Positron emission tomography (PET) has recently emerged as a powerful tool to investigate the progression of Alzheimer's disease (AD) throughout both its clinical and preclinical phases. The field of AD research has emphasized the use of PET to characterize the progression of amyloid-β plaques (Aβ), neurofibrillary tangles (NFTs) and neurodegeneration. This dissertation details the characterization of AD biomarker progression in Down syndrome (DS) using [^{11}C]PiB PET for Aβ, [^{18}F]AV-1451 PET for NFTs, and [^{18}F]FDG PET for glucose metabolism/neurodegeneration.

To improve Aβ PET quantification, the amyloid load metric ($Aβ_L$) was explored and compared to the more conventional standardized uptake value ratio metric (SUVr). The longitudinal $Aβ_L$ data was used to identify the earliest stages of Aβ accumulation in DS, and rates of Aβ change were compared to late-onset AD. Using AV-1451 PET, NFT progression in DS was explored across the conventional Braak staging of NFT pathology in late-onset AD. AV-1451 scores were compared against different groups of DS based on Aβ status to identify whether individuals with DS in the earliest stages of Aβ progression display early NFT progression. Finally, FDG PET was evaluated as a potential marker of neurodegeneration in DS. Glucose metabolism in DS was explored in relation to Aβ using FDG across typically affected regions in late-onset AD. FDG was directly compared to neuropsychological measures of cognition that have been validated for use in DS to monitor AD-related cognitive decline.

Using PiB PET, the $Aβ_L$ metric allowed for improved quantification of Aβ in DS compared to the conventional SUVr. With $Aβ_L$, PET was able to identify Aβ accumulation much earlier than previously achievable in the preclinical AD phase. When combined with NFT PET, these early Aβ accumulators evidenced significant NFT pathology in the early Braak stage regions, potentially indicating that these biomarkers emerge at the same time during AD progression. With FDG PET, glucose hypometabolism was highly associated with measures of cognitive decline. The findings presented in this dissertation highlight the utility of PET imaging for early detection of AD biomarker progression and for characterization of the preclinical and clinical stages of AD in DS.