Cutting Edge: A novel lab-on-a-tube for multimodality neuromonitoring of patients with traumatic brain injury (TBI)

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Traumatic brain injury is a significant health care problem that requires timely intervention, but is as of yet, often difficult to diagnose and monitor. Clinicians often rely on intermittent monitoring or imaging modalities that only provide a snapshot of a highly dynamic injury state. The mechanisms of traumatic brain injury and their relationship to secondary injuries are poorly understood, as well as are the effects of various intervention strategies. Continuous monitoring of multiple parameters in a simple way would potentially improve the ability to track the progression of secondary insults and to guide subsequent interventions.

The approach outlined in the paper published in this issue of *Lab on a Chip* takes advantage of a unique opportunity in TBI to continuously sample CSF that is being drained to relieve pressure.[1] This represents an advantageous situation in microsensing technology to create a continuous monitoring sensor that can be applied to a continuously discarded clinical sample. The relatively large size of ventricular shunts gives ample room to integrate sensors, and the fact that shunts have to be inserted through viable brain tissue presents a unique situation where both global and focal brain sampling can be achieved by placing sensors on both the inside and outside of the shunt.

Although many of the individual MEMS sensor technologies have already been developed, the real challenge here was in fabricating them all within the same device, while still maintaining a flexible and biocompatible substrate to fit the constraints of the TBI monitoring application. This required the integration of a number of disparate fabrication techniques that were likely confounded by numerous processing hurdles. The end result is a good example where integrated multimodal sensing confers a number of advantages over singular sensor elements. For example, most *in vivo* biosensors rely on mediatorless-based detection of hydrogen peroxide (due to potential leaching and toxicity). These types of biosensors are often temperature and oxygen dependent, but the multimodal sensor approach can compensate for these problems by utilizing the output of the onboard temperature and oxygen sensors. The integration of microfluidic channels also presents the opportunity for recalibration of the sensors, as was aptly demonstrated in this article.

Many monitoring techniques only look at overall brain tissue function (*i.e.*, oxygenation, pressure) and don't necessarily reflect the state of the locally injured tissue or the immediately surrounding areas that are vulnerable to secondary insults. Placing sensors both on the inside and outside of the device allows for monitoring of the more global measures that can be inferred from the extracted CSF as well as the local information that can be obtained from the tissue in contact with the outside of the tube (potentially in multiple locations).

The MEMS approach Li *et al.* have taken also makes it relatively straightforward to add other electrical sensors onto the outside of the catheter, such as intracranial EEG sensors, which may also have clinical utility in assessment of brain injury state. The approach should also find itself amenable to the integration of other types of chemical sensors which may be important for brain monitoring (*i.e.* lactate : pyruvate). The multifaceted fabrication approach makes it possible to integrate numerous other types of sensors as well as electrical stimulation and even drug delivery in the same form factor.

New technologies have the potential to provide crucial information about brain physiology and metabolism in a timely fashion. Combining various technologies in a 'multimodal monitoring' approach can produce a more accurate overall picture of brain injury and its response to interventions. While the disparate macrotechnology is cu rrently available to tackle this type of monitoring approach, it requires considerable investment in infrastructure and training as well as a considerable time commitment from staff to administer and monitor. The integrated approach presented in this paper may change the way patients with brain injury are monitored and treated in the future. It also tackles many of the technical issues that will make this type of approach more palatable to 'lab-on-a-tube' applications in other clinical settings.

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References

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