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Influence of Fluid-Structure Interactions on drug distribution in a computational model of the intrathecal space

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1. Introduction

Neurodegenerative diseases and the consequences of damage to the nervous system are among the most ambitious therapeutic challenges we face. The treatment of these pathologies by intrathecal delivery of pharmacological products to the cerebrospinal fluid (CSF) via catheters and access port is recognized for its therapeutic efficacy. While the therapeutic efficacy of intrathecal drug distribution is largely influenced by the characteristics of the product's diffusion within the access port/catheter system and its diffusion into the CSF, knowledge of the mechanical properties that enable the therapeutic approach to be optimized remains limited.

Pulsatile flow of CSF has an effect on drug distribution in spinal canal (Hettiarachchi et al. 2011). Including Fluid-Structure Interactions (FSI) in computational model permit to show that pulsatile flow of CSF generates Spinal Cord (SC) motion and have no impact in pressure (Cheng et al. 2014). In the paper of Cheng (2014), it can be observed variation of the velocity field in cross sectional plane between models with and without FSI.

The objective of this work is to study the influence of FSI on the drug distribution in a three-dimensional model of the intrathecal space. It is considering mechanical behavior of SC and Dura Mater (DM) generated by pulsatile flow of CSF.

2. Methods

2.1 Geometry

The idealized geometry consists in a regular section in transversal plane and a distorted pipe reproducing kyphosis and lordosis in sagittal plane. Curve is based

on MRI data obtained in collaboration with university hospital of Poitiers.

In the middle, a solid distorted cylinder is representing the SC from the base of the skull (BoS) to the caudal end. A thin membrane representing the DM from the BoS to the L5 vertebrae is considered. The space between SC and DM is filled by the fluid representing the CSF.

Fluid and mechanical properties are reported in **Table 1**.

Table 1. Fluid and mechanical properties used in the computational models.

Solid properties	E (MPa)	ν	ρ (kg/m ³)
Dura mater (Li et al. 2011)	31.5	0.45	1174
Spinal cord (Cheng et al. 2014)	0.7	0.45	1050
Fluid properties	μ (kg/(m.s))	ρ (kg/m ³)	
CSF (Kamina 2013)	0.001	1000	
Drug	0.001	1000	

2.2 Boundary conditions

Fluid domain

The mixture CSF+Drug is considered as an incompressible, newtonian fluid and the Drug is supposed to be totally miscible within the CSF. Initially all fluids are at rest.

For CSF, velocity inlet is applied at the BoS as:

$$\vec{v}_{CSF} = A \sin(2\pi ft)$$

With $A = 0.02m$ is the amplitude, $f = 1Hz$ the frequency and t the time.

For drug, velocity inlet is applied at 0.589m/s to be equal as 10 mL/min flow rate. The drug distribution is continued during all the simulation.

Fluid domain is composed by 138157 cells.

Structure domain

The structure domain is composed by DM and SC.

DM is described as a shell with 0.3 mm thickness (Reina et al. 2015). Inner diameter is equal to 15 mm. Fixed support is applied on the totally DM's surface.

SC is described as a solid with 7.5 mm diameter. Fixed support is applied at rostral extremity, caudal extremity is free.

Solid domain is composed by 26638 elements.

2.3 Numerical method

Numerical solver

The whole problem is solved using the commercial package software Ansys Multiphysics. The Navier-Stokes equations coupled with the concentration equation are solved with the software Fluent.

The displacement and deformation of SC and DM are calculated with Finite Element solver Mechanical.

Fluid-Structure Interaction modelling

FSI is accounted since the fluid flow exerts some constraints on the SC and the DM. In return, the modification of fluid domain will influence the fluid flow. Data transfer between the fluid and mechanical solvers are managed with the Ansys System Coupling. Data transfers concern pressure forces and displacement for CSF/SC interface and CSF/DM interface. A time step of 0.01 s was used.

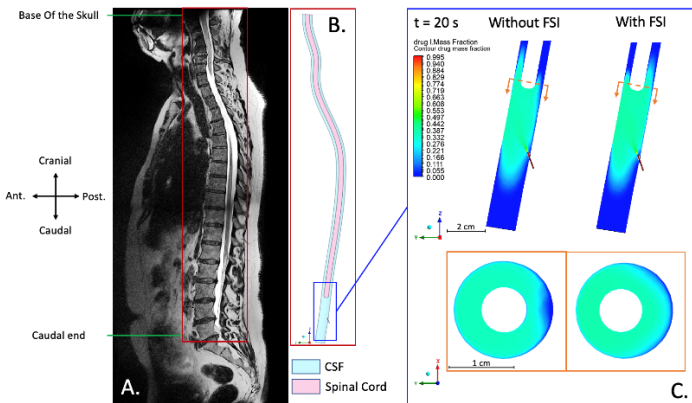


Figure 1. (A.) MRI data, (B.) Idealized geometry based on MRI data, (C.) Results of drug distribution at 20s in sagittal and transversal planes.

3. Results and discussion

Results on **Figure 1** show the mass fraction distribution of drug at 20 s.

As expected, the drug distribution is influenced by pulsatile flow of CSF as it increases the mechanical stirring (Hettiarachchi (2011)).

In transversal plane, the drug can be seen to wrap around the SC. In sagittal plane, the drug appears to flow both upstream and downstream of the injection point because of the incoming jet impacting the opposite wall. As expected, the mass fraction distribution of the drug shows a slight discrepancy between the model with and without FSI.

It can be interesting to simulate the impact of FSI on drug distribution after the injection in future works.

4. Conclusions

In this paper, 3D numerical simulations have been undertaken to compute the drug distribution in the intrathecal space over 20 s. Our simulations show that FSI has an impact on the drug distribution itself. Although moderate, the mechanical behavior of SC due to the fluid flow has an influence on the mixing and should be investigated further in future works.

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Conflict of Interest Statement

The authors declare that they have no conflict of interest

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