G. NON TECHNICAL SUMMARY (NTS)

Project title: Evaluation of innovative, small medical devices for improving current diagnostic and interventional medical procedures
Duration of project - years: 5
Duration of project - months: 0

Purpose of the project (as in ASPA Section 5C(3)):
(a) basic research: **YES**
(b) translational or applied research with one of the following aims:
(i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants: **YES**
(ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants: **NO**
(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes: **NO**

(c) development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the aims mentioned in paragraph (b): **NO**
(d) protection of the natural environment in the interests of the health or welfare of man or animals: **NO**
(e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work: **NO**
(f) higher education or training for the acquisition, maintenance or improvement of vocational skills: **NO**
(g) forensic inquiries: **NO**

Keywords:
Gastrointestinal endoscopy, abdominal surgery, surgical robotics, robotic endoscopy, medical capsule robots

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):
The overall aim of this project is to evaluate feasibility and safety of innovative medical devices for inspection of the digestive tract (gastrointestinal endoscopy) or for abdominal surgery. The following will be answered: *Is the concept feasible? What is the most efficacious design? Is the concept safe and suitable for transitioning to redesign towards clinical use?*

What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?:
The novel devices developed in this project are related to high impact, major clinical needs with millions of individuals potentially benefiting from the successful implementation of the technologies. For example, bowel cancer survival rates could be drastically improved with the adoption of our robotic system which could provide an efficient, easy-to-use, painless alternative to the conventional procedure. Wider groups (e.g. the NHS and the UK as a whole) could also benefit from significant economic savings, particularly with the successful adoption of low-cost concepts. The work will be disseminated in peer reviewed journals and conferences, with the publications being relevant to actively researched areas in medicine and robotics. This will provide valuable knowledge to the wider research

community. The work focuses on high impact, clinically relevant areas where there is still significant scope for innovation. Therefore, the technologies developed have a tangible and significant need, ensuring that support is readily available to push the innovations to clinical use. The extensive facilities, technical expertise and previous research track record of the group will ensure maximum success rate.

What types and approximate numbers of animals do you expect to use and over what period of time?:
We expect to use 60 adult pigs over 5 years. This is the minimum number required to ensure the effective, safe and ethical development of our technologies.

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected levels of severity? What will happen to the animals at the end?:
The devices/technologies developed in engineering laboratories will be extensively tested on benchtop and/or in human and animal tissues before being considered suitable for animal trials. Animal experiments proposed in the applications will be carried out under general anaesthesia. Small moveable devices will be inserted either in colon, stomach and small intestine or in the peritoneal cavity and manipulated by hand or by external sources. After the testing period, animal will be humanely killed without regaining consciousness. Animals will be at risk of the usual complications of general anaesthesia. Balanced anaesthesia will be induced and maintained by a veterinary surgeon. Any animal showing anaesthetic complications that jeopardise animal welfare or scientific aims will be killed immediately by schedule 1 method. In our experience, no adverse effects are expected by the manipulation of devices inserted in the digestive tract or peritoneal cavity by using our minimally invasive technology in anaesthetised animal. The entire procedure may take up to 6 hours during which fluids will be administered intravenously as a routine routinely and temperature maintained via a warming pad. Minimally invasive surgical procedures will be carried out under sterile conditions and every effort made to avoid and control adverse events. As all procedures will be carried out under terminal anaesthesia, we do not expect any adverse effects during manipulation of small medical devices by non-invasive or minimal invasive techniques. At the end of experiment, animal will be killed by a schedule 1 method (overdose of anaesthetic).

Application of the 3Rs
Replacement:

In order to design appropriate medical technologies and evaluate their safety, an environment as close to that of the living human is required. These conditions are necessary to fully assess safety and functionality of the device, including those impossible to recreate synthetically on the bench-top. Testing in an animal model facilitates the refinement of the device design, and specifically the reduction/mitigation of risks associated with its use in humans. This is ethically crucial before investing resources in redesigning a device/technology towards clinical trials.

To-date, no synthetic alternatives are available that can completely recreate conditions found in a human because of the immense complexity. The devices in this project will be developed first in the laboratory using synthetic environments (e.g. silicone) and where possible, in simulation. However, the devices are designed to interact with the living soft tissues and hence their properties are crucial. Therefore, a realistic model is required to ensure the device functions properly before in-human use. Pigs are often used because of their similar size and tissue properties to humans.

Reduction:

Synthetic test environments and/or human cadavers will always be used extensively first and where possible, work with animals will be avoided completely. Benchtop work will be used to answer fundamental questions and to refine the concepts as much as possible. Once operating with satisfactory performance and achieving full functionality, animal models will be used only where is completely necessary for the assessment of device safety and efficacy. If technically feasible, multiple devices will be tested on the same, single animal and thus make most efficient use of the available resources. If we don't have at least 2 devices/technologies ready to be tested in a single animal, the trial will be cancelled and tests will be postponed to the next planned experiment.

This project is aimed at pilot feasibility trials and therefore, data analysis will be descriptive and graphical. No formal statistical comparison will be made. This, combined with the extensive testing on each device that is planned before the animal experiment (i.e. benchtop and human cadavers), results in the minimum number of animals required to test each device. Based upon our extensive experience, three consecutive successful animal trials will be sufficient to establish whether the device/technology is good enough to pass to the next phase (i.e. redesign and specific pre-clinical testing towards pilot human trials).

Refinement:

The pig model is widely accepted as a suitable replacement for the living human model for abdominal surgery and interventions relating to the digestive tract. This is because of its comparable size, tissue properties and - with the exception of the large bowel - anatomy.

All devices will be tested extensively on benchtop and human cadavers prior to animal work and will only be tested in animals if completely necessary. This will ensure the work done in animals is carried out with minimal risk/harm to both the operators and animals.

Experience gained from the animal trials will be used to not only refine the device, but also the procedure itself, ensuring all are performed efficiently and with minimal harm to those involved.

All testing will be performed under terminally anaesthesia under non-recovery conditions.