

## Appendix E1

We investigated the optimal number of subregions into which tumors should be segmented by looking at the change in the likelihood function of the segmentation result with respect to the number of subregions (Fig E1). In general, the likelihood function monotonically increases but becomes saturated beyond a certain point, because adding more subregions does not improve the model. This point is defined as that where the maximum second derivative occurs and represents the optimal trade-off between data fitting and model complexity.

## Appendix E2

To calculate the joint histogram, we decomposed the joint probability distribution of the postcontrast T1-weighted and FLAIR signal intensities as their respective marginal distributions and their copula. Copula is the joint probability of uniformly distributed variables obtained through probability integral transformation (33). In other words, copula can be considered as a special two-dimensional (2D) histogram of two variables (here, the postcontrast T1-weighted and FLAIR signal intensities), which are appropriately standardized so they always lie within the range of 0 and 1 (Fig E2). Such a 2D histogram (ie, copula) no longer depends on the marginal distributions of each variable. Here, it is used as a systematic way to normalize gray scales while preserving the intrinsic correlation between postcontrast T1-weighted and FLAIR signal intensity. Finally, marginal distributions were approximated by their quantiles and copula by the binned 2D histogram. In this study, we used ten bins to compute the quantiles of each of the postcontrast T1-weighted and FLAIR signal intensities and  $5 \times 5$ , or 25, binned 2D histograms to approximate their copula, resulting in a total of 45 image features based on a 2D joint histogram.

## References

33. Durante F, Sempi C. Copula theory: an introduction. *Lect Notes Stat* 2010;198:3–31.