Local Antibiotic Delivery via a Novel Intrawound Device Manages Spinal Hardware Biofilm-Infection Better than Systemic Antibiotics in an Ovine Model

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INTRODUCTION

Implant-associated spine infections are complicated by biofilms, as hardware often cannot be removed after placement. A biofilm is a structured community of microorganisms (e.g., bacteria) embedded in a self-produced matrix that preferentially adheres to surfaces such as implanted hardware (Figure 1A). Bacteria in biofilms can tolerate >**1000x** antibiotic concentrations than planktonic bacteria (Figure 1B).[1]

Current issues with treating these biofilm-associated infections in the spine include:

1. Toxicity from increasing systemic antibiotic doses
2. Limited drug delivery to infection sites due to compromised vasculature[2]
3. Failure to achieve a sustained, high antibiotic concentration

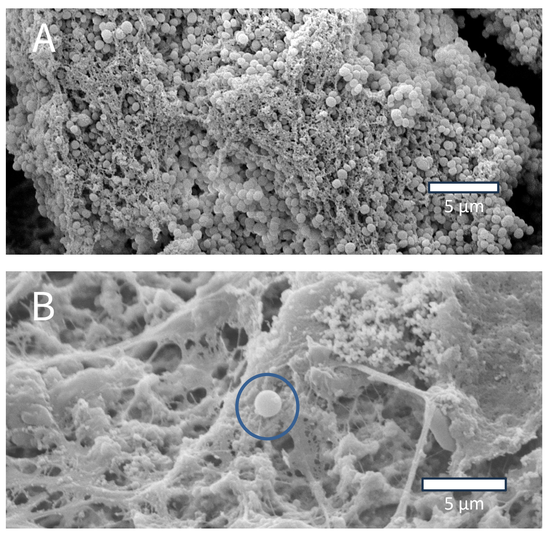


FIGURE 1. SEM Images of Two Bacterial Phenotypes. A) Community of biofilm bacteria. B) Single cell planktonic bacterium.

To address this clinically unmet need, we have been developing a refillable intrawound drug delivery system (Figure 2), referred to herein as a pouch. The device comprises a temporarily implanted (<30 days) antimicrobial-filled reservoir with a permeable rate-controlling membrane. The implanted reservoir communicates externally with a refilling port. Passive diffusion of antibiotics through the rate-controlling membrane and daily refilling maintain high target concentrations of antibiotics in the site tissues. We hypothesized that tobramycin, locally delivered via the pouch, would eliminate biofilms to a greater degree in a sheep model of spinal fusion rod-related infection than systemic antibiotics alone.

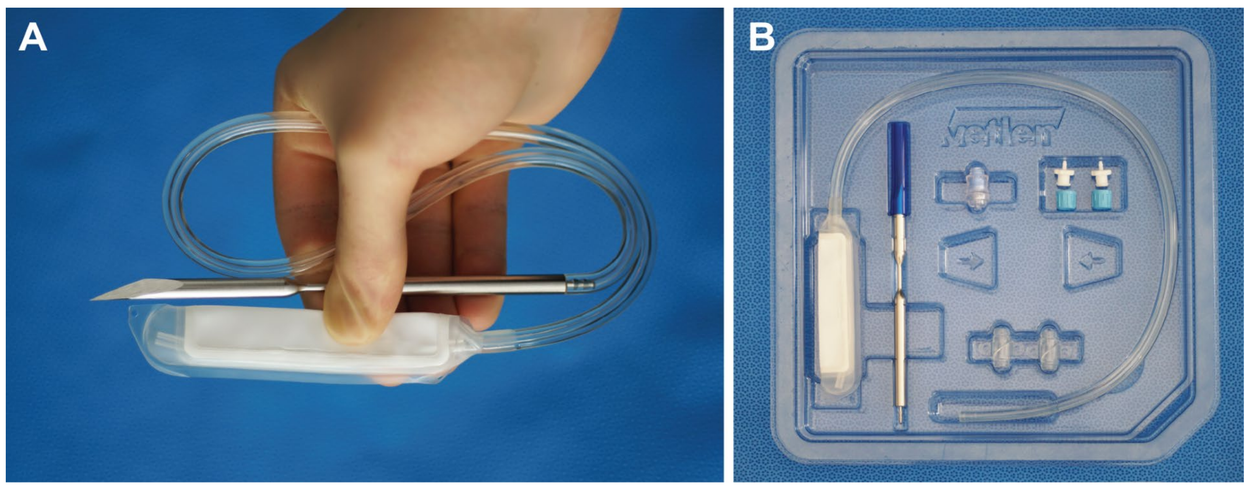


Figure 2: (A) The 10 mL pouch used in this study is in active development toward human clinical use and currently available for veterinary applications. See its function in QR linked video (B) The 10 mL pouch, with the sterile covering peeled back to reveal the kitted components: a bendable stainless-steel trocar, Luer-lock barb fittings, needleless Luer-lock port, Luer-lock caps, and catheter tubing tissue anchors.

