Evaluation of an Investigational Hearing Screening Device *(HeLe)* to Demonstrate Acoustic Brainstem Response among Normal-hearing Adults

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ABSTRACT

Objective. This pilot human trial demonstrates the ability of the investigational newborn hearing screening device to provide acoustic stimulation to produce evoked potentials, as well as its ability to capture and acquire auditory evoked potentials, especially the auditory brainstem response (ABR) wave V. This pilot study also demonstrates the ease of recognizing and identifying ABR waves in the graphical presentation of the evoked potentials over time.

Methods. Fourteen normal-hearing adults or a total of twenty-eight (28) normal-hearing adult ears underwent auditory brainstem response testing using the investigational hearing screening device. A commercially available auditory brainstem response detection device was used to confirm that the acquired ABR waves of the investigational device are normal. The ABR waves displayed by the investigation device were also reviewed by the clinical audiologists to determine their recognizability and identifiability.

Results. The pilot trial demonstrates the ability of the investigational newborn hearing screening device in providing acoustic stimulation to produce evoked potentials, and in acquiring and capturing ABR waves, specifically the wave V, among normal-hearing adult ears. The clinical audiologists recognized and identified the ABR wave V among the evoked potentials at 40dB, 60dB, and 80dB acoustic stimulation. About eighty-nine percent (89.2%) of all ears tested had identifiable and recognizable wave V upon acoustic stimulation at 40dB.

Conclusion. The investigational hearing screening device: (1) can provide acoustic stimulation to produce evoked potentials, (2) can accurately capture and acquire these evoked potentials, (3) can present these evoked potentials in a voltage per time graphical display which an audiologist and trained HCP can easily read and interpret (diagnostic ABR), and (4) can present wave V auditory brainstem potentials that can be easily identified by an audiologist and trained HCP (screening ABR).

Keywords: investigational device, newborn hearing screening device

**Dr. Marcelo and Dr. Sison are project co-leaders.*

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INTRODUCTION

The global burden of congenital hearing loss is at 0.5 to 5 for every 1,000 neonates.[1] This burden is increased three times in developing countries at 6 in 1,000 live births compared with 2 in 1,000 live births in developed countries.[2] In the Philippines, profound bilateral hearing loss is detected in 1.38 per 1,000 live births, which is consistent with global data.[3] Permanent bilateral hearing loss costs a family in

the Philippines an estimated 4.3 million pesos for special education, specialized care, as well as lost income during adulthood. This economic burden is due to delays in speech, intellectual, and emotional development when the hearing loss is not detected and treated early.[4] Timely intervention using hearing aids and cochlear implants will allow normal speech and language development and may result in millions of pesos lifetime savings per patient.[4] The demonstrated cost-effectiveness of early hearing detection and intervention in the Philippines led to the passage of Republic Act 9709 known as the "Universal Newborn Hearing Screening and Intervention Act of 2009" mandating that all newborns must be screened for hearing loss and, if present, treated early. According to data from the National Hearing Screening Reference Center, there are currently 310 Category A Hearing Screening Centers with the capability of providing early hearing screening services to neonates – an increase of 23% in the number of screening centers since the start of the program. There are at least one Category A Hearing Screening centers in each region, but more than half of these centers are situated in Metro Manila. Category B Hearing Screening Centers – where confirmatory testing is done prior to providing early intervention – are not as widely distributed as the majority of centers are within Metro Manila and a few highly urbanized areas.[5] Every year, approximately 1.75 Million babies, or 200 babies per hour are born in the Philippines.[6] Based on the latest census done in 2014, 82% of all live births in the Philippines are delivered in health facilities[7]; and 55% of these live births are born in urban areas. In rural areas, 51% of live births are delivered at home; some regions get birth rates as high as 64-87% outside health facilities.[8]

