Evaluation of Optical Access to the Brain in the Near Infrared Range with a Transparent Cranial Implant

Mildred S. Cano-Velázquez[1], **Nami Davoodzadeh**[2], **David Halaney**[2], **Carrie Jonak**[3],
Devin Binder[3], **Guillermo Aguilar**[2], **Juan A. Hernández-Cordero**[1]

[1]*Instituto de Investigaciones en Materiales, Universidad Nacional Autónoma de México, A.P. 70-360, México City 04510, México.* [2]*Department of Mechanical Engineering, University of California, Riverside, A.P.92507, CA, USA.*
[3]*Division of Biomedical Sciences, University of California, Riverside, A.P.92507, CA, USA*

mildred.cano.vel@gmail.com

Abstract: We report on the improvements in optical access provided by a transparent cranial implant for brain studies in the Near Infrared range. Comparison between the cranial implant and murine native skull by ex-vivo transmittance measurements and Laser Speckle Imaging are presented.

OCIS codes: 170.3660, 170.3880

1. Introduction

Compared to visible wavelengths, the near infrared (NIR) spectral range (800 to 2500 nm), offers advantages such as reduced scattering and absorption, as well a deeper penetration depth in tissue. Hence, NIR wavelengths have shown promising results for brain studies, including imaging, diagnostic and therapeutic applications in brain pathologies. The use of the optically transparent bands of tissue within the NIR range have allowed for noninvasive, optical whole body and brain imaging of small animals [1]. Nevertheless, the main obstacle for optical brain studies at these wavelengths is the highly scattering cranial bone over the cortex, which hinders the observation of optical signals and decreases light penetration.

Different methods have been proposed in order to avoid or at least reduce the highly scattering features of the skull. These include craniotomy, the use of labeling techniques, cranial windows, thinned-skull cranial window, polished thinned skull window and optical clearing of skull. These models are however inadequate for long-term applications. We have addressed this limitation, by introducing a novel cranial prosthesis made of a transparent nanocrystalline yttria-stabilized-zirconia (nc-YSZ). By performing biocompatibility and ageing tests [2], and applying optical coherence tomography, ultrasound transmission, and Laser Speckle Imaging (LSI) [3], we have demonstrated the initial feasibility of nc-YSZ implants for cortical imaging in an acute murine model.

Here, we report on the improvements in optical access provided by the transparent nc-YSZ implant for brain studies in the NIR wavelength range. In particular, we show the transmission features in the spectral range of 800 to 2400 nm of the implant, compared to the cranial bone freshly harvested from. Additionally, LSI images obtained through the native cranium and transparent nc-YSZ implants relative to native cranium are presented to demonstrate the improvements achieved when using this optical imaging technique.

2. Samples and Methods

Male C57BL6 mice were used for this study. All animal experiments were conducted under a protocol approved by the University of California, Riverside Institutional Animal Care and Use Committee, and in conformance with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH Publication No. 85-23, revised 1996). Mice were anesthetized with intraperitoneal injection and additional anesthetic was administered as necessary. A sagittal incision was made to the left of the midline, and the scalp was retracted to expose the skull. Periosteum was removed from the skull, and a square section of cranial bone was excised. The skull excised and the YSZ implant was immediately rinsed in saline and placed between two glass microscope coverslips. The transmission spectra were measured using Ocean Optics spectrometers (SD2000 and NIRQuest 512), covering a total spectral range from 800 to 2400 nm. The nc-YSZ implant was then placed within the craniectomy directly on the intact dura mater, and dental cement was applied to each of the four corners of the implant to prevent displacement. LSI Imaging was conducted immediately after the cranioplasty, while the scalp was still open.

