Development of a Novel Fetal Heart Rate Monitor for Multiple Gestation Pregnancies

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Abstract

Multiple gestation births account for nearly 5% of all births in the United States, of which are more often premature and produce babies who are small for the gestational age and light in birth weight.[1] Additionally, the overall frequency of neonatal mortality in black twin infants was double that of white twins.[2] Given the apparent health disparities in pregnancies, improvements to technology that improve multiple gestation infant outcomes (birthweight, mortality, etc.) are necessary for eliminating these healthcare gaps. Doppler ultrasound (US) is the *de facto* standard technology for fetal heart rate (fHR) monitoring in pregnant individuals.[3] Doppler US is performed by measuring object distances by the reflection of transmitted US sound waves through mediums over time. Commercial transducers only focus on a single heart rate; it is difficult for these monitors to differentiate multiple heart rates nearby, which is the case for multiple gestation pregnancies. We aimed to design a gel phantom to mimic the environment of multiple gestations, use this gel phantom to test a Doppler US device to receive ultrasound data from multiple sources, and to develop an algorithm to filter, analyze, and identify simultaneous fHRs. We began by designing a phantom gel to test our novel device. By purchasing a gel phantom that mimics uterine tissue from Humimic Medical and inserting small speakers, we successfully created a system that models twins *in utero*. We utilized a triangle array of microphones, read the phantom heartbeats, and analyzed the frequency of these beats. We showed that our device can determine heart rates of multiple sound sources by at greatest an error of 1.14% when the sound sources are in-phase and at the same rate (n=1). When the heart rates of each modeled fetus were vastly different (>20 bpm), the error associated with the readings increased to about 43% (n=1).

Keywords: Fetal heart rate, gel phantom, multiple gestation pregnancy

Introduction

Significance

Across the United States, twin births have an eight to ten times higher perinatal mortality rate when compared to singleton births, particularly due to the fact that 40-70% of all twin births are premature.[4] In high-risk pregnancies, such as multiple gestation pregnancies, the well-being of each fetus *in utero* is imperative to reducing the risk of a negative outcome on both the baby as well as the pregnant individual. Fetal well-being is commonly evaluated by monitoring the fHR of each fetus in gestation.[5] Fetal heartbeats begin to appear after approximately five weeks.

However, monitoring fetal heartbeats in the third trimester (29 - 40 weeks) is more pertinent to the fetal outcome at the time of birth.[6] The length (crown to rump) of both normally developing twins in the womb will reach ~25 cm, further expanding the size of the abdomen.[7] The current clinical standard for monitoring fHR is through the use of a Doppler US fHR monitor. While adequate for single fetus gestations, this device has shortcomings in multiple gestation pregnancies.Standard Doppler US fHR monitors currently do not allow for accurate measurements of multiple fetuses in gestation.[5] This is due to the fact that both hearts being measured reside in the same sample volume of the US transducer, leading to inaccurate measurements for both fetuses.[5]

Gel phantoms are an essential tool for mimicking biological tissue when using ultrasound in any application.[8] Moreover, there has been little research regarding the development of an ultrasound gel phantom that specifically addresses modeling the abdomen (from the skin to a fetus inside of the uterus) of a pregnant individual. The development of these types of phantom gels is imperative to be able to effectively and safely test novel US-based devices that aim to alleviate the many unaddressed issues associated with twin pregnancies like the shortcomings of current Doppler US fHR monitors. The goal of this project is to combine both the need of an improved fHR monitoring system for multiple gestation pregnancies and the need for a gel phantom model of these types of pregnancies.

Specific Aim 1

In order to successfully develop and improve upon the current Doppler US fHR monitor used clinically, there must be a way to safely test both the standard device as well as our novel monitor. As mentioned above, there is little known regarding an accurate ultrasound gel phantom that mimics the layers of tissue pertinent to pregnant individuals. We additionally were concerned with the establishment of how fetal heartbeats would be created. Therefore, the first aim of this project involved the development of a novel gel phantom system that provides a method for testing both standard clinical fHR monitors as well as our proposed improved fHR monitor. Once this aim was complete, we began the development of the fHR monitoring device.

