

Poster II-68

Direct Infusion in Brain Tissue: Patient-Specific Planning

Raghavan, Raghu

Image-Guided Neurologics, Baltimore, MD, USA

Intra-parenchymal injection and transport of drugs and other agents have been studied both theoretically and experimentally (see references below). However, beyond these pioneering studies there is a need for a patient-specific model of drug transport to help the planning of such infusions. For example, in a recent study that we will show, fourteen out of sixteen infusions failed to achieve the aimed-for distribution of a surrogate marker. We report on a new systems approach to achieve this aim, based on data obtained by essentially non-invasive means appropriate for human patients.

The poster is divided into three parts. In the first, we discuss the phenomena that occur, and how to exploit them for increased efficacy, and how to observe them *via* magnetic resonance imaging (MRI). When molecules are directly injected into the brain, the phenomena we must account for include: (i) backflow that creates a small fluid-filled cavity along part of the length of the needle or catheter; (ii) flow of fluid into the porous medium which is brain tissue; (iii) flow in a poroelastic medium, where the expansion of extracellular space due to the elasticity of brain tissue is taken into account; and (iv) agent transport, where the molecule in question is carried by the fluid flow, diffuses, leaks into capillaries, is metabolized, and so on.

In the second part, we discuss how we solve the equations that account for the phenomena, and how we may obtain the input parameters needed for the calculation, again principally from MRI. Some new results are: the computation is driven by patient-specific magnetic resonance imaging data (only, *i.e.* no prior atlas, statistical or otherwise is needed although of course such can be used) and a stochastic particle method is used for all the partial difference equations. The particle method has the virtues that the simulation results are available as “real time” as one wants (at the expense of accuracy), no segmentation of brain structures is required provided the fundamental imaging is available at sufficiently high resolution (as one would need for finite element methods), the “weak solution” is automatically obtained and increasing knowledge of the chemical kinetics is easily incorporated. Further, the “roughness” of Brownian motion is actually an advantage, and all modern chips provide true random numbers on call.

Finally, we review the status of the experimental data in checking the predictions. Experiments have been conducted in gels and pigs, and data on humans has been analyzed. In addition, experiments on monkeys and on dogs is being undertaken. The results on the experiments so far, are extremely encouraging. The experimental work has been undertaken in a number of collaborative institutions, which will be duly acknowledged.

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References

1. P. A. Netti, L. T. Baxter, Y. Boucher, R. Skalak, and R. K. Jain, “Macro- and Microscopic fluid transport in living tissues: application to solid tumors”, *AIChE Journal*, vol. 43, pp. 818 - 834, 1997.
2. P. J. Basser, “Interstitial pressure, volume, and flow during infusion into brain tissue”, *Microvascular Research*, vol. 44, pp. 143 - 165, 1992.
3. P. F. Morrison, D. W. Laske, H. Bobo, E. H. Oldfield, and R. L. Dedrick, “High-flow microinfusion: tissue penetration and pharmacodynamics”, *American Journal of Physiology*, vol. 35, pp. R292 - R305, 1994.