Assessment Of Microchip Placement Methods In Immunocompromised Mice

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Introduction

Subcutaneous microchip implants have become a popular means of identification in mice. When compared to other forms of identification, they are less likely to fall out, cause irritation, or be misread. General anesthesia is commonly used for restraint during microchip implantation, but our facility also uses physical restraint devices without complication in immunocompetent mice. This study was designed to determine if any signs of infection or other serious complications would occur when using this method with immunocompromised mice. Mice were microchipped using either physical or chemical restraint, and with or without surgical skin preparation, and responses were compared.

Methods

- NSG (NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ) and NSG-SGM3 [NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl} Tg(CMV-IL3,CSF2,KITLG) 1Eav/MloySzJ] were divided into four groups as follows:

Group	Restraint	Strain	Male	Female
1	Physical restraint	NSG	12	12
2		NSG-SGM3	10	10
3	Anesthesia	NSG-SGM3	9	10
4	Anesthesia with surgical skin prep	NSG-SGM3	10	10

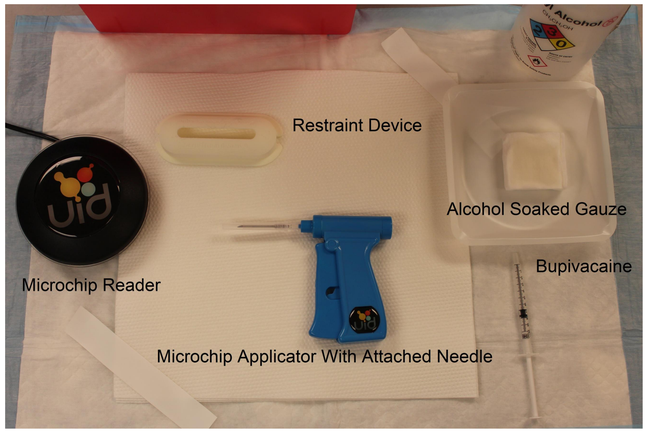
- Two groups were microchipped using physical restraint with a ScruffGuard® by Research Devices, after wiping the insertion site with gauze soaked in 70% ethanol.
- Two groups of mice were microchipped under isoflurane anesthesia, one with and one without surgical skin prep.
- Surgical skin prep was performed by wiping with alternating swabs of 5% Betadine solution and 70% ethanol.
- Microchips were inserted into the subcutaneous space overlying the shoulder blades.
- A drop of bupivacaine was applied at the injection site once microchip insertion was complete.
- All procedures were reviewed and approved by our IACUC.

Data Collection

- 19-24 mice per group (9-12 per sex) were weighed at baseline, week 1, and week 2. Four mice of each sex per group were monitored until week 8.
- Weekly weights for each mouse were compared using two-way ANOVA with Tukey's multiple comparisons test.
- All mice were monitored for signs of infection, skin irritation, barbering, or microchip loss.
- Four mice per group were sent for histology and culture at two weeks post-implantation. The remaining mice were evaluated for gross pathology at 2 or 8 weeks.
- Liver, kidney, and spleen were assessed for signs of systemic disease.
- Histological changes of the skin over the insertion site were graded on a scale of 0-2, as described below, and compared using the Kruskal-Wallis test.

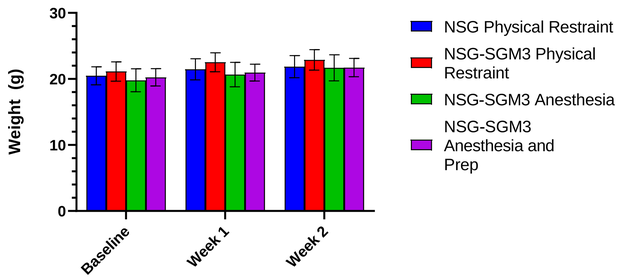
	Score 0	Score 1	Score 2
Dorsal Skin	No significant changes observed	Minimal to mild reactive changes	Mild reactive changes involving two anatomic sites i.e. (epidermis and subcutis)

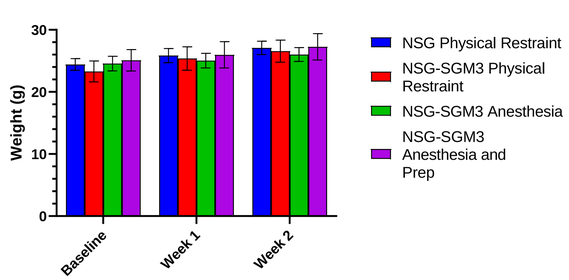
Supplies for Microchipping with Physical Restraint



Supplies and setup for microchipping mice using physical restraint. Necessary supplies include the restraint device, microchip applicator with single use needle containing the microchip, alcohol soaked gauze, and microchip reader.

