Sound analysis of the magnetically levitated left ventricular assist device HeartMate 3™

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Abstract

Introduction: The HeartMate3^{TM} has shown lower rates of adverse events compared to previous devices due to the design and absence of mechanical bearings. For previous devices, sound analysis emerged as a way to assess pump function. The aims of this study were to determine if sound analysis can be applied to the HeartMate3 in vivo and in vitro, and to evaluate an electronic stethoscope.

Method: Sound recordings were performed with microphones and clinical accessible electronic stethoscope. The recordings were studied in both the time and the frequency domains. Recordings from four patients were performed to determine if in vivo and in vitro recordings are comparable.

Results: The results show that it is possible to detect sound from HeartMate3 and the sound spectrum is clear. Pump frequency and frequency of the pulsatile mode are easily determined. Frequency spectra from in vitro and in vivo recordings have the same pattern and the major proportion (96.7 %) of signal power is located at the pump speed frequency ± 40 Hz. The recordings from the patients show low inter-individual differences except from location of peaks originating from pump speed and harmonics. Electronic stethoscopes could be used for sound recordings, but the dedicated equipment showed a clearer sound spectrum.

Discussion: The results show that acoustic analysis can also be performed with the HeartMate3 and that in vivo and in vitro sound spectrum is similar. The

frequency spectra are different from previous devices and methods for assessing pump function or thrombosis need further evaluation.

Introduction

The outcome of patients treated with left ventricular assist devices (LVAD) has improved in recent decades due to improved patient selection, management and the introduction of continuous flow pumps. Despite this, adverse events such as infection, bleeding and pump thrombosis still occur.[1, 2] The HeartMate 3™ (Abbott, Lake Bluff, IL, USA) (HM3) is a compact intrapericardial centrifugal-flow pump that uses magnetic levitation and therefore eliminates the need for mechanical bearings. It was developed to enhance hemocompatibility and minimize the shear stress that resulted in acquired von Willebrand syndrome associated with previous LVAD models.[3-5] Results from the initial trials and follow-up studies, up to two years, showed superiority compared to the axial-flow HeartMate II (Abbott, Lake Bluff, IL, USA) (HMII) with improved clinical outcome due to a lower reoperation rate, lower overall stroke-rate and low reports of pump thrombosis within the device.[6-12]

In recent years, sound analysis has emerged as a novel, non- invasive way to monitor and evaluate pump function in pulsatile, axial and centrifugal LVADs.[13-23] Presence of a third harmonic and an increase in pump frequency amplitude has been shown to be a sign of thrombosis in other centrifugal LVADs.[18, 20] In a recent study, the number of amplitudes was correlated to the presence of thrombosis.[23] The HMII has a different sound spectrum due to its design.[21, 22] However, the sound may be analyzed and *in vitro* studies and *in vivo* cases have shown that pump function and presence of thrombosis can be assessed

with a change in amplitude indicate thrombosis.[17, 21] The electronic stethoscope has been used in multiple studies on sound analysis from LVAD but the reliability of this device has never been discussed.[19, 21]The sound from HM3, with its fully magnetic levitation has never been characterized.

The aim of this study is to characterize and evaluate the sounds from HM3, if they can be recorded and if in vivo and in vitro acoustic analyses are comparable. A further aim was to evaluate whether an electronic stethoscope may be used for recording audio signals from the HM3.

Method

Study settings

Properties of the HM3 are briefly described elsewhere.[8] The HM3 is powered by a 14 Volt (V) Lithium-Ion battery and operates between 10-17V. The winding type and numbers of stators are not accessible.

Mock loop

An experimental model was set-up with a HM3 in a mock- loop circuit with the pump housing immersed in a bag of saline. This set-up ensures a dry surface for recording purposes and a surface to pump distance that is comparable to the position of the HM3 within the thoracic cavity, approximately 2cm (0.78in). The pump was connected to a 2 liter (67,6oz) water chamber, with a 50cm (19.6 in) plastic tubing 2cm (0.78n) in inner diameter, connecting the chamber to the pump inflow. The graft from the HM3 connected the pump outflow and the chamber. The pump speed was increased from 3000 revolutions per minute (rpm) to 8000 rpm in increments of 100rpm, and recordings made after each

increase. The HM3 creates a pulsatile flow by alternating the speed 30 times per minute. This pattern begins when the fixed speed setting is set at a minimum of 4000 rpm. The pump introduces a quick frequency change twice per second. The pump frequency is decreased for 0.15s, and then increased for 0.2s. Both changes are instantaneous as step functions. To simulate obstruction, hemostatic forceps was used to create a constant narrowing of the inflow and outflow conduits to approximately 50%. To determine if the recorded soundwaves were due to surrounding sounds, flow or pump oscillation, an abrupt pump stop was performed.