Specific Aim 2

The second aim of this project regarded the creation of an electronic circuit consisting of a power supply and microphone array to collect and analyze sounds emitted from our previously described fetal heartbeat gel phantom. We were primarily interested in iterating off of similar previous designs of fHR monitors that involved a circular array of ultrasound transducers.[3,5,9] It should be noted, however; we did not end up establishing an array that used a circular array to be described below.

Specific Aim 3

The third and final aim of this project regarded the development of a MATLAB algorithm that could appropriately collect and process the data generated by our gel phantom system and recorded by our novel fHR monitor.This MATLAB code aimed to filter and analyze data while also taking into account the varying acoustical impedances of the tissues surrounding a typical uterus. The code sought to use data filtering and Fourier transformation of collected sound data on top of signal intensity analysis to correctly identify two different heartbeats generated by the gel phantom.

Materials

Gel Phantom Material

Two pounds of material (Gelatin #3) for the gel phantom were purchased from Humimic Medical. We chose this particular gelatin material because it is described to have similar acoustical properties to human uterine tissue. Because we are designing a device to eventually be used on pregnant individuals, this material was the optimal choice when designing a model system for twins *in utero*. During the creation of the gel phantom, we used a convection oven to melt the gel, and we used an oven-safe baking dish lined with aluminum foil to mold the gel and allow for easy removal from the mold.

Phantom Gel Fetal heartbeat Generator

We purchased and used an Arduino Uno from Arduino to develop our fetal heartbeat generator. Two 2-Watt 8-Ohm speakers were purchased from Amazon to be used as heart mimics in the phantom gel.

Fetal Heart Rate Device

The microphones, wires, wire extenders, and cardboard used in the fHR monitor were purchased from Amazon. We also purchased and used an Arduino Uno from Arduino to develop our fetal heart rate monitor.

Methods

Gel Phantom Fetal heartbeat Generator

The fetal heartbeat generator was developed by using an Arduino Uno in conjunction with two speakers. The Arduino Uno was used to generate audible rhythmic pulses from each speaker to mimic a heartbeat *in utero*. We used the Arduino-specific IDE to develop code for the purposes of controlling the pulse duration of each speaker. Because we were able to control each speaker independently, we were able to test a variety of combinations of multiple different heart rates simultaneously.

Gel Phantom Development

We developed our gel phantom in the following steps. We first used 1.5 lbs of the gel phantom material and, per the instructions included in our purchase of the gel, used scissors to cut up the material into approximately 1-inch-sized pieces. We then placed the gel pieces into an oven-safe dish lined with aluminum foil. The material used in conjunction with the size of the dish would yield a gel phantom that measures 2.5 cm in height, 21.6 cm in length, and 11.4 cm in width. The dish was then placed in an oven at 250 ^{o}F (125 ^{o}C) for 4 hours. After 4 hours, the dish was removed from the oven and left to cool for 12 hours. During the cooling process, we covered the dish with aluminum foil to prevent any foreign material from contaminating the gel. After the 12 hours, the, now solid, gel was removed from the dish and placed on Saran Wrap for protection from contamination on any surface. We then sliced two thin (~5 mm) rectangular holes into the side (length-wise) of the gel 6 cm apart and inserted the speaker components of the gel phantom fetal heartbeat generator to create two "phantom hearts" dubbed "Fetus A" and "Fetus B". A representative image of the gel phantom can be seen in Figure 1. The material used for the gel phantom is shelf-stable with no organic components, so we stored the gel phantom by wrapping the gel material in Saran Wrap and placing it on a shelf in a room ~70 ^{o}F (21 ^{o}C) (Figure S1).[10]

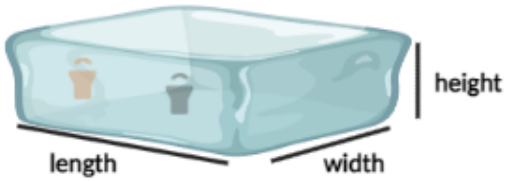

Fig. 1. Representative image of gel phantom Dimensions mentioned are shown along with a depiction of embedded speakers to mimic fetal heart rate shown in orange and grey.

