

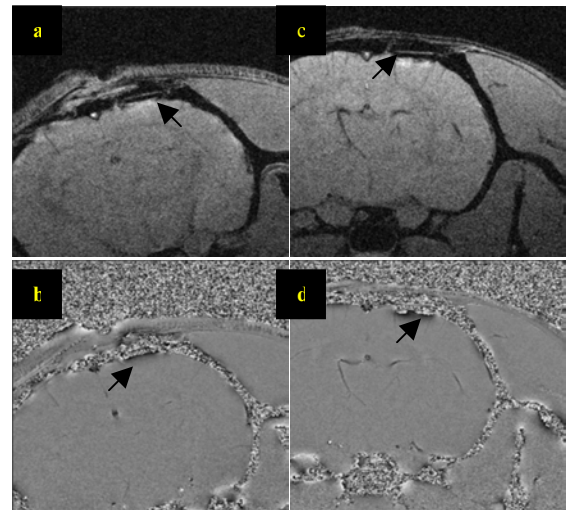
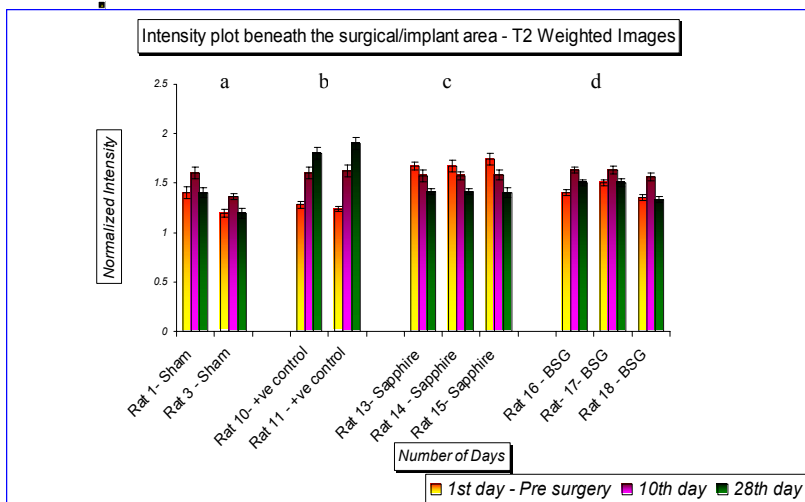
# Biocompatibility of Sapphire and Borosilicate glass for Neural Prosthesis Using MRI and Histopathology

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**Introduction:** Development of new biomaterials for neural implants has been a significant area of research and development for the academic and industrial communities. Our overall goal is to demonstrate the feasibility of a neuroprosthesis interfaced with the cerebral cortex. To achieve this goal we have used high resolution magnetic resonance imaging to evaluate the biocompatibility of sapphire and borosilicate glass implanted onto the brain. Due to its excellent mechanical, optical, electrical and chemical properties, sapphire has found tremendous application potential in opto-electronics, nuclear power, medical and biomedical devices<sup>1,2</sup>. Sapphire based dental implants and hip joint implants have been in use for over 20 years<sup>3,4</sup>. To date, there has not been much research on the use of sapphire based medical devices in neural systems (central or peripheral).

**Materials and Methods:** Twelve healthy adult Sprague-Dawley rats were studied under the institutionally approved animal protocol. The neuro-compatibility of pure sapphire (n=3) and borosilicate glass (n=3) samples (2.5mm diameter x 0.25mm thickness) implanted on the surface of an adult rat cortex for 10 and 28 days was evaluated. Sham-operated and mechanically-lesioned animals were used as controls. Non-invasive testing was performed using MRI on the 1<sup>st</sup> (pre-implantation), 10<sup>th</sup> and 28<sup>th</sup> days (post-implantation) with a 4.7 Tesla BRUKER animal system. A T2 weighted spin echo sequence and 3D high resolution T1 weighted sequence with resolution of 62.5  $\mu\text{m}$  x 62.5  $\mu\text{m}$  x 0.25  $\mu\text{m}$  with TR's of 3664.7ms, 19.5ms, TE's of 67.5ms, 9.35ms respectively were collected in order to evaluate the *in-vivo* biocompatibility of the materials. This method allowed *in vivo* evaluation of edema, inflammation and cortical tissue at the implant interface. The local tissue intensities near the implant from the T2 weighted images were normalized using the intensity of the white matter. In the same animals, light microscopy was used to identify degenerating axons and neurons as well as reactive astrocytes using Nissl and silver stains and GFAP immunocytochemistry at 28-days post-implantation.



**Figure (2):** 3D High resolution (62.5  $\mu\text{m}$  x 62.5  $\mu\text{m}$  x 0.25  $\mu\text{m}$ ) images of sapphire implanted animals. Magnitude and phase images of sapphire implanted animals on the 10<sup>th</sup> day (a & b) and 28<sup>th</sup> day (c & d) showing hemorrhage and/or edema (black arrow)

**Figure (1):** Intensity plots beneath the surgical/implanted region of T2 weighted Images (a) sham, (b) positive control, (c) sapphire, (d) BSG

**Results:** All MRI data was processed with the custom developed software SPIN. The intensity values from the T2 weighted images beneath the sham control and BSG animals on the 10th day were high due to the post surgery effects. However, on the 28th day the intensity values beneath the implant were very similar to that prior to implantation (Figure 1 a & d). Signal intensity increased on the 10<sup>th</sup> and 28<sup>th</sup> day because of the lesion created (Figure 1b). The signal intensity beneath the sapphire implant on the 10th and 28th day reduces due to the presence of hemorrhage and edema in the T2 weighted images (Figure 1c). Neither the histology nor the high resolution MR images showed any effect on the borosilicate glass and sham control animals. High resolution images of sapphire implants showed the presence of hemorrhage (Figure 2) on the 10th and 28th day and scar tissue between the bone and the implant. Since hemorrhage contains hemosiderin which is paramagnetic, it causes a marked change in phase on the 10<sup>th</sup> and 28<sup>th</sup> days. Histology showed reactive astrocytosis, hemorrhage and inflammation adjacent to the sapphire implants and at varying depths through layer III of the cerebral cortex. Increased axonal degeneration was seen in the subcortical white matter.

**Discussion and Conclusion:** MRI and histopathology results correlate with each other in assessing the presence of hemorrhage, inflammation and tissue interference with sapphire implants and for verifying the compatibility of different materials used for the development of cortical visual prosthesis and prototype devices for Parkinson's disease and other movement disorders. These results suggest that in order to enhance the biocompatibility of sapphire by retaining its excellent, mechanical, optical, electrical and chemical properties – surface modification is necessary. Overall, MRI has proven to be a sensitive means by which to monitor the tissue/implant interface and any possible deleterious effects the implant might have on living tissue.

## References:

1. A comparative study of human skin thermal response to sapphire contact and cryogen spray cooling. Anvari B; Milner T E; Tannenbaum B S; Nelson J S IEEE transaction on biomedical engineering (1998 Jul), 45(7), 934-41.
2. Arvindson K, Fartsah B, Moberg LE, Graftsmom R; Ericson I " In vitro and in vivo experimental studies on single crystal sapphire dental implants" Clinical oral implants research (1991 Apr-Jun), 2(2), 47 -55
3. Fartash, B. and K. Arvindson (1997). "Long-term evaluation of single crystal sapphire implants as abutments in fixed prosthodontics." Clinical oral implants research 8(1): 58 – 67
4. Steflik, D. E., D.L.Koth et al. (1995). "Prospective investigation of the single-crystal sapphire endosteal dental implant in humans: ten-year results." Journal of oral implantology 21(1): 8-18

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