The recording devices were placed on the surface of the saline bag. The microphones were placed with the diaphragms facing towards the pump and the windscreen touching the surface of the saline bag with an approximate angle of 90 degrees.

Patients

To be able to compare the acoustics from the mock loop circuit sound was recorded from four consecutive patients with a HM3. The study complies with the Declaration of Helsinki and was approved by regional ethics review board in Linköping University Hospital (Dnr 2011/282-31, 2019-00415). All patients gave informed consent and no clinical adjustments or change in any pump setting was made during the recording sessions to ensure no risk for adverse events.

The recording devices were placed on skin surface above the pumphouse and lateral of the left midclavicular line in intercostal space 8-9. The microphones

were placed with the diaphragms facing towards the pump and the windscreen touching the skin with an approximate angle of 90 degrees.

Recording devices and software

Two microphones, Shure PG58 (Shure Inc. Niles, IL, USA) were connected to an external sound card, Behringer FCA1616 (Behringer, Germany) which in turn was connected to a commercial laptop. For full technical specification, see product specification.[24, 25] The microphones were placed adjacent to each other to determine if there were any inter-individual differences between the recordings. Multiple 10 seconds clips were recorded. The same microphones were used for in vivo and in vitro recordings and no changes in settings of the external sound card was performed. These microphones have previously been used and shown to be acceptable for sound recording of LVAD.[22]

A Littmann™ 3200, electronic stethoscope (3M, St. Paul, MN, USA) was also used. The electronic stethoscope is capable of recording sounds in the frequency range 20-2000 Hz with multiple 30 seconds clips. Three filters may be applied of which we used the extended filter that amplifies sounds between 20-2000 Hz, but emphasizes frequencies of 50-500 Hz. The audio recordings were then transferred by Bluetooth to a computer with the Littmann Stethassist (3M, St. Paul, MN, USA) software. The same stethoscope was used for in vivo and in vitro recordings and the extended filter was used for all recordings. The sampling rate was set at 44.1 kHz for the microphones and 4 kHz for the Littmann 3200™

Recordings with the Shure microphones and all analysis were performed using Matlab (Mathworks, Natick, MA, USA) and the same functions were used for both the stethoscope and the microphones.[26]

Statistical analysis

Statistical analysis was performed with the use of IBM SPSS Version 23. To determine correlation between measured and estimated frequencies the Pearson correlation coefficient was calculated. When assessing the difference between the in vitro and in vivo signal, all recordings for each patient and the recordings in mock loop at the same speed were assessed for estimated frequency and power distribution within the pump frequency ±40Hz. The student´s t-test were used to calculate difference between in vivo and in vitro recordings. Two-tailed P values of less than 0.05 are considered to indicate statistical significance

Recording analysis

First the recording was plotted as a function of time in Matlab. Thereafter customized software computed the estimated frequency by performing fast Fourier transform analysis and automatic finding of the highest peak. A Hamming window, built in as standard in Matlab functions reduced the disruptive effect in the truncated time history. A window-size of 1024 samples was used. To minimize differences in sound volume between different patients and recordings, normalization was performed where the total area under curve was set to 1Watt (W). This generates small numbers of W/Hz and -20dB equals to 0.01W/Hz. Power spectral density (PSD) was computed to assess the

distribution of signal power over various frequencies that could be of interest. Furthermore, the PSD was used to verify the LVAD frequency defined in the set-up to determine reliability.

Results

In vitro recordings

The function of HM3 was assessed by increasing speed and comparing speed towards pulsatility index (PI), flow read from the monitor and power. The results showed significant correlation, ($P<0.01$ for correlation) as expected. When the sounds from the HM3 were plotted as a function of time, a sine wave was seen (Fig 1). When recording at pump speeds above 4000 rpm, i.e. the point at which the pulsatile mode used by the HM3 is activated, a change in amplitude and frequency in the sound signal as a function of time was detected. The changes in amplitude and frequencies were detectable when using the electronic stethoscope but not as clear as with the dedicated equipment (Fig 1).

