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Longitudinal outcomes of distortion product otoacoustic emissions and wideband reflectance in infants

Virginia Ramachandran
Wayne State University,

LONGITUDINAL OUTCOMES OF DISTORTION PRODUCT OTOACOUSTIC EMISSIONS AND WIDEBAND REFLECTANCE IN INFANTS

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VIRGINIA RAMACHANDRAN

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Co-Advisor Date

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Co-Advisor Date

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DEDICATION

To my son, Nathan Ramachandran, for having a smile on his face every day and giving me a soft place to land. I love you.

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CHAPTER 1

INTRODUCTION

Newborn Hearing Screening

Universal newborn hearing screening refers to screening of all infants for hearing loss shortly following birth. Universal newborn hearing screening was first mandated in 1990 in the state of Hawaii. Since that time, all states in the United States have enacted legislation on universal newborn hearing screening. The mandate is due to the known speech, language, and educational consequences of significant hearing loss in children and the technological means to make screening of infants a reasonable task.

The goal of newborn hearing screening is to identify children with sensorineural hearing loss, permanent conductive hearing loss, and auditory neuropathy. The rationale for screening of newborns is that earlier identification of hearing loss leads to earlier intervention and that earlier intervention leads to better outcomes for children. Research has demonstrated that universal screening does lead to earlier identification and earlier intervention (Dalzell, et al, 2000; Durieux-Smith, et al, 2008; Sininger et al, 2009; and Halpin, et al, 2010). Research has also demonstrated that earlier intervention does lead to better outcomes for language development for children with hearing loss (Yoshinaga-Itano, et al, 1998; Moeller, 2000, and Kennedy et al, 2006).

The Joint Committee on Infant Hearing (JCIH) is a multidisciplinary committee whose purpose is to make recommendations to support the identification of children with hearing loss. The administration of newborn hearing screening programs is carried out by Early Hearing Detection and Intervention (EHDI) programs at the state level. The implementation of newborn hearing screening protocols generally follows the

recommendations put forth by the JCIH. The recommendations for screening protocols stem from a timeline for milestones in the process of detection of hearing loss and initiation of intervention. The timeline recommended by the JCIH includes identification of hearing loss (a screening that results in a pass or referral to evaluation) by one month of age, evaluation and diagnosis of hearing loss by three months of age, and initiation of intervention by six months of age (Joint Committee on Infant Hearing, 2007).

Newborn hearing screening typically occurs just following birth, prior to discharge from the hospital. This time frame is due to the availability of nearly all infants following birth, to ensure the highest number of children screened (Joint Committee on Infant Hearing, 2007). Auditory brainstem response (ABR), automated auditory brainstem response (AABR), otoacoustic emissions (OAE), or automated OAE testing are used to screen infants. When infants fail the screening, a follow-up screening or audiologic evaluation is instituted. Other measures of auditory system function, such as immittance or wideband reflectance (WBR), which are used to infer information about the status of the middle ear system, are not typically utilized in screening protocols.

Conductive Hearing Loss in Infants

While the purpose of newborn hearing screening is to identify the presence of sensorineural hearing loss, permanent conductive hearing loss, or auditory neuropathy, some infants who fail a newborn hearing screening do so because of what appears to be a temporary conductive hearing loss.

Permanent conductive hearing loss is due to structural or physiologic abnormalities that will continue to persist indefinitely without intervention. This type of hearing loss has the potential to detrimentally impact speech and language

development. As such, it is a hearing loss of interest for identification with newborn hearing screening. However, in most cases of apparent conductive hearing loss, the circumstances causing the screening failure are temporary in nature, meaning that the indications of conductive hearing loss resolve, without intervention, at some point following the initial screening failure. Because it will resolve independently, temporary conductive hearing loss (TCHL) is not a hearing loss of interest for identification in newborn hearing screening paradigms.

Several potential etiologies have been hypothesized to cause temporary conductive hearing loss in infants. Vernix, (the waxy substance which coats the skin of newborn infants), in the ear canal may be present immediately following birth (McLellan and Webb, 1959). Mesenchyme (loose connective tissue that arises from the mesoderm during embryonic development) and fluids in the middle ear space may be present immediately following birth (deSa, 1973). In addition to actual structural components that attenuate sound energy, immaturity of the ear canal and middle ear structures and function could potentially result in artifactual outcomes due to testing methodology. Systematic investigation into the causes of apparent conductive hearing loss in infants is lacking.

Temporary conductive loss has the potential to cause disruption to the otherwise straightforward process of newborn hearing screening. Conductive loss may cause an attenuation of stimulus intensity, sometimes resulting in a fail on ABR screening. Conductive loss also causes an attenuation of the forward transmission of stimuli for OAE testing and/or the backward transmission of the evoked response, often resulting in a fail on OAE screening. The impact of conductive loss is more pronounced for OAE

testing than for ABR testing. Unfortunately, the same screening and evaluation outcomes that are suggestive of a permanent conductive hearing loss are also those that occur in cases of temporary conductive hearing loss.

Because TCHL is not a hearing loss of interest for identification, a failed screening due to TCHL is considered to be a false positive. On the other hand, consideration of TCHL as a true hit may be valid when considering the guidelines provided for intervention of hearing loss. It is generally assumed that intervention for TCHL is not necessary. However, due to the time course of TCHL, many infants progress beyond re-screening measures and into diagnostic evaluation, during which time the conductive nature of the loss is typically determined. The JCIH guidelines remain silent as to how conductive hearing loss should be handled with regard to differentiating between permanent conductive hearing loss and temporary conductive hearing loss for planning intervention. Research has demonstrated that as much as 34% of infants with sensorineural hearing loss also have abnormal tympanometry consistent with middle ear dysfunction during the first year of life, which would cause outcomes consistent with conductive or mixed hearing loss (Brookhouser, et al, 1993).

Purpose

Temporary conductive hearing loss causes difficulty in identification of hearing loss that is of interest for newborn hearing screening. Due to the problems surrounding temporary conductive hearing loss, it would be of benefit to the clinician to be able to more accurately identify conductive hearing loss in infants and to predict the natural course of conductive hearing loss for the purpose of evaluation and treatment planning.

Measures used to predict middle ear function, such as wideband reflectance have potential to be used for these purposes.

The purpose of this longitudinal descriptive study is to better understand the natural course of screening outcomes in infants, to better understand the use of reflectance measures as they relate to screening outcomes, and to determine whether reflectance measures may be used to predict screening outcomes for the purpose of refining newborn hearing screening programs.

Research Questions

1) Do patient factors at birth, including birth weight, head circumference, and gender, correlate with initial distortion product otoacoustic emissions (DPOAE) testing outcomes? DPOAE outcomes have been evaluated very little according to the criteria of gender or birth weight and head circumference at the time point following birth. DPOAEs have been shown to be larger in female than in male infants (Gordts, et al, 2000), but it is unknown whether this difference would impact hearing screening outcomes immediately following birth. Otoacoustic emissions have also been shown to be poorer in infants in a neonatal intensive care population compared to a regular care population (Chiong et al, 2003), but it is unknown whether this effect is due to size at time of birth, gestational age, or some other confounding factors.

2) What is the longitudinal time course of DPOAE outcomes in infants? DPOAEs are used to evaluate outer hair cell function in the inner ear. However, minimal conductive dysfunction contributes substantially to failing outcomes when DPOAEs are used to screen for hearing loss. Once sensorineural hearing loss has been ruled out, DPOAE testing can be used to infer status of the middle ear in an infant. DPOAE testing

can also be used to provide a means for determining whether a temporary conductive loss in an infant has resolved. Currently, it is unknown how DPOAE outcomes change over time in infants with temporary conductive hearing loss. Longitudinal DPOAE outcomes can be utilized to better understand the timeline of natural resolution of temporary conductive hearing loss in infants for the purpose of creating evidence-based protocols for the follow-up screening and/or evaluation of hearing in infants. In this study, DPOAE screening outcomes will be used to understand the natural time course of resolution of temporary conductive hearing loss in infants over the first three months of life.

3) What frequencies on wideband reflectance testing are best predictive of DPOAE testing outcomes at different ages? Wideband reflectance (WBR) measures are used to describe function of the middle ear system. In cases of conductive hearing loss, measures of reflectance are elevated, as sound energy is reflected from, rather than absorbed by, the middle ear system. WBR measures are generally predictive of DPOAE outcomes in infants and adults, which is important, as both measures can be used to infer function of the middle ear system. The WBR measure uses a range of frequencies to evaluate reflectance. It is known that some frequencies are more useful for predicting middle ear dysfunction than others, and that the optimal frequency depends on the size and other physical characteristics of the ear canal. Currently, it is unknown how the optimal frequency for prediction of DPOAE outcomes changes over time in infants. Cross-sectional studies have investigated WBR measures across groups of infants (Hunter et al, 2008; Keefe et al, 1993; Merchant et al, 2010; Sanford and Feeney, 2008; Vander Werff et al, 2007; Werner et al, 2010) but this type of information has not been

obtained longitudinally in the same group of infants. In this study, WBR measures will be compared to DPOAE outcomes to understand the natural evolution of optimal frequency for predicting DPOAE outcomes in infants over the first three months of life.

4) How useful are WBR measures for predicting DPOAE testing outcomes at later time points? WBR is well correlated with DPOAE outcomes when both are measured at the same time point. However, it is currently unknown whether WBR measures may be used to predict DPOAE outcomes at later time points. Because reflectance is measured at various frequencies, WBR has the potential to be sensitive to various pathologies underlying temporary conductive hearing loss. For example, it may be the case that WBR values would be higher or have a different pattern in the case of resistant "glue ear" compared to the presence of unabsorbed mesenchyme in the middle ear space. It would be of clinical value if WBR measures could be utilized by clinicians to predict which infants with DPOAE refer outcomes are likely to have spontaneous resolution of temporary conductive hearing loss and which are likely to require intervention. In this study, WBR measures will be compared to later DPOAE outcomes to determine the value of WBR measures for predicting the course of temporary conductive hearing loss as characterized by DPOAE outcomes.

CHAPTER 2

LITERATURE REVIEW

Power Reflectance

In 1984, Teele and Teele reported on the development of a device to measure the reflected power of sound presented to the external auditory canal using a broadband (1800 – 7000 Hz) swept signal. In the normal ear, acoustic power is absorbed into the cochlea. Reflectance measurements refer to the measurement of energy reflected from the tympanic membrane into the external ear canal. Power reflectance is a measure of middle ear inefficiency. Reflectance is equal to reflected power/incident power (expressed as percentage 0-100%). Higher reflectance is indicative of less transmittance of power. Lower reflectance is indicative of greater transmittance of power. The transmittance measure is indicative of absorbed power. Function of the structures of the ear canal and middle ear space can be inferred from measures of energy reflectance.

Reflectance (R(f)) is dependent on frequency, so a broadband stimulus (62 – 10,000 Hz) may be used to examine the reflectance across the frequency range. This is known as wideband reflectance. Tone-burst stimuli can also be used. Unlike traditional immittance measures, power reflectance measurements are made at ambient static pressure. In adults and infants transmittance is greatest for the 1000 Hz to 4000 Hz range (Keefe, et al, 1993). Compared to adults, newborns (Shahnaz, 2008) and one- and six-month-old infants (Keefe and Levi, 1996) have been shown to have less reflectance at lower frequencies and greater reflectance at the highest frequencies tested. These effects are hypothesized to be due to amniotic fluid and mesenchyme that

may be present in the middle ear space following birth, causing a mass effect that reduces the conduction of high-frequency energy (Shahnaz, 2010). Age-related effects continue to be seen in older infants of 2-9 months of age (Werner, et al, 2010). Right ears and male ears have been shown to demonstrate lower reflectance than left and female ears in some studies (Keefe, et al, 2000), but not others (Hunter, Tubaugh, et al, 2008). Reflectance has been shown to be increased in infants with cleft palate. This is hypothesized to occur due to reduction in the forward transmission of sound energy due to fluid in the middle ear space, common in children with cleft palate (Hunter, Bagger-Sjöbäck, and Lundberg, 2008). Reflectance has also been shown to be increased in some infants within the first 24 hours after birth. It has been hypothesized that this may be due to vernix in the ear canal following birth (Keefe et al, 2000; and Hunter et al, 2010). Hunter, Tubaugh, and colleagues (2008) and Merchant, Horton, and Voss (2010) have summarized the use of power reflectance measurement in infants and children and have provided data for these populations.

Power reflectance measures have been shown to be sensitive to middle ear status (Hunter, Tubaugh, et al, 2008), and have been used as a test of middle ear dysfunction (Keefe, et al, 2000) and as a test predictive of conductive hearing loss (Keefe and Simmons, 2003). Some studies have found reflectance measures to be more sensitive for detection of presumed middle-ear effusion in infants than high-frequency tympanometry (Hunter, et al, 2008; Sanford, et al, 2009; and Keefe, et al, 2010).

Clinical Application of Power Reflectance

Because the primary goal of newborn infant hearing screening is identification of sensorineural hearing loss and permanent conductive hearing loss, power reflectance measurements, in and of themselves, are inappropriate for screening in the newborn population. However, reflectance measures may provide some additional information which could theoretically assist in more appropriate follow-up strategies. Measurement of middle ear function can be useful in helping to distinguish the presence of conductive hearing loss in infants and therefore may be helpful in interpreting screening outcomes. The inclusion of middle-ear measures greatly assists in targeting potential sensorineural hearing loss for those cases in which middle ear function is determined to be normal, while referral occurs on other tests. Keefe, Gorga, et al. (2003) demonstrated that the inclusion of WBR data into a universal newborn hearing screening two-stage OAE/ABR protocol improved the ability to detect sensorineural hearing loss. Unfortunately, the presence of abnormal middle ear function does not rule out the possibility of sensorineural hearing loss in an infant. Due to the potential for mixed hearing loss, the presence of abnormal power reflectance measurements in a neonate does not exclude the possibility that the child also has a sensorineural hearing loss.

Otoacoustic Emissions

Otoacoustic emissions are sounds generated by the cochlea as a by-product of function of the outer hair cells. Otoacoustic emissions are evoked using stimulus presentations of either transient clicks (transient evoked otoacoustic emissions) or primary tones whose interaction results in distortion products (distortion product otoacoustic emissions). The presence of normal otoacoustic emissions is thought to

reflect normal cochlear function, inferred through the function of outer hair cells. TEOAEs and DPOAEs are typically absent in ears with hearing loss of 30 dB HL or greater (Kemp and Ryan, 1991).

Otoacoustic emissions (both TEOAEs and DPOAEs) are larger in infants than adults, possibly due in part to the smaller ear canal volume of infants and the higher noise floor in infants than adults. DPOAEs have been shown to be larger in female than in male infants (Gordts, et al, 2000), as is the case with adults. Otoacoustic emissions have also been shown to be poorer in infants in a neonatal intensive care population compared to a regular care population (Chiong et al, 2003), but it is unknown whether this affect is due to size at time of birth, gestational age, or some other confounding factors.

Screening Application of Otoacoustic Emissions

Demonstrations of TEOAEs and DPOAEs for hearing screening purposes have shown that both are relatively independent of subject state in reasonably quiet infants, and are relatively independent of test environment, suggesting that the primary source of noise in infants is physiologic (Gorga, et al, 2000; and Norton, Gorga, Widen, Vohr et al, 2000). This is reinforced by the finding that the noise floor is lowest at the highest frequencies tested, as ambient noise tends to be low-frequency in nature.

For the purpose of screening of otoacoustic emissions, automated systems have been developed with associated pass or refer criteria. Automated DPOAE systems work best at higher frequencies, 2000 - 4000 Hz (Gorga et al, 2000), and automated TEOAE systems can be extended to a slightly lower frequency range of 1500 Hz - 4000 Hz (Norton, Gorga, Widen, Vohr et al, 2000). Both can be achieved under most reasonably

quiet states of arousal in infants (Gorga, et al, 2000; and Norton, Gorga, Widen, Vohr, et al, 2000). Kemp and Ryan (1991) describe the use of otoacoustic emissions for newborn screening applications. They report difficulty of proper placement of the probe in the neonate ear canal and ambient room noise as potential barriers to accuracy of test results.

OAEs are generally absent in cases of obstruction of the ear canal, such as might occur shortly after birth, and this is the reason most frequently hypothesized as the cause of higher referral rates in infants with use of OAE screening techniques versus ABR screening techniques (Chang, et al, 1993; Doyle, et al, 1997; McNellis and Klein, 1997; and Norton, Gorga, Widen, Folsom, et al, 2000). Shahnaz (2008) demonstrated a correlation between high reflectance using power reflectance measures, suggestive of middle ear dysfunction, and failure on TEOAE screening. However, other data suggest that maturational factors may play a more important role in increases in TEOAE levels over time. Abdala and Keefe (2006) examined DPOAE measures in adults and infants. They applied a model for an immature ear canal by varying forward and reverse transfer function levels relative to adults. It was found that application of the model for immaturity of the forward transmission system in infants best fit the measured data. Prieve, et al (2009) tested TEOAEs on infants in a well-baby nursery and compared these results to otoscopic examination. They found that ear canal debris was not associated with changes in TEOAE levels over time in infants. They hypothesized that structural changes due to maturation may explain increases in TEOAE levels in infants over time and may be one cause of failure of newborn infant

hearing screening using TEOAEs. OAEs have also been used to estimate severity of hearing loss, but with less success than ABR measures (Hall and Swanepoel, 2010).

