Predict Mathematics

Summary

- Predict takes the form of a competing risk Cox survival model, with fractional polynomial baseline cumulative hazards.
- Approximate intervals for the benefits of treatment can be obtained from the treatment-effects uncertainties.

The form of the Predict V2.1 algorithm

The estimated baseline cumulative hazard for breast cancer mortality H_c at t years post-surgery has the form

$$H_c(t) = \exp[a_c' f(t)]$$

where a_c is a vector of estimated coefficients, and f a (column) vector of fractional polynomial functions of time post-operation (different models are built for ER+ and ER-).

In Predict 2.1,

- if ER+
$$H_c(t) = \exp[0.7424402 - 7.527762/\sqrt{t} - 1.812513 * \log(t)/\sqrt{t}]$$
- if ER-
$$H_c(t) = \exp[-1.156036 + 0.4707332/t^2 - 3.51355/t].$$

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The estimated survival function for breast cancer mortality S_c given risk factors x_R and the ith treatment combination x_T is given by

$$S_c^i(t) = \exp\left[-H_c(t)\exp[b_c' x_R + c' x_T]\right] = \exp\left[-\exp[a_c' f(t) + b_c' x_R + c' x_T]\right]$$

where b, c are vectors of estimated coefficients. This is the chance of living beyond t years after surgery under treatment regime i, assuming only breast cancer mortality.

The estimated baseline cumulative hazard for other-cause mortality H_o has the form

$$H_o(t) = \exp[a_o' g(t)]$$

where a_o is a vector of estimated coefficients, and g a vector of fractional polynomial functions of years post-operation. This is the chance of living beyond t years after surgery, assuming only other-cause mortality.

The estimated survival function for non-breast-cancer mortality S_o, is given by

$$S_o(t) = \exp\left[-H_o(t)\exp[b_o' h(a)]\right]$$

where b_o is a vector of estimated coefficients, and $h(a)$ is a vector of polynomial functions of patient age a at surgery.

In Predict 2.1, the parameters given by

$$H_o(t) = \exp[-6.052919 + (1.079863 * \log(t)) + (.3255321 * \sqrt{t})]$$

$$b_o' h(a) = 0.0698252 * ((a/10)^2 - 34.23391957).$$

$S_o(t)$ is the 'dashed' line in the graphs - the survival of women who are assumed not to die of breast cancer, essentially who are 'cured'.

The overall estimated survival function $S^i(t)$, assuming independent competing risks and treatment combination i, is given by

$$S^i(t) = S_o(t)S_c^i(t),$$

which is the estimated chance of living beyond time t. This is a competing risk Cox survival model.

Overall survival with no treatment ($i = 0$) is then $S^0(t) = S_o(t)S_c^0(t)$.

The benefit at time t of treatment combination i is then given by $S^i(t) - S^0(t) = S_o(t)(S_c^i(t) - S_c^0(t))$, which is the benefit in breast-cancer specific survival $S_c^i(t) - S_c^0(t)$, scaled by the probability of surviving other risks $S_o(t)$.

Each estimated treatment log(hazard ratio) c_j is assumed independent, giving a variance of $V_T = Var(c'x_T) = \sum_j Var(c_j)$, adding over those treatments comprising combination x_T. Then the standard error of the estimated overall treatment effect is $\sqrt{V_T}$, which is used to develop intervals for the overall survival benefit.