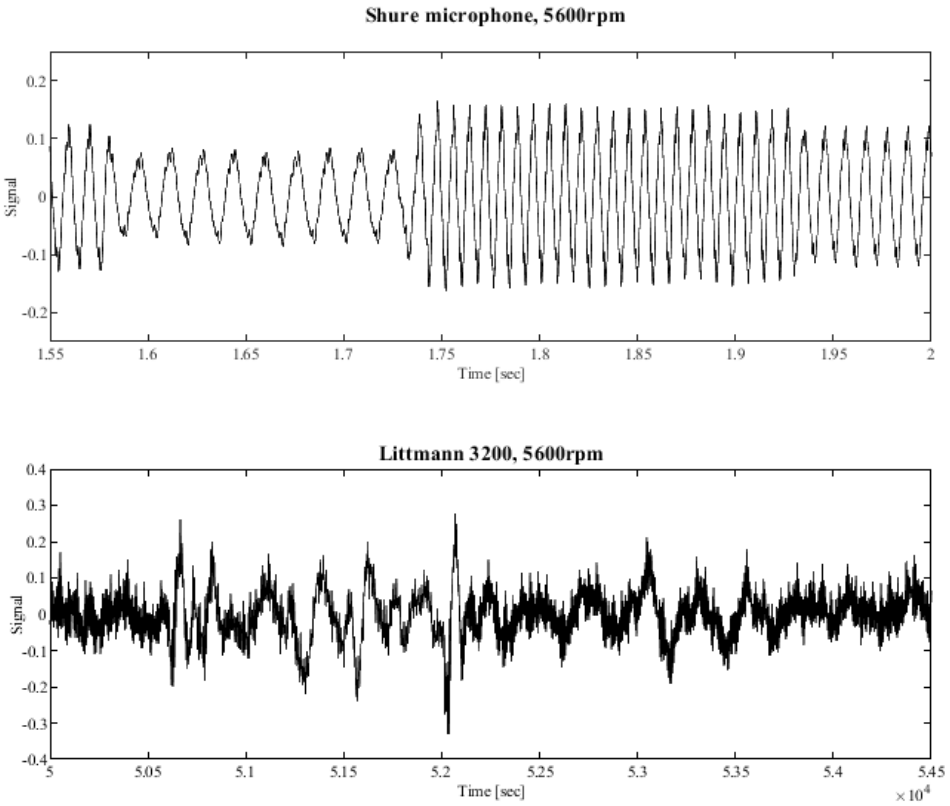

Figure 1. Recordings plotted in time domain, aligned to artificial pulsation within the recordings, and zoomed down to microseconds. A sine wave with different amplitude and frequency due to artificial pulsation is clearly seen with the Shure microphone. The oscillations and change in frequency and amplitude are not so clear with the electronic stethoscope.

When the PSD of the sound was plotted over the entire frequency spectrum, the highest power was present in the lower frequency range with a mean of 96.7% within ±40 Hz of the pump frequency (rpm/60). There was no significant frequency component in the higher frequency range, but clearly visible harmonics of the pump speed could be seen in the low frequency spectrum (Fig

2). The frequency interval was chosen to include the pump frequency and the frequency of the artificial pulse. Above 4000 rpm, symmetrically centered peaks around the pump frequency were detected. These represent modulations due to the increase and decrease in speed used to generate the pulsatile flow (Fig 2). These findings were clearly detected with the Shure microphones when plotted in a frequency spectrum. They could be detected with the electronic stethoscope as well but not as clear (Fig 2). The peaks from pulsatile mode appeared at a mean of +29.5 Hz/– 30.5 Hz from pump frequency, corresponding to a change in speed of approximately 1800 rpm. The peaks that represent a reduction in speed correspond to a mean of 4.3% of the power and the peaks that represent increased speed correspond to 18% of the total power. The higher amount of power for the increase is since the increase last for 0.2s whilst the decrease for 0.15s. This indicates that most of the signal is within the fundamental frequency (pump frequency) and the increment due to pulsation and that this signal and harmonics are due to the system function.

