

Histological Comparison of Tissue Response for Stainless Steel and Teflon Continuous Subcutaneous Insulin Infusion (CSII) Catheters in Live Swine



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INTRODUCTION

- Patients managing their Type I Diabetes with an insulin pump are required to insert a new continuous subcutaneous insulin infusion (CSII) catheter every 2-3 days to minimize the risk for hyperglycemia, hypoglycemia, and DKA.
- The trauma of insertion and indwelling time may cause a local inflammatory response, leading to variable insulin delivery, fibrosis and loss of viable infusion sites.
- Understanding how the tissue responds to trauma and different catheter materials is clinically important.
- Tissue histology was used to evaluate the immune response surrounding commercial Teflon and stainless steel CSII catheters implanted in live swine for 7 days, 5 days, 3 days, 8 hours and 10 minutes.

METHODS

- CSII catheters with a 6 mm Teflon cannula (Inset) and 6 mm steel cannula (Contact-Detach) were implanted within the soft abdominal tissue of ambulatory swine for 7 days (n=8), 5 days (n=4), 3 days (n=4), 8 hours (n=4) and 10 minutes (n=4).
- Insulin Lispro (U-10) was continuously infused through the CSII catheters (5 µL/hour) using multiple insulin pumps.

- A 70 µL bolus of insulin Lispro (U-100) was infused through each CSII catheter the day of excision.
- Five minutes after each bolus, the CSII catheter and surrounding skin/subcutaneous tissue were excised and immediately frozen.
- Specimens were fixed using Formalin 10% and stained using H&E and Trichrome.
- Three investigators and a clinical pathologist blindly evaluated the tissue histology for degree of tissue inflammation, fibrin and collagen deposition, fat necrosis, and volume of debris field.

RESULTS

- Both Teflon and stainless steel CSII catheters produced significant inflammation that increased in size and density over time (See Figures 1 and 2).
- Tissue surrounding the Teflon and steel CSII catheters showed minimal damage and no inflammation at 0 and 8 hours.
- Both catheter materials elicited a more severe inflammatory response from 3 days to 7 days when compared to 0 and 8 hours.
- A difference in inflammatory response is observed between Teflon and stainless steel at 3 days, 5 days, and 7 days.
- Tissue damage and local inflammation was more extensive in specimens with stainless steel catheters compared to Teflon.

