

Nonparametric Multivariate Tests for the Right Censored Data when the Alternative is One-Sided

Hyo-II Park, Department of Statistics, Chongju University, Chongju, 360-764, Korea

Abstract— *In this paper, we formulate the one-sided alternatives for multivariate data and propose an asymptotically nonparametric test for possibly right censored data. We consider obtaining asymptotic tail probability (or p -value) by showing that our proposed test statistics are asymptotically related with multivariate normal distributions. Also we derive the limiting power of our test and compare the performance with other procedures by obtaining empirical powers through simulations for the bivariate case. Finally we illustrate our procedure with an example and discuss properties of our procedure.*

Index Terms— Multivariate data, one-sided alternative, power, right censored data.

I. INTRODUCTION

In survival analysis, we encounter frequently the time-to-event data with multiple endpoints in clinical trial research. The form of observation may be a vector of event times for different outcome types or of successive event times for the same outcome type. Based on these multiple endpoints data, suppose that we are interested in comparing two treatments. In this comparative study, one may come to a conclusion that a treatment is better than the other if at least any one component of a treatment reveals the superiority over that of the other. Then this type of comparative study corresponds to the so-called one-sided alternatives for multiple endpoints. For example, in the National Cooperative Gallstone Study (NCGS) [19], one of the major interests was to study the efficacy of the drug chenodiol for the treatment of cholesterol gallstones. For this study, patients were randomly assigned to the high-dose, low-dose and placebo groups. However [23] raised an issue whether there exists any difference in the progression of gallbladder disease between the placebo and high dose groups as a measure of the efficacy of the drug chenodiol. Progression of disease is indicated by the occurrence of gallbladder pain or the presence of pain accompanied by other symptoms that require surgical removal of the gallbladder (cholecystectomy). Therefore in this case it becomes more appropriate to consider testing hypotheses under the one-sided alternative rather than the general one. Also Wei and Lachin proposed a test statistic in this direction as a sum of univariate test statistics. For the complete bivariate case, [2] and [8] proposed nonparametric tests for the ordered alternatives. The former is based on the concept of two-dimensional layer ranks (cf. [1]) and the latter, the sum of two components of the vector of linear rank

statistics (cf. [18]) for the construction of test statistics. We note that the two test statistics mentioned are of univariate type and so the limiting distributions are univariate normal. Also we note that extensions to the cases with three or more endpoints of the procedure by [2] are not clear since the concept of the layer ranks may not be applicable to the data with three or more endpoints. [3] Considered a nonparametric test based on the maximal T -statistic but did not provide limiting distribution. The reason for this seems non-availability of any software for calculating tail probability of multivariate normal distributions at that time since the limiting distribution of the proposed test statistic should be multivariate normal. Also [12] proposed several parametric and nonparametric procedures. He used linear combination of least squares for the parametric procedure and rank sum type statistic for the nonparametric procedure. [15] Considered a nonparametric procedure using the maximal type of statistics and provided the asymptotic normality. [9] Proposed the one-sided tests for the mean vector using both the Bayesian and frequent approaches. [21] Considered to apply the likelihood ratio principle to obtain the Wald and score statistics for the multivariate one-sided tests for nonlinear mixed-effects models. Very recently, [5] investigated the properties of a one-sided likelihood ratio test for the multivariate data. All the mentioned works in the above except [12], adopted the permutation principle to obtain the null distributions. For censored data, [22] proposed a nonparametric procedure modifying the concept of the layer ranks for the bivariate censored case. Also it can be considered as an extension of the Gehan test for bivariate data. However because of the involvement of censoring distribution, the exact null distribution based on the permutation principle may not be available and the asymptotic normality was derived. Also [16] considered several test procedures based on the weighted linear combination of the vector of univariate statistics for multiple endpoints using the [12] approach. In this paper, we consider a nonparametric test procedure for censored data with multiple endpoints using the rationale of [3]. Thus our procedure may be applicable to the data with three or more endpoints. Then we show that the limiting distributions of our proposed test statistics are multivariate normal distributions. Therefore obtaining of limiting tail probability (or p -value) for any given data depends completely on the software such as S-PLUS (cf. [20]) and (cf. [11]) program. Also we derive the limiting power of our procedure and compare the

performance of our procedure with those of [22] and [16] by obtaining empirical powers through simulation study. For illustration of our procedure, we use the NCGS data with applying two different scores. Finally, we discuss our procedure briefly.