To address these challenges, a collaborative project on both technology infrastructure and healthcare innovation that aims to increase the rate of newborn hearing screening through the development of a cost-efficient newborn hearing screening device, a telehealth/telemedicine system for managing patient information, and a tele-education / e-learning system for newborn hearing screening technology user training and screener accreditation was envisioned. The project, entitled "Increasing the Rates of Newborn Hearing Screening with Novel Technologies and Telehealth" (PCARI IHITM 2015-01), was funded by the Commission on Higher Education under its Philippine-California Advanced Research Institutes. The project was rebranded with the names "Hearing for Life" and HeLe (a Filipino word for "lullaby") to encapsulate the project's mission of bringing music to the ears of children. The HeLe Project developed the HeLe hearing screening device and the HeLe headset to screen all newborns for hearing disability and ensure that those identified to have potential hearing loss will be able to navigate the care pathway from screening to confirmatory. The current beta models of the HeLe hearing screening device and the HeLe headset make up a functional diagnostic ABR device that can (1) provide acoustic stimulation to produce evoked potentials, (2) accurately capture and acquire these evoked potentials, (3) present these evoked potentials in a voltage per time graphical display which an audiologist and trained healthcare provider (HCP) can read and interpret, and (4) has the capacity to exchange demographic and clinical information with an electronic medical record (Community Health Information Tracking System or CHITS, National Telehealth Center, UP Manila) using the HL7-FHIR messaging standard. The Hele devices have passed the electrical safety testing and sound pressure level safety testing, as well as efficacy and repeatability testing. (PCARI IHITM 2015-01 Terminal Report, 2019)

OBJECTIVE

To demonstrate the ability of the investigational newborn hearing screening device in providing acoustic stimulation to produce progressive acoustic/auditory brainstem response (ABR) waveforms, specifically Wave V, with increasing acoustic stimulus among normal-hearing adult volunteers.

Study Design

The study utilized a prospective case series design.

MATERIALS AND METHODS

The Clinical Validation Team was formed to perform data collection during the clinical investigation to determine the accuracy of the HeLe investigational device as a hearing screening device. The HeLe investigational device includes the HeLe Hearing Screening Device (patent application submitted) and the HeLe Headset (patent application submitted). The HeLe Headset provides the acoustic stimulation and houses the electrodes that capture the evoked potentials, while the HeLe Hearing Screening Device processes the evoked potentials and displays them as a voltage over time graph.

Clinical audiologists and clinicians oversaw the clinical validation process. Since the investigational device being developed was an automated auditory brainstem response (AABR), they underwent training and sensitization to the AABR screening modality.

All clinical audiologists underwent a sensitization process to eliminate the learning curve in using the AABR. Different protocols in skin preparation, electrode placement, and AABR screening procedures were explored to pinpoint the most efficient process. Different models of AABR machines were also used during this time. As expert users of hearing screening devices with exposure to all AABR machines available locally, the Clinical Validation Team was also tapped by the Engineering team to give feedback on the design of the investigational device. They were also tapped to support and participate in training activities in the deployment sites of the HeLe project.

Recruitment for all volunteers was done at the Philippine General Hospital Ear Unit. All recruitment procedures were

done following the UPMREB-approved protocol (UPM REB 2016-538-01).

This phase 1 pilot trial involved the detection of auditory brainstem response in healthy adults. A total of 14 normal-hearing adults participated in the study. Thus, there were a total of 28 ears measured using the HeLe Hearing Screening Device and the reference device. The resulting latencies for ABR Waves I, III, and V obtained using the reference ABR were recorded. In cases where waves were not identifiable, no value was recorded.

To eliminate errors, each component and procedure of the device was tested in isolation. The acquired raw ABR Waves are then processed using a defined filtering and smoothing algorithm to attain better and cleaner ABR Wave representation. These post-processed ABR Waves are given to the resident audiologists from PGH Ear Unit to verify the presence of Wave V and conclude that the acquired ABR wave is valid.

RESULTS

The pilot trial obtained multiple ABR recordings using calibrated stimuli of 40 dB, 60 dB, and 80 dB for both the HeLe Hearing Screening Devices and the reference ABR device. The resulting latencies for ABR Waves I, III, and V obtained using the reference ABR are shown in Table 1. The tabulation of clinically identifiable and recognizable ABR waves elicited, captured, and presented by the HeLe Hearing Screening is shown in Table 1. These results demonstrate the ability of the investigational newborn hearing screening device to provide acoustic stimulation and to acquire and capture ABR waves, specifically the wave V, among normal-hearing adult ears. Figure 1 is a representative graphical display of the evoked potentials acquired by the HeLe investigational device over an elapsed amount of time.

