Ecole doctorale sciences mécaniques, acoustique, électronique & robotique de Paris (ED 391)

PROPOSITION DE SUJET DE THESE

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Financement proposé : **Non**

Shock wave propagation in the brain: characterization, imaging, and mechanisms for traumatic injury

Research Summary

Traumatic brain injury is one of the leading causes of disability, especially in young adults. Many of these injuries, such as diffuse axonal injuries, are poorly understood and are undetectable with conventional medical imaging. When the head is subjected to violent impacts, for example in vehicular accidents or falls, elastic shock waves can propagate through the brain. The violent gradients in the shear shock wave tear and damage neurons, starting a biochemical cascade that takes days to develop. Currently there are methods that can describe nonlinear quasi-static (<0.5 Hz) deformations. We wish to investigate the high frequency (>50 Hz) dynamic regime where no characterization of the shock shear wave properties of the brain exist. There are two principal objectives to this project: First, to develop a comprehensive nonlinear heterogeneous model and simulation that will, for the first time, provide a complete mechanical description of shock wave propagation throughout the volume of the skull and brain. Second to develop optical and ultrasonic methods that are capable of measuring displacements in tissue to create high frame-rate images of shock wave propagation in the brain. These methods will be used to quantify the gradients in the shear shock waves and to establish three-dimensional maps of the brain's nonlinear dynamic properties (which cause shock wave formation). By reaching these objectives we will establish the mechanisms of brain injury that arise from the particularly violent gradients in the sharp profiles of shock waves propagating in soft tissue.

Résumé Scientifique

Les lésions traumatiques du cerveau sont une des causes principales de handicap, en particulier chez les jeunes adultes. Beaucoup de ces lésions, en particulier les lésions axonales diffuses, restent peu comprises et sont indétectables par des méthodes d'imagerie conventionnelle. Lorsque la tête est soumise à de violents impacts ou accélérations, par exemple lors de chutes ou d'accidents de voiture, des ondes de choc élastiques peuvent se propager dans le cerveau. Les forts gradients du choc de cisaillement entraînent l'étirement et l'endommagement des neurones, initiant une cascade de réactions biochimiques prenant des jours à se développer. Des méthodes existent pour décrire les déformations nonlinéaires quasistatiques (<0.5 Hz) dans les tissus. Nous souhaitons étudier le régime dynamique (>50 Hz), pour lequel aucune caractérisation des propriétés des ondes de choc de cisaillement dans le cerveau n'est disponible. Ce projet comporte deux objectifs principaux. Premièrement, de développer un modèle et une simulation de propagation en milieu nonlinéaire hétérogène qui permettront, pour la première fois, une description mécanique complète de la propagation d'ondes de choc élastiques dans le crâne et dans le cerveau. Deuxièmement, de développer de nouvelles méthodes acoustiques et optiques capables de mesurer les déplacements dans les tissus et de créer des films haute cadence

de la propagation d'ondes de choc dans le cerveau. Ces méthodes seront utilisées pour quantifier les gradients de cisaillement et cartographier en trois dimensions les propriétés nonlinéaires du cerveau (responsables de la formation de chocs). L'accomplissement de ces deux objectifs permettra d'établir les mécanismes de lésions du cerveau consécutives aux violents gradients liés aux profils raides des ondes de chocs se propageant dans les tissus mous.

Background

Brain injury can occur as a result of compression, tension, and shearing from a direct impact of the head or from acceleration alone. For large amplitude impact loading, a shock shear wave is sent through the skull and into the brain where it propagates throughout the cranial volume. Very little is known about shock wave propagation in the brain, but it is hypothesized that the violent gradients in the propagating shear wave stretch and damage the axons, which subsequently initiates a biochemical cascade beginning with the influx of Ca^{2+} into the cell and unleashing a variety of degrading processes in the minutes to days that follow the trauma. The lack of widely available clinical tools to image these injuries is one of the reasons why so little is known about them.

Competence

The project can be divided into three equal parts: modeling, simulation, and experiments. Depending on the Ph.D. candidate's profile a variable time commitment can be allocated to each. The candidate will nevertheless be expected to develop a high level of competence in shock wave physics, running and interpreting simulation results, and evaluating experimental data. More detail on the different parts of the project are given below.

