THE SCIENCE BEHIND lidoband™

By Dr. Merle Olson & Dr. Steve Roche

Castration is a common procedure conducted in calves and lambs to eliminate sexual behaviour in young males and reduce aggression as well as unwanted pregnancies and indiscriminate breeding (Archer, 2004; Baird and Wolfe, 1998). Tail docking is another procedure commonly completed in lambs to reduce fecal soiling, which is commonly associated with myiasis or fly strike (French et al., 1994). No matter the procedure, castration or tail docking, lambs will commonly exhibit pain associated behaviors, such as vocalization, tail wagging, and restlessness (Grant, 2004; Mellor and Stafford, 2000; Cockram et al., 2012). Pain is a result of the stimulation of nociceptors due to tissue damage which triggers physiological pain pathways (Meintjes, 2012).

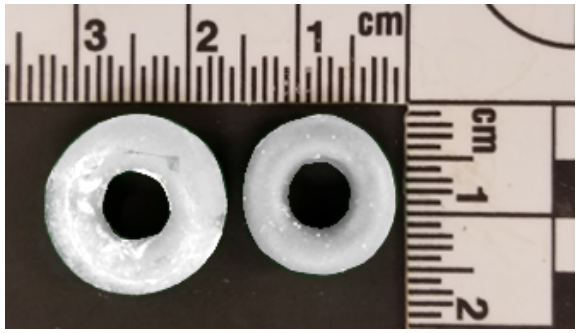
Band castration

Rubber ring castration is commonly used in both castration and tail docking as it is cheap, effective, and easy to apply to young calves and lambs (Stafford and Mellor, 2005). The tight rubber rings will prevent blood from flowing to both the scrotum and testes or tail, causing atrophy and necrosis of the tissues, which eventually slough off. Although this method leads to fewer signs of pain at its application compared to other methods (Petherick et al., 2015), the presence of the tight band does not prevent the conduction of nerve impulses from the painful, ischemic tail, and can cause a protracted pain response (Molony et al., 1993; Kent et al., 1995).

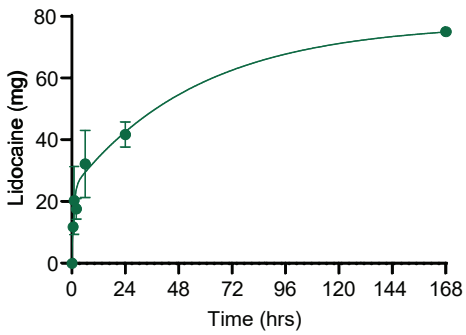
Pain control for these procedures

The use of local anesthetics and non-steroidal anti-inflammatories drugs (NSAIDs) at the time of application have been shown to mitigate pain associated with these procedures. Specifically, the use of a local anesthetic administered subcutaneously at the site of application or into the scrotal neck, cord, or testis has been shown to reduce cortisol (Thorton and Waterman-Pearson, 1999) in the 3 to 6 hours following castration and reduce cortisol responses and pain behavior in the hours following application of the rubber band for tail docking in lambs (Kells et al., 2020; Graham et al., 1997; Kent et al., 1998). The use of NSAIDs has also been shown to reduce the pain responses in the hours to day following the procedures (Stafford et al., 2002). However, despite the utility of a multi-modal approach for pain control, the use of rubber rings can create long-term pain, as it can take considerable time for the procedure to be completed; for example, castration takes more than 4 weeks following the application of the rubber ring (Cockram et al., 2012). Given that the scrotum remains swollen and appears to cause behavioral signs of discomfort prior to casting (i.e., detachment), the development of longer-term pain control strategies is needed. Furthermore, Nogues et al. (2021) found that calves that underwent rubber ring castration gained less weight over the study and had lower grain intake compared to surgical castration, highlighting the importance of prolonged pain control. It is therefore critical that innovative strategies for pain management are investigated and developed.

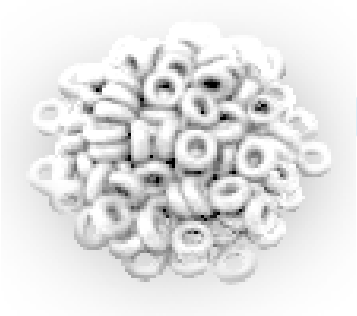
Lidoband is a latex elastration device that has lidocaine impregnated directly into the band (US patent #11596510) (Saville et al., 2020). Lidocaine is impregnated into the latex along with a penetrating agent (isopropyl myristate). Each band contains 80 mg of lidocaine (equal to 4 cc of injection) and a penetrating agent, isopropyl myristate (IPM). The bands are slightly "plumper" than a regular band (figure below) as they have the lidocaine and penetrating agent impregnated into the latex matrix. (Figure below)



The bands were developed to allow for an initial rapid delivery of lidocaine into the tissues followed by a slower continuous delivery of local anesthetic until the band and tissue are casted. This aligns the need for and initial rapid local anesthesia and longer-term pain management with the current standards of practice requirements.