II. ASYMPTOTICALLY NONPARAMETRIC ONE-SIDED TESTS FOR RIGHT CENSORED DATA WITH MULTIPLE END-POINTS

Let $\{X_{ij} = (X_{1j}, \dots, X_{dj})', j = 1, \dots, n_i\}$ be independently and identically distributed d -variate life-time random vectors with positive components and an unknown but continuous survival function $S_j(x_1, \dots, x_d)$ for each $j = 1, 2$. Also let $\{U_{ij} = (U_{1j}, \dots, U_{dj})', j = 1, \dots, n_i\}$ be independently and identically distributed d -variate censoring random vectors with an arbitrary distribution function $C_j(x_1, \dots, x_d)$ for each $j = 1, 2$. In order to avoid the identifiability problem, we assume that the life time random vectors are independent of the censoring random vectors. Since the random censoring schemes are involved, we may only observe that for each $k, K = 1, \dots, d$

$$T_{ikj} = \min(X_{ikj}, U_{ikj}) \text{ and } \delta_{ikj} = I(X_{ikj} \leq U_{ikj})$$

for $j = 1, 2$ and $k = 1, \dots, d$, where $I(\bullet)$ is the indicator function. Since we are interested in the one-sided alternatives, the hypotheses for the multiple endpoints data can be formulated as follows:

$$H_0 : S_{11}(x_1) \leq S_{21}(x_1), \dots, S_{1d}(x_d) \leq S_{2d}(x_d)$$

v.s. $H_1 : \text{at least one strict inequality holds}$

for some $x = (x_1, \dots, x_d)' \in R^d$, where S_{ij} is the j th marginal survival function of S_j . Also it is known as ordered alternatives in the literature (cf. [2]). In order to construct the test statistics for this problem, first of all, we introduce some notation. For each k th component, let

$$N_{ik}(t) = \sum_{j=1}^{n_i} I(T_{ikj} \leq t, \delta_{ikj} = 1)$$

be the number of deaths that occur no later than time t in group i and

$$Y_{ik}(t) = \sum_{j=1}^{n_i} I(T_{ikj} \geq t)$$

be the number of deaths that occur no later than time t in group i and

$$T_{kn} = \frac{1}{\sqrt{n}} \int_0^\infty \frac{Q_k(t) Y_{1k}(t) Y_{2k}(t)}{Y_{1k}(t) + Y_{2k}(t)} \left[\frac{dN_{1k}(t)}{Y_{1k}(t)} - \frac{dN_{2k}(t)}{Y_{2k}(t)} \right],$$

where the score function, $Q_k(t)$, is a uniformly bounded nonnegative predictable process (cf. Gill, 1980), which is a function of $\{T_{ikj}, \delta_{ikj}; i = 1, 2; j = 1, \dots, n_i\}$ and vanishes whenever $\min(Y_{1k}(t), Y_{2k}(t)) = 0$. We note that $T_{kn}(t)$ can be used for testing $H_0^k : \theta_k \leq 0$ against the one-sided alternatives $H_1^k : \theta_k > 0$ in case of univariate data. Also we note that we may construct various linear rank statistics

according to the choice of $Q_k(t)$. For example, the Gehan and log-rank statistics correspond to $Q_k(t) = t$ and $Q_k(t) = \log t$, respectively. Now we assume the following:

Condition 1. $n_i/n \rightarrow \lambda_i \in (0,1)$ as $n \rightarrow \infty, i = 1, 2$.

Condition 2. The score function, Q_k converges uniformly on each closed sub-interval of $[0, \infty)$ in probability to a function q_k as $n \rightarrow \infty$.

