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FIRST ANNUAL REPORT ON PERCUTANEOUS CONNECTORS

by

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First Annual Report on
Percutaneous Connectors

Abstract

A unique surface possessing a regular array of micro-pillars was evaluated with regard to its ability to control epithelial downgrowth at the percutaneous interface. A range of pillar sizes were applied to the vertical segment of "T" shaped Biomer^{R} implants. These percutaneous tabs were implanted into the dorsum of cats for a period of 6 weeks using a standardized surgical technique. Comments were made post-operatively and at the time of retrieval. A quantitative scoring system was applied to these observations as well as histological results. As observed, the pillar morphology used in this investigation displayed the ability to control epithelial downgrowth. Collagen ingrowth into the interpillar spaces and possibly direct interactions of the epithelial cells with the morphology may account for the inhibition. The reproducibility of epithelial inhibition is, however, limited by other factors which are currently not well understood. These factors and potential methods of assessment are discussed.

Acknowledgments

We would like to express our appreciation to Dr. Donald F. Gibbons, Ms. Elizabeth Powell, and Mrs. Sue Heffernan for their invaluable help, guidance, and consultation on this project.

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INTRODUCTION

The development of a functional percutaneous device would find immediate and wide spread application in both medical research and clinical practice. A few of the potential applications include:

Blood access devices for dialysis, hyperalimentation, and drug delivery
Direct skeletal attachment of artificial limbs
Monitoring of physiological processes
Power access for artifical organs
Stimulation of neurological systems
Dental prosthesis

Despite the tremendous need and widespread application that a percutaneous device could provide, results from previous attempts to develop a functioning connector have been unpredictable and inconsistent. However, it has been agreed that the limiting factors to the success of a percutaneous device is the establishment of the epithetial and dermal seal. Without an adequate seal, the device will fail primarily by either infection or externalization.

When an incision is made in a transcutaneous fashion, initially a clot of fibrinous exudate and blood will collect between the cut surfaces of the dermis and epidermis. The epithelial cells in this case would typically move across the wound surface between the interface of the dried fibrin clot and the viable tissue until they contact homologous cells restoring continuity. However, in the presence of a foreign material, this response will be altered in any one of a number of ways depending on the material's chemistry and, more importantly, surface morphology. Typically, the epithelial response to a smooth implant is that of downward migration between the interface of the implant and the skin eventually externalizing or marsupializing the implant. However, if the implant surface allows for tissue ingrowth, epithelial downgrowth can be inhibited (1, 2, 3). In select situations it has been observed that the surface morphology of the percutaneous device has outweighed other material variables in determining the epithelial response (1).

A range of chemically different materials have been investigated with regards to percutaneous implants: carbons (4, 5, 6), Hydron^{R} (PHEMA)(1), Silastic^{R} (7), PTFE (Teflon^{R}) (8), polyurethane (9), polyethylene (10), as well as various metals (11, 12). The characteristic response is epithelial downgrowth with the formation of a sinus tract between the epithelium and implant. The sinus then predisposes the transcutaneous implant to infection. Additionally, exudate which collects between the implant and surrounding tissue provides an environment conducive to bacterial growth ultimately resulting in implant failure and eventual removal.

In contrast, porous materials (1, 8, 9) and fabrics (felts and velours) (2, 3, 8, 13, 14) have been used in an attempt to produce tissue ingrowth and prevention of epithelial downgrowth. It has been reported that if collagen fills the interstices of the material, it will in very select situations allow a functional epithelial seal (1, 14). However, porous implants lend themselves to the problem of cell necrosis deep within the interstices which can lead to rapid and irreversible infection, again, eventuating in implant removal. If an epithelial seal is established, the chromic percutaneous device can be subject to yet another problem, namely extrusion. Normal migration of maturing epithelial cells from the basal layers toward the outer keratinized layers can produce vertical forces on the implant and result in extrusion (1, 15). Although porous materials and fabrics which allow collagen ingrowth might appear to provide a potential solution to the issue of an epithelial seal, a device which incorporates these surfaces and performs in a reliable and acceptable fashion is not available.

The advent of ion technology at NASA (16, 17) has allowed the development of a series of unique surface sutructures. One of these morphologies, developed in conjunction with Applied Medical Technology, Inc. (Cleveland, Ohio), is that of a rectangular array of mico-pillars. Previous work has indicated that this particular surface topology when used in association with a percutaneous implant has the ability to allow collagen ingrowth (18, 19). In addition, there may be direct epithelial/morphology interactions to aid in the inhibition of epithelial downgrowth. An advantage of this surface morphology is that all dimensional parameters can be varied

(Figure 1); the base width of the pillar, the heighth of the pillar, and the inter-pillar spacing. Earlier work has shown that variation of these parameters can alter the soft tissue response subcutaneously (20). Therefore, the major objective of this report is to develop a model that would allow for evaluation and optimization of a pillar morphology as it applies to the percutaneous seal.

MATERIALS AND METHODS

The principal goal of the first year's percutaneous efforts has been to determine the optimal pillar morphology with regard to its influence on the epithelial response at the percutaneous interface. This morphology, once optimized, will then be applied to several different percutaneous devices.

The techniques of implant manufacture and implantation are those developed by Picha (18), and Taylor (19) in conjunction with Applied Medical Technology, Inc. Devices in the shape of a "T" (Figure 2) were implanted into the dorsum of mongrel male cats. The pillar morphologies were incorporated into the vertical segment of the "T" which was placed transcutaneously, while the horizontal segment was located subcutaneously for stabilization. After a predetermined time, animals were sacrificed and implants retrieved for histological analysis. Details of the protocol will be addressed subsequently.

Morphology Assessment: To assess the accuracy of morphology production, Biomer^{R} casts were fabricated by AMT. Sections of the cast which were representative of the mold were selected for SEM examination. Sections were mounted on aluminum stubs, sputter coated with gold-palladium and examined on an ISI-III A SEM. Biomer^{R} casts were photographed at various angles of tilt and magnification for accuracy of pillar dimensions and fabrication technique. A high degree of quality control was used to select only those molds which possessed accurate pillar dimensions and shape over a uniform area. The selected morphologies are discribed in terms of their base width and aspect ratio (a 100μ(1:3) morphology means the pillar base is 100u wide and pillar heighth is 300μ). Figures 3 through 9 show representative areas of the mprphologies examined in this study.

Implant Fabrication: All implants were fabricated from Biomer^{R}, a polyether polyurethane which has shown considerable application in the biomedical field (21). Pillared Biomer^{R} surfaces were produced by methods described by Picha (20). Once

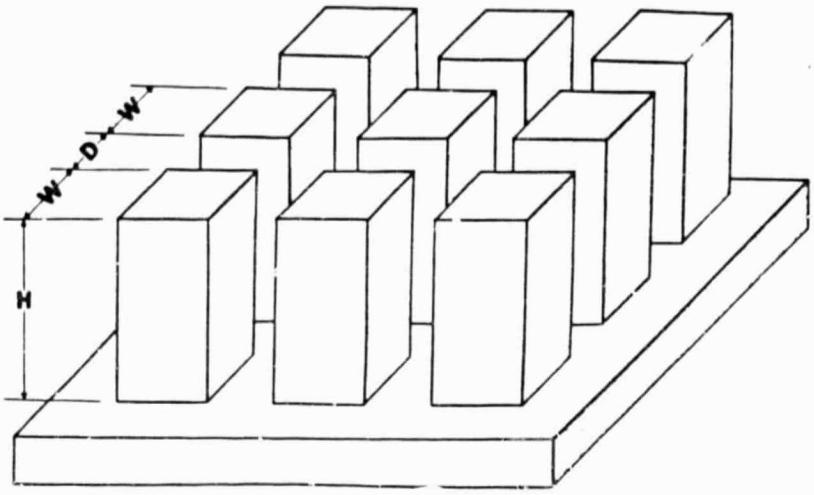


Figure 1. A graphic representation of a pillar morphology. All dimensional parameters (D,W,H) have the capability of being varied from 10 micra to several hundred micra.

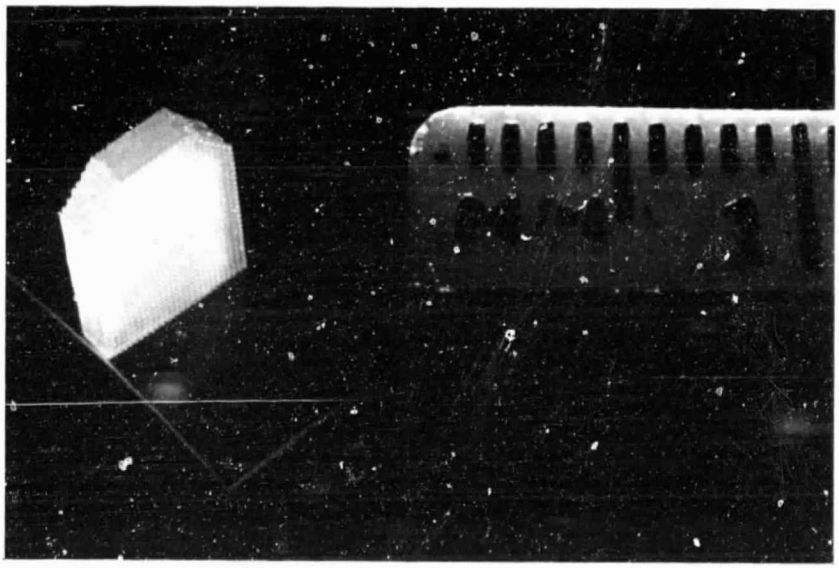


Figure 2. A close-up of the "T" shaped implant. The 100μ wide pillars can be seen on the percutaneous segment.

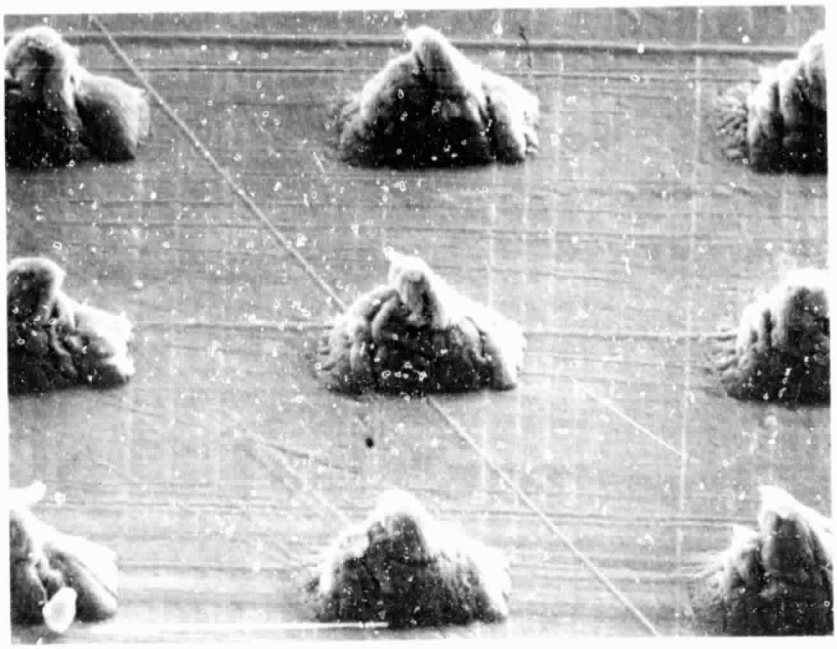


Figure 3. Representative area of a 28μ 1·1 morphology (560X, 35^{o} tilt).