Problems Encountered in the Hearing Screening Process Due to TCHL

The JCIH suggests a quality indicator of less than 4% for the percentage of infants who fail initial screening and any subsequent rescreening before comprehensive evaluation. The most recent data available from the Centers for Disease Control found the referral rate of infants not passing the final or most recent screening to be 2.1%. (Centers for Disease Control, 2007). However, the caveat of final or most recent screening does not take into account the numbers of children who are re-screened due to temporary conductive hearing loss (TCHL). It is unknown how many infants are re-screened prior to referral for audiologic evaluation. Re-screening may take place prior to hospital discharge, or may require follow-up at a later date or in an outpatient facility.

If TCHL is considered to be a false positive for newborn hearing screening, there are numerous costs associated with the inability to separate TCHL from the population with hearing loss of interest. The financial cost of re-screening or evaluating the infant, potentially numerous times over the course of resolution of the TCHL, and the services needed for attempts to locate infants to minimize loss to follow-up are an issue. An excessive referral rate may also lead to delay in identification of hearing loss of interest when resources are burdened. Diminished confidence in screening outcomes, and consequently diminished emphasis on follow-up, may occur when providers and patients believe that most hearing screening failures are primarily false positives. The current rate of lack of follow-up for infants failing an initial newborn hearing screening is an average of 46%, with individual states having loss to follow-up rates as high as a

staggering 95.6% (Centers for Disease Control, 2007), making this a substantial concern, as newborn hearing screening is completely ineffective if follow-up of screening failure is not pursued. Parent or caregiver distress over a failed screening result and the time and effort required by parents or caregivers to have the infant re-screened or evaluated are other issues related to false positive outcomes.

On the other hand, consideration of TCHL as a true hit may be valid when considering the guidelines provided for intervention of hearing loss. It is generally assumed that intervention for TCHL is not necessary. However, in clinical practice it has been noted that due to the time course of TCHL, many infants progress beyond re-screening measures and into diagnostic evaluation, during which time the conductive nature of the loss is typically determined. The JCIH guidelines remain quiet on how conductive hearing loss should be handled with regard to differentiating between permanent conductive hearing loss and temporary conductive hearing loss. For instance, should physician referral be instituted immediately, or should the child be followed for some time to determine whether the hearing loss resolves on its own, as most do? Should or would a physician pursue diagnostic measures, such as computed tomography which may require sedation and would subject the infant to radiation exposure, to differentiate permanent from conductive hearing loss in a three-month old? If obvious causes of permanent conductive hearing loss are ruled out, at what point is conductive hearing loss considered permanent? When, if ever, should TCHL become a hearing loss of interest, requiring medical treatment? The ability to pursue newborn infant hearing screening has allowed for tremendous improvement in timelines for identification of hearing loss and improvement in outcomes for children, but the logistical

problems created by TCHL appear to have been an unexpected source of difficulty in screening paradigms and questions regarding how to handle TCHL continue to plague clinicians.

Conductive Hearing Loss in Newborns

There are numerous potential causes that are hypothesized to result in temporary conductive hearing loss and/or false positive hearing screening failures in newborns.

Debris in the Ear Canal

In a study of the ear canal and tympanic membrane of neonates, McLellan and Webb (1959) found at least some vernix in the ear canals of all ears of 102 infants within the first 24 hours of life. In a separate study following infants for the first week of life, repeated otoscopic examination showed approximately half of infants had clear ear canals by day six of life, compared to 10.5% in the first three days of life (McLellan and Webb, 1961). Cavanaugh (1987) found vernix obscuring the tympanic membrane in 56% of ears on the first day after birth. This decreased to 19% on the third day, and 2% at two weeks. McNellis and Klein (1997) found that otoacoustic emission screening failures correlated with the partial or complete presence of vernix occluding the ear canals of neonates. Doyle and colleagues (1997) found that removal of vernix from the ear canal reduced the referral rate of infants re-screened using OAEs and ABR. Chang and colleagues (1993) found vernix in the ear canals of 43% of 82 ears of infants 22-64 hours following birth. They found that the rate of ears passing the OAE screening increased from 76% of 91% after removal of the vernix from the ear canals.

Middle Ear Pathology in Intensive Care Infants

Middle ear pathology, which could result in conductive hearing loss, has been found in samples of infants who died shortly after birth. Temporal bone studies of infants by deSa (1973) showed evidence of amniotic fluid in the middle ear space of 55 of 130 infants. Piza and colleagues (1989) demonstrated that infants who were born with meconium contamination had a higher volume of cellular content in the middle ear and mastoid cavities. The origin or type of cellular material was unspecified in the study, presumably because it was not evaluated, although this is not specified. Instead the volume of cellular material was evaluated and correlated with the presence of meconium-stained fluid. They speculate that the presence of this cellular content could provoke a foreign-body inflammatory reaction, causing a true otitis media in neonates. Similarly, deSa (1977) found evidence of amniotic squamous debris in the wall of the middle-ear cavity in a series of a total of three infants upon histopathological examination. In 1983, deSa reported on a series of 72 infants postmortem. Abnormal histopathological findings were present in all but five of the infants and included metaplastic epithelial lesions, inflammatory lesions, otitis media, and destruction of ossicles. Reasons for abnormal findings were hypothesized to include infections, aspirated amniotic squamous debris, effects of oxygen therapy, and obstruction of the eustachian tube by a nasal airway. Balkany and colleagues (1978) reported on the presence of suppurative middle ear effusions in 30% of 125 consecutive infants from a neonatal intensive care unit. Hemsath (1936) reported histopathological results indicating either foreign body reaction to amniotic fluid constituents or acute purulent

otitis media in seven infants. Middle-ear pathology has been shown to be a potential factor in conductive hearing loss in infants in at least the intensive care population.

Decreased Tympanic Membrane Mobility at Birth

In addition to frank or confirmed cases of pathology of the middle ear, decreased tympanic membrane mobility has been found in infants from regular care nurseries. Fluid in the middle ear space is one hypothesized cause of decreased tympanic membrane mobility in infants. Jaffe and colleagues (1970) found poor tympanic membrane mobility in 18% of 101 newborns using pneumatic otoscopy within the first 48 hours after birth. Cavanaugh (1987) found poor tympanic membrane mobility in 88% of 18 infants on the first day following birth and in 57% of 29 infants on the third day following birth. Roberts and colleagues (1995) used a battery of pneumatic otoscopy, tympanometry, and acoustic reflex measures to determine presence of effusion in the middle ear space in neonates. It was found that all of 68 infants exhibited effusion when tested in the first three hours after birth. Effusion resolved within 72 hours in 73% of 24 full-term neonates. Decreased tympanic membrane mobility, evaluated using pneumotoscopy, was found in 9% of 214 infants able to be evaluated by Doyle and colleagues (1997), and the decreased mobility correlated with screening pass rates for both ABR and OAEs.

Otitis Media Following Birth

While some infants may present with conductive hearing loss at birth, other infants may develop conductive hearing loss over time, and this may manifest during hearing screenings which occur at later time points in the infant's development. In some cases, infants are screened later than the recommended pre-hospital discharge

timeframe for various reasons. In other cases, infants may refer on a single ear and, per JCIH recommendations (2007), will be re-screened in both ears. In these cases, infants may develop otitis media over time, and this finding would be reflected in the later-occurring screening or re-screening results.

The finding of otitis media in young infants is not an uncommon occurrence. Marchant and colleagues (1984) found onset of otitis media in 33% of 24 infants before two months of age. Roberts and colleagues (1995) found that at two weeks and at two months following birth, new cases of effusion (not present at birth) had appeared in their sample of infants, at a rate of 9%. The finding of new cases of effusion is consistent with that of Teele and colleagues (1989) who found effusion in 9% of 877 infants by three months of age in a longitudinal study. Similarly, Sipilä and colleagues (1987) found evidence of effusion using otoscopy in 17% of 284 infants during the first seven months of life.

Relationships of Testing Outcomes to Conductive Hearing Loss

Complicating the issue of understanding auditory function in infants is that almost no studies utilize a gold standard of tympanocentesis for determining presence of middle ear effusion as the reason for absence of otoacoustic emissions or abnormal immittance or reflectance measures. This is due to ethical concerns of performing such procedures in infants when other courses of treatment may be effective, such as medications, or when the condition is expected to be time-limited or self-resolving in nature, as is commonly the case with conductive hearing loss in infants.

It is currently unknown whether WBR measures can be used to predict middle ear function in infants in a longitudinal fashion. Cross-sectional studies involving WBR

measures have typically involved comparison to OAE outcomes that are thought to indicate middle ear dysfunction. Wideband reflectance measures have been shown to be useful in predicting OAE outcomes in infants (Hunter, et al, 2010; Keefe, Zhao, et al, 2003; Merchant et al, 2010; Sanford, et al, 2009; Shahnaz, 2008; Vander Werff, et al, 2007) and adults (Ellison and Keefe, 2005). WBR measures have been shown to be superior to 1000 Hz tympanometry at predicting OAE outcomes in infants (Hunter, et al, 2008; Hunter, et al, 2010; Keefe, et al, 2010; Sanford, et al, 2009). WBR has also been shown to be predictive of otherwise known conductive disorder in school-aged children (Beers, et al, 2010; Hunter, et al, 2008; Kaf, 2011) and adults (Feeney, et al, 2003; Feeney, et al, 2009; Keefe and Simmons, 2003; Shahnaz, et al, 2009). WBR may therefore be useful as a cross-sectional adjunct to other screening methods for the purpose of understanding the conductive component of hearing loss in infants.

CHAPTER 3

METHODS

This longitudinal, descriptive study characterizes auditory function in infants prior to time of discharge following birth, and one, four, eight, and twelve weeks following birth. The testing process is depicted in Figure 1. During the initial testing period, infants were screened using various measures to determine potential for, or presence of, sensorineural hearing loss, for the purpose of determining study candidacy. Infants were then tested using DPOAE and WBR measures at each time point to answer the research questions. At the final time point, infants still at risk for progressive sensorineural hearing loss were screened to rule out this occurrence for the purpose of re-evaluating study candidacy.

Subjects

Subjects were recruited from the infants in the well-infant nursery, born at Henry Ford Hospital in Detroit, Michigan and from the West Bloomfield Henry Ford Hospital in West Bloomfield, Michigan.

The total subject sample size was 54, with four subjects being removed from the study by the investigator when they were unable to be contacted for the purpose of continued participation. It is unknown why subjects became unavailable. Subjects were removed at various points, and replaced with new, for a total of 54 subjects at birth, 52 subjects at week one, 52 subjects at week 4, 50 subjects at week 8, and 50 at week 12. Both ears were tested for a total sample size of 108 ears at birth, 104 at week one, 104 at week four, 100 at week eight, and 100 at week 12. Subjects were recruited so that there were an equal numbers of passing and referring ears at birth. The calculation of

subject sample size of 50 was based on the findings of Hunter et al. (2010). In this study, the area under the curve for the WBR frequency which best predicts DP outcome is 0.90. Using the analyses provided by Hanley and McNeil (1982) for determining standard error which would accompany such an area under the curve, a standard error of .06 is estimated for a sample size of 50. Given an area under the curve outcome of 0.90, such as that found by Hunter et al. (2010), a sample size of 50 would provide a 95% confidence interval of 0.11, for a range of 0.79-1. Based on the calculation of Hanley and McNeil, this would provide 99% power to determine whether the test is different from chance (H_0: Area under the curve ≤0.5; H_1: Area under the curve > 0.5).

Subject Recruitment Procedures

The process of subject recruitment followed the process depicted in Figure 1. Following the automated auditory brainstem response test (AABR), a risk factor questionnaire was verbally administered to determine whether the infant had risk factors for sensorineural hearing loss. Although a risk factor questionnaire is administered as a standard component of the hospital's infant hearing screening program, the specific questionnaire used in this study (Appendix) differed slightly from the standard completed by the hospital. Subjects who had any of the following risk factors were excluded from the study:

- family history of permanent childhood hearing loss
- time spent in the neonatal intensive care unit
- history of in utero infections
- craniofacial anomalies, including those that involve the pinna, ear canal, ear tags, ear pits, and temporal bone anomalies

- physical findings that may be associated with syndromes know to include hearing loss
- postnatal infections associated with sensorineural hearing loss, including confirmed bacterial and viral meningitis, or head trauma.

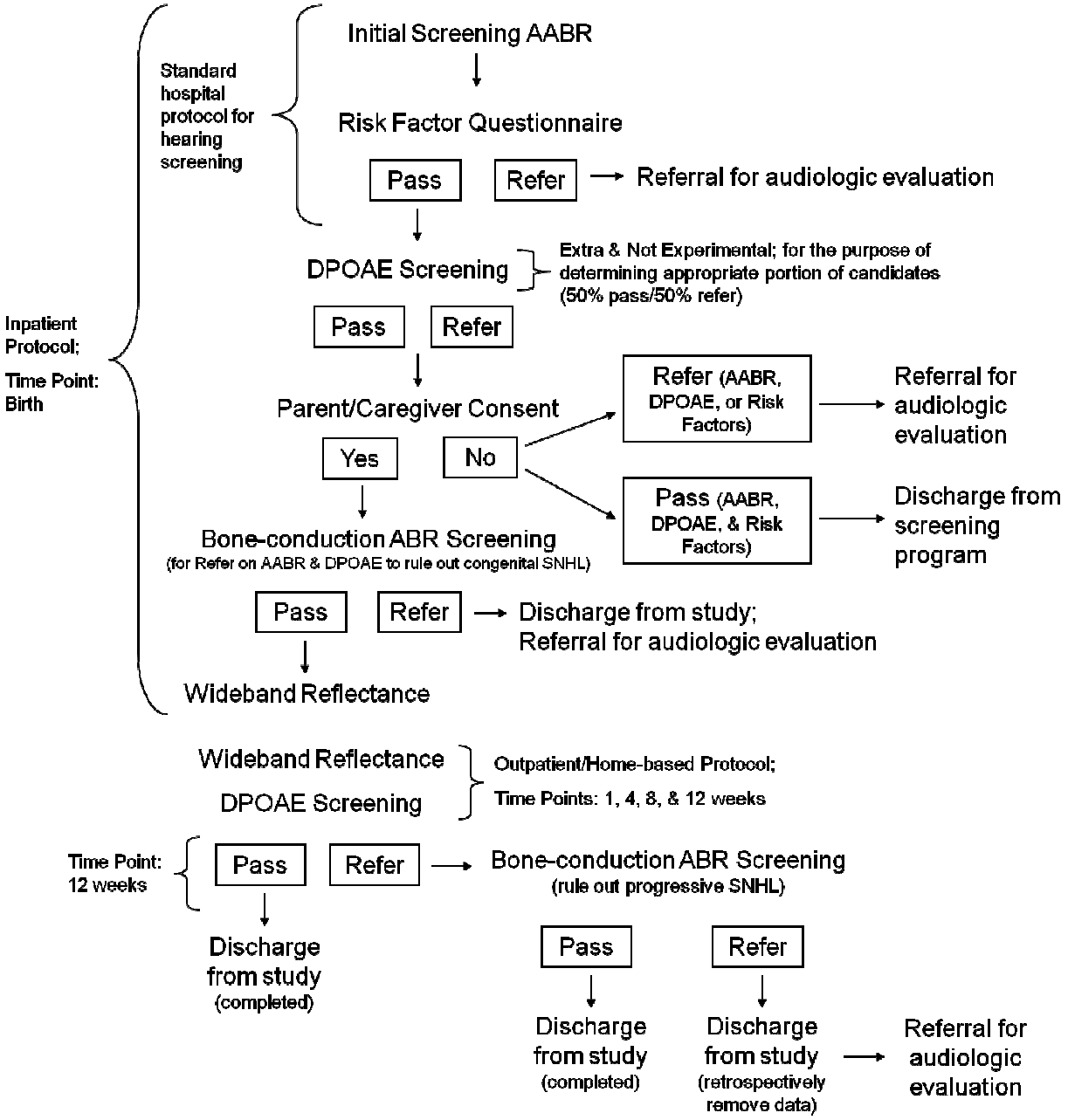
In addition, it was the intent that subjects who were suspected of or were found to have sensorineural hearing loss based on ABR bone-conduction screening at the initial or final time points (as described below) would also be excluded from the study, although no such infants were encountered in the recruitment or follow-up process. Infants who failed the risk factor screening were instructed to continue with the hospital's standard process for infant evaluation and treatment.

Infants who passed the risk factor screening and whose parents consented were screened during their stay in the well-infant nursery using DPOAE to determine pass or refer status. The DPOAE screening was an extra, but not experimental, step in the screening process which allowed determination of pass or refer status for the purposes of the study. Infants were recruited for the study as needed based on DPOAE outcomes to obtain 50% passing and 50% referring ears.

Study objectives and methods were explained to parents. Caregivers were paid a minimal amount ($7.20 per testing session) for their participation. Beyond the initial assessment, caregivers of all subjects chose to have further testing completed in the home.

Gender of infants, birth weight, and head circumference were recorded as described in the infants’ inpatient medical record chart.

Figure 1. Depiction of process from initial screening through study end.



Instrumentation & Testing Methods

The protocol of the study was discussed with caregivers of subjects prior to obtaining consent. Following the consent process, testing continued while infants were still admitted to the hospital. In addition to the initial DPOAE screening outcome, testing

for “Time point: Birth” included WBR in all cases and ABR bone-conduction screening in infants who failed the initial AABR screening, which occurred in five cases.

