Brain computer interfaces (BCI’s) and implantable cortical devices have recently emerged in research as promising treatment methods for a variety of neurological problems such as motor dysfunction, memory loss, and sudden onset seizures. The number of people currently suffering from a loss of nervous system function as a result of neurodegenerative diseases or injury creates a need for reliable neural prostheses. The autoimmune response of the Central Nervous System (CNS) when introduced with a foreign object such as an electrode shank quickly impedes signal strength and degrades the functional life of the device. Two different experimental methods were used to analyze the host tissue responses to implantation with silicon micro-electrodes and micro-wires. In situ device capture histology was used to obtain fluorescent images of neurons and activated microglia in rat and mouse brain slices with an electrode still present. A recent method, CLARITY, was used to obtain images of green fluorescent microglia in un-sectioned mouse brains post mortem. Both methods utilized a laser-equipped inverted confocal microscope to obtain the images. The results show that increasing tissue transparency with CLARITY and two photon imaging can give detailed information about the tissue immune response in an implanted brain. Through comparison to various controls, changes in density, movement, and conformation of neurons and microglia surrounding electrode implants will help increase the understanding of the cellular mechanisms involved and likely be used to identify future targets for research.