METHODS

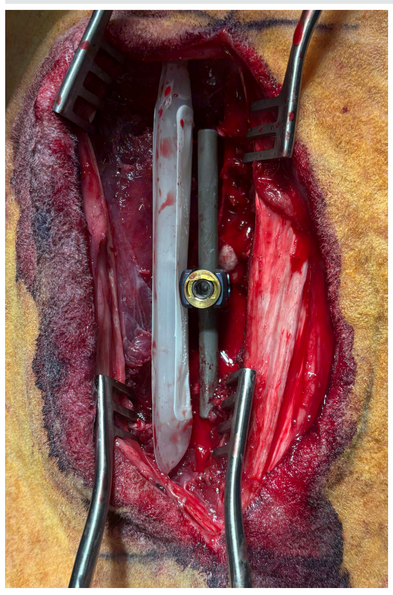


FIGURE 3. Established Ovine Deep Spine Infection Model. Surgically implanted spinal hardware (Right) with the Purgo Pouch (Left).

Our study objective was to compare the Purgo Pouch against a systemic antibiotic clinical standard using an established sheep spine infection model.[3] This model uses a *Staphylococcus aureus* biofilm grown on a spinal fusion rod, which is then surgically implanted into the lumbar spine of sheep using a pedicle screw and locking cap (Figure 4). Sheep (age 1-3 years) were randomly assigned to 1 of 5 treatment groups (with approximately equal amounts male and female) as shown in Table 1. The implanted cap and rod, along with tissue and bone samples were collected at necropsy for histological and quantitative microbiological analysis.

TABLE 1. Study Groups

Group Name	Daily Treatment	Group Size	Duration
+ Control	None	n = 5	30 Days
- Control	None	n = 5	30 Days
Systemic Only	Systemic Rifampin (600 mg) + Levofloxacin (750 mg)	n = 5	14 or 30 Days
Pouch Only	Local Tobramycin (352 mg)	n = 5	14 or 30 Days
Pouch + Systemic	Systemic Rifampin (600 mg) + Levofloxacin (750 mg), Local Tobramycin (352 mg)	n = 5	14 or 30 Days

References:

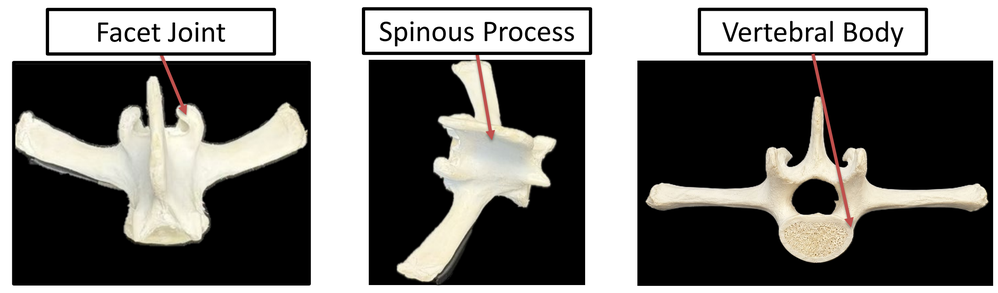
1. Stewart, Philip & Costerton, J. (2001). Stewart PS, Costerton JW. Antibiotic resistance of bacteria in biofilms. Lancet 2001; 358: 135-138. Lancet. 358. 135-8. 10.1016/S0140-6736(01)05321-1.
2. Falconer, R., Rothberg, D., Kay, W., Hunt, C., Epperson, R. T., Kawaguchi, B., Ashton, N., & Williams, D. (2025). Assessing the efficacy of systemic antibiotics for biofilm-associated infection in an ovine model of simulated fracture-related infection. *Journal of bone and joint infection*, *10*(6)
3. Shaw, J. D., Bailey, T. L., Ong, J., Brodke, D. S., Williams, D. L., Wawrose, R. A., Epperson, R. T., Kawaguchi, B., & Ashton, N. N. (2023). Development and validation of a large animal ovine model for implant-associated spine infection using biofilm based inocula. *Biofilm*, *6*, 100138. https://doi.org/10.1016/j.bioflm.2023.100138

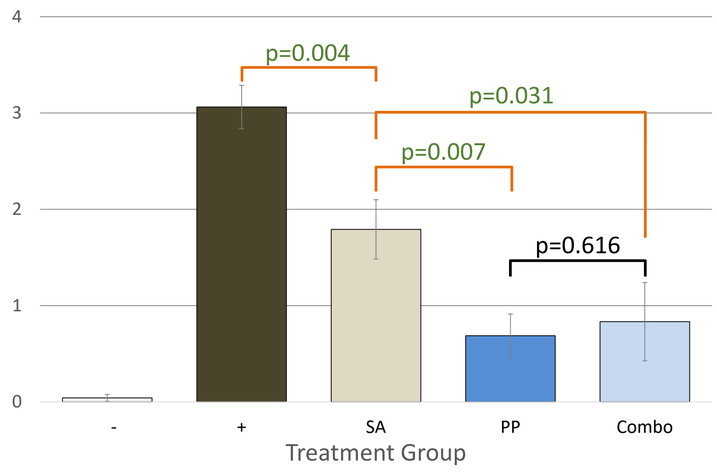
RESULTS

Microbiologically, there was no statistically significant difference in bioburden between the antibiotic treatment groups after 30 days of treatment. However, there was a significant difference between the pouch groups and the systemic only group with the 14-day treatment duration, indicating that infection was cleared faster with the Pouch.