For infants who did not pass the initial AABR screening, ABR bone-conduction screening was performed to rule out congenital sensorineural hearing loss on those infants who were eligible for the study (i.e. those who had passed the risk factor questionnaire, had DPOAE testing resulting in a pass or refer, and had parental consent). All five infants who did not pass the AABR screening did pass the ABR bone-conduction screening at the initial time point. Infants who passed the initial AABR screening were assumed to have no worse than a mild sensorineural hearing loss (screening intensity level of 35 dB nHL which correlates to behavioral thresholds in older children of 25 dB HL in the 1000-4000 Hz range).

For time points one, four, and eight weeks, testing included DPOAE screening and WBR. At the twelve-week time point if an infant did not pass the DPOAE screening ABR bone-conduction and/or air-conduction screening was performed. Two of these infants met this criterion and did pass the subsequent ABR screening.

Infants who passed the final DPOAE or ABR screening at the final time point were considered to have completed the study.

ABR Equipment and Methods

Equipment. ABR screening was completed using the Vivosonic Integrity V500 system (Vivosonic, Inc., Toronto, Ontario). The system was connected to a Lenevo notebook computer with a 1.19 GHz Intel Core 2 Duo processor, 1.86 GB RAM, run on Windows XP Professional 2002 SP3 operating system. The Vivosonic system differs from traditional ABR systems in that it utilizes Bluetooth communication between the

computer and the data collection module. This wireless feature reduces the antennae effect of long electrode leads and eliminates line noise in the recording. In addition, the data collection module utilizes an amplifier on the electrode itself. This allows for filtering to occur prior to amplification, reducing the addition of electrical artifact. The system also utilizes a Kalman weighted averaging system that estimates the noise in each raw response and weights each sweep based on its noise estimate. In this paradigm, noisy signals are weighted less than cleaner signals. The combined features of the system allowed for excellent ABR recordings in relatively noisy situations.

Calibration. Output calibration of the bone vibrator was made at periodic intervals to ensure maintenance of pre-existing calibration parameters. Calibration was performed by coupling the bone vibrator to a Beltone 5A artificial mastoid system. The output of the artificial mastoid was recorded using a Brüel & Kjær Type 2209 precision sound level meter set with a slow mode linear weighting network to average the output of transient signals. It was found that bone vibrator output did not result in a change of 5 dB or greater during calibrations.

Subject preparation. To prepare infants for testing, the skin was cleansed with a standard alcohol pad. Ambu Neuroline 720 disposable self-adhering electrodes (Ambu A/S, Denmark) were used. A single-channel recording montage was used, with a non-inverting electrode placed at the high forehead. The inverting electrode was placed on the mastoid of the test ear. The common electrode was placed on the mastoid of the non-test ear. Preparation ensured that an interelectrode impedance difference of ≤3kΩ was obtained for each electrode. Following testing preparation, the tester waited for the infant to sleep naturally.

Stimulus parameters. Bone-conduction stimuli were delivered via a Radioear B-71 bone-conductor (Radioear Corp., New Eagle, PA) positioned anterior and superior to the mastoid electrode and held in place by a pediatric metal headband and foam beneath the headband. Wideband masking was presented to the non-test ear at 30 dB HL. Stimuli consisted of 2-0-2 ramp number of cycles, 12 dB/octave high pass filter roll off and 24 dB/octave low pass filter roll off, Blackman windowing, 2000 and 500 Hz tone-bursts presented at a rate of 37.7 Hz. The intensity used was 15 dBnHL.

Recording parameters. High-pass filters were set at 30 Hz. Low-pass filters were set at 1500 Hz. The recording window was 25 ms. Recordings were replicated during testing, with alternate sweeps being stored in bin A or bin B. The resulting waveforms were added to achieve the displayed waveform.

Response analysis. Immediately following recording of the waveforms, using the Vivosonic Integrity software, the area surrounding the presumed Wave V location was marked to indicate start and end points for statistical analysis. The A and B waveforms were then used to determine a correlation coefficient to indicate the degree to which the collected waveforms in A and B were repeatable in the specified interval. Correlation coefficient values of at least 0.50 were deemed to be replicable waveforms, indicating when a replicable Wave V was identified.

DPOAE Equipment and Methods

Equipment. Distortion product otoacoustic emissions testing was performed using the Mimosa Acoustics Hear ID MEPA 3 + DP Otoacoustic Emissions Module (Mimosa Acoustics, 2007).

Calibration. Calibration was performed prior to testing with the probe tip in the ear canal. A 1000 Hz tone was presented automatically during the calibration to establish the level of output for the tonal stimuli. In addition, the cavity of the canal was estimated during calibration to ensure that the probe tip was not occluded and the noise floor was measured to ensure an appropriate level of ambient noise prior to testing.

Recording parameters. The probe was coupled to the ear using a pediatric foam tip. The protocol was run following a successful preset calibration trial. Distortion product stimuli consisted of L1 signal at 65 dB SPL and L2 signal at 55 dB SPL with an F2/F1 ratio of 1.22. Stopping rules for the protocol were as follows: Minimum DP amplitude of 0 dB SPL and minimum DP-NF amplitude of 10 dB SPL. The protocol included distortion products of $2f_1$-f_2, targeting 2000, 3000, 4000, and 6000 Hz.

Response analysis. Distortion product otoacoustic emission data were recorded as the response - the noise floor in decibels. This value was recorded for 2000, 3000, 4000, and 6000 Hz. Presence or absence of DPOAE was recorded for each response. "Present" was recorded for DPs of responses with a SNR ≥ 6 dB and a noise level < 0 dB SPL. "Absent" was recorded for responses with a DP <10 dB SPL and a noise level < 0 dB SPL. The decision of pass or fail was recorded. "Pass" consisted of DPOAE responses wherein at least 3/4 frequencies were present. Criterion for pass or fail for most otoacoustic emission screening equipment was originally based on work by Gorga and colleagues from Boystown Hospital (2000). DPOAE screening is designed to target those frequencies that are most important for speech and language development and which can be most accurately measured. Gorga et al (2000) found that measurements were most reliable in infants for 2000, 3000, and 4000 Hz, but not at 1000 Hz and that

these frequencies were most important for screening in sensorineural hearing loss. The criterion of three of four frequencies being present was based on this work. The 6000 Hz DPOAE frequency was included in this protocol because of its potential relationship to WBR outcomes and 1000 Hz was excluded because of its unreliability in the Gorga et al (2000) study and because testing occurred in non-acoustically treated environments, which are more likely to have low-frequency noise present in the room that could mask low-frequency sounds involved in testing, such as 1000 Hz.

Power Reflectance Equipment and Methods

Power reflectance was performed using the Mimosa Acoustics Hear ID MEPA 3 + DP Middle Ear Power Analyzer (Mimosa Acoustics, 2007). Calibration was performed prior to each subject measurement using the calibration cavity set to determine the acoustic impedance of the sound source prior to measurement in the ear. Three sources of impedance are possible when measuring impedance in the ear canal: the middle ear, the ear canal wall, and the sound source. The ear canal wall has been shown to have negligible absorption of sound energy (Voss et al, 2008), leaving the sound source and middle ear as contributing to impedance mismatches. Calibration of the sound source allows for the impedance to be determined prior to measurement in the ear canal, so that the known impedance of the sound source can be used in calculations to determine the unknown impedance of the remaining load, the middle ear. The sound source impedance is calculated from measurements of the acoustic response of the sound source in a set of four cavities.

The probe was coupled to the ear using the same pediatric foam tip used for DPOAE measures. In-the-ear pressure calibration was made with the probe in the

subject's ear. Results of power reflectance were recorded as the value of power reflectance for each tone-burst frequency tested. This value was recorded for 1000, 1500, 2000, 3000, 4000, and 6000 Hz. Stimuli below 1000 Hz were not utilized due to findings that reflectance across test sites may differ below 1000 Hz (Hunter et al, 2010).

Measurement of Ambient Noise Levels

Soundfield measurements were made prior to performing tests using a RadioShack 33-2055 sound level meter set to a fast mode "A" weighting network, which is appropriate for a 24-55 dB SPL environment (Decker and Carrell, 2004), as well as a "C" weighting network. Measures were recorded for the purpose of minimizing ambient noise as much as possible when present. In general, measurements indicated ambient noise levels to be quieter than the 50 dB SPL noise floor of the instrument. Comparison of "C" and "A" weighted readings indicated that when noise was present in the environment, it was typically low-frequency in nature.

CHAPTER 4

RESULTS

Gender

The subject pool at birth consisted of a total of 54 infants. Of these, 35 (64.8%) were female and 19 (35.2%) were male. Results are shown in Table 1. For females 54.3% passed while 45.7% failed at birth. For males, 42.1% passed and 57.9% failed at birth. Chi-square analysis using expected observed passing values of 35 for females and 19 for males yields a value of 0.731 and two-tailed p=0.3926, suggesting that these differences are not significant.

Table 1: Initial pass or fail outcome as a function of gender. Numbers shown refer to ears tested (i.e. two per subject).

	Pass	Fail	Total
Female	38 (54.3%)	32 (45.7%)	70 (64.8%)
Male	16 (42.1%)	22 (57.9%)	38 (35.2%)
Total	54 (50%)	54 (50%)	108 (100%)

Birth Weight

Birth weight of infants was determined by first removing those infants who had both a failing and passing ear, which resulted in a total of 16 infants being removed. Mean birth weight was then calculated for bilaterally passing (n=19) and bilaterally failing (n=19) groups of infants. Results are shown in Table 2. Unpaired t-test analysis with p=0.9574 suggests that differences between groups are not significant.

Table 2: Initial pass or fail outcome as a function of birth weight

	Pass	Fail
Mean	3270.00	3279.47
Standard Deviation	449.58	623.09
N	19	19
Two tailed p = .9574		

Head Circumference

Head circumference of infants was determined by first removing those infants who had both a failing and passing ear as described above. Mean head circumference was then calculated for bilaterally passing and failing groups of infants. Results are shown in Table 3. Unpaired t-test analysis with p=0.8292 suggests that differences between groups are not significant.

Table 3: Initial pass or fail outcome as a function of head circumference

	Pass	Fail
Mean	34.73	34.69
Standard Deviation	1.46	1.53
Standard Error of the Mean	0.33	0.35
N	19	19
Two tailed p = .8292		

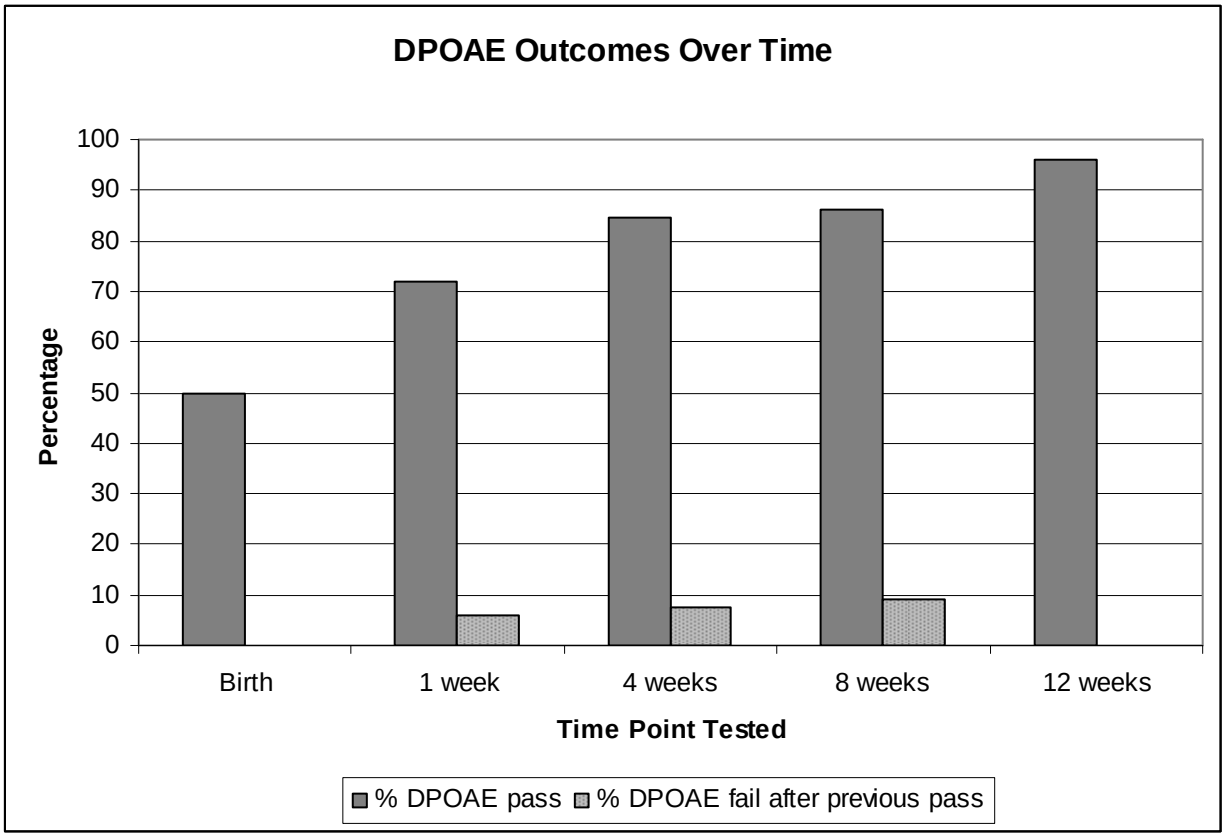
Longitudinal DPOAE Screening Outcomes

Per the study design, 50% of ears were passing at birth and 50% failed at birth. At week one, 72.1% of ears passed. Ears then passed at a rate of 84.6%, 86.0%, and 96.0% at weeks four, eight, and twelve, respectively. The percentages of infants who failed following any previous pass were 5.8% at week one, 7.7% at week four, 9.0% at week eight, and 0 at week twelve. Results are shown in Table 4 and Figure 2.

Table 4. Percentages of DPOAE pass and fail outcomes for ears at time points following birth.

Time Point	**% Pass**	**% Fail**	**% Fail Following Pass**
Birth	54 (50%)	54 (50%)	N/A
1 week	75 (72.1%)	29 (27.9%)	6 (5.8%)
4 weeks	88 (84.6%)	16 (15.4%)	8 (7.7%)
8 weeks	86 (86.0%)	14 (14.0%)	9 (9.0%)
12 weeks	96 (96.0%)	4 (4.0%)	0 (0.0%)

Figure 2. DPOAE pass and fail outcomes following birth.



Longitudinal WBR Outcomes

Mean reflectance outcomes are shown as a function of frequency for ears that passed DPOAE screening in Figure 3. These data show little change in the reflectance

of the highest frequencies in the time between birth and twelve weeks. For the lower frequencies, particularly 1500 Hz, there was a systematic decrease in mean reflectance over the first twelve weeks following birth.

Preliminary analysis of data for failing ears demonstrated substantially different patterns for those ears that failed at twelve weeks, relative to the other failing ears. Because of the possibility that these differences represented differing etiologies for failure (i.e. the ears that failed at twelve weeks were failing due to dysfunction that was different than the other infants who failed but eventually passed), the longitudinal data for these groups is displayed separately. Figure 4 shows the mean reflectance data as a function of frequency for ears that failed the DPOAE screening, excluding subjects 18 and 40 who continued to fail the screening at twelve weeks. Figure 5 shows the mean reflectance data for the four ears of these two subjects. In order to understand the longitudinal reflectance differences between ears that passed and ears that failed DPOAE screenings, mean difference values were plotted as a function of frequency. These differences can be seen in Figure 6 for those ears that failed the DPOAE screening excluding subjects 18 and 40 who continued to fail the screening at twelve weeks. Figure 7 shows this same information for subjects 18 and 40.

The overall trends for both Figures 6 and 7 can be described as increased reflectance in the higher-frequency range when compared to passing ears. Reflectance values were also higher at 1000 Hz than for passing ears. This resulted in an “S-shaped” configuration, in which the 1500-2000 Hz range had much lower reflectance than higher and lower frequencies in referring ears. At some time points these values were even lower than in the group of passing ears.

Figure 3. Mean WBR outcomes for DPOAE passing ears. Note that standard deviations are not represented here for the sake of visual clarity. However, the range of values can be seen in Figures 8 through 12, which show the percentiles for passing ears.