Weight Data for Groups 1-4





Histology Scores Per Group

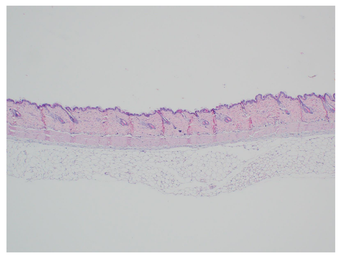
Group (n=4/Group)	Score: 0	Score: 1	Score: 2
1	2	2	0
2	3	0	1
3	3	1	0
4	3	1	0
Total	11	4	1

Clinical Findings

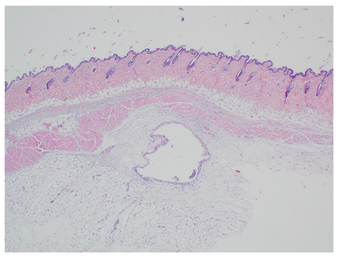
Complication	Mice (N)
Barbering/Scabbing/Bruising	16
Microchip Loss	6

Very mild barbering and scabbing was observed in 16 mice out of the 127 total mice (Groups 1-7) within the first week post-implantation. This resolved by the end of the study.

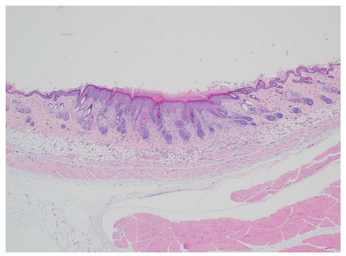
Histology



Score of 0 (Group 4): No significant findings.



Score of 1 (Group 1): Peripheral fibrosis in the subcutis. This is a non-specific and expected response to a sterile implant.



Score of 2 (Group 2): Focal scar represented by epidermal hyperplasia, dermal fibrosis and hyperkeratosis. Visible grossly as a ~1mm scab. Peripheral fibrosis in the subcutis.

Additional Strain Validation

- The physical restraint method was also validated in Nude (J:NU) and humanized NSG and NSG-SGM3 mice.
- Mice were weighed weekly and screened for gross pathology after two weeks. Weight data was analyzed using one-way ANOVA.
- Lost microchips were replaced five days after first implantation.

Group	Males	Females
5. J:NU	12	12
6. Hu-NSG	0	11
7. Hu-NSG-SGM3	0	9

Results

- There were no significant differences in weight between Groups 1-4 during the first two weeks of the study ($p>0.08$).
- Mice kept past week 2 (n=4 per Group 1-4) did not show significant difference in weight at week 8 ($P>0.05$).
- Group 5 females showed an increase in weight ($P<0.05$), while all other mice in Groups 5-7 showed no significant change in weight ($P> 0.5$).
- No signs of infection were noted throughout the study. Mild barbering and scabbing at the insertion site was isolated to two cages in Groups 2 and 3. Bruising was seen in two J:Nu mice. All clinical signs resolved within two weeks without intervention, with the exception of one small scab. Approximately 12.5% of mice experienced these reactions.
- Microchip loss was seen predominately in the physical restraint groups. The microchip fell out immediately after insertion in most cases. Approximately 5% of all mice (Groups 1-7) experienced microchip loss.
- When microchips were replaced 5 days after loss, no additional complications were seen.
- No major adverse reactions were observed histologically. The most common finding (N=5) was minor subcuticular fibrosis. There were no significant differences between groups based on histological scores ($p>0.999$).
- No pathology was seen in the liver, kidney, or spleen of any mice in the study.

Conclusions

- Both physical restraint or general anesthesia were acceptable for microchipping immunocompromised mice.
- All clinical changes seen in all groups were minimal and were resolved or nearly resolved within two weeks.
- Though microchip loss occasionally occurred with the physical restraint method, we have found that it is acceptable to replace microchips after 5 days without complication.
- The physical restraint method is considered easier to implement and more cost effective, due to time constraints, labor costs, and equipment needs.

Acknowledgments

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