Then with Conditions 1 and 2, it is well-known that T_{kn} converges in distribution to a normal random variable with mean 0 and variance σ_k^2 , which can be consistently estimated by $\hat{\sigma}_k^2$ (cf. [23]), where

$$\sigma_k^2 = \frac{n_1}{n} \sigma_{1k}^2 + \frac{n_2}{n} \sigma_{2k}^2,$$

$$\hat{\sigma}_{ik}^2 = \frac{n_i}{n} \sum_{j=1}^{n_i} [\hat{\mu}_{ik}(T_{ikj}) \delta_{ikj} - \hat{\psi}_{ik}(T_{ikj})]^2,$$

$$\hat{\mu}_{ik}(t) = Q_k(t) \left(1 - \frac{Y_{ik}(t)}{Y_{1k}(t) + Y_{2k}(t)} \right)$$

$$\text{and } \hat{\psi}_{ik}(s) = \sum_{j=1}^{n_i} \left[\frac{\delta_{ikj} \hat{\mu}_{ik}(T_{ikj}) I(T_{ikj} \leq s)}{Y_{ik}(T_{ikj})} \right].$$

Without loss of generality, for each k , we may assume that for testing $H_0^k : S_{1k}(x_k) \leq S_{2k}(x_k)$ against $H_1^k : S_{1k}(x_k) > S_{2k}(x_k)$ for some x_k , we can reject H_0^k for large values of T_{kn} in favor of H_1^k . Then we may propose the asymptotically nonparametric one-sided test statistics for censored data with multiple endpoints in the light of the rationale of [3] as follows:

$$T_n = \max \left\{ \frac{T_{1n}}{\hat{\sigma}_1}, \dots, \frac{T_{dn}}{\hat{\sigma}_d} \right\},$$

where $\hat{\sigma}_k = (\hat{\sigma}_k^2)^{1/2}$ for each k . When H_1 is true, at least one of d numbers of $T_{kn} / \hat{\sigma}_k$'s would tend to have large positive values. Therefore we may reject H_0 for large values of T_n in favor of H_1 . Then for any given significance level, in order to determine the critical value, we need to obtain the null distribution of T_n . For this end, first of all, we note that for any $t > 0$,

$$\begin{aligned} \Pr\{T_n > t\} &= \Pr\{\max\{T_{1n}/\hat{\sigma}_1, \dots, T_{dn}/\hat{\sigma}_d\} > t\} \\ &= 1 - \Pr\{\max\{T_{1n}/\hat{\sigma}_1, \dots, T_{dn}/\hat{\sigma}_d\} \leq t\} \\ &= 1 - \Pr\{T_{1n}/\hat{\sigma}_1 \leq t, \dots, T_{dn}/\hat{\sigma}_d \leq t\}. \end{aligned}$$

Therefore we have to consider the d -variate joint distribution of $(T_{1n}/\hat{\sigma}_1, \dots, T_{dn}/\hat{\sigma}_d)'$ or equivalently that of $(T_{1n}, \dots, T_{dn})'$ for the distribution of T_n . Since the unknown censoring distributions are involved in the distribution of $(T_{1n}, \dots, T_{dn})'$, it is not feasible to obtain the null distribution of T_n by applying the permutation principle even for the small sample case. Therefore we have to consider applying the large

sample approximation. From [23], we see that under Conditions 1 and 2, the random vector $(T_{n_1}, \dots, T_{n_d})'$ converges in distribution to a d -variate normal random vector with 0 mean vector and covariance matrix $\Sigma = (\sigma_{kj})$, which can be consistently estimated by $\hat{\Sigma} = (\hat{\sigma}_{kj})$, where $\hat{\sigma}_{kk} = \hat{\sigma}_k^2$ and for $k \neq l$,

$$\hat{\sigma}_{kl} = \frac{n_1}{n} \hat{\sigma}_{1kl} + \frac{n_2}{n} \hat{\sigma}_{2kl},$$