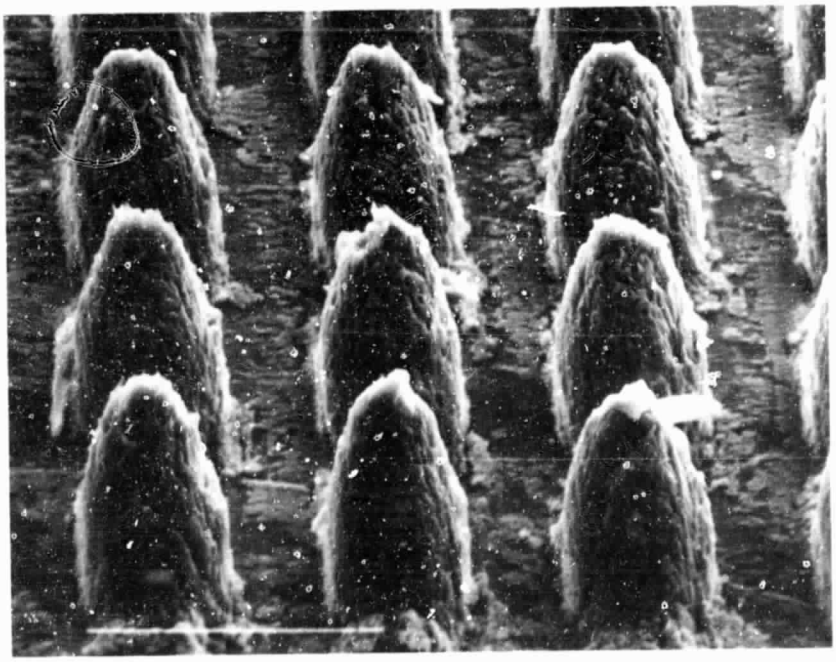


Figure 4. Representative area of a 28μ 1:2 morphology (560X, 35^{o} tilt).

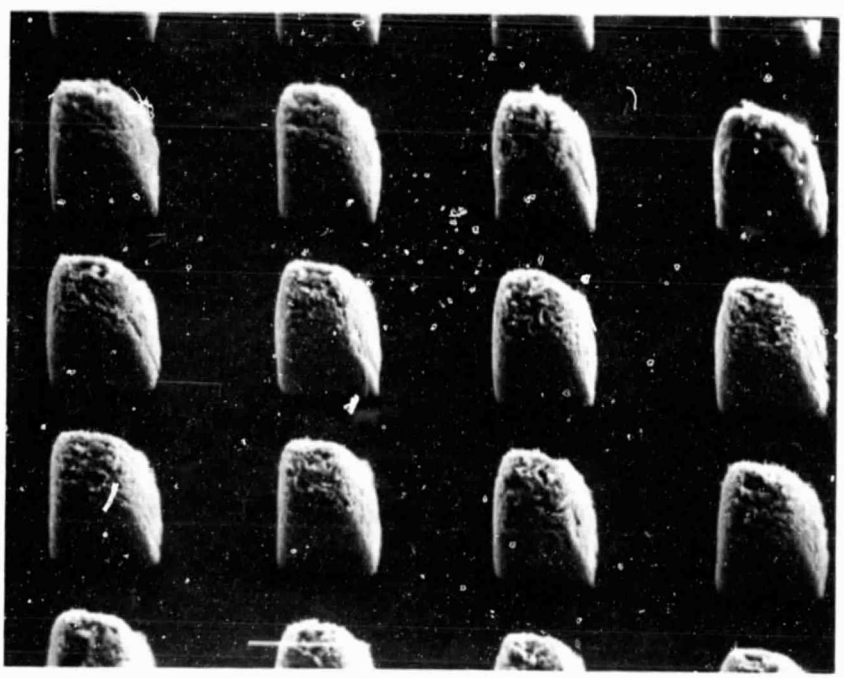


Figure 5. Representative area of a 50μ 1:1 morphology (240X, 45° tilt).

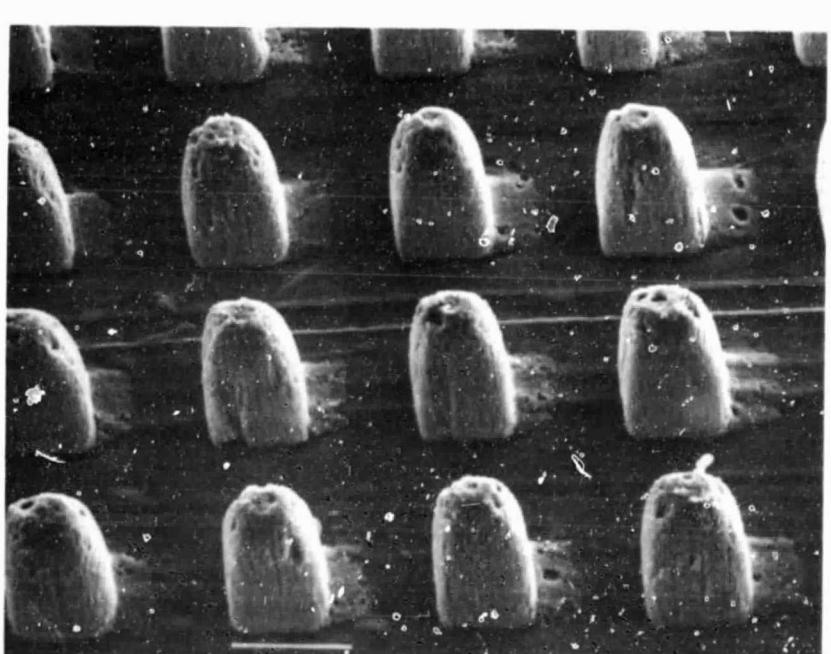


Figure 6. Representative area of a 50μ 1:2 morphology (240X, 35° tilt).

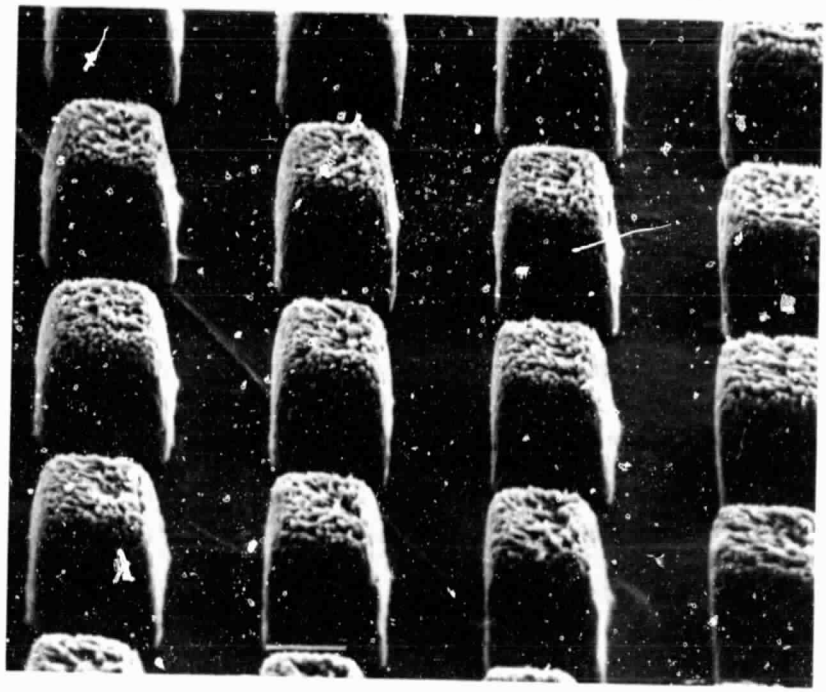


Figure 7. Representative area of a 100μ 1:1 morphology (160X, 45° tilt).

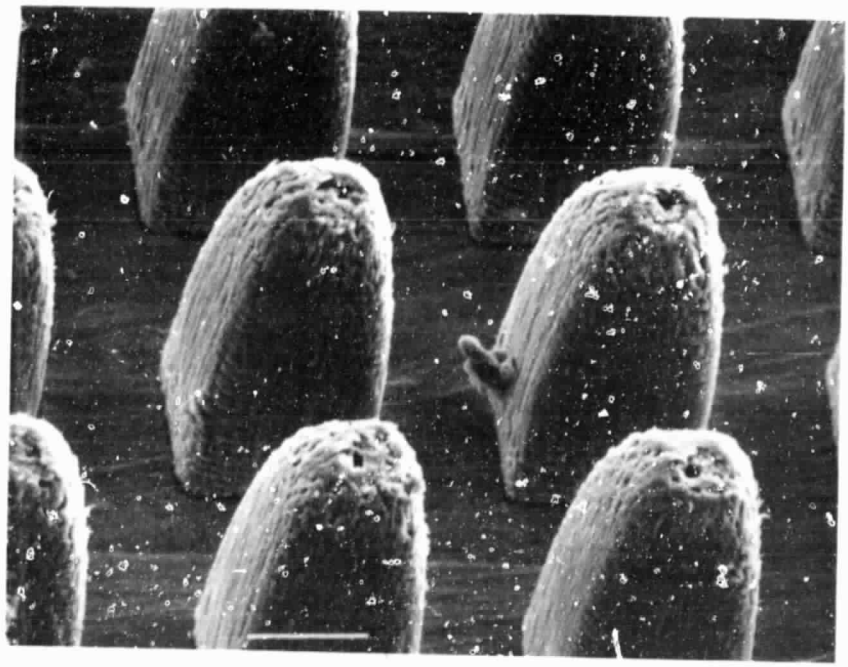


Figure 8. Representative area of a 100μ 1·2 morphology (240X, 35° tilt).

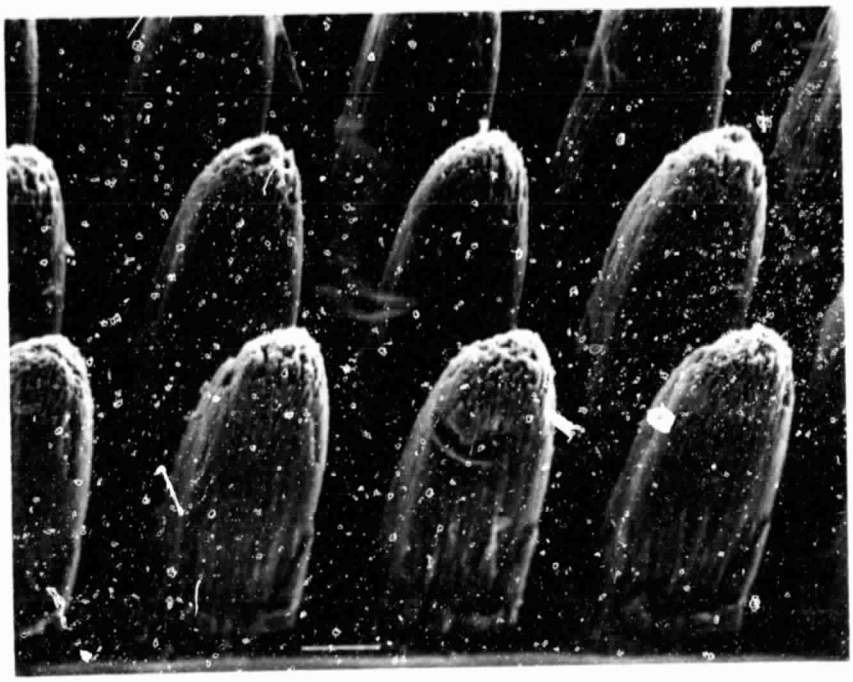


Figure 9. Representative area of a 100μ 1.3 morphology (160X, 45° tilt).

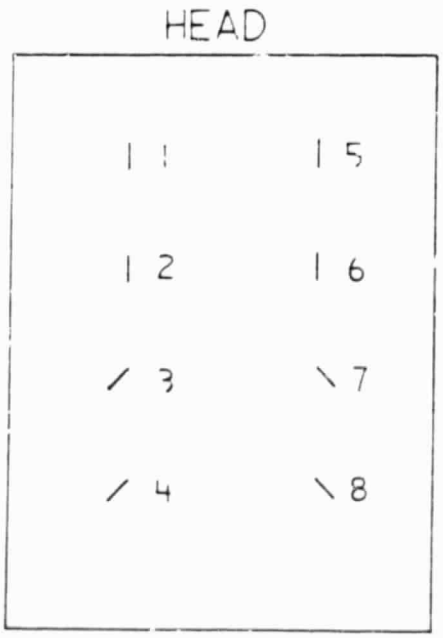


Figure 10. A schematic of the surgical field showing the orientation of the exit wounds.

an implant morphology was cast and removed from the mold, it was then incorporated into an implant by methods described in Appendix A; smooth controls were also made in a similar fashion.

Implant Surface Analysis: To insure that no chemical contaminants were being transferred from the mold to the Biomer^{R} casts, a series of casts were made for Electron Spectroscopy for Chemical Analysis (ESCA)[1]. The major contaminant of interest was nickel, which in sufficient quantities can cause hypersensitivity, necrosis, and carcinogenesis. Four samples were examined: (a) a smooth glass cast control, (b) a 6th casting from a mold having 1 coat of releasing agent, (c) a 6th casting but boiled for 15 minutes, and (d) a 5th casting without releasing agent. To determine whether a contaminant was restricted to the surface or was actually in the bulk polymer, the Biomer^{R} samples were sputtered to remove the surface molecular layers. The data is presented in Table 1. As can be seen, the contaminant of interest, nickel, can be eliminated by using one coat of releasing agent on the mold, taking five casts, and then boiling subsequent casts. This procedure was followed for all implants used in this study.

