# THE EFFECT OF POSITION ON CARDIOPULMONARY OUTCOMES IN PRETERM INFANTS DURING BOTTLE FEEDING

BY

Caryn Bradley

Dissertation Committee:

Phyllis Guarrera-Bowlby, PT, EdD., PCS, Chair
Sudarshan R. Jadcherla, MD, FRCP (Irel), DCH, AGAF
Beth McManus, PT, PhD
Dinesh P. Mital, PhD
Frances Rieth Ward, PhD, RN, MBE

Approved by the Dissertation Committee:

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## DEDICATION

This is dedicated to my children Bradley, Danielle and Jonathon, who provided their love, encouragement and endless patience throughout this journey. This is also dedicated to the extraordinary NICU infants and their parents, who participated in this study in the hopes that this academic endeavor will provide better understanding of the feeding challenges of preterm infants.

TABLE OF CONTENTS

**ABSTRACT**

**Background.** Feeding in preterm infants is a complex motor activity requiring physiologic stability, behavioral readiness and the sensorimotor synchronization of multiple muscle groups; to effectively coordinate sucking, swallowing and breathing. The elevated sidelying position is suggested as a potential therapeutic intervention strategy to support bottle feeding in preterm infants.

**Purpose.** The primary purpose of this study was to investigate the effect of position on cardiopulmonary parameters in preterm infants during oral feeding. In addition, nonlinear methods of analysis of respiratory waveforms (Approximate Entrophy) were used to examine respiratory variability during oral feeding.

**Methods.** Twelve healthy preterm infants were studied using a within-subject cross over design to compare semiupright and the elevated sidelying position during bottle feeding. Outcomes measures were cardiopulmonary physiology (heart rate, respiratory rate, oxygen saturation and respiratory pattern variability), behavioral state and feeding efficiency (volume intake and length of feeding).

**Results.** The principle findings related to cardiopulmonary physiology revealed no significant difference in heart rate, respiratory rate, percent hemoglobin oxygen saturation or respiratory variability between the semiupright and elevated sidelying position, during oral feeding in healthy preterm infants. Feeding outcomes did not differ significantly between the semiupright and elevated sidelying position. Nonlinear measures of respiratory waveforms proved useful in assessing variability in respiratory patterns in healthy preterm during bottle feeding.

**Conclusions**. Either the semiupright position or the elevated sidelying may be beneficial for healthy preterm infants transitioning to oral feeding. Analysis of respiratory waveforms may prove useful clinically for assessing variability in infant breathing patterns.

**Key words:** oral feeding; preterm infant; positioning; cardiopulmonary outcomes; respiratory variability

## DEFINITION OF CONCEPTS

### Measures of Cardiopulmonary Physiology

**Heart rate** (beats per minute). A measure of electrical activity of the heart, sensed by standard ECG leads connected to a Phillips Intellivue Patient Monitor MP70.

**Respiratory rate** (breaths per minute). A measure of change in impedance due to thoracic movement between two ECG electrodes on an infant's chest, connected to a Phillips Intellivue Patient Monitor MP70.

**Percent hemoglobin oxygen saturation** (%SaO2). A functional measure of the percentage of hemoglobin molecules in the arterial blood, monitored using a Radical-7 pulse oximeter.

**Cardiorespiratory stability**.

- Respiratory rate of 30 to 60 breaths per minute
- Heart rate of 100 to 160 beats per minute at rest
  100 to 180 beats per minute during feeding
- Hemoglobin oxygen saturation of greater than 95%

**Respiratory waveform**. A measure of thoracic impedance and an indirect measure of respiratory wave form variability. Variability analysis refers to the assessment of patterns of variation over time intervals.

**Respiratory waveform variability**. Calculated using Approximate Entropy (ApEn), a statistical measure of the change in complexity of physiologic processes.

## Measures of Feeding Outcomes

**Proficiency.** Defined as the percentage of milk taken during the first five minutes per milliliter prescribed and used an index of oral motor skill.

**Rate of Milk Transfer**. Measured as the milliliters/minute over an entire feeding and used as an index of endurance.

**Oral feeding performance**. Defined as the percentage of milliliters taken during the feeding per milliliters prescribed and used as a reflection of oral motor skill as well as fatigue.

**Duration of feeding**. Measured as the time of completion of nutritive sucking minus the time at first presentation of the nipple.

## Measure of Behavioral State

Behavioral state. A constellation of behaviors that signal level of alertness or consciousness, measured using the Anderson Behavioral State Scale.

## Measures of Feeding Position

**Semiupright position**. The preterm infant is held with trunk and head up to approximately 70 degrees in relation to the feeder's lap.

**Elevated Sidelying**. The preterm infant is held perpendicular to the feeder, with the trunk and head up to approximately 45 degrees in relation to the feeder's lap.

# Chapter I

# Introduction and Background

## Context and Background of the Problem

The semiupright position is traditionally used in the Newborn Intensive Care Unit (NICU) when bottle feeding preterm infants. However, the elevated sidelying position for bottle feeding preterm infants is an emerging clinical practice within NICUs employed as a therapeutic feeding intervention. Little is known about the influence of feeding position on bottle feeding in preterm infants or its efficacy as a feeding technique.

Oral feeding problems in preterm neonates are multifactorial and different strategies to support bottle feeding have been studied in the past: feeding readiness, nonnutritive sucking, pacing, nipple flow rates, oral support measures, and feeding practices (Dodrill, Donovan, Cleghorn, McMahan, & Davis, 2008; Elder et al., 2011; Howe, Sheu, Hinojosa, Lin, & Holzman, 2007; Jadcherla, Wang, Vijayapal, & Leuthner, 2010; Lau & Smith, 2011; Thoyre & Carlson, 2003). One factor impacting the transition from gavage to oral feeding is position

(Lau, 2013). Although presumed developmentally supportive, limited research exists comparing positioning in elevated sidelying with traditional semiupright positioning and the effect on cardiopulmonary outcomes in neonates during feeding. Five published research studies (Clark, Kennedy, Pring, & Hind, 2007; Dawson et al., 2013; Lau, C., 2013; Park, Thoyre, Knafl, Hodges & Nix, 2014; Thoyre, Holditch-Davis, Schwartz, Roman, & Nix, 2012) examined the relationship between feeding position and physiologic stability during transition from gavage feeding to bottle feeding in premature infants. Two unpublished PhD dissertations (Daley, 2002; Steven, 2007) studied the relationship between feeding position and feeding proficiency in premature infants during nipple feeding.

**Research Purpose and Goals**

This research investigated the effect of positioning on cardiopulmonary parameters in preterm infants during oral feeding. Outcome measures were cardiopulmonary physiology (heart rate, respiratory rate, oxygen saturation, respiratory pattern variability), behavioral state, and feeding performance (total volume intake and length of feeding).

**Significance/Need for Study**

The dissertation research study satisfied important gaps in the literature by providing a detailed feeding protocol, including reliable positions using goniometric measures, to facilitate a consistent methodology during feeding and improving accuracy in measurement by using the Masimo Radical-7 pulse oximeter with Signal Extraction Technology. Additionally, this study examined healthy preterm infants with less experience in bottle feeding than previously reported in the literature.

