Replacing the need for anaesthesia and refining your study initiation by using pre-microchipped rodents

SARAH CARLISLE[1], NATALIE CURETON[2], LAUREN KELLY[2], LAURA LEFEVRE[1] and ANI OBAYAA[1]

[1] Envigo RMS (UK), an Inotiv Company

[2] Oncology R&D, AstraZeneca, Cambridge

Correspondence: sarah.carlisle@inotiv.com

Introduction

Envigo RMS (UK), an Inotiv company, have been microchipping models to support our customers' research programmes. Originally developed to support our internal rabbit breeding operations; more recently we have refined this programme to further develop the service for our rodents due to increased client requests.

Working with our customer AstraZeneca, a large pharmaceutical company focussing on oncology research, we have collaborated to perform microchipping of mice prior to delivery, that does not require the use of anaesthesia and with a focus on the 3R principles.

This was achieved by bringing together the veterinary and operational teams from both institutes and developed a plan of action striving to maintain the 3R principles.

The impact to AstraZeneca was important, as it meant that the mice were already microchipped upon delivery and it shortened the time in starting an experiment. In adhering to the 3R principles, these mice also experienced less handling on the actual procedure days. A great 3Rs' improvement (Figure 1).

Anaesthesia vs non-anaesthesia

Microchip implantation is a common and widely employed means of animal identification in laboratory animal facilities. Until recently, we would anaesthetise the mice before implantation which is a regulated procedure and requires the technician to be a Personal Licence holder (PIL).

The animals would be anaesthetised via a gaseous anaesthetic and then placed on a flat surface for the implantation to take place. They would then be monitored to ensure full recovery.

Challenges of use of anaesthesia

- Impact of anaesthetising large numbers of mice.
- Implication on the 3Rs and harm benefit analysis, animal and staff welfare

Alternative approach: microchipping without anaesthesia

- Improved process, balancing Animal Welfare with the logistical aspects of the procedure.
- Move away from anaesthetising while still ensuring minimal discomfort for the animals.
- Good example of the 3Rs in practice, especially the emphasis on refinement by reducing potential harm.
- Alternative method is also commonly used in veterinary practice by veterinary surgeons.
- It took time and dedication from all parties (NVS, NTCO and the operations team) to make sure no adverse effects on the animal were observed. Welfare was paramount (for both the animal and staff) and the concern of momentary discomfort of the injection was evaluated as low compared to the additional impact of the anaesthesia event and recovery.