$$\hat{\sigma}_{1kl} = \frac{1}{n_1} \sum_{j=1}^{n_1} [\hat{\mu}_{1k}(T_{1kj})\delta_{1kj} - \hat{\psi}_{1k}(T_{1kj})]$$

$$[\hat{\mu}_{1l}(T_{1lj})\delta_{1lj} - \hat{\psi}_{1l}(T_{1lj})].$$

Thus one can show easily with the Slutsky's theorem that the random vector $(T_{n_1} / \hat{\sigma}_1, \dots, T_{n_d} / \hat{\sigma}_d)'$ converges in distribution to a d -variate normal random vector with 0 mean vector and covariance matrix $P = (\rho_{kj})$, whose diagonal elements are all one and off-diagonal elements can be consistently estimated by $\hat{\rho}_{kl} = \hat{\sigma}_{kl} / (\hat{\sigma}_k \hat{\sigma}_l)$ for $k \neq l$. Therefore we have to approximate the tail probability, $\Pr\{T_n > t\}$ from the d -variate normal distribution to obtain the p -value. In case of the bivariate normal distributions with 0 mean vector and unit variances by varying the values of correlation coefficient, [13] tabulated the cumulative probability when both coordinates have the same values. However the tables are not sufficient for our purpose since they can not contain the cases for all values of correlation coefficient. Nowadays we may obtain the approximate probability of $\Pr\{T_n > t\}$ by using the pmvnorm function, which is provided by S-PLUS in case of bivariate data. For d -variate case with $d \geq 3$, we may use M_X program (cf. [11]) to obtain the approximate probability of $\Pr\{T_n > t\}$. By using the M_X program, we can compute the multiple integrals of the multivariate normal distribution up to dimension 10. The program and documentation can be downloaded from the website <http://www.vipbg.vcu.edu/mxgui>.

III. LIMITING POWER AND SIMULATION RESULTS

In this section, we consider the following location translation model for the consideration of the limiting power. For all $x \in R^d$, there is a $\theta = (\theta_1, \dots, \theta_d)' \in R^d$ such that $S_1(x) = S_2(x - \theta)$. Then under this model, our one-sided alternative can be restated as follows:

$$H_0 : \theta_1 \leq 0, \dots, \theta_d \leq 0 \quad \text{v.s.}$$

$H_1 : \text{at least one of } \theta_k \text{'s is strict greater than 0.}$

For the derivation of the limiting power of our tests, we consider the Pitman translation alternatives of the form: For each n and for each k , $k = 1, \dots, d$, let

$$H_{1n}^k : \theta_{kn} = c_{kn} / \sqrt{n},$$

where c_k is a fixed positive real number. Also let $\theta_n = (\theta_{n_1}, \dots, \theta_{n_d})'$. We assume that all the univariate test statistics which we consider in this paper, satisfy the assumptions and conditions of the section 3.8.3 (pp. 120-121) in [18]. Then from some straightforward calculations, we have the limiting power of the tests based on T_n as follows:

$$\lim_{n \rightarrow \infty} \Pr_{\theta_n} \{T_n > C_n(\alpha)\}$$

$$= 1 - \lim_{n \rightarrow \infty} \Phi_{\Sigma(\theta_n)} \left(C_n(\alpha) \frac{\sigma_{1n}(0)}{\sigma_{1n}(\theta_{1n})} - \frac{\mu_{1n}(\theta_{1n})}{\sigma_{1n}(\theta_{1n})}, \right.$$

$$\left. \dots, C_n(\alpha) \frac{\sigma_{dn}(0)}{\sigma_{dn}(\theta_{dn})} - \frac{\mu_{dn}(\theta_{dn})}{\sigma_{dn}(\theta_{dn})} \right)$$

$$= 1 - \Phi_{\Sigma(0)}(C(\alpha) - c_1 m_1, \dots, C(\alpha) - c_d m_d),$$

where $\Phi_{\Sigma(\theta_n)}$ and $\Phi_{\Sigma(0)}$ are the d -variate normal cumulative distribution functions with θ_n and 0 mean vectors and covariance matrices under Pitman translation alternatives and the null hypothesis, respectively. $C(\alpha)$ is such that

$$\lim_{n \rightarrow \infty} \Pr\{T_n > C(\alpha)\} = \alpha$$

$$\text{and } m_k = \lim_{n \rightarrow \infty} \mu'_{kn}(0) / (\sqrt{n} \sigma_{kn}(0))$$

for each k with the notation that μ'_{kn} is the first derivative of μ_{kn} .

