ISTU 2016

Program Booklet

The 16th International Symposium on Therapeutic Ultrasound

March 14–16, 2016
Dan Panorama Hotel, Tel Aviv, Israel

www.istu.org

SAP5 T-ARRAY: A SOFTWARE PACKAGE FOR FAST SIMULATION OF THERAPEUTIC ULTRASOUND FIELDS RADIATED BY MULTI-ELEMENT PHASED ARRAYS

Pavel B. Rosnitskiy[1], *Sergey A. Ilyin*[1], *Oleg Sapozhnikov*[1], *Leonid Gavrilov*[2], *Petr V. Yuldashev*[1], *Vera Khokhlova*[1]

[1]Physics Faculty, Lomonosov Moscow State University, Moscow, Russian Federation, [2]Andreev Acoustical Institute, Moscow, Russian Federation

OBJECTIVES

Multi-element phased arrays are widely used in various applications of HIFU therapy. A possibility of fast and convenient analysis of acoustic fields generated by such therapeutic arrays for testing their designs and different configurations of dynamic focusing is important for researchers and engineers. To facilitate developments in this field, a software package "T-Array" with a graphical user interface (GUI) is proposed (Fig. 1a).

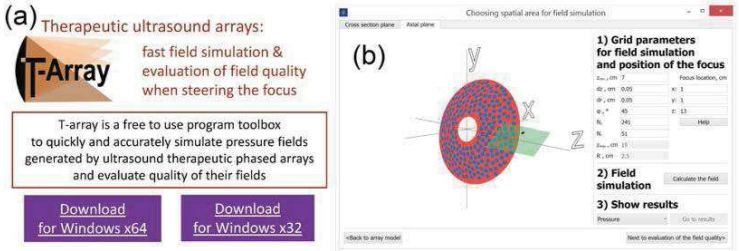

Figure 1: (a) Web page about T-array program with a brief description and options for downloading. (b) Demo page 1 showing the first step in executing the program: a window for setting parameters of the array, position of the focus, spatial window and grid steps for calculating the field with a 3D visualization of the array and simulation area.

METHODS

A multi-element array is considered as a spherical cup comprising flat circular elements distributed over its surface. The coordinates of the array elements are set through an external data file. The diameter of the elements and the curvature radius of the cup as well as parameters of numerical grid for the modelling are set through the GUI of the program (Fig. 1b). The amplitude and phase of each element of the array can be varied independently. Assuming linear wave propagation, the field of the entire array can be represented as superposition of acoustic fields radiating from its elements. For therapeutic treatments, the region near the geometric focus is of interest and thus the distance to the focus from each array element is much larger than the length of its near field. In the T-array program it is proposed to use an approximate analytic solution to the Rayleigh integral in the far field of a flat circular source to calculate contribution of each element to the total field of the array. This method significantly accelerates calculations while preserving high accuracy of the results. Such an approach has been validated by comparing analytical solution for a typical HIFU array to the conventional direct numerical integration [Ilyin et al., Acoust. Phys., 61(1): 52-59, 2015]. Analytic method appeared to be about 500 times faster than the numerical one, so in T-Array software it is used to perform multiple calculations and analyse array fields in real time.

One of the major properties of multi-element arrays is the possibility of electronic steering their foci. When considering this property, it is necessary to account for undesirable side effects caused by the discrete structure of the arrays. In particular, the field amplitude in the main focus decreases and side lobes appear when translating the focus. As suggested earlier, the degree of manifestation of these effects is used here as a quality criterion for the field generated by a given array [Gavrilov L.R. et al., IEEE UFFC, 47(1): 125–139, 2000]. To evaluate the side effects, multiple calculations of 2D fields in the steering plane are performed for different locations of the array focus. A level of the 10% intensity maximum in any side lobe is used as a parameter of safety, and various levels of intensity in the main focus as compared to the maximum achievable level can be set for evaluating the efficacy of the focus steering.

