A Preliminary Proof-of-Concept for an Electronic Circuit Board that Uniquely Intensifies the Acoustic Output of a Muscle and Bone Resonance Signal Such that It Can Be Used for Clinical Diagnosis—Such Electronic Circuit and Amplifying Electric Circuit Being Based on a Fibonacci Sequence Design

Stan Beran[1], Adrian Harrison[2]

[1]Coral Gables, FL, USA; [2]Section for Physiology, Department for Veterinary and Animal Sciences (IVH), Faculty of Health & Medical Sciences, University of Copenhagen, Frederiksberg, Denmark

Correspondence to: Adrian Harrison, adh@sund.ku.dk
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ABSTRACT

To date, accurate assessment of muscle tissue and bone has proven difficult due to lack of definition and detail of the recorded signal. With the use of an SMB pre-amplifier electronic unit, which uses a unique system to intensify and clarify acoustic output, we present a proof-of-concept that such a device is now capable of assessing and diagnosing differences in bone structure as well as soft body tissues, in a rapid, safe and non-invasive manner. It is proposed that the SMB pre-amplifier has potential as a diagnostic tool, pending validation in a larger more diverse patient cohort, and that it could be of benefit in a clinical and microgravity setting, as well as being an acoustic delivery phenomenon producing a perceived enhanced listening experience.

1. INTRODUCTION

There are many instances where an accurate and very detailed amplified acoustic signal is essential [1]. One additional instance is the assessment and diagnosis of soft and hard tissues of the body (muscle, bone etc.) employing the technique of resonant frequency [2]. This technique is of current importance since exposure to microgravity during spaceflight causes rapid and preferential changes to body tissue [3]. One example is atrophy of skeletal muscle, including a decrease in strength, predominantly in the lower limb and trunk muscles, most likely due ambulatory changes at μG compared to earth [4]. Likewise detrimental changes have also been observed in the skeletal system. Findings to date indicate that μG exposure affects the porous nature of trabecular bone tissue and accelerates bone resorption [5].

Studies of bone loss in ISS astronauts using Quantitative Computed Tomography (QCT) of the hip and spine and High-Resolution-peripheral QCT (HR-pQCT) of the lower leg have shown loss of trabecular bone mineral density that is not detectable by standard clinical testing for osteoporosis [3]. Recently, a 6-month spaceflight revealed biologically significant declines in the hip trabecular bone and deficient or delayed bone recovery in some crewmembers. Indeed, it was found that deterioration in trabecular BMD immediately following long-duration spaceflight continued in some crewmembers for a year or more post-flight. Combined, these findings suggest that astronauts are at risk of premature or irreversible skeletal fragility.

It is documented that trabecular deterioration is associated with skeletal fragility and fractures in populations undergoing age-related bone loss [6]. However, trabecular characterization has not been performed for the astronaut cohort which is much younger and instead exposed to disuse-induced bone loss. It is therefore critical to assess changes in skeletal structure in astronauts during and after spaceflight missions. Moreover, the inclusion of a non-invasive and quick bone structure assessment for astronauts would enable in-flight bone health monitoring and the efficacy of such countermeasures as ARED on ISS. To this end, it is known that resistive exercise using ARED prevents reductions in cortical BMD of the femoral neck of astronauts, and that bisphosphonate, when combined with resistive exercise, enhances the preservation of bone mass [5].

The strength of acoustic signals, particularly those from living organisms, can be improved through amplification, whereby the amplitude or energy of a sound or audio signal is increased [7]. This can be achieved with the aid of transistors and circuits for use with low-voltage electrical signals from sources like microphones or piezoelectric ceramic sensors. Acoustic signals can often be affected by extraneous issues that affect the signal-to-noise ratio and result in distortion or humming and buzzing noise or simply a low output signal. Often in order to amplify a low-output signal, equipment and circuits that require an external power source are used, but this in itself can result in signal distortion. When dealing with very low-output or noisy signals a pre-amplifier is typically used, but here again the design of such circuits involves the choice of the right amplifier type, configuration and components [8].

This study has therefore sought to test the use of a unique amplifier device alongside the technique of resonant frequency of soft tissue and bone to test the hypothesis that: 1) real-time monitoring of BMD can be achieved non-invasively and with a sufficient clarity and definition to be of clinical diagnostic use, and 2) that a unique amplifier device can be used in combination with the technique of resonant frequency to detect soft tissue structures.

