Home Office

NON-TECHNICAL SUMMARY

Validating computer models of mastication

Project duration

5 years 0 months

Project purpose

- (a) Basic research

Key words

feeding, dental implants, modelling, rabbit

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?

The goal of this research study is to demonstrate that computer models are capable of accurately predicting the internal forces generated and sustained by the muscles and bones of rabbits while they feed. This will be achieved by comparing the predictions from models to a new set of direct experimental measurements on rabbit muscles and bone. This will be pursued through the following specific objectives:

1. collect in-vivo data on bone motion and muscle physiology on rabbit mastication

2. collect in-situ/ in-vitro data on the physiology of rabbit masticatory muscles and the mechanical properties of hard tissues from the skull and mandible

3. collect anatomical and image data on bone and muscle morphology in rabbits

4. combine data from (1), (2) and (3) to build and validate computer models of rabbit mastication.

{KS110719 These are different to the objectives in the application]

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?

The goal of this project is to demonstrate that computer simulation approaches can contribute significantly to reduction, replacement and refining of the use of animals in biomechanical research. Many experimental studies in animal biomechanics are highly invasive, causing pain and distress to the animals before they are euthanized. In theory, once a digital model has been created, computer simulation has the potential to completely replace (or maximally reduce) the use of animals in that area of biomechanical research and/or medical device design. The anatomy and/or behaviour of a digital model can manipulated or altered continuously without any harm or distress to a real animal. This can allow, for example: a model analysis to be extended to a different strain/breed of the same species (or a morphologically similar species) by digital modification of the anatomy/behaviour; elements of anatomy to be modified in multiple ways (e.g. removal of teeth/bone) to examine the consequences of different surgical approaches; and for implant devices to be digitally inserted into models to examine their mechanical impact and performance, all without the need for any experimentation on real animals.

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?

We will use approximately 45 male New Zealand White rabbits over the course of the next four years to generate the data required to build and thoroughly test our models. The maximum of 45 rabbits was decided on based on analysis of previously published data and a power analysis.

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?

The likelihood of adverse reactions to the experimental interventions are low. There is potential for inappropriate anaesthetic depth that could result in moderate pain or death (less than 1% likely incidence). All animals will be killed by a Schedule 1 method at the end of the experiment.

Replacement

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

To validate a computer model requires a large amount of data about the anatomy and mechanics of feeding used by rabbits. This data does not exist for rabbits, or indeed any other experimental animal. Therefore a systematic anatomical and biomechanical investigation of rabbit feeding is required in which all the primary determinants and measures of feeding are measured from a small cohort of rabbits. Constructing models from medical imaging data of those same rabbits can then directly and immediately validate computers simulation. Only in this way can models we truly validated and their potential for achieving 3R's in future studies be demonstrated.

Reduction

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

Our experience with the experimental protocols will be applied to ensure appropriate group sizes are used to identify statistically significant differences between groups, whilst minimising the numbers of animals undergoing the protocol. Group sizes are constantly reviewed and experts in statistics consulted to ensure the minimum number of animals is used

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.

Rabbits are the first-choice experimental animal for dental implant design studies because of their size and easy handling. According to international standards regarding species suitable for testing implants in bone, rabbits represent an important species. Although the rat is also a frequently used model, it is not really regarded as a suitable model for testing dental implants and bone remodelling due to significant differences in bone composition, healing, and anatomy to humans. Therefore because rabbits represent by far the most widely used species in this context we proposed to use them to

demonstrate the capacity of validated computer modelling as a means of achieving replacement, reduction and refinement of animal use in future studies of dental surgeries and implant design. We have the facilities and expertise for housing this species. In this project we will use male New Zealand White rabbits because their large body size (~3kg) is more amenable to the surgical procedures and x-ray imaging than smaller breeds of rabbits.