Comparison of gross and histologic tissue responses of skin incisions closed by use of absorbable subcuticular staples, cutaneous metal staples, and polyglactin 910 suture in pigs

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Objective—To assess gross and histologic tissue responses of skin incisions closed by use of absorbable subcuticular staples, cutaneous metal staples, and polyglactin 910 suture in pigs.

Animals—8 purpose-bred disease-free pigs.

Procedure—Pigs were randomly allocated to 1 of 4 groups from which tissues were collected after death on postoperative days (PODs) 7, 14, 21, or 42. In each pig, 4 incisions were made; 1 was closed subcuticularly with 3-0 polyglactin 910 suture, 1 was closed with metal staples, and 2 were closed with absorbable subcuticular staples. Incision sites were grossly evaluated every 3 days after closure. At necropsy, incision sites and surrounding tissues were examined histologically; a histopathologic scoring system was used to quantitate healing and tissue response directed against the closure material.

Results—Postoperatively, the metal staples induced a severe inflammatory response, compared with minimal inflammation associated with the suture or absorbable subcuticular staples. Histologic evaluation of incisions on PODs 7, 14, and 21 revealed less severe inflammation associated with absorbable subcuticular staples than that associated with the other materials.


Surgical skin wound closure is primarily accomplished through cutaneous or buried subcutaneous suture placement. Placement of cutaneous sutures provides excellent apposition of the edges of incisions or wounds and is easy to perform; reported disadvantages include the need for removal of the sutures (often requiring further attendance at a medical facility), bacterial migration along suture tracts, skin irritation that may result in self-mutilation, and scarring. Problems with suture tract infection and crosshatch scarring led to the development of a subcuticular suture placement technique, which was first reported in 1895. This so-called buried suture pattern is frequently used in human and veterinary patients as the primary means of wound closure. Subcuticular placement of sutures reduces skin irritation, compared with cutaneous sutures; in animals, licking and scratching at the incision after closure are thereby decreased. Another advantage of the continuous subcuticular suture pattern is that it provides exceptional skin edge apposition and eversion, resulting in decreased tension along the wound margins and decreased scar formation, respectively.

Application of stainless-steel skin staples is an alternative to traditional cutaneous wound closure. Compared with the use of suture for skin closure, the speed and precision of staple placement are advantages; the use of staples has been reported to decrease closure time by as much as 80%, with no increase in complication rate. However, metal staples do require removal, which has been associated with considerable pain in humans. A high degree of visibility and large size of the remaining scar are additional problems associated with use of metal staples for skin closure.

Recently, absorbable staples designed for subcuticular placement have become commercially available. These staples are composed of polyglycolic-polyactic acid copolymers that lose 60% of their holding strength within 14 days of placement and undergo complete breakdown by hydrolysis and subsequent absorption (tissue half-life of 10 weeks). Each staple has 2 barbs to facilitate grip of the subcutaneous tissue and is placed with a multifire stapling device (Figure 1). Use of subcuticular staples has the potential to combine the advantages of subcuticular closure with the speed and precision of stapling.

The purpose of the study reported here was to assess the clinical and tissue responses of skin incisions closed by use of absorbable subcuticular staples, cutaneous metal staples, and polyglactin 910 suture placed in a continuous subcuticular pattern in pigs. Our hypothesis was that there would be no difference in the...
inflammatory response and wound healing associated with skin closure involving absorbable staples, compared with findings after skin closure involving polyglactin 910 suture or metal staples.

Materials and Methods

Animals and groups—Eight purpose-bred disease-free pigs were purchased from a local supplier. Pigs were approximately 6 weeks old; there were 6 females and 2 males. Pigs were ear tagged and housed as pairs. Prior to surgery, a pair of pigs was randomly assigned to 1 of 4 groups from which tissues were collected at necropsy on postoperative days (PODs) 7 (group 1), 14 (group 2), 21 (group 3), or 42 (group 4). Mean weight on the day of surgery was 13.6 kg (range, 11.5 to 15.9 kg). This study was approved by the University of Minnesota Institutional Animal Care and Use Committee, and all animal welfare standards were upheld.

Surgical procedures—Surgery to create skin incisions were performed on 2 days. Pigs in groups 1 and 3 underwent surgery on the first day, and pigs in groups 2 and 4 underwent surgery on the second day. Each pig received an injection of ketamine (10 mg/kg, IM) and xylazine (2 mg/kg, IM) as preanesthetic medication; anesthesia was induced with isoflurane via a mask. Each pig was intubated, and anesthesia was maintained with isoflurane and oxygen with a circle rebreathing system. Lactated Ringer’s solution was administered IV at a rate of 10 mL/kg/h. Within the first 5 minutes of anesthetic induction, an injection of penicillin G procaine (6,600 U/kg, IM) was administered. On completion of surgery, an injection of buprenorphine (10 µg/kg, IM) was given for pain control.

