In the literature, there are few reports describing the attempts to modulate the rotary pump's speed, which only focus on asynchronous speed modulation [7], mathematical modelling [8-10] and in vitro investigation of pump speed modulation using sinusoidal waveforms [11]. A promising application of VADs, besides their usage in the bridgeto-transplantation and destination therapy, is the bridgeto-myocardial recovery [12, 13]. Although the mechanism of functional recovery of a failing heart is not completely understood, cardiac unloading by assist devices has been suggested as a mechanical tool to promote recovery [14, 15]. We hypothesized that a synchronized speed-modulated pump could yield better control over the heart device interaction, and it might provide pathways to heart recovery and device weaning. Furthermore, to overcome the aforementioned limitations of RBPs and effectively control the load on the heart, the main objective of this study was to modulate the speed of a centrifugal RBP and investigate the effect of pump speed variation during systole and diastole on cardiac unloading. We have examined different levels of support during systole and diastole (comparable with co-pulsation and counter-pulsation) to investigate whether the systolic duration of modulated pulses matters.

## **METHODS**

## Pulsatile speed pattern of rotary blood pump

The CentriMag<sup>TM</sup> RBP (Levitronix GmbH, Zürich, Switzerland) is a magnetically levitated centrifugal-flow pump designed to provide haemodynamic support for the periods of up to 30 days during extracorporeal procedures. This pump is based on a bearing-less motor technology and operates without mechanical bearings or seals, which results in minimal friction in the blood path. It is composed of a disposable pump head and a reusable motor that works with a direct drive yielding firm control over the speed. A Levitronix industrial controller was modified and tuned to run with the CentriMag pump. This modified proportional-integral controller yields a direct speed control via analogue voltage and feedback of the actual speed. The control algorithm used to modulate the pump speed was written in LabVIEW (National Instruments, Austin, TX, USA) and communicates in real time via a data acquisition system (c-RIO-9074, National Instruments) with the pump controller, while continuously receiving the animal's electrocardiographic (ECG) signal using a patient monitor (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland). The programme detects the QRS complexes in the ECG signal using a peak detector algorithm based on the Pan-Tompkins technique [16] and then produces the pump control signal in synchrony with the heart rate. Figure 1 presents different levels of pump command speed during systole and diastole. All the pump speed scenarios have the same mean speed (2000 rpm), and therefore, the number of pump impeller revolutions per each heartbeat is equal. Moreover, this figure shows the actual pump speed derived from the motor's Hall sensors, demonstrating how well the pump can follow the command speed. Pump systole starts at the beginning of the QRS complex and is defined as one-third of the heart cycle, which is based on the length of the previous cycle, while the rest of the heart cycle is considered as diastole.

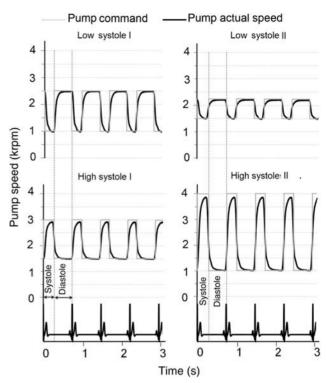


Figure 1: Pump command speed and actual pump speed derived from the motor's Hall sensors; systole starts at the beginning of the QRS complex and last for one-third of the heart cycle and the rest of the heart cycle is considered as diastole.

## Surgical preparation and instrumentation

The CentriMag<sup>TM</sup> RBP was implanted in four healthy female sheep (56-83 kg). All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals (National Academy of Sciences, 1996), and the study was approved by the Swiss Federal Veterinary Office. After premedication and induction of anaesthesia, the animals were intubated and anaesthesia and analgesia were maintained with isoflurane in oxygen (1.6%) and fentanyl (5-10 µg/kg/h). A left thoracotomy was used to enter the thorax and expose the left ventricular (LV) apex and the descending aorta (used as a surrogate for the very short ascending aorta). The animals were heparinized to maintain the whole-blood activated clotting time of >400 s. For the surgical implantation of pump inflow, LV apical cannulation was performed using a modified 32 Fr angled venous cannula (DLP 67532, Medtronic Inc., Minneapolis, MN, USA), and a 22 Fr arterial cannula (EOPA 77522, Medtronic) was placed in the descending aorta. The inlet/outlet cannulation was kept short  $(30 \pm 5 \text{ cm})$  in order to simulate the implantable VADs. Following pump priming and the connection of the cannulas to the inlet/outlet ports, pump operation commenced. Coronary flow (CF) and pump flow (PF) were measured using ultrasonic flow probes (Transonic Systems Inc., Ithaca, NY, USA) on the left main coronary artery (8PAU) and the outlet cannula of the pump (9PXL). Fluorescence-based optical sensors (Foxy AL-300) and portable spectroscopes (NeoFox, Ocean Optics, Dunedin, FL, USA) were placed in the coronary sinus and the left carotid artery to measure continuous venous and arterial oxygen partial pressure, respectively. The hemi-azygous vein was ligated to prevent blood mixing in the sinus. Aortic pressure, LV pressure