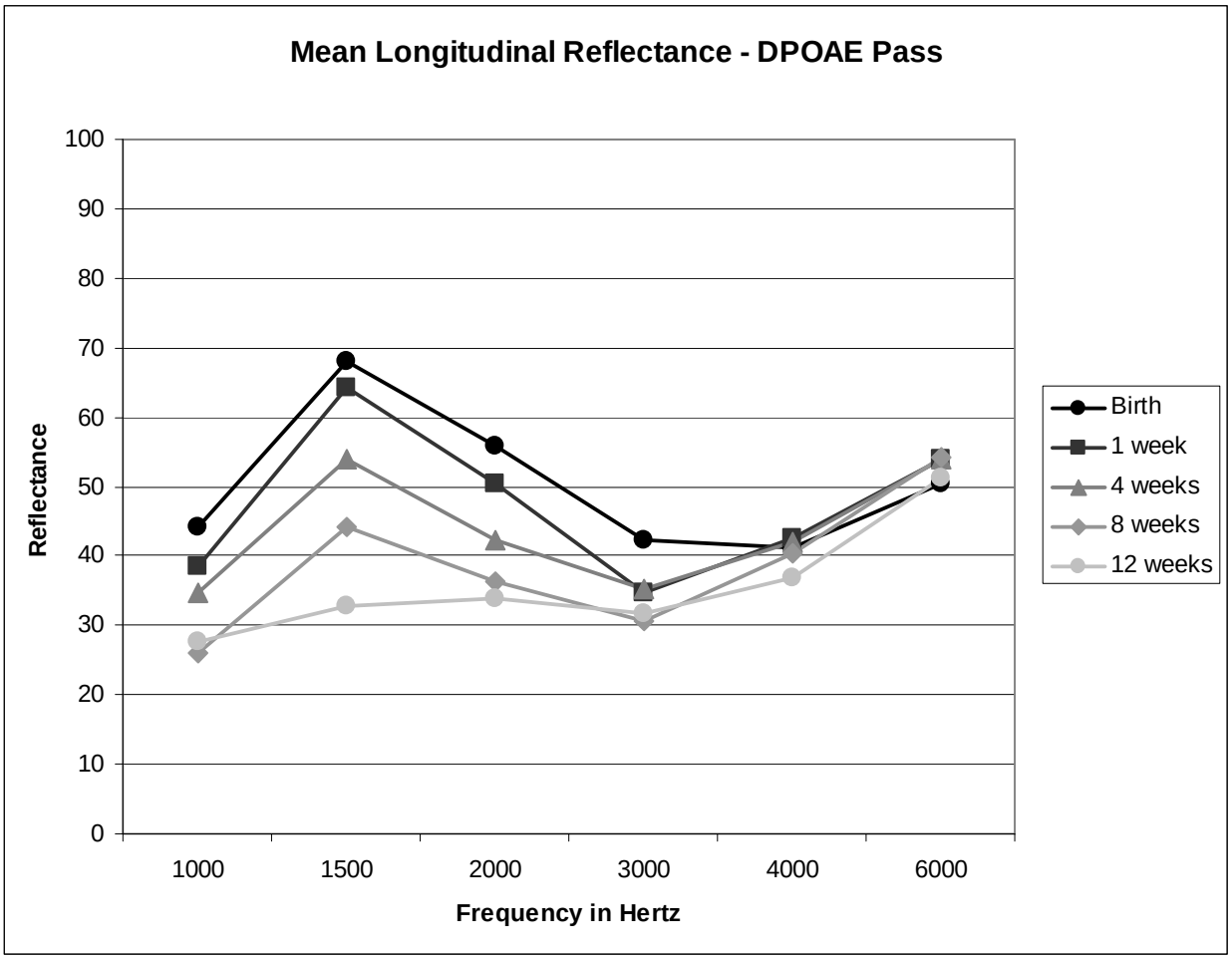


Figure 4. Mean WBR outcomes for DPOAE failing ears, excluding subjects 18 and 40. Note that standard deviations are not represented here for the sake of visual clarity. However, the range of values can be seen in Figures 8 through 12, which show the percentiles for passing ears.

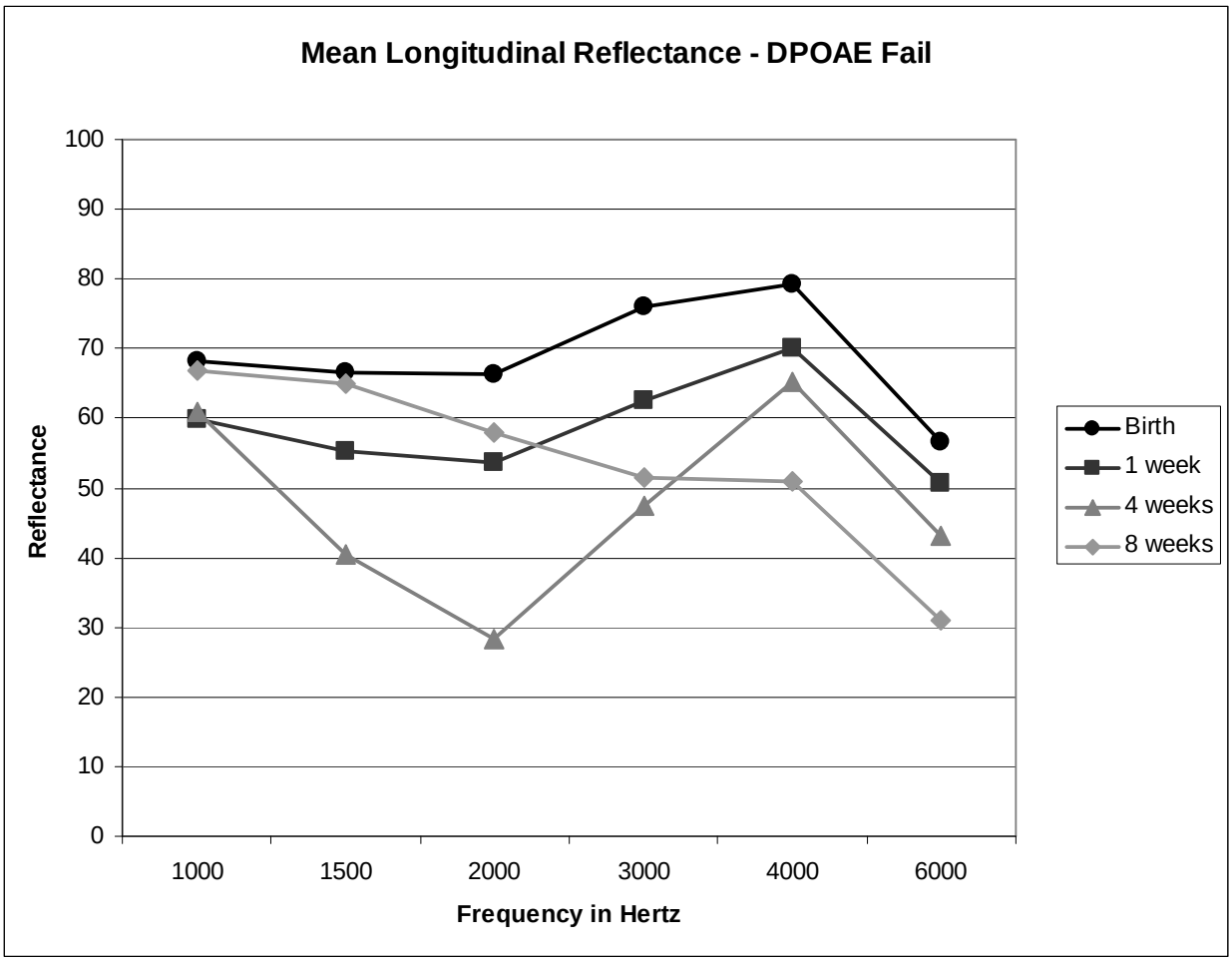


Figure 5. Mean WBR outcomes for subjects 18 and 40, who had four failing ears throughout the entire protocol.

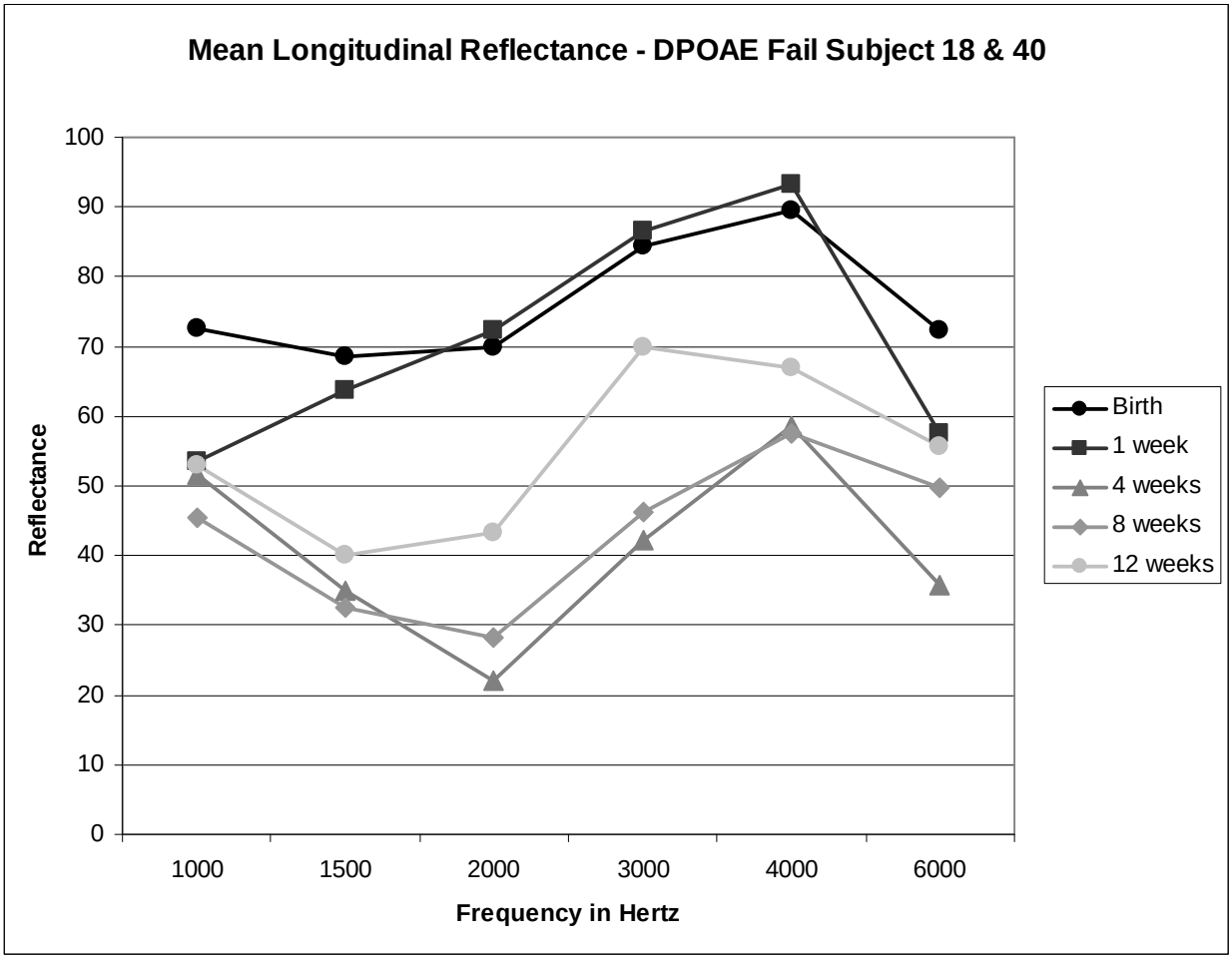


Figure 6. Differences between mean WBR outcomes for DPOAE failing (excluding subjects 18 & 40) and passing ears.

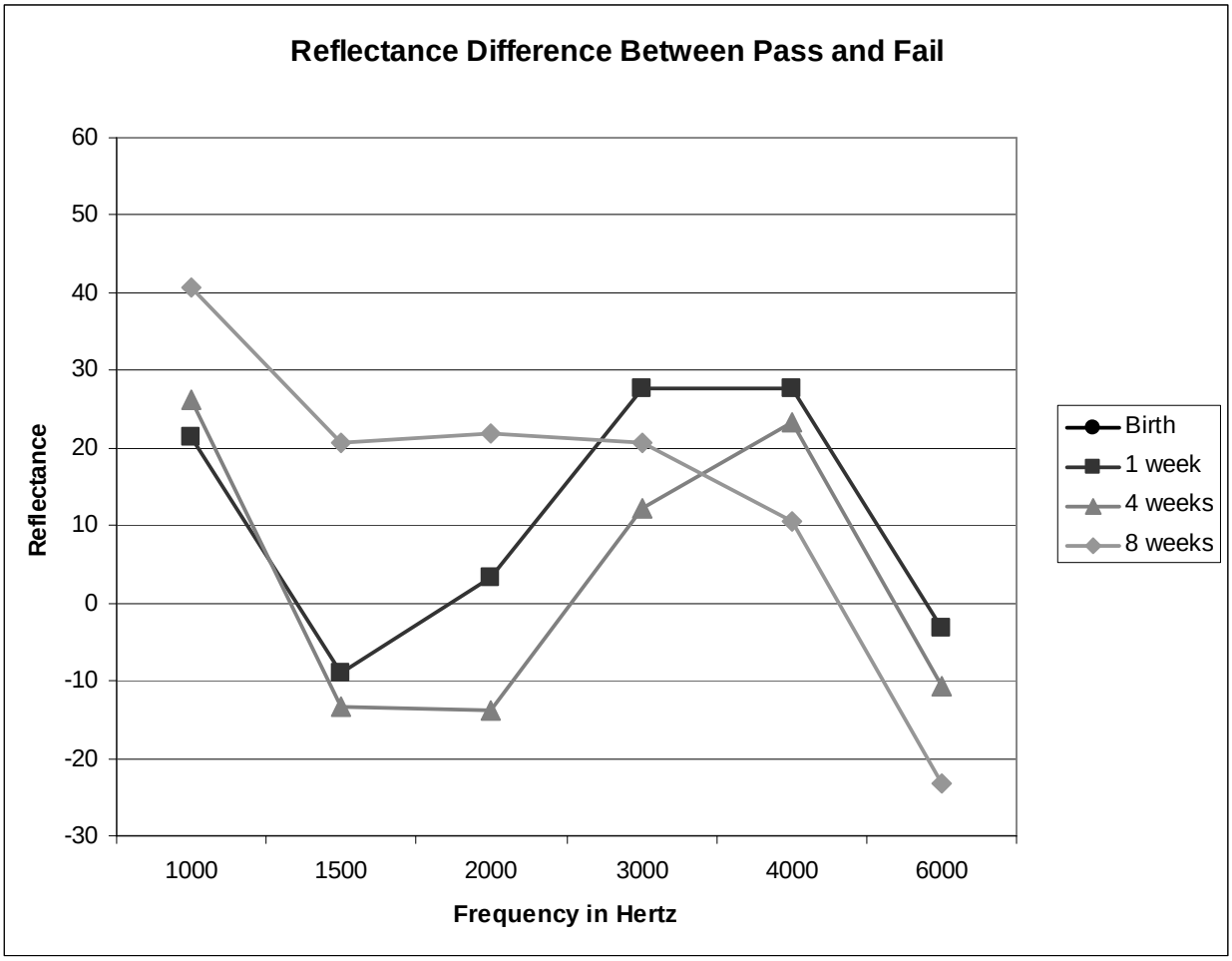
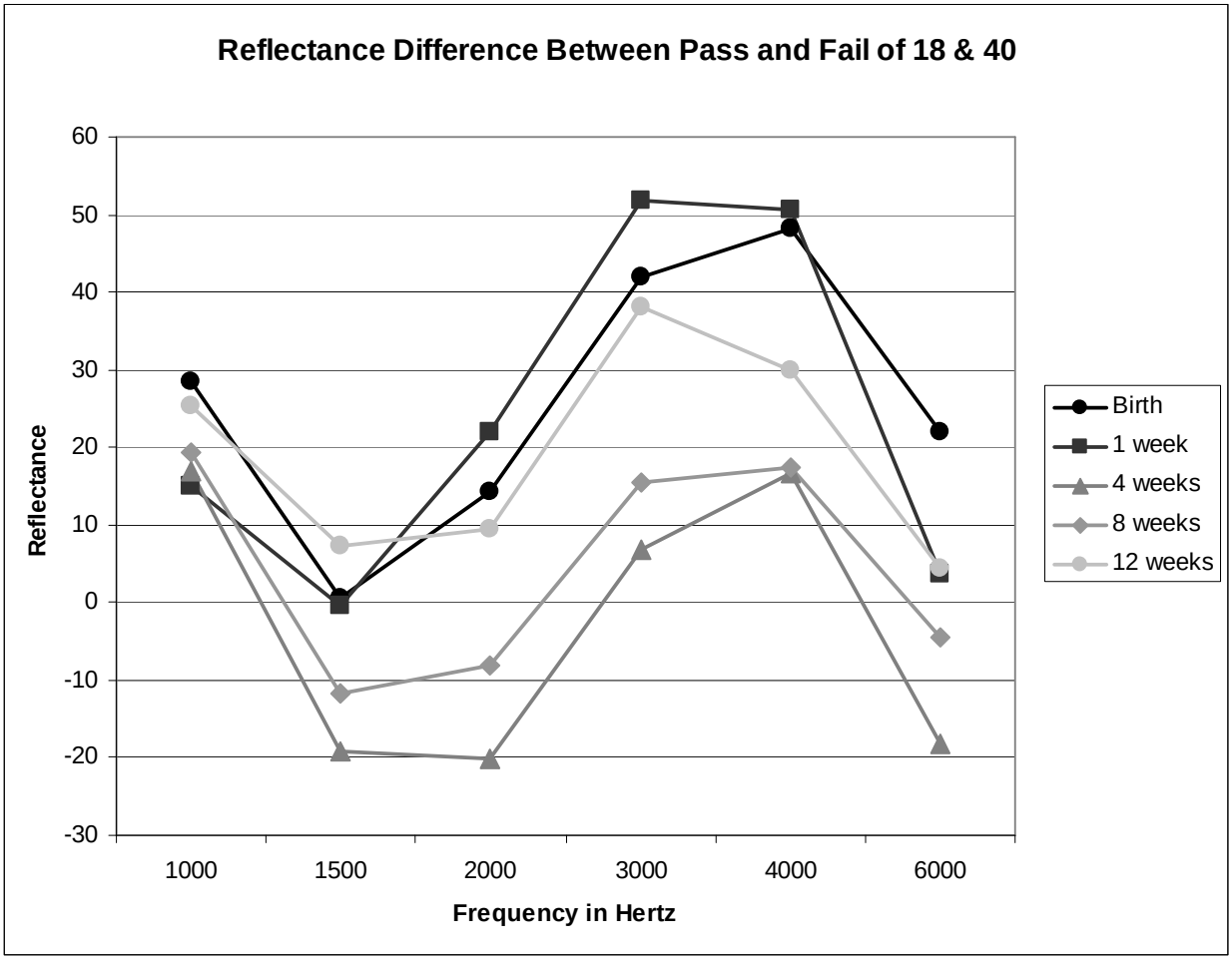


Figure 7. Differences between mean WBR outcomes for DPOAE failing ears of subjects 18 & 40 and passing ears.