Most notably, this study was unique in the use of respiratory waveform analysis as a measure of respiratory variability during feeding. Nonlinear methods of analysis of the respiratory data provided a unique perspective on the adaptability of infants' breathing patterns while feeding. Since this approach has not been done in prior related research, this analysis examined behavioral rigidity or conversely the disorganization of breathing for the premature infant during early attempts to feed. These types of analyses had been performed with respiratory patterns however, not for the NICU population. Therefore this was a novel application of this type of analysis (Burkioka et al., 2003; Caldirola, Bellodi, Caumo, Migliarese, & Perna, 2004). As such, analysis of respiratory waveforms may provide a more sensitive measure of cardiorespiratory effort during feeding in preterm infants.

# Chapter II

# Review of the Literature

## Introduction

The transition from gavage feeding to oral feeding is a major challenge for premature infants and their caregivers (Barlow, 2009; Thomas, 2007). Ongoing assessment of an infant's neuromotor maturation, as well as their cardiopulmonary response to oral feeding, is required to make clinical decisions about the ability of an infant to progress to full oral feedings (Amaizu, Shulman, Schanler, & Lau, 2008). Most nurseries use criteria related to the efficiency and safety of oral feeding as a guide for discharge (Pickler, Best, & Crosson, 2009). According to the American Academy of Pediatrics Committee on Fetus and Newborn (Bell et al., 2008), the criteria for discharge from a neonatal intensive care unit includes successful oral feeding along with physiologic stability and consistent weight gain. Success implies the ability to take all of the prescribed volume by mouth within an allotted time and maintain a sustained pattern of growth. Safety implies proper coordination of suck, swallow and breathing while maintaining cardiorespiratory stability.

Feeding in preterm infants is a complex motor activity. Oral feeding requires physiologic stability, behavioral organization, and the sensorimotor synchronization of multiple muscle groups for appropriate coordination of the suck, swallow, and breathe pattern (Brown & Ross, 2011; Jadcherla et al., 2012). Although this pattern is present in preterm infants, it is often immature and frequently nonfunctional to obtain the amount of nutrition needed for growth (Amaizu et al., 2008). Therefore, the process of oral feeding results in significant physiologic stress for many preterm infants including: thermal alterations, apnea, bradycardia, and decreased oxygen saturation levels (Slocum, Arko, Di Fiore, Martin, & Hibbs, 2009). When inefficient preterm infant feeders experience cardiopulmonary stress, vital signs change rapidly. Thus, effective means of monitoring heart rate, respiration, and hemoglobin oxygen saturation during feeding is essential (Martin, Fanaroff, & Walsh, 2011).

The relationship between position and cardiopulmonary response has been identified previously in the literature as affecting a preterm infant's ability to transition from gavage to oral feeding, (Brown & Ross, 2011; Dimitrious et al., 2002; Thomas, 2007). The importance of examining behavioral state, coordination of the suck swallow breathe pattern and physiologic stability is consistently demonstrated across studies (Emeriaud et al., 2010; Lau, Smith, & Schanler, 2003; Mizuno & Ueda, 2003; Rhein et al., 2012; Thoyre & Carlson, 2003; Vice & Gewolb, 2008). Thus, this analytic synthesis is an exploration of current published literature on the relationship between position and cardiopulmonary outcomes during bottle feeding in preterm infants. The specific focus of inquiry includes: a) maturation of oral feeding skills and the mechanics of feeding, b) the relationship between position and cardiopulmonary outcomes and c) measures of cardiopulmonary physiology and infant behavior.

**Search Strategies.** A comprehensive review of the primary research served as a foundation for the planned research study. The method section of this analytic synthesis provides details on the literature search strategy, selection criteria, and data extraction methods related to each specific area of focused inquiry. For all topic areas, the search results were limited to publications written in English and pertaining to human infant subjects newborn to 1 month of age. All articles included in the review were analyzed, applying a PICO model, for Population, Intervention, Comparison and Outcomes. Sampling design, methodology, data collection procedures, statistical analysis, and results were all evaluated.  Reports were examined for validity and reliability and were scrutinized for potential biases.

This literature search analyzed previous research studies and includes published journal articles, dissertations, meeting abstracts and personal communications.  Secondary sources (textbooks, equipment manuals) were included either as contextual material or for methodological guidance.  In an effort to acquire all significant literature, references list from all articles selected for review were manually searched for relevant articles cited in the paper. Additionally, five older papers of central importance to this research topic were included in the review of the literature:  Bullock, Woolridge & Baum (1990), Hanlon et al. (1990), Koenig, Davis, & Thach, (1990), Mathew (1988), and Shivpuri, Martin, Carlo, & Fanaroff (1983).  These seminal papers are pertinent as they influence the body of knowledge related to the coordination and maturation of suck, swallow and respiration during bottle feeding in preterm infants.  In performing literature searches on this topic, these papers were frequently cited in research articles.

## Review of the Literature

**Maturation of oral feeding skills and mechanics of feeding.** The purpose of this review of the literature was to determine if there is a relationship between maturation and suck, swallow, breathe coordination during bottle feeding in infants born prematurely. The bibliographic database Medline and the Quinnipiac University Library Embase were utilized for this review of the literature on the topics of maturation of feeding skills, mechanics of oral feeding, and respiration during feeding. Embase is a search engine that provides access to scholarly resources at Quinnipiac University through an integrated search of all Quinnipiac databases, e-books, print books, full-text journals and the library catalog. The search strategy incorporated the concepts from the topics along with identified MeSH (Medical Subject Headings) terms relating to the topics. These included: bottle feeding; suck, swallow, breathe coordination and cardiopulmonary physiology. This review of the literature covered a period, from 2003-2014. From these initial 97 search results, abstracts were reviewed and only publications identified as a primary research study were considered. A total of 27 articles met this set of criteria. Several factors have been previously identified in the literature as important for assessing readiness to initiate bottle feeding in preterm infants: feeding protocol, behavioral responses, nonnutritive sucking, infant morbidity, maturation, feeding experience, and sucking pattern (Garber, 2013; Howe et al., 2007; Pickler et al., 2005; Thoyre & Carlson, 2003). Variables identified as influencing feeding efficiency include: infant morbidity, postmenstrual age, behavioral state, feeding opportunities, feeding schedule, and position (Dodrill et al., 2008; Elder, Campbell, Larsen, & Galletly, 2011; Howe, Sheu, Hinojosa, Lin, & Holzman, 2007; Jadcherla, Wang, Vijayapal, & Leuthner, 2010; Lau & Smith, 2011; Thoyre, 2012). Variables identified as influencing cardiopulmonary outcomes during bottle feeding include: development of ventilatory control, maturation of oral feeding skills, coordination of respiration with sucking and swallowing during feeding, behavioral and sleep state, and adjusted gestational age at time of study (Bullock, Woolridge, & Baum, 1990; Lau, Smith & Schanler, 2003; Mizuno & Ueda, 2003; Lau, 2013; Vice & Gewolb, 2008).