Now we compare the performance of our procedure (T_n) with those of the procedures of [22] (U_n) and [16] (S_n) through simulation studies with S-PLUS. The following tables summarize the empirical powers for the bivariate case with a life time distribution and four different censoring distributions. The results are based on 1000 simulations with sample sizes $n_1 = 30$ and $n_2 = 40$ and the simulations have been carried out under the nominal significance level $\alpha = 0.05$. For the life time distribution, we considered the Marshall-Olkin type of bivariate exponential distribution, whose joint survival function is as follows: For each $i, i=1,2$,

$$S(x_{11}, x_{12}) = \Pr\{X_{11} > x_{11}, X_{12} > x_{12}\}$$

$$= \exp[-\lambda_{11}x_{11} - \lambda_{12}x_{12} - \lambda_{13} \min(x_{11}, x_{12})].$$

In all cases, we have generated the life time random vectors, (X_{11}, X_{12}) , with $\lambda_{11} = \lambda_{12} = \lambda_{13} = 1$ for each i and allowed to vary the values of the first component (θ_1) only of the second sample by adding values from 0.05 up to 0.7 in order to emphasize that we are dealing with the one-sided alternatives for the multiple endpoints data. For the censoring distributions, we considered the bivariate exponential distributions $E(\lambda_{11}, \lambda_{12})$ whose joint survival functions are of the form,

$$S_c(u_{11}, u_{12}) = \Pr\{U_{11} > u_{11}, U_{12} > u_{12}\}$$

$$= \exp[-\lambda_{11}u_{11} - \lambda_{12}u_{12}].$$

We note that the two components are independent for the censoring distributions. We considered four different cases

such as $\lambda_{11} = \lambda_{12} = \lambda_{21} = \lambda_{22} = 1$, $\lambda_{11} = \lambda_{21} = 1$ and $\lambda_{12} = \lambda_{22} = 2$, $\lambda_{11} = \lambda_{12} = 1$ and $\lambda_{21} = \lambda_{22} = 2$ and $\lambda_{11} = \lambda_{22} = 1$ and $\lambda_{12} = \lambda_{21} = 2$ for Tables 1 through 4, respectively. In all tables, we note that our procedure achieves better performance than those based on U_n and S_n regardless of censoring patterns. Therefore our procedure may be a reasonable alternative for nonparametric one-sided test of the right censored data with multiple endpoints with suitable choice of scores. Also we note that the procedures based on U_n and S_n show their performances in alternate fashion and the empirical powers vary with the censoring patterns. Thus one may consider that unknown censoring distribution may be one of the elements which determine the efficiency of test. Finally we note that the tests using the Gehan score obtain slightly higher empirical powers than those using the log-rank score in both procedures based on S_n and T_n and achieve the nominal significance level well.

