Modern radiation therapy techniques allow for improved target conformity and normal tissue sparing. These highly conformal treatment plans have allowed dose escalation techniques increasing the probability of tumor control. At the same time this conformation has introduced inhomogeneous dose distributions, making delivered dose characterizations more difficult. The concept of equivalent uniform dose (EUD) characterizes a heterogeneous dose distribution within irradiated structures as a single value and has been used in biologically based treatment planning (BBTP); however, there are no substantial validation studies on clinical outcome data supporting EUD’s use and therefore has not been widely adopted as decision-making support.

These highly conformal treatment plans have also introduced the need for safety margins around the target volume. These margins are designed to minimize geometrical misses, and to compensate for dosimetric and treatment delivery uncertainties. The margin’s purpose is to reduce the chance of tumor recurrence.

This dissertation introduces a new EUD formulation designed especially for tumor volumes, called generalized Tumor Dose (gTD). It also investigates, as a second objective, margins extensions for potential improvements in local control while maintaining or minimizing toxicity.

The suitability of gTD to rank LC was assessed by means of retrospective studies in a head and neck (HN) squamous cell carcinoma (SCC) and non-small cell lung cancer (NSCLC) cohorts. The formulation was optimized based on two datasets (one of each type) and then, model validation was assessed on independent cohorts.

The second objective of this dissertation was investigated by ranking the probability of LC of the primary disease adding different margin sizes. In order to do so, an already published EUD formula was used retrospectively in a HN and a NSCLC datasets.

Finally, recommendations for the viability to implement this new formulation into a routine treatment planning process as well as the revision of safety margins to improve local tumor control maximizing normal tissue sparing in SCC of the HN and NSCLC are discussed.