***Feeding performance***. Howe et al. (2007) examined the relationship between physical indicators (PMA, weight, oral motor skills and signs of physiologic distress) and bottle feeding performance. Bottle feeding performance was measured by rate of milk transfer and volume intake (percentage of prescribed volume over the feeding time). These researchers found multiple factors related to bottle feeding performance in preterm infants including: age, weight, oral motor skills, feeding experience, and feeding technique. Pickler et al. (2005) found a strong relationship between indicators of feeding readiness and feeding performance outcomes (proficiency, efficiency, and volume consumed). Infant feeding readiness indicators were morbidity, maturity, behavioral state at start and feeding experience. Using pulse oximetry and observation of behavioral state, Thoyre and Carlson (2003) found changes in respiratory control when an infant became fatigued during feeding. They theorized these changes may be due to loss of muscle tone, decreased muscle activity in the intercostals and in the upper airway; and changes in quality of breathing pattern (shallow breaths, breathing pauses). Changes in behavior however, were insufficient to detect oxygen desaturation decline. In 2012, Thoyre et al. described markers of infant dysregulation adversely impacting oral feeding as behavioral disorganization, poor fluid management, and increased work of breathing.

Dodrill, Donovan, Cleghorn, McMahon, and Devies (2008), Jadcherla et al. (2010), and Pickler et al. (2005) studied the relationship between gestational age (GA) at birth and neonatal morbidity in relation to age of initiation of oral feeding and age at full volume oral feeding. These researchers found that neonates who were less mature at birth and/or who had a greater degree of neonatal morbidity took longer to transition from start of oral feeding to attainment of full volume oral feeding. The relationship of gestational age to attainment of full volume oral feedings is consistent with the findings by Lau and Smith (2011). Additionally, Lau and Smith found a correlation between feeding skills and feeding performance. Oral feeding skills were reflected as the combination of proficiency (percentage taken during the first 5 minutes per milliliter prescribed), rate of milk transfer over an entire feeding (milliliters/minute), and feeding performance (percentage of milliliters taken during the feeding per milliliters prescribed). Oral feeding was defined as successful if infants completed greater than or equal to 80%; as opposed to unsuccessful if infants took less than 80% of prescribed feeding (Lau & Smith, 2011). Pickler et al. (2005) define proficiency, efficiency, and performance similarly to Lau and Smith (2011) stating oral feeding success incorporates oral motor skill and level of endurance. To objectively define volume consumed, Thoyre et al. (2012) weighed a burp cloth before and after the feeding. The amount of spilled milk was subtracted from the total volume using the formula that I gram weight of cloth equated to I milliliter of milk. Multiple factors influencing feeding performance were considered In the dissertation research design: GA, PMA, days of life at study entry, morbidity, behavioral state and cardiopulmonary stability.

***Cardiopulmonary outcomes***. Several researchers investigated the development of coordination of sucking, swallowing, and breathing during bottle feeding in preterm infants (Blackburn, 2013; Bu'Lock, Woolridge, & Baum, 1990; Gewolb & Vice, 2006; Goldfield, Richardson, Lee, & Margetts, 2006; Hanlon et al., 1990; Koenig, Davies, & Thach, 1990; Lau, Smith, & Schanler, 2003; Mathew, 1988; Mizuno & Ueda, 2003; Shivpuri, Martin, Carlo, & Fanaroff, 1983; Vice & Gewolb, 2008).

This review was intended to acquire an understanding of the development of suck and swallow in coordination with breathing in healthy preterm infants. Safe and efficient feeding requires the simultaneous coordination of various muscle groups with protection of the airway while maintaining regular respiration (Bu'Lock et al., 1990; Hanlon et al., 1990, Jadcherla et al., 2010). This coordination of sucking, swallowing, and breathing is integrated with development of the musculoskeletal, neurologic and gastrointestinal systems, and required for oral feeding efficiency in preterm neonates.

The development of nutritive sucking typically matures about 34 weeks gestation and includes both a suction and an expression component that alternates rhythmically (Lau, 2003; Mizuno & Ueda, 2003). The expression phase is characterized by compression of the nipple by the tongue against the hard palate to eject milk; while the suction phase is described as negative intraoral pressure produced by lowering the jaw and closing the nasopharynx, that draws the milk into the oral cavity (Barlow, 2009; Garber, 2013). Maturation of sucking skills progress sequentially and are correlated with PMA (Lau, 2003). During early bottle feeding in healthy preterm infants, there may be two distinct phases: a) continuous sucking phase and b) intermittent sucking phase. The continuous sucking phase occurs during the first two minutes of feeding and is characterized by uninterrupted sucking. The intermittent sucking phase follows and is characterized by runs of several sucks punctuated by periods of no sucking (Koenig et al., 1990). However patterns of sucking during feeding can be variable among preterm infants as the relationship of swallow to phase in respiratory varies and as pauses in sucking fluctuate with pauses in swallow (Gewolb & Vice, 2006; Jadcherla, 2012).

Coordination of swallowing with respiration may be challenging for the preterm infant as feeding requires integration with neuromotor control and cardiorespiratory stability (Mizuno & Ueda, 2003). The pharynx is the shared anatomic pathway for both swallowing and breathing (Goldfield et al., 2006; Koenig et al., 1990). During infant feeding, swallow influences respiratory efforts, as respiration is inhibited centrally during pharyngeal swallowing (Gewolb & Vice, 2006; Vice & Gewolb, 2008). Therefore, precise coordination of sucking, swallowing, and breathing is necessary during bottle feeding. In a coordinated nutritive sucking cycle, breathing is interposed between swallows in a sequential pattern (Bu'Lock et al., 1990).

Respiration can be interrupted at any point in the cycle of inspiration or expiration by the swallow (Vice & Gewolb, 2008). Lau et al. (2003) found the frequency of swallowing was correlated with sucking frequency. Shivpuri et al. (1983) found both ventilation and oxygenation are reduced during the course of nipple feeding in preterm infants; both of which are influenced by sucking pattern and postmenstrual age of the infant. Breathing efforts appear to be the last function integrated into more mature feeding patterns in preterm infants (Vice & Gewolb, 2008). Therefore, coordination of swallowing and breathing is linked to blood oxygenation during feeding. Alterations in blood oxygen levels are due to decreased ventilation which may be due to airway closure during swallowing and decreased ventilator effort (Goldfield et al., 2006; Koenig et al., 1990; Shivpuri et al., 1983). Interestingly, Goldfield et al., (2006) found lower oxygen saturation levels following feeding than during actual feeding. They attributed this change in oxygen saturation to burping and gastric distress after feeding.

Respiratory rhythms during feeding undergo developmental changes with maturation (Vice & Gewolb, 2008) and the patterns of suck, swallow breathe coordination follow maturational patterns that correlate with postmenstrual age (Gewolb & Vice, 2006). Bu'Lock et al. (1990), Gewolb & Vice (2006), and Hanlon et al. (1990) found that coordination of sucking, swallowing and breathing improved with maturation. Mizuno & Ueda (2003) found a significant difference in the coordination of swallowing and breathing in infants less than 34 weeks gestation as compared to infants greater than 34 weeks postmenstrual age (PMA) ($p < 0. 05$). Before 34 weeks PMA, swallowing occurred usually during a respiratory pause while after 35 weeks, swallowing occurred typically at the end of inspiration (Mizuno & Ueda, 2003). Premature infants typically attain maximal oral feedings by the median age of 35 to 37 weeks PMA (Jadcherla et al., 2010). With maturation, the swallowing process becomes more adaptable to handling more rapid and larger bolus sizes (Amaizo et al. 2007; Barlow, 2009). However, respiratory control during feeding is still immature at 35-36 weeks PMA (Mathew, 1988). Coordination of each of the feeding components (suck, swallow, breathe) may mature at different rates in individual infants and patterns vary between infants (Vice & Gewolb, 2008). Hanlon et al. (1990) found that preterm infants feeding skills were significantly different from term infants even when they reached term postmenstrual age. Prolonged deglutition apnea in preterm infants occurred significantly more frequently at term PMA compared to full term infants ($p < 0.001$).

