# Abstract

Multiple sclerosis (MS) is a demyelinating neurological disorder with unknown etiology. Even though several drugs are approved for modifying the disease course, the effect is limited to slowing down the disease progression. Also, in relatively large group of patients disease continues to progress, resulting in permanent disability. It is believed that developing preclinical animal model with improved clinical relevance will speed up the progress of finding the successful therapy. In case of MS, disease modeling is practically exclusively done in rodents. Currently, the most popular model of MS is experimental autoimmune encephalomyelitis (EAE). Even though this model reproduces quite well the pathomechanism of clinical MS, the clinical course of the disease is highly dependent on animal strain. Moreover, lesions mostly localize within the spinal cord, in contrary to clinical MS, where pathology is primarily localized in the brain. Multifocal and unpredictable lesion distribution is particularly undesired when targeted delivery of therapeutic agents is explored, such as with intraarterial or intracerebral injections. To address these limitations, it is essential to develop a local model of EAE, where the lesion can be placed precisely in desirable brain area. Rats with larger brain compared to mice are still cost-effective for high throughput screening and as such are the focus of this dissertation project. The main goal of this project and paradigm shifting approach was to achieve precise control over the lesion size and placement. Such model is expected to contribute to accelerating the progress of developing successful therapy for this devastating disease.