A. Hartlep, C. Pedain, I. Rodríguez, M. Brady, R. Raghavan

Targeted Infusion – Physiological Simulations for Treatment Optimization

Purpose:
Computer-assisted surgery (CAS) provides assistance during surgery but also during planning and monitoring of the treatment. Here we describe a novel application in the planning of surgeries based on the simulation of physiological and therapeutic processes. Motivated in part by the profound difficulties in treating malignant brain cancer (glioblastoma multiforme), various groups have been exploring direct infusion of therapeutic substances into solid brain tissue to bypass the problem of the blood-brain barrier. However, brain parenchyma is an extremely inhomogeneous and physiologically reactive tissue so that the treatment has to be tailored to the individual properties. In this framework, convection-enhanced delivery (CED) based on the direct infusion of the drug into tissue under the application of a pressure gradient has shown to be a very promising and effective technique. However, improvements to minimize the risk of leakage of drugs as well as the optimal coverage of the target area are still necessary. A simulation tool able to predict such adverse scenarios in relation to the actual catheter position and the properties of the individual brain tissue as well as the final distribution of the drug in tissue appears to be a very valuable tool.

Method:
Anatomical MR and DTI data sets are used as basis for calculation of fluid distribution in individual brain tissue. In clinical studies, BrainLAB investigated the usefulness of the simulation for the particular case of the treatment of gliobastoma multiforme.

Result:
Based on new infusion simulation algorithms, we developed surgical planning software that can be used by the physician for planning CED catheter trajectories taking into account the predicted resulting fluid distribution. Once the trajectories are optimized so that the predicted distribution pattern matches the target region best, the surgical plan can be executed using stereotactic surgery, either frameless or frame-based.
Results of clinical studies conclude that the pre-operative simulation helps to avoid catheter placements prone to subarachnoid leakage, aid in defining the most effective treatment plan.

Conclusion:
Mathematical modeling of tissue fluid dynamics in individual patients integrated into treatment planning procedures provides a powerful tool not only for clinical research but also for clinical practice, and will support and increase the use individually tailored treatment.