Components of sucking, swallowing and breathing and the coordination between these motor activities require consideration during oral feeding. The achievement of safe and efficient oral feeding in preterm infants may be challenging as immaturities in neurodevelopmental may contribute to difficulties in achieving cardiorespiratory stability and feeding progress.

**Relationship between position and cardiopulmonary outcomes.** The purpose of this literature review was to examine the relationship between position and cardiopulmonary responses during bottle feeding in premature infants.

The search strategy incorporated concepts from the topic along with identified MeSH (Medical Subject Headings) terms. These included: posture, position, and cardiopulmonary outcomes. This review of the literature covered a ten-year period, from 2004-2014. From the initial 40 search results, abstracts were reviewed and only publications identified as a primary research study were considered. A total of 8 articles met this set of criteria.

Select studies were used in development of the research protocol to: a) operationally define cardiopulmonary outcomes (Poets et al., 2009; Shiraishi et al., 2009), b) describe mechanics of breathing to support purpose and significance (Oliveira et al., 2009; Shiraishi et al., 2009), c) identify infant characteristics for inclusion (Elder et al., 2011; Oliveria et al., 2009) and d) outline criteria to discontinue the study (Shiraishi et al., 2009).

Only four articles (Clark, Kennedy, Pring, & Hird, 2007; Dawson et al., 2013; Park et al., 2014; Thoyre et al., 2012) compared positioning in elevated sidelying versus semiupright and the effect on cardiopulmonary outcomes in neonates. Two unpublished PhD dissertations (Daly, 2002; Steven, 2007) and one unpublished Master's thesis (Bradley, 2002) on the topic of feeding and positioning in neonates, were considered for research methodology. Additionally, the evidence from this review was used in part to develop the feeding method protocol for elevated sidelying.

***Right versus left sidelying***. A review of the literature by Elser (2012), examined the positioning after feeding to reduce feeding intolerances. The evidence from this review was used in part to develop the feeding method protocol for elevated sidelying. Research supports the lateral right side position for infants with slow gastric motility while other research supports lateral left side and prone position for infants with gastroesophageal reflux (GER). Research findings conclude the right side position enhances the rate of gastric emptying while left side position reduces the quality, length, and degree of reflux events (Elser, 2012). Positioning is recommended on the left side because the decreased musculature of the lower esophageal sphincter allows the stomach content to remain angled toward the fundus of the stomach. On the right lateral side, stomach content above the lower esophageal sphincter remains in the esophagus and flows toward the mouth (Elser, 2012). Many infants born prematurely experience gastroesophageal reflux and most nurses who will be feeding during the study are right handed and will typically feed with the infant lying on the left side. Therefore, this review provided support for feeding infants in left lateral side position during the elevated sidelying feeding method.

***Measures of cardiopulmonary physiology.*** Many measures of cardiopulmonary outcomes in neonates are identified in the literature: heart rate and respiratory monitoring, pulse oximetry, heart rate variability, near-infrared spectroscopy, nasal airflow oscillimetry, polysomnography, indirect calorimetry, and respiratory inductance plethysmography.

The purpose of this third literature review was to make an informed decision on research instrumentation. A review of the literature was conducted to acquire knowledge of standards of measurement, physiological interpretation and clinical use of instrumentation used for measuring neonatal cardiopulmonary outcomes. The benefits and limitations of each measurement system are examined: 1) within the context of the proposed research study and 2) in relation to the ability and feasibility to measure respiration.

The bibliographic database Medline and the Quinnipiac University Library Database One Search were utilized for this review of the literature on the topic of neonatal cardiopulmonary physiology. The search strategy incorporated concepts from the topic along with identified MeSH (Medical Subject Headings) terms. These included: cardiopulmonary outcomes, measures of cardiopulmonary function, and nonlinear measures of respiration. This review of the literature covered a ten-year period, from 2002-2012. From the initial 60 search results, abstracts were reviewed and only publications identified as a primary research study were considered. A total of 18 articles met this set of criteria. Operator manuals for the Philips Intellivue Monitor MP70 and Massimo Radical-7 pulse oximeter were studied to understand basic operations, patient applications, data collection, and data export capabilities. A textbook (Stergiou, 2004) and three articles (Bravi & Seely, 2011; Brown, 2003; Burioka et al., 2003) on nonlinear methods provided an introduction to the theory and potential use of this analysis for studying respiratory variability in neonates.

Several parameters that are important in designing a research protocol were studied: outcome variables, data collection procedures, measures of reliability and validity, data analysis, and data interpretation. Variables that were identified as influencing cardiopulmonary outcomes included: behavioral and sleep state, adjusted gestational age at time of study, thermoregulation, and timing of data collection in relation to feeding schedule. These confounding variables were explored further in a subsequent review of the literature.

Many measures of cardiopulmonary outcomes in neonates are identified in the literature: heart rate and respiratory monitoring, pulse oximetry, heart rate variability, near-infrared spectroscopy, nasal airflow oscillimetry, polysomnography, indirect calorimetry and respiratory inductance plethysmography. Each of these methods was reviewed in an effort to clarify and define outcome measures for this research study.

***Heart rate variability.*** Heart rate variability (HRV) provides an indirect measure of the autonomic nervous system's influence on heart rate (McCain, Knupp, Fontaine, Pino, & Vasquez, 2010). Analysis of HRV differentiates parasympathetic from sympathetic components of the autonomic nervous system (Cong, Ludington-Hoe, McCain, & Fu, 2009). The main parasympathetic inputs are the influence of the vagus nerve on the heart rate rhythmicity and the variation in vagal impulses related to respiration known as respiratory sinus arrhythmia (McCain et al., 2010). The beat-to-beat fluctuations in the heart rate occur at the same frequency as respiration and are under the control of the parasympathetic nervous system (Brown, 2007).

HRV is analyzed by measuring the variation in the time interval between heartbeats and is a measure of cardiorespiratory stability. Greater variability in heart rate is an indicator of better regulation by the vagus nerve and ability to adapt to physiologic and environmental demands (Brown, 2007). Time series analysis generates two power spectra frequencies: high frequency associated with respiration reflecting parasympathetic activity and low frequency which is primarily an indication of sympathetic activity (Cong et al., 2009).

Although an indirect measure of cardiorespiratory stability, HRV (i.e. the balance between parasympathetic and sympathetic activity) is primarily an indicator of physiologic response and reactivity to stress and imposed demands as opposed to a measure of respiratory function (McCain et al., 2010).

***Near-infrared spectroscopy.*** Near-infrared spectroscopy (NIRS) is a noninvasive monitoring technique that continuously measures tissue oxygenation (Marin & Moore, 2011). Similar to pulse oximetry, NIRS uses light wavelengths to measure tissue oxygenation. Differently though, unlike pulse oximetry which measures oxyhemoglobin in arterial blood, NIRS "measures the difference between oxygen oxyhemoglobin and deoxyhemoglobin, which reflects oxygen uptake in the tissue bed" (Marin & Moore, 2011, p. 382). By placing probes on different areas of the body, NIRS provides real time tissue oxygenation status to a particular tissue bed which reflects its perfusion status (Marin & Moore, 2011; Elser, Holditch-Davis, & Brandon, 2011). Each probe consists of a light source and two photodetectors to measure tissue oxygen levels at different tissue depths (surface level tissue oxygenation and deep tissue oxygenation) (Marin & Moore, 2011). NIRS values represent the average of arterial, venous, and capillary oxygenation at the tissue level (Marin & Moore, 2011).