After anesthetic induction, each pig was placed in dorsal recumbency and the ventral aspects of the thorax and abdomen were aseptically prepared. Incisions (7 cm long) were made to the right and left of the ventral midline, approximately 2 to 3 cm lateral to the mammary tissue. Two incisions were placed on the ventral aspect of the thorax, and 2 were placed on the ventral aspect of the abdomen. Each incision extended to the level of the subcutaneous tissue (a depth of approx 3 mm below the dermis). All incisions were performed by the same surgeon (JLF) using a No. 10 scalpel blade.

The method of incision closure was predetermined such that each pig had 1 incision that was closed with metal skin staples,1 incision that was closed with 3-0 polyglactin 910 suture,2 and 2 incisions closed with absorbable subcuticular staples. The locations of incisions closed with metal staples, suture, or absorbable staples were randomized for each pig. However, within each group of 2 animals (groups 1 through 4), the total number of thoracic incisions closed with absorbable subcuticular staples equaled the total number of thoracic incisions closed with polyglactin 910 suture or metal staples combined. Likewise, within each study group, the total number of abdominal incisions closed with absorbable subcuticular staples equaled the total number of abdominal incisions closed with polyglactin 910 suture or metal staples combined.

To achieve skin closure with metal staples, 1 surgeon (REN) held the incision edges in apposition with Adson forceps while the primary surgeon (JLF) placed and fired the stapler in routine fashion. The distance between staples was approximately 6 mm. Skin closure with polyglactin 910 suture was performed in a continuous subcuticular pattern, with 4 throws placed on each knot. To achieve skin closure with absorbable subcuticular staples, 1 surgeon (REN) held the incision edges in apposition and elevated the edges within the stapler device by use of 2 Adson forceps while the primary surgeon (JLF) placed and fired the stapler. On the first surgery day, a single-fire stapler was used. On the second surgery day, a multifire stapler was used. Absorbable subcuticular staples were placed 1 cm apart. On closure of all 4 incisions in each pig, each surgical site was photographed.

Postoperative monitoring, euthanasia, and necropsy of pigs—Pigs were monitored after surgery in compliance with the university of Minnesota Institutional Animal Care and Use Committee guidelines. For each pig, gross findings were recorded and photographs of all surgical wounds on PODS 1, 4, 7, 11, 14, 17, 21, 28, 35, and 42 were obtained. Data recorded included assessments of the extent of dehiscence, erythema, and swelling and the type of exudate, if any. Metal staples were removed at necropsy (POD 7) for pigs in group 1; for pigs in groups 2, 3, and 4, metal staples were removed on POD 11.

Euthanasia was performed on PODS 7, 14, 21, and 42 for groups 1, 2, 3, and 4, respectively. Pigs were first administered an injection of ketamine (40 mg/kg, IM) and xylazine (4 mg/kg, IM); once the pigs were no longer responsive to manipulation, heparin (3,000 units) was administered IV. Euthanasia was carried out 5 minutes after heparin administration via intracardiac injection of potassium chloride (40 mEq). Pigs underwent a complete necropsy. After the gross appearance of all incision wounds was recorded, wounds were excised with approximately 2-cm margins of adjacent skin and associated deeper tissues (to the first muscle plane). Specimens were placed in neutral-buffered 10% formalin.

Histologic evaluation—After fixation of the excised tissues, specimens were transversely cut at 2-mm intervals, beginning from the midpoint of the wound and extending to its cranial end. In the remaining caudal half of the specimen, a longitudinal cut was made parallel to and 1 mm from the midline. For each wound specimen, 1 transverse and 1 longitudinal sample were each embedded in paraffin. Two sections (each 5 mm thick) were obtained from each sample: 1 section was stained with H&E, and the other was stained with Masson trichrome to better visualize dermal collagen fibers.