Fetal Heart Rate Monitor Development

Similarly to the fetal heartbeat generator, the fHR monitor was developed by using an Arduino Uno as the circuit board to power and collect data from six microphones connected to six different analog voltage pins. We mounted the six microphones in a triangular shape onto a cardboard base for stability. A hole was placed in the center of the cardboard base to reliably align the device in the center of the two gel phantom heartbeat generators. A schematic of the fHR monitor is shown in Figure 2. Speakers 2, 4, and 6 were placed 1.3 cm from the center of the triangular base, and speakers 1, 3, and 5 were placed 2.6 cm from the center of the triangular base. These distances were chosen to fall equally distributed on a circle with a radius of the same respective length. A novel MATLAB algorithm was created to control the Arduino Uno and perform data acquisition. An image of our novel fHR monitor interfacing with our gel phantom can be seen in Supplementary Figure 1.

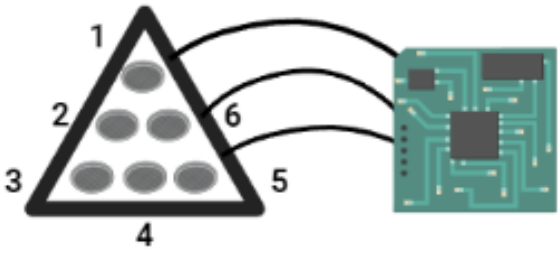

Fig. 2. Representative image of fHR Monitor. All 6 microphones are shown in a triangular layout with each microphone being labeled radially "1" through "6". Representative wires are shown to connect the microphone array with a representative Arduino Uno circuit board.

Gel Phantom Heartbeat Mimic Characterization

After creating the novel fHR monitor, we characterized each individual speaker. To test each speaker, one heartbeat mimic was set to pulse at 0 beats per minute (BPM) while the other heartbeat mimic was set to pulse at either 130 BPM, 150 BPM, or 180 BPM. We repeated this experiment with the same conditions for both heartbeat mimics. To test the fHR monitor, we centered the device between the two heartbeat mimics using the aforementioned hole in the center of the triangular base. A representative image of the heartbeat monitoring setup is shown in Figure 3. We powered on the heartbeat generator by connecting its respective Arduino to a personal laptop and powered on the fHR monitor by connecting its respective Arduino to a second laptop running the aforementioned MATLAB data collection code. While each speaker was pulsing at its set frequency, the MATLAB code was run for 10 seconds and data was stored in a .XLS file for future analysis.

Fetal Heart Rate Monitor Testing

Identical parameters were used to test the fHR monitor with both heartbeats mimics active (BPM > 0). A total of nine trials were performed, one for each combination of 130 BPM, 150 BPM, and 180 BPM.

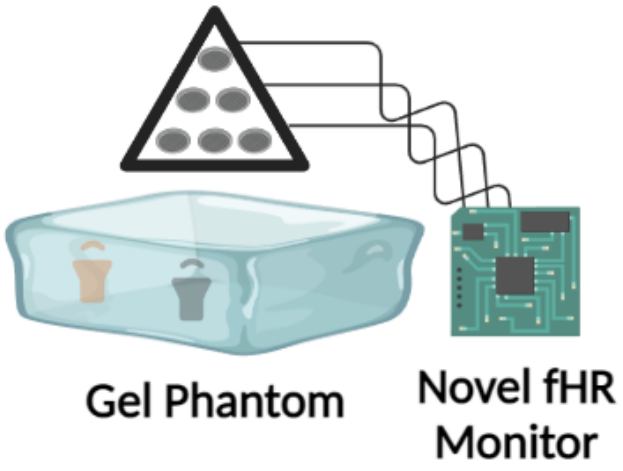

Fig. 3. Representative image of fHR monitor testing. The gel phantom is shown with the novel fHR monitor on top. The speakers in the gel phantom pulse at a desired frequency to mimic fetal heart rate *in utero* for the fHR monitor to read using its 6 microphones.

