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Material-tissue interface

M S VALIATHAN

Department of Cardiothoracic Surgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum 695011, India

Abstract. The interface between prosthetic materials and body tissues has become important thanks to the extensive use of bioimplants and artificial internal organs. The long-term function and survival of implanted prostheses depend on the stability of the material-tissue interface. The methods in current use for the fixation of implanted prostheses are mainly based on mechanical linkages which are inherently unstable. The manifestations of instability are seen in clinical phenomena such as prosthetic thrombosis and failure of skin-prosthetic linkage. A less vulnerable approach to stablising material-prosthetic interface would be the development of chemical bonding which has already been accomplished at the bone-bioglass ceramic level. The approach may have wider relevance to the linkage of polymeric materials to body tissues.

Keywords. Prosthetic materials; tissue ingrowth; clinical complications; chemical bonding

1. Introduction

The steep rise in the clinical use of prosthetic materials has brought into sharp focus the junctional zone between non-living materials and living tissues. A material tissue interface exists whenever a material is placed within the external and internal boundaries or integuments of the body, namely skin and mucous membranes. The major problem of the interface is its instability which is no less a constraint for the implant than those imposed by biomechanical factors, by candidate materials and by the many biological conditions under which it must function within the body. The clinical disturbances listed in table 1 are manifestations of the unstable nature of the prosthetic interface which reacts differently in diverse environment.

As an important example from table 1, endocardial thrombosis may be considered. Its dramatic presentation is seen when prosthetic valves undergo postoperative thrombosis and demand urgent reoperation (figure 1). While abnormal cardiac rhythms, haemodynamics of the valve and other factors may contribute to valve thrombosis, its most important cause has been experimentally shown to be the triggering effect of the prosthetic-endocardial junction (Valiathan *et al* 1966). The material-tissue interface is no less vulnerable in other organs.

In general, it would appear that a clinically satisfactory linkage with prosthetic materials is currently feasible for only connective tissue which is derived from the embryonic layer of mesoderm. The derivatives of the two other germinal layers namely ectoderm and endoderm which include epithelium, neural tissues and endothelium are not amenable to prosthetic linkage. The more highly specialised the tissue, the less would seem to be its ability to form stable links with prosthetic materials.

Table 1. Tissue responses to materials.

Tissues	Materials	Interface clinical reactions
Integuments		
Skin	Polyester	Microbial tract formation.
	PTFE	
	Silicon	Loosening of implant.
Tracheal mucosa	Polypropylene silicone	"
Bladder mucosa	Silicone	"
		urinary fistula
Cardio vascular		
Endocardium	Polyester	Thrombosis
	PTFE	
	Titanium	
	Stellite 21.	
Vascular wall	Polyester	Thrombosis
	PTFE	Perigraft haematoma
Musculoskeletal		
Bone	Stainless steel	Bone resorption
	Titanium	Release of corrosion products
	Vitallium	Loosening of implant
Dental		
Teeth	Silver amalgam silicate	Track formation Recurrent decay

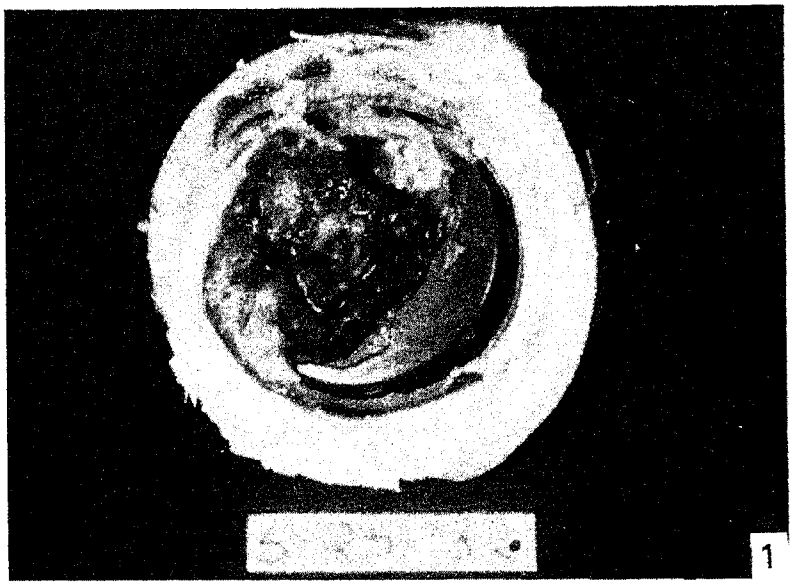
2. Linkage of prosthetic materials to tissues

