

| Project Details |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| Project Code    | CMD27Br Hart                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Title           | Vascular morphology and haemodynamic risk of intracranial aneurysm in aortic coarctation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Research Theme  | Cardiometabolic Disease                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Project Type    | Dry lab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Summary         | Aortic coarctation (CoA) is a common congenital heart disease, and even after successful repair, patients face elevated lifelong risk of hypertension, stroke, and intracranial aneurysm (IA). Why only a subset of patients develop these complications remains poorly understood, and no validated tools exist to identify who is at highest risk. This project will combine patient-specific 3D vascular reconstruction, machine learning, and computational fluid dynamics (CFD) to characterise the relationship between aortic and cerebrovascular morphology, blood flow patterns, and aneurysm risk in CoA. The aim is to generate the anatomical and haemodynamic evidence base needed for more targeted, personalised screening strategies.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Description     | <p><b>BACKGROUND.</b> Aortic coarctation accounts for 5-8% of congenital heart disease and, despite successful surgical repair, leaves patients at persistently elevated risk of hypertension, coronary artery disease, heart failure and stroke. Evidence links CoA specifically to intracranial aneurysm (IA): population studies report higher rates of subarachnoid haemorrhage and unruptured IA among CoA patients compared with stroke patients without CoA, and a recent meta-analysis across five studies estimated IA prevalence at 3.8% in CoA, with systemic hypertension the only factor significantly associated with IA presence. Notably, reported IA prevalence has declined in more recent cohorts, plausibly reflecting earlier diagnosis, earlier repair and improved long-term hypertension management — but this trend also underscores how little is understood about which specific patients remain at risk. Current evidence cannot distinguish whether cerebrovascular abnormalities in CoA arise from an underlying congenital arteriopathy, cumulative hypertension exposure, altered haemodynamic forces, or some interaction of these. Increased aortic stiffness is documented from the neonatal period and persists after technically successful repair, suggesting an intrinsic vascular abnormality, while reduced cerebral artery elasticity and increased carotid intima-media thickness point toward a hypertension-driven mechanism. Conventional imaging and clinical risk stratification cannot resolve this ambiguity, and consequently no evidence-based tool exists to identify which CoA patients should be screened for IA. Routine screening of all patients is not currently supported by evidence; a more selective, risk-informed approach is needed but requires a mechanistic understanding this project aims to provide.</p> <p><b>AIM.</b> To improve understanding of the mechanisms underlying cerebral aneurysm development in patients with CoA, with the long-term goal of improving risk stratification and informing future screening strategies.</p> <p><b>OBJECTIVES.</b> 1) Develop patient-specific 3D models of the aorta and cerebral vasculature from clinical imaging (CT/MRI angiography), enabling detailed morphometric characterisation of vascular anatomy and identification of structural features associated with aneurysm</p> |

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|  | <p>formation. 2) Apply machine learning to integrated clinical, anatomical and haemodynamic datasets to identify previously unrecognised patient subgroups and risk phenotypes. 3) Develop computational fluid dynamics (CFD) models of the coarctation segment and head/neck vessels to investigate how altered flow patterns and haemodynamic forces contribute to aneurysm development and progression.</p> <p>APPROACH. This retrospective and prospective observational computational imaging study will recruit approximately 70-100 CoA patients, using routinely acquired clinical imaging to reconstruct patient-specific geometries of the thoracic aorta and cerebral circulation (including carotid and vertebrobasilar systems) via standardised, reproducible segmentation pipelines. Three complementary analytical strands will be integrated. First, morphometric analysis will extract quantitative descriptors — vessel diameter, curvature, tortuosity, branching angles — with statistical shape modelling (SSM) capturing population-level modes of anatomical variation. Second, unsupervised machine learning (e.g. hierarchical clustering, principal component analysis alongside SSM) will be applied to combined morphological and clinical data to identify stable, clinically interpretable phenotypic subgroups, validated against hypertension burden and available cerebrovascular outcomes. Third, CFD simulations on the reconstructed geometries will quantify patient-specific haemodynamic parameters — wall shear stress, oscillatory shear index, pressure gradients — with a parametric modelling approach systematically varying anatomical and physiological inputs to identify flow conditions associated with adverse remodelling and aneurysm risk. These three strands will be integrated into a combined anatomical-haemodynamic risk framework, testing whether specific vascular phenotypes carry distinct haemodynamic signatures correlating with known clinical risk factors such as hypertension burden and age at repair. These computational insights will be enriched through an additional physiological experiment. Participants with repaired CoA (n=25-30) will be invited to a single study visit (estimate 60-90 minutes). Brief clinical screen will be performed (resting blood pressure, baseline oxygen levels) ensuring appropriate exclusion for contraindications (e.g. recent cardiovascular events). Continuous near-infrared spectroscopy (NIRS) optodes will be used to monitor cerebral tissue oxygenation index (TOI), while assessing cerebral blood flow velocity with ultrasound. Following normoxic baseline recording, a controlled graded hypoxic challenge will be performed. Cerebral blood flow velocity and tissue oxygenation would be compared (normoxic baseline vs. hypoxia) to assess whether cerebral autoregulatory vasodilation is sufficient to preserve tissue oxygenation. This is especially relevant in CoA patients given altered upstream vascular mechanics and blood pressure dynamics (even after successful repair) providing extremely useful physiological data to complement computational observations.</p> <p>INCLUSIVITY AND PPIE. The study will be shaped by ongoing involvement of patients with lived experience of CoA, consulted on study design, dissemination materials, and how risk and uncertainty around screening and incidental findings are communicated. Inclusive design principles will examine whether morphological and haemodynamic patterns differ by</p> |
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|                             | sex, given known sex-based differences in vascular biology, with minimal, clinically justified exclusion criteria to ensure the cohort reflects real-world NHS CHD populations rather than a highly selected subgroup. IMPACT. Beyond disease-specific insights into IA mechanisms in CoA, the project will produce a transferable computational framework combining 3D vascular modelling, machine learning and CFD, applicable to other cardiovascular and cerebrovascular conditions where morphologyhaemodynamic- outcome relationships remain poorly understood — extending the project's value well beyond the immediate CoA population. |
| Can be completed part time? | Yes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Supervisory Team            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Lead Supervisor             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Name                        | Dr Emma Hart                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Affiliation                 | Bristol                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| College/Faculty             | Faculty of Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Department/School           | Bristol Medical School                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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| Co-Supervisor 1             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Name                        | Dr Andrew Cookson                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Affiliation                 | Bath                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| College/Faculty             | Faculty of Engineering                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Department/School           | Department of Mechanical Engineering & Centre for Therapeutic Innovation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Co-Supervisor 2             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Name                        | Dr Giovanni Biglino                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Affiliation                 | Bristol                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| College/Faculty             | Faculty of Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Department/School           | Bristol Medical School                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Co-Supervisor 3             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| Affiliation                 | Bristol                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| College/Faculty             | Faculty of Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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