Fetal Heart Rate Data Filtering

After the collection of sound data given by the gel phantom, a MATLAB algorithm was used to process the data. The Fast Fourier transform was used to transform the time-series data into frequency-series data for further analysis (Figure 4, 5). This transformation was done because as heartbeats are a measure of frequency, we needed to identify various frequencies appearing in our collected data.

Fetal Heart Rate Determination

The measured heart rate of each phantom heart was determined after applying the Fast Fourier transform to the data using MATLAB. The highest magnitude signals for each trial were declared to be a result of the phantom hearts and recorded as such. A percent error value with respect to the true heart rate of each phantom heart was used to determine the efficacy of our novel fHR monitor in each trial.

Results

Data Filtering

For each of the six single heartbeat trials and nine simultaneous heartbeat trials, voltage data was collected from each of the six analog probes. The mean of each of the six analog probes was subtracted from the original data to create normalized microphone signals over a given recording time (Figure 4).

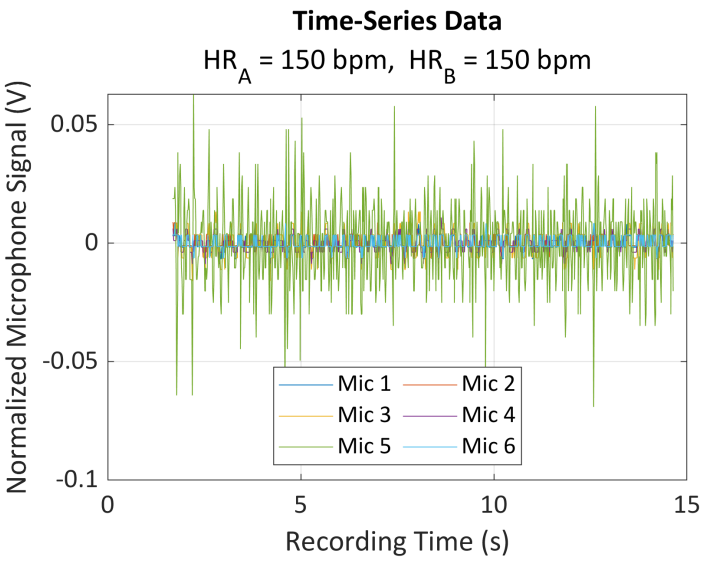

Fig 4. Normalized time-series data of one trial The data of a trial was collected over 10-15 seconds as voltages between 0 and 5.0 V across six microphones. Then, the data was normalized by subtracting the mean voltage signal for each of the six microphones. Microphone 5 received the signal with the greatest amplitude.

The time-series data of each trial was Fast Fourier transformed to produce the respective spectral data. Below is the spectral data of the 150-bpm-and-150-bpm trial. Non-zero frequencies exist greater than 250 bpm but were omitted because we want to capture frequencies between 100 bpm and 200 bpm, the nominal range of heart range for fetuses. The frequency with the greatest amplitude in each trial represented the signal for a given microphone, which is assumed to be the measured heart rate. An example, spectral data for the 150-bpm-and-150-bpm trial is shown (Figure S2).

However, both low-frequency (<50 bpm) and high-frequency (>250 bpm) exist within this measured signal. Because of this, a MATLAB band-pass filter between 100 bpm and 200 bpm was applied to the spectral data, which is the nominal heart-rate range. Below is the filtered spectral data for 150-bpm-and-150-bpm trial (Figure 5).