The tissue sections were randomized and evaluated in a masked fashion by 1 pathologist (NK). During microscopic examination, the wound healing response and the tissue response directed against the closure material were scored by use of a system modified from that of Sewell et al.11 In the scoring system of Sewell et al, different weighting factors are applied to different variables so that variations in cell types and cell densities are considered in the interpretation of the tissue reaction.12,13

The wound healing response that was directed against the mechanical damage from the incision and the introduc-
tion of the closure material was evaluated semiquantitatively by scored assessment of 11 variables (Appendix 1). Absence of a variable was scored as 0; if present, the extent of the variable was scored (in increasing order) as 1 or 2, 1 through 3, or 1 through 5, depending on the feature of interest. Assessed variables included completeness of closure and recepithelialization at the incision, ability to trace the incision (as evidenced by parallel alignment of nuclei or fibers in the connective tissue or loss of birefringence under polarized light in the dermis beneath a scab or an area of epithelial irregularity), alignment of collagen, and remodeling of collagen to native whirls. The mean width of the connective tissue filling the incision gap between superficial and deep dermis was measured digitally. The extent and degree of epidermal hyperplasia in the vicinity of the incision and the amount of granulation tissue present in dermis or subcutis were scored. Lastly, presence of multinucleate giant cells and dislocated epidermal cysts was assessed. Findings consistent with poor or delayed wound healing were assigned negative values for their weighting factor. Scores were multiplied by their weighting factors, and the products were summed to develop an aggregate wound healing score. The more negative the final score, the poorer the wound healing response; for instance, the score for the worst possible wound healing was ~30, whereas the score for the best possible wound healing was +7.

The tissue response directed against the closure material was evaluated semiquantitatively by scored assessment of 11 variables (Appendix 2). Absence of a variable was scored as 0; if present, the extent of the variable was scored (in increasing order) as 1 through 3 or 1 through 5, depending on the feature of interest. Assessed variables included the estimated numbers of neutrophils, macrophages and histiocytes, epithelioid cells, multinucleate giant cells, lymphocytes, and fibroblasts. The overall severity of the inflammatory response (total estimated cell number) was scored separately. For incisions closed with metal staples, the lateral skin penetration sites were scored. For all closures, the connective tissue capsule surrounding the surgical material and the presence of bacterial colonies were scored. Findings consistent with increased inflammation were assigned negative values for their weighting factor. Scores were multiplied by their weighting factors, and the products were summed to develop an aggregate tissue irritation score. A more negative score was associated with greater tissue irritation. The score representing the worst possible tissue irritation was ~105, whereas the score representing the least possible tissue irritation was +6.

Statistical analyses—Data were analyzed by use of computer software. Aggregate wound healing scores for incisions closed with absorbable subcuticular staples, metal staples, and polyglactin 910 suture were compared. Aggregate tissue irritation scores for incisions closed with absorbable subcuticular staples, metal staples, and polyglactin 910 suture were compared. A nonparametric Mann-Whitney U test was performed. Results were considered significant at a value of P ≤ 0.05.

Results The absorbable subcuticular staples, metal staples, and polyglactin 910 suture were easy to manipulate, and successful wound closure was achieved by use of each. All pigs recovered from anesthesia without incident. In the immediate postoperative period, there was good apposition of skin edges (with no visible separation) in all closed incisions. No incision dehisced along its entire length throughout the study period. However, 1 pig in group 1 and 1 pig in group 3 each had some separation along 1 of the 4 incision lines. On POD 4, the pig in group 1 had separation (5 mm in width) along the central 3-cm portion of the incision closed with metal staples because 4 metal staples had been pulled out of 1 or both edges of the skin; the separation gap had crusted over by POD 7. On POD 4, the pig in group 3 had skin edge separation (<3 mm in width) at the cranial and caudal margins of the incision closed with polyglactin 910 suture. All separation gaps were permitted to close by second intention healing.

Two pigs developed incisional abscesses as determined by purulent exudate from the surgical wounds. In the pig in group 3 in which separation was detected along the incision closed with metal staples, exudate was detected along that incision on POD 2. A pig in group 4 developed purulent discharge along the incision closed with polyglactin 910 suture on POD 14. These pigs were administered an additional injection of penicillin G procaine (6,600 U/kg, IM) daily for 4 days. At the time that the surgical wound abscesses were detected, a generalized distribution of papules and pustules was identified along the ventral aspects of the abdomen and thorax of both pigs.

Gross observations during the study period—Typically, wound edges of incisions closed by use of metal staples were everted after surgery and on POD 1; thereafter, swelling obscured the appearance of the incision. Marked erythema and firm swelling along the incision sites worsened from PODs 4 through 7 and persisted until staple removal (Figure 2). Of the 6 pigs that remained in the study at POD 11, 5 had some bleeding at the skin-staple interface after staple removal. Erythema resolved within 3 to 10 days of staple removal. Firmness of tissue resolved within 6 to 10 days of staple removal, although a visible crosshatch scar was still visible even at POD 35.