Implantation: A total of 12 cats (3.5 - 6.0 kg.) were each implanted with eight implants. The implants were spaced and oriented in the dorsum (Figure 10) taking into account the influence of Langer lines (19). The implant morphologies were sequenced such that each morphology was implanted in a different location on the cat's back to eliminate location as a variable.

Anaesthesia was induced with Ketamine chloride (30mg/hg.) and Atropine (0.2 mg.) was given to reduce respiratory secretions. When sedated, the animal was secured with full ties. The back was shaved and scrubbed with tinted amphyl (3 times), forllowed by a Phisohex^{R} scrub. The operative site was then rinsed with sterile saline and draped for surgery. Sterile surgical procedures were followed throughout. Antibiotics were not used at any time during this study.

1. ESCA analysis was kindly performed by Dr. D. Dwight and Steve McCartney at Virginia Polytechnic Institute (Blacksburg, VA.)

TABLE 1 ESCA Data for Cast Biomer Surfaces

SAMPLE		C		O		F		N		Si		Ni	
		BE*	%	BE	%	BE	%	BE	%	BE	%	BE	%
A	BEFORE SPUTTERING	285	73	532.2	19		0	399.6	4	102.4	4		0.0
	AFTER SPUTTERING	285	86	532.7	10		0	400.0	2	103.0	2		0.0
B	BEFORE	285	66	532.0	22	689.8	6		0	102.4	6	856.6	0.2
	AFTER	285	76	532.4	20		0			103.2	4	856.2	0.2
C	BEFORE	285	65	532.1	24	689.5	1	400.5	3	102.5	7		0.0
	AFTER	285	70	532.3	21		0	400.8	2	102.7	6		0.0
D	BEFORE	285	69	532.0	23	689.4	3		0	102.6	5	855.4	0.1
	AFTER	285	73	532.2	20		0		0	102.8	6	854.4	0.3

A=Smooth glass cast control
B=6th cast from mold having 1 coat of releasing agent
C=6th cast, but boiled for 15 min.
D=5th cast without releasing agent

*BE=Binding energy (ev)
%=Atom composition calculated from peak areas and Schofield cross-sections

Figure 11. Intradermal injection of epinephrine.

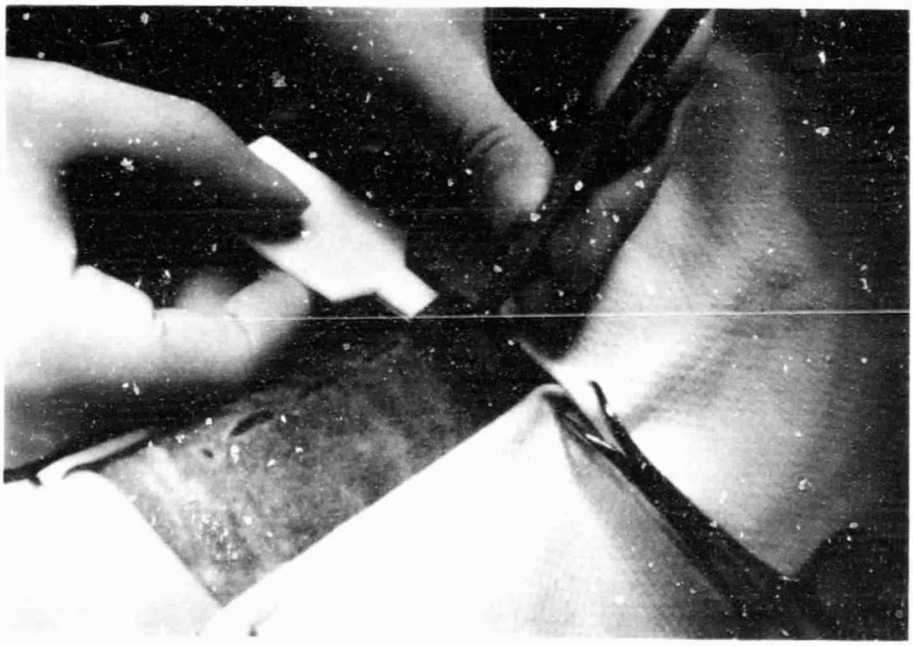


Figure 12. PTFE cutting surface placed subcutaneously for the 4.7mm exit wound.

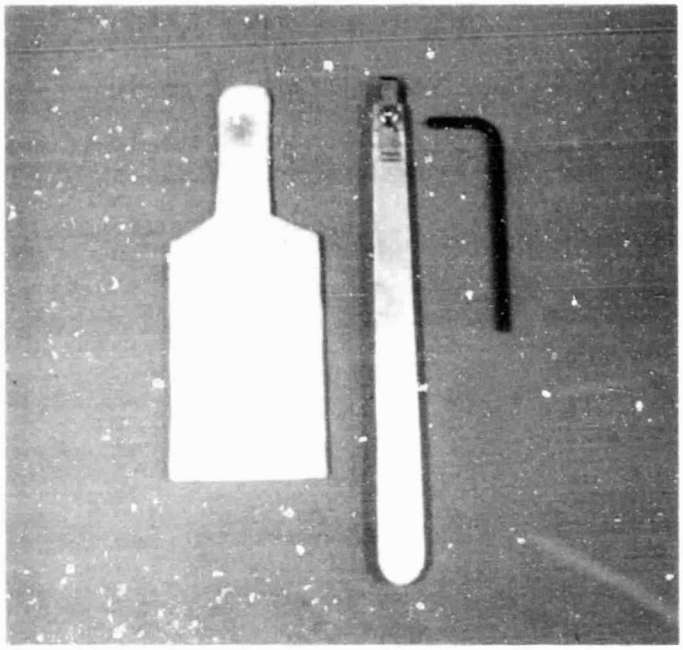


Figure 13. From left to right: a. Teflon which was inserted subcutaneously through the initial incision providing a cutting surface when making the exit wound; b. Blade and handle used to make 4.7mm stab wound for the exit site; c. Allen wrench used to secure blade to handle.

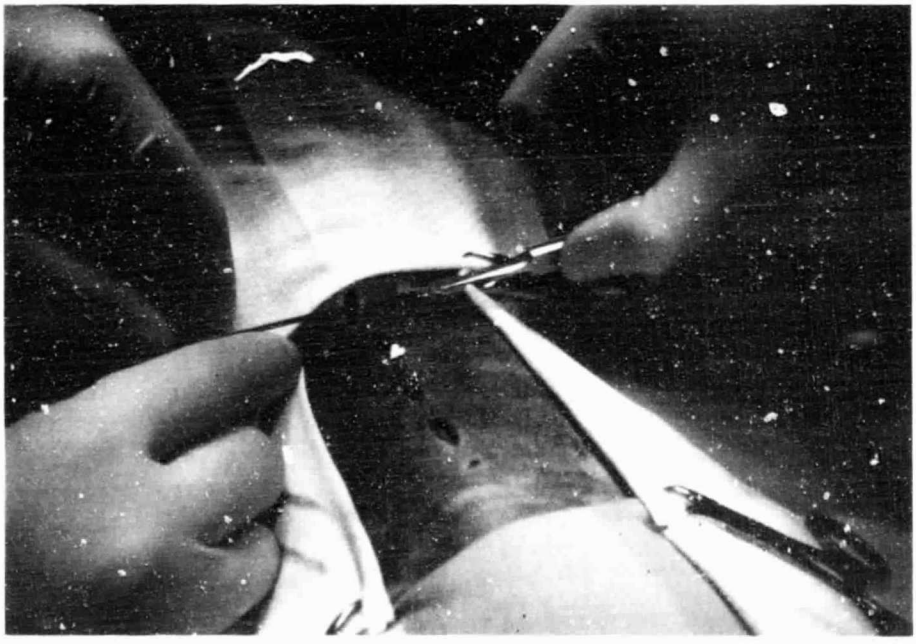


Figure 14. The Wullstein ear forcep is passed subcutaneously through the exit wound to grasp the top of the implant.

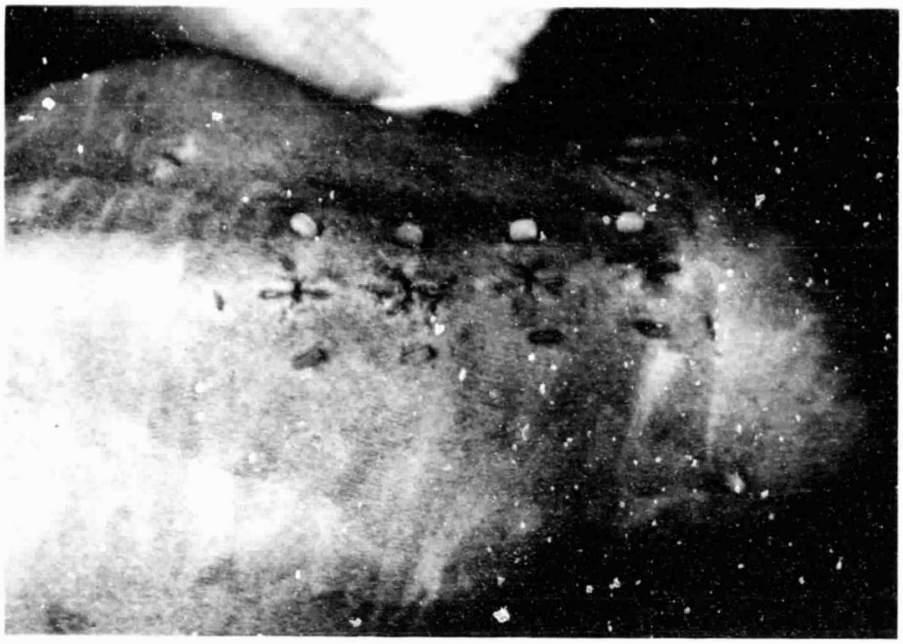


Figure 15. Back of cat following surgery.

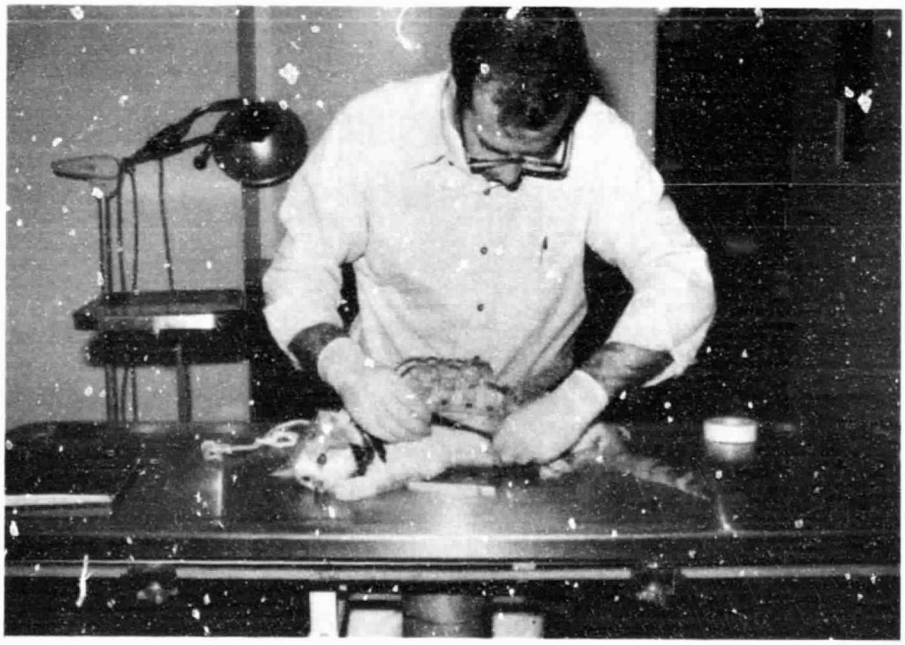
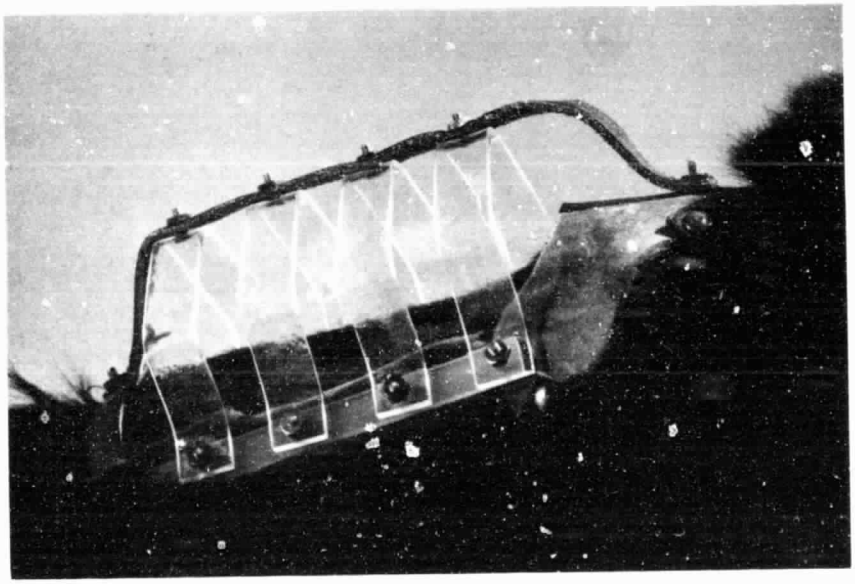


Figure 16. Placement of protective harness following surgery.