RESULTS

T-Array software package was designed to comprehensively analyze the fields generated by multi-element arrays and their focus steering capabilities. The program was developed using C++ (Qt) without using any external commercial products, so it is an open source program. To make the application user-friendly it is divided into three major steps. These steps are illustrated here for the specific array with the following parameters: 1 MHz operating frequency, 256 elements of 7 mm diameter each distributed in quasi-random manner, 170 mm aperture, and 130 mm geometric focal distance [Hand et al., Phys. Med. Biol., 54: 5675-5693, 2009].

The first step in the simulation process is to set the parameters of the array and the propagation medium, the position of the electronic focus, the spatial window and grid steps for field calculations (Fig. 1b). The array can be visualized in 3D, rotated, and zoomed for checking and analyzing its geometry. The program calculates the acoustic field in two planes: one plane passing through the array axis at arbitrary angle ("Axial plane") and another one perpendicular to the axis ("Cross-section plane"). After entering the input data, the area of calculation (green rectangle in the Fig. 1b) and the position of the focus (black dot) appear in the image. Then, parallel concurrent computing calculations can be started.

The second step of the program is to visualize 2D field distributions calculated during the initial step. As shown in Fig. 2, two side effects appear when the focus is shifted by 2 cm off the axis from the center of curvature of the array. The pressure amplitude in the main maximum decreases by approximately 60% comparing to the case without steering; at the same time, a region of discrete scattered grating maxima is formed in the field pattern.

The last step is to determine spatial areas of efficient and safe steering capabilities of the array taking into account the side effects. Multiple field simulations with different dynamic focusing are performed and the results are presented as contours of regions, in which dynamic focusing can be used (Fig. 3). For example, the black contours represent the regions of focus steering where the main pressure maximum decreases by less than 10, 30, and 50% of the maximum achievable value. Red contour indicates the region of focus steering in which the intensity of the largest grating lobe does not exceed 10% of the intensity (32% of the pressure amplitude) in the main maximum, which is the accepted criterion of safe irradiation [Gavrilov et al., IEEE UFFC, 41(1), 125-139, 2000]. The user may enter different values to define the contour levels.

CONCLUSIONS

The software package T-Array was designed for calculating the fields of therapeutic arrays consisting of circular elements and evaluating spatial regions of safe and efficient dynamic focus steering. Calculations, visualization of the results, and saving data for further analysis are performed in real time. Further extensions of the program is planned: simulations for elements of different shape, multi-foci configurations, modelling propagation of ultrasound in absorbing medium, simulation of heat deposition and radiation force. The program can be downloaded for free from the website http://limu.msu.ru starting from March 1, 2016 if not earlier.

Acknowledgements: The work was supported by the Russian Science Foundation grant 14-12-00974.

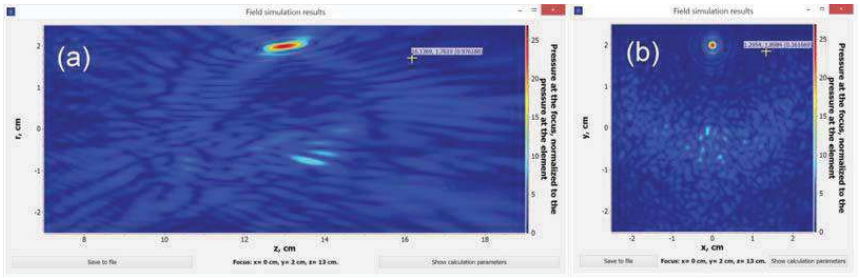

Figure 2: Demo page 2 showing the second step of working with the program: results of the 2D simulation of the pressure field generated by the array. Results are normalized to the pressure at the array element. (a) Acoustic pressure in the axial plane showing the focus electronically shifted vertically by 2 cm off the axis. (b) Acoustic pressure in the focal plane showing the position of the focus and the side effect of appearance of scattered elevated pressure spots.

