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Flow Alterations in Different Transcatheter Aortic Valve Implantation Scenarios

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Experimental in-vitro modelling of left coronary blood flow

In 2017 Trans-Aortic Valve Implantation (TAVI) became more prevalent than Surgical Aortic Valve Replacement in Denmark and is increasingly considered for younger and lower risk patients placing an increased demand on the durability of TAVI valves. Pathologies such as Subclinical Leaflet Thrombosis and Hypoattenuated Leaflet Thickening have been associated with deterioration of prosthetic valve function. Understanding how coronary blood flow interacts with the aortic valve and affects stasis and washout in the aortic sinuses might be a valuable tool in understanding the development of thrombus related pathologies after TAVI and help improve valve positioning.

LCA flow has been described as phasic and diastolic dominant, and several literature-referenced metrics have been identified for the characterization of LCA flow including diastolic-systolic velocity ratio and diastolic-systolic resistance ratio. Three experimental models for replicating physiological LCA flow were developed and evaluated: A simple model with a static resistance element, a ventricular coupled starling resistor model and a phasic mechanical resistance model. A simplified CFD model of the experimental setup was constructed applying experimentally derived pressure, flow and resistance values as boundary conditions.

Of the three models, the phasic resistance model showed closest agreement with literature values based on the identified coronary flow metrics. It is concluded that a phasic resistance model is the best option for further work on modelling left coronary blood flow. Some agreement between experimental and numerical LCA flow curves were achieved with the numerical model underestimating diastolic dominance by 26 %.

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Development of a pulsatile in vitro model of the native porcine mitral valve

Background

Pulsatile in vitro models allow mitral valve function and surgical techniques to be investigated under controlled haemodynamic conditions. Reproducing physiological mitral valve function remains challenging because of the interaction between the leaflets, annulus, chordae tendineae, and papillary muscles. We developed a pulsatile in vitro model for native porcine mitral valves to reproduce physiological haemodynamics and valve dynamics while maintaining direct surgical access.

Methods

Native porcine mitral valves were mounted in an in-house-developed pulsatile flow-loop system. The papillary muscles were secured to holders using running horizontal mattress sutures with 4-0 Prolene. Papillary muscle position was adjusted under low-pressure conditions to obtain appropriate leaflet coaptation before increasing system pressure. Five valves were tested at 70 beats/min. Left ventricular pressure, aortic pressure, and peripheral flow were recorded. Valve motion, coaptation, and competence were assessed visually and by ultrasound.

Results

In preliminary testing, all five valves were successfully evaluated under pulsatile conditions. Physiological systolic and diastolic pressures were achieved, with a cardiac output of approximately 4.5 L/min. All valves showed consistent leaflet opening and closure with adequate coaptation. No

mitral regurgitation was detected visually or by ultrasound. Further optimisation is ongoing to refine cardiac output and stroke volume.

Conclusion

These preliminary experiments show that the model can reproduce physiological pressure conditions and competent dynamic function of native porcine mitral valves. Further optimisation and haemodynamic characterisation are required before the model is used for experimental evaluation of mitral valve repair techniques.

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Using automated speech recognition to gain insights into the relationship between verbal fluency and deep brain stimulation in Parkinson's patients

Deep brain stimulation (DBS) of the subthalamic nucleus is an effective treatment for advanced Parkinson's disease but has been linked to declines in verbal fluency, traditionally assessed through labour-intensive manual transcription of verbal fluency tasks (VFTs). This study examined whether automated speech recognition (ASR) can support this process, and whether DBS condition affects verbal fluency and its underlying linguistic structure. Ninety-six audio recordings from 12 Danish-speaking Parkinson's patients performing phonemic VFTs under three DBS conditions (off, dorsal, ventral) were manually annotated and transcribed using a locally deployed Whisper ASR pipeline, with and without audio enhancement and task-specific prompting. Transcription accuracy was benchmarked against manual annotations (inter-rater $\kappa = .736$), and temporal word clusters, derived via curve-fitting, were analysed using hierarchical regression models to test associations between DBS condition, cluster count, and within-cluster semantic and phonemic similarity. Whisper achieved a mean transcription accuracy of only 25%, well below levels considered clinically usable; neither audio enhancement nor prompting improved performance, with prompting significantly reducing accuracy. No significant associations were found between DBS condition and verbal fluency or linguistic cluster structure. These findings indicate that off-the-shelf ASR models are not yet suitable for annotating clinical VFT recordings of this type, and that domain-specific fine-tuning is likely required before automated pipelines can reliably support this area of clinical research. The absence of a measurable DBS effect in this sample further suggests that larger, better-powered studies are needed before conclusions about DBS-related cognitive-linguistic decline can inform clinical decision-making.