Figures 17 and 18. These fugures show the harness which was designed to protect the implants and allow observation of the surgical field.

Once prepped, four longitudinal incisions were made along the dorsal midline using electrocautery. Subcutaneous pockets were dissected bilaterally from each incision. Approximately one inch lateral to the midline, 0.1 ml of epinephrine (1:10,000) was injected subcutaneously to constrict local dermal vasculature (Figure 11). Approximately 5 minutes following epinephrine injection, a narrow piece of PTFE was inserted into the subcutaneous pocket to funcion as a cutting surface for the exit wound. A 4.7mm[1] longitudinal stab wound was then made at the original site of epinephrine injection (Figure 12). This 4.7mm incision functioned as the exit site for the percutaneous segment of the implant. All exit wound blades were cut from the ends of single edge GEM^{R} blades.

Actual implantation required inserting Wullstein ear forceps into the 4.7mm stab wound and directing the forcep tips to the original midline incision. Concurrently, the midline incision was retracted such that when the tips of the forceps were exposed, the implant could be grasped by the top of the percutaneous segment and pulled into the exit site (Figure 14). All wounds as well as the implant were irrigated with sterile saline prior to implantation.

Implant Management: Of equal importance to the surgical technique is the post-operative care of the implants. A protective harness shown in Figures 17 and 18 was utilized to prevent the animal from contacting and abraiding the operative site. This harness also allowed for observation of the implants (19). The animal was fitted with the harness one week prior to surgery to allow acclimation and adjustments for fit. The brace was removed for surgery and replace immediately afterwards. Animals were maintained on Purina Cat Chow and water ad libidum.

Implant Analysis: Immediately following surgery each implant was assessed for the quality of interfacial fit (i.e. tight, eversion, or gap) and whether blood was present on both the medial and/or lateral sides. This procedure was repeated after

1. The first 4 experiments employed a 5.0mm blade, however, it was felt that a 4.7mm exit wound would encourage improved tissue/implant apposition. The 4.7mm blade was used in all subsequent experiments.

six weeks at the time of implant retrieval (see Table Z). Implants were retrieved and fixed in 10% buffered formation en bloc. Once fixed, the implant and surrounding tissue block were cut on the midline (along the long axis of base) and processed for normal parafin embedding (acetone used in place of xylene). The cut planes of the implant and tissue were presented for histological sectioning, and subsequently stained with Masson's trichrome and standard H&E. The methods used for histological analysis are presented in Chapter III - Results.

RESULTS

A total of 12 cats were implanted with 8 implants each and retrieved after 6 weeks. A system was employed for analysis which assigned a quantifiable score to qualitative comments made at the following times: (a) post-operatively, (b) at the time of retrieval, and (c) on the histologic results.

Method of Analysis: The methods used to assess and quantify the "Post-Operative Comments" and "Comments at Time of Retrieval" have been discussed earlier (19). Table 2 lists the descriptions used and corresponding scores. Each interface (medial and lateral) was visually scored with regard to the implant fit (i.e. tightness, gap, eversion, etc.) and the quality of the interface (dry, bloody, exudate, etc.).

A percentage score was assigned to: (a) missing implants, (b) implants that slipped subcutaneously, (c) inflamed implants, and (d) interfaces which could be scored (epithelium contacted implant). The percentage of missing and subcutaneous implants was calculated from the total number of implants (Figure 22). This population was then excluded from any further analysis. The remaining implants were then subdivided into scorable and non-scorable groups. The criterion for this distinction will be discussed subsequently. The population of inflamed implants represents a unique group calculated from the combined populations of scorable and non-scorable implants.

Histologically, the epithelium was scored in terms of the presence of a sulcus and the extent of epithelial downgrowth. A distinction was made such that epithelial downgrowth was graded only when actual epithelial contact was made with the implant. A second score was assigned to the general cellularity seen in the vicinity of the implant interface. The descriptions and corresponding values used to assess the histological sections are listed in Table 2.

In several instances, epithelial contact with the implant surface was not observed. It was felt in some cases, the wound edge may not have apposed the implant adequately, consequently the epithelium appears to approach the interface at an oblique angle (Figure 25a). More often, however, blood, exudate, and cellular debris collected

TABLE 2 Observations with Corresponding Scores

	Score
I. Post-Operative Comments	
A. Fit	
1. Tight (no gap)	1
2. Puckering (eversion)	2
3. Gap	3
B. Interface	
1. Dry (no blood)	1
2. Slightly bloody	2
3. Very bloody	3
4. Subcutaneous Membrane	4
II. Comments at Retrieval	
A. Fit	
1. Tight (no gap)	1
2. Gap (sulcus)	2
B. Interface	
1. Dry	
a. No crustaceous exudate	1
b. With crustaceous exudate	2
2. Moist and red	
a. No crustaceous exudate	3
b. With crustaceous exudate	4
c. Perulent exudate	5
III. Histology	
A. Epithelial Response	
1. No Data	no score
2. No downgrowth	
a. No sulcus	1
b. Sulcus $< \frac{1}{2}$ dermal thickness	2
c. Sulcus $> \frac{1}{2}$ dermal thickness	3
3. Downgrowth $< \frac{1}{2}$ way to base starting from the point where the epithelium contacts the material	
a. No sulcus	4
b. Sulcus $< \frac{1}{2}$ of dermal thickness	5
c. Sulcus $> \frac{1}{2}$ of dermal thickness	6
4. Downgrowth $> \frac{1}{2}$ way to base starting from the point where the eipthelium contacts the material	
a. No sulcus	7
b. Sulcus < 1	8
c. Sulcus $> \frac{1}{2}$	9

Table 2 Continued

III. Histology - continued

5. Complete downgrowth	
a. No sulcus	10
b. Sulcus < ½	11
c. Sulcus > ½	12

Cellular Response

1. Predominately fibroblasts with some macrophages	1
2. Predominately macrophages	5
3. Predominately PMN's with some macrophages	10

between the implant and tissue, forming a new interface and effectively masking the morphology (Figure 25b). Consequently, the epithelium advanced down this new interface. In other cases, the advancing epithelium was inhibited by inflammation, creating yet another example of inadequate epithelial/implant contact. Under any of the circumstances just described, the sample was assigned the status of "no score", which eliminated it from further analysis. Of those samples remaining, scores for each morphology were pooled and averaged as presented in Table 3.

Although the primary variable of interest is the pillar morphology, the effect of exit wound size was also evaluated. The first four experiments were performed using a 5.0mm blade for the exit wound. The data for these four experiments was not considered in the morphology assessment, however the data from these experiments (5.0mm) is compared to the data of the remaining experiments (4.7mm) to examine the effect of exit wound size (Table 4).

Post-Operative Comments: All implants were similar with regards to post-operative comments (Table 3). There were no statistically significant differences in scores for fit, interface quality, or combined scores (fit + interface). This, however, might be expected since the basic implantation technique was the same for each implant.

In comparing the 5.0mm blade to the 4.7mm blade, the 4.7mm blade revealed a trend toward uniformly better scores. This trend can be seen for the control, 50μ 1:2, and 100μ 1:3 morphologies (Table 4).

Comments at Time of Retrieval: All implant morphologies demonstrate similar responses with regard to implant fit, interfacial quality, and combined scores. The 4.7mm blade suggests a trend of better average scores than the 5.0 mm blade, but again these differences are not statistically significant.

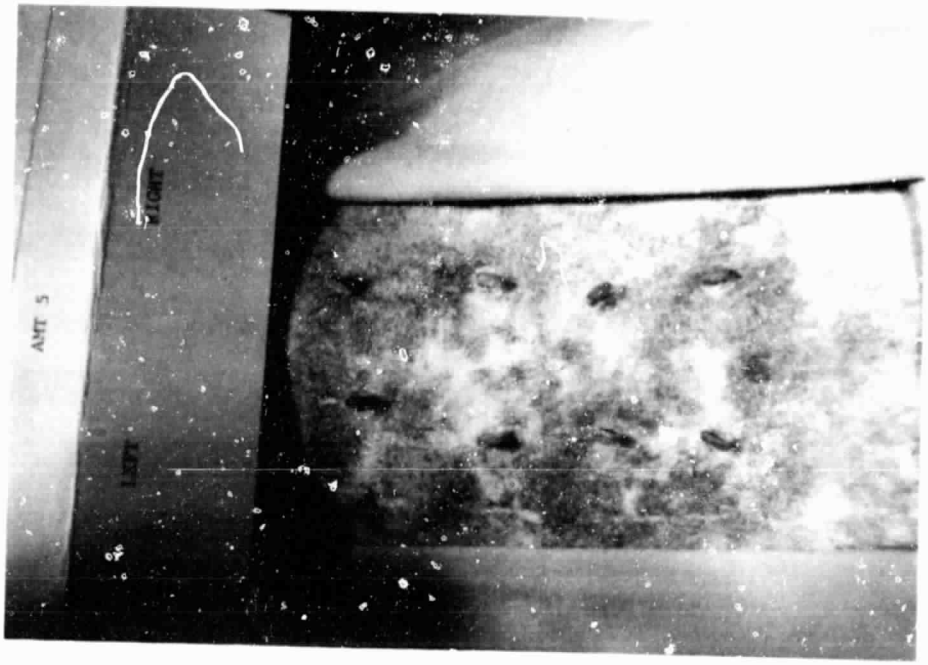


Figure 19. Implant region showing condition of implants after 6 weeks.

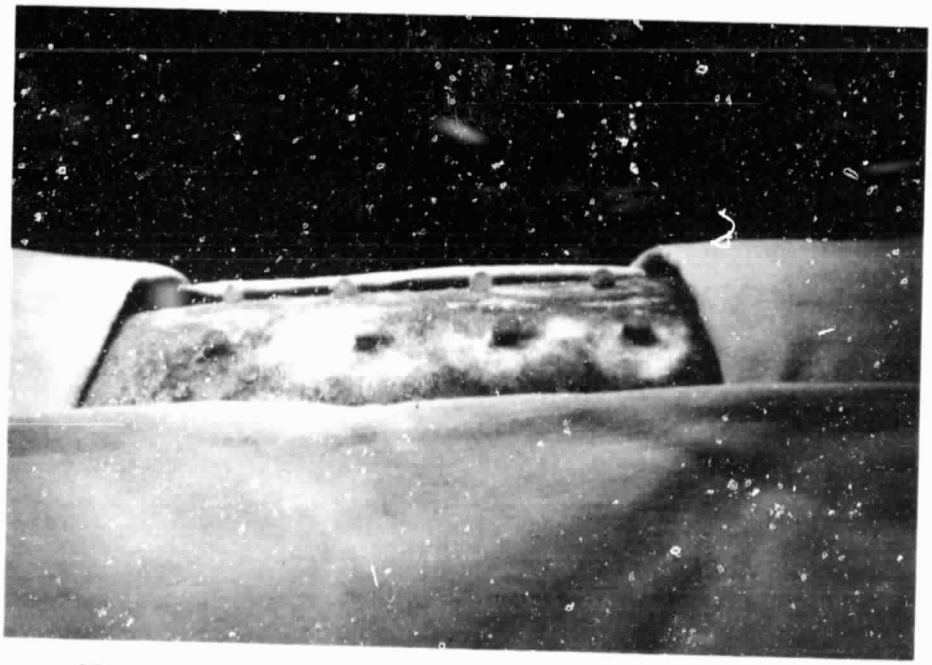


Figure 20. Side view of Figure 19.