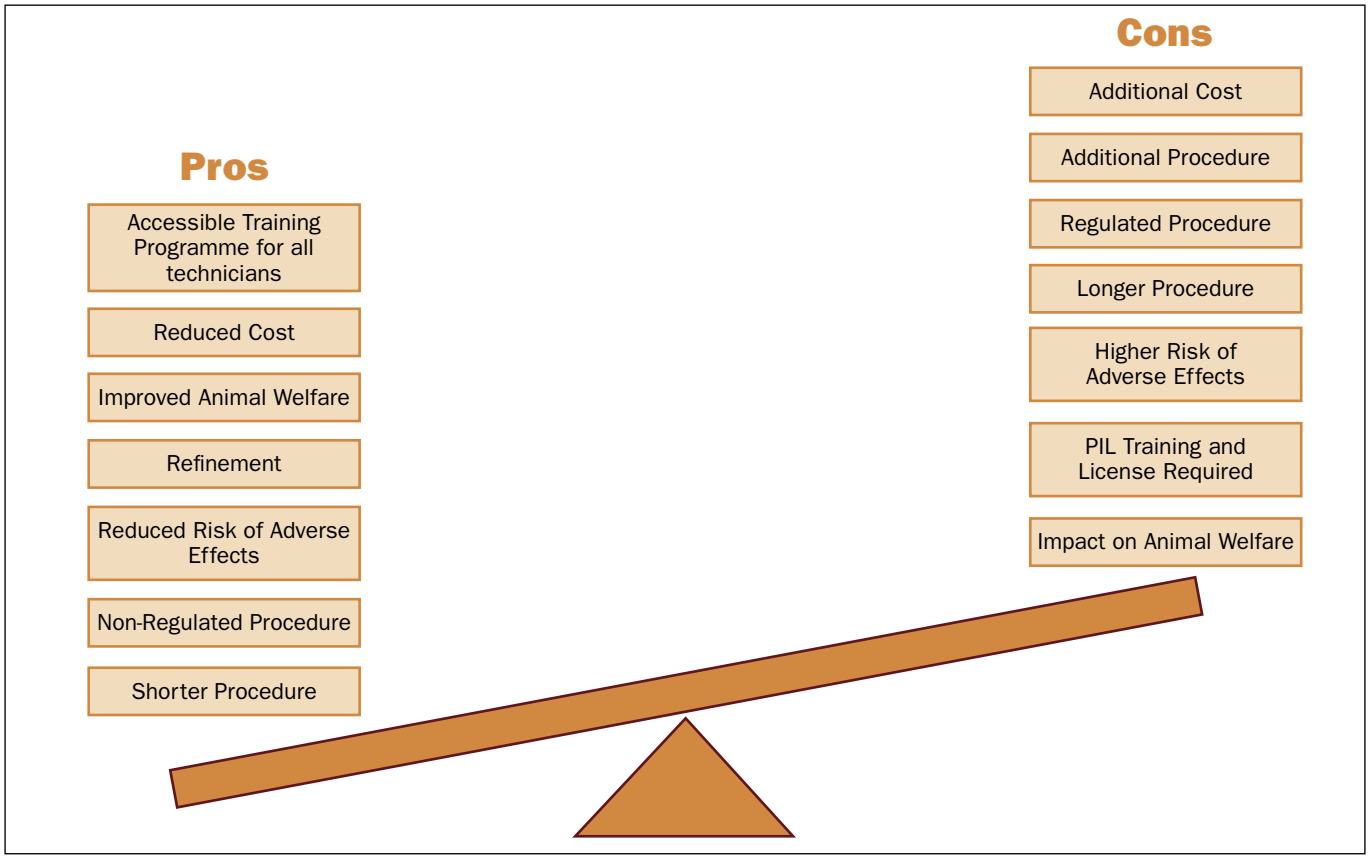

Figure 1. Pros and cons.

Method

Three technicians will be required to complete the procedure (Figure 2):

One dirty technician, working outside of the laminar flow hood (handling cages).

One clean technician, inserting the microchip into the animal.

A second clean technician, to restrain the animal during the implantation.

1. The dirty technician will select animal cage and pre-scan the microchip within its sterile packaging before implantation. This confirms the chip is providing a readable signal.
2. A clean technician will select animal from cage and will restrain the animal. It is important that the handler does not cover or pull the skin of the scruff as this will impede the implantation of the microchip.
3. The other clean technician will create a tent of skin behind the animal's neck between shoulders. The needle is inserted in the lower dorsal area at the base of the tent parallel with the animal's body. The needle is angled away from the body and against the direction of the fur. This angle of injection is important to deliver the microchip subcutaneously.
4. Fully depress the plunger on the applicator to administer the microchip.
5. Apply a pinch pressure on the injection site as the needle is withdrawn to ensure the microchip remains in place and that the skin edges are brought together to minimise bleeding.
6. Using fingers, gently work the microchip away from the injection site.

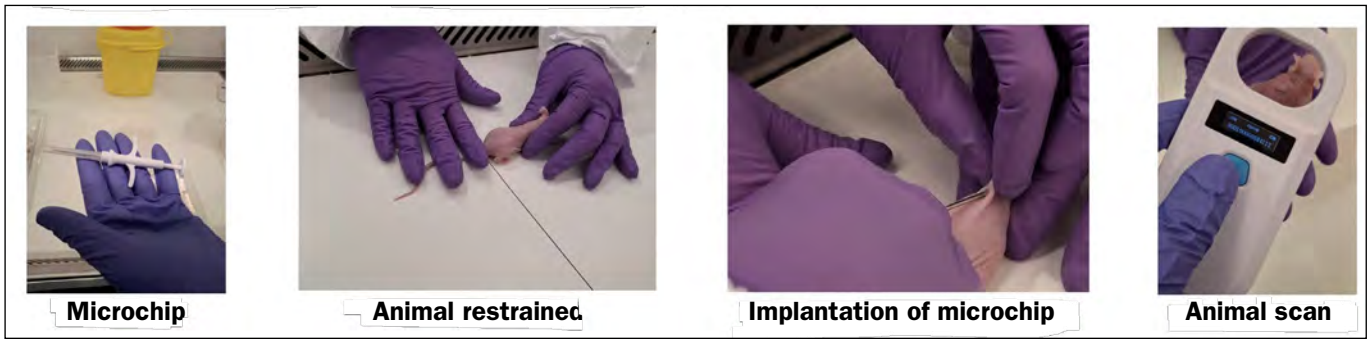

Figure 2.

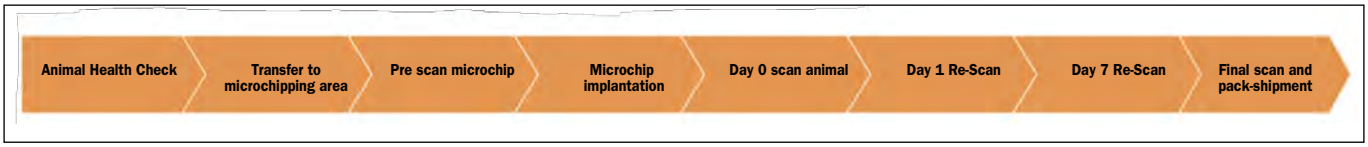

Figure 3.