The advantage of NIRS is the ability to provide noninvasive real-time data to clinicians which allows for immediate intervention and feedback of effect (Elser et al., 2011). Despite NIRS being used in neonatology to measure cerebral perfusion and mesenteric perfusion, research efficacy studies report limitations in use. NIRS monitoring does not provide information on how much an organ is metabolizing the oxygen (Elser et al., 2011). Additionally, only the tissue under each probe will be measured for oxygenation with a large amount of organ tissue unmonitored (Elser et al., 2011) while added probe monitoring creates a potential risk of irritation to infant skin integrity. Finally, normative values for premature infants are not available (Marin & Moore, 2011; Elser et al., 2011). The potential for NIRS to provide a more direct assessment of oxygenation is being researched. However, NIRS is not yet accepted as a clinical standard of care in the newborn intensive care unit.

***Estimate of energy expenditure.*** The amount of energy expended by preterm infants can be estimated from measures of inspired and expired oxygen and carbon dioxide (Pridham et al., 2005). Energy expenditure (EE) can be defined as the kilocalorie of heat produced/day and can be indirectly estimated from the volume of carbon dioxide produced relative to the volume of oxygen consumed during a defined interval of time. Contributing variables to energy expenditure in the preterm infant include: growth, caloric intake, level of motor activity, postnatal and postmenstrual age, and history of respiratory distress syndrome (Pridham et al., 2005). A metabolic gas monitor indirect calorimeter for infants can be used to study energy expenditure. The calorimetric system assesses an infant's EE by continuous measurement of the volume of oxygen consumed (VO2 mL/min) and the volume of carbon dioxide produced (VCO2 mL/min) by drawing expired gases through a pneumotachometer (Pridham et al., 2005). The rate of flow is measured and expired gases are sampled. Estimates of energy expenditure are an important measure of the physiologic oxygen consumption at the cellular level and a clinical indicator of an infant's ability to sustain biological processes (growth, digestion, thermoregulation). This equipment is not typically found in a NICU, therefore, this was not a feasible clinical measure of respiration for this study.

***Nasal airflow oscillimetry.*** Nasal airflow oscillimetry in neonates is measured with thermistors taped under both of the infant's nostrils (Bhat et al., 2006; Razi, DeLauter, & Pandit, 2002). Thermistors are used to indicate airflow by detecting temperature oscillation between inhaled room air temperature and warmer exhaled air (Bhat et al., 2006). Often, airflow is first identified by the thermistor signal and then correlated to EEG, thoracic respiratory movement, or polysomnographic recordings. Apnea is then defined by lack of nasal airflow and presence or absence of chest and abdominal wall movement (Bhat et al., 2006; Rhazi et al., 2002). Thermistors are widely used due to their ease of use and relative patient comfort. However, thermistors are less sensitive to detection of reduced airflow and therefore may under-detect respiratory events (Di Fiore, 2004).

***Polysomnography.*** Polysomnography (PSG) is one of the noninvasive methods for studying breathing abnormalities that may be exacerbated or seen during rapid eye movement (REM) sleep. Neonatal polysomnographies are recorded in a neurophysiology laboratory for the duration of a complete sleep cycle. Polysomnography typically includes a multichannel electroencephologography (EEG) recorder, electromyogram (EMG), electrocardiogram (ECG), nasal thermistor, and thoracic respiratory movement recording (Oliveria, Nunes, Fojo-Olmos, Reis, & da Costa, 2004). Along with assessment of respiratory patterns, polysomnographic recordings have been used to examine sleep organization and behavioral state regulation (Ludington-Hoe et.al, 2006). Polysomnographic recording and interpretation is typically performed by a skilled EEG technician, pediatric pulmonologist and a neonatal nurse, making clinical use of this methodology challenging for the purpose of this research study.

***Respiratory inductance plethysmograph.*** Respiratory inductance plethysmography (RIP) is a noninvasive method for measuring respiratory timing and volume measurements (Emeriaud, Eberhard, Benchetrit, Debillon, & Baconnier, 2008). The method involves wearing two inductance bands around the rib cage and abdomen creating a magnetic field (Mazeika & Swanson, 2007). The adjustments in the inductance of the coils produce a signal of the cross sectional area that reflect the changes of thoracic and abdominal compartment volumes (Emeriaud et al., 2008; Mazeika & Swanson). The tidal volume can be estimated from the weighted sum of the ribcage and abdominal inductance signals (Emeriaud et al., 2008). RIP can be measured along with nasal or oral airflow. Researchers in France developed a RIP jacket specifically sized for preterm neonates. This jacket was calibrated against other standard respiratory measures and found to be reliable (Emeriaud et al., 2008). Additional research with this jacket proved valuable in analysis of breath-to-breath variability and measures of end-expiratory lung volume (Emeriaud et al., 2010). According to the Director of Pulmonology at Connecticut Children's

Medical Center, respiratory inductance plethysmography equipment is not available locally. Contact with the primary investigator Dr. Emeriaud revealed the RIP device Visurep was designed by a French company and developed in collaboration with the Universite J Fourier. The monitoring software was adapted for neonates and is the property of the development team at the Univesite J Fourier. Additionally, the device is not currently FDA approved so it is not available for use at this time.

***Heart rate and respiratory monitoring.*** Clinical bedside monitoring is commonly used to evaluate cardiopulmonary stability and to detect episodes of apnea, desaturations, and bradycardia in hospitalized preterm neonates (Di Fiore, 2004). In the Newborn Intensive Care Unit cardiopulmonary monitoring is the standard of care (Martin, Farnoff, & Walsh, 2011). A cardiorespiratory monitor is a physiologic monitor attached to sensors on a baby that provides a constant read-out of the baby's heart rate and rhythm, breathing rate, arterial or central venous pressure, and oxygen saturation (Philips, 2010). Heart rate monitoring is used to monitor sudden changes in heart rate that may or may not be a consequence of respiratory events. Cardiorespiratory event identification is dependent on the method of monitoring used: alarm setting, inclusion of continuous pulse oximetry, and the type of respiratory monitoring (Di Fiore, 2004). Heart rate monitoring is based on impedance monitoring. Impedance technology measures time dependent alterations in electric impedance across the chest wall that occur during respiration (Di Fiore, 2004; Martin et al., 2011).

The most common cause of ECG (electrocardiogram) artifact is poor skin contact with electrodes (Martin, Farnoff, & Walsh, 2011). Cardiac overlay occurs when the respiratory electrodes pick up impedance changes caused by cardiac activity (blood flow) and can affect the respiratory waveform (Philips, 2010). Correct electrode placement, particularly in neonates, can reduce cardiac overlay, resulting in the optimal respiratory and EKG signal (Martin et al., 2011; Philips, 2010). For term infants, the best probe positioning is one lead at the right midclavicular line at the level of T4 and the other at the xiphoid; while the lead placement in a line parallel but shifted to the left is best in premature infants to optimize the cardiorespiratory wave (Martin et al., 2011).