Figure 21. A close-up of one of the implants from Figures 19 and 20.

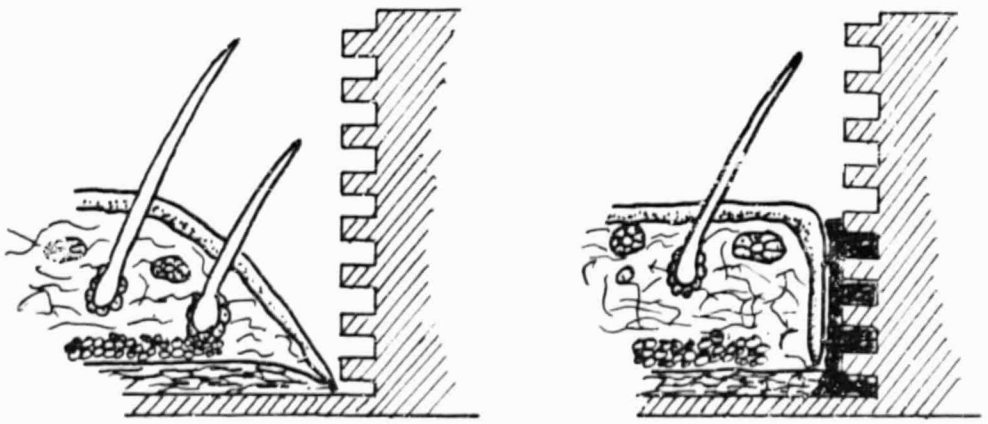


Figure 25. Tissue responses which were assigned a status of "no score": a. The tissue approaches the implant in such a way that little or no apposition occurred; b. The morphology of the implant is masked by dried blood and exudate so that the epithelium never contacted the implant.

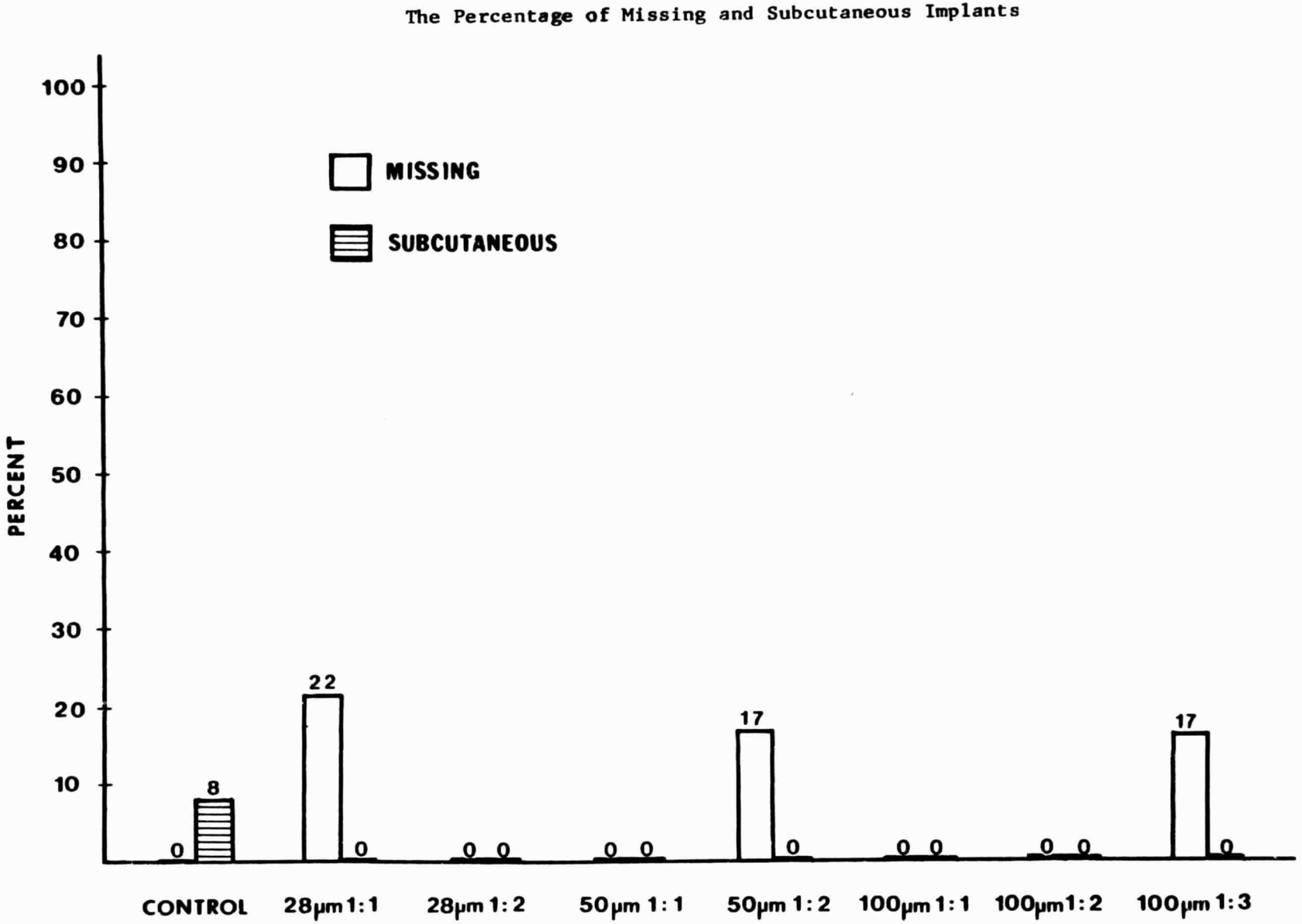


Figure 22. A graph of implant surface morphology VS. the percentage of missing and subcutaneous implants.

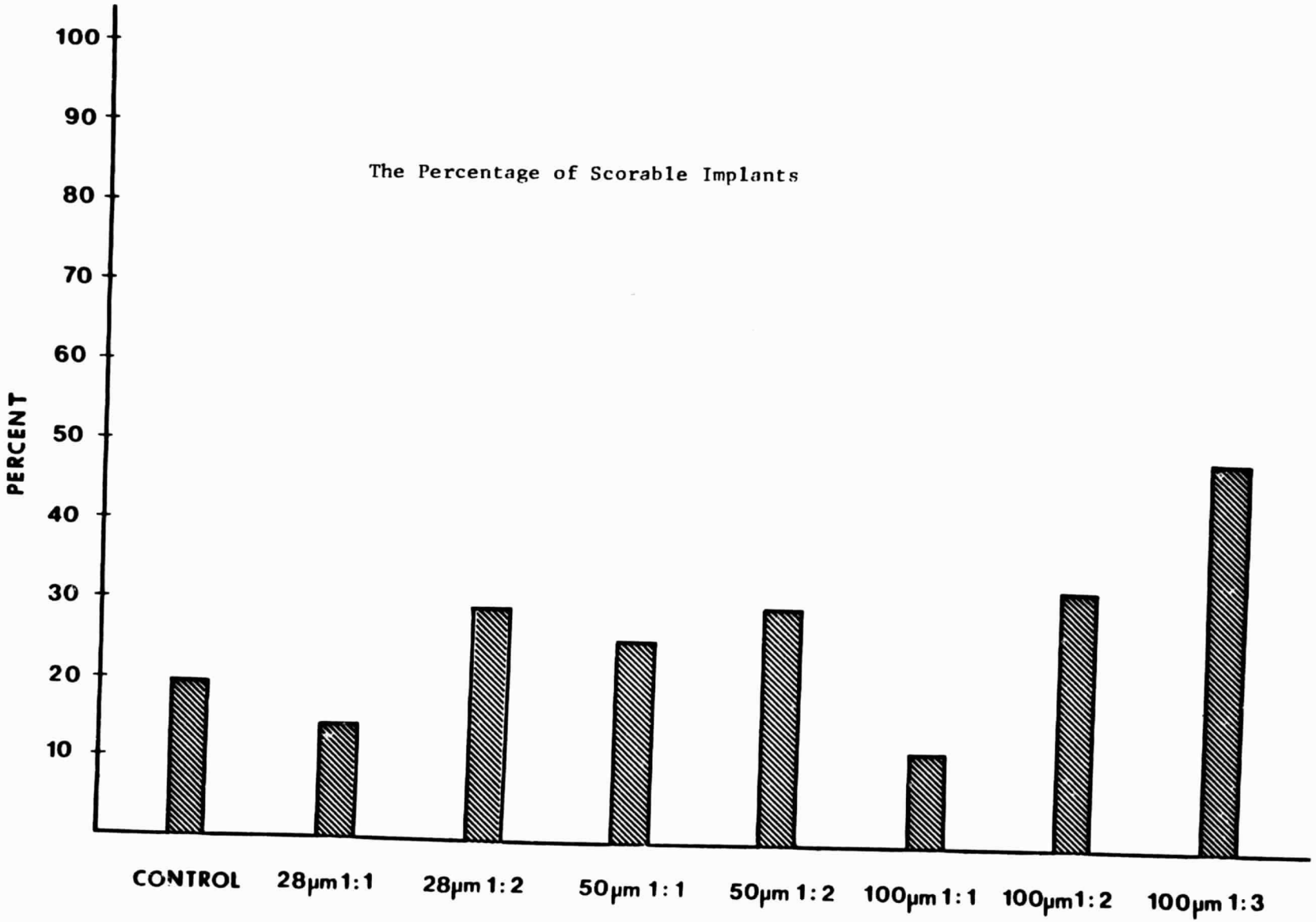


Figure 23. A graph of implant surface morphology VS. The percentage of implants which could be scored histologically.

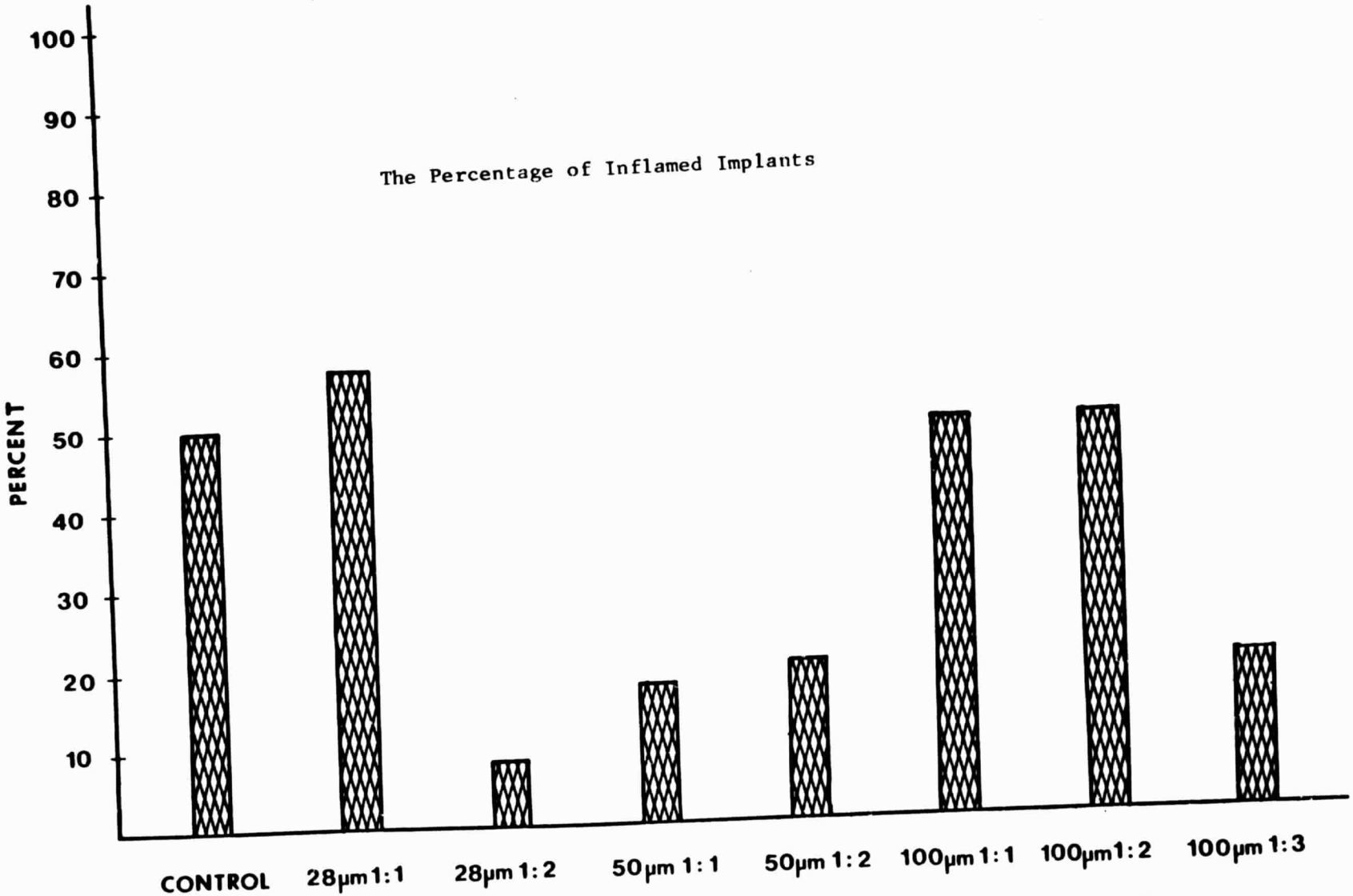


Figure 24. A graph of implant surface morphology VS. the percentage of inflamed implants.