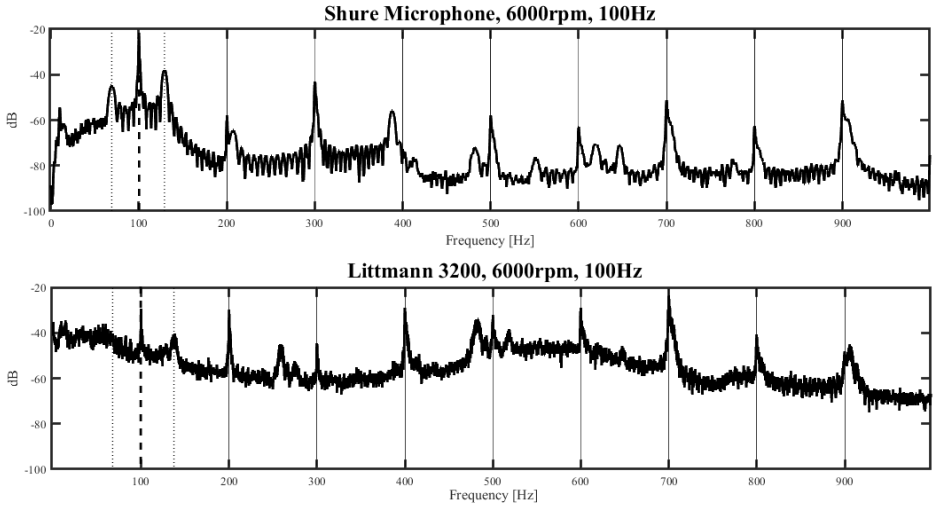

Figure 2. The signal from HM3 after PSD, plotted in the low frequency range. Both devices show the estimated pump frequency and harmonics. The decrease in frequency due to artificial pulsation is not as clear with the electronic stethoscope and the spectrum holds more interference. -20db equal to 0.01W/Hz.

The largest peak in the PSD was significantly correlated to the set fixed speed, showing a linear relationship with the Shure microphones ($p<0.0001$). The electronic stethoscope determined the correct pump speed in approximately 50% of recordings with the peak from pump speed clearly visible but another peak with higher PSD.

When the pump was suddenly turned off by unplugging the controller, the alarm signal appeared after exactly 0.5 seconds and greatly affected the signal in time domain. The recording of the HM3 at this point revealed that pump rotation terminated abruptly and no continuous oscillation in time domain was seen. This indicates that the magnetic rotor do not produce any further rotation and is abruptly stopped and most likely fixed to one of the magnetic stators (Fig 3). When the inflow and outflow were obstructed, there was no change in the frequency nor in the time domain, except a small increase in the first harmonic but the flow rate on the monitor dropped and the pump signaled for low flow after a few seconds.

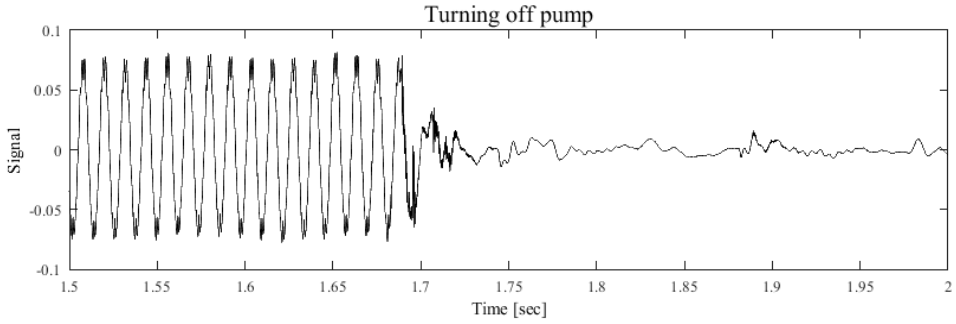

Figure 3. Signal in time domain from the pump in vitro, when the pump was abruptly turned off. The sinewave disappears immediately and no signal indicating rotation can be seen. This indicates that the signal arises from the LVAD

HM3; In vivo recordings

When comparing *in vivo* recordings with *in vitro* recordings using the Shure microphones, there was no significant difference between estimated speed in the patients and estimated pump speed in the mock loop circuit (P=0.88 for difference between groups). When using the electronic stethoscope *in vivo*, results were not consistent with pump speed estimated with the microphones and with the electronic stethoscope in the mock loop circuit. When comparing signals from the mock loop circuit with those from the four patients, in time domain, the sine wave, change in frequency and amplitude of the spectrum were similar except for a small amplitude difference in the harmonics (Fig 4).

When comparing the power distribution within the frequency spectrum there was no statistical significant difference between the *in vitro* and *in vivo* recordings (Fig 5).