3. Results and Discussion

3.1. *Ex-vivo transmittance measurements*

Freshly cranial bone and implant samples were used for ex vivo optical measurements. The transmittance spectra of Figure 1(a) show that the transparency of the nc-YSZ implant is higher in comparison to the native skull throughout the tested IR range. This demonstrates a significant reduction in scattering with when using the proposed cranial implant. In terms of relative differences in the optical properties between skull and the implant, the nc-YSZ implant improves the light transmission in the water absorption bands because of its reduced water content compared to the native skull (70 75%) [1]. The water absorption bands apparent in the implant spectrum are due to the saline solution added for a fair comparison with the treated skull. The percentage of light transmitted in these bands using the nc-YSZ implant had an increase of 53% compared to the transmittance in the native skull.

3.2. *In-vivo LSI*

To prove the feasibility of using the transparent nc-YSZ implant for brain imaging, we performed LSI imaging and compared it with transcranial imaging obtained in the same mice [3]. The LSI images were acquired with laser light at 810 nm, where light transmitted through the implant that reaches the brain tissue is increased by 20% compared to the native skull (Fig. 1 (a)). The results, presented in the Figure 1(b), show that LSI imaging allows for blood vessel mapping unlike in a regular image. In addition, as it is visually evident, the image acquired through the implant is sharper and less blurred than the transcranial images allowing micro-vessels visualization.

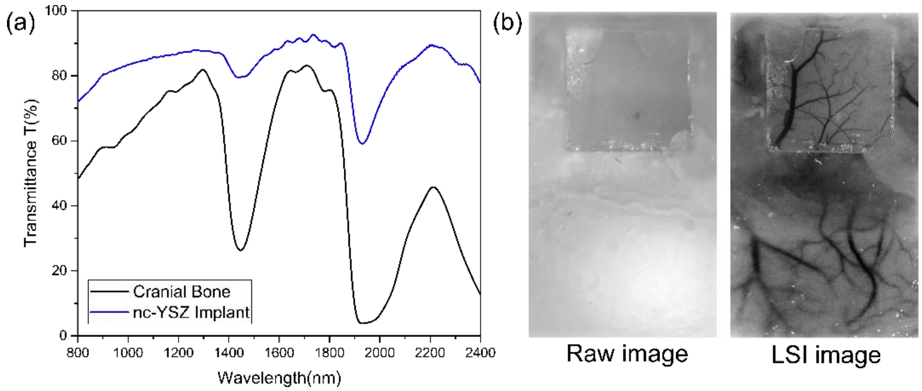

Fig. 1. (a) Transmittance of the nc-YSZ implant and cranial bone for the 800-2400 nm range. The transmitted light increases until 50% through the implant. (b) Regular image (left) vs. LSI (right) of the mouse brain. Sharper images with improved resolution are obtained through the implant compared to thus obtained through the native skull.

4. Conclusions

The use of transparent nc-YSZ provide enhanced optical access to the brain. While the current study represents only the first step towards realization of the long-term deep brain imaging through an implant, it is helpful to consider the opportunities this may eventually render. For example, opportunities may arise for chronic monitoring of cerebral edema. Finally, it could provide a platform to develop a novel tool for long-term optical diagnosis and therapy for brain pathologies in the NIR wavelengths range that us not usually considered due to the water absorption inherent to transcranial techniques.

Acknowledgments: The WttB project is being funded by NSF through grants NSF-PIRE 1545852, NSF-EAGER 1547014 and by CONACYT (México) through FONCICYT, grant 246648. M.C. acknowledge the support by "Beca Mixta" from CONACYT.

References

1. Golovynskyi, S., et. al., "Optical transparence windows for head tissues in near and short-wave infrared regions," presented at ICPIBM, OSA, China, 2017.
2. Damestani, Y., et. al., "Transparent nanocrystalline yttria-stabilized-zirconia calvarium prosthesis." *Nanomedicine*, 2013. 9(8): p. 1135-8.
3. Davoodzadeh, N., et.al., "Laser speckle imaging of brain blood flow through a transparent nanocrystalline yttria-stabilized-zirconia cranial implant." presented at SPIE BiOS2018, CA, 2018.