(243 words)

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Machine Learning Driven Prognostic Tool for Identifying CTEPH-Patients with Insufficient Effect of Pulmonary Thromboendarterectomy

Prediction tools are increasingly being used in surgery but have not been developed for the expensive and very invasive operation, pulmonary thromboendarterectomy (PTE), in CTEPH-patients. Around 15% of CTEPH-patients who receive PTE get no positive effect from it. I have developed and validated a prediction tool that can help to predict patient's outcome of PTE before the operation.

40 patients from Aarhus University Hospital Denmark (AUH) where included in the in the dataset. For each patient a pressure volume loop (PV-loop) was created and different physiological measures were included. 11 different machine learning models were created and validated with LOOCV.

A combination of Support Vector Machine model (SVM) and Gradient Boosting model (GB) had the best predictive accuracy for patient's outcome. The combination of the SVM and GB could predict one third of the patients who didn't have an effect from PTE.

Max right ventricular pressure (Pmax) before operation, was with 95%CI the most predictive singular variable of a patient's outcome.

This study only has an n=40, which is low for machine learning, so this study is a proof of concept of what is possible. Variables like how well the PTE-operation was conducted was not available and therefore not included in the predictions.

Predictions of patients' outcomes after PTE is a promising tool to help make better and more precise decisions of which patients to give the extensive and costly PTE-operation. But more research is needed for more precise predictions.

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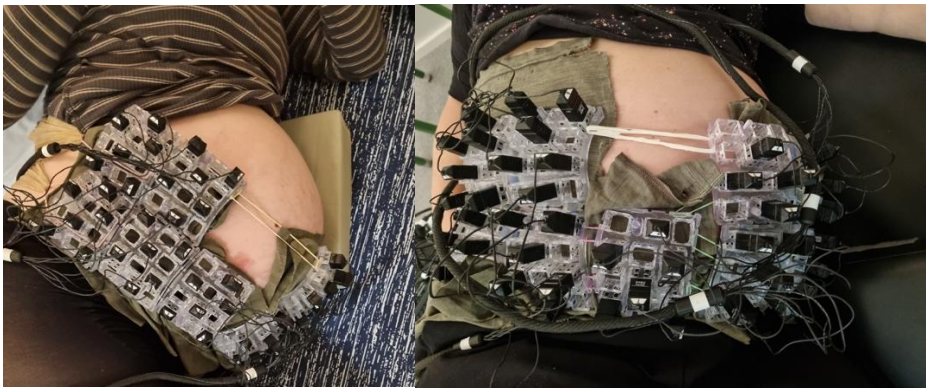
Listening Before Birth: Measuring Foetal Brain Responses to the Maternal Heartbeat Using OPM-MEG

Our understanding of prenatal functional brain development is limited by the challenges of recording foetal brain activity in utero. Novel imaging approaches such as magnetoencephalography (MEG) with optically pumped magnetometers (OPMs) offer a promising approach to investigating foetal brain function. Given the foetus' continuous exposure to the sound of the maternal heartbeat, this study investigated foetal auditory evoked responses (AERs) to the maternal heartbeat using OPMs. To rule out non-auditory explanations, such as cardiac activity or physiological coupling, brain responses to naturally occurring maternal heartbeat sounds were compared with those elicited by externally presented heartbeat sounds temporally decoupled from the maternal heartbeat. In a within-subjects design, eight recordings of fMEG responses to maternal and external heartbeat sounds were obtained from women in the third trimester of pregnancy (≥32 weeks gestation), using OPM sensors positioned on the maternal abdomen. Following noise reduction and artefact removal, data were epoched and averaged to obtain stimulus-locked AERs. Peak AER latencies did not differ significantly between maternal and external heartbeat responses, and the Bayes factor provided anecdotal evidence for similarity in latency. However, responses in the maternal heartbeat condition showed substantially larger amplitudes and generally smoother waveforms, suggesting that the activity in the maternal-heartbeat condition may reflect residual maternal physiological activity, such as the pulse wave. Although findings were inconclusive, this study demonstrates a first application of OPM-based fMEG to naturalistic

auditory stimuli and emphasises the key methodological challenges that must be addressed to advance this approach to studying prenatal brain functioning.

Figure 1.

Experimental setup of OPM sensors on a pregnant participant's abdomen.



