There is an urgent need for innovative diagnostic strategies to improve the classification of ischemic stroke (IS) of undetermined etiology, which continues to affect approximately one-third of patients despite advances in current classification systems. In such cases, therapeutic uncertainty increases the risk of adverse outcomes. Given the global impact of stroke as a leading cause of death and long-term disability, this project seeks to provide the foundation for more accurate etiological diagnosis.

We will advance IS classification by performing a comprehensive spectroscopic characterization of thrombectomy-retrieved clots (TRCs), utilizing vibrational spectroscopy (VS)—specifically Raman spectroscopy (RS) and Fourier-transform infrared spectroscopy (FTIR)—in combination with complementary reference methods. These include atomic force microscopy (AFM) to assess topography, mechanical properties, and fibrin architecture; histological and immunohistochemical staining for morphological evaluation; chiroptical spectroscopy and proteomics for detailed protein profiling. This multimodal analytical approach will significantly expand current knowledge of TRC composition and its relevance to stroke pathophysiology.

The primary scientific objective is to generate novel insights into the biochemical and structural heterogeneity of TRCs across various IS subtypes. Identified spectroscopic signatures will serve as a valuable resource for translational research and potential clinical applications. The project will also establish the groundwork for an operator-independent, label-free, and fully automated method for TRC characterization, intended for integration into clinical workflows following intervention. The resulting spectroscopic profiles will introduce an innovative biochemical parameter capable of refining and extending current IS classification frameworks. Incorporating this advanced data into clinical practice could substantially improve etiological prediction, guide treatment selection, and enhance the effectiveness of secondary prevention strategies.

Our prior findings, have demonstrated the diagnostic potential of VS in differentiating large vessel disease from cardioembolic stroke. Building on this foundation, the project will proceed in three stages: (1) detailed chemical, morphological, and structural characterization of TRCs across IS subtypes; (2) development of classification algorithms based on RS/FTIR data for semi-automated TRC diagnosis; and (3) application of these methods to improve classification of TRCs from patients with previously undetermined stroke etiology.

The anticipated outcome is a comprehensive biochemical and spectroscopic framework for TRC characterization, forming the basis for future automated diagnostic tools. Integration of this data into existing clinical algorithms has the potential to transform IS classification, enhance patient stratification, and enable more precise therapeutic decision-making. Moreover, the insights generated will contribute to a broader understanding of stroke pathophysiology and inform future updates to clinical classification guidelines.