

NSA SERVICES: IMAGE ANALYSIS

ALZHEIMER PLAQUE BURDEN: PARTICLE COUNT AND DENSITOMETRY

Mouse models of Alzheimer disease are designed to display neuritic plaques similar to those found in humans with the disease. Drugs that may potentially retard plaque development or prevent the creation of plaques are then tested on these mouse models. Part of the determination of the efficacy of a drug candidate is to measure the plaque load, the percent of cortex and/or hippocampus that is occupied by plaques. Other meaningful measures that should be considered when measuring efficacy include quantification of the total number of plaques and the frequency of plaque sizes. Below is an illustration of how NSA gathers the data.



NSA Neurohistology: Neuritic plaques are revealed in freeze-cut, free-floating sections with the Campbell-Switzer staining method. Image analysis is performed on other stains, such as A β 1-40, A β 1-42, Thioflavin S, Congo Red, or any other stains that would reveal Alzheimer plaques.

NSA Analysis: High-resolution digital images of designated sections are captured. The percent of the area of cortex-hippocampus occupied by plaques is obtained through the following steps:

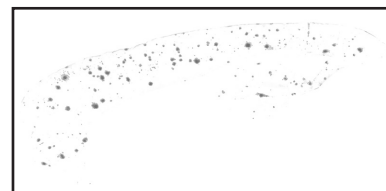
- Outline cortex and hippocampus and create a separate “traced” image.
- From the traced image, two other images are created in order to:
 1. Determine the total area of cortex-hippocampus.
 2. Determine the individual and total area of the plaques.



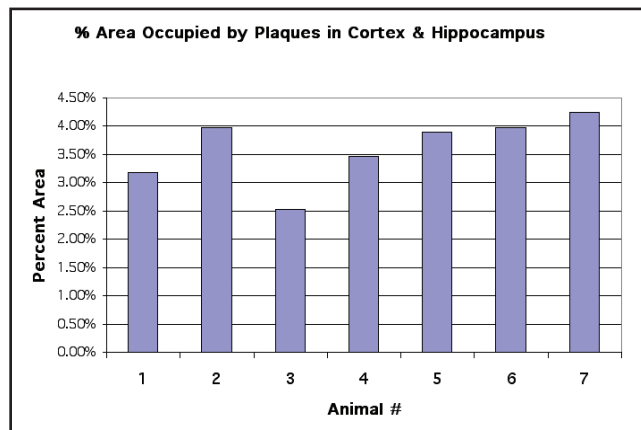
Traced image



The area of interest is rendered totally black to get total area.



Analyze Particles: Individual plaques are automatically outlined, and the area is calculated for each.



Compilation of data from several animals yields a histogram within which comparisons of different treatment groups and controls can be made.

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ALZHEIMER PLAQUE BURDEN: PARTICLE COUNT AND DENSITOMETRY (continued)

In addition to percent area occupied and plaque density, visualizing the number of plaques of different sizes may prove valuable. In the two images below, case #1 appears to have numerous large plaques but not many small ones. In #2, however, many small plaques accompany numerous large plaques. This qualitative difference is graphically depicted by plotting the cumulative frequency of sizes for each as shown here, from which quantitative comparisons can be derived.