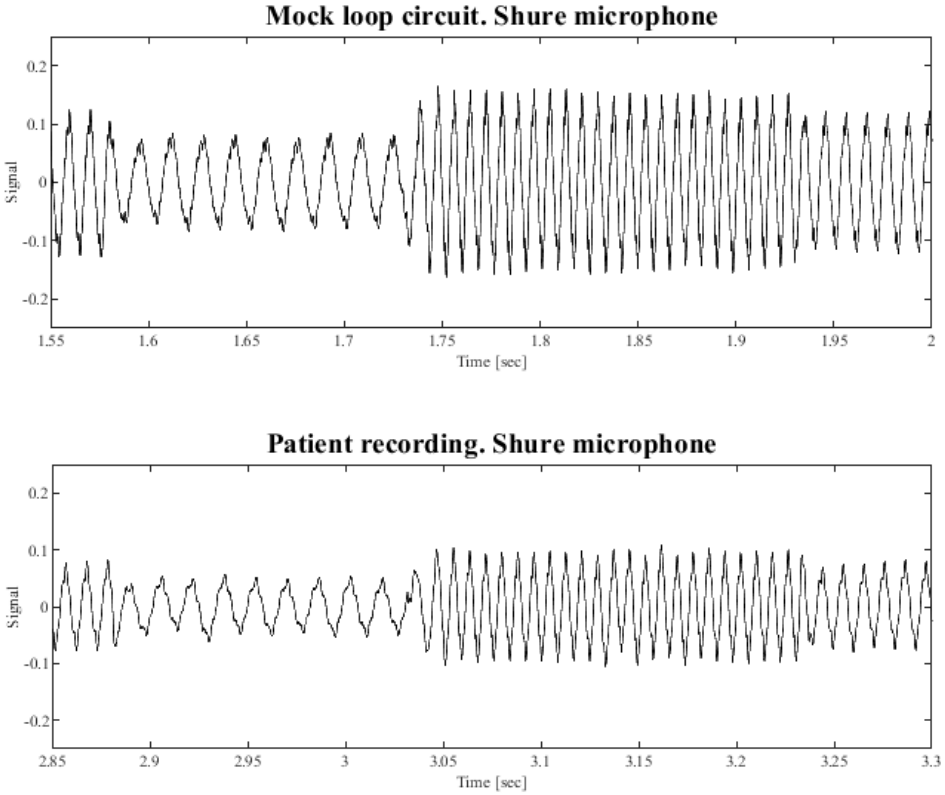

Figure 4. Zoom- in on recordings using the Shure microphone in vivo and in vitro circuit. The signals are clearly similar.

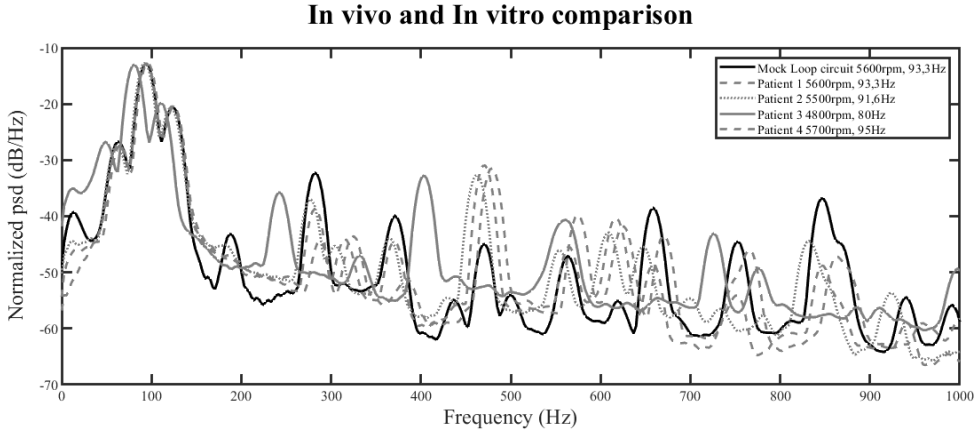

Figure 5. Recordings from the four in vivo recordings and one mock loop recording presented in a low frequency spectrum up to 1 kHz after normalization (area under curve =1). Pump frequency and artificial pulsation

peaks are clearly visible. Multiple harmonics can be seen. All recordings look alike with minor changes in amplitude in harmonics and due to speed . -20db equal to 0.01W/Hz. Rpm=revolutions per minute.