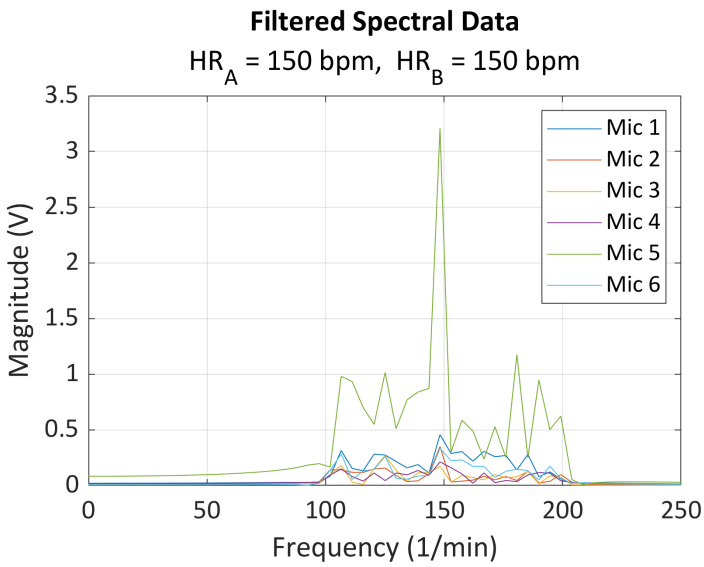

Fig. 5. Filtered spectral data of one trial The data was Fast Fourier transformed and MATLAB bandpass filtered to produced a range of frequencies nominal for fetal heart rates which were measured by the six microphones.

The frequency with the greatest magnitude is one very close to 150 bpm. In each trial, we selected this frequency as the measured heart rate of two fetuses. Additionally, microphone 2 received the greatest signal, followed by microphone 1 and 6. This suggests that the measured heart rate was closest to microphone 2.

Heartbeat Mimic Characterization Results

With the MATLAB data-collection pipeline established, we conducted two scenarios: single heartbeat measurements and simultaneous heartbeat measurements (Figure 6).

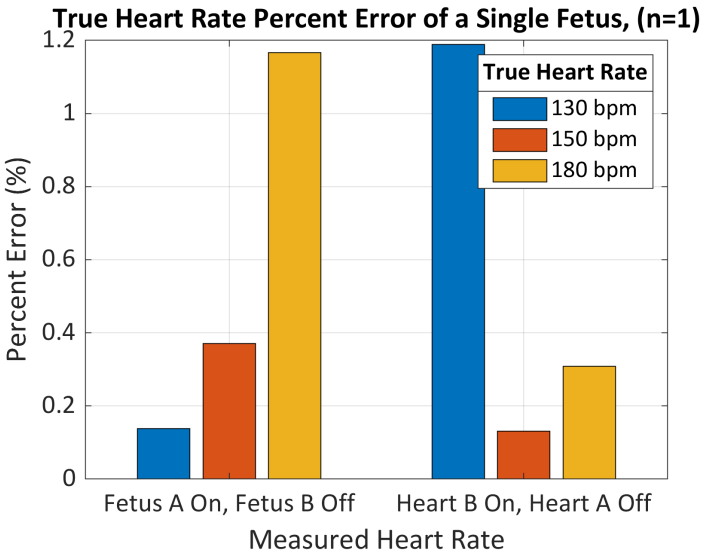

Fig. 6. Percent error for single heartbeat measurements Two sets of trials were conducted: three trials for each fetal heartbeat at 130 bpm, 150 bpm, and 180 bpm (n=1).

Six heart rate scenarios were recorded (n=1). Of which, fetus A and fetus B were isolated and measured at 130, 150, and 180 bpm. The measured heart rates were recorded according to the greatest spectral peak. The percent error between true and measured heart rates were calculated and are displayed in the figure above, of which we measured a maximum of about 1.2 percent from the six scenarios. We believe that this error is a result of the frequency granularity in the measured spectral data. There is approximately 4.6 bpm between each spectral datum, which is a result of the duration of the recorded time-series data. This error could be minimized by increasing the sampling time.

Simultaneous Heartbeats Results

In a similar way to the single heartbeat measurements, we measured the heart rate of fetus A and fetus B and compared the results against the respective true heart rate. Like single heartbeat measurements, the measured heart rate of each trial was determined by the frequency of the greatest amplitude. Below are the results of the nine trials (Figure 7).

