Diagnostics and Biomarkers

Novel Smart Catheter for Multimodal Monitoring of the Head-Injured Warrior

Traumatic brain injury (TBI) is a major focus of combat casualty care, as it remains a principal cause of mortality and morbidity in the military setting. This is especially because of the enemy's use of low cost, yet powerful, improvised explosive devices (IEDs). The critical period during which the injured brain is very vulnerable to secondary injury is approximately one week after severe head trauma; for severe blast-related TBI, ischemic insults may even persist for several weeks. Current standard-of-care for severely brain injured patients calls for monitoring intracranial pressure (ICP) and possibly brain oxygenation, using multiple devices. Unfortunately, the use of this technology has not kept pace and has remained essentially unchanged for two decades. One cannot overstate the need for a compact but sophisticated neuromonitoring device which can be used in hospitals or during transport and is capable of allowing for targeted interventions before irreversible brain damage occurs. Collaborators at the Feinstein Institute for Medical Research and the University of Cincinnati received funding from the Psychological Health/Traumatic Brain Injury Research Program (PH/TBIRP) managed by CDMRP to develop a single, novel, multimodality neuromonitoring device, or 'smart catheter'. The researchers developed and took this catheter through initial design, small scale production, laboratory refinement, and early animal testing. Recent studies have shown that a phenomenon known as spreading depolarization may be the pathophysiological basis of neurological deterioration in severe TBI patients.[1,2,3] However, the technology to study this phenomenon and to understand what causes it in humans has been limited until this catheter was developed. This one-of-a-kind catheter was successfully designed and microfabricated with seven microsensors (ICP, temperature, cerebral blood flow (CBF), oxygen tension, glucose, lactate, and electrocorticograph) using a flexible polyimide substrate that was spirally rolled to form a catheter for multimodal sensing of critical intracerebral variables. The function and performance of the complete system was tested and validated in both rat and pig animal models.[4,5,6] Both the individual sensing technologies as well as the capabilities to monitor multiple variables represent tremendous advances in brain monitoring and neuroscience. The sensors developed individually or in various combinations, hold great commercialization potential for biomedical research applications since, presently, combined probes

1 Li, C., Wu, P., Wu, Z., Limnuson, K., Mehan, N., Mozayan, C., … Narayan, R. K. (2015). Highly accurate thermal flow microsensor for continuous and quantitative measurement of cerebral blood flow. Biomedical Microdevices, 17(5), 87. https://doi.org/10.1007/s10544-015-9992-3

2 Li, C., Limnuson, K., Wu, Z., Amin, A., Narayan, A., Golanov, E. V., … Narayan, R. K. (2016). Single probe for real-time simultaneous monitoring of neurochemistry and direct-current electrocorticography. Biosensors & Bioelectronics, 77, 62–68. https://doi.org/10.1016/j.bios.2015.09.021

3 Li, C., Wu, Z., Limnuson, K., Cheyuo, C., Wang, P., Ahn, C. H., … Hartings, J. A. (2016). Development and application of a microfabricated multimodal neural catheter for neuroscience. Biomedical Microdevices, 18(1), 8. https://doi.org/10.1007/s10544-016-0034-6

4 Li, C., Narayan, R. K., Wu, P.-M., Rajan, N., Wu, Z., Mehan, N., … Hartings, J. A. (2016). Evaluation of microelectrode materials for direct-current electrocorticography. Journal of Neural Engineering, 13(1), 16008. https://doi. org/10.1088/1741-2560/13/1/016008

5 Li, C., Chaung, W., Mozayan, C., Chabra, R., Wang, P., & Narayan, R. K. (2016). A New Approach for On-Demand Generation of Various Oxygen Tensions for In Vitro Hypoxia Models. PloS One, 11(5), e0155921. https://doi. org/10.1371/journal.pone.0155921

6 Wu, Z., Li, C., Hartings, J. A., Narayan, R., & Ahn, C. (2016). Polysilicon Thin Film Developed on Flexible Polyimide for Biomedical Applications. Journal of Microelectromechanical Systems, 25(4), 585–592. https://doi.org/10.1109/JMEMS.2016.2554358

are not commercially available. Furthermore, the individual sensing technologies, such as the quantitative CBF monitor, represent significant advances compared to the best monitoring techniques available to biomedical researchers today, and also have application for other tissues besides the nervous system. The collaborating institutions have filed several patent applications covering the technology developed by the researchers and a patent has been issued for the 'smart catheter' (patent number 8,628,493). Members of the research team received two awards at the 2016 Annual Meeting of the American Academy of Neurological Surgeons: the Synthes Cerebrovascular Section Resident/Fellow Award and the ThinkFirst Head Injury Prevention Presentation Award.[7,8]

The ability to understand the dynamic and unique pathophysiology of severe neurotrauma from explosive blasts using an advanced 'smart catheter' advances the field of neurocritical care which is important to the care of critically injured Service Members who are being transported across long distances during periods of maximum vulnerability to secondary injury.

7 Krueger, B., York, J., Mahoney, E. J., Dreier, J. P., Zuccarello, M., & Hartings, J. A. (2016). Subarachnoid hemorrhage induces spreading depolarizations and cortical infarction. Presented at the Annual Meeting of the American Academy of Neurological Surgeons.

8 Li, C., Limnuson, K., Golanov, E. V., Ahn, C. H., Narayan, R. K., & Hartings, J. A. (2016). Transient brain temperature elevation as a surrogate indicator of cortical spreading depolarization. Presented at the Annual Meeting of the American Academy of Neurological Surgeons.