Wideband Reflectance and Current DPOAE Outcomes

Wideband reflectance values are reported in Table 5 as a function of DPOAE screening outcome, time point, and reflectance frequency tested. Minimum and maximum scores are recorded, as well as 10^{th} and 90^{th} percentiles. Due to the small number of failing subjects at week 12 (four in number), 25^{th} and 75^{th} percentile were calculated instead. A percentile is a measure that tells what percentage of scores were below a given score. So in Table 5, for example, in the case of DPOAE passes, at birth,

for 1000 Hz, the minimum reflectance value was 5.8. Ten percent of the reflectance values for this group fell below a reflectance score of 29.90. Ninety percent of the reflectance values for this group fell below 68.30. The maximum value for the group was 73.90. Use of percentiles is one method that provides a sense of the range and distribution of values found for the group. In this case, eighty percent of the passing ears had reflectance values at 1000 Hz between 29.90 and 68.30.

Table 5. Percentiles of WBR values as a function of time point tested, frequency, and DPOAE outcome.

		DPOAE Outcome Pass Percentiles				**DPOAE Outcome Fail Percentiles**			
Time Point	**Frequency**	**Min**	**10**	**90**	**Max**	**Min**	**10**	**90**	**Max**
Birth	1000	5.8	29.90	68.30	73.90	23.40	39.75	88.45	93.90
Birth	1500	16.00	22.60	63.45	68.80	2.00	37.15	89.55	93.90
Birth	2000	20.60	23.25	75.00	61.35	9.40	30.30	89.10	95.20
Birth	3000	22.10	31.90	75.55	88.80	29.70	51.00	97.65	100.30
Birth	4000	33.60	49.10	87.75	120.50	12.30	49.10	104.30	118.10
Birth	6000	2.70	17.15	78.50	86.90	1.70	17.95	90.60	98.50
1 week	1000	26.30	32.76	75.60	84.20	27.80	36.00	80.60	92.00
1 week	1500	14.90	25.50	63.44	107.10	28.10	35.40	80.10	90.30
1 week	2000	5.80	14.44	54.72	92.80	25.90	31.40	84.40	90.80
1 week	3000	8.20	32.24	67.56	88.40	16.00	29.20	93.20	99.70
1 week	4000	15.70	40.06	81.00	98.00	16.00	16.20	103.30	106.30
1 week	6000	1.50	14.74	70.80	95.80	7.60	13.50	84.70	91.00
4 weeks	1000	14.50	33.26	71.04	112.10	27.90	39.94	72.10	72.80
4 weeks	1500	6.00	22.18	62.25	73.90	10.20	18.39	56.95	57.30

4 weeks	2000	7.00	16.00	59.15	70.00	10.80	10.87	45.38	52.10
4 weeks	3000	0.60	18.37	65.65	81.70	18.50	22.28	66.12	67.10
4 weeks	4000	4.70	27.06	76.52	88.60	37.10	37.10	84.22	89.40
4 weeks	6000	0.40	3.04	69.69	100.70	6.40	13.96	61.16	69.00
8 weeks	1000	11.80	36.60	68.97	95.00	32.80	37.20	82.20	85.90
8 weeks	1500	9.50	19.12	58.04	77.40	13.70	19.15	88.70	93.30
8 weeks	2000	1.10	12.91	54.19	79.20	5.30	9.25	92.60	95.40
8 weeks	3000	0.70	14.38	58.76	79.60	20.70	22.50	92.80	93.10
8 weeks	4000	0.10	20.20	69.59	101.20	6.30	9.15	89.70	97.60
8 weeks	6000	0.00	5.00	55.44	100.50	8.10	9.00	82.50	85.00
Time Point	**Frequency**	**Min**	**10**	**90**	**Max**	**Min**	**25**	**75**	**Max**
12 weeks	1000	21.50	35.10	69.11	82.20	50.20	50.75	54.83	55.10
12 weeks	1500	2.7	17.87	59.81	73.30	18.40	21.08	64.03	71.60
12 weeks	2000	0.70	12.05	58.56	93.10	18.30	20.2	73.25	82.20
12 weeks	3000	4.40	12.47	56.35	76.00	43.70	48.1	93.8	100.30
12 weeks	4000	0.80	6.14	65.26	85.70	32.80	39.95	94.95	103.00
12 weeks	6000	0.00	3.21	63.21	101.10	13.50	23.28	86.45	94.60

The values from Table 5 are displayed as function of frequency in Figures, 6, 7, 8, 9, and 10. In the figures, differences between the 10^{th} percentile for failing ears and minimum values for passing ears represent an area of WBR that correlated with a passing outcome on DPOAE screening. Differences between maximum values for failing ears and 90^{th} percentile for passing ears represent an area of WBR that correlated with failing outcome on DPOAE screening. Differences between the 90^{th} percentile of passing ears and the 10^{th} percentile of failing ears represent an area of ambiguity, where WBR values were similar among passing and failing ears. For the

twelve week time point, 25th and 75th percentiles were calculated instead of 10th and 90th percentiles. This is because only four ears were available for analysis in the group of "failing" ears. This sample size precludes calculation of 10th and 90th percentiles and only allows for analysis of 25th and 75th percentiles.

Figure 8. Percentiles for birth time point. The "Pass" area represents the difference between the 10th percentile for failing ears and minimum value for passing ears. The "Fail" area represents the difference between the maximum value and the 90th percentile for passing ears. The "Ambiguous" area represents the difference between the 90th percentile for passing ears and the 10th percentile for failing ears.

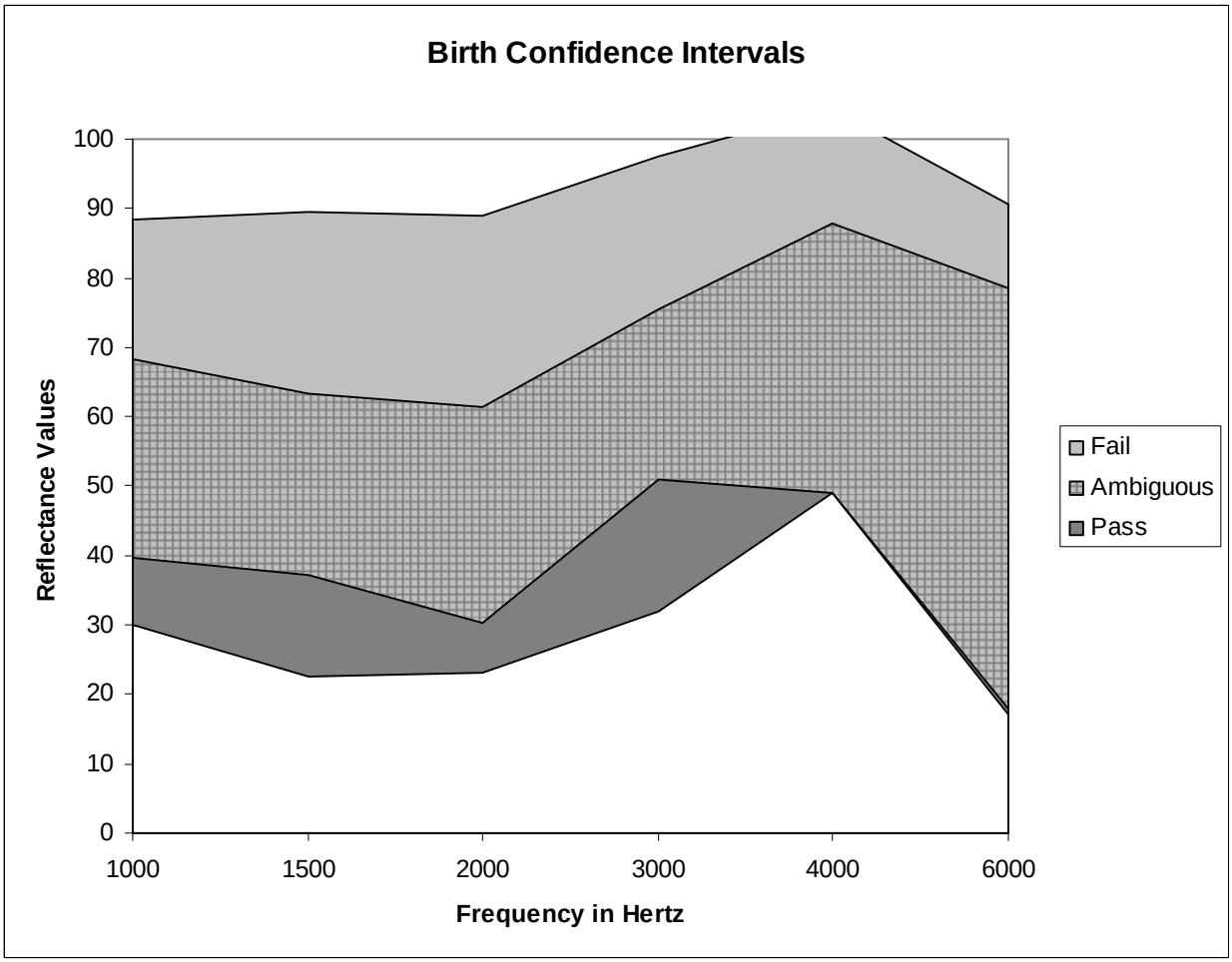


Figure 9. Percentiles for one-week time point as described in Figure 8.

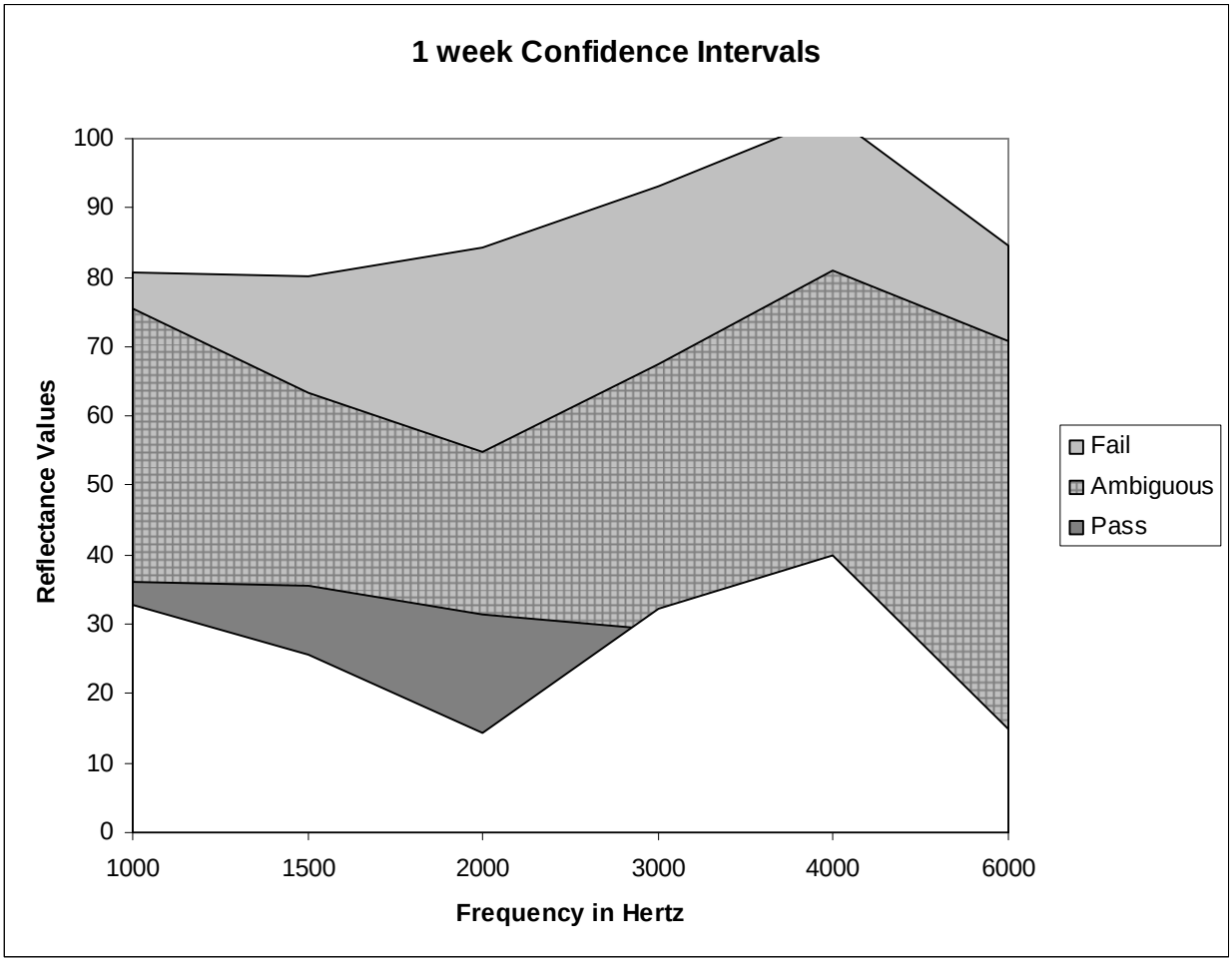


Figure 10. Percentiles for four-weeks time point as described in Figure 8.

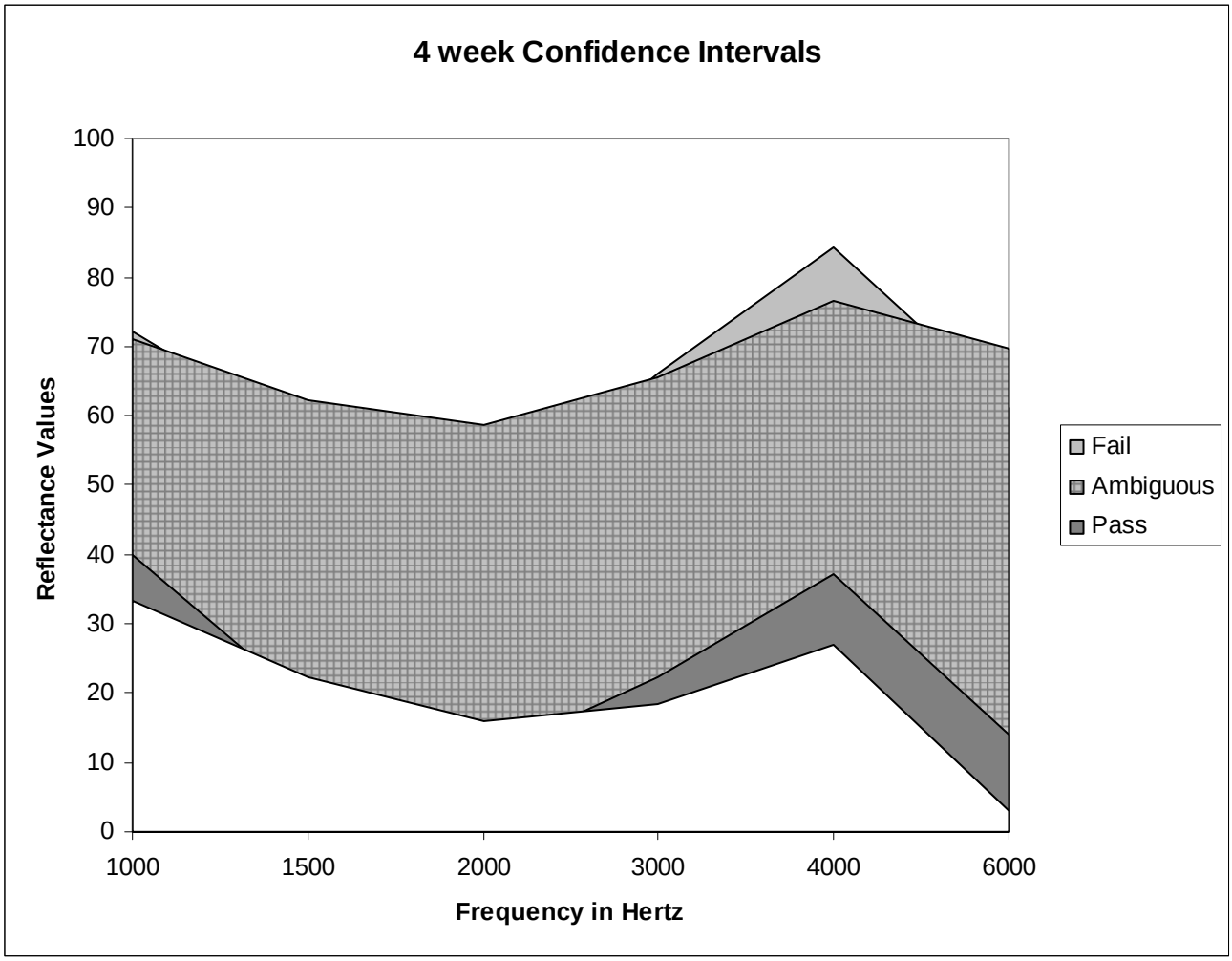


Figure 11. Percentiles for eight-weeks time point as described in Figure 8.

