

# ROUNDUP<sup>360</sup>

## Research

### Contact patch to rim distance and metal ions

■ The voluminous research concerning metal-on-metal arthroplasty has identified a huge number of predictors of metal ion levels and outcome, including component design, size, orientation, patient gender and body mass index. What is currently missing is a single, easy-to-use rule of thumb that might be able to predict metal ion levels. Researchers in **Los Angeles (USA)** have described and validated a contact patch rim distance (CPR) as a predictor of metal ion levels. The authors point out that many of the known predictors of failure have an effect on the CPR distance. The research team used a retrospective series of patients to evaluate the utility of this new method. They included 182 patients who underwent arthroplasty with a Conserve Plus prosthesis followed up to a minimum of 12 months. Patients had Co and Cr serum levels measured using the (now standard) inductively coupled mass spectrometer method. Data were analysed using a multiple logistic regression model to determine which factors related to serum ion levels. The results were astoundingly good. In patients with a CPR < 10 mm there was a 37 × increased risk of elevated Co levels (> 7 µg/l) and an 11 × increased risk of elevated Cr levels (> 7 µg/l).<sup>1</sup> When combined with negative predictive values in the high 90% range, we would agree with the authors of this paper that it would be reasonable to exclude those patients from a

serum-based follow-up programme. The difficulty, of course, is accurately determining the contact patch in the normal clinical environment.

### Hypoxic cartilage has good matrix

■ In vivo cartilage is in a mostly hypoxic environment, with oxygen tensions within a native joint rarely rising above 10% and well below 1% in the deepest cartilage layers. In addition to this concentration gradient within the cartilage layers (spatial gradient), there are temporal changes in oxygen tension during cartilage development which may have an effect on the tissue itself. It is curious to us here at 360 HQ to find that the majority of tissue culture protocols used in chondrocyte cultivation do so at ambient oxygen concentrations. We understand the very good reasons why this might be (chondrocytes are difficult to culture, and become increasingly difficult to do so in a hypoxic environment), but, by altering normal conditions, are we in fact compromising the engineered tissue? Researchers in **New York (USA)** set out to examine the effects of oxygen tension on engineered cartilaginous extracellular matrix by comparing the quality of tissue produced in normoxia (21% PaO<sub>2</sub>), hypoxia (5% PaO<sub>2</sub>) and transient hypoxia (5% PaO<sub>2</sub> for seven days, then 21% PaO<sub>2</sub> for 21 days) on engineered cartilage constructs over a month of incubation. They were then able to measure the effects on cartilage and matrix production through gene expression. In a very

well rounded study the research team demonstrated that most effective up regulation of collagen and chondrogenic genes (COL2A1, ACAN and SOX9) was seen in the transient hypoxia group and when combined with increased tissue expression of GAG's and type II collagen this forms a fairly conclusive picture: transient hypoxia improves expression of matrix proteins. How this affects the quality of engineered cartilage was also addressed in this study. The research team tested the Young's modulus of elasticity for these constructs, and found hypoxic tissue culture (but not normoxic or transient hypoxia) to result in eroded mechanical properties.<sup>2</sup> It certainly seems, from this investigation at least, that current tissue culture protocols might be missing a bit of a trick. Perhaps it's time to revisit the 'standard' culture protocols.

### CT assessment of early fracture healing

■ The early stages of fracture healing do not result in radio-opaque cartilage or matrix formation. Visualisation of early callus on radiographs and CT is impossible. This causes problems with diagnosis of nonunion as well as making basic science investigation of fracture healing difficult. Researchers in **Boston (USA)** have investigated the value of a novel contrast-enhanced CT (CECT) scan as a non-destructive method of identification of early callus formation. The researchers investigated the method using a mouse model of a closed stabilised femoral

fracture. The mice were killed at day nine and subsequently imaged with micro-computed tomography (µCT), both before and after staining with a cationic contrast agent that preferentially accumulates in early cartilage. The researchers used co-registration of two images; pre- and post-contrast. Two- and three-dimensional images of bone, soft callus and cartilage were then produced using a combination of the CT and CECT. Subsequent testing with histomorphometric measurements was able to confirm that the CECT was able to accurately determine callus and cartilage areas in addition to identification of mineralised cartilage. The advantage of the CECT method is that, as it is non-destructive, the tissue can be used for further analysis.<sup>3</sup>

### Pressure of relief?

■ At least part of the pathophysiology of carpal tunnel syndrome is increased pressure within the tunnel, although evidence suggests that this is only part of the pathophysiology. Studies investigating the pathoanatomy of carpal tunnel syndrome have demonstrated that the pressure within the tunnel varies with posture, and that there are typical morphological changes seen with increasing pressure within the intact canal. With patients who have undergone transverse ligament release, the relationship is unknown. Researchers in **Cleveland (USA)** undertook endoscopic release of cadaveric transverse carpal ligaments to simulate carpal tunnel surgery. The pressure within the canal was

then increased dynamically from 10 mmHg to 120 mmHg and recorded using an implanted pressure transducer. Changes in morphology of the carpal tunnels were studied using ultrasound scanning as the pressure was increased within the tunnels. Interestingly, despite the release having been undertaken, there were significant changes in morphology of the tunnel with an increase in carpal arch area of 62 mm<sup>2</sup> with 120 mmHg pressure. The increasing pressure affected arch height, length (increased) and width (decreased) significantly. Comparisons made with unreleased carpal tunnels previously investigated, suggested an order of magnitude increase in compliance following transverse ligament release.<sup>4</sup> Although a small basic science paper published in a relatively specialised journal, we can't help but feel a small twinge of satisfaction here; this paper represents for us the final piece in the puzzle. Despite some arguments to the contrary there is now ample evidence that this condition is caused by intrinsic pressure within the tunnel, that the tunnel has limited compliance prior to release, and that following release the compliance increases markedly, accommodating more space with the increase in pressure. As the mathematicians would say, 'QED'.

