Introduction: The key processes during prenatal joint development are interzone formation, cavitation and morphogenesis [1]. Joint morphogenesis is the process during which two opposing cartilaginous rudiments develop their reciprocal and interlocking shapes [1], and is highly relevant to postnatal skeletal abnormalities, particularly to developmental dysplasia of the hip (DDH). DDH is a condition in which hip joint morphogenesis does not proceed correctly and has an incidence of 1.3 per 1000 births [2]. It is known that reduced or restricted movements in utero, due to neuromuscular disorders or breech positioning, increase the risk of DDH [3], but the effects of abnormal movements on the prenatal onset of DDH have never been quantified. Normal hip joint development has been described by Ralis et al. [4], who showed that the very early prenatal human hip joint is formed from a deep acetabular cavity which almost totally encloses the femoral head. By the time of birth, the acetabulum has become shallower and the femoral head has lost substantial sphericity (which is then regained after birth) [4]. In this study, we use a dynamic mechanobiological simulation to explore the effects of normal, restricted and abnormal prenatal movements on hip joint shape, giving new insights into the etiology of DDH.

Methods: A 2D biomechanical model of an idealised prenatal hip joint, consisting of two opposing rudiments, was constructed using a modified version of our previously published model [5] (Figure 1A). All material properties were assumed to be linear elastic, isotropic and homogeneous; E=1.1 MPa and v=0.49 [5]. Using the mechanobiological theory for cartilage developed previously, growth and adaptation were directed by biological (i.e. intrinsic growth of the rudiments) and mechanobiological factors. Mechanobiological growth was driven by a region-specific biophysical stimulus (hydrostatic stress), where static hydrostatic compression inhibits cartilage growth and dynamic hydrostatic compression promotes cartilage growth. Three phases of development were modelled; early, middle and late, where the growth rates and range of movement decreased step-wise over the three developmental phases. “Physiological loading” was defined as the application of symmetric movements (Figure 1A), with a range of motion of ±40° in the early phase, ±30° in the middle phase and ±10° in the late phase. Three different parameters were analysed to quantify the changes in shape of the hip joint: acetabular angle, which reveals the opening of the acetabulum; acetabular shape, which is the ratio between the greatest width of the cavity and the acetabular depth; and the femoral head sphericity, calculated as the ratio between the greatest head diameter and the femoral head height. We also explored the effect of decreased movements on joint shape by reducing the extent of motion to ±10° in the early or middle phases. Finally, we simulated hip joint shape development when asymmetric movements were applied (Figure 1D).

Results: With physiological symmetric loading, our model predicted a progressive opening of the acetabulum, making it increasingly shallow, and a gradual decrease in sphericity of the femoral head (Figure 1A-C). These trends correlate well with anatomical changes in shape reported previously [4]. When reduced movement at the early phase was simulated, the femoral head sphericity decreased further and the acetabulum became shallower compared to the physiological simulation (Figure 2A, B),
resulting in a less stable joint. Reduced movements at the middle phase of development resulted in minimal joint shape changes and no severe loss in joint stability (Figure 2, A, B). The rates at which the acetabular depth and the femoral head sphericity decreased were inversely proportional to the ranges of movement, suggesting that fetal movements help to maintain the ball & socket configuration, while reduced or absent movements contribute to the loss of joint stability (data not shown). When an asymmetric movement pattern was applied, the acetabulum tended to open in the same direction as the applied loads. The acetabulum no longer acquired a symmetric shape, and the shape of the femoral head was also affected, leading to a dysplastic hip joint shape (Figure 1D-F).

**Discussion:** This study demonstrates how fetal movements are extremely important for hip joint stability at birth. Symmetric movements help to maintain the ball & socket configuration of the hip by maintaining acetabular depth and femoral head sphericity. Reduced movements, especially at an early stage of development, contribute to the loss of joint congruity making it less stable and increasing the risk of subluxation or dislocation of the hip. Our model predicts that asymmetric movements lead to an abnormal joint shape, providing further evidence for the importance of fetal movements for the manifestation of congenital disorders such as DDH in the infantile hip.

**Significance:** Mechanical forces due to normal fetal movements contribute to the stability of the developing hip joint by maintaining acetabular depth and femoral head sphericity, while reduced or asymmetric movements lead to decreased joint stability, providing insight into the etiology of DDH.
Figure 1. A) Initial model configuration with symmetric movements. B, C) rounding shapes after 10 and 28 steps respectively of symmetrical movements. The acetabulum progressively opens and the sphericity of the femoral head gradually decreases. D, E) Model configuration with asymmetric movement (E). F) rounding shapes after 10 and 28 steps respectively of asymmetric movements. The acetabulum loses its round shape and the femoral head becomes deformed.

Acetabular Shape

Femoral Head Sphericity

Figure 2. Changes in acetabular depth (A) and femoral head sphericity (B) during early and middle phases of development. Reduction in acetabular size during early phases of development had a substantial impact on final joint shape, while reduced acetabular size during the middle phase did not have a large effect on joint shape.