Analysis of Dose-response Relationship in Number of Intestinal Crypts for Exposed Mice to Radiation Using Multi-target Model

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1 Introduction

Consider a gene of exposed object as a target. By assuming that damage-free rate of each target be $e^{-\beta D}$, where β is a coefficient of exposure effect and D denotes irradiation dose, we obtain that probability of one target having damage is $1 - e^{-\beta D}$. We assume that survival rate of the cell could be written as $1 - (1 - e^{-\beta D})^m$, where m is a number of targets that provides vital condition of the object.

Observational data that employed in this paper contains number of intestinal crypts of mice as radioprotective effects of miso (fermented soy bean paste), and X-irradiation dose (Gy). X-irradiated mice are separated in three different fermentation-stages of miso that administered in mice, i.e. short-, medium-, and long-term fermented miso.

For the purposes of our research, we would like to establish a model to assess the effects of miso at various fermentation-stages on crypt survival after X-irradiation in mice.

2 Models

In analysis, we apply two models, namely Poisson model and Poisson-Gamma model.

For a given group, assume that the observational number of intestinal crypts Y is a random variable having Poisson distribution with

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mean $\lambda = \mu(D)$, where $\mu(D) = \mu_0\{1 - (1 - e^{-\beta D})^m\}$ and μ_0 is expected number of intestinal crypts for un-irradiated mice.

Then, the Poisson model with parameters (μ_0, β, m) can be specified as

$$Pr(Y = y) = \frac{\left[\mu_0\{1 - (1 - e^{-\beta D})^m\}\right]^y}{y!} e^{-\mu_0\{1-(1-e^{-\beta D})^m\}}. \qquad (2.1)$$

A frailty version of the Poisson model is derived from replacing $\mu(D)$ by $\mu(D)Z$, where Z is a latent variable, which describes term of relative risk, measurable or nonmeasurable and $Z \sim i.i.d$ $\mathrm{G}(\nu, \nu)$, gamma distribution with mean 1 and variance $\frac{1}{\nu}$.

The joint density of Y and Z is expressed as

$$Pr(Y = y; Z = z) = \frac{(\mu(D)z)^y}{y!} e^{-\mu(D)z} \frac{\nu^\nu}{\Gamma(\nu)} z^{\nu-1} e^{\nu z}. \qquad (2.2)$$

The marginal probability density function of $Y = y$ for given D is then

$$Pr(Y = y) = \frac{\Gamma(y + \nu)}{y!\Gamma(\nu)} \left(\frac{\mu(D)}{\mu(D) + \nu}\right)^y \left(\frac{\nu}{\mu(D) + \nu}\right)^\nu, \qquad (2.3)$$

which follows negative binomial distribution.

3 Results

The results show that there is substantial frailty for all fermentation-stages of miso. The long-term fermented miso group provides the smallest coefficient of exposure effect, which means that the crypt survival of this group has a higher rate as compared with the other groups.

Restriction for parameters of frailty model approach is an improvement on the power of Likelihood ratio test for coefficient of exposure effect. The resulting LR test suggests that short-term and medium-term fermented miso have the similar effect on survival crypt after X-irradiation.

References

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