Linear Mixed Effect Model for Setup positioning uncertainty

The vector magnitude (VM) of table shifts was calculated, providing a 3-dimensional expression of table shifts following CBCT. VM is defined as:

$$\text{Vector Magnitude} = \sqrt{(\Delta x^2 + \Delta y^2 + \Delta z^2)}$$

where x= table shift in the transverse direction, y= table shift in the superior-inferior direction, and z = table shift in the anterior-posterior direction. The table shifts in the x, y, and z direction as well as the VM were each analyzed as a dependent variable using a linear mixed-effect (LME) model. A LME model is the extension of the regular linear regression model by simultaneously adjusting for the fixed effects and random effects. An explanatory variable is treated as a fixed effect when its systematic (non-random) association with the dependent variable is of interest. An explanatory variable is treated as a random effect when its contribution to any particular measurement of the dependent variable may be viewed as a random "error" from an infinite population of values. In our work, institutions and subjects may be considered as random effects as there are no known associations between them and the dependent variable respectively, nor such association is of interest. We assumed that the random effect variables were normally distributed with a zero mean and an unknown standard deviation that was estimated during the overall model fitting procedure. The use of random effects allow one to account for the random errors (which are integral to any regression model) that may be attributed to different sources, such that our estimation and inference on the fixed effects become more appropriate and relevant.

Formally, we considered the following LME model:

$$Y_{ijk} = \beta_0 + v_{0k} + u_{0jk} + X\beta + e_{ijk}$$

Where Y_{ijk} is the table shifts (x, y, z, or VM) of the *i*th measurements of patient *j* at institution *k*, v_{0k}, u_{0jk} and e_{ijk} are random effects which each follows a normal distribution with mean 0 and variance σ_v^2 , $\sigma_u^2$and σ_e^2 respectively. σ_v^2 is the inter-institution variance that quantifies the uncertainty at the institutional level, σ_u^2 is the inter-patients variance that quantifies the uncertainty at the patient level across multiple measurements, and σ_e^2 is the within patients variance that quantifies the random uncertainty applicable to every measurement. After accounting for the systematic uncertainties (inter-patient and inter-institution error) and random uncertainty (within patient error) for table shifts in the x, y, and z directions as well as for the VM, the intercept β_0 represents the group mean error that universally exists across all measurements. The fixed effect β corresponds to the difference in the dependent variable between various levels of some explanatory variable of interest, e.g., male vs. female. Of note, routine repeat CBCT was not performed after treatment. As such, there was no estimation of the intra-fraction uncertainty.