IV. AN EXAMPLE AND SOME CONCLUDING REMARKS

For illustration of our procedure, we consider the NCGS data, which are presented in Table 1 of [23]. The data consist of the ordered paired times in days of the occurrence of gallbladder pain (the first component) and cholecystectomy (the second component) for 113 patients with floating gallstones of the placebo ($n_1 = 48$) and high dose of the drug chenodiol groups ($n_2 = 65$). In this example, it is of our interest to detect whether the high dose of the drug chenodiol for the treatment of cholesterol gallstones has any efficacy, which is indicated by delaying the occurrence of gallbladder pain or cholecystectomy in terms of time. Under the general alternatives, [23] obtained 0.042 and 0.145 as p -values by using the Gehan and log-rank scores, respectively. For the one-sided alternatives, the procedure by [22] gave 0.037 as its p -value. Also the procedure of [16] gave 0.016 and 0.036 as p -values for the Gehan and log-rank scores, respectively. In our case, when we use the Gehan score for both components, the values of T_n and $\hat{\rho}_{12}$ are 2.4579 and 0.637, respectively. The corresponding p -value is 0.013, which shows strong evidence of delay of the occurrence of gallbladder pain or cholecystectomy for the patients of the high dose group. Also if we use the log-rank score for both components, then we obtain that $T_n = 1.9735$ and $\hat{\rho}_{12} = 0.605$ and the corresponding p -value is 0.042. In this example, our procedure shows similar pattern with that of [16]. We note that in general, the procedures for the one-sided alternative produce more significant results than that of [23] and the tests based on the Gehan score give less p -value than those based on the log-rank score. We have noted that T_{kn} forms a class of linear rank statistics with varying the score function Q_k . Also [17] proposed another type of linear rank

statistics for right censored data based on the marginal likelihood, which may produce locally most powerful tests in linear model. [10] and [14] showed that the two types of linear rank statistics are equivalent. Thus one may consider improving power of tests by choosing some suitable form for Q_k . Thus we allowed Q_k to vary from component to component in this study. Also we note that it does not matter whether the covariance matrix of T_n is singular or not since we do not use the quadratic form for test statistics, which require the inverse of the covariance matrix. Therefore this point may be an advantage of our approach. In passing, we note that for each k , the sequence (T_{kn}) is consistent for testing $H_0^k : S_{1k} \leq S_{2k}$ against the one-sided alternatives $H_1^k : S_{1k} > S_{2k}$. This, in turn, implies that the sequence (T_n) is also consistent against the one-sided alternatives for the data with multiple endpoints. For the consideration of obtaining null distribution of T_n , we have used the large sample approximation theory. Therefore all the p -values obtained in the example are approximate. Also for obtaining these approximate probabilities, one may consider using the permutation principle (cf. [7]) or the bootstrap method (cf. [4]). Both the methods are extensively computer-oriented methodologies because of re-sampling procedures. The only difference between the two methods is as follows: The permutation principle re-samples without replacement whereas the bootstrap method does with replacement. In general, for multiple endpoints, when we apply the permutation principle or the bootstrap method to obtain the distribution for a given test statistic approximately, we have to consider obtaining the covariance matrix and its inverse for each stage of re-sampling, which may induce some problems such as large amount of computing time or singularity problem for covariance matrix when the form of test statistics is quadratic. For the maximal type of statistics, as we have already noted, we do not need to worry about the singularity problem. Also it takes much less time for computing since the inverse of covariance matrix is not necessary. On the other hand, when we use the maximal form, it is impossible to collaborate with the covariance structure into the distribution of test statistics explicitly. Therefore it would be worthwhile to investigate the asymptotic probability obtained from re-sampling methods in more detail. We will take the opportunity to report the results for this subject in the near future. Finally we note that [16] considered applying their nonparametric test to the bivariate data such as one endpoint is survival time and the other, binary response. Since our procedure is also nonparametric, we can also apply our procedure to the data with different types of endpoints.

REFERENCES

- [1] O. Barndorff-Nielsen and M. Sobel, "On the distribution of the number of admissible points in a vector random sample," Theory of Probability and its Applications, vol. 11, pp. 249-269, 1966.