Post procedural checks

Each animal must receive a visual daily check for seven days following implantation. During these checks particular attention is taken to ensure there are no adverse effects or abnormal behaviours observed following microchipping.

Microchips are to be checked with the reader on the day of insertion (day 0), the day after insertion (day 1), seven days after insertion (day 7) and at the time of packing (Figure 3).

All checks and observations are captured and recorded on a log form.

Throughout the process all animals receive a daily health and welfare check.

Importance of microchip placement

It is well known that the microchip can significantly migrate from the initial implantation site. As part of our commitment to support our customers we have been recently discussing about the refinement of the implantation site aiming to focus on implanting to the left of the dorsal area (left shoulder) instead of central to dorsal area (between shoulders) (Figure 4).

Why? – client perspective:

– Due to the type studies conducted (tumour growth) the right flank (red zone) is the desired area for the implantation of the tumour cells. The green zone shows the ideal chip placement which will not impede on the progression of the tumour growth. The risk of the microchip being positioned on the right side could compromise the quality of the data.

AstraZeneca's feedback

The ability to bring in mice pre-chipped from Envigo RMS (UK), an Inotiv company has resulted in a number of 3Rs' benefits to the mice on our studies.

– Prior to moving to receiving pre-chipped mice, on the day of tumour implant we would need to pre-weigh, shave, tail mark and then implant tumour cells and microchip mice under anaesthesia, then re-handle after implant to map the microchip to our software. This was resulting in 5 to 10% of mice developing scabs at the microchip insertion site, due to handling post-implant disrupting the healing process. With pre-chipped mice, mice have a 1 to 2 week period of reduced handling following microchipping, allowing uninterrupted healing. This workflow also reduces the number of times mice are handled on the day of cell implant as they can be weighed, shaved and mapped in the days leading up to implant.

– Another major benefit has been the reduction in the length of time it takes to implant tumour cells. Previously microchips were inserted at the same time as cells but with pre-chipped mice the time taken to complete the cell implant is reduced meaning mice spend less time under anaesthesia. This also improves cell viability, reduces tumour growth variability and ultimately results in a more robust data package.

Overall, introduction of pre-chipping of mice at Envigo RMS (UK), an Inotiv Company has improved Animal Welfare as well as benefitted study delivery.

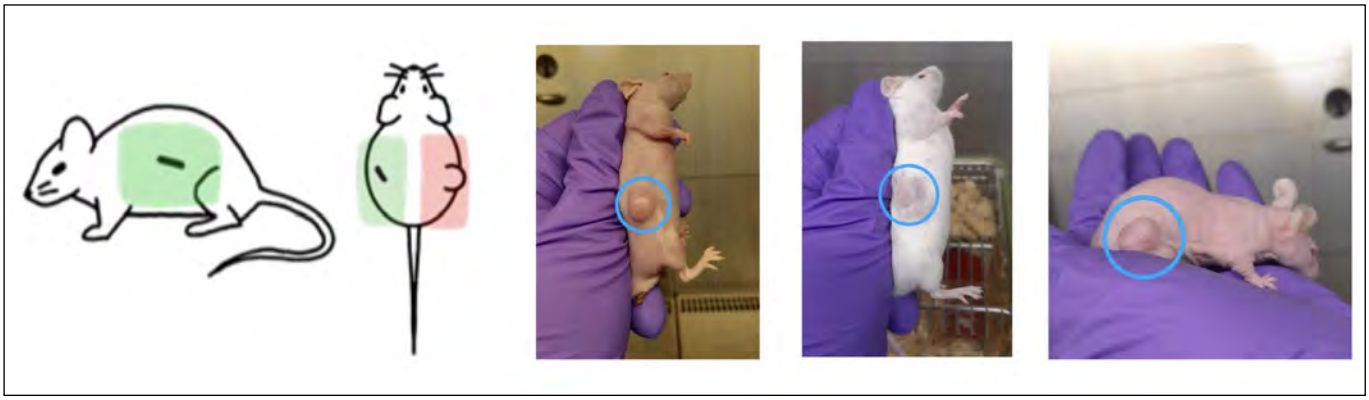

Figure 4.