The two methods currently employed in linking prosthetic materials to host tissues and the likely advances in this field of biomaterials will be reviewed in this article.

2.1 *Fibrous ingrowth*

2.1a *Fibrous ingrowth and implants*: The most common method for linking a prosthetic surface to body tissues is mechanical which takes advantage of the physiological process of healing. The classic response of healing to diverse forms of tissue injury is a process of great evolutionary significance. A skin injury uncomplicated by tissue loss or infection will, for example, be followed by a series of tissue reactions which are mediated by hormones and chemical agents. The sequential reactions include dilatation of blood vessels, exudation of blood and tissue fluid, growth of capillaries and formation of granulation tissue, laying down of collagen which matures into scar tissue and the final closure of the gap by the contraction of scar tissue (figures 2 and 3).

When a prosthetic material is implanted, the healing response is similar except in so far as the material will partially block the union of scar tissue which in turn tends to grip the material (figure 4). The tissue changes associated with prosthetic healing have



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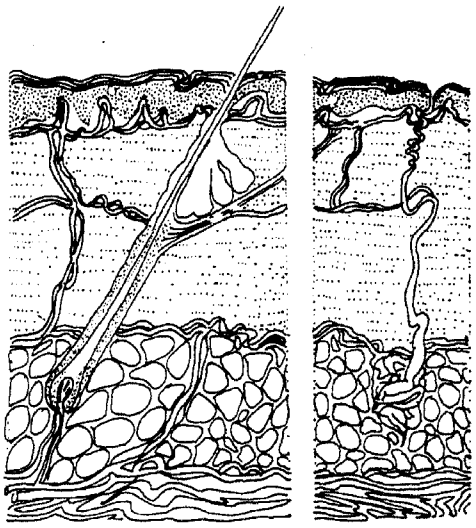

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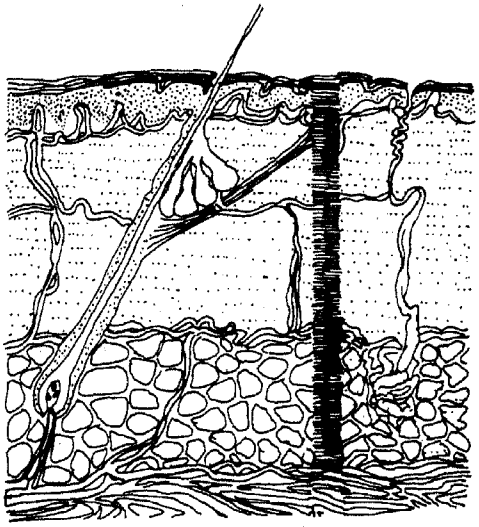

