceive textual information presented on a tactile display. It was shown in this work that arrays with a random distribution of elements over the array surface can generate regions of action by focused ultrasound with predetermined shapes and provide higher quality intensity distributions (estimated in terms of the intensity levels in the grating lobes and secondary maxima) for synthesis of complex symbols relative to comparable regular arrays.

Acknowledgments

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