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Therapeutic applications of biodegradable and bioactive forms of silicon.

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Introduction

This invited presentation will give a brief overview with regard the evolution of microelectronic implants and then describe how the dominant semiconductor, silicon, can be made much more biocompatible than previously imagined. A summary of perceived applications in different clinical areas will then be given.

Biomedical MEMS : Clinical use of silicon technology

Microelectronic implants within the human body have a history almost as long as that of microelectronics. The most well known, the cardiac "pacemaker", was first implanted in 1960 but even prior to this "radio pills" were being swallowed and tested in-vivo. Today, there are a range of electrical stimulation devices for both cardiovascular and neurological conditions. There are programmable pumps for terminal cancer patients and cochlear implants for the profoundly deaf.

To date it has been necessary in all FDA-approved devices to completely isolate the chip from the body by packaging with other biomaterials.

The emergence of bioMEMS and some synergistic major trends in clinical medicine, namely ;

- minimally invasive & robotic surgery
- home-based monitoring systems and telemedicine
- smarter, more reactive prostheses will converge to make biomedical applications the fastest growing MEMS market over the next few years. This market pressure will further promote development of smaller and interactive systems for implantation.

Nanostructured silicon as a biomedical material

Surprisingly little development of silicon for biomaterial use occurred prior to the 1990's, although in cortical tissue it had been earlier found to be "non-reactive" (1). Non-porous monocrystalline silicon and many sintered polycrystalline structures do not exhibit pronounced corrosion in physiological environments. Very thin (2 micron) pieces of silicon have been soaked in saline for years and implanted in guinea pigs for over 11 months with negligible dissolution in either case (2). In striking contrast, it was shown in 1995 (3) that a 1 micron thick layer of high porosity silicon completely dissolved away within a day of in-vitro immersion in simulated human plasma. In addition, poly-Si of nanometre grain size was subsequently shown to undergo appreciable corrosion (4). It was proposed (3) that nanostructured forms of silicon could be resorbable, breaking down into silicic acid by hydrolysis, which is efficiently excreted by the kidneys. This exciting prospect received in-vivo confirmation from a 6 month study of bulk and porous silicon discs in subcutaneous tissue of guinea pigs (5). Here the partially porosified discs continually lost weight, as opposed to the bulk silicon and titanium controls. Combined monitoring of systemic response and histopathology also demonstrated that silicon could be simultaneously biodegradable and biocompatible.

Research within pSiMedica Ltd has now shown biodegradability in a number of different body fluids, corresponding to placement within different body sites. These include simulated lung fluid, intestinal fluid, sweat and cerebrospinal fluid. Gastric fluid was notable in terms of there being minmal corrosion : attributed to its acidic environment compared to all other body fluids.

BioSilicon: A material platform for clinical therapy

Biocompatible silicon will facilitate many clinical applications of Si technology in and on the human body. In summary these include :

- **controlled drug delivery**
  High porosity silicon provides a reservoir from which a range of drugs can be released in a controlled fashion.

- **oncology**
  Radioactive & biodegradable seeds are under development for brachytherapy. Here we exploit the machinability of silicon, neutron transmutation doping and its radiation hardness.

- **orthopaedics**
  Osteoinductive coatings, scaffolds and composites are under development for bone fixation, replacement and repair.

- **in-vivo diagnostics**
  Porous multilayer structures, when derivitised can function as slowly degradable mirrors, useful in minimally invasive optical monitoring of analytes in blood.

- **bioMEMS implant packaging**
  Porous silicon coatings, when combined with hermetic sealing via wafer-to-wafer bonding or "poly-Si bubble" processing, enable Si packaging designs that will enable integration of the chip itself with living tissue.

(1) Histopathological evaluation of materials implanted in the cerebral cortex. S.S.Stensaas, L.J.Stensaas. Acta Neuropathologica 41,145-155 (1978)

(2) A hermetic glass-silicon micropackage with high density on-chip feedthroughs for sensors and actuators. B.Ziaie,A.Von Arx,M.R.Dokmeci,K.Najafi J.Microelectromech.Syst.5,166-179 (1996).

(3) Bioactive silicon structure fabrication through nanoetching techniques. L.T.Canham Adv.Mater. 7,1033-1037 (1995).

(4) Bioactive polycrystalline silicon. L.T.Canham,C.L.Reeves,D.O.King,P.J.Branfield,J.G.Crabb, M.C.L.Ward. Adv.Mater.8,850 - 852(1996).

(5) Implants for administering substances and methods of producing implants. PCT Patent WO 99/53898.