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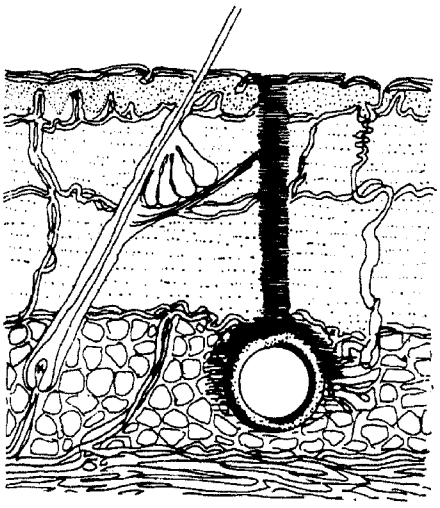
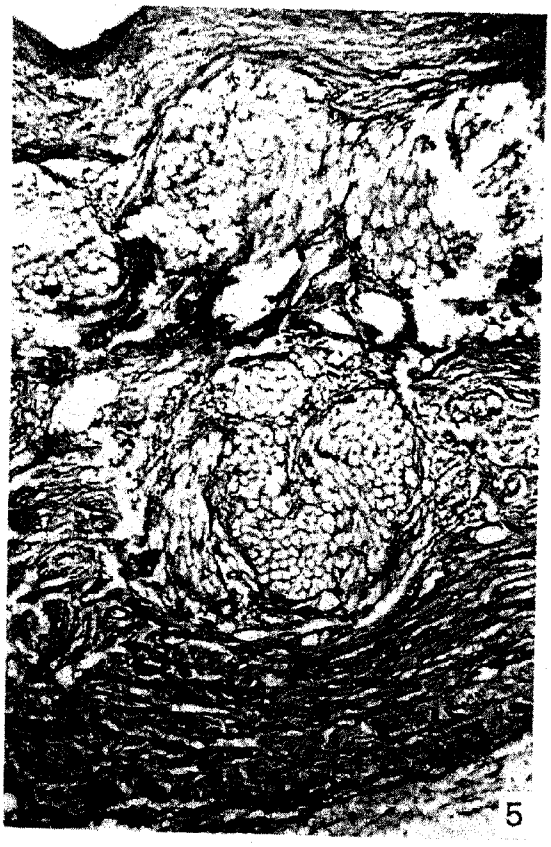
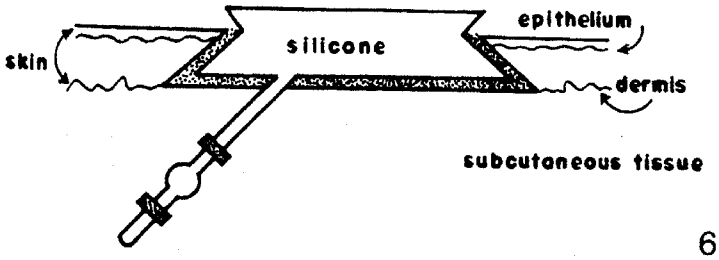
Figures 1–3. **1.** Postoperative thrombosis of Bjork-Shiley valve. **2, 3.** Stages of natural healing of skin.







Figures 4–6 **4.** Healing of an implant. **5.** Photomicrograph showing ingrowth of connective tissue into the interstices of fabric. **6.** Diagram of silicone skin button.

been confirmed for an indigenous textile fabric in a recent series of experiments (Bhuvaneshwar *et al* 1981). In this study, circular patches of polyester fabric which had been implanted in the right atrial wall of dogs were seen to be lined by a thin layer of thrombus within hours, the patch itself being held in position by surgical sutures. At 48 hrs, the border zone of atrial wall showed coagulative necrosis, interstitial oedema and polymorphonuclear infiltration. At 21 days, the histological picture had changed with several plump fibroblasts, polymorphs and macrophages in appearance, all riding on granulation tissue which protruded into the interstices of the graft. At 60 days, the turbulence of inflammation had settled with the appearance of a smooth, fibrous internal lining on the prosthetic patch which resembled normal endocardium. During this final stage, the ingrowth of fibrous tissue was complete into the interstices of the fabric which no longer depended on surgical sutures for its fixation (figure 5).

The ingrowth of fibrous tissue would seem to be a mechanical process, largely controlled by the inertness of the prothesis and the distribution and size of pores on its surface. The optimal size and distribution of pores which vary for different materials and tissues are determined experimentally. For example, when high strength is required for skeletal applications, the mechanical interlock is provided by large pores in the material. When the strength requirements are low, pores of 50–200 μm cross-sectional diameter can be used to establish mechanical linkage by tissue ingrowth (Hulbert *et al* 1972; Leonard *et al* 1973).

