Supplementary Information

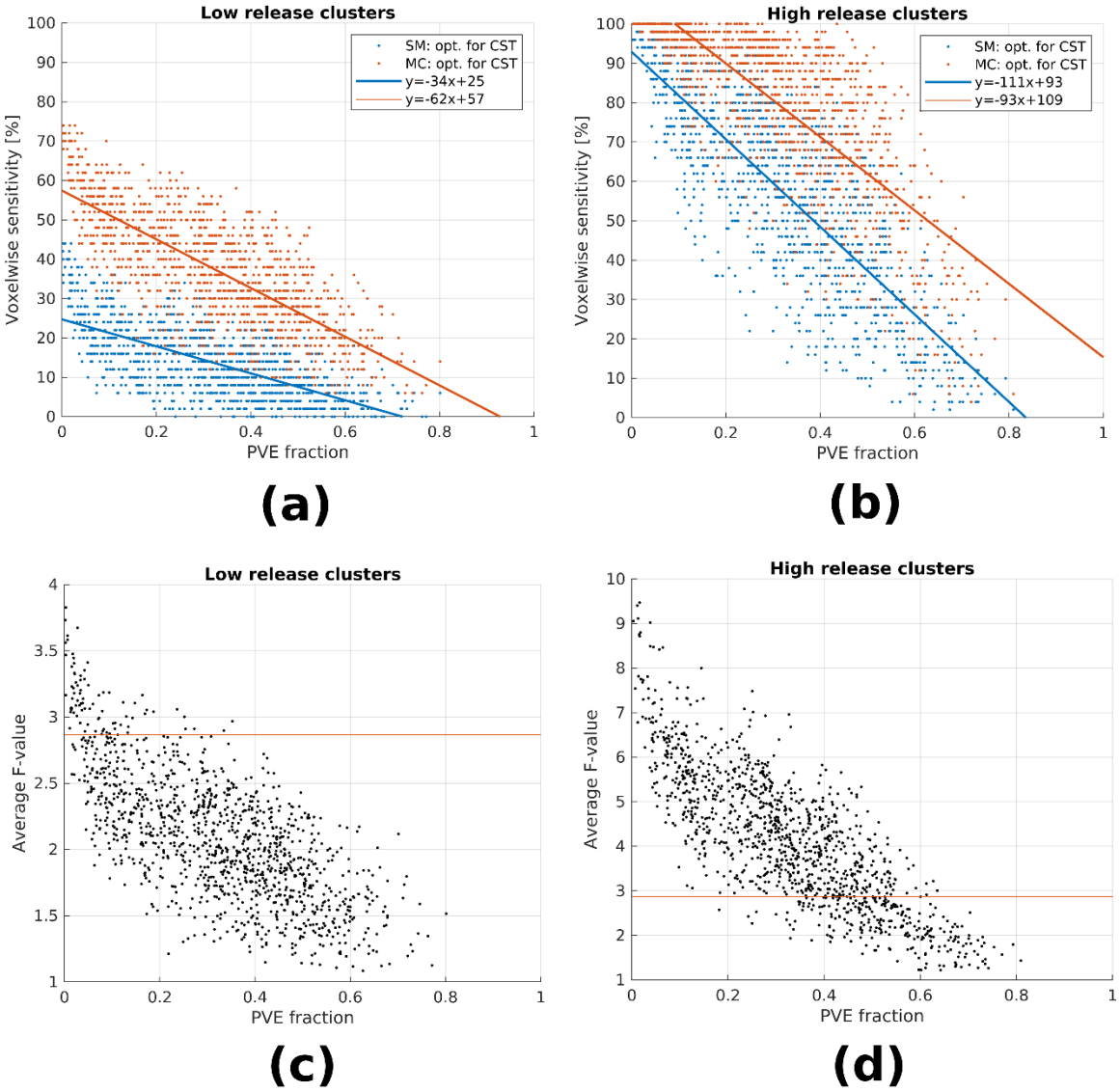

Figure S1: Scatter plots of voxelwise sensitivity as a function of PVE fraction for **(a)** low release clusters and **(b)** high release clusters. The average voxel F-values over all 50 noisy realizations are plotted in **(c)** for low release clusters and in **(d)** for high release clusters. The red line indicates the F-test threshold value.

The voxelwise sensitivity maps of Figure 3a in the main text demonstrate how DA release in edge voxels in a cluster is generally detected with lower sensitivity than in the central voxels of a cluster. Edge voxels are especially corrupted by PVE through mixing the release TAC in the voxel with adjacent high binding baseline TACs—diminishing the observable DA-induced perturbation in the release TAC. Consequently, the computed F-value will be lower than that of the uncorrupted version of the TAC, potentially falling below the F-test threshold

and thus reducing sensitivity. As the MC method probabilistically allows such voxels to still be accepted, we expect that the voxelwise sensitivity of voxels with PVE will be improved. A visual inspection of Figure 3a demonstrates that this is indeed the case.

We assess the amount of PVE corruption to a voxel by starting with a binary mask of each cluster and filtering the mask with the PSF of the scanner (modeled as a 2.5 mm Gaussian). Subtracting the voxelwise values within the cluster after filtering from the value before filtering (i.e. one) defines the PVE fraction; values close to zero are relatively uncorrupted by voxels outside the cluster, and values close to one are almost entirely corrupted. Even with the high resolution of our scanner (~2.5 mm), as see in Figure S1 almost all voxels are affected by PVE to some degree for the cluster size range tested in this work (300-500 $(1.22\ mm)^3$ voxels).

In Figure S1a-b, we plot the voxelwise sensitivity as a function of PVE fraction for the standard and MC methods optimized for CST, stratified by cluster release level. In both release levels, there is a strong negative relationship between voxelwise sensitivity and PVE fraction, as expected. The improvements in sensitivity in high PVE fraction voxels can be explained by the MC method probabilistically allowing these voxels—falling below the significance threshold more often (Figure S1c-d)—to be reclassified as release voxels. As well, in low release clusters, lower PVE fraction voxels may be detected fairly reliably in the standard method, but because they only comprise a subset of the voxels within the true cluster, the detected cluster size may be lower than the CST. The MC method encourages the cluster size to increase beyond the CST through the parity term and through allowing DA release in higher PVE fraction voxels to be more reliably detected. This claim is supported by not only higher voxelwise sensitivity across all PVE fractions, but by higher binary sensitivity in all low release clusters as well (Figure 3c in the main text).