ON THE USE OF FRACTIONAL POLYNOMIALS TO MODEL TIME-VARYING EFFECTS IN THE COX MODEL

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The hazards model of Cox is the standard for the analysis of survival times. Often proportional hazards (PH) are assumed for covariate effects, implying that the effect on the hazard function is unchanged in time. However, with long-term follow-up this assumption may be questionable. Furthermore, for a continuous factor the assumption of a linear effect on the log hazard function may be violated, in which case a non-linear risk function may be required.

We will propose a new approach based on fractional polynomials (FP) to model time-varying effects in survival data. The principles for selecting an FP function are transferred to selecting a function of time describing the variation over time of a regression coefficient. To protect against spurious time-varying effects caused by mis-modeling of time-fixed non-linear effects of continuous covariates, the procedure uses in its first step the multivariable FP (MFP) approach (Sauerbrei & Royston 1999, JRSS, A, 162:71-94). This time-fixed MFP model is extended by including time-varying functions, if strongly supported by the data.

We will illustrate the procedure by analysing the joint effect of several prognostic factors for patients with breast cancer. We will investigate the stability of selected models by using the bootstrap. Using another breast cancer data set, we will discuss validation of a model with non-linear and time-dependent effects.