Testing of Lidoband and regular bands has shown that they are biomechanically similar and function the same for castration and tail docking.



So, is Lidoband effective?

In order to answer this question, we first need to understand the effects of injectable lidocaine. Effective concentrations of local anesthetics, such as the tissue concentration yielding a 50% and 95% reduction in tissue sensation (EC50 and EC95, respectively), are important metrics of an anesthetic's potency (Dimmit 2017; Nakamura 2003; Yartsev 2015). Moreover, by measuring the tissue concentration over time and comparing it to the EC50, the time of onset and duration of local anesthesia can be established. You might expect that we know a lot about this already, but despite lidocaine being a well-studied local anesthetic in humans (Gordh, 2010; Weinberg, 2015; Yang 2020), few studies investigated lidocaine's pharmacokinetics, pharmacodynamics, and effective concentrations for local anesthesia in scrotal or tail tissue. Given the widespread recommendation—and, in many cases, requirements (see Canadian Codes of Practice for the Care and Handling of different livestock species)—for use of pain control (often citing the importance of local anesthetics), more research is clearly needed to provide a more comprehensive understanding of lidocaine use in these species.

How effective is a traditional lidocaine block?

Two studies have recently been conducted by Chinook Contract Research and Solvet, one in lambs and one in calves, to explore the use of traditional local-anesthetic application in castration and tail-docking and to understand if Lidoband is effective at preventing long-term pain after application.

Lambs, for tail docking and castration, and calves, for castration, were injected with 2% lidocaine without epinephrine into the scrotal neck tissue and/or tail tissue (for lambs) to form a ring block and had a regular rubber ring applied at the castration or tail docking site. At 30, 60, 90, 120, 180 and 240 minutes after injection, a punch biopsy was collected from an injection site and the amount of lidocaine in the tissue was quantified. Furthermore, the tail or scrotal tissue had electrocutaneous stimulation conducted at the same biopsy time points and the local anesthetic activity was graded using the responses in Table 1.

Table 1. Electrocutaneous stimulation rubric for sensitivity at biopsy location.

Graded Response	Description of positive avoidance response
0	No reaction
1	Slight reaction: Moves side to side and tail flick
2	Moderate reaction: Moves side to side and tail flick, slight kick, or jump
3	Severe reaction: Moves side to side and tail flick, pronounced kick or jump, bawling, head shaking, or vocalization

In lambs, lidocaine was not detected prior to injection (Time (T) = 0) and reached a peak by 30 minutes post-injection in scrotal and tail tissues, respectively, before dropping back toward zero over the time-course (**Figure 1 A**: Lamb Scrotum; **Figure 1 B:** Lamb Tail).

For the electrostimulation response score, in both the scrotums and tail, it was near maximum prior to lidocaine injection, and dropped to no reaction for all animals by 30 minutes post-injection (**Figure 1 C-D**), indicating a complete loss of sensation in the injected tissues. However, by 120 to 180 min post-injection, the response scores for the scrotum and tail were not significantly different (P > 0.05) from the T = 0 level (**Figure 1 C-D**), indicating a return of sensation.

