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OPTIMIZATION OF PERFUSION/CONDUCTION FREEZING PROTOCOLS FOR PRESERVATION OF THREE-DIMENSIONAL ORGANS

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ABSTRACT

In this substantiated proof-of-concept study it has been successfully demonstrated that it is possible to numerically simulate the entire freezing protocol of realistic three-dimensional organs using simultaneously heat conduction via external cooling and heat convection via internal perfusion. It has been successfully demonstrated numerically that it is possible to control the thermoelastic stresses during freezing of organs by periodically optimizing time-varying temperature distribution on the surface of the freezing container. This suggests that it may be possible to develop optimally controlled protocols for freezing organs. Using more diverse tissue sub-domains, more accurate non-isotropic thermophysical tissue data, finer spatial and temporal discretization, and more geometrically complicated configurations of organs and containers is a relatively straightforward future extension of this work. However, a considerably more challenging extension of this work would be to incorporate effects of viscoplasticity of the freezing tissue.

INTRODUCTION

One of the serious difficulties encountered by surgeons involved with organ transplantation is the shortage of available organs. It would be invaluable to establish organ banks that could store organs with different immunological properties in a frozen state for lengthy periods of time. The organs could be cooled in a special gelatin while being internally perfused by a cooling liquid. Because of the difficulties in controlling the local cooling rates within a three-dimensional organ, extreme thermal stresses develop that cause fractures of the organ tissue. Consequently, over the past four decades, experimental attempts at viably freezing organs have been unsuccessful. However, there is the possibility that mathematically optimum freezing protocols could be determined that will maximize the survivability of organs. The authors have developed a preliminary mathematical model and computer simulation and optimization of this process. A time-accurate finite element computer program was used to predict unsteady heat conduction with phase change, thermal stresses and coolant flow within the realistically shaped organs. A micro-genetic optimization algorithm and a robust response surface based self-adapting optimizer were then used to achieve nonlinear constrained optimization of time-varying container wall temperature distribution so that the prescribed maximum allowable thermal stress levels are never exceeded throughout the organ.

The objective of this paper is to present a fully automatic computational procedure that can determine the optimum time variation of temperature distribution on the surface of the freezing container and the optimum time variation of temperature and flow rate of the perfusing coolant so that the local thermal stresses can be maintained below a specified level at each instant of time at every point in the arbitrarily shaped and sized organ. Most significantly, the results of this research will offer substantial evidence towards answering the still open question: is freezing of three-dimensional organs possible without causing irreparable damage due to fracturing of the organ tissue?

MULTILEVEL PARALLELISM IN OPTIMIZATION

The usual approach to parallel optimization is to run a single analysis on each processor per optimization iteration. However, a mesh for a geometrically complex design may be large; sometimes the finite element analysis requires more memory than is available on a single processor. For this reason, the finite element analysis must be distributed among several processors. If a large number of processors are available, we can use all of them by running several simultaneous parallel analyses to evaluate several candidate design configurations. We have developed an optimization communication module with the MPI library that utilizes this multilevel hierarchy of parallelism. This module can be used with any parallel optimization method including GA and IOSO algorithms.

THERMAL AND FLUID FLOW ANALYSIS

The thermal, thermoelastic, and coolant fluid flow analysis is performed by a set of parallelized finite element analysis computer codes. The finite element analysis codes and tools for mesh generation, mesh partitioning, and others are freely available as a part of the ADVENTURE project lead by the University of Tokyo. The finite element solvers are geared towards large-scale parallel analysis and are well suited to the efficient analysis of complicated geometries.

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