

Application for QIBA Project Funding

<b>Title of Proposal:</b> Analyses to Support Amyloid Imaging Profile Development		
QIBA Committee/Subgroup: Amyloid Imaging Profile Working Group		
NIBIB Task Number(s) which this project addresses: 13, 18		
<b>PI (Project Coordinator or Lead Investigator Information)</b>		
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Institution/Company: ADM Diagnostics, LLC		
Total Amount Requested:		

**1. Project Description**

The purpose of the proposed project is to address information gaps relevant to the development of image processing and analysis recommendations for the amyloid imaging profile. The first of these is the impact of subject motion. The second two are reference region definition and target region of interest definition, as evaluated under non-motion conditions and as related to subject motion effects. To provide this information, we propose to perform a set of motion simulations and reconstructions using de-identified florbetapir scans, analyze the resulting scans using variations in reference and target region definitions, evaluate the impact on test-retest variability, and put into context of other analyses we have performed and with the literature. We have identified, through a collaborative approach with Siemens and Avid Radiopharmaceuticals, the raw amyloid image data and reconstruction hardware and software platform necessary to accomplish these objectives.

**2. Objectives and rationale**

The specific objectives of this work are to:

- 2.1 Quantify the effect of subject motion, including misalignment between emission and transmission scan, on measured SUVR

*Rationale:* Subject motion is a major source of variability impacting the SUVR measurement that is the focus of the Profile claim(s). There are a limited number of studies on the effects of motion and motion correction; Mourik et al, 2009 and Ikari et al, 2012 are among the most informative and relevant. However, there is a gap in specific information for the amyloid target, likely processing and analysis methods, and context of use of the Amyloid Imaging Profile. A systematically generated set of data using a relevant amyloid tracer, applicable processing and analysis approaches, and controlled motion conditions would enable specific quality control recommendations and tolerance definition.

- 2.2 Quantify the effect of reference region selection, boundary definition, and spatial positioning upon measured SUVR

*Rationale:* A major influence (or confound) in SUVR repeatability is the reference region. Several published studies have made use of ADNI and other data to compare the group means and variance across different reference regions (Chen et al, 2015; Landau et al, 2015; Brendel et al, 2015; Matthews et al, 2014). Since different tracer manufacturers and protocols may recommend different reference regions, the Profile is not intended to prescribe use of a particular reference. However, in

order to enable recommendations achieving the tolerances cited by the Profile Claim(s), it is important to extend this work to quantify impact at an individual level of variations in tissue selection, boundary definition, mask placement, and susceptibility to the motion effects studied in objective 2.1 above.

#### 2.4 Quantify the effect of target region definition upon measured SUVR

*Rationale:* A lesser, but still significant influence (or confound) in SUVR repeatability is target region definition. While some studies (e.g. Landau et al, 2014) have shown correlation between different overall methods (composites of target, reference, and boundary definition methods), there is a gap in quantifying the impact of well-defined variations in target region definition at the individual level, including susceptibility to motion. Filling this gap would enable specific Profile recommendations.