Home Office

NON-TECHNICAL SUMMARY

In-vivo assessment of new coatings for joint replacement implants.

Project duration

5 years 0 months

Project purpose

- (a) Basic research
- (b) Translational or applied research with one of the following aims:
  - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants.

Key words

Joint replacement, prosthesis, coating, sheep, bone

Retrospective assessment

The Secretary of State has determined that a retrospective assessment of this licence is not required.

Objectives and benefits

Description of the project's objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.

What's the aim of this project?

Joint replacements are commonly performed on people who have severe joint pain due to conditions like arthritis. Joint replacements describe the process of replacing a damaged joint with an artificial implant. To keep the implant more securely in the bone most implants have a coating that encourages the bone to stick to the implant. In this project we are investigating whether a new generation of coatings, based on glass technology, can stick the implant to the bone better than the coating that is currently used in human surgery and to investigate the claim that the glass coatings may help prevent infection at the site of surgery. The latter aim - whether the glass coatings are able to prevent infection will be studied in the laboratory and not in the animal models.

Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.

What are the potential benefits that will derive from this project?

Joint replacements are usually successful, however 12% fail due to loosening of the joint replacement implant within the remaining bone or infection.
If successful this project will have discovered a new coating that can be used to stick implants into bones more securely and with a reduced risk of infection to the patient. This will have significant implications for human joint replacements. It will reduce the time that the patient takes to get back to normal daily life, reduce the likelihood of loosening of the implant (making a second surgery less likely) and reduce the likelihood of infection from the joint replacement.

Species and numbers of animals expected to be used

What types and approximate numbers of animals will you use over the course of this project?

96 sheep over 5 years

Predicted harms

Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?

There are two protocols within the project. In the first protocol (80 sheep) the sheep will have a general anaesthetic and have small (6mm diameter) pins placed across one of the bones in one hind leg (all the pins will be placed during one anaesthetic). The number of pins that can be safely implanted will be determined in a pilot study but will be no more than 4. The purpose of this protocol is to identify which pins provide the best interface between the bone and the pin (bone integration and growth). The expected adverse effects of this protocol are pain lasting a short time associated with the placement of the pins and all animals will receive drugs to prevent pain after surgery. There is also a theoretical (but very small chance) of fracture of the bone after pin placement. In the second protocol (16 sheep) the

animals will undergo a hip replacement surgery. The possible adverse effects of this protocol are hip dislocation and fracture of the bone associated with the joint replacement. To help prevent this, all animals will be weight supported by a body sling for the first day after surgery and then be kept in a small pen (approximately 9m2) for 3wks after surgery to minimise exercise movement that may predispose to hip dislocation before being kept together in a larger pen. At all times, sheep will be kept together with at least one companion to avoid separation anxiety. All animals will receive drugs to prevent pain after surgery including the use of an 'epidural' – a long-acting injection that reduces pain from the pelvis and back legs.

At the end of the study the animals will be killed humanely so that we are able to collect information from the tissues to verify whether the study has been successful.

Replacement

State why you need to use animals and why you cannot use non-animal alternatives.

Developing new technology to improve surgical implants takes many years. The materials that will be used as coatings on the transcortical pins and hip implants in this study have been tested thoroughly in the laboratory prior to be used in animals and many possible materials that are not suitable for this purpose have been abandoned. We now need to use animals in the final part of this study so that we can show that the proposed coating materials fit well with bone (in a transcortical pin mode)and that they are successful in fixing a hip replacement into position in the animal model.

Reduction

Explain how you will assure the use of minimum numbers of animals.

We will always use the least number of animals necessary to achieve the aims of the project whilst getting meaningful results. For this study we will use 6 per group in the bone pin model and 8 animals per group in the hip replacement study. These numbers have been worked out statistically from previous studies. In our research we randomise our experiments – for example we randomise which animals get which treatment and in what order they undergo surgery. In some instances we ask researchers we work with outside our laboratory to randomly allocate animals to experimental groups. We believe that these methods contribute to the robustness of our data interpretation by removing bias. . In addition we use 'pilot' studies of a small number of animals to check what we plan to do is well tolerated by the animals before we apply the experiment to larger groups of animals.

Refinement

Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.

We have chosen the sheep as our model for a number of reasons. Whilst sheep do walk on 4 legs, not 2 like humans, the structure of the hip joint is similar to humans and so provides a good model in which to perform this work. If successful, the new coatings could be used in human patients without further experiments in animals being undertaken.

We will minimise animal suffering by ensuring that animals receive anti-inflammatory medication, similar to ibuprofen, during and after surgery and that the animals having the joint replacement receive a long-acting injection that reduces pain from the pelvis and back legs.For the majority of this work, of our animals are kept in groups and are kept as naturally as possible out in a grass field. A small number of animals will be kept in indoor pens immediately after their surgery (first 1-2 weeks), but will always be kept in close proximity with and within sight of other sheep to avoid separation stress during this time.

. We monitor our animals movement continuously through the experiment using measures of how much weight they are placing on their operated legs using clinical scoring and a force plate and a 'Fitbit tracker' [(this is a tracker placed on a collar around the neck of the sheep that records the activity of the sheep). Any animal that is showing abnormal movement or behaviour (as assessed by clinical examination, weight bearing and Fitbit activity monitoring can be quickly identified, examinedand any necessary treatment given.