The Philips Intellivue Patient Monitor MP70 provides surveillance of neonates, multi-measurement monitoring, and data management (Philips, 2010). The Intellivue electrocardiogram (ECG) measures the electrical activity of the heart and displays it on the monitor both as a waveform and a numeric (Philips, 2010). The Intellivue monitor stores data in trend, event, and calculation databases. The monitor measures the thoracic impedance between two ECG electrodes on the infant's chest for the respiratory measurement. Changes in impedance due to thoracic movement produce a respiratory waveform. The monitor counts the waveform cycles to calculate the respiratory rate (RR) (Philips, 2010). To monitor pulse rate, the monitor counts the arterial pulsations that result from the mechanical activity of the heart in beats per minute (bpm). The pulse can also be measured from a SpO2 signal (pleth wave) or any arterial pressure, and a numeric pulse is displayed (Philips, 2010).

The Philips Intellivue Monitor provides trend data and event surveillance. Trends are patient data collected over time and displayed in graphic, tabular, or histogram form (Philips, 2010). Event surveillance detects and records event episodes (i.e. apnea, bradycardia, desaturations). Additionally, the Neonatal Event Review and Oxy-CRG (oxy-cardiorespirography) detect and document any combination of apnea, bradycardia, or hypoxia as a significant neonatal event. Oxy-CRG is an indicator of breathing efficiency and brain maturity (Philips, 2010).

The Philips pulse oximetry provides four measurements: oxygen saturation of arterial blood ($SpO_2$), pleth waveform (a visual indication of the patient's pulse), pulse rate (derived from pleth wave), and perfusion indicator (numerical value for arterial pulsation) (Philips, 2010).

***Pulse oximetry.*** Pulse oximetry is a commonly used monitoring method that assesses oxygenation saturation measurements in neonates (Shiao, 2005; Shiao & Ou, 2007). Pulse oximeters measure blood oxygen saturation noninvasively and continuously. A blood-oxygen saturation reading (SaO2) is a *functional measurement* that indicates the percentage of hemoglobin molecules in the arterial blood which are saturated with oxygen at the time of the measurement (Masimo Corporation, 2006; Philips Medical Systems, 2002). The term $SpO_2$ means the SaO2 measurement determined by pulse oximetry and is usually expressed as a percentage. Measurement is taken by placing a sensor on the hand or foot for neonates. The Radical-7 pulse oximeter uses a two wavelength pulsatile system to discriminate between oxygenated and deoxygenated blood (Masimo Corporation, 2006). Pulse oximetry works by emitting two sources of light (red and infrared light) that are absorbed by hemoglobin and transmitted through tissue to a light sensitive detector opposite the light (photodetector) (Phillips Medical System, 2002). With each heart beat, a pulse of oxygenated arterial blood travels by the sensor (Di Fiore, 2004). The amount of light received by the detector indicates the amount of oxygen bound to the hemoglobin in the blood. The instrument can calculate the measurement and convert the reading to a digital value representing the percentage of hemoglobin saturated with oxygen (Di Fiore, 2004; Philips Medical System, 2002).

The accuracy of $SpO_2$ measurements is dependent on a number of physiologic variables such as: hemoglobin level, arterial blood flow to and temperature of the digit where the sensor is located, amount of ambient light seen by the sensor, and movement artifact (Shiao 2005; Shiao & Ou, 2007).

Accuracy in interpretation of pulse oximetry is based on the accurate measurement of oxygen saturation. In neonates, the level of oxyhemoglobin is dependent on the effects of fetal hemoglobin and levels of carbon monoxide hemoglobin and methemoglobin. In neonates, most of the circulating hemoglobin in the blood is fetal hemoglobin (HbF). Fetal hemoglobin has a high affinity for oxygen (i.e. releases less to the tissues) resulting in a left shifted hemoglobin-oxygen dissociation curve (Shiao, 2005). The measurements from clinical pulse oximeters should be used with caution as they cannot account for variations in types of hemoglobin. Additionally based on the oxygen dissociation curve, the accuracy of pulse oximetry is limited at lower levels of oxygen saturation (i.e. 70-80%) (Di Fiore, 2004; Shiao, 2005). Temperature also affects the oxyhemoglobin curve. Decreased temperature results in an increased affinity of hemoglobin for oxygen while the opposite occurs with increased temperature (Phillips Medical System, 2002). Therefore, maintaining neurothermoregulation is important in securing accurate measurement. A major limitation of pulse oximetry is false alarms or loss of signal due to body motion. Accuracy in interpretation is dependent on software algorithms, types of hemoglobin (fractional versus functional), and averaging time to calculate saturation levels (Di Fiore, 2004).

The Radial-7 Pulse Oximeter is a noninvasive, arterial oxygen saturation and pulse rate monitor (Masimo Corporation, 2006). The Radial-7 displays SpO2, pulse rate, plethysmographic waveform and Signal Identification and Quality Indicator (Signal IQ™). It measures functional oxygen saturation of arterial hemoglobin (SpO2). The Radial-7 pulse oximeter uses a sensor that passes light through the site to a photodetector. The photodetector receives the light, converts it to an electronic signal, and sends it to the Radical-7 for calculation (Masimo Corporation). The Radical-7 measures functional saturation:

the amount of oxygenated hemoglobin expressed as a percentage of the hemolobin that can transport oxygen (Masimo Corporation, 2006).

*Masimo set signal extraction technology***.** Masimo Signal Extraction Technology identifies, separates, and filters varying physiologic signals ("noise") to report accurate arterial oxygen saturation (Masimo Corporation, 2006). The sensor is connected to the pulse oximetry instrument with a patient cable.

**Variability analysis.** Nonlinear methods of analysis is the most appropriate option for data analysis of respiratory waveforms. Nonlinear analysis is based on the Dynamic Systems Theory which is built on the dynamical properties of: 1) nonlinearity, 2) nonstationarity, 3) time irreversibility and 4) multiscale variability (Stergiou, 2004). When applied to biologic systems, this theory identifies variability as a range of behaviors within a system characterized by nonlinear mathematical equations (Stergiou; Bravi, Longtin, and Seely, 2011). The pattern of variability is assessed over time intervals. This mathematic concept of variability can also be applied to the study of complex physiologic parameters (Bravi et al.2011; Elder, Campbell, Larsen, & Galletly, 2010). According to traditional concepts of physiologic control, healthy systems auto-regulate to reduce variability and maintain physiologic constancy (Goldberger, 2002). Contrarily, the output of a wide variety of healthy physiologic systems, such as respiration, reveals a type of complex variability along with distinct nonlinear interactions (Goldberger, 2002). For instance, the breathing pattern of preterm infants often exhibits wide variation or variability in the timing of breaths (interbreath intervals) that may be clinically manifested as desaturation or apnea (Bloch-Salisbury, Indic, Bednarek, & Paydarfar, 2009).

Bloch-Salisbury et al. (2009) explained the nonlinear properties of the immature respiratory control system by illustrating how the breathing pattern of preterm infants often exhibits wide variation or variability in the timing of breaths (interbreath intervals). Prematurity may interfere with an infant's ability to develop a stable coordination pattern resulting in dysrhythmic sucking, swallowing, and breathing patterns. Through the use of physiologic time series analyses (wavelet transform of the respiratory signal), these authors point out that certain types of variability may be biomarkers of healthy physiological control.