Moreover, the clinical audiologists were able to recognize and identify auditory brainstem response waves (Figure 1), especially the wave V, on the graphically displayed voltage/

Table 1. Clinically Identifiable Auditory Brainstem Response Waves per Ear

Ear	Auditory brainstem-evoked potentials detected by HeLe device																	
	80dB						60dB						40dB					
	I		III		V		I		III		V		I		III		V	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
1R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
2R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
3R	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
4R	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
5R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
6R	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
7R	✓	-	✓	-	✓	-	✓	-	✓	-	✓	-	-	-	-	-	✓	✓
8R	✓	✓	✓	✓	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
9R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
10R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
11R	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12R	✓	✓	✓	✓	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
13R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
14R	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
1L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-		-		✓	✓
2L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
3L	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
4L	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
5L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
6L	-	-	-	-	✓	-	-	-	-	-	✓	-	-	-	-	-	✓	-
7L	✓	-	✓	-	✓	-	✓	-	✓	-	✓	-	-	-	-	-	✓	✓
8L	✓	✓	✓	✓	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
9L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
10L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
11L	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12L	✓	✓	✓	✓	✓	✓	-	-	✓	✓	✓	✓	-	-	-	-	✓	✓
13L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
14L	-	-	-	-	✓	✓	-	-	-	-	✓	✓	-	-	-	-	✓	✓
TOT	8	5	8	6	28	20	4	2	5	3	28	20	2	2	2	2	28	22
ABR	5		6		20		2		3		20		2		2		22	

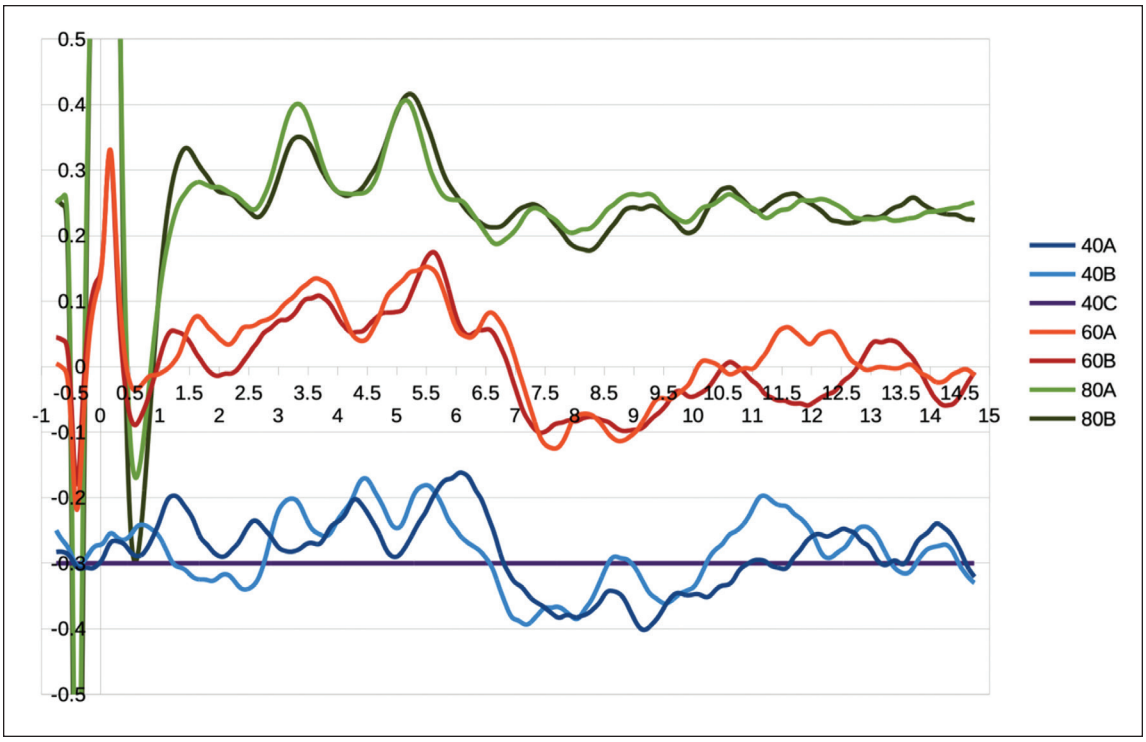

Figure 1. Graphical display of evoked potentials at 40dB, 60dB, and 80dB acoustic stimulation **(A)** right ear, **(B)** left ear, **(C)** ground.