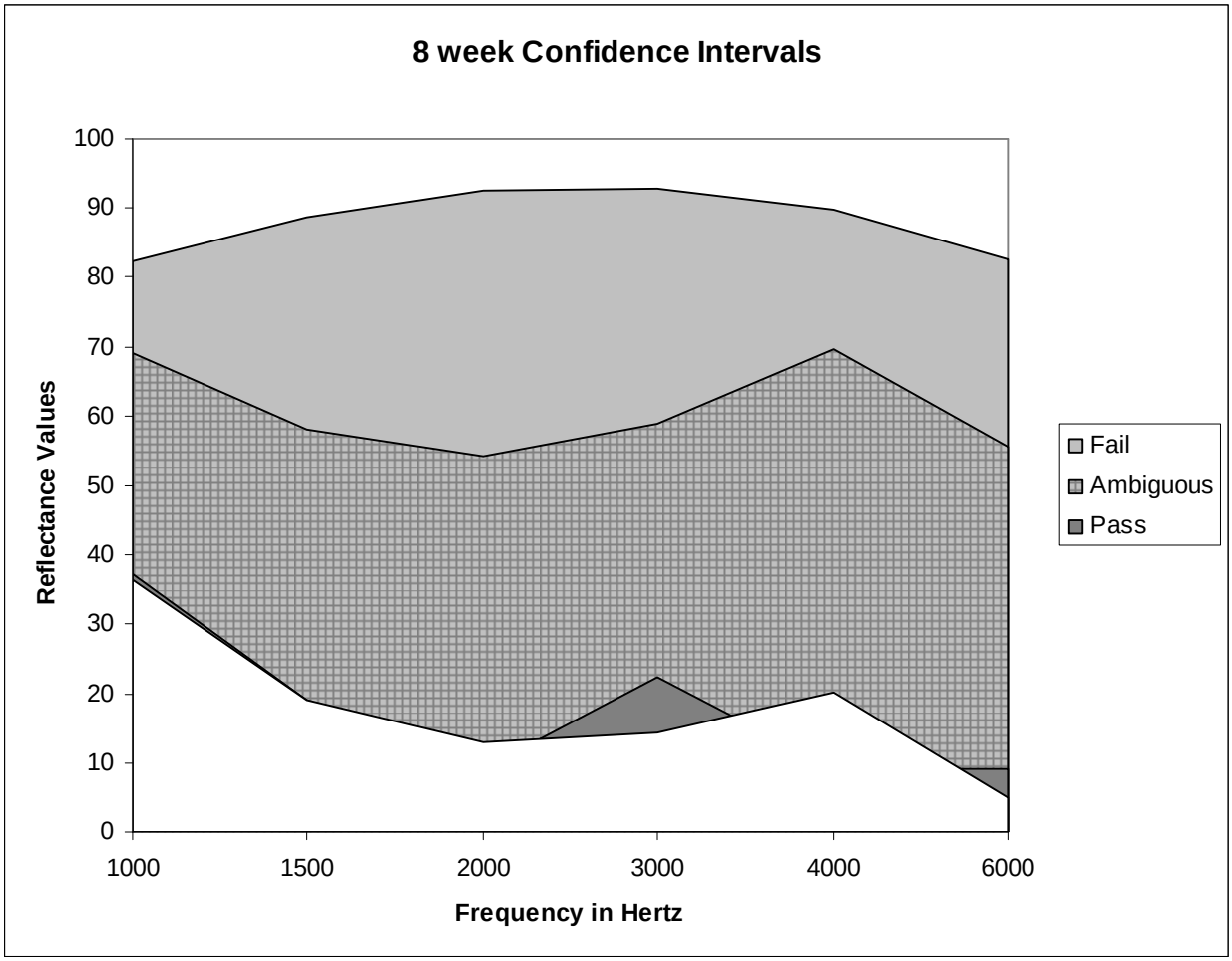
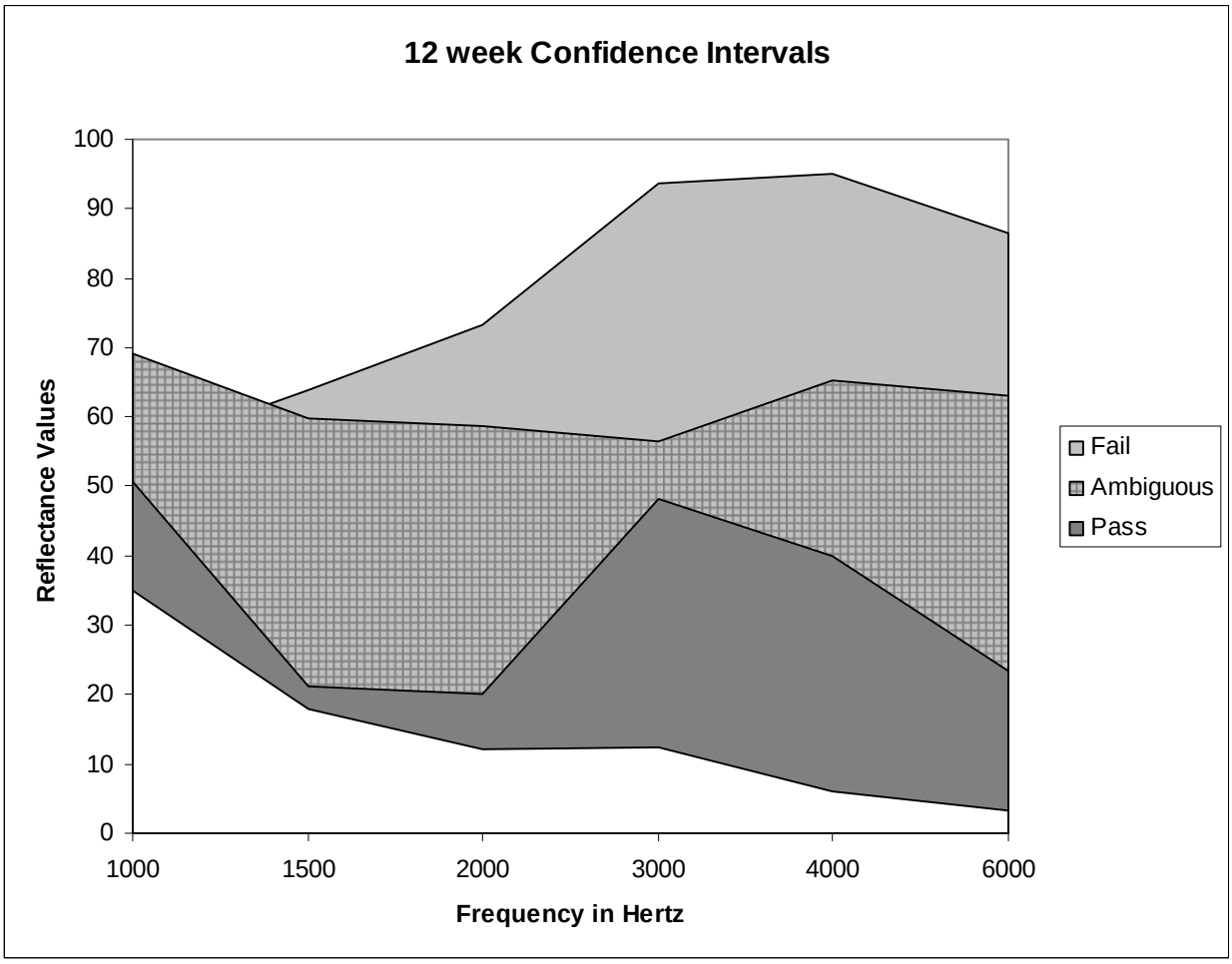


Figure 12. Percentiles for twelve-weeks time point. The “Pass” area represents the difference between the 25th percentile for failing ears and minimum value for passing ears. The “Fail” area represents the difference between the maximum value for failing ears and the 90th percentile for passing ears. The “Ambiguous” area represents the difference between the 90th percentile for passing ears and the 25th percentile for failing ears.



The sensitivity of a test, the degree to which the test is able to predict a true positive outcome, is generally at odds with the specificity of a test, the ability of a test to correctly reject false positive outcomes, but the degree to which this is true differs with each test. The best tests are those which have maximum sensitivity and specificity.

Receiver operating characteristic (ROC) curves are plots of the proportion of true positive outcomes (hits), which relate to sensitivity, and to false positive outcomes (false alarms), which relate to specificity. The higher the true positive proportion and the lower the false positive proportion, the better the predictive ability of the test. A value that can characterize these two components is the area under the curve (AUC). Literally, the AUC is the portion of a unit of 1 that exists under the ROC curve. In general, the higher the AUC value, the better the predictive value of the test.

ROC curves are generated from the distributions of values from two populations. In this case, the two groups are DP passes and DP refers. The values that make up the distributions are WBR outcomes. The distributions for these two groups will overlap to some extent. These distributions are available for each WBR frequency measured. So for each frequency, there will be differing degree of overlap of the distributions. The greater the separation of the WBR distributions for DP pass and DP refer groups, the greater the ability to predict DP outcome with a given WBR measure. ROC values range from 0 to 1 and the higher the value, the more the reflectance measure accurately predicts DPOAE outcomes.

Receiver operating characteristic (ROC) curves were generated via IBM SPSS Statistics Version 20 (IBM Corp.) from the distributions of WBR values from the current time point DPOAE pass and DPOAE fail groups. Data are shown in Table 6. In this table, as well as Table 7, ROC values were calculated for each frequency used for reflectance testing. In this way, the frequency which is best predictive of DPOAE outcomes can be ascertained. This information can help direct the audiologist's attention toward frequencies that are most important for interpretation of clinical data. In

Table 6, this information is displayed for each time point tested. For example, the ROC value of .787 at 1000 Hz at birth provides a metric for how well the 1000 Hz reflectance values found at birth accurately predict DPOAE outcomes at birth.

Table 6. ROC values based on DPOAE pass and DPOAE fail outcomes for WBR values at time points following birth.

Frequency	**Birth**	**1 week**	**4 weeks**	**8 weeks**	**12 weeks**
1000	.787	.584	.618	.635	.576
1500	.832	.737	.444	.708	.525
2000	.807	.806	.335	.703	.615
3000	.808	.726	.581	.669	.927
4000	.702	.668	.646	.631	.836
6000	.663	.652	.616	.616	.760

Wideband Reflectance and Future DPOAE Outcomes

Receiver operating characteristic (ROC) curves were generated via IBM SPSS Statistics Version 20 (IBM Corp.) from the distributions of WBR values from an earlier time point to the DPOAE outcomes of a later time point. Data are shown in Table 7. In Table 7, this information is displayed for the reflectance data from one time point and the DPOAE outcomes at a later time point. For example, the ROC value of .574 at 1000 Hz at “birth – 1 week” provides a metric for how well the 1000 Hz reflectance values found at birth accurately predict DPOAE outcomes at one week.

Table 7. ROC values based on DPOAE pass and DPOAE fail reflectance distributions for WBR frequencies. Each time point compares the current or final DPOAE outcome to a previous time point WBR.

Freq	**Birth – 1 wk**	**Birth – 4 wks**	**Birth – 8 wks**	**Birth – 12 wks**	**1 wk – 4 wks**	**1 wk – 8 wks**	**1 wk – 12 wks**	**4 wks – 8 wks**	**4 wks – 12 wks**	**8 wks – 12 wks**
1000	.574	.719	.634	.692	.565	.611	.478	.456	.461	.263
1500	.618	.686	.616	.692	.634	.742	.828	.459	.393	.349
2000	.596	.611	.611	.708	.620	.683	.903	.395	.230	.418
3000	.594	.625	.676	.784	.516	.681	.943	.494	.511	.577
4000	.563	.656	.696	.770	.499	.676	.940	.496	.508	.686
6000	.537	.621	.598	.760	.487	.536	.639	.385	.518	.820

The percentiles for the WBR to future time point are displayed as function of frequency in Figures 13-16. In the figures, differences between the 10^{th} percentile for failing ears and minimum values for passing ears represent an area of WBR that correlated with a passing outcome on a future DPOAE screening. Differences between maximum values for failing ears and 90^{th} percentile for passing ears represent an area of WBR that correlated with failing outcome on a future DPOAE screening. Differences between the 90^{th} percentile of passing ears and the 10^{th} percentile of failing ears represent an area of ambiguity, where WBR values were similar among passing and failing ears. For the twelve week time point predictions, 25^{th} and 75^{th} percentiles were calculated instead of 10^{th} and 90^{th} percentiles. This is because only four ears were available for analysis in the group of “failing” ears. This sample size precludes calculation of 10^{th} and 90^{th} percentiles and only allows for analysis of 25^{th} and 75^{th} percentiles.

Figure 13. Percentiles for the birth time point WBR values compared to future DPOAE pass or fail.

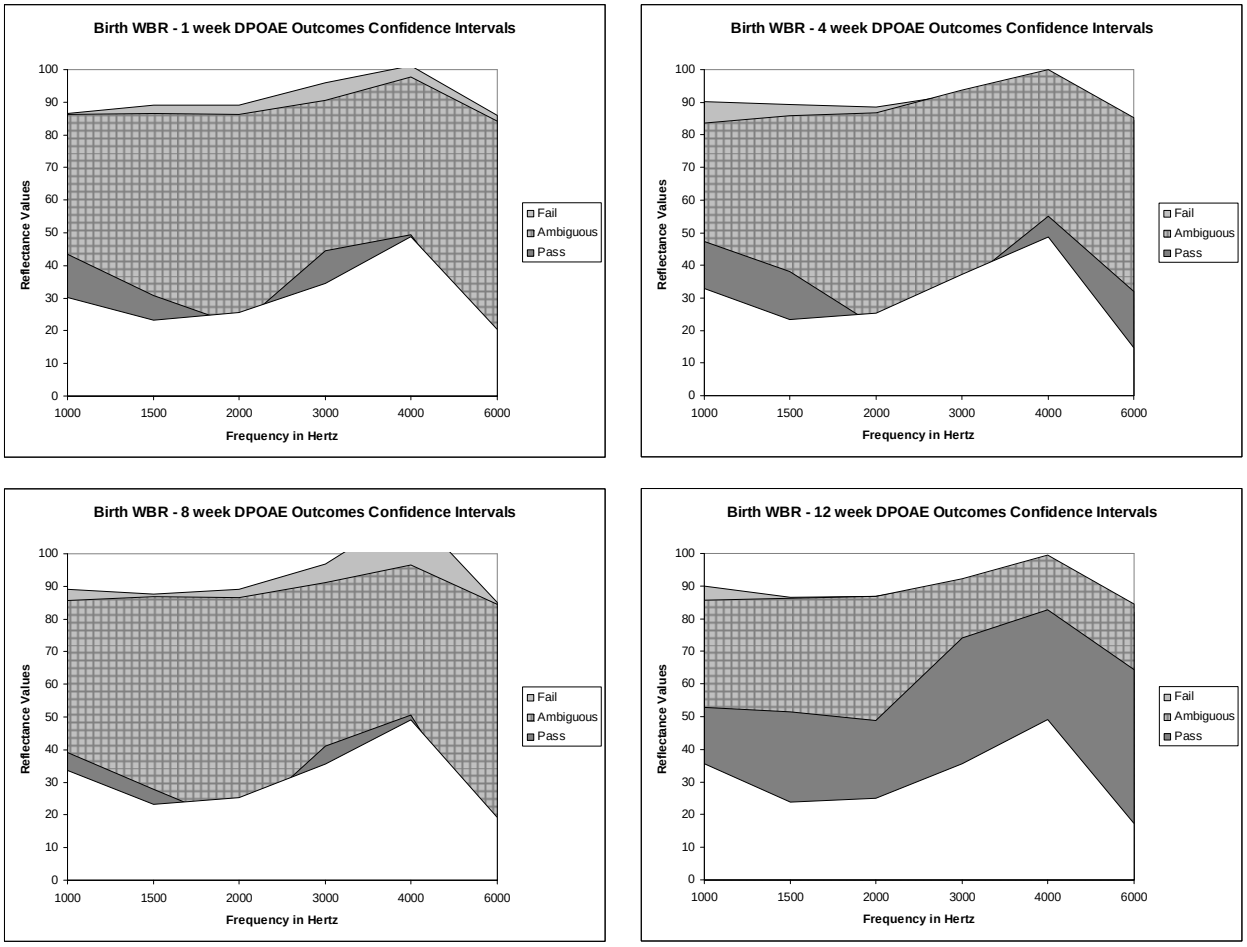
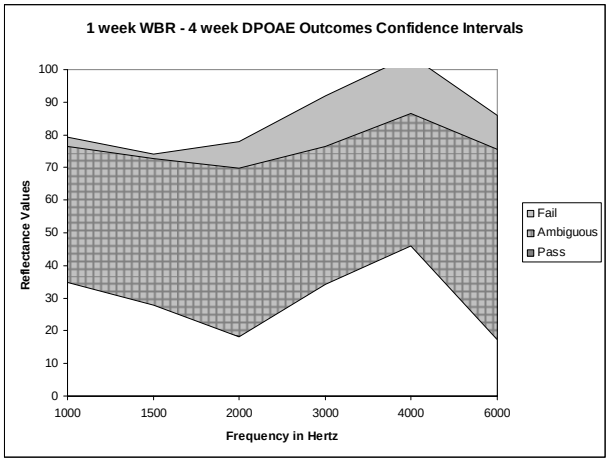
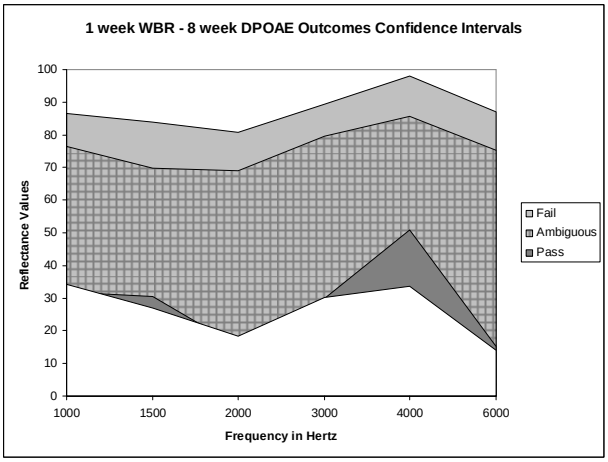


Figure 14. Percentiles for the one-week time point WBR values compared to future DPOAE pass or fail.





