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Risk Modeling and Treatment Planning: a Breast Cancer Case

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Summary

Predicting the outcome of the treatment is important, however, difficult. Especially, a typical randomized control trial takes about 10 years in order to compare the long-term outcome of different treatments. In this thesis, I demonstrated a risk modeling framework which predict the treatment outcome and has added value to the current practice of breast conserving therapy. Further, I applied the analytics framework in planning new type of treatments.

Specifically in this thesis, I explained why surgical resection margin is not recognized as a prognostic factor in breast-conserving therapy and why doctors reported different results in Chapter 3. The reason is that the impact of a negative margin width on local recurrence is limited due to the large variation of microscopic disease across patient population. Chapter 2 contains a complementary experiment to testify an important assumption in Chapter 3 that the distribution of *in-vivo* microscopic disease can be reliably estimated through *ex-vivo* breast specimen tissue. Unlike lung tissue, limited deformation of breast tissue was observed in our study. In Chapter 4, I built an analytical framework to estimate the outcome of breast-conserving therapy through simulations. I applied this framework to estimate the difference between younger and older patients in Chapter 5, and found that the higher local recurrence rate in younger patients could be explained by larger clonogenic tumor cell quantity, even though the tumor cells were found to be more radiosensitive. I also predicted the outcome of the Young-Boost trial as tumor control probability of 92% at 10 years using the same framework. In Chapter 6, I further developed this concept and estimated the benefit of switching to 'dose-painting' strategy from the current practice of using homogeneous dose. The overall tumor control probability of a patient population is significantly improved under the dose-painting plan compared to the homogeneous dose plan with the same mean dose. However, the adoption of dose-painting plan should depend on

target TCP and setup error in practice. Finally, I discussed state of the art of risk modeling and treatment planning methods, limitations of my thesis and future direction of research (decision support analytics) in Chapter 7.