Purpose & Objectives
Ictal and interictal SPECT have commonly been used to help guide electrode placement as part of the presurgical localization of the seizure focus in epilepsy. Visual detection of the hyperperfused area on the ictal scan relative to the interictal can be challenging. Our goal is to utilize an automated method for highlighting statistically significant differences in images and apply this to ictal and interictal SPECT.

Methods & Materials
Ten patients with ictal and interictal SPECT scans were evaluated using an automated tool which rigidly registered the ictal to interictal scan, auto-normalized the image contrast to allow for subtraction of the images, subtracted the normalized activity values in the two images, and then performed cluster analysis to highlight statistically significant differences based on the size and magnitude of the differences (see flow diagram). A cluster requirement of p < 0.05 and a Z-score > 2.4 was used. The minimum cluster size was automatically calculated based on the p-value and Z-score. Significant clusters were compared to localization determined using post-surgical resolution of seizure symptoms (n = 5) or intracranial EEG localization (n = 5).

Auto-Normalization Method:
The Auto-Normalization algorithm seeks to minimize the differences in voxel values between two scans. To reduce the influence of outliers an iteratively-reweighted least-squares fit (IRLS) method is used. First a normal least-squares fit of the data is performed, outlier voxels are identified, a scaling factor is applied to minimize their influence, and then the fitting is repeated. This process is repeated until there is a convergence on the best fit for the normal data.

Cluster Analysis Method:
The cluster analysis algorithm models the distribution of subtraction values and filters out any subtraction values less than the Z-score (standard deviation) threshold. The Gaussian Random Field Theory is used to determine the cluster size which corresponds with the p-value specified. Any voxels which are individually significant beyond the threshold, but which are not part of a cluster the specified size or greater, are removed from the subtraction image.

Results
For all 10 patients the location of the largest (2.9-34.8ml) and most statistically significant cluster corresponded to the location of surgical resection or intracranial EEG localization. Additional smaller (1.75-3.36ml) and less statistically significant clusters were also found in 5/10 patients at a distant location: cerebellum (n=3), left thalamus (n=1), and right temporal lobe (n=1).

Conclusion
The automated subtraction method for highlighting statistically significant differences between ictal and interictal SPECT showed excellent agreement with surgical and intracranial EEG results for seizure localization. This method shows promise as an aid in the presurgical seizure localization for epilepsy.