- [2] G. K. Bhattacharyya and R. A. Johnson, "A layer rank test for ordered bivariate alternatives," *The Annals of Mathematical Statistics*, vol. 41, pp. 1296-1310, 1970.
- [3] J. M. Boyett, and J. J. Shuster, "nonparametric one-sided tests in multivariate analysis with medical applications," *Journal of American Statistical Association*, vol. 72, pp. 665-668, 1977.
- [4] B. Efron, B. "Censored data and the bootstrap," *Journal of American Statistical Association*, vol. 76, pp. 312-319, 1981.
- [5] H. Gao, I. B. Aban and C. R. Katholi, "Properties of a one-sided likelihood ratio test as applied to pool screening," *Communications in Statistics-Theory and Method*, vol. 43, pp. 4546-4565, 2014.
- [6] R. D. Gill, "Censoring and Stochastic Integrals," *Mathematical Center Tract 124: Mathematische Centrum, Amsterdam*, 1980.
- [7] P. Good, "Permutation Tests: A practical Guide to Resampling Methods for Testing Hypotheses," Second Edition, New York, Springer, 2000.
- [8] R. A. Johnson and K. G. Mehrotra, "Nonparametric tests for ordered alternatives in the bivariate case." *Journal of Multivariate Analysis*, vol. 2, pp. 219-229, 1972.
- [9] B. Kline, "The Bayesian and frequent approaches to testing a one-sided hypothesis about a multivariate mean," *Journal of Statistical Planning and Inference*, vol. 141, pp. 3131-3141, 2011.
- [10] K. G. Mehrotra, J. E. Michalek and D. Mihalko, (1982) A relationship between two forms of linear rank procedures for censored data," *Biometrika*, vol. 69, pp. 674-676, 1982.
- [11] M. C. Neale, G. Xie, W. M. Hadady and S. M. Boker, "Introduction to the Graphical User Interface," Department of Psychiatry, Medical College of Virginia, Richmond, 1998.
- [12] P. C. O'Brien, "Procedures for comparing samples with multiple endpoints," *Biometrics*, vol. 40, pp. 1079-1087, 1984.
- [13] D. B. Owen, "Handbook of Statistical Tables," Addison-Wesley, New York, 1962.
- [14] H. I. Park, "A Study on the scores for right censored data," *Journal of Statistical Planning and Inference*, vol. 86, pp. 101-111, 2000.
- [15] H. I. Park, J. H. Na and M. M. Desu, "Nonparametric one-sided tests for multivariate data," *Sankhya*, vol. 63, Series B, pp. 286-297, 2001.
- [16] S. J. Pocock, N. L. Geller and A. A. Tsiatis, "The analysis of multiple endpoints in clinical trials," *Biometrics*, vol. 43, pp. 487-498, 1987.
- [17] R. L. Prentice, "Linear rank tests with right censored data," *Biometrika*, vol. 65, pp. 167-179, 1978.
- [18] M. L. Puri and P. K. Sen, "Nonparametric Methods in Multivariate Analysis," Wiley, New York, 1971.
- [19] L. J. Schoenfeld and Lachin. The STEERING COMMITTEE and the NCGS GROUP, "Chenodiol (Chendeoxycholic Acid) for dissolution of gallstones: The National Cooperative Gallstone Study," *Annals of Internal Medicine*, vol. 95, pp. 257-282, 1981.
- [20] S-Plus 4 Programmer's Guide, Data Analysis Product Division, Mathsoft Inc., Seattle, Washington, 1997.
- [21] T. Wang and L. Wu, "Multivariate one-sided tests for nonlinear mixed-effects models," *Canadian Journal of Statistics* vol. 41, pp. 453-465, 2013.
- [22] L. J. Wei and M. W. Knuiman, "A one-sided rank test for multivariate censored data," *Australian Journal of Statistics*, vol. 29, pp. 214-219, 1987.
- [23] L. J. Wei and J. M. Lachin, "two-sample asymptotically distribution-free test for incomplete multivariate observations," *Journal of American Statistical Association*, vol. 79, pp. 653-661, 1984.

AUTHOR'S PROFILE

Professor Hyo-Il Park had been educated and received his B.E. degree at the Korea University in Korea and Ph.D. degree in Statistics at the State University of New York at Buffalo in USA. He had published more than 30 research papers at the international journals including *Biometrika* with the title of 'A note on the relation between two forms of linear rank statistics for right censored and grouped data in 1997. He is a member of Korean Statistical Society and International Indian Statistical Association. His main academic interests are of the overall statistical applications with the testing problems and application of the permutation principle.