2. METHODS

The raw data presented in this study were collected from a Healthy Control subject (male, 59 years) and an Osteoporosis subject (female, 70 years) after giving their informed consent. This study has followed the guidelines set by the Helsinki Declaration 2013 (https://www.wma.net/wp-content/uploads/2016/11/DoH-Oct2013-JAMA.pdf), and the technique of acoustic measurement was approved by the University of Copenhagen: Ethics Institutional Review Board No. 2023-09-PAS-014A.

2.1. PRE-AMPLIFICATION

An electronic unit (SMB pre-amplifier; Miami, FL, USA) has been designed based on a vacuum tube circuit with a unique construction, placement and housing which provides an exceptional frequency response and signal-to-noise ratio, with variable gain and extremely low distortion. The SMB electronic unit was designed for use as an insertion into a pre-amplifier or tape-out unit. Prior to and separate from power amplification, active signal amplification takes place through a vertically arranged circuit board design that isolates the signal of importance from any stray energies arising from a toroidal-based power supply. For a diagram of the construction details see Figure 1. The SMB pre-amplifier was tested against a standard commercial device (Advanced Myographic Technology, LLC; Ocala, FL, USA) both in combination with a smartphone (Apple Inc., Cupertino, CA, USA). The SMB pre-amplifier was built from hand-selected components that were tested with a variety of triode vacuum tubes to arrive at the finished device with its unique properties.

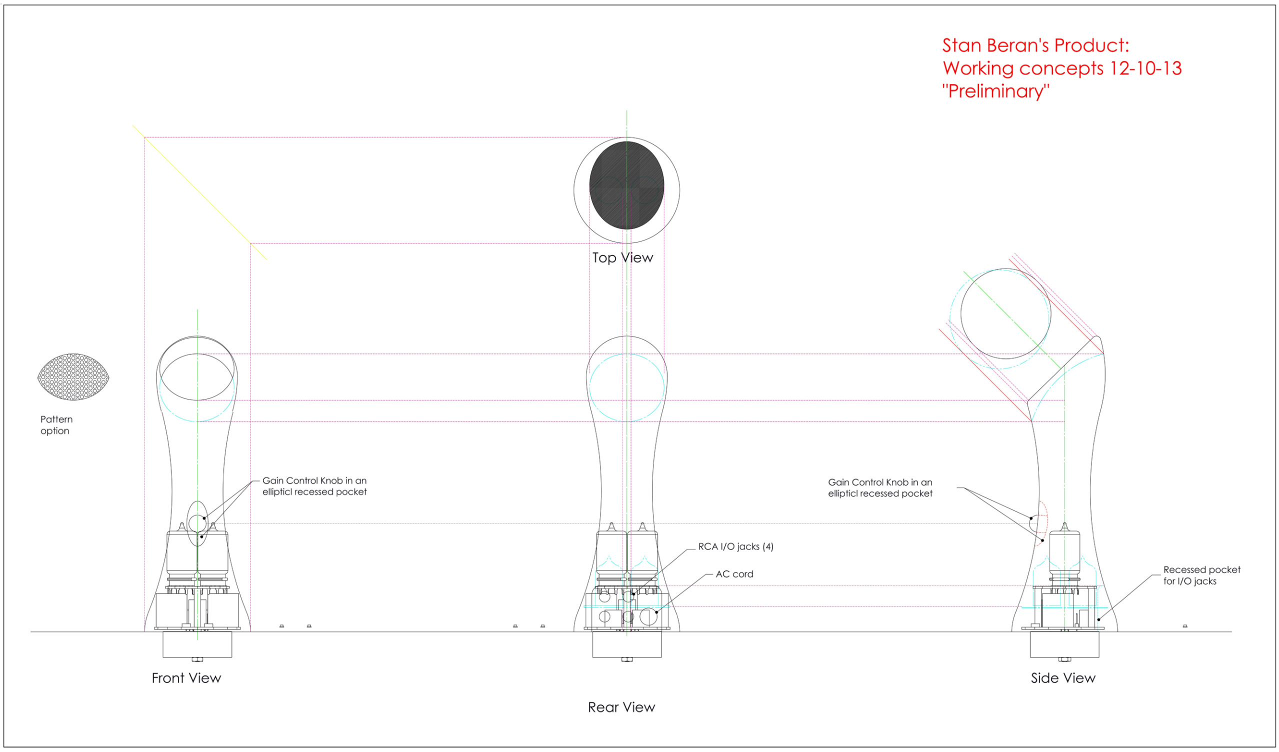


Figure 1. Details of the SMB pre-amplifier unit. A diagram of the housing used and an overview of the circuitry placement.