Discussion

HM3 represents a new generation of LVAD that shows great potential, with low risk for pump thrombosis and other hemo-incompatibility related adverse events.[6-8, 11] The previous LVAD, were associated with complications of which pump thrombosis has been frequently addressed.[27-29] The etiology of pump thrombosis is multifactorial and the phenomenon is related to multiple risks.[30]. The design of the HM3 is different to previous pump systems and due to magnetic levitation, the distance between the rotor and wall is greater, minimizing the risk for pump thrombosis.[8] The incidence of pump thrombosis in HM3 is rare, indicating the importance of more diagnostic possibilities.[31]

The absence of mechanical bearings results in a clear sine wave with few disturbances visible on audio recordings using both dedicated equipment and the electronic stethoscope. The use of sound analysis as a way to detect malfunction and assess thrombosis has been developed and applied to previous pumps with encouraging results.[17, 18, 20, 21] In this study, sound signals from the HM3 were characterized and the results indicate that sound analysis may be used as one of the tools to evaluate pump function in this system in the same way as with previous systems, and that future studies on evaluation on pump function and changes in frequency and time domain during different clinical circumstances initially can be performed *in vitro* and thereafter verified *in vivo* studies. Compared to the HMII, the HM3 has a more distinct frequency

spectrum where peaks and harmonics are clearly seen. The frequency spectrum from the HM3 resembles the ones from other centrifugal pumps in which sound analysis has shown changes in the frequency spectrum caused by the presence of thrombosis, a change in amplitude and the presence of a peak at three times the pump frequency were significant findings.[18, 20]. With the HM3, a peak at three times the pump frequency was seen in both the mock loop circuit simulation and in recordings from actual patients. This would suggest that the same findings might also be valid for the HM3 but with increases in amplitude or increase in number of peaks as recently seen.[23] Perhaps a change in the power distribution or amplitude of specific peaks is more valid, but this remains to be studied and future clinical studies are ongoing. Function of the pulsatile mode was easily assessed by sound analysis and according to frequency analyses the change in speed is ±1800 rpm. This result differs from the interval delivered from the manufacture but might valid since the intervals were consistent for all our recordings.

In this study, we used both dedicated recording equipment and an electronic stethoscope to record HM3 sounds. The reason was to evaluate the electronic stethoscope. Both equipment could be used to create a valid signal in both time and frequency domain. However, the dedicated recording equipment showed clearer signals and were more accurate in determining pump frequency in both *in vivo* and *in vitro* recordings indicating that the results found in studies with the electronic stethoscopes must be validated with a more reliable equipment.[19, 21] The electronic stethoscopes main advantage is the accessibility as a clinical instrument and therefore might be used as a screening tool in the clinical

setting. If there is an indication of malfunction, a more thorough recording should be performed. The relative low sample rate of the stethoscope also results in its inability to assess frequencies higher than 2 kHz according to the sampling theorem. In one patient, the sound recording was performed at the intensive care unit, resulting in disturbance, that might have affected the analysis to some extent, but the spectra were still similar. A limitation of this study is the lack of results from mock loop simulation of pump thrombus, but the study lies the foundation for future studies were simulation of thrombosis in different location could be one application. Another limitation of the study is the small number of in vivo recordings. However, we performed multiple recordings in each patient, and they all were similar, indicating reproducibility. The results imply that future research into the sound analysis of thrombosis, for instance, can be performed *in vitro* and thereafter studied and verified *in vivo*. This approach can minimize the risk of patients and minimize use of animal research. Further research on sound analyses of the HM3 is necessary to determine the specific changes related to thrombosis and mechanical failure but this study points out the possibilities to perform such studies in mock loop circuits. If specific parameters in the acoustic spectra are found, as for instance number of peaks or a peak at a specific frequency, the stethoscope can be adjusted and artificial intelligence added, and by that used for identifying thrombosis or mechanical problems.

Conclusion

The sounds from HM3 can be recorded and is similar in vivo and in vitro, indicating that the findings from mock loop circuit can be tested in clinical

settings. The highest power of the sound signal is located at the pump frequency, and there are also multiple harmonics. The pulsatile mode resulting from alternating high and low speeds can easily be detected by sound analysis, revealing a speed variation of 1800 rpm (approximately 30Hz) around the pump speed. A dedicated microphone system is superior to the stethoscope in recording sounds from the HM3, but both methods may be used for acoustic sampling and consecutive acoustic analysis and assessment of pump functions.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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