PhD proposal

CSC program – 2020

Title

Development of a numerical reconstruction tool to investigate brain microstructure by Magnetic Resonance Elastography

Supervisors

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Scientific context

Doctors have long used palpation as a method of diagnosing pathologies. Thus a breast tumour can be detected, from a certain size, by this type of qualitative method. The use of mechanical property measurements to monitor tissue alterations has therefore become a fully-fledged field of biomedical research, both fundamental and applied. Moreover, for more than a decade, the field of mechanotransduction, which raises the opposite question of whether mechanical effects could alter tissues on a microscopic scale at the biochemical or biocellular level, has been booming. The link between the properties of tissue on a macroscopic scale and its multi-scale components (cells, extracellular matrix, etc) has therefore been the subject of numerous studies, but mainly by rheological methods on ex vivo samples. This link is still poorly explored in vivo, but the development of non-invasive imaging methods now makes it possible to consider drawing up maps of mechanical organ parameters.

Among them, Magnetic Resonance Imaging (MRI) allows to record in 3D in a 3D volume the propagation of low frequency mechanical waves (10Hz-1000Hz) induced by a mechanical actuator and propagating in a tissue under in vivo conditions: it is Magnetic Resonance Elastography (MRE). In this proposal, the focus is on the brain, for which MRI is the only in vivo investigation modality. This organ is a particularly interesting object of study: in a nutshell, the brain is made up of several zones, each of which has its own proportion of tissue components. In this project, we believe that it would be possible using numerical methods to model shear wave propagation (those used for MRE) to discriminate at the macroscopic scale between the four main tissue components of the brain: vessels, neural networks, cells and the extracellular matrix.

At present, the velocity map acquired by IRM is postprocessed using simple constitutive laws in small deformations and analytical mechanical models. By a reverse approach, material parameters can be evaluated locally. Nevertheless, these methods are based on simplifying mechanical hypotheses (homogeneity, linearity, isotropy, wave type, ideal boundary conditions) while the tissues studied exhibit complex behaviours (viscosity, hyperelasticity, anisotropy, poroelasticity) resulting from the elaborate microstructure mentioned above. To allow the identification of more complex constitutive laws that are more adapted to soft biological tissues, a numerical finite element wave propagation model seems appropriate: it could include strong local heterogeneities, prefered directions or even conditions with complex boundaries. An approach that aims to combine different models of brain tissue behaviour depending on the area being explored is a way considered in this project to discriminate in imaging between the different tissue components of the brain.

Recently, a numerical wave propagation simulation model was developed at LaMCoS that includes advanced numerical methods to ensure a calculation time compatible with clinical practice. It allows the simulation of the propagation of plane and non-plane waves in a non-linear and anisotropic tissue. Validated in the case of transient elastography, i.e. for the first passage of the wave in the tissue, without wave conversion or reflection, it requires additional developments to be applied to MRE, where the low MRI acquisition frequency implies the presence of reflected and converted waves in the measured signal. The very structure of the Finite Elements code allows the implementation of any constitutive law that would seem relevant for our object of study; in particular, we are considering a law that includes the mechanical contributions of each of the components of brain tissue. The comparison of the numerical model and the images would allow the identification of the parameters of this law for the different cerebral zones.

Scientific challenges

The main scientific challenges associated with MRI elastography are:

- Reducing the sensitivity of the reconstruction of property maps to measurement noise. The filtering of experimental data involves artifacts that could be removed by constructing an inverse method that strongly couples image processing and numerical simulation.
- Taking into account the complexity of the behaviour of biological tissues. Only a few recent studies have studied anisotropy or poroelasticity by MRE; these aspects require further investigation, particularly using a component approach based on known anatomical data.
- The cost of calculating inverse methods based on numerical methods by Finite Elements. Based on previous work at LaMCoS, a compromise will be sought between a very accurate description of compression and shear waves and an acceptable computation time in clinical practice.

Aim and organization

The objective of the thesis is to develop a tool for reconstructing MRI elastography data based on a finite element numerical simulation of wave propagation in brain tissue. This tool will aim to integrate the multiple tissue components of the brain and their variations by brain zone at a macroscopic scale. It will be based on previous numerical developments performed in two PhD thesis at LaMCoS, including one focused on MRE and on-going. The steps envisaged for this thesis work are as follows:

TASK 1

Develop and validate the existing Finite Element code for monofrequential wave propagation at interfaces (reflections, conversions) using existing experimental data; interfaces may represent inclusion boundaries or boundary conditions (skull box).

TASK 2

To construct a constitutive law allowing to take into account in numerical simulation the different structural components of the brain (mainly neural network, vascularization, cells, extra-cellular matrix) in order to model as well as possible the in vivo wave propagation in the brain.

TASK 3

Build a numerical brain model from medical imaging and vascular and neural segmentation.

TASK 4

Develop from the previous model a method for reconstructing elastography data acquired in MRI.