

specifically in the mesenchyme of developing limb buds as early as embryonic day 9.5. These mice were then crossed to mice with conditional (floxed) alleles of the Gsk3b gene, resulting in knockout (KO) GSK-3 $\beta$  specifically in the limb buds. These KO mouse mutants were then compared to their control littermates to examine any physical and molecular differences through whole skeletal preparations, immunohistochemistry on tissue sections, and a variety of other techniques.

In addition to my *in vivo* studies, I will perform *in vitro* micromass cultures utilizing both an adenoviral delivery of Cre recombinase (with adenovirus-GFP as control) and pharmacological inhibitor to inactivate GSK-3. The *in vitro* studies will allow for further investigations into the molecular mechanisms associated with GSK-3 function in limb development, with a focus on the canonical Wnt/ $\beta$ -catenin pathway.

**C. Results:** My preliminary analyses of the first mutants I obtained indeed suggest that their limbs are shorter, with a noted difference in digit length. Tissue sections of different long bones show a slight difference within the growth plate between the mutant mice and their control littermates.

The *in vitro* micromasses cultures stained with alcian blue, which represents glycosaminoglycans in cartilage, show an increase in alcian blue stain with increasing concentration of the GSK-3 inhibitor SB86. Real-time PCR data of day 3 micromasses treated with SB86 indicates that there is a decrease in Aggrecan, Col2a1, and Sox9 markers, while Col1a1 remains relatively stable. Preliminary western blots show an increase in  $\beta$ -catenin accumulation within the micromasses treated with increasing concentrations of SB86.

**D. Conclusions:** Together, these studies will provide insights into the mechanisms controlling limb development. Previous studies indicate that disruption of the Wnt pathway, as we expect to occur in our model, causes limb malformations including brachydactyly and syndactyly, which are clinically important birth defects in humans. Our studies are therefore highly relevant to these birth defects, as well as adult skeletal diseases such as osteoarthritis that show a clear connection to skeletal development.

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### DIAGNOSTIC VALUE OF INTRA-ARTICULAR ANAESTHETIC HIP JOINT INJECTION IN PATIENTS WITH ATYPICAL HIP PAIN: A SYSTEMATIC REVIEW

D.M. Dorleijn, P.A. Luijsterburg, S.M. Bierma-Zeinstra, P.K. Bos. *Erasmus MC, Rotterdam, The Netherlands*

**Purpose:** Pain in the hip region can arise from different sources. These include intra-articular hip joint pathologies such as osteoarthritis, acetabulofemoral impingement, labral pathology as well as extra-articular causes such as greater trochanter pain syndrome, inguinal hernia, and referred or radicular pain from the lumbosacral spine. Although with careful history and examination hip osteoarthritis can often be distinguished from other origins, sometimes symptoms are atypical. In these cases, when total hip replacement surgery is being considered, an intra-articular anaesthetic hip injection is frequently used as a diagnostic tool for excluding or confirming an intra-articular source of hip pain.

To assess the diagnostic value of intra-articular anaesthetic hip injection in patients with atypical hip pain.

**Methods:** Searched databases were PubMed, Embase, PEDro and the Cochrane Library (until December 2011). Included were cohort studies, randomized controlled trials and case series assessing the diagnostic value of anaesthetic hip injections in differentiating between hip pain caused by osteoarthritis or another source in patients with atypical hip pain. Key terms used were: "osteoarthritis", "hip", "spine", "diagnostic" and "intra-articular".

Two reviewers independently selected studies for inclusion, extracted data and assessed methodological quality. Depending on homogeneity of the studies, we calculated pooled estimates of sensitivity and specificity with 95% confidence intervals (CI).

Positive effect of total hip replacement surgery after a positive test and positive effect of spinal treatment after a negative test were used as reference test. Additional calculations were done for a total hip replacement-only scenario.

Methodological quality of the studies was assessed with the Quadas2 tool.

**Results:** The search yielded 1387 eligible studies. Finally, 9 articles were included representing 556 patients with hip pain; seven studies were included in the meta-analysis.

The studies were heterogeneous as to patient characteristics and outcome measurements.

The pooled estimates of sensitivity and specificity were .97 (95% CI .87, .99) and .91 (95% CI .83, .95). This corresponds with a positive likelihood ratio of 10.6 (95% CI 5.6, 20.1) and a negative likelihood ratio of 0.04 (95% CI 0.01, 0.15).

