Modulation of Foreign Body Response towards Implanted Microdialysis Probes

by

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Abstract

Implantable chemical sensors and drug delivery devices hold great promise for continuous disease monitoring and therapy. Developing reliable *in vivo* sensors or devices is impeded by a lack of understanding of localized implant biochemistry and how it affects the *in vivo* performance of the sensor/device. Experiments described in this dissertation aimed to elucidate some of the underlying parameters that can affect long-term implanted device calibration performance.

Microdialysis sampling probes were used in this study because they provided a convenient way to simultaneously collect and deliver different solutes when implanted subcutaneously in Sprague-Dawley rats. Microdialysis probes with either polycarbonate, PC (MWCO 20 kDa), or polyethersulfone, PES (MWCO 100 kDa), membranes were calibrated in awake and freely moving rats using internal standards 2-deoxyglucose (MW 164), antipyrine (MW 188), and vitamin B12 (MW 1355). Alterations in the local recovery of endogenous glucose and the loss (delivery) of the internal standards through the probes was used to determine the influence of glucose metabolism, capillary and membrane permeability changes during the long term implantation of the probes. Additionally, monocyte chemoattractant protein-1 (MCP-1) and dexamethasone-21-phophate disodium (Dex-Phos) were infused to affect the inflammatory response.

After one week of implantation, all probes were found to be encapsulated. Three layers (compact cells, collagen, and rich blood vessels) containing inflammatory cells (macrophages and fibroblasts) were observed inside the capsule. Capsules ranged in size between (200-250 μm) for controls and probes were infused with Dex-Phos to (500-600 μm) for probes that infused MCP-1. Delivery of Dex-Phos through the probe caused a significant decrease in the density of inflammatory cells at the implant site.

For controls, the fibrous capsule appeared to block the diffusional pathway of the larger molecular weight analyte (VB_{12}), but did not significantly affect the diffusion of the lower molecular weight molecules (antipyrine and 2-deoxyglucose). Interestingly, the infusion of MCP-1 or Dex-Phos did not significantly affect the delivery of the different internal standards compared to controls. For all the implanted probes, the

delivery of VB_{12} and the collected glucose concentrations dramatically decreased by over 70% throughout the implant time.

The conclusions from these studies are two-fold. First, blood supply is primarily affected during the foreign body response and the change in blood supply will affect localized solute concentrations near any device. Second, low molecular weight solutes are able to freely diffuse through a fibrous capsule, whereas large molecules such as VB_{12} cannot. This study indicated how the capsule tissue affected glucose collection and large molecule delivery at the implant site in different ways and provided possible guidance towards the improvement of *in vivo* calibration of implantable sensor/device.