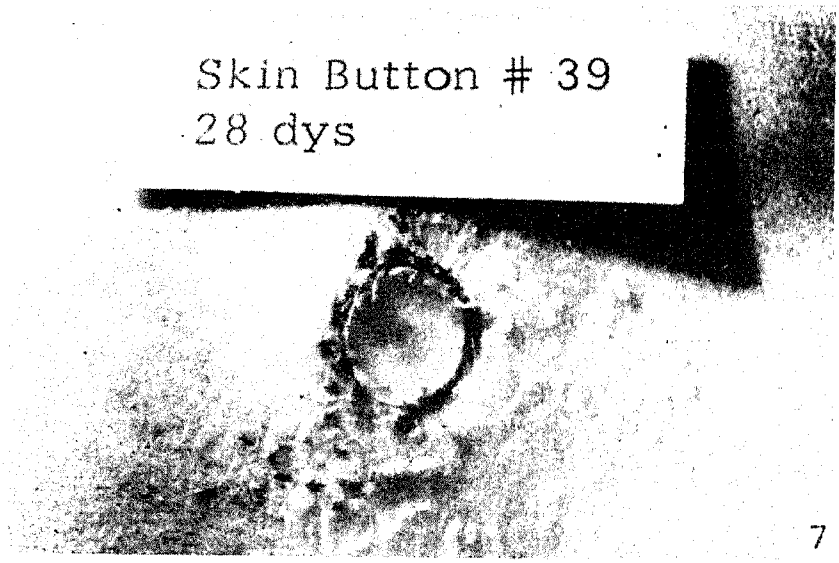
While the mechanical linkage of prosthesis can be successfully used for the fixation of vascular grafts, prosthetic valves, fabric reinforcements and similar applications, its underlying basis of tissue ingrowth must be seen as an attempt by the body to microencapsulate the implant which has no links with the fibrous tissue at the molecular level. The absence of a bond at the molecular level and the isolation of the implant may indeed be desirable for certain applications such as an implantable pacemaker which needs periodic replacement, but they may create serious problems in other locations. For example, polyester fabric which links satisfactorily to the vascular wall does not permit the ingrowth of connective tissue from the integuments and causes implant failure. At the integuments, the implant faces the dual challenge of body tissues within and the external environment without.

2.1b *Fibrous ingrowth and integuments:* As long as an implant depends upon external sources for power supply or control, access to it through the skin or other bodily integuments is essential. The Jarvik heart which was recently implanted in a patient owed its drive to a compressed air line which had to transit through the patient's chest wall from an external source. A more common example is the plastic cannula of patients with terminal kidney disease who depend on haemodialysis for survivial. The two ends of the *U*-shaped cannula enter a peripheral vein and artery of the patient while the body of the plastic device remains outside the skin for intermittent connection to a haemodialysis machine. In these situations, transcutaneous access to the heart or blood vessels demands a 'bacteria proof' seal at the point of entry of the prosthetic device through the skin. But, unlike what happens for implants in the atrial wall, the ingrowth of fibrous tissue from the dermal layer of skin to a prosthetic surface is neither strong nor reproducible as noted in the following observations.

With the objective of promoting a mechanical bond between skin and prosthetic surfaces, silicone buttons of various diameters were implanted in rabbit skin under aseptic conditions. The construction of the buttons was such that it provided a surface

of highly porous polyester fabric for the ingrowth of fibrous tissue from the skin (figure 6).

The experiments showed that if the diameter of the silicone button was less than 1 cm, the skin tended to grow over and bury the implant. When the diameter of the button exceeded 1 cm, the epithelium dipped at the junction and grew parallel to the fabric which was thereby prevented from developing bonds with the connective tissue in the dermal layer (figure 7). This also resulted in the formation of a potential track for