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Flow Alterations in Different Transcatheter Aortic Valve Implantation Scenarios

Background:

In Denmark, approximately 100,000 people suffer from heart valve diseases, with aortic valve stenosis being one of the most common. Severe aortic valve stenosis can be treated by surgical or transcatheter aortic valve replacement (TAVR), with the majority today being the latter. However, compared with surgical valves, potential flow alterations in the sinus of Valsalva may increase the risk of leaflet thrombosis following TAVR. The TAVR stent frame can create regions of reduced flow velocity and blood stasis, which are known from Virchow's triad to promote thrombus formation. One possible mechanism is that the presence of the TAVR frame impedes blood flow in the lower part of the sinus, particularly with increasing implantation height.

Aims:

To investigate the relationship between TAVR implantation height and rotation on local flow velocities in the sinus of Valsalva, which hypothetically could be associated with thrombus formation.

Method:

An in vitro flow loop equipped with a TAVR model was developed to facilitate various implantation scenarios, including valve implantation heights of 50-90% above annulus and

rotation with either valve-to-sinus commissural alignment (anatomical) or 60° rotation (anti-anatomical). The flow loop was constructed without ferromagnetic components allowing MR scanning. Testing conditions were a cardiac output at 5 L/min (± 10%) and aortic pressure of 120/80 mmHg (±10%). Flow measurements were performed using 4D flow MRI, for quantifying spatial and temporal velocity distribution in the sinus of Valsalva throughout the cardiac cycle.

Results:

Preliminary data show a difference in flow between the native configuration and configurations with 50-90% implantation height from the aortic annulus.

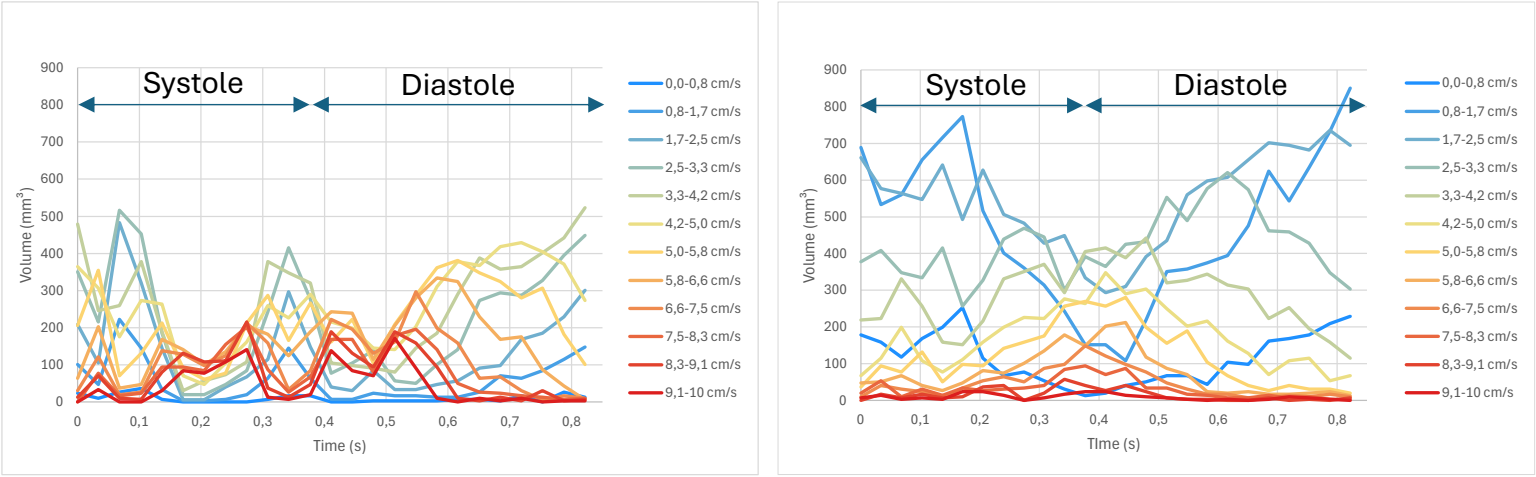

Figure 1. Assessment of stagnation volumes in one of the sinuses, showing volume over time across different velocity intervals.
Left - Control configuration with a silicone replica of a native aortic valve (no TAVR).
Right - Implantation at 90% and anatomical orientation (commissural alignment) of a TAVR model comprising silicone-replicated leaflets and a 3D-printed TAVR stent structure.
Systole and Diastole identified from cross section flow profile of the native configuration, distal to the Sinutubular Junction level.
Color indicates velocity, ranging from low (blue) to high (red).