At incision sites closed by use of polyglactin 910 suture, a mild to moderate amount of swelling and erythema that was initially associated with the complete length of the incision resolved between PODs 4 and 7. After this generalized swelling had resolved, distinct nodular swellings (approx 1 cm in diameter) were observed at the cranial and caudal extents of the incisions after POD 7 (Figure 2). In 3 of the pigs (1 each in groups 2, 3, and 4), these swellings were not associated with erythema and the incisions remained soft. In the 2 other pigs (in groups 2 and 3), the caudal swellings became firm and erythematous. At necropsy, similar swellings were observed in both pigs of group 1. In the other pig in group 4, peri-incisional firmness was detected on POD 7 and progressed to swelling, erythema, and purulent discharge from the incision on POD 14. With the exception of this pig, scarring at the incision sites closed by use of polyglactin 910 suture was minimal.

Wound edges of incisions closed by use of absorbable subcuticular staples were everted after surgery and on POD 1; erosion resolved by POD 4. Between PODs 4 and 7, mild to moderate amounts of swelling and erythema were present along these incisions, similar to that observed in association with the incisions closed with polyglactin 910 suture. Wounds
remained palpably soft throughout the observation period, except in areas of more pronounced swelling. Nodular swellings (0.5 to 1 cm in diameter) were observed at the cranial end of one of the incisions closed with absorbable subcuticular staples in 2 pigs (1 each in group 2 and 4), at the center of one such incision in the other pig in group 2, and in both such incisions in a pig in group 3. Typically, remnants of

Figure 2—Photographs of the gross appearance of skin incisions closed by use of polyglactin 910 suture in a continuous subcuticular pattern (A and B), metal staples (C and D), or absorbable subcuticular staples (E and F) in 1 pig (from group 4) on days 7 and 21 after closure. The cranial end of the incision is to the left in each panel. A—Incision closed with suture 7 days earlier. Notice that scab material covers most of the incision line. Moderate erythema is present, most noticeably at the caudal end where a nodular swelling is present. B—Incision closed with suture 21 days earlier. At this time, erythema is minimal and a small nodular swelling persists at the caudal extent of the incision. C—Incision closed with metal staples 7 days earlier. Severe erythema and swelling are present along entire length of incision. Notice that bedding and particulate food matter are present on the surface of the skin. D—Incision closed with metal staples 21 days earlier. Staples were removed 11 days after closure of the incision. Erythema is minimal, and swelling has resolved. Notice that crosshatch scarring is visible. E—Incision closed with absorbable subcuticular staples 7 days earlier. Scab material covers 50% of the wound, and erythema is mild. F—Incision closed with absorbable subcuticular staples 21 days earlier. Notice that erythema and scarring are minimal.
Figure 3—Photomicrographs of cross sections of skin incisions closed by use of polyglactin 910 suture in a continuous subcuticular pattern (A and B), metal staples (C and D), or absorbable subcuticular staples (E and F) in 3 pigs (groups 1 and 3) on days 7 and 21 after closure. A—Section of an incision closed with suture 7 days earlier. A severe neutrophilic infiltrate is directed toward the multifilamented suture with a wide zone in the dermis containing numerous macrophages and occasional lymphocytes. B—Section of an incision closed with suture 21 days earlier. Notice that a moderate pyogranulomatous response with mineralization of suture fragments is present. C—Section of an incision closed with metal staples 7 days earlier. The penetration of a staple caused severe neutrophilic inflammation in this region of the dermis, hyperplasia of the overlying epidermis, and accumulation of macrophages in deeper dermal layers. D—Section of an incision closed with metal staples 21 days earlier. The area is almost fully remodeled and of normal appearance; there is only slight, irregular epidermal thickening and hyperkeratosis over the incision. E—Section of an incision closed with absorbable subcuticular staples 7 days earlier. The staple material is surrounded by a thin zone of macrophages mixed with occasional lymphocytes and neutrophils, corresponding to the early stages of fibrous capsule development. F—Section of an incision closed with absorbable subcuticular staples 21 days earlier. Histologic findings are similar to those determined 7 days after closure. In all panels, H&E stain; bars = 500 μm.
absorbable subcuticular staples were still palpable on POD 42, but the skin and underlying tissue remained soft. Scarring was minimal, and the incision lines became increasingly difficult to identify during the study period (Figure 2).

Gross observations at necropsy—No drainage or dehiscence of wound edges was detected along any of the incisions. A scab (dried exudate) was tightly adhered along all incisions of the pigs euthanatized on POD 7. Scabs were present at the previous metal staple–skin interface of pigs euthanatized on POD 14 (staples were removed on POD 11 in pigs of groups 2, 3, and 4). At euthanasia on POD 21, scabs along the previous metal staple–skin interface had resolved in 1 pig of group 3 but persisted in the second pig. No scabs were present along incisions of pigs euthanatized on POD 42 (group 4). No relevant pathologic changes were detected in liver, lungs, spleen, heart, or kidneys of any pig.