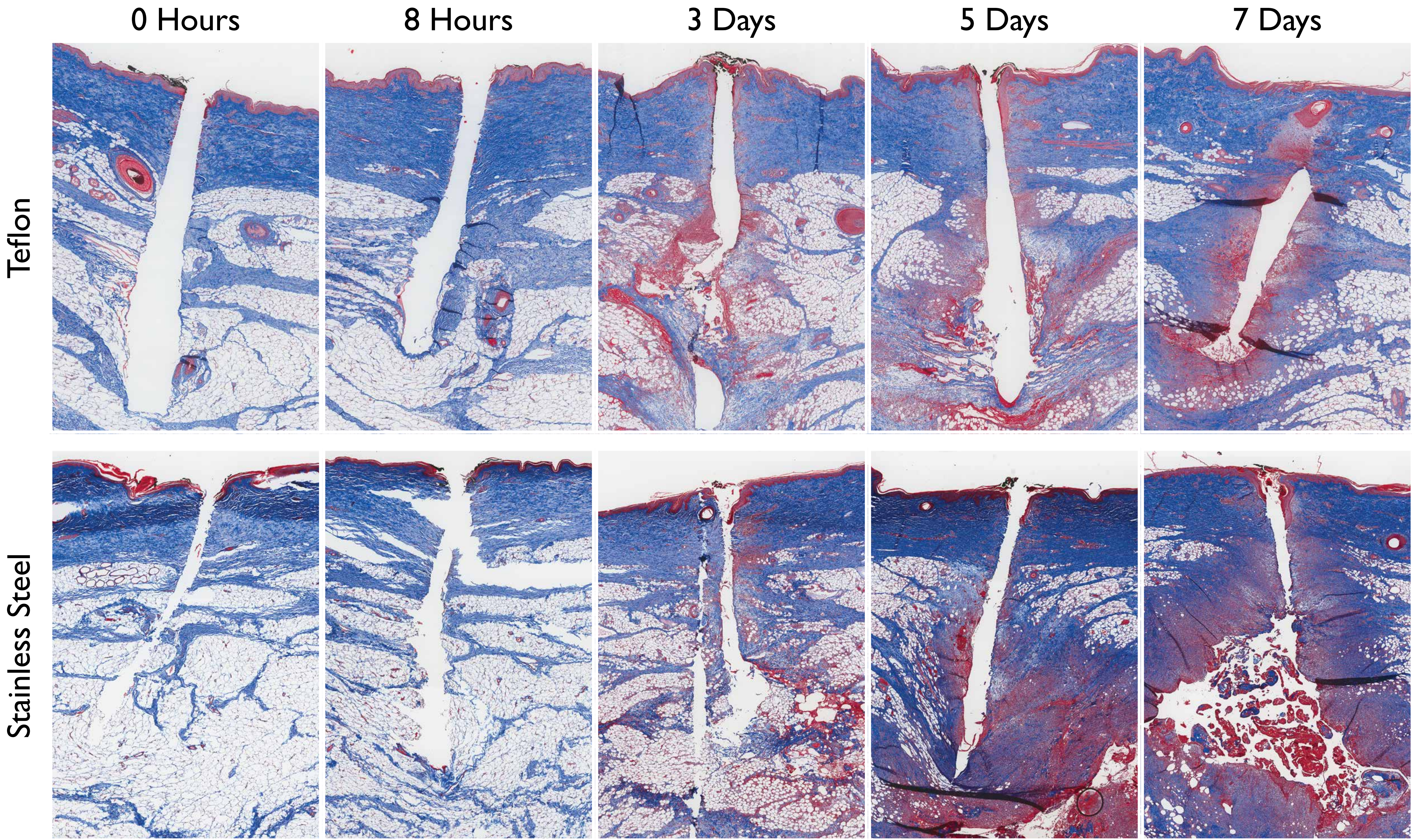


Figure 1. Longitudinal sequence of representative histology specimens for Teflon (top) and stainless steel (bottom) CSII catheters indwelling for 0 hours, 8 hours, 3 days, 5 days, and 7 days (left to right). Degree of tissue inflammation increased with prolonged indwelling time for both catheter types. Extent of inflammation and tissue damage was more severe for steel versus Teflon catheters.

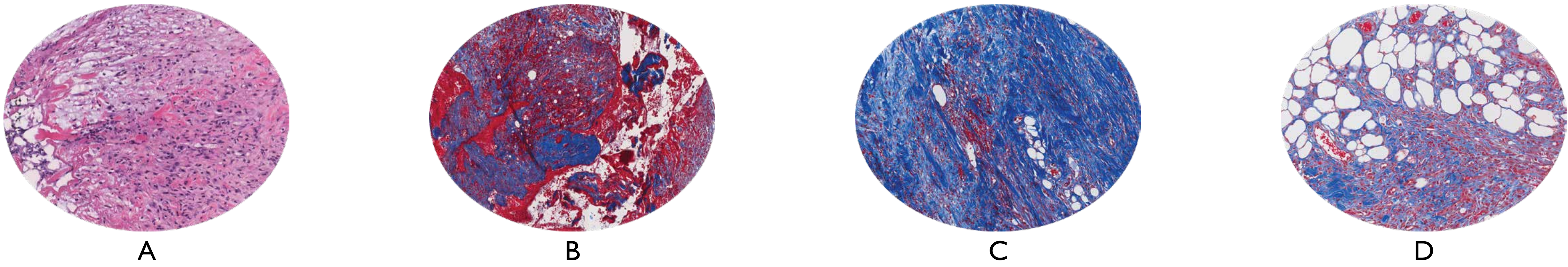


Figure 2. Tissue Histology was evaluated by qualifying: A) Degree of Tissue Inflammation, B) Fibrin Deposition, C) Collagen Deposition, and D) Fat Necrosis. H&E (Haematoxylin and Eosin) staining (A) allows for the visualization of cell nuclei and a visual estimate of inflammation density. Trichrome stains (B, C, and D) allow for the visualization of erythrocytes and thrombus (B), new collagen deposition (C), muscle, and digested or lysed adipose cells (D).

DISCUSSION

- CSII cannula insertion initiated an acute inflammatory response due to damaged cells, connective tissue, and extracellular matrix.
- A layer of inflammatory tissue formed around the cannula consisting of thrombus, neutrophils, macrophages, fibroblasts, and cellular debris.
- The layer of inflammatory tissue became thicker, denser, and more continuous over time in both Teflon and steel specimens.
- The layer of inflammatory tissue may function as a mechanical barrier; slowing or inhibiting the movement of insulin into adjacent subcutaneous tissue containing capillary and lymph vessels.
- Although structurally stable, stainless steel catheters elicit a more severe tissue response surrounding the insertion site, which may interfere with insulin absorption and increase loss of viable sites.

- Presented results provide information about biocompatibility and the acute inflammatory response that may cause insulin absorption variability and help guide the development of more effective, next generation insulin infusion catheters.

Slow/variable insulin absorption into circulation may be due to:

1. Insulin movement onto skin surface.
2. Insulin degradation within inflammatory tissue by proteases.
3. Variable distance to functioning capillary vessels.
4. Variable local capillary blood flow.
5. Variable insulin absorption across capillary endothelial cells.
6. Variable distance to functioning lymph vessels.
7. Variable absorption into local lymph vessels.
8. Insulin degradation within lymph nodes by proteases.
9. Variable rate of insulin diffusion through inflammatory and SC tissue.

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