The total hip replacement-only scenario contained patients who had received a total hip replacement and their pain outcome was scored afterwards. The pooled estimates of sensitivity and specificity were .96 (95% CI .87, .99) and .42 (95% CI .09, .84).

**Conclusions:** These results show that complete or partial hip pain relief after intra-articular anaesthetic hip injection is reasonably predictive of pain relief after total hip replacement surgery. However, the value of a negative test (no pain relief after hip injection) is unclear. As our results may have been influenced by heterogeneity and missing data, the evidence for the diagnostic value of an intra-articular anaesthetic hip injection is not conclusive.

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### ASSESSING HAND OSTEOARTHRITIS USING DIGITAL PHOTOGRAPHS IN A COMMUNITY-DWELLING POPULATION: RELIABILITY AND ASSOCIATIONS WITH RADIOGRAPHIC AND CLINICAL FEATURES

M. Marshall<sup>†</sup>, H. Jonsson<sup>‡</sup>, G.P. Helgadóttir<sup>§</sup>, E. Nicholls<sup>†</sup>, D. van der Windt<sup>†</sup>, H. Myers<sup>†</sup>, K. Dziedzic<sup>†</sup>. <sup>†</sup>Keele Univ., Staffordshire, United Kingdom; <sup>‡</sup>Landsþítalinn Univ. Hosp., Univ. of Iceland, Reykjavik, Iceland; <sup>§</sup>Univ. of Iceland, Reykjavik, Iceland

**Purpose:** An atlas for grading hand osteoarthritis (OA) on photographs has been shown to be reliable and associated with clinical examination and radiographic features in a population of older adults (aged  $\geq 69$  years) from the AGES-Reykjavik study. The objective of this research was to determine if this atlas was reliable and to assess its association with radiographic and clinical features in a different younger community-dwelling population.

**Methods:** Participants were community-dwelling older adults ( $\geq 50$  years) in North Staffordshire, UK with self-reported hand pain or hand problems in the last year who attended a research clinic. High quality photographs taken at a set distance in a standardised position were graded for the presence of hand OA using an established atlas. Hand radiographs were graded for OA using the Kellgren Lawrence grading system and the presence of clinical features (nodes, bony enlargement, deformity) was determined on physical examination by trained assessors.

**Results:** Following exclusions 558 participants (mean age 64 years, 62% female) were included in the analyses. Overall reliability for scoring each joint and joint group was good (mean intra-rater ICC = 0.79, mean inter-rater ICC = 0.71). For each joint and joint group photographic hand OA was positively associated with grade of radiographic OA ( $\rho$  0.19–0.57,  $p < 0.001$ ) and the number of clinical features present on an examination ( $\rho$  0.36–0.59,  $p < 0.001$ ). At the person level, individuals with higher global photographic hand OA scores had higher summed K&L scores and had higher percentages meeting the ACR clinical hand OA criteria.

**Conclusions:** This photographic scoring system for hand OA has been shown to be reliable and associated with both radiographic and clinical features in a different and younger community-dwelling population to that in which it was developed. This method of data collection offers researchers an feasible alternative to the physical examination and maybe of particular use to large studies and those spread over a wide geographic areas.

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### LOW SURGEON VOLUME IS ASSOCIATED WITH INCREASED COMPLICATIONS FOLLOWING TOTAL HIP ARTHROPLASTY, AFTER ACCOUNTING FOR EXPERIENCE

B. Ravi<sup>†</sup>, R. Croxford<sup>‡</sup>, G.A. Hawker<sup>†</sup>. <sup>†</sup>Univ. of Toronto, Toronto, ON, Canada; <sup>‡</sup>Inst. of Clinical Evaluative Sci. (ICES), Toronto, ON, Canada

**Purpose:** Provider volume-outcome relationships for total hip arthroplasty (THA) have been demonstrated in the US, but, to date, not in Canada. Potential explanations for differences include a relatively low proportion of surgeons in Canada with low arthroplasty volumes. A previous study which examined this relationship in Canada pooled the surgeon's total volume over the entire time period, to avoid penalizing surgeons with less experience. We sought to re-examine this issue by determining the surgeon's procedure volume in the year prior to the