Histologic findings—In specimens of wound sites closed by use of metal staples, bilateral skin penetration sites of the staple ends were histologically evaluated as a substitute for actual closure material. On POD 7, severe inflammation was present (Figure 3). The overlying epithelium was hyperplastic and had an irregular trabecular extension into the underlying dermis. At the site of trabecular extension into the underlying dermis, a severe pyogranulomatous inflammation was detected, particularly in areas where the epithelium was dislocated (ie, overlapping). The inflammation extended into the deep dermal layers. On POD 14, the inflammatory reaction was more quiescent and the number of lymphocytes had increased, whereas the number of neutrophils had decreased. On POD 21, the inflammation was barely detectable, and by POD 42, it had completely resolved.

In specimens of wound sites closed by use of polyglactin 910 suture that were collected on POD 7, a closely aligned cluster of monofilaments was visible as numerous white foci that appeared intact (Figure 3). Neutrophils were rare to absent. The inflammatory reaction of incisions closed with absorbable subcuticular staples was significantly different from that of incisions closed with metal staples or polyglactin 910 suture (Table 1). On POD 14, the inflammatory response of incisions closed with absorbable subcuticular staples was significantly different from that of incisions closed with metal staples; however, there was no significant difference between the inflammatory response of incisions closed with absorbable subcuticular staples and that of incisions closed with polyglactin 910 suture. By POD 42, no sig-

### Table 1—Mean aggregate wound healing scores* (representing overall tissue responses) for incisions at 7, 14, 21, and 42 days after closure by use of cutaneous metal staples, polyglactin 910 suture in a continuous subcuticular pattern, or absorbable subcuticular staples in 8 pigs.†

<table>
<thead>
<tr>
<th>Postoperative day</th>
<th>Metal staples</th>
<th>Polyglactin 910 suture</th>
<th>Absorbable subcuticular staples</th>
<th>Comparison (P value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>–20.5</td>
<td>–17.5</td>
<td>–9.5</td>
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<td>21</td>
<td>–13.8</td>
<td>–11.3</td>
<td>–6.4</td>
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<td>42</td>
<td>–2.75</td>
<td>–5.75</td>
<td>–6.9</td>
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</table>

*Each value represents the mean of scores obtained from longitudinal and transverse sections of incision sites excised from 2 pigs. All scores were converted from negative to positive values for the sake of statistical analysis. †Four incisions were made in each pig; 1 was closed with metal staples, 1 was closed with suture, and 2 were closed with absorbable subcuticular staples. ‡Significant (P < 0.05) difference between the 2 methods of closure.

Postoperative day = Day after incision closure on which incision sites were excised from pigs.
significant differences in inflammatory responses were detected between incisions closed with metal staples or absorbable subcuticular staples and between incisions closed with polyglactin 910 suture or absorbable subcuticular staples. This difference between the wound healing response of incisions closed with polyglactin 910 suture and the response of incisions closed with metal staples was not significant at any time point.

For each incision, tissue response directed against the closure material was also assessed semiquantitatively by use of the aggregate tissue irritation score (Table 2). On POD 7, the inflammatory responses directed against the metal staples and polyglactin 910 suture exceeded the inflammatory response against the absorbable subcuticular staples. Although the aggregate tissue irritation score for the absorbable subcuticular staples was better (ie, less negative) than scores for the other 2 closure materials (−27 vs −43.8 and −34.5) on POD 14, the differences in scores among the metal staples, polyglactin 910 suture, and absorbable subcuticular staples were not significant. On POD 21, the inflammatory responses against the metal staples and absorbable subcuticular staples were similar; however, the response against the polyglactin 910 suture was significantly lower than that against the absorbable subcuticular staples. On POD 42, the only significant difference in inflammatory responses against closure materials was between polyglactin 910 suture and metal staple incisions.

Histologic examination of tissue sections revealed a moderate amount of bacteria associated with incisions closed by use of polyglactin 910 suture in both pigs in group 3; there was no purulent exudate associated with these incisions. However, in 1 of those 2 pigs, purulent exudate was detected on POD 2 at the incision closed by use of metal staples, but bacteria were not observed histologically (POD 21). Bacteria were also detected in association with incisions closed with metal staples in 1 pig each in groups 1, 3, and 4. The pig in group 1 had many bacteria, and the pigs in groups 3 and 4 had few bacteria associated with the incisions; however, none of those incisions had purulent exudate. In that pig in group 4, purulent exudate was detected on POD 14 at the incision closed by use of polyglactin 910 suture, but bacteria were not observed histologically (POD 42). In one of the incisions closed with absorbable subcuticular staples in 1 pig in group 2, a moderate amount of bacteria was detected but no purulent exudate was present.