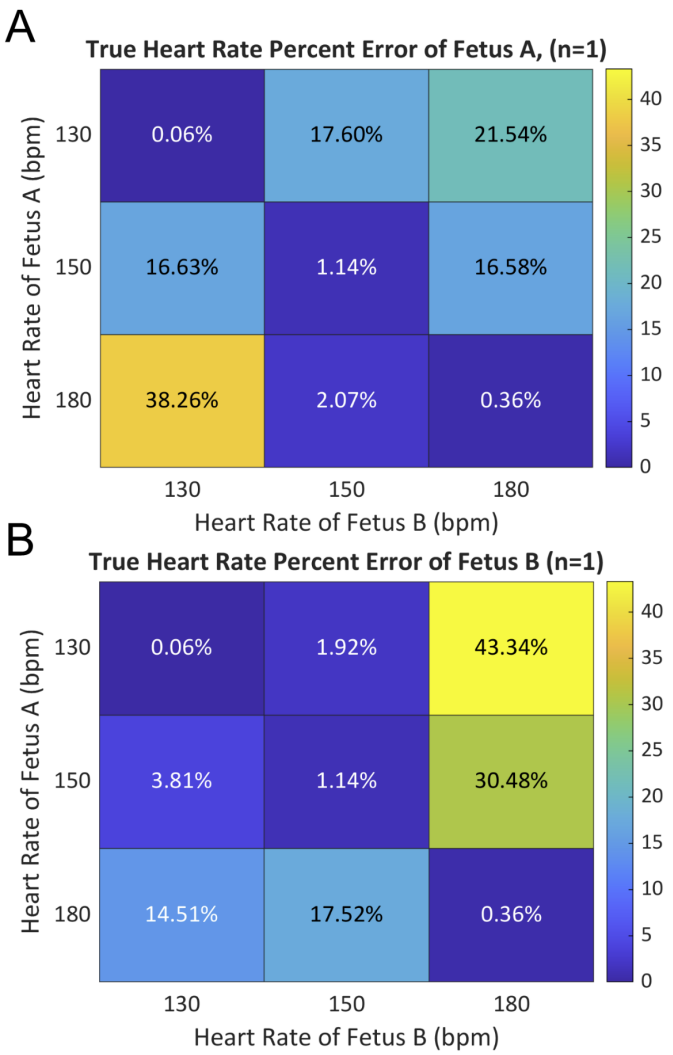

Fig. 7. Percent error for multiple heartbeat measurements Two sets of measurements were conducted, one against each heartbeat: nine trials of pairs of heartbeats of 130 bpm, 150 bpm, and 180 bpm (n=1). Each value represents the percent error of the reading for the heart rate of fetus "A" (Fig. 7a) or the heart rate of fetus "B" (Fig. 7b).

We can see that the true heart rate percent error is low when the difference in heart rates between the two fetuses are low Conversely, we can see that the true heart rate percent error is high when the difference in hearts rates between the two fetus are high (Figure 7). As much as a 43 percent error is seen when the difference is high (Figure 7b). We believe the reasons for the high-error to be two-fold: the gain of each microphone was not normalized to each other, resulting in all microphones receiving one heart rate as the dominate heart rate in a trial, and our algorithm is not able to separate noise from heart rate A

and heart rate B as it naively selects the frequency with greatest amplitude as the one recorded signal.

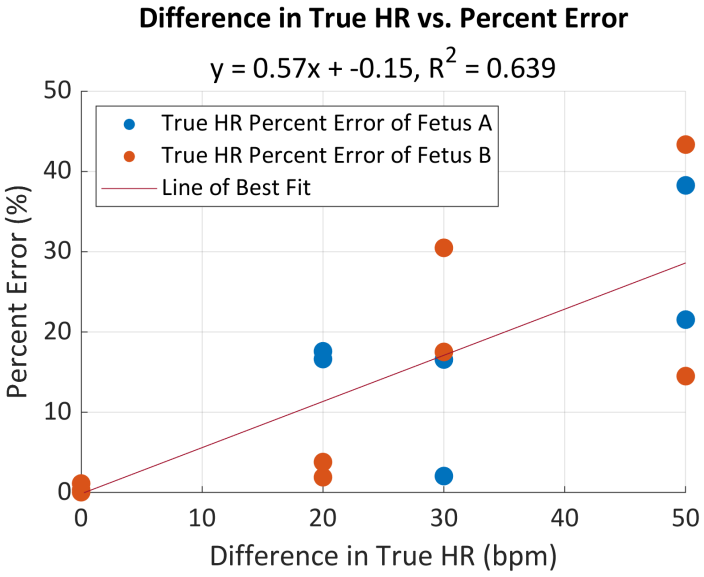

Fig. 8. Percent error correlation plot The correlation between difference in heart rates between the two fetuses and the percent error are shown. As the difference in heart rates increases, the percent error also increases.