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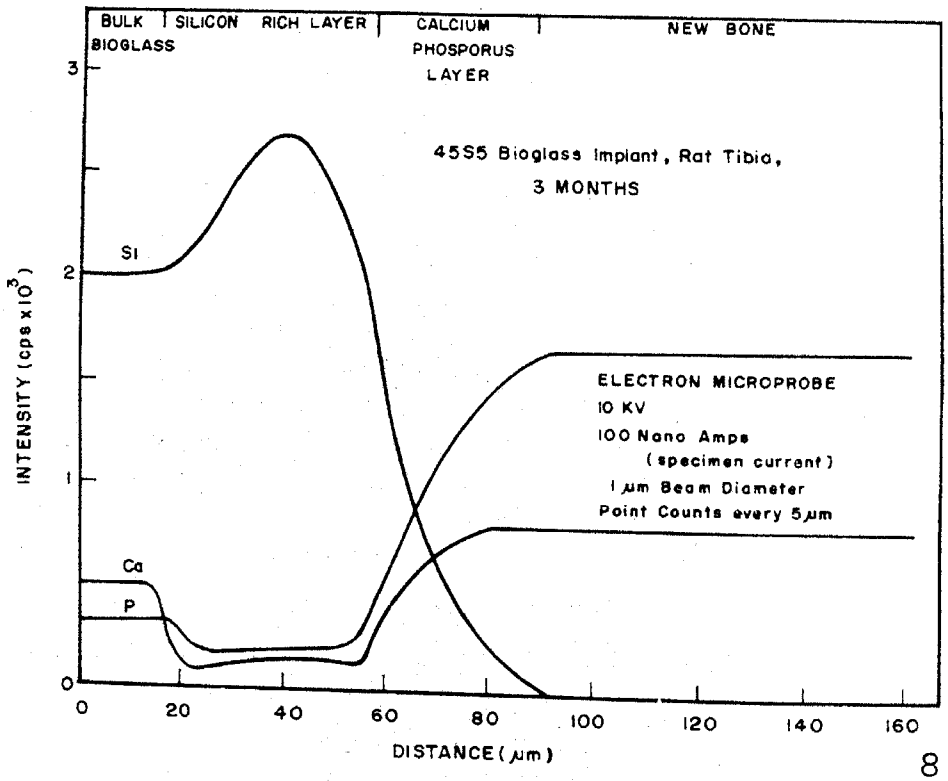

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Figures 7–8. **7.** Photograph of implanted silicone button at 28 days. **8.** Electron microprobe profile of three month bioglass implant in rat tibia. (Hench, by permission).

bacteria between the fabric and epithelium and the gradual loosening of the button. In a series of over thirty experiments, no instance of a strong mechanical bond could be observed between the polyester cuff of the silicone button and rabbit skin (Valiathan and Hufnagel 1971).

To summarise, the mechanical approach to prosthetic-tissue linkage suffers from the complications listed in table 1 and offers a poor alternative for transcutaneous applications. Apart from the difficulty in controlling the deposition and growth of fibrous tissue, the mechanical approach also remains unsatisfactory for linking prosthetic materials to bone because the development of a porous structure to promote tissue ingrowth will weaken the bone. These drawbacks have led to intensive efforts to develop a chemical bond between prosthetic surfaces and tissues.

2.2 *Chemical bonding*

2.2a *Bonding bioglass ceramics to bone:* The outstanding example of the chemical approach to bonding prosthetic materials to tissues is the work of Hench and colleagues who bonded surface active glass and glass ceramic materials to bone (Hench and Paschall 1973; Hench 1973; Clark *et al* 1975). As component materials, they used mainly (by weight %) 45% S_1O_2, 24·5% CaO, 24·5% Na_2O and 6% P_2O_5. The S_1O_2 functioned as the primary network former, Na_2O/CaO as net work modifers and P_2O_5 as an internal nucleant for surface hydroxyapatite formation. While the spectrum of tissue reactions to these formulations ranged from the formation of a thin fibrous capsule to total absorption of the material, certain glass surfaces in the series were noted to be surface active and capable of incorporating physiologic constituents such as muco-polysaccharides, collagen and calcium-phosphate mineral salts following implantation. The surface active glass and glass ceramics showed uniform network dissolution and the formation of an amorphous calcium-phosphate film which developed with time into a crystalline hydroxyapatite layer. Because of the similarity of the hydroxy-apatitic layer to that formed when bone crystallises, the glass with 6% P_2O_5 formed a chemical bond with bone. An electron microprobe compositional profile across a bone-bioglass interface after three months implantation in rat tibia is shown in figure 8. The interfacial bond was strong and resisted fracture which occurred either in the implant or the bone to values of stress from 8000 to 11000 psi at the interface.