potential vs time graph presented by the HeLe investigational device. The tabulation of the percentage of clinically identifiable auditory brainstem response waves at various auditory stimulation levels is shown in Table 2. At auditory stimulation levels of 40dB, 60dB, and 80dB, the HeLe device was able to elicit, capture, and acquire recognizable and identifiable evoked potentials, specifically ABR Wave V, in the majority of the ears of the trial participants. In the first run of the ABR testing, 100% of all ears tested had identifiable and recognizable wave V's upon stimulation with 40dB, 60dB, and 80dB auditory stimuli (Table 2). However, in terms of reproducibility (Table 3), the HeLe device was only able to present the ABR wave V in 71.43% of the test ears at 80dB auditory stimuli, 71.43% at 60dB auditory stimuli, and 78.57% at 40dB auditory stimuli on the second run of ABR testing, the percentage of ears with identifiable and recognizable wave V's decreased as follows: 71.43% at 80dB auditory stimuli, 71.43% at 60dB auditory stimuli, and 78.57% at 40dB auditory stimuli. These discrepancies may be explained by patient and device factors during prolonged and repeated patient testing. However, since waves are only considered as ABR waves if they are reproducible in at least 2 test runs, the device fell short of being able to consistently present identifiable ABR waves. It is also noteworthy that a 40dB auditory stimulation demonstrated reproducible and clinically identifiable ABR wave V (78.57%).

The HeLe hearing screening device was not able to consistently elicit, capture, and acquire the other auditory brainstem response waves (i.e., I and III). These waves were only recognized and identified between 7.14% and 28.57% of the ears tested.

Table 2. Percentage of Clinically Identifiable Auditory Brainstem Response Waves at Various Auditory Stimulation Levels

	80dB			60dB			40dB		
	I	III	V	I	III	V	I	III	V
Trial 1	28.57%	28.57%	100%	14.29%	17.85%	100%	7.14%	7.14%	100%
Trial 2	17.86%	21.43%	71.43%	7.14%	10.71%	71.43%	7.14%	7.14%	78.57%

Table 3. Reproducibility of the Auditory Brainstem Response Waves at Various Auditory Stimulation Levels

Wave	80dB			60dB			40dB		
	I	III	V	I	III	V	I	III	V
ABR	17.86%	21.43%	71.43%	7.14%	10.71%	71.43%	7.14%	7.14%	78.57%

Table 4. Technology Readiness Levels[13,15]

TRL Level	Definition
TRL 1	Basic principles observed
TRL 2	Technology concept formulated
TRL 3	Experimental proof of concept
TRL 4	Technology validated in laboratory
TRL 5	Technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies)
TRL 6	Technology demonstrated in relevant environment (industrially relevant environment in the case of key enabling technologies)
TRL 7	System prototype demonstration in operational environment
TRL 8	System complete and qualified
TRL 9	Actual system proven in operational environment (competitive manufacturing in the case of key enabling technologies or in space)

DISCUSSION

Auditory Brainstem Response (ABR) also known as Brainstem Auditory Evoked Response (BAER) is a valuable objective measurement of the integrity of the auditory pathway. It is a diagnostic test that provides an estimation of the hearing sensitivity of patients who are unable to give reliable subjective responses or unable to tolerate conventional behavioral audiometry. This could be performed not only among infants but also among those hard-to-test children or those with other medical conditions that need hearing evaluation.

Among the Auditory Evoked Potentials (AEP), ABR is identified as "early or short" - latency, occurring in the first 10 to 15 milliseconds after the introduction of either a click or a tone burst stimulus.[9]

The auditory brainstem evoked potential latencies are measured from time 0 (acoustic stimulation) to the time coinciding with the highest peak of the waves. Wave amplitude is the difference in potentials from one wave to the next. Interwave latencies are the time difference between waves.[10] ABR waveform changes in response to a progressively decreasing stimulus intensity.[10] For any ABR wave, the peaks are labeled as waves I, II, III, IV, and V. Each of these waves is believed to be produced by the following generator sites: Waves I & II - auditory nerve, Wave III - cochlear nucleus, Wave IV - superior olivary complex, Wave V - lateral lemniscus & inferior colliculus.[11]