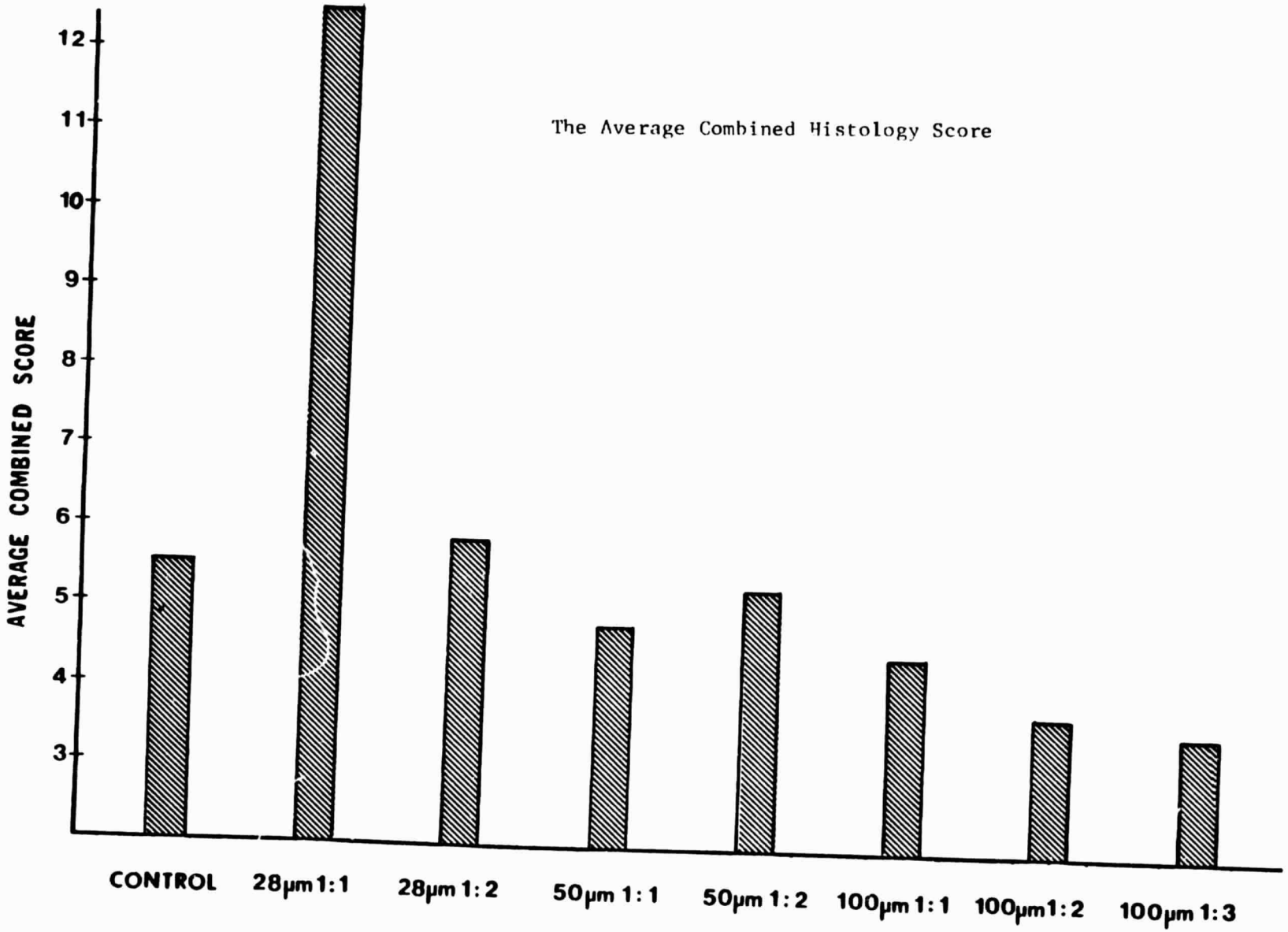


Figure 26. A graph of implant surface morphology VS. the average combined histological score (epithelial score + cell response score). A lower number represents a more optimal response.

TABLE 3 The Effect of Surface Morphology - Data Comparison[1] (average ±S.D.)

	Post-Operative Comments[3]			Comments at Retrieval[3]			Histology[3]		
	Fit	Inter-face	Combined[2]	Fit	Inter-face	Combined	Epith.	Cells	Combined
CONTROL	1.0±0	1.4±.5	2.4±.5	1.1±.3	2.9±1.3	4.0±1.4	4.5±1.5	1.0±0	5.5±1.5
28μm 1:1	1.1±.3	1.4±.6	2.5±.6	1.0±0	2.0±0	3.0±0	11.5±.5	1.0±0	12.5±.5
28μm 1:2	1.0±.2	1.3±.5	2.3±.5	1.1±.3	2.2±.7	3.3±.7	4.9±2.4	1.0±0	5.9±2.4
50μm 1:1	1.1±.4	1.4±.5	2.5±.7	1.2±.4	2.6±1.0	3.8±1.0	3.8±3.0	1.0±0	4.8±3.0
50μm 1:2	1.0±0	1.3±.4	2.3±.4	1.0±0	2.2±.6	3.2±.6	4.3±1.9	1.0±0	5.3±1.9
100μm 1:1	1.0±0	1.8±.6	2.8±.6	1.2±.4	2.0±.7	3.2±.8	3.5±1.5	1.0±0	4.5±1.5
100μm 1:2	1.2±.6	1.4±.6	2.6±1.1	1.0±0	2.4±1.0	3.4±1.0	2.8±.4	1.0±0	3.8±.4
100μm 1:3	1.0±0	2.1±1.8	3.1±1.8	1.0±0	2.3±.9	2.3±.9	2.6±.5	1.0±0	3.6±.5

1. All experiments employed a 4.7mm exit site
2. Combined = Fit + Interface
3. A lower score represents a more optimal response

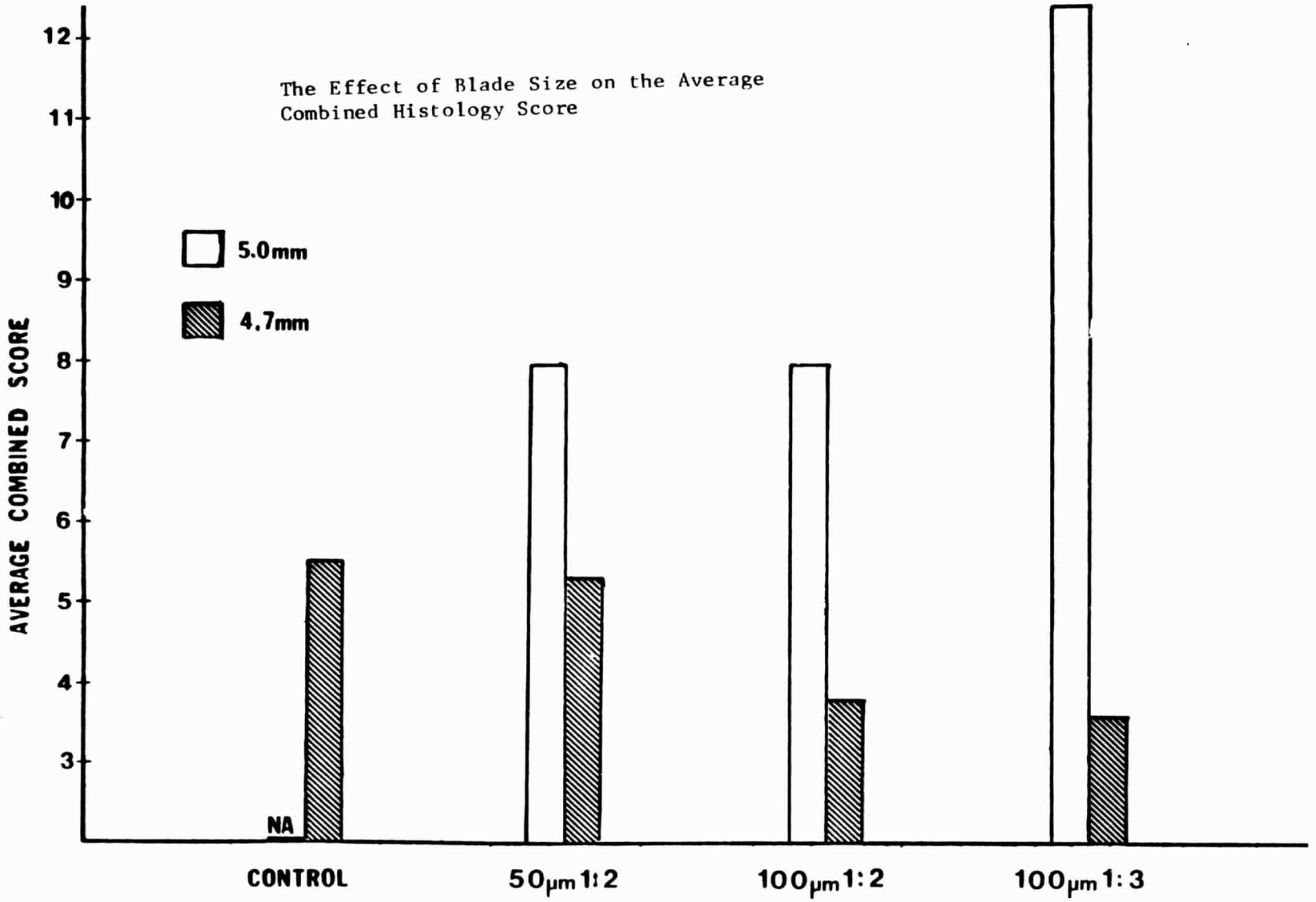


Figure 27. A graph showing the effect of blade size on the average combined histology score. A lower number represents a more optimal response.

TABLE 4 The Effect of Exit Wound Size (average ± S.D.)