### Table 2—Mean aggregate tissue irritation scores* (representing tissue response against closure material) for incisions at 7, 14, 21, and 42 days after closure by use of cutaneous metal staples, polyglactin 910 suture in a continuous subcuticular pattern, or absorbable subcuticular staples in 8 pigs.

<table>
<thead>
<tr>
<th>Postoperative day</th>
<th>Metal staples</th>
<th>Polyglactin 910 suture</th>
<th>Absorbable subcuticular staples</th>
<th>Metal staples versus absorbable subcuticular staples</th>
<th>Suture versus absorbable subcuticular staples</th>
<th>Metal staples versus suture</th>
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<tbody>
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<td>−55</td>
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<td>−17.8</td>
<td>0.297</td>
<td>0.180</td>
<td>0.050†</td>
</tr>
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See Table 1 for key.

### Discussion

Most commonly, surgeons rely on suture to hold wound edges in apposition until sufficient healing of tissue has occurred.2,3,12 Although a wide variety of suture types are currently available for wound closure, no one suture type is ideal for use in every situation.2,3,6 Factors such as wound environment, degree of contamination, rate of healing, suture handling characteristics, tensile strength, and reactivity must be considered when selecting suture.2,13,16 Compared with suture material that causes minimal inflammation, suture that causes a greater amount of inflammation may have a detrimental impact on wound healing.2 Consequently, in the development of new suture material, minimization of the inflammatory reaction through complete absorption or encapsulation of the material has been a goal.1

In the present study, closures of skin incisions with polyglactin 910 suture in a subcuticular pattern, absorbable subcuticular staples, and metal staples were compared in terms of wound healing responses and tissue irritation against the closure materials; in addition, the handling characteristics of each material were assessed. Because of the lack of suture memory as well as familiarity with the handling characteristics of the polyglactin 910 suture, the authors found the ease of wound closure with this material far outweighed any detrimental effect of tissue drag. Metal staples were likewise easy to apply, although periodically they had to be removed and replaced; because of improper placement, staples did not always equally grasp the skin edges. A few practice applications of the absorbable staples were required to master the art of subcuticular placement. However, despite the authors’ previous unfamiliarity with the technique, absorbable staple application was quickly mastered, and wound closure was accomplished with ease and relative speed.

Within the first 21 days of healing after closure of incisions in the present study, gross assessment of the wounds revealed severe tissue reaction against the metal staples as evidenced by firm, swollen, erythematous tissue; this response far exceeded the reaction observed along incisions closed with polyglactin 910 suture or the absorbable subcuticular staples. These differences in the appearance of the closed wounds were less apparent once the metal staples were removed and the inciting cause of inflammation (ie, foreign bodies) was no longer present. The extreme
reaction of porcine skin tissue against the metal staples surpassed anything that the authors had witnessed in clinical use of metal staples in dogs and cats.

The gross differences between skin closures by use of polyglactin 910 suture and absorbable subcuticular staples were more difficult to assess. Both methods of closure resulted in complete wound healing with minimal visible inflammatory response. However, along some of the incisions closed with polyglactin 910 suture, 1-cm swellings were visible and palpable at the cranial or caudal ends, likely because of the presence of suture knots. These swellings were not appreciable along every incision closed with polyglactin 910 suture, and we speculate that their presence may be a consequence of more superficial knot placement at some incision sites.

A wide variety of evaluation methods have been described13-24 as objective means of histologic assessment of wound healing; yet, no single method is universally accepted. In our study, we attempted to eliminate individual bias by creating a histologic scoring system modeled after that first reported by Sewell et al12 in 1955. That scoring system quantifies the inflammatory response on the basis of the predominance of specific immune cell types and overall cell numbers.12,13 Wound healing follows a series of predictable phases (lag, debridement, repair, and maturation) that are defined by the cell types that are present.17 Evaluation of wound healing involves assessment of the inflammation that results from the initial surgical trauma as well as the ongoing reaction against the closure material.9,10 Our scoring system, although slightly less detailed than that of Sewell et al.,enabled us to produce objective values for overall wound healing response and tissue reaction against the closure materials.

On PODs 7, 14, and 21, incisions closed with absorbable subcuticular staples had less negative aggregate wound healing scores than those associated with incisions closed with metal staples or polyglactin 910 suture, indicating a less severe overall inflammatory response within the incisions closed with absorbable staples. These differences in aggregate wound healing scores were significant on PODs 7 and 21 but not on POD 14 (which may be a result of the small sample size in our study). By POD 42, wound healing scores decreased with no significant differences among scores for incisions closed by use of metal staples, polyglactin 910 suture, or absorbable subcuticular staples. The similarity in scores among closure techniques on POD 42 was consistent with development of less severe inflammation. By POD 14, there were no significant differences among the scores for incisions closed by any of the 3 methods, which was consistent with decreased inflammation as the polyglactin 910 suture and absorbable subcuticular staples were degraded and absorbed and because the wounds closed with metal staples had been left open for >2 weeks.

