THE ANALYSIS OF LOCAL RECURRENCE AND DISTANT METASTASES IN EARLY-STAGE BREAST CANCER USING A MIXTURE MARKOV MODEL

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The role of local recurrence (LR) in the risk of distant metastases (DM) and survival has been a controversial topic. It is uncertain whether an LR indicates a more biologically aggressive tumor that had been established at inception or it is responsible for an increase in the rate of DM through secondary dissemination. Such knowledge is important in determining the salvage treatment for local recurrence which impacts survival outcomes. Several studies based on large databases have shown evidence to support both explanations. It is likely that such observations were a consequence of mixed patient or tumor subtypes in the population. Therefore, we propose a mixture model of two independent continuous-time multistate Markov processes to incorporate population heterogeneity. Transition and mixing probabilities will be estimated by the likelihood method through a modified EM algorithm. Nelson-Aalen estimator is used for the cumulative intensity functions. We will focus on the probability of metastatic dissemination. Extension to include covariate information will be discussed. The methodology is applied using data from 1293 women with Stage I-II breast carcinoma treated with breast-conserving therapy (BCT) between 1977 and 1995. The median follow-up was 8.5 years (range, 1.5-24 years).