### John Charnley may have been right

■ In the early days of joint replacement (and other forms of orthopaedic surgery), patients across the British Isles (and indeed in other countries) were customarily asked to take a shower or bath prior to their attendance at the OR. This is a custom that has all but disappeared in many hospitals as it is time-consuming and lacks an evidence base; that is, of course, excepting those patients who are MRSA positive where the extensive decolonisation regime necessitates regular bathing in antiseptic. Our interest was reignited in this process, having read a completely non-orthopaedic research paper published in a recent edition of the

Lancet. Researchers in **Baltimore (USA)** taking part in the SCRUB trial have published some of their results. In their large study, critically ill children were randomised to either daily bathing in chlorhexidine gluconate or standard bathing. Their chosen outcome measure was incidence of bacteraemia. In a slightly complex cluster-randomised two-period cross-over trial, the investigators randomised specific paediatric high dependency and intensive care units to a specific daily bathing protocol. These were then

switched after six months for a second six-month period. The study team were able to enrol 4947 patients (1521 were excluded for length of stay < 48 hours). The researchers identified a significantly lower incidence of bacteraemia in the chlorhexidine group (3.28 per 1000 days) as compared with the standard practice group (4.93 per 1000 days). There were no serious adverse events although the incidence of chlorhexidine skin reactions was 1.2 per 1000 days.<sup>5</sup> The research team concluded that daily chlorhexidine bathing reduces the incidence of bacteraemia in critically ill children. This has direct implications for the management of paediatric trauma victims, but also caused us to stop and think – perhaps we should go back to some of the old-fashioned nursing practices. If skin decontamination can reduce the incidence of bacteraemia, it certainly could reduce infection rates following surgery.

### Hawthornes and radiographs

■ Sometimes the smallest changes can have the biggest impact on clinical practice. A research team in **Cork (Ireland)** introduced weekly quality reviews of all intra-operative radiographs as part of the hospital's risk management and clinical governance framework. The research

team used the "Tip Apex Distance" as an objective surrogate measure of surgical quality and to monitor any changes in surgical outcomes following the implementation of the new outcome system. The researchers demonstrated effectively that the number of TAD measurements over 25 mm decreased significantly following the introduction of the quality control system - an illustration of the Hawthorne (audit) effect in action.<sup>6</sup>

### Cardiovascular mortality and fragility fractures

■ It is a well described relationship between osteoporotic fractures and excess mortality. Age-matched controls demonstrate excess mortality, an effect that is most pronounced during the first six months after fracture. Despite this well described association, what is unclear are the timing and causes of death within the early post fracture period. Researchers in **Innsbruck (Austria)** studied the causes of death following a fragility fracture (pelvic, proximal femoral, spinal, or proximal humeral) at the 30- and 90-day time points. The study included 1630 patients sustaining 1630 fractures admitted for inpatient management over a six-year period. The majority of patients were women and the median age was 83 years. The study group suffered 58 deaths within 30 days of fracture (3.6%) and 122 deaths (7.5%) by 90 days following fracture. The most common cause of death was cardiovascular in all fracture groups. There was a significant excess mortality associated with spinal fractures.<sup>7</sup> The effect of spinal fractures on mortality has often been underestimated and the particular focus on proximal femoral fractures over the past few years may have overshadowed the not-insignificant disease burden

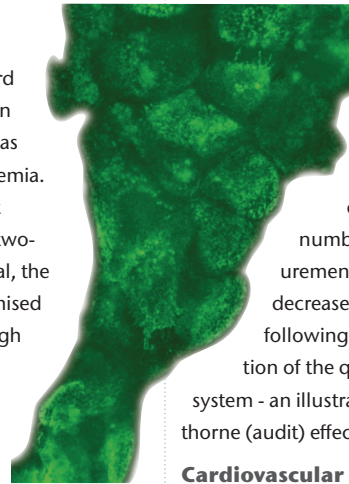
shared by these patients.

### Muscle strength decline precedes OA changes

■ The debate surrounding muscle strength and osteoarthritis has an element of 'chicken and egg'. Which came first; the OA or the muscle weakness? The difficulty with unpicking such a complex problem is that capturing patients before they develop osteoarthritis is extremely difficult. Researchers in **Salzburg (Austria)** have utilised an Osteoarthritis Initiative to establish if cross-sectional longitudinal measures of muscle isometric strength differ between knees that subsequently develop OA and those that do not. The study participants consisted of 4796 participants, of whom 2835 knees with Kellgren Lawrence (KL) grades < 3 underwent annual radiographs, quantitative joint space width and isometric muscle strength measurements. Of the initial 4796 participants, 466 knees progressed to developing OA during the observation intervals (two years apart) and 946 did not. Females with progressive disease, no matter how severe, exhibited lower extensor and flexor muscle strength by the second year than those without progression, but this was a non-significant difference. There were no other significant changes observed in any group of progressors or non-progressors.<sup>8</sup> This study provides no strong evidence that isometric muscle strength changes are associated with osteoarthritic changes. The evidence presented here supports the hypothesis that muscle strength-related changes are purely a symptom of osteoarthritic change and not part of the disease process itself.

### REFERENCES

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