EAR SOLVERS FOR HIGH-INTENSITY FOCUSED ULTRASOUND WITH APPLICATION TO CANCER TRE

organized by
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Workshop Summary

This workshop was concerned with the development of numerical methods for problems of nonlinear wave propagation, with a focus on cancer treatment based on High Intensity Focused Ultrasound (HIFU). A rich set of exchanges occurred during the five days of this workshop; the organizers feel much was accomplished in this period of time with regards to bridging gaps between experts in various related fields, including mathematics, physics, engineering and clinical practice.

Workshop activities

Two leading talks during the first day of the workshop focused on the application of HIFU to cancer treatment. In the first talk, Michael Bailey explained how applications of HIFU can be used to destroy cells using predominantly thermal effects. During this talk treatments for a variety of cancers were considered, including prostate, kidney, liver and breast cancer, and mention was made of applications to bone healing as well as non-cancerous diseases such as uterine fibroids. Some barriers to wider use of HIFU techniques were reviewed. In the second talk, in turn, Brian Fowlkes described applications of the mechanical effects of HIFU, which exploit cavitation in order to emulsify tissue. The physics of the processes associated with creation of bubbles and bubble-cloud dynamics were described. Applications to prostate cancer were presented. A brainstorming exercise in the afternoon, lead by Tom Hagstrom, helped identify a set of topics relevant to HIFU, which were further discussed in small-group break-out sessions on Monday afternoon as well as other workshop days.

The second day focused on the physics of the HIFU problem. In the first talk Vera Khokhlova presented a review of the state-of-the-art of modeling and simulations in HIFU, including numerical simulations and comparisons with experimental data. It was shown how calculations of the acoustic field at various levels of approximation diverged from each other as well as from the experimental data resulting from a clinical HIFU source. In the second talk Charlie Church described the use of ultrasound to induce bioeffects in soft tissue through either mechanical or thermal means. The mechanical processes considered result mainly from cavitation and included lysis and sonoporation due to jetting or shear stresses due to bubble collapse, high-temperature chemistry (including free radical production) inside collapsing bubbles. In the first part of the afternoon the participants broke up into four focus groups. This was followed by an "ask the experts" session in which Josh Soneson, from the Food and Drug Administration (US) and Richard Findlay from the Health Protection Agency (UK) gave brief presentations about regulatory issues, and discussed the matters concerning use of numerical tools for treatment planning. There was then a lively Q&A session concerning the process necessary to bring HIFU machines to market.

The third day focused on mathematical methods for solution of PDEs. Tom Hagstrom gave a review on the use of high-order PDE solvers, and he described the advantages brought about by such algorithms, namely improved dispersion behavior, even for coarse spatial discretizations, computational cost, and boundary treatment. He contrasted the different techniques that can be employed for nonlinear problems and ended with a list of freely available PDE solvers. Oscar Bruno presented the Fourier-Continuation technique to solve PDEs, including a description of dispersionless numerics and fast computing times resulting from this method, which enable solution of very large non-linear acoustic problems of the type arising in HIFU applications, in acceptable computing times. In the afternoon a lively discussion arose as the Monday break-out groups reported on the discussions and findings. The participants then broke up into groups once again, some of which continued discussions from the previous day.

On the fourth day Jan Nordstrom started the morning with a presentation concerning numerical treatment of boundary conditions in PDE problems. Robin Cleveland gave a presentation on the derivation of the nonlinear wave equations from first principles in order to clarify the approximations made for the various equations used in the field. The afternoon session consisted of a debate of the output from the groups that met on Day 3. The participants then broke up into new groupings.

On the fifth day, finally, Martin Verweij gave a talk on the use of integral methods for solving PDEs used in nonlinear acoustics. This was followed by a talk by John Ballard concerning HIFU treatment across the rib cage. A discussion concerning topics treated in the group meetings the previous day and general discussions completed the days activities and the workshop adjourned.

Outcomes the workshop

(1) A set of benchmarks was identified, which are recommended by the attendees as fundamental test problems for numerical methods that seek address the difficulties inherent in HIFU simulation. The benchmarks proposed are as follows:
   — A homogeneous medium including nonlinearity and frequency-dependent attenuation.
   — A multi-layered medium with differing tissue properties in each layer
   — A multi-layered absorptive nonlinear medium containing a strongly scattering obstacle.

(2) A number of problems concomitant with HIFU were identified which were not previously treated in the mathematical literature, including 1) Oscillation of bubbles of sizes comparable with or larger than the acoustic wavelength embedded in a nonlinear medium, with application to mechanical treatment of tissue; 2) Mathematically correct implementation of boundary conditions for absorptive media; 3) Inverse problems for beam-forming across the rib-cage; 4) Nucleation and dynamics of bubble clouds; and 5) Rupture of bubbles under intense non-linear acoustic fields.

(3) A number of concrete exchanges concerning high-order numerical methods and the Fourier continuation method were made, leading to initial efforts towards implementation of such advanced numerical solvers in the nonlinear acoustics community.