Predicting calvarial growth in normal and craniosynostosic mice using finite element analysis

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The cranium consists of several bones that are joined together at their edges by soft tissue called sutures. Early fusion of sutures is a medical condition, known as craniosynostosis. Cruzon mouse is a well-established animal model displaying bicorporal suture fusion and an invaluable model to understand the biomechanics of the skull growth. The aim of this study was to predict calvarial growth in wild type (WT) and mutant, cruzon, (MT - *Fgfr2*$^{C342Y/+}$) mice.

Two ontogenetic series of WT and MT mice were scanned using micro-computed tomography. A 3D finite element model of a WT mouse skull at day 3 postnatal development age (P3) was created, including the bones, sutures and brain. The model was used to predict the WT and MT calvarial growth at P7, P10, and P20 where intracranial volume in mouse plateau. Input parameters to the model were estimated based on a series of parallel experimental studies. Nevertheless, several sensitivity analyses to the input parameters were performed and outputs were compared to *ex vivo* specimens in terms of the overall calvarial shape and bone formation at the sutures.

Sensitivity analyses showed that model predictions were sensitive to the input parameters. However, using the experimental data, the model could predict the radial expansion of the calvarial bones and bone formation at the sutures at P7 and P10 in WT mouse. For example, the difference of calvarial length, width and height between the *ex vivo* and FE predictions were 5%, 13% and 12% respectively. Further, the model predicted the overall shape of the MT skull at P10, which has a slightly taller, wider and shorter profile compared to the equivalent WT skull at P10.

The models developed in this study are the first validated models of mouse calvarial growth. The close match between the predicted shape of the models and *ex vivo* data build confidence in the modelling approach. However, further studies are required to refine the models. Such models can be used in long term for patient-specific modelling of craniosynostosis.