NON-TECHNICAL SUMMARY

# Spine surgery: a new treatment

5 years 0 months

- (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

Orthopaedic, Surgery, Minimally invasive, Ultrasound, Implant

| | |
|---|---|
| Cattle | adult |
| Sheep | adult |
| Goats | adult |

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

The aim is to assess the safety and feasibility of novel medical devices, injectable implants, test articles or test substances used either as part of or in association with surgical procedures, or as part of or in association with non-invasive or minimally invasive procedures for tissue disruption or treatment, or for the treatment of conditions which may be simulated by surgical procedures. The context of this work is spinal disorders and in the first instance we are focusing on lower back pain.

Around 500 million people suffer from lower back pain, the 1st cause of disability and the 3rd largest cause of healthcare spending ($87.6 billion) globally. Patients with persistent, recurrent lower back pain currently only have two diametrically opposed treatment options: conservative therapy, involving either physiotherapy or minimally invasive injections; and major surgery, most commonly spinal fusion, a complex high-cost procedure associated with significant complications ultimately leading to reduced range of motion and quality-of-life. In 2017/2018, the NHS undertook 211,000 pain injections and 52,523 spinal procedures, whilst in the US there were 9m treatments and 520,000 surgeries. Across Europe and the US, some 120,000 patients present with discogenic pain and an intact annulus, the initial target population for the technology at the heart of this application. The aim is to provide these patients with an intermediate treatment option, enabling percutaneous, minimally invasive nucleus pulposus replacement as a day case procedure, at a fraction of the cost ($15K vs $113K) of current surgical options, and leading to restoration of spinal function.

At the end of this project, in the first instance the expectation is a validation of the new spinal treatment and prototype, plus the collection of data for regulatory submission.

The outcomes from this study will feed into a clinical trials application that has the potential to impact sufferers of lower back pain. Around 500 million people suffer from low back pain, the 1st cause of disability and the 3rd largest cause of healthcare spending ($87.6 billion) globally. Patients with persistent, recurrent lower back pain currently only have two diametrically opposed treatment options: conservative therapy, involving either physiotherapy or minimally invasive injections; and major

surgery, most commonly spinal fusion, a complex high-cost procedure associated with significant complications ultimately leading to reduced range of motion and quality-of-life.  In 2017/2018, the NHS undertook 211,000 pain injections and 52,523 spinal procedures, whilst in the US there were 9m treatments and 520,000 surgeries. Across Europe and the US, some 120,000 patients present with discogenic pain and an intact annulus, the initial target population for the technology at the heart of this application.  The aim is to provide these patients with an intermediate treatment option, enabling percutaneous, minimally invasive nucleus pulposus replacement as a day case procedure, at a fraction of the cost ($15K vs $113K) of current surgical options, and leading to restoration of spinal function.

The outputs from this work will be disseminated to the wider scientific community through publication in peer reviewed journals and by presentation at international meetings. Negative data will also be published and shared within the scientific community. Where appropriate, patients and the public will be informed of the outcomes through appropriate avenues.

Where appropriate, this work will lead to patent applications.

- Cattle: 80
- Sheep: 80
- Goats: 80

,

,

.

.

For non-recovery studies approximately 20 animals in total will be used; this may be composed of goats, and / or sheep and / or cattle.

For recovery studies up to 60 animals in total will be used (determined to be the best species from the non-recovery studies); this may be composed of goats, and / or sheep, or cattle.

Adult animals are ideal for this study for fulfilling scientific objectives, based on anatomy, size and expertise of scientists and animal care staff.

,

Animals will be acclimatised and trained for handling purposes.

Each animal will be anaesthetised on up to 2 occasions and up to 5 intervertebral discs will be treated. Analgesia and antibiotic treatments will be provided post recovery and animals will be monitored by clinical observations.

The animals for the long-term study will go through a recovery period of up to 12 months following the final procedure and up to 30 blood tests could be performed for the assessment of the long-term effects.

Animals will be killed and post mortem assessments performed.

/

Some short-term mild pain may be expected following the procedure, which will be controlled with appropriate treatment. Any adverse effects resulting from treatment failure will result in humane killing.

, .

(

For recovery studies, moderate in all animal types.

2- Human cadavers were not suitable as gas is entrapped in the tissue and blood vessels after death and prevents any attempt to use ultrasound for both therapy and imaging. Embalmed human cadavers were not suitable as the mechanical properties of the tissues were changed having both an impact on non-external technology such as ultrasound and invasive techniques such as needle introduction.

Human cadavers failed to provide any inflammatory response, and any biological live feedback of the procedure.

.
, .
, . . , ,
.

The present project is divided into a non-recovery pilot study and a long-term recovery study.

One species from goats, sheep or cattle will be selected based on cadaver studies for the majority of the work. It is not expected that the cummulative total of 80 sheep + 80 goats + 80 cattle will be required.

The pilot study is designed as well to spot at an early stage any obvious correction of the protocol that would be required, and the rough quantification of the observed effect can also be assessed.

The animal number for preclinical safety and efficacy studies will be based on the requirements of the relevant testing protocol for the regulatory authority to obtain the preclinical evidence on safety, biocompatibility and biomechanical.

Initially, cadavers have been used to evaluate the suitability of the treatment in a large animal model.

Finally, using within the same animal up to 5 spinal segments for the treatment groups will reduce the number of animals needed by up to 5 times.

,

Computer modelling: The acquisition of x-ray imaging during or after the procedure will be used to model and adjust the experimental procedure and re-assess further animal need.

Cadavers will be shared with other groups where possible.

. , ( , - ,
) , , ,
( .
.

, , , .

Deer had been investigated and rejected based on intervertebral space, therefore a dual model combining goats/sheep and cattle is required.

Cattle have been selected as their intervertebral discs space and intervertebral disc type of cells are similar to human.

In the first instance, the surgical method involves minimally invasive techniques designed to minimise peri-operative pain and replace the disc structure with an implant capable of withstanding the appropriate mechanical strain. In initial cadaver and imaging studies already performed by the PPL holder, cattle have a correct anatomical disc space and furthermore, in recovery studies will provide an optimal model.

Optimisation will be performed under terminal anaesthesia. Once the protocol is defined and refined, recovery studies with general anaesthesia will be started.

Local anaesthetic may be used wherever possible, for example, to reduce stress prior to taking blood samples.

The human spine is unique as human are bipedal and have a vertical load bearing. Only mammals can provide the relevant spine mechanical properties, inflammatory response. The prototype that we are creating is unique and is very dependent on the size and the geometry of the subject which requires large animal models. At a later stage, among the large mammals only a subset is losing notochordal cells at an adult age like human.

Terminal anaesthesia studies will be used for the pilot studhe$e