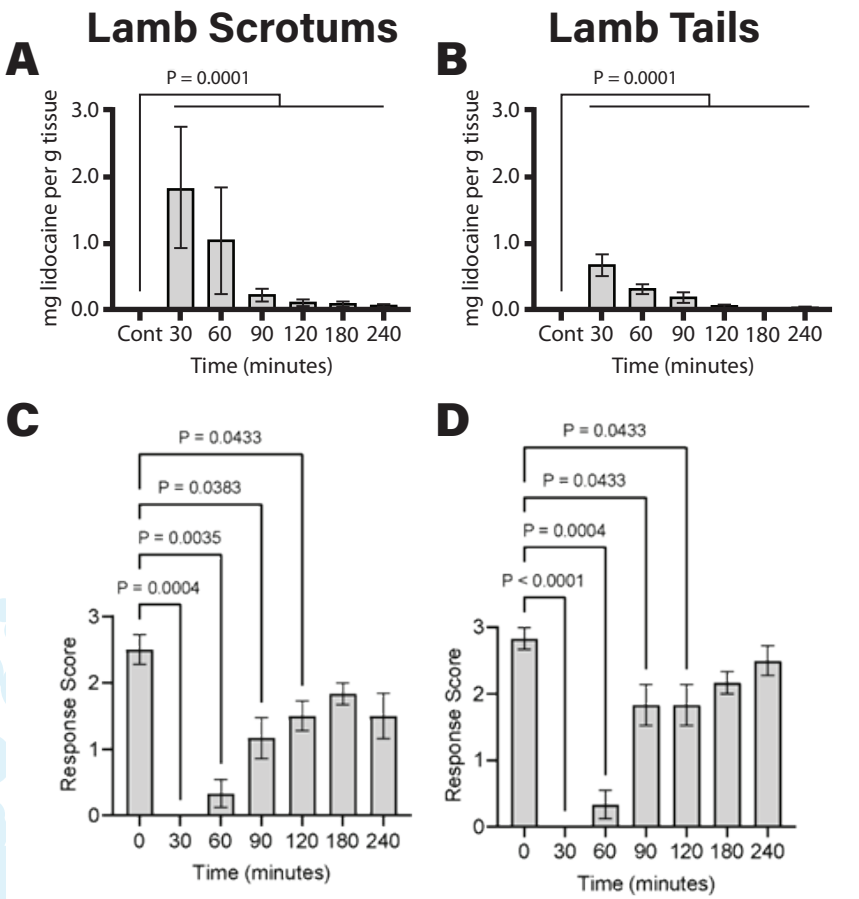


Figure 1. Tissue lidocaine concentration for Lamb Scrotums (A) and Lamb Tails (B) and Electrocutaneous Stimulation Response Scores for Lamb Scrotums (C), Lamb Tails (D).

A similar effect was noted for calves, where prior to lidocaine injection, no lidocaine was found (Time = 0) (**Figure 2 A**); however, the concentrations of lidocaine rose and reached a peak by 30 min before declining through time. With regard to electrostimulation score, the response was at a maximum prior to lidocaine injection and dropped to no reaction for all animals by 30 minutes post-injection. However, by 90 min post-injection, the response scores for the scrotum was not significantly different (P > 0.05) from the T = 0 level (**Figure 2 B**), indicating a return to sensation.

Calf Scrotums

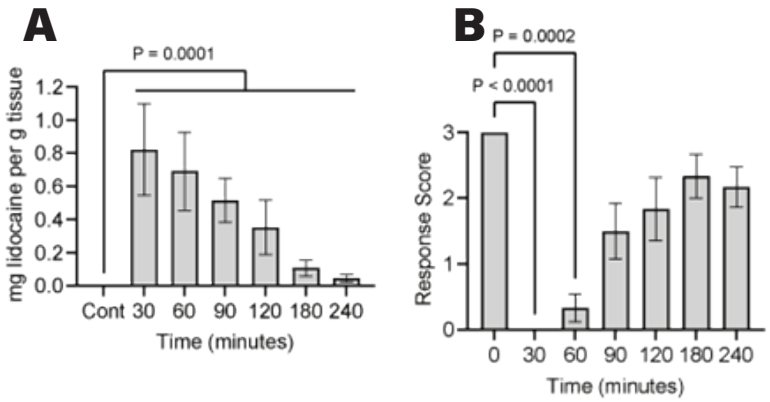


Figure 2. Tissue lidocaine concentration for Calf Scrotums (A) and Electrocutaneous Stimulation Response Scores for Calf Scrotums (A).

The effective concentration (EC50) of lidocaine was also calculated, which is the concentration of lidocaine expected to yield a 50% reduction in tissue sensation. For lambs, it was found to be 0.17 and 0.08 mg of lidocaine per g of scrotal and tail tissue, respectively, whereas for calves, it was found to be 0.54 mg of lidocaine per g of scrotal tissue.

Bottom line: Injectable local anesthetic has a short duration of activity and can't be relied on for long-term pain control.

How does Lidoband compare to a traditional lidocaine block?
Lidoband offers a unique approach to pain control following rubber ring castration. This product has lidocaine impregnated directly in the band, which allows for the slow release of lidocaine into the site of application.

In a similar approach to what was described above, lambs had a Lidoband attached to their tail or scrotum and calves had a Lidoband attached to their scrotum with no additional anesthetic applied. The lambs had a punch biopsy and electrocutaneous stimulation, as described above, at the time points 0.5 h, 1 h, 2 h, 4 h, 24 h, 48 h, 72 h, 7 d, 14 d, 21 d, and 28 d after banding. For calves, punch biopsies were conducted at 2 h, 72 h, 14 d, and 28 d after banding.