The use of metal staples for skin closure has the advantages of speed and ease of application. However, previous reports7,9 in the human medical literature of patient discomfort at the site of skin penetration as well as during the process of suture removal may prevent metal staples from becoming the optimal choice for wound closure. Furthermore, metal staple wound closure results in a more visible, larger surgical scar than that achieved with subcuticular or percutaneous nylon suture closure.10 The incisions closed with metal staples in the present study were the most visible and were associated with the most palpable tissue irritation of any of the 3 closure methods. Although this tissue reaction generally subsided within 10 days after staple removal, the large degree of irritation and visibility of the remaining scar may outweigh the benefit of speed of closure when determining whether to use metal staples in veterinary practice.

Speed of closure was not evaluated in the present study because a single-fire stapling device for the absorbable subcuticular staples was used on the first surgery day and a multishot stapling device was used on the second surgery day. There was a learning curve associated with subcuticular placement of the absorbable staples; however, secure wound closure was generally accomplished after 3 or 4 practice staples had been placed at the beginning of each surgery day. The assistant surgeon held skin edges in apposition for metal and absorbable staple placement to accomplish near perfect skin alignment and to mimic the closure technique used in surgeries in humans. Considering that surgery performed on a veterinary patient is frequently accomplished by only 1 surgeon, the authors believe that the stapling device used for placement of the absorbable subcuticular staples could effectively be applied by 1 individual using 1-handed skin edge approximation.

Investigation of tensile strength of the incisions was not a focus of our study. However, all incisions closed with absorbable subcuticular staples healed without any sign of dehiscence, and most of the incisions closed with polyglactin 910 suture or metal sta-
wounds is relatively low. Metal staples have been defenses against infection. Despite these factors, the polyglactin 910 suture and metal staples).

Adequate healing (comparable to that provided by the incisions in the pigs used in our study for adequate healing (comparable to that provided by polyglactin 910 suture and metal staples).

Sutures act as foreign bodies within a wound, thereby increasing inflammation and altering host defenses against infection. Despite these factors, the incidence of infection in noncontaminated surgical wounds is relatively low. Metal staples have been reported to provide a tighter closure than buried subcuticular or cutaneous nylon suture, thus decreasing the ability of surface bacteria to migrate through the incision line. In the present study, only 2 dogs developed purulent exudate along 1 incision (an incision closed with polyglactin 910 suture and the other closed with metal staples), and both pigs were treated for 4 days with an antimicrobial. Although the authors speculate that these incisions were infected, without results of bacterial culture, the possibility of a sterile abscess cannot be ruled out. The presumed infection along the incision closed with metal staples in that pig was likely secondary to environmental contamination through the partial dehiscence that resulted from staple pullout. Microscopic examination of these 2 clinically inflamed incisions revealed no bacterial infection at the time of necropsy; this finding suggests that the administration of an antimicrobial or time (or both) enabled the pigs' immune defenses to clear the infection prior to euthanasia or that the abscesses were sterile. However, bacteria were detected via histologic examination of clinically noninfected incisions in those same pigs despite treatment with penicillin during the observation period. The presence of bacteria along other incisions suggests that these pigs may have had more generalized skin infections. This assertion is further supported by the diffuse distribution of papules and pusules identified on these pigs at the time that the abscessed incisions were detected.

Although bacteria were detected via histologic assessment in 6 of 24 (25%) incisions, there was no overt evidence of clinical infection (i.e., purulent exudate) in these 6 incisions at any time during the observation period. Incisions closed with metal staples had the highest incidence (3/8 incisions) of bacteria present at necropsy, followed by incisions closed with polyglactin 910 suture (2/8 incisions); incisions closed with absorbable subcuticular staples had the lowest incidence of bacteria present at necropsy (1/16 incisions). These findings suggest that absorbable subcuticular staples may have a comparatively decreased tendency to harbor bacteria. Furthermore, it is not surprising that the metal staple incisions had the highest incidence of bacteria given that metal staples were the only skin closure material that penetrated the skin, thereby providing an avenue for bacterial invasion. However, the true relevance of the bacteria in these incisions may be minimal given that surgical preparation does not eliminate bacteria from skin but merely reduces the quantity. It is unknown how these closure materials would compare in a larger study of contaminated wounds. Yet, the low overall presence of bacteria in the incisions is noteworthy given that pigs do not live in a sterile environment. Despite efforts to clean the runs frequently and keep the pigs on a tenderfoot grate system, pigs typically had fecal material on or near the incisions when the authors examined them.