The design of the SMB pre-amplifier unit is based on the so-called golden ratio, derived from the Fibonacci sequence. Not only is the casing for the SMB pre-amplifier unit based on the Fibonacci sequence, providing a unique circuit to vacuum tube separation that serves to reduce internal electrical interference, it also provides a natural path for heat dissipation. The Fibonacci sequence is also an integral part of the design of the SMB pre-amplifier circuit itself, and contributes significantly, in the author's opinion, in combination with the other design features, to both optimized gain and signal processing.

2.2. Bone Structure Assessment

An acoustic recording made from the lower leg bone Tibia (tibial tuberosity—human subjects) using a unique SMB pre-amplifier, reveals the difference in bone structure occurring with osteoporosis (female subject, 70 years of age), over the frequency range of 290 - 5 Hz, compared with a healthy control subject (male subject, 59 years of age).

2.3. Soft Tissue Assessment

An acoustic recording made from the forearm muscle Flexor carpi radialis using a unique SMB pre-amplifier reveals the difference in soft tissue structure over the frequency range of 400 - 5 Hz in a healthy control subject (male subject, 59 years of age).

2.4. Acoustic Signals

Acoustic recordings were made using a SOFi M² (Advanced Myographic Technologies, LLC, Ocala, FL, USA) unit and an AMT piezo sensor placed on the tibial tuberosity and m.Flexor carpi radialis and held in place using hydrogel (Promeon Hi-Adhesion Gel 032—M863X; R&D Medical Products CA, USA). Signals were recorded at 100 per second at a 32 dB gain setting and were transferred to a smartphone for data storage [9] [10]. The SOFi M² unit weighs 10 g, has a gain setting range of 0, 6, 12, 15, 18, 21, 24, 27 and 32 dB which can be adjusted in real-time via an app, uses a piezoelectric crystal sensor of 2 cm or 5 cm diameter connected via a 2.5 mm audio jack and has an input impedance of 50 kOhm. At the 32 dB gain setting a SOFi M² unit has a signal amplitude of 123 mV.

