

### **Supplemental Appendix III. Unsupervised Hierarchical Clustering.**

In the present study, we used unsupervised clustering to measure the efficacy of the texture based radiomic features in distinguishing between the Super Responders and the Non-super Responders. Specifically, hierarchical clustering was used to evaluate the discriminative ability of the different groups of features.<sup>48</sup> Hierarchical clustering, also known as hierarchical cluster analysis, is an algorithm that groups similar objects into groups called clusters. The endpoint is a set of clusters, where each cluster is distinct from each other cluster, and the objects within each cluster are broadly similar to each other. Hierarchical clustering starts by treating each observation as a separate cluster. Then, it repeatedly identifies the two clusters that are closest together followed by merging the two most similar clusters. This iterative process continues until all the clusters are merged together. The main output of hierarchical clustering is a dendrogram, which shows the hierarchical relationship between the clusters. Hierarchical clustering typically works by sequentially merging similar clusters. This is known as agglomerative hierarchical clustering. Theoretically, it can also be done by initially grouping all the observations into one cluster, and then successively splitting these clusters. This is known as divisive hierarchical clustering. However, the agglomerative clustering technique is the one which is most commonly used for clustering of medical images.