Designed Extension of Survial Studies: Applications to Clinical Trials with Unrecognized Heterogeneity

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It is well known that unrecognized heterogeneity among patients, such as is conferred by genetic subtype, can undermine the power of a randomized trial, designed under the assumption of homogeneity, to detect a truly beneficial treatment. We consider the conditional power approach to allow for recovery of power under unexplained heterogeneity. While Proschan and Hunsberger [Biometrics 51 (1995):1315–24] confined the application of conditional power design to normally distributed observations, we consider more general and difficult settings in which the data are in the framework of continuous time and are subject to censoring. In particular, we derive a procedure appropriate for the analysis of the weighted log rank test under the assumption of a proportional hazards frailty model. The proposed method is illustrated through application to a brain tumor trial.

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