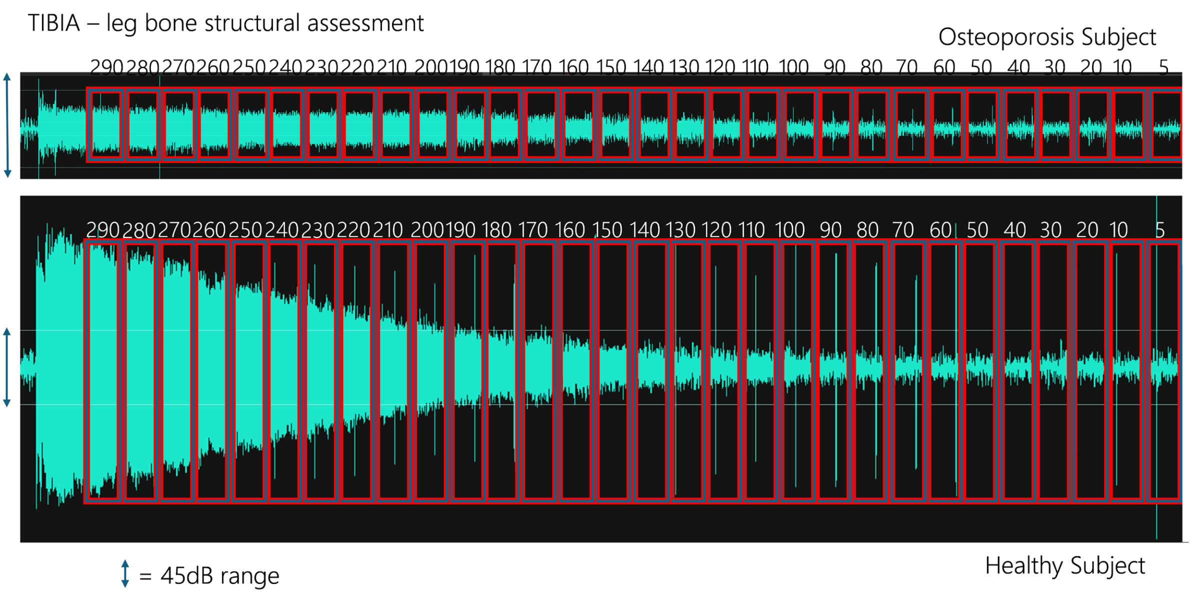
2.5. Sound Generation

The audible signals used in this study were generated using a Tone Generator App (Michael Heinz, Lifegrit 2023; Lifegrit Development, DE), which were sent to a hand-held speaker with an open membrane design (Lifetrons Drumbass IIIe Mini Bluetooth Speaker, Lifetrons, CH) via a USB connector. The hand-held speaker was then placed onto the tissue of interest and sound waves generated by the device were transmitted directly to the tissue. The AMT piezo sensor was placed 1 cm away from the hand-held speaker and care was taken to avoid contact with the hand-held speaker.

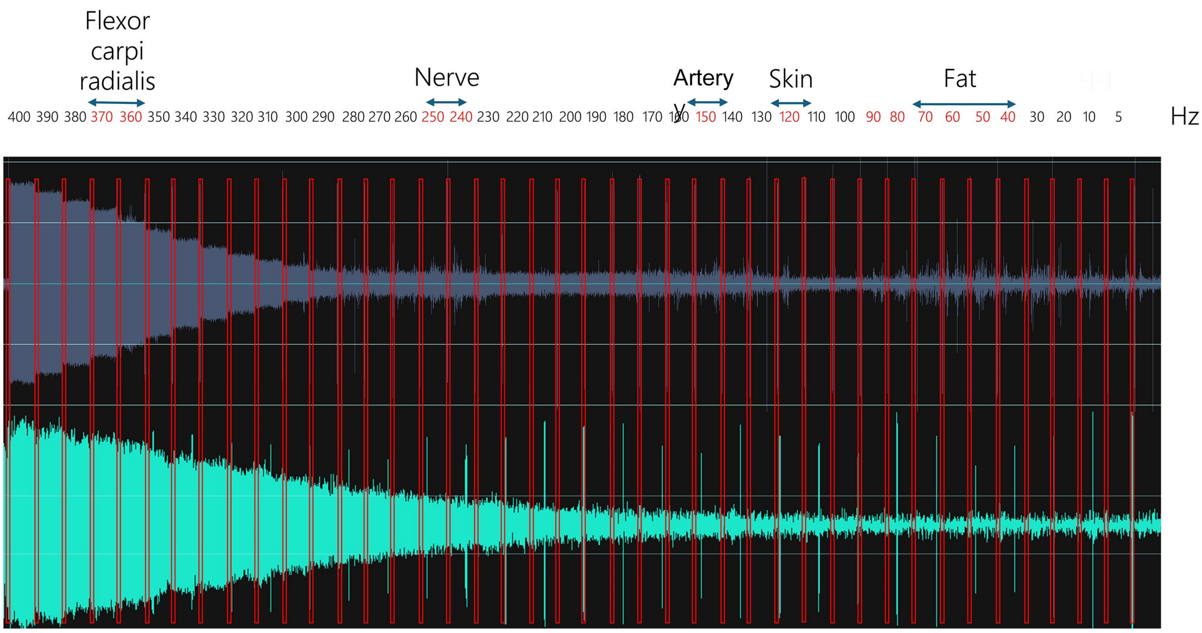
3. RESULTS

An example of the clarity and improved definition achieved using the SMB pre-amplifier unit can be seen in **Figure 2**. Note in the image (see **Figure 2(a)**) that the 45 dB range for the healthy and the osteoporotic bone measurements differ greatly, with osteoporosis the recorded signal does not exceed the 45 dB range, whilst with the healthy control subject it exceeds the 45 dB range and approaches the 24 dB range.

Figure 2(b) shows a recording comparing the signal from the SMB pre-amplifier (upper panel) with a signal from a standard amplified signal achieved using a SOFi M² unit alone (lower panel). The figure highlights frequency bands known to be the resonant frequency of human tissues, such as the forearm muscle Flexor carpi radialis, nerve tissue, artery, skin and fat [2]. Note how the frequency bands have a more stable plateau with the SMB pre-amplifier and that there is improved detail at set frequencies; e.g., 250 - 240 Hz, 150 Hz, 120 Hz and 90 - 40 Hz.