Microchipping demand

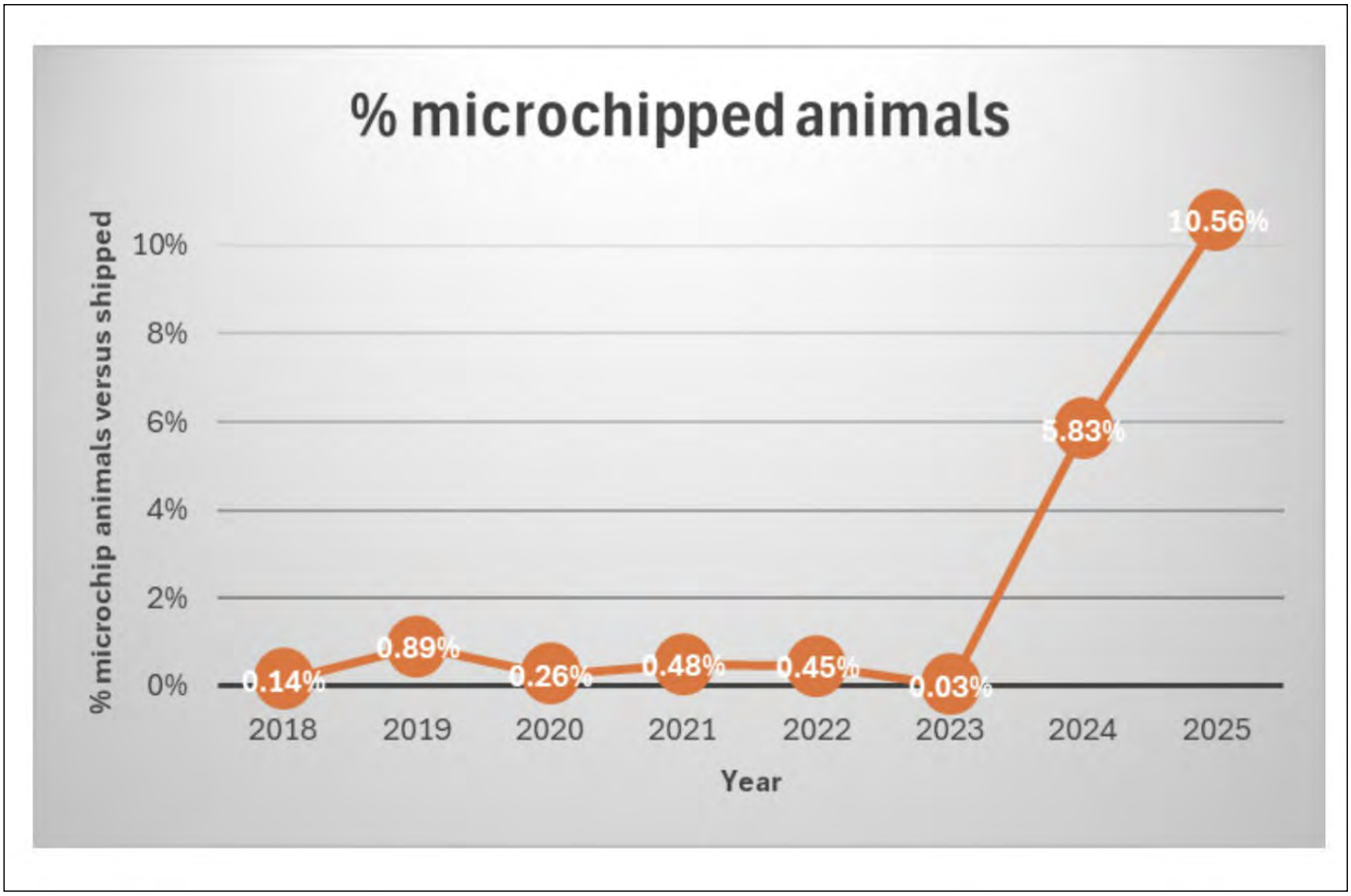

Figure 5.

Significant increase in customer demand for microchipping (<1% of animals sold between 2018 to 2023, to 5 to 10% in 2024 and 2025) (Figure 5).

– Bespoke service developed to meet our client's needs as well as refine our internal processes.

Our commitments:

– Providing a tailored, ethical and cost-effective solutions.

– Maintain the highest standards for data integrity and Animal Welfare.

Conclusion

This poster advocates for the use of pre-implanted naïve animals in study establishments as a refinement of Animal Welfare and an enhancement of study design and data integrity.

We continue to collaborate with our customers to address their needs and requirements related to study initiation, ensuring that animals arrive without the need for pre-study manipulation.

We emphasise ongoing training, continuous refinement of techniques and improvements in Animal Welfare. Additionally, we are exploring various types of chips, such as temperature recording, which are already present on our PPL.

This poster is a collaboration between Envigo RMS (UK), an Inotiv Company and AstraZeneca. All animals described within this poster were bred and maintained under authorised Home Office Licence, and methods approved under the guidance of the named people.