For lambs, tissue lidocaine levels reached or exceeded the EC50 in as little as 30 minutes (**Figure 3A and C**) and remained well above the EC50 for 21-28 days for tails and scrotums, respectively (**Figure B and D**).

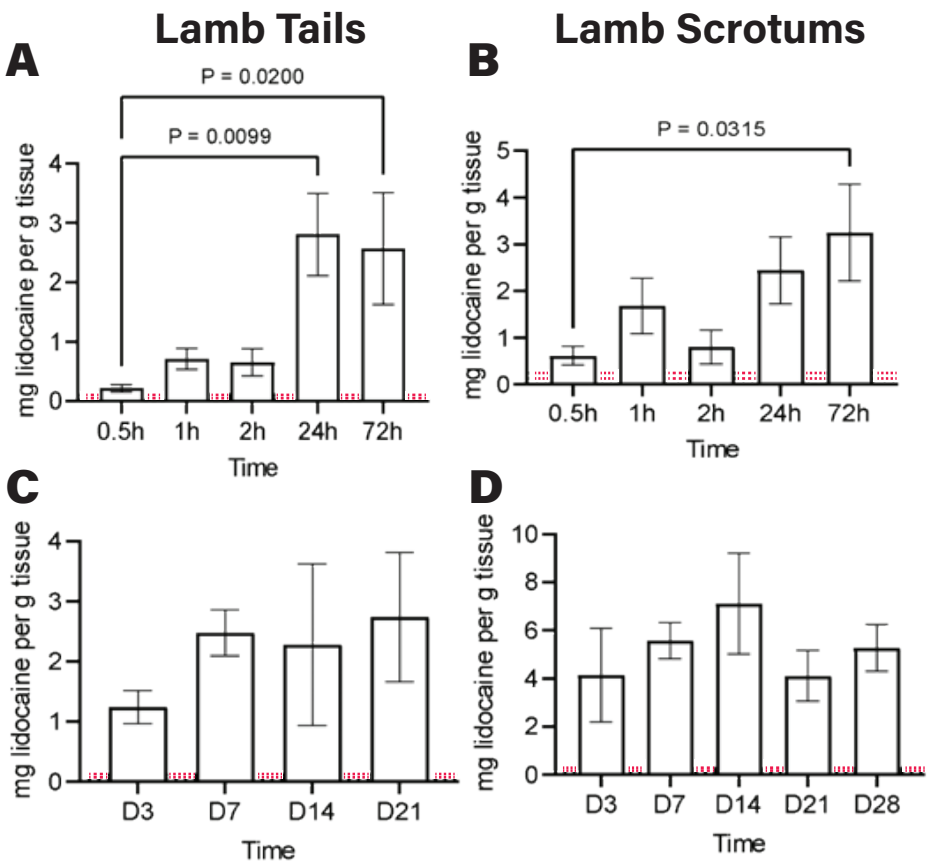


Figure 3. Lidocaine Levels in Lamb Tail (A, B) and Lamb Scrotal (C, D) Tissues Biopsied at the Indicated Times After Banding with LidoBands. For reference, the dotted lines denote the 95% CI of the EC50.

In calves, tissue lidocaine levels reached or exceeded the EC50 by 72 hours (**Figure 4**) and remained well above the EC50 for the remaining 28 days, respectively.

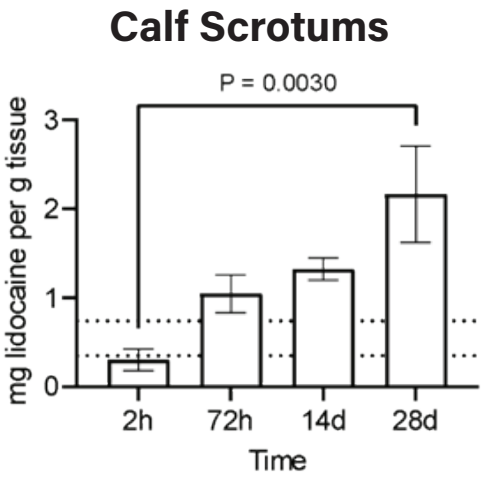


Figure 4. Lidocaine Levels in Calf Scrotal (C, D) Tissues Biopsied at the Indicated Times After Banding with LidoBands. For reference, the dotted lines denote the 95% CI of the EC50.

