Quantitative magnetization transfer (qMT) imaging is a magnetic resonance imaging (MRI) technique that has demonstrated considerable promise for multiple sclerosis (MS) research. qMT improves on conventional MRI by probing the macromolecules present in myelin, providing a quantitative estimate called the pool-size ratio, which correlates strongly with myelin density in brain white matter. qMT requires several other quantitative MRI maps for calibration purposes: the main magnetic field (B0), the radiofrequency amplitude (B1), and the longitudinal relaxation time (T1). These maps can also depend on each other (e.g. some T1 mapping techniques require B1), meaning that the impact of B1-inaccuracies on the fitted pool-size ratio may depend on the choice of T1 mapping technique. The focus of this thesis is to characterize and minimize the B1-sensitivity of qMT.

The first aim of this thesis was to compare several whole-brain B1 mapping techniques, their potential sources of inaccuracies, and their impact on a widely used, B1-sensitive, T1 mapping technique (variable flip angle – VFA). This study was done in the context of validating a B1 mapping technique using a standard MRI pulse sequence and comparing it against two other advanced B1-mapping techniques. The second aim was to characterize the B1-sensitivity of qMT for two different T1 mapping techniques: B1-dependent (VFA) and B1-independent (inversion recovery– IR). qMT data were simulated and fitted for a wide range of B1-inaccuracies, and *in vivo* qMT data were acquired in healthy subjects using both VFA and IR T1 mapping, along with multiple B1 mapping techniques. The final aim was to develop an optimization framework for qMT protocols to further improve the robustness against B1-inaccuacies. A sensitivity-regularized Cramér-Rao lower bound expression was developed theoretically as an iterative optimization condition, and the iteratively optimized protocols were tested for a wide range of conditions (signal-to-noise ratios, B1-inaccuracies, tissue types) using Monte Carlo simulations. Overall, this thesis presents a characterization and optimization of the robustness of qMT to B1-inaccuracies, and concludes that it may be even possible to develop an imaging protocol that could omit B1 maps altogether without substantially impacting the accuracy of the pool-size ratio estimates.