Deep vein thrombosis (DVT) of the lower limb is a health condition that arises when blood clots develop in the deep veins of the leg. This occurs due to pathological changes in the blood vessels or the blood itself. This research will focus on PTS which can be defined as chronic venous insufficiency presenting symptoms in the limb following DVT. Patients may experience pain, swelling, heaviness of the limb and in extreme cases, ulceration of the affected limb - all significantly reducing the quality of life. One of the factors responsible for clinical symptoms of venous thrombosis are blood flow changes, such as abnormal vortices and retrograde flow which may occur especially at vessel bifurcations and behind valves. Therefore, understanding the influence of thrombosis on blood flow could aid the treatment of PTS.

Computational Fluid Dynamics (CFD) approaches have been applied to the cardiovascular system for several decades and vary in their complexity. Three-dimensional models provide detailed information about the haemodynamics of local vascular regions (e.g., regions prone to thrombosis such as venous bifurcations). The computational cost and challenging design of 3D CFD models hinders their translation to routine clinical practice. Statistical shape models (SSM) provide an effective method to quantify the geometric properties of a number of complex shapes. The combination of SSM and CFD has the potential to improve clinical interpretation of computational analysis, characterising the influence of complex 3D anatomy on local haemodynamics, and may also reduce the computational cost of translating these technologies to the clinic.

Sensitivity analysis is crucial when developing a model to understand how uncertainty propagates from inputs to outputs, especially, when model outputs identify biomarkers of disease states or support clinical decisions. Recent publications have demonstrated the feasibility of using Statistical Shape Models (SSM) to reduce the complexity of variation of 3D anatomy to the form of shape modes which can be used to represent complex variability within patient cohorts. Such a representation allows sensitivity analyses to be undertaken in relation to the characterisation of individual patient anatomy in terms of individual shape modes, significantly reducing the degrees of freedom to be considered.

This project will use both idealised complex geometries described using CAD models and patient-specific anatomical data obtained by segmentation of 3D medical imaging modalities (e.g. MRI and CT) to examine the relationship between local 3D venous anatomy and CFD metrics associated with risk of thrombosis (e.g. low wall shear stress). SSM approaches will then be used to quantify shape variation in the patient cohort and sensitivity analysis will be used to quantify the relationship between shape modes and CFD metrics. This research will investigate the possibility of changing typical CFD workflow to reduce the number of computationally expensive 3D simulations. The hypothesis of the proposed project is that an SSM approach can be used to characterise the link between local 3D venous anatomy and the potential for thrombus formation, informed by CFD analysis. Once established such a workflow could deliver significant benefits in improving clinical decision making by delivering computational efficient approaches to patient-specific simulation.

The approaches described in this proposal are state-of-the-art with recent publications focussing on research questions associated with coronary and cardiac disease. The application of these technologies to the study of DVT and PTS is novel and has potential to significantly enhance the information available to clinicians to inform decision making both before and during interventions (e.g., choice of stent size and location). The project will develop quantitative metrics to characterise anatomical features (e.g., shape metrics) and the nature of blood flow for individual patients (using computational fluid dynamics, CFD) which are not currently available in the clinic. The project will use retrospective clinical data collected at the Royal Free London Vascular Surgery clinic, London, UK (for which HRA approval was granted in May 2023). All data will be anonymised prior to use.

The project will address novel scientific questions in particular contributing to emerging frameworks for model Verification, Validation and Uncertainty Quantification (VVUQ) both in this specific clinical application and more generally. Such activity is strongly aligned with state-of-the-art developments in clinical translation of computational models and complements broader activities in both the Sano Centre and the wider scientific community (as evidenced by the establishment of the VPH institute (www.vph-institute.org/) and the Avicenna Alliance (https://avicenna-alliance.com/)).

Ultimately, this research project will provide a workflow to assess whether patient-specific CFD is necessary or whether SSM can provide sufficient geometric information to characterise new patient-specific data sets and accurately predict clinically relevant blood flow metrics.