(a)



(b)

Figure 2. (a) A recording made using a standard pre-amplifier (Upper Panel) compared with a signal from a standard amplified signal (Lower Panel) taken from the tibia of an Osteoporosis subject and a healthy subject; (b) A recording made using the SMB pre-amplifier unit (Upper Purple signal) compared with a signal from a standard amplified signal (Lower Green signal) taken from the forearm muscle Flexor carpi radialis longus—note that the improved upper signal has more clarity and detail than the lower recorded signal over the low frequency range (5 - 450 Hz).

In a more detailed recording made using frequencies ranging from 12 to 170 Hz, it can be seen how the SMB pre-amplifier unit consistently produces a signal with a greater amplitude but also a greater definition; 170 Hz - SMB pre-amplifier exhibited a −29 dB (7.09e−10 kPa) signal compared with the standard amplified signal which exhibited a −34 dB (3.99e−10 kPa) signal: 12 Hz - SMB pre-amplifier exhibited a −14 dB (3.99e−9 kPa) signal compared with the standard amplified signal which exhibited a −23 dB (1.41e−9 kPa) signal (see Figure 3).

The signal amplitude is clearly not only improved with the SMB pre-amplifier compared with standard amplification it is also more stable with level plateaus at each step frequency, and clearer definition at key diagnostic frequencies.

4. DISCUSSION

In this study, we focus on the application of a unique and novel SMB pre-amplifier for the detection of differences in bone and soft tissue structure in human subjects, a technique of importance for terrestrial diagnostic purposes, but also of importance for prolonged space flight changes. Of course, the SMB pre-amplifier can also be used for other purposes, such as the improvement of low-voltage electrical signals from sources like microphones or simply for playing music.

This study has a primary limitation in that a very small sample size (n = 2) was used, and as such readers should be aware that whilst promising, these findings warrant further validation in a larger, more diverse patient cohort. Despite this, however, the present study demonstrates information that an MRI would typically provide without the discomfort, expense or immediate advantages of a real-time analysis. Furthermore, the details provided by this device represent a quality of information and speed of analysis that are currently not available in a clinical setting and additionally lend themselves to a microgravity environment. The cost savings of discovery using the SMB pre-amplifier unit over the costs of MRI to provide the same level of detail are also many times reduced. It is envisioned that the SMB pre-amplifier unit can be used by non-medically trained technicians and readily adopted in a home or a less formal setting.

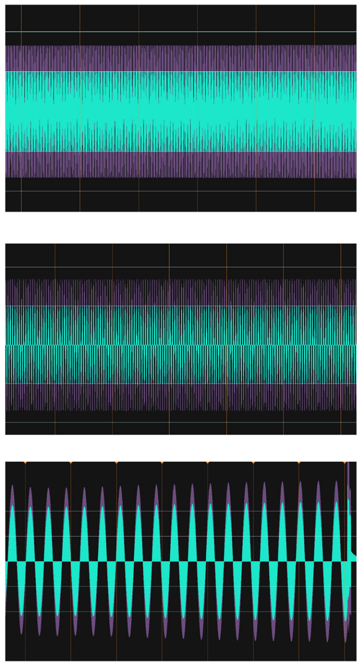


Figure 3. A recording made using the SMB pre-amplifier unit (Purple signal) compared with a signal from a standard amplified signal (Green signal)—note that the improved signal is consistently better across the frequency spectrum tested (12 - 170 Hz). At high frequency the SMB pre-amplifier exhibited a −29 dB (7.09e−10 kPa) maintaining the details of the response and at the lower frequencies it generated a −14 dB (3.99e−9 kPa) signal with a greater level of detail compared with the standard amplified signal. The standard amplified signal exhibited a −34 dB (3.99e−10 kPa) signal which was measured at lower frequencies to be −23 dB (1.41e−9 kPa).