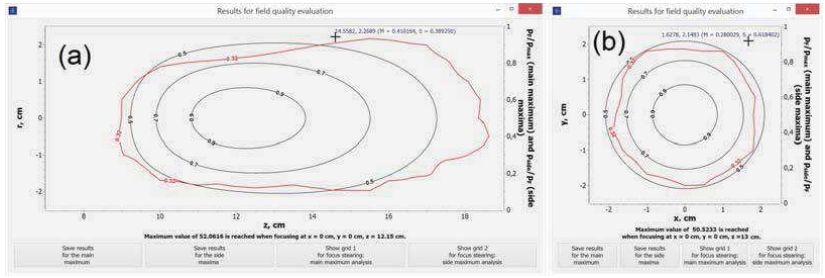

Figure 3: Demo page 3 showing the third step of working with the program: evaluation of the quality of the array field while steering the focus. Contours of regions of focus steering in which the pressure in the main maximum decreases by less than 10, 30, and 50% of the largest achievable value (black curves) and in which the intensity of the largest grating lobe does not exceed 10% of the intensity in the main maximum (red curves). The results are given (a) in the axial and (b) in the focal plane of the array.

SAP6 THE EFFECT OF ULTRASOUND AND MODIFIED PECTIC GALACTAN/DNA COMPLEXES: NEW APPROACH FOR TREATING BRAIN CANCER IN VIVO

Nitsa Buaron[1], Antonella Mangravita[2], Yuan Wang[2], Ann Liu[2], Mariangela Pedone[2], Eric Sankey[2], Ramesh Chintacunta[1], Tamar Traitel[1], Riki Goldbart[1], Henry Brem[2], Betty Tyler[2], Joseph Kost[1]

[1]Chemical Engineering, Ben-Gurion University of the Negev, Be'er Sheva, Israel, [2]Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States

OBJECTIVES

In this novel study, we utilize a targeted gene delivery system based on modified pectic galactan, which was developed in our lab, in combination with Ultrasound (US) in order to achieve successful DNA delivery to an in vivo 9L gliosarcoma tumour model in Fischer rats. The main objective of this research is to develop a safe and stable platform approach for a non-viral cancer gene delivery system based on pectin derivatives, utilizing US as a means for improving complexes' distribution and effective gene transfection. Our hypothesis is based on the highly specific carbohydrate interaction between pectic galactan side chains and galectin-3 receptors on the glioma cell membrane that will result in a higher concentration of complexes at the cell surface, and therefore, increase their chances for internalization. In this manner, modified pectin would not just prevent metastasis, but also might have a preferred incorporation pathway into cells as a DNA carrier. US will enhance the complexes' distribution through a solid tumour mass, and will increase transfection in two ways: by changing membrane permeability and by overcoming intracellular barriers.

METHODS

Experiments were performed on a well-established 9L gliosarcoma tumour model on Fischer 344 rats that was developed in Professor Brem's neurosurgical laboratory. The targeted delivery system that was examined in this study is pectic galactan modified with quaternary ammonium groups (Q=N+ (CH3)3), Q-galactan. The complexation process was carried with plasmid DNA encoding the Green Fluorescence Protein (pGFP). Complexes of Q-galactan/pGFP that were found to be the most successful in vitro were examined in this study.
Experimental system: Experiments were performed to choose the type of tumour inoculation and the strategy of intracranial administration of complexes. Two types of tumour inoculations were examined: 9L cell injection and 9L tumour piece implantation. In addition, two types of intracranial treatment administration were examined for each: manual injection and convection-enhanced delivery (CED) infusion. Injected labelled complexes were tracked by fluorescence microscopy, while the brains were examined by histological analyses.
Safety study: Safety studies were performed by examining the complexes' toxicity and US effect on the brain tissue. 90 Fischer 344 rats (6 rats per group) were used in this study. Intracranial administration of the complexes was performed through a small hole drilled in the skull. The US probe was immersed in a gel-filled cylinder, <2 mm above the drilled hole in the skull. For safety evaluation, complexes toxicity in different DNA concentrations (0.5-2 µg/µL) was performed; the US irradiation effect was assessed at intensities between 11-15