Assessment of Graphene Oxide Hydrogel Treatment for Osteoporotic Hip Strengthening

Project team
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Background
Osteoporosis is a disease that causes fragile bones, increasing the risk of fracture. It is estimated that the disease affects 3 million people in the UK [1] and it is particularly problematic in the elderly and post-menopausal women [2]. Total hip arthroplasty (THA) is a common treatment for osteoporotic fracture that costs the NHS approximately £1.5 billion annually [3]. Osteoporosis can lead to complications in hip replacements including delay in osseo-integration and aseptic loosening [4-6]. Consequently, potential treatments to improve bone mineral density in osteoporotic bones have been developed [7-9] including a graphene/stem cell impregnated hydrogel developed by the Co-I, Dr Hidalgo-Bastida. This biomaterial has demonstrated superior mechanical and antimicrobial properties [10], with applications not only for bone regeneration but also for cardiac and neural, promising a step change in biomaterials to deliver cell and/or drugs for regenerative treatments.

Our research team wish to test the feasibility of injecting graphene/stem cell impregnated hydrogels into osteoporotic bones to improve the clinical outcomes of total hip arthroplasty. This project will produce essential pilot results to support a £900 thousand EPSRC project application to develop new treatment technology.

Methodology and Outcomes
We will undertake two work packages (WP) to prove feasibility of the hydrogel injection approach:

WP1: In vitro osteoporotic ovine bone models (January-February 2019)
Decalcification of Ovine hips: will achieved by treating them with 10% formalin followed by treatment with 0.5 M of DTA decalcification solution (pH 7.4; Sigma) at room temperature. Bone Mineral Density (BMD): will be measured using DEXA (QDR 1000; Hologic, Inc.) and a QCT scanner (Siemens Sensation 16 CT Scanner; 120 kV, 100 mA, 1 × 10–mm/ pixel resolution) with a high-resolution bone algorithm. Usually osteoporosis is defined as a loss of trabecular bone with an area BMD level less than 0.75 g/ cm². The ovine hips will be treated to produce a range of bone mineral densities. Biomechanical Axial Compression tests: will be conducted to measure the failure stress and strain of control and decalcified hips (5 specimens in each group). Samples will be placed between 2 loaded platen rods on a Model 858 MTS Universal Testing Machine (MTS Systems) in quasi-static conditions until compressive failure occurs. CT imaging: will be used on one bone sample with an area BMD level less than 0.75g/cm².
Output 1: Data for relationships of compressive failure and bone mineral density and a medical image of the bone

WP2: Computational modelling (March-June 2019)
Finite element analysis: of a hip with a hip implant will be created from CAD models to determine the stress and mechanical failure risks from BMD changes in the hip. The model will be used to predict success and failure for a range of bone mineral densities (simulating severities of osteoporosis). Computational fluid dynamics (CFD): model created from CT imaging in WP1 will be used to predict the perfusion of the injected hydrogel in the osteoporotic bone. This treatment will only be successful if the hydrogel is injected in the right place and if it is able to travel through the porous bone structure. The CFD model will be used to investigate the relationship of hydrogel viscosity in a range of osteoporotic severities of bone.
Output 2: Conference paper for Biomechanics or Regenerative Medicine conference.

WP3: Grant preparation (May-June 2019)
Meetings with key stakeholders including Prof Gordon Blunn (University of Portsmouth) to discuss animal model, as well as with Dr Elisabetta Ferrari (Johnson & Johnson-Leeds) to discuss industrial involvement.
Output 3: Preparation and submission of an EPSRC grant application – approximate value £900k
Budget

Consumables = £2,303
- Demineralising solution (40L @£31.70/L + delivery £35) = £1,303
- Ovine hips (10, each at £50) = £500
- Lab consumables (plasticware, scalpels, containers, PPE) = £500

Dissemination in Conferences = £2030
ISB (Biomechanics theme)* - Canada 2019 (£530 reg, £800 flights, £700 acc. + subsistence) = £2,030
TERMIS (Clinical Translation theme)* - Rhodes 2019 (£700 reg, £400 flights, £700 acc. + subs) = £1,700
*The team will submit to both conferences but only attend one, depending upon acceptance and type of session.

UK Travel to meet stakeholders (Leeds £50 x 2 PI & Co-I, Portsmouth £200 x2 PI & Co-I) = £500

TOTAL £4,833

References
[1] Calculated using mid 2013 population data [i] and osteoporosis incidence from [ii].