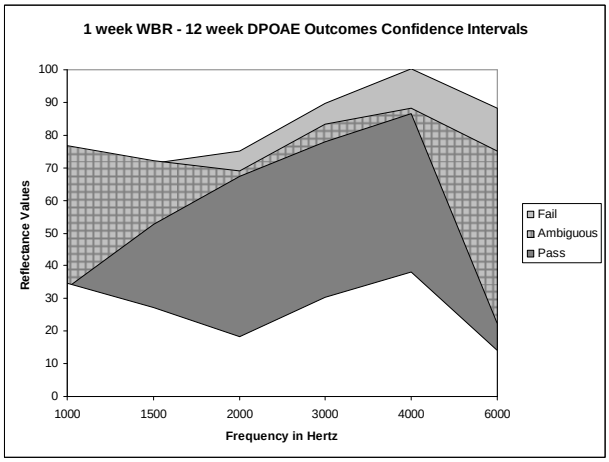


Figure 15. Percentiles for the four-weeks time point WBR values compared to future DPOAE pass or fail.

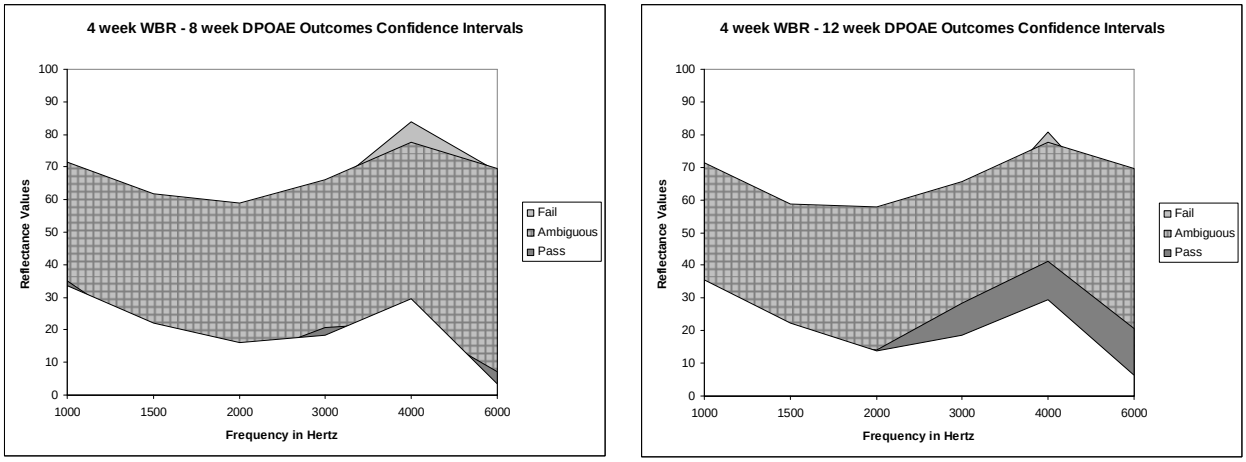
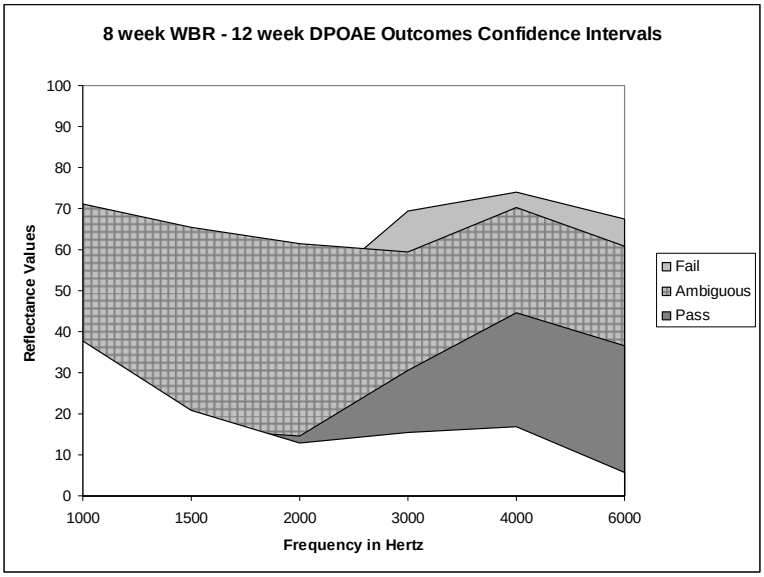


Figure 16. Percentiles for the eight-weeks time point WBR values compared to future DPOAE pass or fail.



CHAPTER 5

DISCUSSION AND CONCLUSIONS

The results of this study provide evidence to address the research questions as follows.

Do patient factors at birth, including birth weight, head circumference, and gender correlate with initial DPOAE screening outcomes?

Gender was not a factor in initial DPOAE screening outcomes in this study. Previous work (Gordts, et al, 2000) has demonstrated that DPOAEs are larger in female than in male infants, but such differences, if present, are likely to be too small to be observed when utilizing a screening level for evaluation. Interestingly, infant gender did appear to be a factor in the willingness of parents to enroll subjects into the study and the recruited group was ultimately skewed toward females. Given that only about half of infants born are female, it is unknown why more parents of females chose to participate than parents of male infants.

Birth weight and head circumference were not significantly different for passing and failing groups in this study. Infants in intensive care nurseries have previously been shown to have poorer otoacoustic emission outcomes than the regular care population (Chiong et al, 2003), and because such infants tend, as a group, to be smaller than infants in the regular care population, it could be hypothesized that size differences could affect DPOAE outcomes. However, other correlated factors can account for these differences, such as gestational age and other health factors, and in this study the

relationship between infants size, as measured by birth weight and head circumference, was unrelated to DPOAE screening outcomes.

What is the longitudinal time course of DPOAE outcomes in infants?

As expected, the rates of DPOAE passes increased over the time course of the study. Also, the rate of ears that failed following some previous pass increased at each time point, with the exception of week twelve in which no new failing ears were generated. The greatest increase in passing ears was seen within the period between birth and one week (an additional 21 ears), but with a change in six ears from a passing to a failing outcome. There is also a reasonably large increase between one and four weeks of age (an additional 12 ears) but with only two additional ears failing that had passed at some previous time point. This improvement in passing outcome would suggest that beyond birth, four weeks is preferable to one week for retesting. Eight weeks of age does not appear to provide much additional advantage over four weeks of age in that there were only two additional passing ears and one additional new fail.

The twelve week time point clearly provided the most efficient time point in this study. By this time, 96% of ears had passed, with no new referrals occurring. It is surprising, however, that there were no new referrals when the rate of referrals had been steadily increasing from birth. It is possible that there may be ear canal maturational effects that caused referrals throughout the first three months of life that were resolved by the twelve week time point. Another possibility is that there were seasonal effects that contributed to referrals occurring at early time points than the final measurement, as most interim measures were taken during winter months, while the final time point measurements primarily occurred in the spring. Perhaps otitis media

occurred during the interim time points and had resolved by the final time point when incidence of otitis media would naturally begin to wane. Of course, a simple anomalous situation cannot be ruled out either. If the pattern of results were unrelated to situational factors and were rather related to maturational factors, then the twelve week time point would represent the most efficient opportunity for re-evaluation for infants who fail on testing. If the pattern were due to situational factors, such as seasonal otologic issues, waiting until the twelve week time point could potentially result in higher rates of new referrals, diminishing the positive effect of waiting.

Another potential concern is that of loss to follow up for infants who fail. In this study subject attrition was limited to four infants, but this was likely due to considerable effort on the part of the investigator to maintain subjects in the study by conducting testing in the homes of patients. The nationwide average for follow-up before three months of age is a mere 46% in real-world clinical situations (Centers for Disease Control, 2007). It is unknown whether waiting a longer period of time, such as twelve weeks versus four, might contribute to increases in loss to follow up. An answer to this question requires future study.

What is the longitudinal time course of WBR outcomes in infants?

Post-hoc analysis demonstrated interesting development changes in WBR over the first twelve weeks following birth. Figure 3 shows that in infants who pass DPOAE screenings, lower-frequency reflectance values (1000 – 2000 Hz and especially 1500 Hz) decrease systematically following birth, while the higher frequency reflectance values are stable. This clearly suggests an early developmental trend in normal infants which has not been previously shown in the literature.

In ears that failed the DPOAE screening (Figures 4 and 5), there is a trend toward higher reflectance values in the highest frequencies, relative to the passing ears. This trend can be seen more clearly in Figures 6 and 7, (more pronounced in Figure 7) which show the difference between reflectance scores for failing and passing ears as a function of frequency and time point tested. There is an “S-shaped” trend that is present in both figures that indicates low reflectance for the 1500 - 2000 Hz range and higher reflectance for the 3000 – 4000 Hz range than the trends for passing ears. The mechanism underlying the inability to record DPOAEs in these ears appears to have its impact on both the mass (high-frequency) and stiffness (low-frequency, 1000 Hz) of the middle ear and ear canal systems. There are numerous developmental factors that occur in the ear canal and middle ear following birth that can help to explain the developmental changes in the passing ears. Among the many factors that can help to explain the mass and stiffness effects apparent in the failing ears, fluid in the middle ear space has the potential to generate these forces.

What frequencies on wideband reflectance testing are best predictive of DPOAE testing outcomes at different ages and later time points?

ROC calculations demonstrate that the WBR frequencies with the highest predictive level of DPOAE outcomes were 1500 Hz at birth, 2000 Hz at one week, 4000 Hz at four weeks, 1500 Hz at eight weeks, and 3000 Hz at twelve weeks. Overall and not surprisingly, the ROC values were smaller for the relationship of WBR measures to future DPOAE outcomes (Table 7) than they were for current DPOAE outcomes (Table 6). Interpretation of these values will be discussed further in the section on clinical utility.

A challenge inherent in the design of this study is that there is a smaller subject pool of failing ears at each additional time point to evaluate the relationship of WBR to DPOAE outcome, dropping from 54 ears at birth to 29 at one week, 16 at four weeks, 14 at eight weeks, and only 4 at twelve weeks. As such, the data must be interpreted cautiously and with the knowledge that a small subject pool cannot be assumed to be representative of population data.

It is beyond the scope of this study to determine the primary mechanisms responsible for changes in the frequencies that are characteristically useful in the infant ear canal, but some possibilities include developmental changes in the resonance characteristics of the ear canal related to size and outer and middle ear structures. Due the mechanics involved in various dysfunctions in the outer or middle ear, there would presumably be different patterns of energy transfer into the middle ear space, depending on the dysfunction. These differences would manifest as different frequencies having characteristic outcomes that are representative of the type of dysfunction. Because WBR measurements are made in the ear canal, it is presumed that, like tympanometry, this frequency-specificity would reflect the most peripheral level of dysfunction.

Clinical Utility

To help interpret the data found herein, it is important to consider the diagnostic questions facing the clinician. If an infant has failed a DPOAE hearing screening at birth, the following questions would be of interest to the clinician:

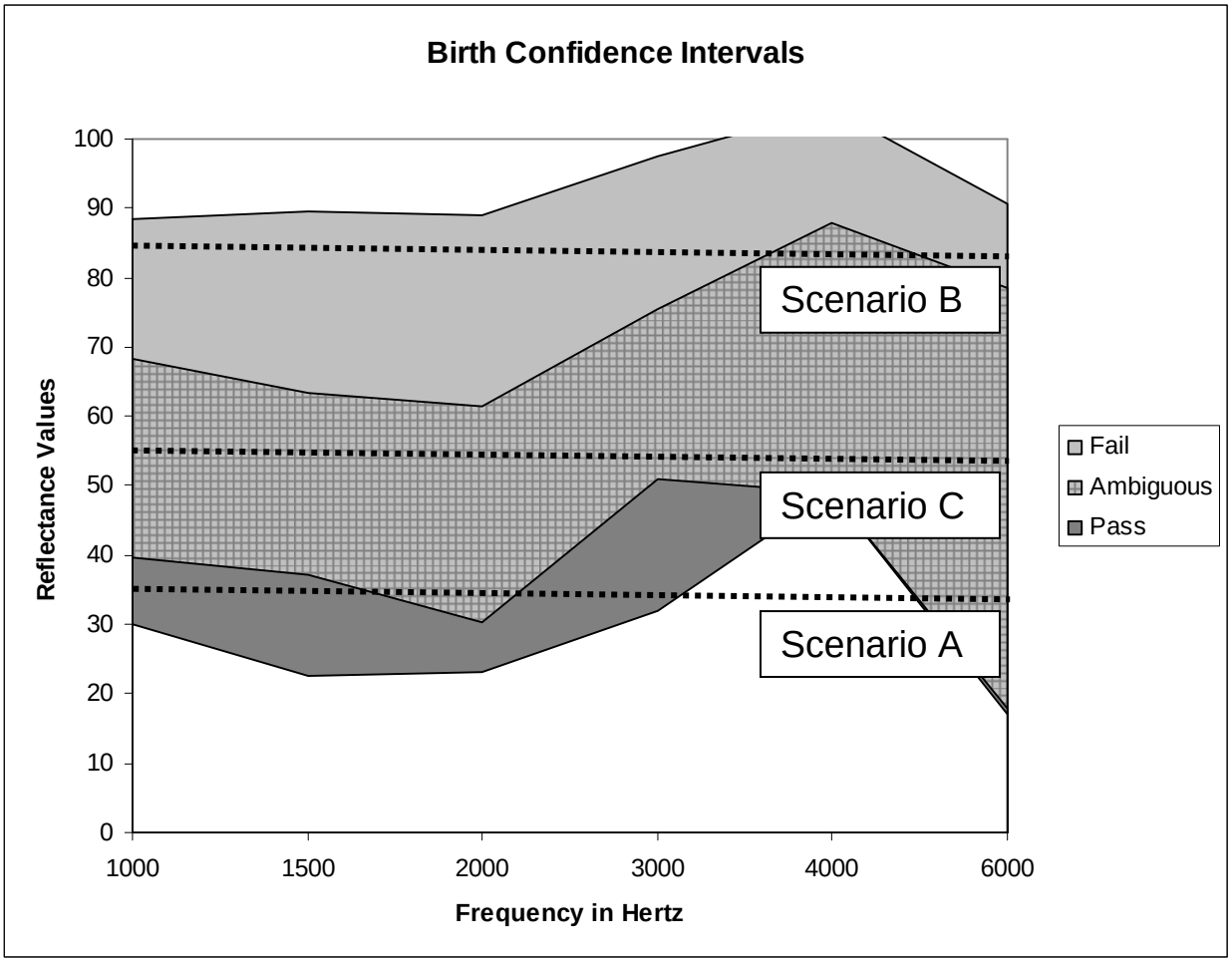
1. Is there heightened suspicion for sensorineural hearing loss?
2. Is there concern that a conductive component will be persistent?

3. When should the infant be re-tested?

To understand how the data presented here can inform this question, consider the percentiles for measurements taken at birth (shown again in Figure 17). In these scenarios, assume that the audiologist has obtained DPOAE and WBR data.

Scenario A: Imagine that the infant failed the DPOAE screening and had (for the sake of simplicity) WBR values of 35 across all frequencies. The WBR values for 1000 – 3000 Hz fall within the “pass” area of the percentiles, while those values for and 6000 Hz fall within the “ambiguous” area. (In this case 4000 Hz would be below the minimum values recorded in this population. Again, this value was chosen only for convenience of display). If we only had access to WBR data for 2000, 4000 or 6000 Hz, this information would not be helpful in answering whether there is heightened suspicion for sensorineural hearing loss because there is no clear “pass” area for these frequencies. However, the data for the 1000 – 3000 Hz range suggests that the infant does not have a conductive component. In the face of a failed DPOAE screening, the clinician should have heightened concern for sensorineural hearing loss, little to no concern for persistent conductive loss, and should recommend re-testing in the immediate future.

Figure 17. Percentiles for WBR values at the birth time point for DPOAE pass or fail outcomes. Various scenarios of WBR outcomes are highlighted for descriptive purposes.