The results of our study indicated that there was a significant difference between tissue irritation scores at POD 7 for the absorbable subcuticular staples, compared with those associated with the metal staples or polyglactin 910 suture, allowing us to reject the null hypothesis. On the basis of histologic evaluation of incision site tissues, there was a greatly reduced inflammatory response against the absorbable subcuticular staples during the early stages of healing, compared with the response against metal staples or polyglactin 910 suture. Furthermore, clinical evaluation revealed a severe inflammatory response against the metal staples, whereas inflammation associated with the polyglactin 910 suture or absorbable subcuticular staples was minimal.

The clinical impact of the applications of absorbable subcuticular staples remains to be determined. Pigs are commonly used in testing of human medical products, and many of the closure materials used in veterinary surgery are derived from the human medical field. The findings of our study suggest that absorbable subcuticular staples are safe to use as a means of wound closure and evoke a less severe inflammatory response with minimal scarring, compared with the effects of other commonly used methods of wound closure.

References

Appendix 1—Variables assessed to obtain the aggregate wound healing score (indicating the scale on which assessments were made and the weighting factor assigned to each variable).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score*</th>
<th>Weighting factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent of incision closure</td>
<td>0–2</td>
<td>1</td>
</tr>
<tr>
<td>Extent of reepithelialization with respect to normal thickness</td>
<td>0–2</td>
<td>1</td>
</tr>
<tr>
<td>Ability to trace incision†</td>
<td>0–3</td>
<td>-1</td>
</tr>
<tr>
<td>Parallel alignment of collagen</td>
<td>0–1</td>
<td>1</td>
</tr>
<tr>
<td>Remodeling of collagen to native whirs</td>
<td>0–1</td>
<td>2</td>
</tr>
<tr>
<td>Width of epidermal hyperplasia along surface</td>
<td>mm</td>
<td>-1</td>
</tr>
<tr>
<td>Degree of epidermal hyperplasia in vicinity of incision</td>
<td>0–2</td>
<td>-1</td>
</tr>
<tr>
<td>Overall cell density of granulation tissue in dermis</td>
<td>0–5</td>
<td>-1</td>
</tr>
<tr>
<td>Degree of acute inflammatory component in granulation tissue</td>
<td>0–5</td>
<td>-1</td>
</tr>
<tr>
<td>Presence of dispersed multinucleate giant cells</td>
<td>0–3</td>
<td>-1</td>
</tr>
<tr>
<td>Presence of epidermal cysts</td>
<td>0–2</td>
<td>-1</td>
</tr>
</tbody>
</table>

*Absence of a variable was scored as 0; if present, the extent of the variable was scored (in increasing order) as 1 or 2, 1 through 3, or 1 through 5, depending on the feature of interest. Ability to trace incision refers to evidence of parallel alignment of nuclei in fibers in the connective tissue or the loss of birefringence under polarized light in the dermis beneath a scab or an area of epithelial irregularity.*

Appendix 2—Variables assessed to obtain the aggregate tissue irritation score (indicating the scale on which assessments were made and the weighting factor assigned to each variable).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score*</th>
<th>Weighting factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of extravascular neutrophils</td>
<td>0–5</td>
<td>6</td>
</tr>
<tr>
<td>Presence of intravascular neutrophils</td>
<td>0–5</td>
<td>3</td>
</tr>
<tr>
<td>Presence of macrophages</td>
<td>0–5</td>
<td>-1</td>
</tr>
<tr>
<td>Presence of multinucleate giant cells</td>
<td>0–5</td>
<td>-2</td>
</tr>
<tr>
<td>Presence of lymphocytes</td>
<td>0–5</td>
<td>-1</td>
</tr>
<tr>
<td>Presence of fibroblasts</td>
<td>0–5</td>
<td>-1</td>
</tr>
<tr>
<td>Overall severity of inflammatory response against closure material</td>
<td>0–5</td>
<td>-3</td>
</tr>
<tr>
<td>Presence of bacterial colonies</td>
<td>0–3</td>
<td>-3</td>
</tr>
<tr>
<td>Capsule width around closure material</td>
<td>0–3</td>
<td>-1</td>
</tr>
<tr>
<td>Inflammatory cells within active fibrous capsule around closure material</td>
<td>0–3</td>
<td>-1</td>
</tr>
<tr>
<td>Complement of fibrous tissue capsule formation</td>
<td>0–3</td>
<td>2</td>
</tr>
</tbody>
</table>

*Absence of a variable was scored as 0; if present, the extent of the variable was scored (in increasing order) as 1 through 3 or 1 through 5, depending on the feature of interest.*