Even though chemical bonding of glass ceramic to bone and teeth has shown highly promising results, bulk bioglass and bioglass-ceramics are likely to have insufficient long-term mechanical reliability for load-bearing prosthetic applications. Therefore, bioglass and bioglass-ceramics are currently being used as coatings on high strength surgical alloys. Another limitation of these materials is their inability to form chemical bonds with soft tissues. Notwithstanding these limitations, bioglass-ceramic coatings on high strength alloys do represent the successful application of chemical bonding in clinical practice. It also illustrates the flexibility and usefulness of a composite system which combines a controlled biological interface with high strength substrate performance.

3. Future developments

So long as accidents, war and disease stalk the world, the loss and destruction of organs

will remain inescapable tragedies for mankind. The human and economic dimensions of these mishaps and their inevitable escalation with population growth have been a powerful stimulus to research in biomaterials and bioimplants. While bioimplants and artificial internal organs have given new life to patients who would have died otherwise, they continue to suffer from the serious drawback that less than 50% of the recipients remain 'event-free' after 5 years. These 'events' in the form of thrombosis, calcification, loosening of implant and other complications will often necessitate costly and difficult reoperations and impose a heavy psychological burden on the patients and their families. The future will therefore see intensified research in the characterisation and matching of tissues and materials, analysis of implant failures, improvement of tests for function, development of surfaces with active groups to perform different functions and above all, the chemical bonding of tissues to materials. The successful bonding of bioglass ceramics to bone has opened up bright possibilities of bonding tissues to bioactive groups on polymers and composites which will greatly enlarge the usefulness and durability of bioimplants. The observation by Pantano and Hench that collagen fibres are readily incorporated with the growing hydroxy-apatite crystallites on the silica-rich and calciumphosphate layers of a bioglass surface is strongly suggestive of a similar approach to bonding collagen to other bioactive surfaces. It would also imply a corresponding departure from mechanical linkages. The common objective of this endeavour will be the achievement of total reliability for implants which must cause no anxiety to the patient or his family. The current upsurge of interest in biomaterials science encourages the hope that this ambitious goal may be realised before the turn of the century.

4. Conclusion

The instablity of the material-tissue interface has been discussed. The merits and demerits of mechanical linkage which is currently employed for linking prosthetic materials to tissues have been reviewed. On the basis of current experience with bioglass bone bonding, chemical bonding between materials and tissues would seem to be potentially superior to any form of mechnical linkage. Future directions of research in bioimplants have been indicated.

References

Bhuvaneshwar G S, Venkatesan V S, Pattankar V L, Kartha C C, Arthur Vijayan Lal V and Valiathan M S 1981 *Indian J. Med. Res.* **74** 580

Clark A E Jr, Paschall H A, Hench L L and Harrell 1975 *J. Biomed. Mater. Res. Symp.* (Clemson University)

Hench L L and Paschall H A 1973 *J. Biomed. Mater. Res. Symp.* **4** 25

Hench L L 1973 *Med. Instrum.* 7 136

Hulbert S F, Morrison S J and Klawitter J J 1972 *J. Biomed. Mater. Res.* **6** 346

Leonard R B, Sauer B W and Hulbert S F 1973 *J. Biomed. Mater. Res. Symp.* **4** 85

Pantano C G and Hench L L 1983 to be submitted

Valiathan M S and Hufnagel C A 1971 (unpublished observations)

Valiathan M S, Whiffen J D, Weldon C S and Gott V L 1966 *Trans. Am. Soc. Artif. Intern. Organs* **12** 174