Test Statistics	(θ_1, θ_2)								
	(0, 0)	(0.05, 0)	(0.1, 0)	(0.2, 0)	(0.3, 0)	(0.4, 0)	(0.5, 0)	(0.6, 0)	(0.7, 0)
U_n	0.046	0.103	0.209	0.464	0.694	0.848	0.936	0.972	0.982
S_n (Gehan)	0.054	0.130	0.245	0.450	0.626	0.750	0.823	0.878	0.907
S_n (log-rank)	0.057	0.101	0.186	0.305	0.492	0.576	0.682	0.796	0.834
T_n (Gehan)	0.046	0.145	0.362	0.780	0.958	0.993	1.000	1.000	1.000
T_n (log-rank)	0.059	0.104	0.203	0.490	0.748	0.905	0.940	0.985	0.996

Table 1. Empirical powers when $\lambda_{11} = \lambda_{12} = \lambda_{21} = \lambda_{22} = 1$

Test Statistics	(θ_1, θ_2)								
	(0, 0)	(0.05, 0)	(0.1, 0)	(0.2, 0)	(0.3, 0)	(0.4, 0)	(0.5, 0)	(0.6, 0)	(0.7, 0)
U_n	0.029	0.102	0.166	0.360	0.554	0.768	0.849	0.917	0.945
S_n (Gehan)	0.052	0.110	0.258	0.453	0.687	0.830	0.906	0.922	0.950
S_n (log-rank)	0.060	0.115	0.176	0.319	0.502	0.623	0.786	0.825	0.898
T_n (Gehan)	0.049	0.119	0.331	0.777	0.956	0.996	1.000	1.000	1.000
T_n (log-rank)	0.061	0.112	0.201	0.407	0.736	0.902	0.969	0.985	0.994

Table 2. Empirical powers when $\lambda_{11} = \lambda_{21} = 1$ and $\lambda_{12} = \lambda_{22} = 2$

Test Statistics	(θ_1, θ_2)								
	(0, 0)	(0.05, 0)	(0.1, 0)	(0.2, 0)	(0.3, 0)	(0.4, 0)	(0.5, 0)	(0.6, 0)	(0.7, 0)
U_n	0.035	0.112	0.203	0.461	0.703	0.874	0.939	0.971	0.984
S_n (Gehan)	0.040	0.117	0.244	0.448	0.636	0.698	0.774	0.812	0.837
S_n (log-rank)	0.054	0.097	0.176	0.311	0.479	0.594	0.723	0.783	0.836
T_n (Gehan)	0.049	0.146	0.396	0.823	0.968	0.999	1.000	1.000	1.000
T_n (log-rank)	0.055	0.114	0.226	0.531	0.775	0.921	0.976	0.993	0.999

Table 3. Empirical powers when $\lambda_{11} = \lambda_{12} = 1$ and $\lambda_{21} = \lambda_{22} = 2$

Test Statistics	(θ_1, θ_2)								
	(0, 0)	(0.05, 0)	(0.1, 0)	(0.2, 0)	(0.3, 0)	(0.4, 0)	(0.5, 0)	(0.6, 0)	(0.7, 0)
U_n	0.032	0.098	0.201	0.449	0.688	0.855	0.938	0.962	0.981
S_n (Gehan)	0.049	0.127	0.243	0.449	0.626	0.752	0.770	0.830	0.843
S_n (log-rank)	0.058	0.094	0.163	0.346	0.492	0.630	0.708	0.807	0.848
T_n	0.044	0.154	0.367	0.815	0.977	0.999	1.000	1.000	1.000

(Gehan)									
T_n (log-rank)	0.058	0.128	0.223	0.517	0.811	0.920	0.966	0.991	0.997

Table 4. Empirical powers when $\lambda_{11} = \lambda_{22} = 1$ and $\lambda_{12} = \lambda_{21} = 2$