With regard to electrocutaneous stimulation, differences were noted at 1 and 3 days following band application, with lambs with a Lidoband have a lower stimulation score compared to lambs banded with no pain control (**Figure 5**).

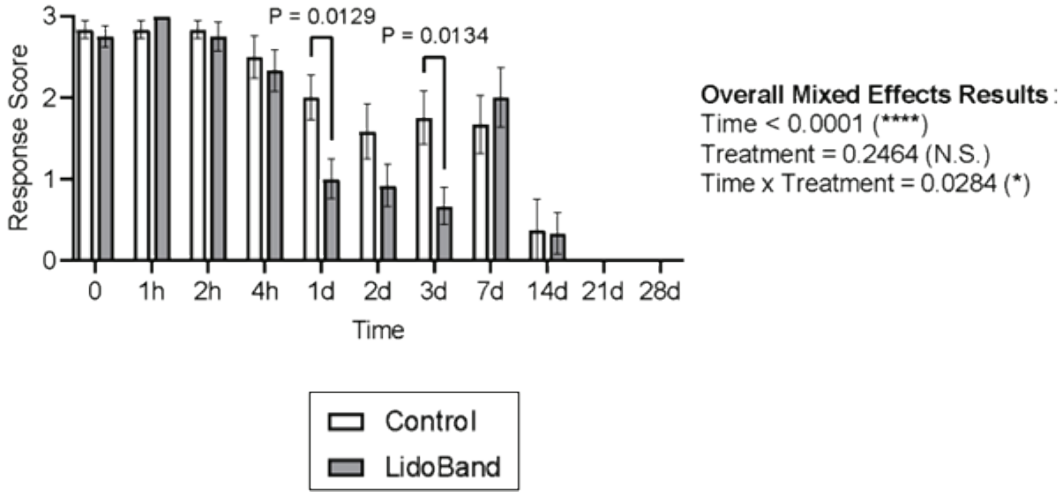
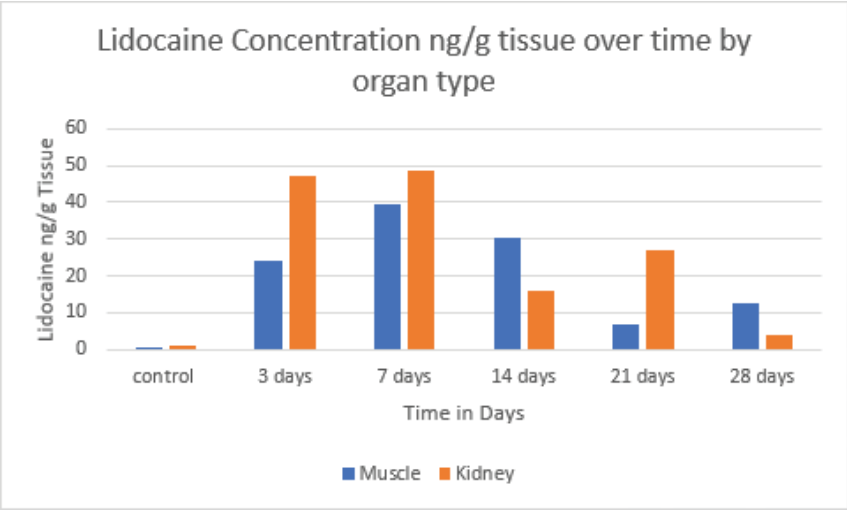


Figure 5. Electrocutaneous Stimulation Response Scores Over Time for Lamb Tails Treated With Control Bands or LidoBands.

Bottom Line: The Lidoband has rapid and sustained release of lidocaine, allowing for concentrations to be above the effective concentration for prolonged periods of time.

Tissue Residues

When lidocaine is injected into tissues there is a rapid release of drug into distant tissues resulting in withdrawal time issues. With Lidoband the lidocaine is very slowly released into adjacent tissues and at very low concentrations. Residue depletions studies are ongoing for lambs and calves. For lambs, serum lidocaine is undetectable (below detection limit of 1 ng/g) and tissue lidocaine are very low for the entire banding process (figure below). It has been shown in all cases distant tissues are well below established maximum residue limits (MRL) for lambs and calves (200 ng/g) (APVMA 2023).



What's next for Lidoband?

More research is currently underway to evaluate other impacts of the bands, from additional residue work and confirmatory studies to build out our understanding of what is reported above, to evaluating more comprehensive markers of pain (cortisol, acute phase proteins, algometry), as well as the antimicrobial and anti-inflammatory properties of lidocaine when administered this way.

Stay tuned for more!

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