ESTIMATING THE DOSE RESPONSE PATTERNS IN A PHASE 2 CLINICAL TRIAL

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There is a large literature for the test and estimation problems in the dose response analysis. They are however, not answering well for proposing an optimal dose level to be employed in actual clinical treatments. For the purpose more appropriate approach will be the multiple comparisons of several interesting isotonic contrasts. It seems that to employ more basic contrasts for multiple comparisons will meet better for a wide range of isotonic contrasts but with an inevitable loss of efficiency. Then an interesting problem will be which and how many isotonic contrasts should be included in the basic contrasts for multiple comparisons. Now it is shown in this paper that a most appropriate choice will be the set of K-1 change-point type contrasts for K dose levels, which are characterized as the corner vectors of the polyhedral cone defined by the monotone response patterns. Then all the isotonic contrasts can be expressed as a unique and positive linear combination of those basic contrasts so that the simultaneous confidence intervals (SCI) can be easily extended to all the isotonic contrasts. If we replace one of those basic contrasts by another isotonic contrast then the positiveness fails and we cannot extend the SCI to some of the isotonic contrasts. Adding other contrasts to basic contrasts will lose the uniqueness. Regarding the efficiency it is remarkable that even for detecting the linear trend adding linear trend type contrast cannot contribute anything.