**Behavioral State.** Behavioral state is a constellation of behaviors that signal level of alertness or consciousness (Gill, Behnke, Conlon, & Anderson, 1992; Gill et al., 1988; Thoyre & Carlson, 2003). Behavioral states also indicate how available a baby is for interaction or for functional skills such as feeding. The Anderson Behavioral State Scale (ABSS) is a standard assessment of an infant and is a 12 category scale that was used for assessments of behavioral state (Pickler et al., 2005). Several studies have reported that a quiet alert state is optimal for feeding success (Pickler et al., 2005; Thoyre & Carlson, 2003).

**Evaluation of Related Studies**

A review of the studies examining the effect of position on cardiopulmonary outcomes during oral feeding in preterm infants, lent support to the proposed theoretical framework and guidance in research proposal design (Clark, Kennedy, Pring, & Hind, 2007; Daley, 2002; Dawson et al, 2013; Lau, 2013; Park, Thoyre, Knafl, Hodges & Nix, 2014; Steven, 2007; Thoyre, Holditch-Davis, Schwartz, & Nix, 2012).

Clark et al. (2007) described and pilot tested a method for researching bottle feeding preterm infants in the elevated sidelying position. Six premature infants born less than or equal to 29 weeks gestation were enrolled in the study. The study employed a within-subject design whereby each infant was fed in both semiupright and elevated sidelying with feedings (one in each position) recorded every 3-5 days during the transition to oral feeding. The study period for each infant covered a span of approximately one to three weeks. These researchers measured physiologic stability (mean oxygen saturation and standard deviation of heart rate) using a Masimo Radical pulse oximeter and equipment used for pediatric sleep studies (CIU-2 unit). Data was collected for a two minute period prior to the feeding and throughout the feeding. Feedings were video recorded to collect data on feeder techniques and infant behavioral responses. The equipment integrated pulse oximetry with video recording for analysis. Collection of measures was performed through Winvisi software program onto a laptop computer. The primary purpose of this pilot was to test methodology to see if the design was sensitive enough to detect differences between feeding positions and warrant a larger study. Clark et al. found improved physiologic stability and feeding efficiency in elevated sidelying position during the midpoint of feeding. There was a significant interaction between time and feeding position ($F(2,10) = 11.42$, $p<0.01$). In the first three minutes, oxygen saturation decreased for both positions, improved in the middle three minutes in elevated sidelying position while decreasing further in semiupright. No other effects were significant. They reported a need for a larger study to confirm the benefits of elevated sidelying position for feeding.

Thoyre et al. (2012) used a within-subject crossover design to study 20 premature infants over two consecutive days for an average of four feedings for each infant. Infants in the intervention group in this study were positioned in elevated sidelying. Infants in the control group were positioned in either semiupright or elevated sidelying at nursing discretion. The purpose of the study by Thoyre et al., was to determine the preliminary effectiveness of an approach to oral feeding preterm infants called coregulated feeding. As position in the control group was at the discretion of nursing, this study does not look specifically at position as an intervention. Physiologic variables (oxygen saturation and heart rate), measures of infant regulation (behavioral organization, fluid management, work of breathing), feeding efficiency (length of feeding and feeding intake) and observation of intervention protocol and caregiver feeding behaviors (feeding position, infant preparation, infant readiness, pacing, and stimulation) were measured. Oxygen saturation and heart rate were collected using Ohmeda 4700 pulse oximeter and Gould electrocardiogram (ECG) monitor. Physiologic data were recorded with WINDAQ data acquisition software onto a laptop computer. All feeding observations/caregiver behaviors were videotaped using Observer software program and coded using the Dynamic Early Feeding Skills™ system by Thoyre. Sounds were transmitted from a microphone (attached to the infant's neck) to the video camera to code fluid management and work of breathing. Thoyre et al., reported findings on multiple components of the coregulated feeding intervention:

physiologic stability, behavioral organization, fluid management and work and breathing, and length of time to feed and nutritional intake. Infants fed by coregulated feeding had less SaO2 variability (SaO2 < 85%, $p=0.023$), less heart rate decline ($p=0.002$) and less increased work of breathing ($p<0.001$). The total length of feedings and the proportion of infant's prescribed volume was not statistically different between the groups.

Park et al. (2014) used a within-subjects crossover design to study the effects of head elevated supine (HES) i.e. semiupright, compared to elevated sidelying (HEL) in six premature infants. Each infant was bottle fed twice on one day in both the HES and HEL position in a random order. Infants were enrolled in the study once they were able to consume 50% of their prescribed volume by mouth for three consecutive days. Heart rate, oxygen saturation, and respiratory characteristics were recorded continuously for 30 minutes before the feeding until the feeding was completed. Analysis of the respiratory waveform was done using the AcqKnowledge software (BioPac) system. Respiratory effort was measured using a monitoring system which measures chest expansion associated with respiratory effort via elastic straps around the infant's chest. A microphone attached to the infant's neck measured breathing and swallowing sounds. The software was used to calculate the intervals between breaths, breathing pauses >3 seconds, amplitude of breaths, and respiratory rate per minute. Mean, standard deviation, and coefficient of variation were used to quantify the variability of the physiologic parameters. A test with one infant trialed data collection procedures, intervention plans, and measurement analysis. Because this was a pilot study, Park set the significance level at $p = 0.10$ and p values less than 0.20 were considered to be indicative of trends. Based on Park's analysis, infants fed in the head elevated sidelying position showed significantly less variability in heart rate, less severe and fewer decreases in heart rate, shorter and more regular intervals between breaths, breathing frequency closer to prefeeding state, and more variation in breath duration. Additionally, heart rate was more stable over time and regulated breathing improved over time in the head elevated sidelying position. No significant findings for SpO2 nor feeding performance were found.

Dawson et al. (2013) used a within-subject cross over design and studied infants on successive days rather than the same day. Twenty-five Infants were enrolled in the study when they were receiving at least two feeds (either breast feeding or bottle feeding) daily; percentage of intake was not specified. Oxygen saturation and heart rate were measured before, during, and 30 minutes after the feeding using a Massimo pulse oximetery monitor. Data was downloaded to a computer for analysis. Respiratory rate was recorded before and after the feeding and every 5 minutes during the feeding. The method for recording respiratory rate was not specified. Infants' level of alertness was measured using the Brazelton activity scale. Unlike Park but similar to Daley (2002), Dawson positioned the infants cradled in the caregivers arms in the semiupright position. Unlike any of the previously described studies, parents or nurses primarily provided feedings to infants. Infants enrolled in the study had significantly variable levels of respiratory support. Eight infants were receiving respiratory support (low flow oxygen, nasal continuous positive airway pressure, or high flow oxygen greater than 4L/min) at the time of the study. Dawson found no significant difference in level of alertness nor mean heart rate, respiratory rate or oxygen saturation between the semiupright cradle hold and sidelying position.

Lau (2013) randomized 41 very low birth weight infants to one of 3 study groups (upright, sidelying, and semi-reclined control feeding position) to compare the length of time (days) to full volume oral feeding and oral feeding skill maturation levels. Oral feeding skill level was defined as proficiency (percent volume taken at 5 min/volume prescribed) and rate of milk transfer over the entire feeding (ml/min). No differences in oral feeding skill maturation levels or length of time to attain full volume feeding was found between the upright and sidelying positions.