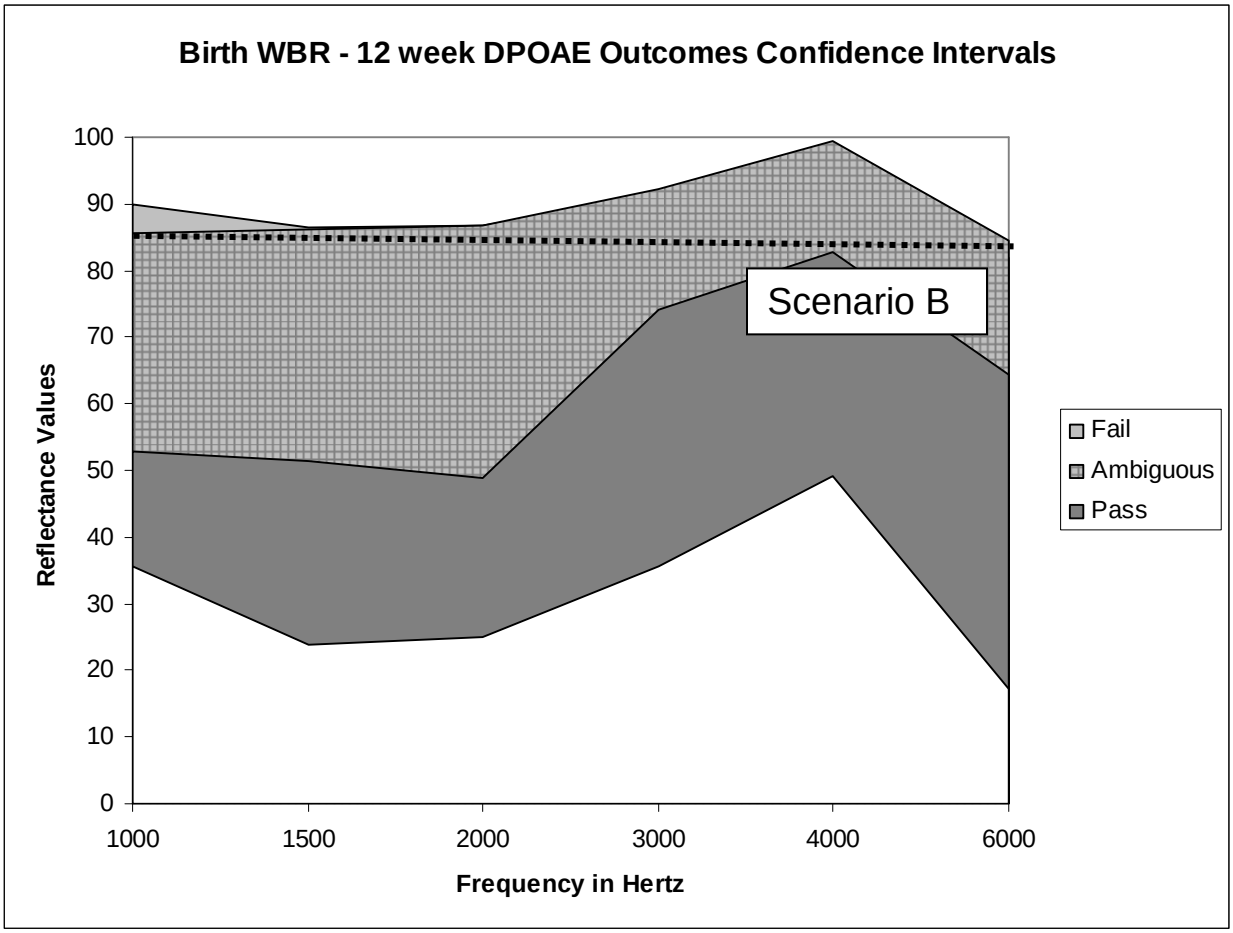


Scenario B: Imagine that the infant failed the DPOAE screening and (for the sake of simplicity) had WBR values of 85 across all frequencies. In the case of the second clinical question, WBR values fall within the “fail” area at all frequencies except 4000 Hz. This is consistent with a conductive dysfunction of some type. Note that this does not rule out the possibility of sensorineural hearing loss, which can co-exist with conductive loss. So, in answer to the first clinical question, we do not have heightened

concern for sensorineural hearing loss; just that which is typical for any other infant who fails a screening. We do expect that the infant has conductive hearing loss, but we do not know whether this is expected to be persistent.

The question of persistence, whether a conductive component is likely to resolve independently, or may require medical treatment, is important for the purpose of planning the assessment process for the patient. If the conductive component is likely to be persistent, it may be of interest to refer the infant for medical follow up at an earlier age, rather than waiting several months and repeatedly testing the infant to see if it will resolve on its own. On the other hand, if the conductive component is likely to resolve independently, it would be helpful to anticipate this and to know when resolution is likely to occur. To assist in answering the third clinical question of when the infant should be re-evaluated, we would examine the value of WBR in predicting future outcomes. Figure 18 shows the figure that depicts the WBR values at birth as a tool for predicting DPOAE outcomes at twelve weeks. The reflectance values at birth for Scenario B, 85, are plotted for reference.

Figure 18. Percentiles for WBR values at the birth time point for predicting DPOAE pass or fail outcomes at twelve weeks. The scenario of WBR outcomes is highlighted for descriptive purposes.



It can be seen that in this case WBR values are not a useful predictor for whether the conductive component will persist to twelve weeks because the reflectance values found at birth fall within the “ambiguous” area of the graph, meaning that the values for passing and failing ears overlap. Indeed, there is almost no clear “fail” area on the graph. (However, if the values were at 35, as in the previous scenario, the predictive utility would be greatly heightened because there is a clear “pass” area to be seen).

The ROC calculations in Tables 6 and 7 provide a value that captures the overall relationship between WBR measures and DPOAE outcomes. The reader will recall that ROC values to be lower for future predictions than for concurrent predictions. The functional consequences of this can be seen in these scenarios. When looking at the birth time point Percentiles (concurrent predictions), there are distinct regions of pass, fail, and ambiguous outcomes. The audiologist could use this information in a meaningful way to guide clinical decision making. However, in the birth to twelve week Percentiles (future predictions), the area of ambiguity is much larger and there is no region that clearly predicts fail outcomes. This is of much less utility to the audiologist because there is no more useful information that can be gleaned from these data to assist in decision-making. Overall, ,the utility of the predictive value that is represented by the calculated ROC values does not depend on the particular ROC value per se. This value is merely descriptive. Rather the utility depends on the clinical question which is being asked and whether the confidence-interval data can provide information to assist in the decision-making process. The audiologist must use the information accordingly.

Scenario C: Imagine that the infant failed the DPOAE screening and (for the sake of simplicity) WBR values of 55 were found across all frequencies (Figure 17). In this case the reflectance data is of no value because the these values fall within the area of ambiguity where there is complete overlap of values that occur for passing and failing ears. In this case, the longitudinal DPOAE outcome data will be most helpful in informing the clinician’s next recommendation of when the infant should be re-tested.

Longitudinal assessment demonstrated that referral on DPOAE screening declined with each additional time point, even though the rate of referral following an earlier passing outcome increased at each time point, with the exception of the final time point. Based on these data, twelve weeks would be optimal time for re-evaluation of infants who fail at birth. However, in the clinical population, it is unknown whether waiting this amount of time would be detrimental to the rate at which patients received follow up care. Furthermore, an infant who is found to fail at twelve weeks of age would then require further diagnostic follow up, including auditory brainstem response evaluation. While DPOAE measures can reasonably be performed in infants who are awake, ABR evaluation cannot, and waiting until twelve weeks of age for this possibility may be inadvisable as infants at three months of age do not spend as much time in natural sleep as younger infants. Therefore, the next best recommendation would be to re-screen at four weeks following birth. This would yield the greatest improvement in passes without substantial new referrals. An additional advantage is that re-screening at four weeks would fall within the JCIH guidelines, which are based on theoretically ideal timelines for speech and language development. The JCIH guidelines are for re-screening by one month, and identification and quantification of hearing loss (which requires further audiologic evaluation) by three months of age. Due to these factors, it would likely be in the best interest of the clinician to recommend re-testing at four weeks of age.

Study Limitations

The intensive nature of data collection for this study necessarily limited sample size, which contributed to limitations of the study. As subjects had a natural resolution of

conductive hearing loss over time there was a progressively smaller sample size available for understanding the wideband reflectance results of failing ears. This small sample size compromises the ability to generalize study results for the latest time points, particularly eight and twelve weeks of age. In addition, those infants who did continue to have conductive hearing loss at the later stages may have had a fundamentally different mechanism underlying the conductive disorders than those who resolved spontaneously at earlier time points. A larger sample size would have allowed for more infants to be examined with conductive hearing loss at the latest time points. A larger sample size might also allow for effects of race and ethnicity to be evaluated. It is the author's opinion that a useful sample size, while not impossible, will be ambitious to achieve. The JCIH recommended referral rate is 4%. However, institutions such as where these data were collected have a much higher referral rate; closer to 15%. If a realistic referral rate of around 10% is assumed, there would be a need for ten infants to be tested for one to refer. Further, the author estimates that approximately 90% of the population asked to participate in the study either declined or were ineligible for some reason. Following the inclusion criteria for this study and in a population similar to this, it is estimated then that about one infant out of 100 will refer on initial screening, will be eligible to participate, and will have caregivers willing to participate. In this study, of those infants who fail the screening, 96% of ears resolved, leaving only 4% that did not. Based on these data, if we were to desire to have a sample size of 50 ears that did not resolve by twelve weeks of age, for the purpose of characterizing wideband reflectance results in a sample of ears that is resistant to spontaneous recovery of TCHL, a population size of approximately 122,500 infants would be required for the study.

The home-based evaluation of infants was deemed necessary to secure the ongoing participation of subjects in the study. However, this method limited the type of data collected. Because data was collected in the home by a single investigator, there was no ability to evaluate otoscopic status of infants during testing. Even if the investigator was adequately trained to perform such evaluations, there would be no corroboration of this subjective assessment by another rater.

Another limitation of the study was the inability to ascertain the underlying cause of the apparent conductive hearing losses in these infants. Other assessment beyond otoscopic examination, such as tympanocentesis could provide important information to understand the mechanisms underlying the results that were used to infer conductive hearing loss. Unfortunately, this type of procedure has some potential for harm and could not be ethically performed in infants who do not require such a procedure for treatment purposes.

Future Directions

This study provided useful information regarding the natural course of temporary conductive hearing loss in infants. However, prior to providing recommendations based upon such findings, it is important to understand potential unintended consequences of suggesting that parents wait for a particular period of time prior to having infants re-evaluated. It is known that while nearly all infants are screened for hearing at birth, approximately half of all infants are lost to follow-up for re-evaluation. One important piece of information to know is whether the duration of time between initial screening and outpatient rescreening would contribute to loss to follow up. If waiting a particular period of time for re-evaluation results in an increase in loss to follow up, then the

savings of resources that would be achieved by waiting may not be worth the cost of losing infants who require re-evaluation.

Another important question of interest is whether reflectance measures performed in conjunction with universal newborn hearing screening protocols could, in fact, improve the age of identification of sensorineural hearing loss in infants. A prospective study, using data such as these as normative values for passing and referring groups would allow determination of whether reflectance should be used as an adjunct measure in screening protocols.

In this study, the time points selected for examination were largely arbitrary. Future studies which examine more discrete time points, particularly in the first few days following birth might be useful in further refining the screening process.

Lastly, the vast majority of infants who failed the screening in this sample and were assumed to have TCHL passed their AABR screening. Only five ears failed this screening. It is important to understand the natural resolution of TCHL in infants screened with DPOAEs because this technology is widely used in various regions of the world as the primary newborn hearing screening mechanism. However, in much of the United States, AABR is the method of choice for newborn hearing screening. While the “failing” group of infants in this study was presumed to have TCHL, the vast majority of these infants would have “passed” the typical AABR screening protocol. This is because of the different mechanisms underlying measurement using these systems and the impact of conductive dysfunction on the outcomes. For AABR screening, conductive hearing loss attenuates the intensity of the stimulus signal which can potentially result in a failure on screening. For DPOAE screening, conductive dysfunction can attenuate the

intensity of the stimulus but, more importantly, attenuates the “backward” traveling OAE signal. The attenuation of the evoked emission nearly always results in a failure on screening because the signal is too low in intensity to be measured in the ear canal. The difference that the conductive mechanism has upon these test outcomes can be seen in this population, wherein 49 of the 54 ears that failed the DPOAE screening had passed the AABR screening. The degree of conductive dysfunction, which results in a pass on AABR and a failure on DPOAE screening, is likely mild, and it is this degree of dysfunction which is primarily represented in this study. An outcome of failure on AABR and DPOAE screenings (in the face of confirmed normal sensorineural reserve), suggests a more severe degree of conductive dysfunction. The differences in degree of dysfunction could potentially be caused by fundamentally different mechanisms. Therefore, a replication of this study in infants who fail on both AABR and DPOAE screenings should be performed to investigate this possibility.

Summary

Universal newborn infant hearing screening has been an unmitigated success at reducing the age of identification of hearing loss in children and the age of intervention. There is, however, room for improvement, particularly in the area of follow-up evaluation. Knowledge obtained from longitudinal examination of the development of normal and abnormal function in infants can be useful in refining screening and follow-up protocols.

These data have demonstrated no differences in the gender, birth weight, or head circumference of ears that pass or fail on initial screenings using DPOAEs in a normal and diverse clinical population.

Reflectance data demonstrated developmental trends in normal passing ears and trends in failing ears that are consistent with a conductive etiology. WBR may be utilized as means to predict DPOAE screening outcomes, but the usefulness of this measure can only be interpreted in light of the clinical answer that is sought.

DPOAE longitudinal data suggests that re-evaluation at either four or twelve weeks would be optimal due to high rates of infants who pass, without a substantial number of new cases of fails. The decision to re-test at four or twelve weeks may ultimately be based on psychosocial factors that impact rate of follow-up, rather than physical outcomes per se. However, until clinical evidence is accumulated to provide guidance, it is the opinion of the investigator that: 1) if there is heightened concern for sensorineural hearing loss based on WBR outcomes, audiologic evaluation should occur as soon as possible, to characterize degree and type of hearing loss; 2) if WBR data at a particular time point predicts that a conductive loss is likely to be persistent, the clinician should make a medical referral and defer re-evaluation until after medical evaluation (but preferably before twelve weeks of age); and 3) if WBR provides ambiguous information regarding either of the aforementioned concerns, the clinician should re-evaluate at around four weeks of age.

APPENDIX

CAREGIVER INTERVIEW TO DETERMINE STUDY CANDIDACY

1. Is there anybody in your family who has or has had hearing loss at a young age?
2. Has your baby spent any time in the neonatal intensive care unit?
3. Did you have any infections during your pregnancy?
4. Does your baby have any health issues that you are aware of?

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ABSTRACT

LONGITUDINAL OUTCOMES OF DISTORTION PRODUCT OTOACOUSTIC EMISSIONS AND WIDEBAND REFLECTANCE IN INFANTS

by

VIRGINIA RAMACHANDRAN

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Co-Advisors: Dr. Jean E. Andruski and Dr. Kenneth R. Bouchard

Major: Communication Sciences and Disorders

Degree: Doctor of Philosophy

Clinical practice has shown that some infants are born with, or develop a temporary conductive hearing loss characterized by the absence of measurable otoacoustic emissions (OAEs) but normal sensorineural hearing. This transient situation interferes with the process of universal newborn hearing screening and identification.

The purpose of this prospective, longitudinal study was to describe outcomes of distortion product OAE (DPOAE) screening in infants at birth, and one, four, eight, and twelve weeks of age. In addition, wideband reflectance (WBR) measures, which have the potential to help characterize outer-ear canal and middle-ear function, were examined to determine their potential utility in identifying DPOAE screening outcomes.

Beginning with a sample of 50% of ears that passed the initial DPOAE screening at birth, results showed that passing outcomes rose over the course of time, at rates of 72.1%, 84.6%, 86.0%, and 96.0% at weeks one, four, eight, and twelve, respectively. Rates of new fails – ears that had passed the screening at a previous time point – also increased over time, with the exception of the last time point, at which no new failing outcomes were seen. These data suggest that twelve weeks would be the most efficient

time for re-evaluation of infants, and that four weeks would be an appropriate alternative.

Percentiles of reflectance measures were calculated for DPOAE outcomes at each time point. Reflectance outcomes were distributed such that fail and pass DPOAE outcomes could be predicted from the highest and lowest values, with an area of ambiguity in between. Receiver operating characteristic curves were calculated to determine the reflectance frequencies that would provide the highest predictive value at each time point. In addition, this method was used to determine how well WBR could be used to predict DPOAE outcomes at future time points. The predictive value of WBR for future DPOAE outcomes was poorer than concurrent prediction and likely has little clinical utility at present. However, low WBR values in the face DPOAE screening failures should cause concern for sensorineural hearing loss and can be used to prioritize such infants for follow-up audiologic evaluation.

AUTOBIOGRAPHICAL STATEMENT

Virginia Ramachandran is a Senior Staff Audiologist and Research Coordinator in the Division of Audiology, Department of Otolaryngology-Head and Neck Surgery, of the Henry Ford Hospital in Detroit, Michigan. She received her Bachelor of Social Work (B.S.W.), Master of Social Work (M.S.W.), and Doctor of Audiology (Au.D.) degrees from Wayne State University.

Virginia is an adjunct faculty member in the Department of Communication Sciences and Disorders. She coordinates the clinical education for the Au.D. program and teaches courses in the department. Virginia is the current President of the Michigan Academy of Audiology. She also serves as a member-at-large of Board of Directors of the Accreditation Commission for Audiology Education. Other professional activities include serving on the Coding and Reimbursement Committee, the Nominations Committee, and the Education Committee of the American Academy of Audiology. She also serves as chair of the Professional Education subcommittee of the Strategic Documents Committee of the American Academy of Audiology.

Virginia is co-author of the “Basic Audiometry Learning Manual” and has co-authored several book chapters. She has authored several papers and presented at numerous national meetings. She has served as an ad hoc reviewer for several journals and is an Associate Consulting Editor for Plural Publishing, Inc.