Micro-CT imaging showed that bone was healthier in the facet joint, spinous process, and vertebral body of sheep treated with (Figure 4). Average bone necrosis grading showed a statistically significant difference between the pouch groups and systemic antibiotics only (Figure 5).

FIGURE 4. Vertebral Landmarks





Facet	**0.0**	4.0	3.0	**0.7**	**0.7**
Spinous	**0.0**	3.0	1.3	**0.3**	**0.7**
Body	**0.0**	3.0	1.7	**0.7**	**0.7**
Screw	**0.2**	2.3	1.2	1.1	1.3
	-	+	SA	PP	Combo

FIGURE 5. Bone Necrosis Grading at 30 Days. Graded on a scale from 0-4. A 4 indicates significant resorption, while 0 indicates no resorption.

The micro-CT data showed that sheep receiving systemic antibiotics only had high bone resorption (degradation) in the spinous process (Figure 6A) and especially the facet joint (Figure 6B). Sheep that received locally delivered antibiotics through the pouch showed minimal bone resorption.

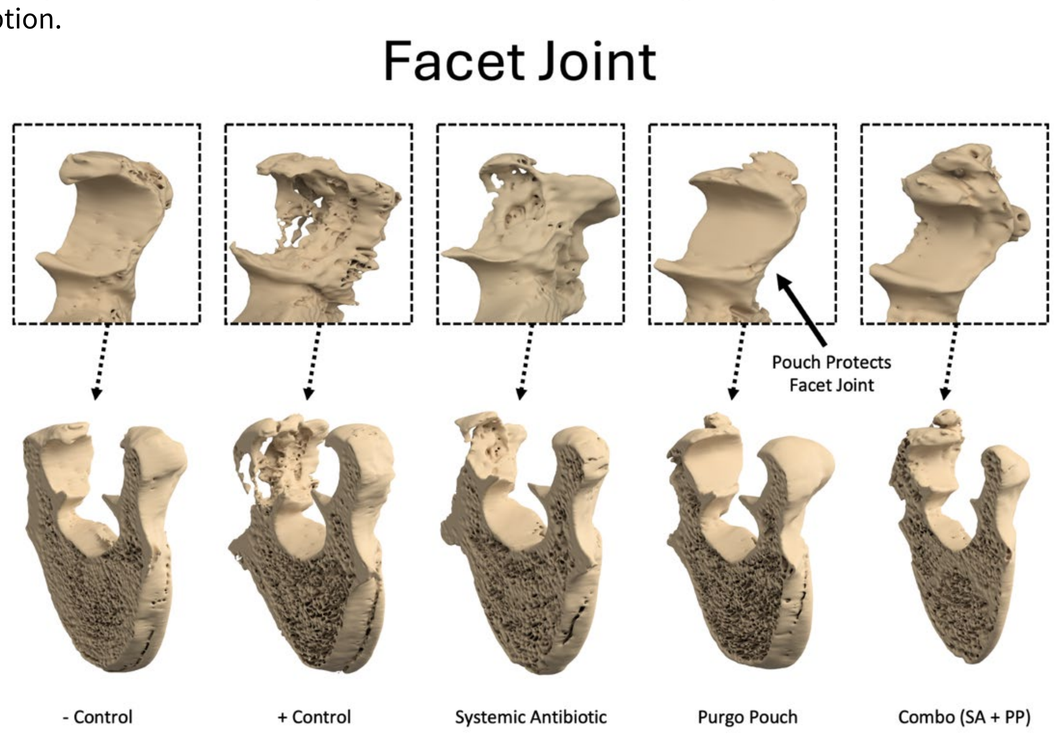


FIGURE 6. 3D-Renderings of Spinous Process (A) and Facet Joint (B) at 30 Days. Note that these are representative images from each treatment group. The systemic antibiotics group is most similar to the positive control in both vertebral regions, with large pockets of "moth-eaten" bone. The Purgo Pouch groups showed smooth, healthy bone similar to negative controls.

DISCUSSION

Conclusion:

- Bacteria in sheep with the pouch were killed **sooner** than those with systemic therapy alone.
- Sheep treated with the pouch had far **less** bone resorption.

Future Work:

- Compare the pouch to sprinkled antibiotic powder using the same model.
- Analyze histology with the 14-day treatment groups.
- Determine release kinetics of the pouch.