Detailed description of the research project

Question to be addressed

The aim of the research is to conduct a rigorous examination of the hydrodynamics affecting syrinx filling. For this purpose it is necessary to build a computer model of spinal CSF dynamics along the lines of that which I have developed previously, but now incorporating poroelastic effects without sacrificing treatment of transient behaviour.

In four major published papers since 2005 (two with co-authors), I have developed a computer model of the spinal cord hydrodynamics. The model is based on interaction between flexible solid structures representing the spinal cord and the dura mater on the one hand, and incompressible fluid flow in the intervening spinal subarachnoid space (SSS). Besides these basic elements, variants of the model have included a fluid-filled syrinx in the cord tissue, stenosis of the SSS by a flexible partial occluder attached to the dural surface, subdivision of the cord into a tough outer membrane (pia mater) and soft parenchyma, the ligament called the *filum terminale* connecting the end of the spinal cord to the coccyx, the widening of the SSS called the lumbar cistern, and string-like elements connecting the dura and cord to simulate arachnoiditis. The model can be excited by transient or repetitive pressure changes applied either at the cranial end of the SSS, to represent the effects of cranial arterial pulsation, or externally to the abdominal dura, in an approximation of cough. To maintain enough simplicity to allow cause and effect to be discerned, the model is axisymmetric and two-dimensional. All dimensions and parameter values are based on measured reality, allowing a limited degree of quantitative comparison of the model's predictions with measurements *in vivo*.

The judicious choice of just enough complexity to allow the model to simulate reality in a simplified but largely faithful way, while eschewing the three-dimensional burden of detail that turns a model into a large-team project, has allowed it to be used to investigate a number of questions which are central to the possible hydrodynamic generation of syrinxes, and to establish a number of fundamentals about spinal hydrodynamics. These include (among others) the existence of four different wave types, the role of reflected and refracted waves, the effect of SSS waves and pulsatile flows on syrinx fluid motion, the possible influence of arachnoiditis on syringogenesis, the protective effect of the *pia mater* for a syrinx-including cord, and the ways in which co-located SSS stenosis affects the mechanical environment experienced by a syrinx. The model's findings have influenced current thinking on many of the physical processes involved in initial genesis and subsequent growth of a syrinx, helping to define what is mechanically feasible and what is not.

However, the further development of the model requires inclusion of effects which cannot be achieved using the software on which it is currently based. In particular, up to now the model has been limited to an impermeable syrinx, where the reality is that syrinx fluid is thought [1] to be continuous with cerebrospinal fluid (CSF) in the perivascular spaces around the blood vessels which penetrate the cord tissue.

Rationale

The model can potentially address the conundrum that syrinxes have been reported [2] to have pressure exceeding that in the SSS from which their fluid is thought to be derived. There is currently no consensus about this; some authors (e.g. [3]) have found no difference between syrinx pressure and SSS pressure. It may be that some syrinxes have raised pressure and some do not, and that the location of the syrinx in relation to the local abnormality that caused it (typically Chiari malformation, or scarring from old trauma) determines whether the pressure is elevated. (There is also a school of thought [4] that syrinx fluid is derived from extracellular fluid exuded from cord capillaries, and not

from CSF.) There is currently only one physics-based hypothesis for how elevated pressure might arise [5] if the source of syrinx fluid is the CSF. I have developed an alternative hypothesis, arising out of the modeling reported in my 2010 paper. However, it cannot be tested properly using the current model. The present limitation of the model whereby the syrinx has fixed volume and the cord is a simple viscoelastic solid must be relaxed, if it is to address these questions. This in turn demands that the model be adapted to include the fluid-phase flow through pores in the cord parenchyma.

Research plan

The model is currently realized in the commercial code ADINA. This is well suited to the modeling of the interactions between flexible solids and adjacent fluids. However, it does not permit the simultaneous inclusion of poroelastic and viscoelastic properties for the solids. Viscoelasticity is an essential part of the damping of the transient excitations of the system, by arterial pulsation or by coughing, sneezing, straining, etc. The excitations give rise to wave phenomena which are not handled in ADINA's poroelastic set-up, which is essentially based on Darcy flow, i.e. is quasi-steady in concept. Thus even if poroelastic and viscoelastic options could be combined, the poroelastic formulation in ADINA is inappropriate.

The intention is to move the model to the open-source software oomph-lib, which is "an object-oriented, open-source finite-element library for the simulation of multi- (and single-)physics problems, developed and maintained by Matthias Heil and Andrew Hazel of the School of Mathematics at The University of Manchester"— http://oomph-lib.maths.man.ac.uk/doc/html/index.html. Correspondence with Prof. Heil has confirmed that the library is capable of realizing a version of the model including all the desired phenomena. Once it has been confirmed that the model coded in oomph-lib gives quantitatively identical results to the existing model, the model will be extended to include dynamic poroelastic behaviour. Much existing work on poroelasticity involves assumptions of quasi-steadiness which are incompatible with treatment of the pressure wave-induced transients in the SSS, but a new paper by my ex-student and current collaborator Elliott [6] sets out the analytical framework for their simultaneous incorporation. This extended model will then be used to test the new hypothesis for syrinx filling exhaustively, and to assess the merit of existing theories on this vital topic.

[1] Stoodley MA, Brown SA, Brown CJ, Jones NR. Arterial pulsation-dependent perivascular cerebrospinal fluid flow into the central canal in the sheep spinal cord. J Neurosurg. 1997;86:686–93.

[2] Milhorat TH, Capocelli AL, Kotzen RM, Bolognese P, Heger IM, Cottrell JE. Intramedullary pressure in syringomyelia: clinical and pathophysiological correlates of syrinx distension. Neurosurgery. 1997;41:1102–10.

[3] Heiss JD, Patronas N, DeVroom HL, Shawker T, Ennis R, Kammerer W, et al. Elucidating the pathophysiology of syringomyelia. J Neurosurg. 1999;91:553–62.

[4] Greitz D. Unravelling the riddle of syringomyelia. Neurosurgical Review. 2006;29:251–64.

[5] Bilston LE, Stoodley MA, Fletcher DF. The influence of the relative timing of arterial and subarachnoid space pulse waves on spinal perivascular cerebrospinal fluid flow as a possible factor in syrinx developments. J Neurosurg. 2010;112:808–13.

[6] Elliott NSJ. Syrinx fluid transport: modeling pressure-wave-induced flux across the spinal pial membrane. ASME J Biomech Eng. 2012 (in press).