	Post-Operative Comments[3]			Comments at Retrieval[3]			Histology[3]		
	Fit	Inter-face	Combined	Fit	Inter-face	Combined	Epith.	Cells	Combined
5.0[1] **CONTROL**	1.4±.8	2.3±1.6	3.6±1.8	1.6±.5	2.6±1.0	4.2±1.6			
4.7[2]	1.0±0	1.4±.5	2.4±.5	1.1±.3	2.9±1.3	4.0±1.4	4.5±1.5	1.0±0	5.5±1.5
5.0 **50µm 1:2**	1.4±.8	2.0±.9	3.4±1.2	1.4±.5	2.4±.9	3.8±1.3	6.0±3.1	2.0±1.7	8.0±4.1
4.7	1.0±0	1.3±.4	2.3±.4	1.0±0	2.2±.6	3.2±.6	4.3±1.9	1.0±0	5.3±1.9
5.0 **100µm 1:2**	1.3±.7	2.3±1.7	3.5±1.6	1.3±.4	2.5±.9	3.8±1.3	2.8±1.9	5.3±3.2	8.0±2.3
4.7	1.2±.6	1.4±.6	2.6±1.1	1.0±0	2.4±1.0	3.4±1.0	2.8±.4	1.0±0	3.8±.4
5.0 **100µm 1:3**	1.0±0	2.1±1.2	3.1±1.2	1.4±.5	3.0±1.2	4.4±1.7	2.3±.5	10.0±0	12.3±.5
4.7	1.0±0	2.1±1.8	3.1±1.8	1.0±0	2.3±.9	3.3±.9	2.6±.5	1.0±0	3.6±.5

1. 5.0mm exit wound
2. 4.7mm exit wound
3. A lower score represents a more optimal response

TABLE 5 The Effect of Exit Wound Size on the Percentage of Missing, Subcutaneous Inflamed, and Scorable Implants

	Missing	Sub-cutaneous	Inflamed	Scorable
5.0[1] CONTROL	13%	13%	43	0
4.7[2]	0	0	50	20
5.0 50µm 1:2	25	0	50	33
4.7	17	0	20	30
5.0 100µm 1:2	38	0	40	40
4.7	0	0	50	33
5.0 100µm 1:3	0	0	50	19
4.7	17	0	50	50

1. 5.0mm blade size
2. 4.7mm blade size

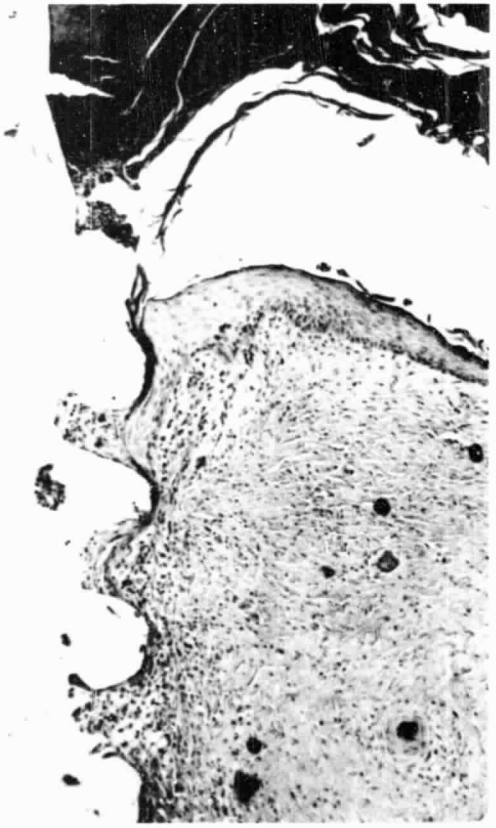
Histology: When comparing the epithelial response for all morphologies, only the 28μ 1:1 appeared to be significantly different ($p < .001$)(Table 3). The 100μ 1:2 and 100μ 1:3 morphologies demonstrated the best average scores for the epithelial response but this was not statistically significant. All morphologies demonstrated a similar cellular response, therefore, the combined scores reflect the same trends described for the epithelial response.

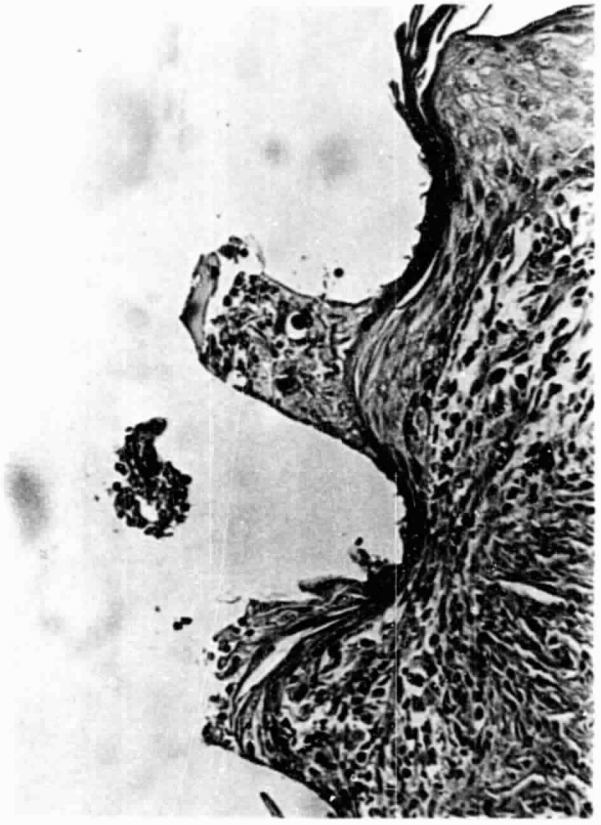
In comparing the 5.0mm blade with the 4.7mm blade, the 4.7mm blade demonstrated generally better histological results (Table 4). The cellular response is consistently better for the 4.7mm experiments giving the combined scores (epithelial + cellular) a similar bias.

Other Comments: There does not appear to be any relationship between surface morphology and percentage of missing implants. However, the only implant which slipped subcutaneously was the control. In comparing blade experiments, 4.7mm blade had better overall scores for the control, 50μ 1:2 and 100μ 1:2 morphologies in the categories of percent missing and subcutaneous.

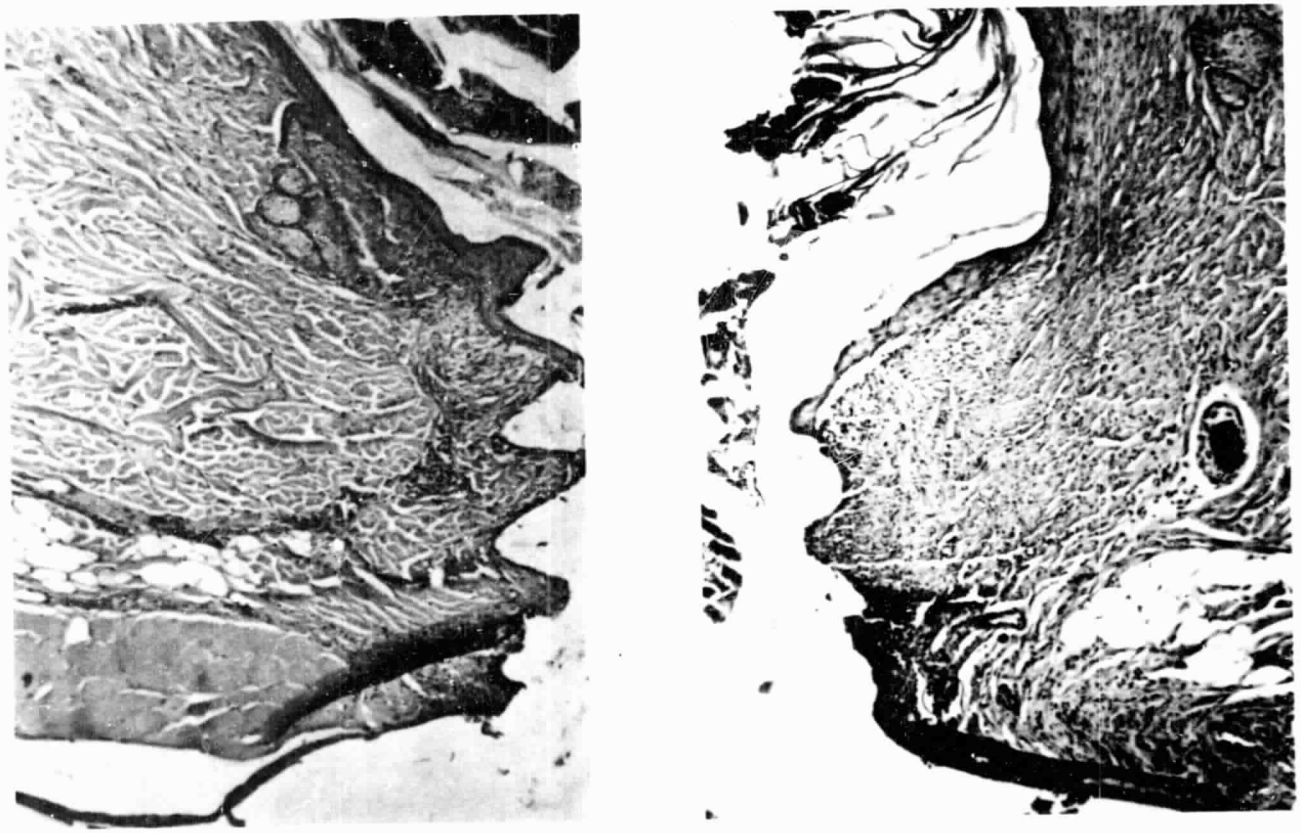
The percentage of scorable implants revealed two trends. When comparing the height to base ratio, a ratio greater than 1 resulted in a better score in all cases. A second trend was also noted: with increasing pillar base size, the percentage of scorable implants also increased.

When comparing the percentate of inflammed implants to surface morphology, no relationship was seen. Likewise, blade size did not appear to have any correlation with the inflammatory response.





Figures 28 and 29. An example of collagen ingrowth into the interpillar spacing of a 100μ 1:2 morphology. The epithelium inconsequently inhibited from further downgrowth (260X).



Figures 30 and 31. This represents a situation where the epithelium has come in contact with the collagen within the interpillar space. A sulcus exists above this area which is filled with dried blood and exudate (260X).

DISCUSSION

The establishment of an effective percutaneous interface requires the successful manipulation of an array of variables: surface morphology, implant design, tissue mechanics, surgical technique, and post-operative care. This study has begun to examine the effect of a unique surface structure on the epithelial response and has demonstrated that a regular array of micro-pillars can inhibit epithelial down-growth (Figures 28 and 29). Consistent and reproducible success of this morphology is, however, limited by non-optimization of some of the previously mentioned variables (implant design, tissue mechanics, surgical technique, etc.).

The tissue response to the percutaneous connector must consider factors other than surface structure. For example, the initial approximation of the skin to the implant is felt to be of fundamental importance in determining the tissue response. One of the possible mechanisms is a critical appositional tension between the implant and skin that will encourage collagen ingrowth and penetration into the interpillar spaces. Below this tension a gap may form allowing exudate and blood to collect with associated problems, and above this tension, pressure necrosis may occur. The interfacial forces will be a function of: wound size, shape and orientation; implant size and shape; and tissue mechanics. Some of these factors will now be considered.

The skin is always in a state of static tension (22). Due to the action of muscles, distribution of cellular tissue, and gravity (23), these cutaneous tensions become directionally oriented. The lines of maximum tension, known as Langer Lines (22, 24), were accounted for (19), however it is felt that additional consideration of this variable is warranted.

The relationship between the size of the implant and the incision is equally important. In these experiments the implant sides possessing the morphologies of interest were positioned normal to the lines of maximum tension in an effort to optimize appositional forces. An attempt was made to alter these forces by changing the wound size (5.0mm to 4.7mm). Comparing the data for the two blade sizes suggests a significant influence on histological results.

