535g Surface Modification of Sapphire to Enhance Its Neural Biocompatibility

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Due to its excellent mechanical, optical, electrical and chemical properties, sapphire has found tremendous potential for applications in opto-electronics, nuclear power, medical and scientific instruments, military/aerospace, and biomedical devices, among others. Sapphire is the hardest natural material next to diamond, with a high resistance to scratching and abrasion. It provides a very wide optical transmission band from UV to near-IR. Sapphire is extremely chemically inert, and unaffected by essentially all chemicals, even at elevated temperature up to hundreds of degrees Celsius. It has high electrical resistance, yet high thermal conductivity as a non-conductor.

Sapphire-based dental implants have been in clinical use for over 20 years, and it is also regarded as the top candidate for hip joint implants, and prosthetic heart valves. Sapphire-based laser technology has been used in optical tomography in clinical trials. To date, there has not been research on the development of sapphire-based medical devices to be used in the nervous systems. Meanwhile, sapphire is an important material in the development of high-performance sensors for the continuous monitoring of pressure, pH, temperature and other parameters in the diagnosis and treatment of patients with neurological disorders.

No adverse tissue reactions have been reported for sapphire as orthopedic implants, and none to only slight tissue reactions were observed while implanted subcutaneously for up to 12 weeks. However, we found that among the various candidate neuroprosthetic materials (including aluminum nitride, borosilicate glass, cover-slip glass, silicon and sapphire), sapphire caused the most severe tissue reaction while implanted on the cortical surface of adult rats. The human body has the tendency to reject or isolate alien materials, which is one of the biggest concerns in the design and implementation of implantable biomedical devices. Therefore, surface modification is a necessary practice to enhance the biocompatibility of these materials. In addition to the improvement of biocompatibility by surface modification, tissue integration, microbial inhibition and lubricity were often enhanced as well.

In this study, sapphire wafers (2.5mm dia x 0.25mm thick) were modified by the deposition of a self-assembled monolayer (SAM) of o**ctadecyltrichlorosilane** (OTS), followed by the photo-immobilization of heparin and hyaluronan, two naturally occurring biocompatible polysaccharides. Figure 1 shows the scheme of the surface modification approach. Heparin coating has demonstrated dramatic improvement in biocompatibility, especially for blood contacting devices. Hyaluronan also brings biocompatibility, lubricity and hydrophilicity to the underlying substrates. Unmodified and modified sapphire wafers were implanted on the cortical surfaces of adult rats for 10, 28 and 90 days. The brain tissue directly under the wafers was analyzed histopathologically to evaluate the neural biocompatibility of the modified sapphire substrates. As shown in Figure 2, unmodified sapphire caused significantly elevated astrocytic gliosis (or GFAP reaction) in all groups (10-, 28- and 90-day). All of the surface-modified sapphire wafers exhibited reduced astrocytic gliosis. Heparin coated sapphire caused the least tissue damage in all groups, and there was essentially no difference when compared to sham-operated animals (Figure 2). Meanwhile there was no statistical difference with regard to the neuron and axon degeneration (silver staining in the cortex and white matter) between the sapphire implanted and sham-operated animals in all groups. All the SAM and biopolymer coatings have no noticeable effect on the neuron and axon degeneration as well.

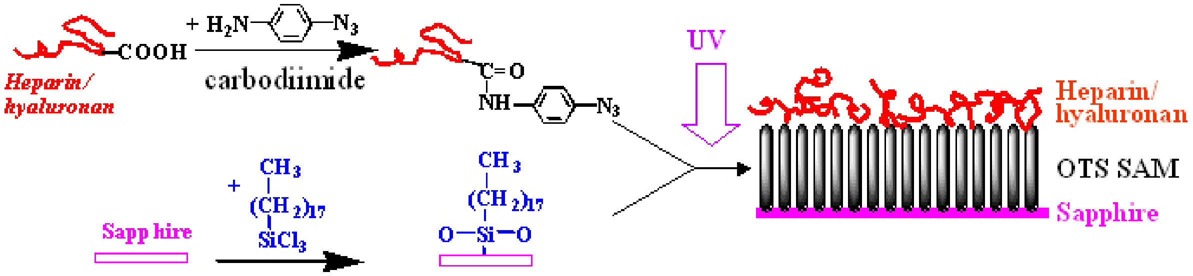

Figure 1. Schematic illustration of the surface modification procedure for sapphire.

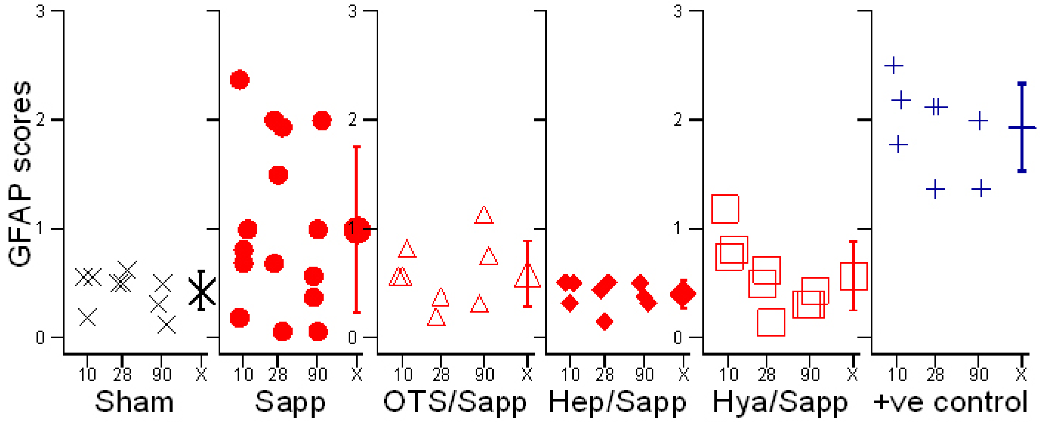

Figure 2. Comparison of astrocytic gliosis (GFAP reaction) in sham-operated animals (Sham), positive control animals and animals implanted with sapphire wafers with or without surface coatings. The data is plotted as a function of days implanted (10, 28 and 90 days; individual points are offset to illustrate all points), and as a grand mean (x) with standard deviation (S.D.) of all animals in each group.

The wafers were also characterized by optical microscopy, atomic force microscopy (AFM) and X-ray photoelectron spectroscopy (XPS) before and after implantation to evaluate the change in surface morphology and chemical composition. No cells were found on the surfaces of all the extracted sapphire wafers, and a very thin layer of proteins and extracellular matrix was deposited on all unmodified or modified sapphire surfaces after 10, 28 and 90 days. Unlike silicon, no corrosion was observed on the surfaces of extracted sapphire wafers with or without coatings in all aging groups. XPS results indicated that the OTS SAM coating was stable *in vivo* for up to 90 days.

In conclusion, the short and long-term neural biocompatibility of sapphire could be significantly enhanced by surface heparin immobilization. It is generally believed that only the topmost layer (maybe only a few nanometers thick) determines the biocompatibility of the alien materials, and thus this surface modification protocol has the potential to enhance the neural biocompatibility of all materials for implantation.