ABR waveform changes in response to a progressively decreasing stimulus intensity. With wave V typically having the largest amplitude, the ABR threshold is obtained as the lowest intensity at which it is present or observed.[9]

Based on data from R. Kelley and J.W. Hall III in 2007, testing both left and right ears of 26 subjects, the mean wave V absolute latency at 80 dB is 6.16 ms (right) and 6.18 ms (left).[12] The wave V absolute latencies acquired using the ABR reference device range from 5.15 - 6.10 ms at 80 dB, 5.65 - 6.70 ms at 60 dB, and 5.55 - 7.33ms at 40 dB, and conform with the published standard normal values.

ABR is therefore a diagnostic audiological assessment that permits early diagnosis of hearing loss. The information from ABR testing is vital for the determination of the appropriate hearing intervention. This pilot study has demonstrated that the current model and build of the HeLe headset/electrode system was able to successfully provide an acoustic stimulation to elicit an evoked auditory brainstem response, as well as capture the ABR wave V and display the evoked potentials as a voltage vs time graph. The latencies of the ABR waves captured and acquired by the HeLe investigational device appear to fall within the normal range of values for ABR waves I, III, and V. It is important to note that ABR wave V is reproducible, identified, and recognized in 78.57% of all ears tested at 40dB acoustic stimulation, and in 71.43% of all ears at both 60 and 80dB acoustic stimulation. The results are promising since it can detect and capture the ABR wave V upon auditory stimulation of 40dB which makes the device a capable screening tool for detecting hearing loss. Further development is recommended to make the device more consistent in acquiring and presenting reproducible ABR wave V.

The HeLe investigational devices appear to be ready for further clinical testing together with the algorithm for automating the detection of ABR wave V. This algorithm was developed in parallel with the device development and a patent application is being prepared. In the context of device development, the consistency of identifying and recognizing ABR wave V acquired by the HeLe device provides the development team a firm basis to continue its plan for algorithm development for automating the detection of ABR wave V. Further development to improve the capture and acquisition of the evoked potentials is underway to ensure close to 100% detection of ABR wave V.

At this point, the HeLe investigational hearing screening devices can be considered to be at least Technology Readiness Level 4 (and in the early stage of TRL 5, Table 4). That is, the HeLe hearing screening device and the HeLe headset proof-of-concept technologies are ready to function as each one is intended to do, confirmed in the laboratory setting, and tested in among controls – patients with known clinical findings. The Technology Readiness Levels (TRL) assesses the maturity – capacity and readiness - level of a specific technology.[13] In parallel, the World Health

Organization, in its guidance to innovators in the use of information and communications technologies for health, describes this early stage of technology development as the prototype stage.[14] Inventors seek answers to the question "Does it work?" that is, "Do the HeLe technologies work"? This study affirms this and has demonstrated that the HeLe system meets the defined technical specifications. That is, the HeLe headset can provide the acoustic stimulation to elicit an evoked auditory brainstem response, and the HeLe hearing screening device can capture the ABR wave V and display the evoked potentials. For these two functionalities, the HeLe hearing screening device and the HeLe headset are now in the early TRL 5 phase: testing in a "relevant environment" where adults with known ABR findings are subjected to the HeLe technologies. Further development can improve the device performance and further studies should determine if the HeLe system is stable and error-free, and perform its functions consistently and faithfully especially among its intended patients - including those with hearing impairment - in the controlled clinical setting. An increase in sample size is recommended; the WHO cites at least 100 to meet functionality and stability goals for the technology. Similarly, usability studies should also coincide in order to establish ease-of-use and provide better information on the feasibility of integration of the HeLe technologies in the clinical workflow. These studies will inform how the stable and clinically-validated HeLe investigational hearing screening devices are best deployed in over 2500 primary care health facilities nationwide, envisioned to be NHS Category A centers more accessible to Filipino families.

CONCLUSION

The current model and build of the investigational hearing screening device: (1) can provide acoustic stimulation to produce evoked potentials, (2) can accurately capture and acquire these evoked potentials, (3) can present these evoked potentials in a voltage per time graphical display which an audiologist and trained HCP can easily read and interpret (diagnostic ABR), and (4) can present wave V auditory brainstem potentials that can be easily identified by an audiologist and trained HCP (screening ABR).

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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