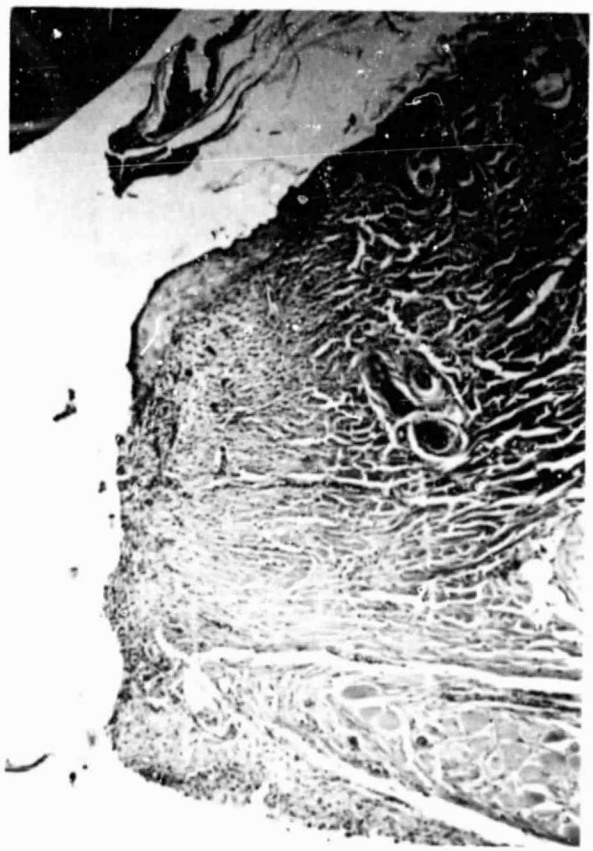
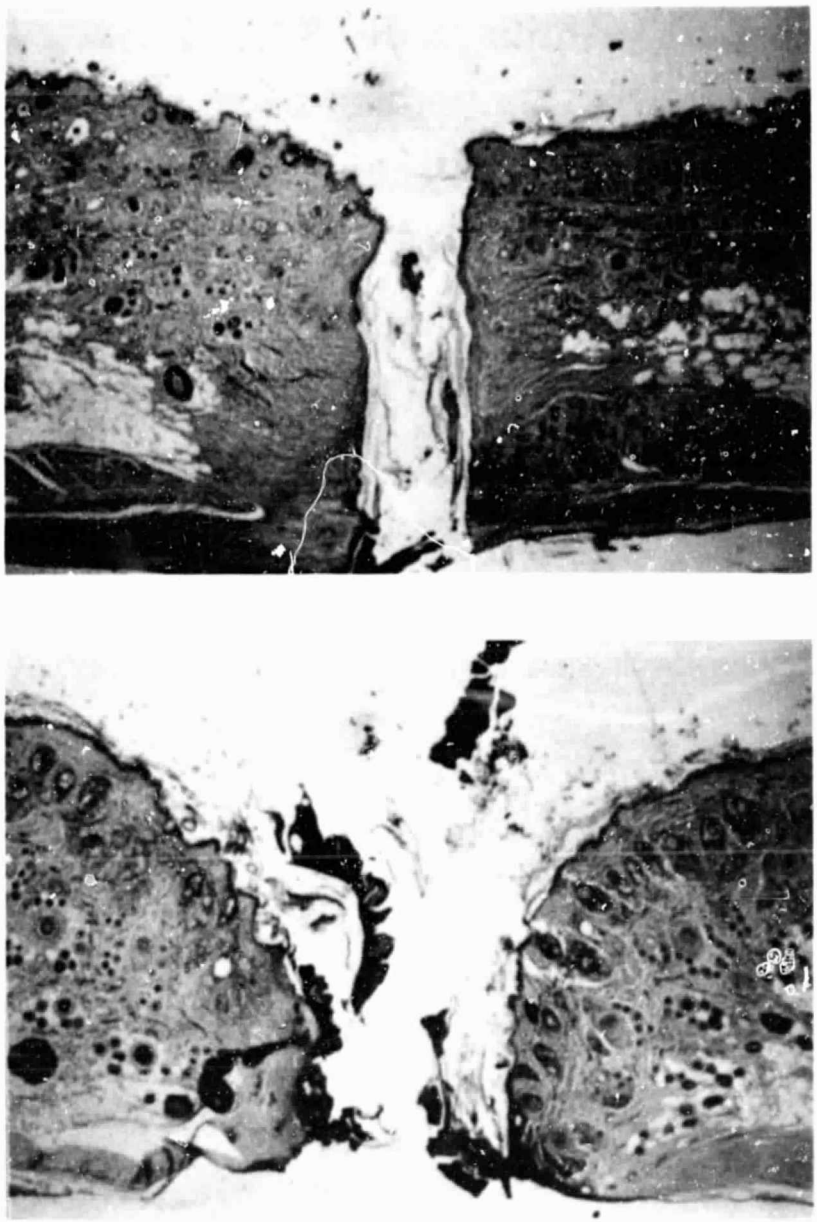
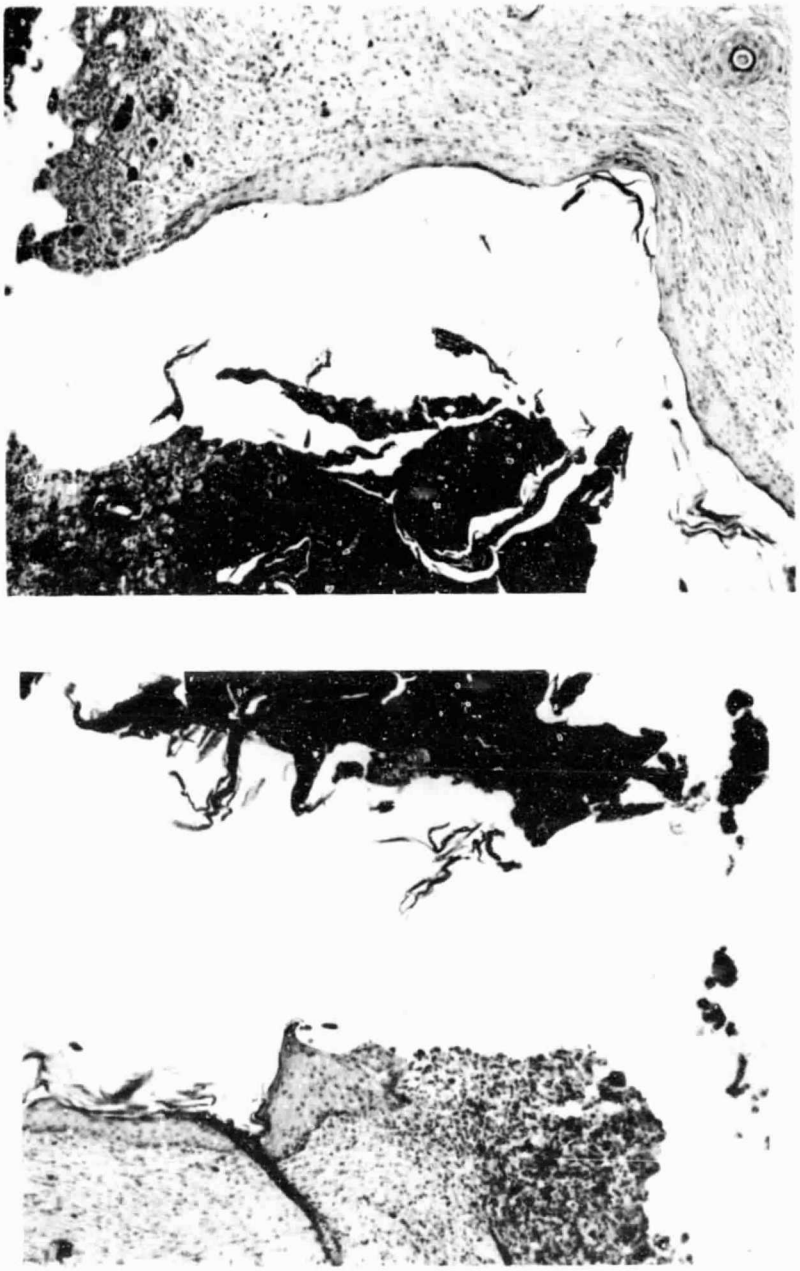


Figure 32. The epithelium has contacted the implant and partially grown down. A sulcus is also present. The depth of the sulcus along with the extent of epithelial downgrowth determine the epithelial score (260X).



Figures 33 and 34. The sections represent examples of interfaces which could not be scored. Due to the accumulation of blood and exudate between the tissue and implant, the epithelium never contacted the implant (15X).



Figures 35 and 36. In some situations, the epithelium was inhibited by a local inflammatory response. In this situation the epithelium never contacted the implant and consequently no score was assigned histologically (260X).

The implant/tissue apposition could also be altered by changing the implant size and/or shape. By increasing the implant width (5.0mm) or thickness (1.25mm) the appositional forces will increase in a similar manner as with decreasing wound size. However, stress distribution at the implant/tissue interface is the important issue to be considered. A linear incision will normally retract into an elliptical shape with time. Thus, by placing a rectangular (in cross-section) implant in a linear incision, the stress distribution will be nonuniform with the corners acting as point stress raisers, while minimizing appositional forces at the interface possessing the morphology. Therefore, the interrelationship between the shape and size of the wound and implant is extremely important. An improvement in design would allow for more uniform stress distribution between the skin and implant, consequently producing appostitional forces more favorable for tissue ingrowth.

It is also felt that a better understanding and characterization of skin dynamics would be advantageous in understanding the percutaneous seal. Skin represents a viscoelastic substance with varying properties depending upon body location, age, and disease state. In the normal state, skin will be a composite of tightly packed surface cells (epithelium), loose connective tissue, blood vessels, sweat and sebaceous glands, and hair follicles. Although mechanical testing of skin has been routinely performed, it is likely that the anatomical layers may each impart different mechanical characteristics to the skin. For example, the elasticity and stress relaxation properties of the epidermis may be significantly different when compared to the underlying dermis, a composite of loose connective tissue, glands, follicles, and blood vessels. It is felt that a better understanding of the skin mechanics will aid implant design and implantation technique so that stresses can be optimized for tissue apposition.

Another factor which can influence the response of a percutaneous implant is bleeding at the implant site. Initially, if a clot is present it can provide an immediate seal between the implant and tissue. However, excessive bleeding may mask the implant morphology. Consequently, the epithelial front will advance down the clot resulting in externalization of the implant.

shown that this microtexture can activate monocytic cells at the interface which have been suggested to inhibit collagen formation (25). Thus, it would be of interest to evaluate these surface parameters in their ability to encourage or discourage collagen ingrowth as it relates to the percutaneous seal.

The results of this study also suggest that the appropriate pillar dimensions can minimize the masking effect of adsorbed blood and exudate. If, for example, a 50μl:1 morphology is used a layer of blood approximately 10 red blood cell diameters thick would effectively mask the morphology from the tissue. However, the larger pillar structures could overcome this problem.

A final area to be considered is the establishment of an effective bacterial seal at the epithelial/implant junction which is of principal importance when considering the success of a chronic percutaneous device (2, 12, 13). Although infection was not conclusively determined in this study, an overall inflammation rate of 35% was observed. This is not optimum, however significantly better when compared to previous investigations - Yamamato (100%)(26), Von Recum (100%)(27), Al-Nakeeb (40%)(28), Pae (77%)(15).

This investigation has demonstrated the ability of a unique pillar morphology to inhibit epithelial downgrowth and encourage a functioning chronic percutaneous seal. By the careful manipulation and control of surface morphology, implant design, and surgical techniques this surface topology has the potential to produce a functional and dependable percutaneous device.

Suggested Efforts: Many unresolved issues have been brought out in this investigation. A list of areas worthy of further research include:

- Implant shape and size
- Exit wound shape and size
- The tissue dynamics of skin
- The micro mechanics of the anatomical layers of the skin (i.e. epidermis, dermis, etc.)
- Methods for hemostasis
- The animal model
- The implant material and surface charge
- Further modifications of implant surface structures
- Quality of the percutaneous seal
- Wound dressings
- Techniques for evaluating implants designed for acute vs. chronic duration

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APPENDIX A

(1) Once an implant morphology is cast and removed from the mold, its thickness is measured with a micrometer. Since a total thickness of 1.25 $\pm$ .05mm. is desired for the percutaneous segment, the Biomer^R morphology casts (which are typically .3 to .5mm. in thickness) must be sandwiched agains a piece of Biomer^R of the necessary thickness.

(2) A Cardner knife is used to cast sheets of Biomer^R on glass slides which are cured in the oven for 24 hours at 65^{o}C. A series of multiple cast were made to give a series of Biomer^R thicknesses to be used in the sandwich described in step 1.

(3) The pillar casting is cut into two pieces which are each approximately 1.0 x 1.0cm. One of these pieces is welded to a 1.2 x 1.2 cm. piece of smooth Biomer^R with 30% Biomer^R solution. This assembly is placed between two glass slides and dried in an oven (65^o) for one hour. The other piece of pillar morphology is welded to the opposite side of the sandwich, placed between glass slides, and dried in the oven for one hour.

(4) Percutaneous segments having a width of 5.0mm. and heighth of 7mm. were cut from the constructed lamination. The critical dimension is the width - 5.0mm.

(5) These segments are welded to base segments of smooth cast Biomer^R (5.0 x 1.2 x .4mm.) with 30% Biomer^R solution. This assembly is placed in the oven (65^{o}C) for 24 hours.

(6) Smooth controls were made by the same process using laminations of smooth glass cast Biomer^R. No effort was made to expose the glass dried or air dried surface in the percutaneous segment.