Modeling

There is a three order of magnitude difference between the longitudinal (compression) wave speed (1500 m/s) and the transverse (shear) wave speed (2 m/s) in soft tissue. It is often convenient to consider the two modes independently, for both models and numerical simulations. For example a generalized description of the shock wave physics in soft solids can be simplified to a scalar equation by assuming a polarized geometry and a paraxial approximation.

A first step in the evolution of this model and in the Ph.D. project is to reduce the simplifying assumptions to obtain a scalar model for nonlinear shear wave propagation in a heterogeneous representation of the brain. This will allow us to model the brain as an elastic medium with slow wave speeds surrounded by a rigid boundary imposed by the skull. In this first model wave propagation in the skull, would be ignored. The model and subsequent numerical simulations can therefore be optimized to treat a single time scale associated with slow wave speeds in soft tissue.

A more comprehensive and challenging model for shock wave propagation in the brain will include both transverse and shear waves (and thus fast and slow time scales). In the skull bone, the shear wave speed (1800 m/s) and the transverse wave speed (3000 m/s) are the same order of magnitude as the transverse wave speed in soft tissue (1500 m/s). Taking both into account will allow us to model the complex interaction between the two, such as mode conversion and the coupling of the nonlinear terms. With a nonlinear model we will also be able to determine how important mode conversion and nonlinear coupling are in describing shock waves within the brain. The physical models developed for this project will require numerical solutions.

Simulations

To tackle the new models heterogenous elastic shock wave propagation models we will develop new finite volume and discontinuous Galerkin simulation tools. In finite volume methods the flux is evaluated at the surface of each finite volume so that by construction the flux entering a volume is the same as the flux leaving adjacent volumes. This shock capturing method is therefore conservative and is particularly well suited to wave propagation.

The discontinuous Galerkin method is a class of numerical methods that combines features of finite elements and finite volumes. Within each element the solution is represented by a polynomial approximation (as in FE) and the interelement flux is solved by upwind numerical flux formulas (as in finite volumes). This method, which will be developed in collaboration with R. Marchiano (Prof. UMPC), is more complex than finite volume methods but it is better suited to higher order developments due to it's low numerical dispersion.

Experiments

The Ph.D. student will be expected to participate in experiments that measure and characterize the nonlinear properties of soft tissue and to image shock propagation.

Optical techniques, in particular high frame-rate cameras, are especially promising and have demonstrated the ability to accurately measure small displacements in tissue mimicking phantoms with a high resolution. This would allow us to observe the thin shock profile of an elastic wave on a scale that is consistent with cellular mechanisms for injury.

Camera-based optical detection schemes have been used to detect the transient elastic motion induced by acoustic radiation force in soft solids. In optically transparent tissue-mimicking gels this technique can obtain sub-surface images of wave propagation with spatial a resolution that is equivalent to a low-power microscope, i.e. approximately 1 μm and an elastic displacement resolution of approximately 100 nm. These experimental techniques are being developed in our laboratory and the Ph.D. student may participate in the setup and development of the experimental protocols (in collaboration with A. Antkowiak, MCF UPMC).

Compared to ultrasound, optical techniques have the advantage of a higher spatial resolution and the ability to measure displacement in three dimensions rather than only along the imaging axis but it can only be used to measure shallow displacements. Ultrasound has the advantage of larger penetration depths that can span the entire brain.

In collaboration with our partner, the Institut Langevin, ultrasonic methods will be used to generate real time images of shear displacements. We will use this imaging technique in conjunction with strong mechanical excitations to image and quantify nonlinear wave propagation at depth (up to 10 cm) and in three dimensions, which will yield information about the nonlinear properties throughout the entire brain volume.

Clinical applications

The clinical application of this project is to aid in the precise evaluation of brain damage in the first days of severe traumatic brain injury (this early stage is especially promising because patients with severe trauma are precluded from a prone position and the MRI restricts ventilation). For example X-ray computed tomography images, in conjunction with a traumatological assessment of the impact areas, could be used as an input to the simulation tool that calculates the mechanical environment in the head and brain. This could establish areas at increased risk of a) diffuse axonal injury, which are invisible at this early stage, b) cerebral hemorrhage in the days that follow, and of c) hemorrhagic softening in the days that follow.