This study illustrates that a combination of an SMB pre-amplifier circuit and a toroidal-based power supply circuit, uniquely positioned one from the other, greatly improves the quality and the detail of the recorded signal compared to that of standard amplification. A pre-amplifier is typically used to improve sound, and thereby enhance audio systems. They serve to amplify and condition weak signals from sources like microphones or turntables to a "line level", which is stronger and clearer [1]. Thus, high-quality pre-amplifiers facilitate the reduction of both noise and distortion and the result is a cleaner, more detailed sound with improved dynamic range. Pre-amplifiers also function by improving the signal-to-noise ratio. They ensure that the desired audio signal is louder and more distinguishable from background noise. One should, however, bear in mind that not all pre-amplifiers when they are built, end up clean. In some instances the input and output transformers within the circuitry can generate harmonic distortion when the signal's input or output volume is close to its limit. However, with the design of the SMB pre-amplifier and its variable amplitude control, a better signal-to-noise ratio and sonic detail have been achieved.

The signal presented in the present study from the tibia of a human subject diagnosed with osteoporosis compared with that of a healthy subject, shows how the resonant frequency of the tissue differs, most markedly the amplitude of the signal (see **Figure 2(a)**). The speaker and sensor were placed onto the skin above the tibial tuberosity, and care was taken to ensure good contact throughout the recording. The recorded signal presented in Figure 2(b) clearly illustrates not only how stable the SMB pre-amplified signal is at each frequency step, with a level plateau, but it also reveals definition and details that are not detectable using standard amplification (see Figure 2(b))—e.g., nerve, artery, skin and fat [2].

A comparison of the SMB pre-amplifier *versus* a standard amplifier revealed that at higher frequencies (290 Hz) the SMB pre-amplifier exhibited a 2.00e−9 kPa signal which increased at the lower frequencies to 3.99e−9 kPa. In contrast, the standard amplified signal exhibited a 1.26e−9 kPa signal which increased at the lower frequencies to 2.82e−9 kPa. This represents a sound pressure increase in recorded signal with the SMB pre-amplifier of 0.74e−9 kPa at the higher frequencies and 1.17e−9 kPa at the lower frequencies—percentage-wise, this represents a 58% improvement at higher frequencies and a 41% improvement at lower frequencies, for the SMB pre-amplifier compared with the standard amplified signal. Quantitative improvements in bone density measurement are currently not typically described in kPa, but rather in decibel (dB) or kilohertz (kHz) for ultrasound techniques, and in millimeters per year or percent change from a baseline for clinical assessment [11]. Hence, if this technique were to be adopted in a more clinical setting, then it would be necessary to collate kPa data so it could be readily relevant and recognisable in a clinical setting. Moreover, in bone density measurement, the clinical relevance of dB relates to the signal-to-noise ratio and the clarity of the sound waves, which influence detection accuracy. Yet another consideration of importance when using such techniques as these as a diagnostic tool is that whilst higher frequencies provide better resolution for detecting subtle changes in tissue density, they also limit penetration depth, something that might be avoided using a resonance signal and a SMB pre-amplifier unit where a the observed improvement in signal pressure in the present study was 58% at higher frequencies.

It is likely, based on the results of this study, that an SMB pre-amplifier with a sound generator preset with a suitable frequency range and coupled to a device like the SOFi M^2 can be of use in a micro-gravity setting. Indeed, it is anticipated that such a setup could be of use in addressing such issues raised by NASA as, MA-201: Determine the required exercise countermeasure or countermeasures (*i.e.*, modality or modalities, prescription, monitoring) to protect mission-specific task performance and crew health outcomes, or Bone-101: Characterize skeletal changes on bone mass (Bone Density) and bone structure (Bone Quality) of astronauts [12].

5. CONCLUSION

The present findings indicate that the use of a unique SMB pre-amplifier can greatly improve the clarity and definition of a recorded acoustic signal originating from human tissue exposed to different sound frequencies. As such, this equipment and technique now warrants more focus as a potential diagnostic tool for assessing differences in bone structure as well as soft body tissues, in a rapid, safe and non-invasive manner. There is now a need for a validation study involving a larger cohort of human subjects and with a more diverse background. Besides this, the SMB pre-amplifier unit clearly has potential as an acoustic delivery phenomenon that is more satisfying to listen to than the original content, particularly in a digital setting.

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CONFLICTS OF INTEREST

SMB designed and built the pre-amplifier used in this study and is currently trying to commercialize the device. For details about the SMB pre-amplifier design contact stan@soundperformance.com. AH was responsible for the BMD recordings and soft tissue measurements as well as signal analysis. For details concerning the SMB pre-amplifier contact SMB.

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