There is a slight correlation (~0.639) between the difference in true heart rate and the percent error of measured heart rate against the true heart rate (Figure 8). This suggests that as the difference in true heart rate increases, the percent error from the true heart rate also increases. Future work will aim to decrease the slope of the correlation line of best fit, which would be a measure of improving fetal heart rate measurements.

Discussion

Limitations

Many of the issues we faced during this project were a result of inadequate experimental design and hardware. With respect to experimental design, we do not believe that the gel phantom perfectly models a twin gestation *in utero*. This is primarily because of the methods used to insert the speakers that acted as phantom hearts. Because of the high temperature of the material and limited accessibility of the side of the material during gel phantom creation, we had to forcibly make incisions in the phantom. Although the knife used to cut the phantom was sharp, the inherent elasticity of the gel made it difficult to get a clean and level cut. This difficulty resulted in the potential for a speaker-air interface for sound waves before it reaches the gel material, adding undesired noise to the data collection.

Additionally, we assumed that the heart rates of the simultaneous phantom heartbeat measurements were in-phase. This phenomenon resulted in trials for which the two heart rates were equal in frequency–trials 130-bpm and 130-bpm, 150-bpm-and-150-bpm, and 180-bpm, and 180-bpm–the audio generators produced sound at the same time, rather than at a non-zero displaced time.

We encountered numerous hardware issues during this project. Firstly, the speakers used to act as the phantom hearts in our gel phantom system produced their respective sound pulses at a relatively (unmeasured) low magnitude. Additionally, we were not able to change the intensity of sound emitted from these speakers. The speakers also did not emulate a natural human heartbeat, rather they simply generated a single pulse at the desired frequencies. Secondly, the microphones used in the novel fHR monitor picked up on a fair amount of ambient noise during all aforementioned trials. Although the intensity of the phantom heartbeats could be seen in our measurements, the addition of noise potentially added to inaccuracies in our data collection. We believe that with microphones that produced less noise, the efficacy of our device would improve. Lastly, the Arduino Uno used as the microcontroller for our device had a limit of 6 analog pins. In our proposal, we suggested using 7 microphones arranged in a circular pattern (6 microphones equally distributed in a circle with 1 microphone in the center) as shown in previous studies to work well in systems measuring heart rate.[9] Because of this limitation, our array design shifted to the aforementioned triangular array, which we assume has lower efficacy when measuring heart rate, especially multiple heart rates, due to a lower degree of equal distribution. Overall, we believe that the efficacy of our novel fHR monitor would improve with more appropriate hardware.

Future Work

Hardware Improvements

As mentioned previously, the implementation of better hardware would increase the efficacy of this device. In the future, we would aim to seek out speakers (that are able to interface with our microcontroller system) that are thinner and can better emulate the particular wave pattern of a natural human heartbeat. This particular improvement would establish a more accurate model describing a twin gestation pregnancy *in utero*. We would also attempt to

find microphones (that again are able to interface with our microcontroller system) that have a higher signal-to-noise ratio. A potential solution without purchasing different microphones would be to build a physical bandpass filter as part of the circuit. Moreover, we would aim to seek out a microcontroller with more than 6 analog pins such that we can create an ideal array of 7 microphones mentioned previously to improve the efficacy of measurement as well as improve our ability to implement triangulation to identify the location of the phantom heartbeats.

Human Mounting Apparatus

Laid out in our capstone proposal in the fall, we intended on designing a mounting apparatus for our device to successfully be used on a pregnant patient. Commercial standard clinical fHR monitors wrap around the lower abdomen. While this securely fastens the monitor for more accurate readings, obstruction of the lower back prevents an efficient and effective administration of an epidural, which can be highly desired during labor and delivery. Future work would attempt to design a way for the novel fHR monitor to be secured to a patient without obstructing their lower back.

Clinical Standard fHR Monitor Testing

Although we intended to, we were unable to use a standard fHR monitor on our gel phantom to compare our novel fHR monitor. Future work in this area would involve going into a local clinic to borrow a standard fHR monitor to use on our gel phantom. This experiment would not only allow us to compare the efficacy of our device to the gold standard in this field but also validate the gel phantom as a model for pregnancy.

Triangulation

One way of representing the collection of data is by a relative heatmap over time. Although an animation would show color values across the entire measurement duration, below is an instance of the 150-bpm-and-150-bpm trial (Figure S3).

Each microphone dot is located relative to the center of the probe, and the two "X's" represent the locations of the measured heartbeats relative to the

However, future work includes conducting "reverse triangulation", in which the amplitude of each of the six microphones could be used to mathematically determine a position of the two heart rates. This can be done only with equal gain across the six microphones, which this project did not do. This is hinted at by microphone 2 having a much higher gain than that the other five microphones in each trial.

End Matter

Author Contributions and Notes

The authors declare no conflict of interest.

Acknowledgments

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Dr. Natasha Sheybani, PhD, Assistant Professor of Biomedical Engineering

Dr. Christopher Ennen, MD, Assistant Professor, Maternal - Fetal Medicine

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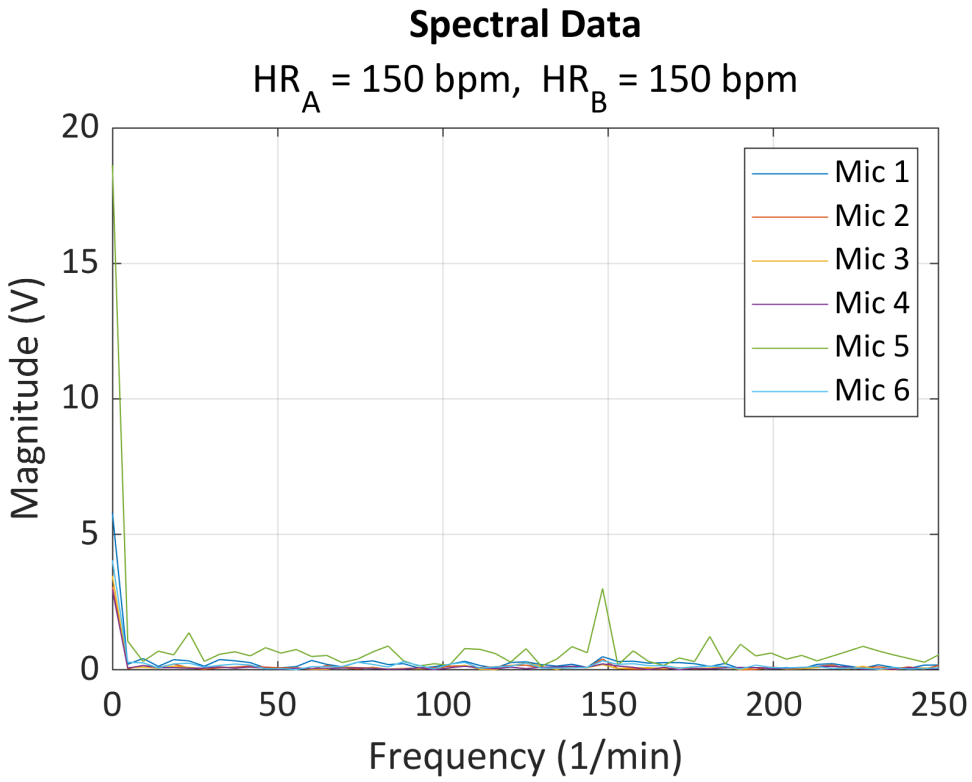
Supplementary Material

Supplementary Figure 1. Image of our gel phantom setup

Supplementary Figure 2. Unfiltered spectral data of a given trial