Similar to Clark et al. (2007), Daley (2002) used a longitudinal, within-subject design to study the relationship between two positions and feeding performance in premature infants. However, unlike the Clark et al. (2007) study, Daley positioned the infants cradled in the arms of the nurse (ARM position) or held in the nurse's lap with one hand supporting the infant's head, i.e. semiupright (LAP position); and 51 infants were observed weekly during two oral feedings, one in each position, until discharged or reached 38 weeks PMA. The order of feeding position was randomly assigned for each infant's first feeding. Thereafter, the order of the feeding positions remained the same for each infant. Daley measured feeding performance as volume intake, feeding duration, physiologic stability (heart rate, respiratory rate, oxygen saturation), distress (apnea, bradycardia, oxygen desaturation, color change, gag, cough, hiccup and emesis) and behavioral state. Data was collected at one minute prior to the start of the feeding, at five minute intervals throughout the feeding up to a 30 minute maximum and five minutes after completion of feeding. Heart rate, respiratory rate, and oxygen saturation were measured using Marquette Electronics Tram 200SL cardiorespiratory monitors. The behavioral state scale from the Neonatal Behavioral Assessment Scale (NBAS) was used in this study. Daley's results for feeding performance were similar to Lau (2013), Park (2014), and Thoyre et al. (2012). No significant difference was found for volume consumed between the two positions. Differently though, Daly found a significant difference in duration of feeding when the infants were fed cradled in the nurses arm (ARM) versus held in semiupright (LAP) (p=0.006). Infants fed in the ARM position took half the time to take the mean volume. The mean physiological signs (heart rates, respiration rates, and oxygen saturation) were not significantly different between positions in premature infants during bottle feeding. Additionally, no significant difference between the number and type of behavioral distress signs was found between the two feeding positions.

Stevens (2007) used a randomized, two period, crossover design to test upright (45 degree head up) and cradle (15 degrees head up) feeding positions on 12 preterm infant's cardiorespiratory stability while feeding. Each baby was assigned to one condition and each condition had a 6 hour washout period with a scheduled nasogastric feeding between oral feeding positions. Stevens used the Philips

IntelliVue MP50 cardiorespiratory monitor to record infant heart rate, respiration, and oxygen saturation over three time periods: 30 minutes baseline recording immediately prior to the feeding, maximum of 30 minute during feeding recording and 30 minute recovery recordings immediately after the feeding. Occurrence of apnea, bradycardia, and oxygen desaturations were recorded on an observation form. A goniometer was used to measure the feeding position angle and the Anderson Behavioral State Scale (ABSS) was used to assess behavioral state. Data collection procedures, observation forms and intervention plan were pilot tested. Findings indicated that neither the cradle (15 degree head up) nor upright (45 degree head up) feeding positions had a statistically significant effect on the preterm infant's cardiorespiratory stability. No significant relationships were found between feeding positions and volume consumed, gestational age nor postmenstrual age. Infants experienced a somewhat slower heart rate ($p=0.005$) and higher oxygen saturation level ($p=0.02$) when held in the upright position as compared to the cradle position. Although non-significant, infants held in the upright position had a slighter shorter feeding duration ($p = 0.27$).

**Study limitations.** Evaluation of related studies reveals limitations related to: 1) lack of sensitivity of instrumentation and measurement bias (Clark et al., 2007; Daley, 2002; Dawson et al., 2013), 2) small sample size (Clark et al., 2007; Park et al., 2014; Thoyre et al., 2012; Stevens, 2007), 3) inconsistent approach to feeding (Clark et al., 2007; Park, 2014; Thoyre et al., 2012) 4) variety of feeders with differing levels of experience (Dawson, 2013; Stevens, 2007) and 5) differences in infant respiratory system stability (Clark, 2007, Dawson, 2013, Park, 2014).

Lau (2013) reports limitations in study design as caregivers were not blinded to group assignment. This will be a limitation in the dissertation study as well as caregivers will know whether the infant was fed first in sidelying or semiupright; and this can limit knowledge of the hypotheses.

The use of multiple caregivers is clinically relevant. To address a variety of feeders, in the proposed study clear instructions to act in response to infant behavioral cues, were used across both feeding methods to ensure consistency and safety during feeding. To provide a consistent approach to feeding, a comprehensive feeding protocol, including specific caregiver training (demonstration, handout and verbal instruction) was developed to facilitate consistency in positioning during oral feeding. Instrumentation for data was checked and calibrated by a biomedical engineer to ensure reliability and a goniometer was used to measure and maintain consistency in positioning as defined in the protocol. A sample of infants with similar respiratory capabilities (all infants breathing room air at time of study), provides for more accurate interpretation of cardiopulmonary findings. To address limitations in sample size a power analysis was performed. The power analysis revealed that a sample size of 12 infants (i.e. a total of 24 feedings) would be sufficient to detect a difference in heart rate at an alpha level of <0.05 with 80% power.

**Relationship between Literature Review and Dissertation Research**

The analysis of the literature provided a conceptual model for the dissertation research and for development of the research study protocol.

**Theoretical framework.** Investigators and clinicians alike propose conceptual frameworks regarding the effect of positioning on cardiopulmonary outcomes during feeding in preterm infants. Three primary theories have emerged suggesting support for positioning as a method to optimize bottle feeding in preterm infants by improving physiologic stability and improving feeding outcomes: 1) the relationship of positioning to breast feeding, 2) the impact of milk flow rate on support of swallowing and 3) a physiologic model for preterm infant position and cardiopulmonary stability.

***The relationship to breast feeding.*** Sidelying positioning has been proposed as an intervention to support positive bottle feeding experiences in preterm infants in that sidelying is very similar to the cross cradle position typically used for breast feeding preterm infants (Clark et al., 2007; Dawson et al., 2013; Park et al., 2014; Stevens, 2007; Thoyre et al., 2012). Thoyre et al. (2012) asserts that many preterm infants are offered both bottle and breast feeding, therefore, bottle feeding an infant in sidelying provides consistency across feeding conditions. Better coordination with swallowing and less disruption of breathing has been reported in breastfeeding versus bottle feeding; therefore it is hypothesized that infants fed in sidelying may adopt some of the advantages of breastfeeding (Park, 2014). However, the demands of bottle feeding are significantly different from those of breastfeeding. Comparison of feeding behaviors by breast versus bottle reveal differences in latch, sucking pressures, characteristics of sucking rate, rhythm and pattern, and rates of milk fluid flow. All of these factors affect overall ventilation, oxygen saturation, and energy expenditure (Berger et al., 2009; Goldfield et al., 2006; Hallowell & Spatz, 2012; Spatz, 2011). Additionally, in the cross cradle position during breast feeding the infant's body is turned toward the mother and he/she is held in close contact against her body. In an elevated sidelying position, the infant is most often held perpendicular and away from the caregiver. Research acknowledges breast milk fed from a bottle as a very different experience for the infant than direct breastfeeding from the mother (Hallowell & Spatz, 2012). Although health care professionals suggest that elevated sidelying may be beneficial due to the similarity in positioning to breastfeeding, there is little evidence to support this hypothesis.

***Support of swallowing.*** The elevated head sidelying position is perceived to promote safe feeding by providing support to swallowing during the oral phase of feeding in preterm infants. The oral phase is the preparatory stage of swallowing. During the oral phase, the infant sucks milk from the bottle, forms a bolus, and transports the bolus to the back of the oral cavity to generate the swallowing reflex (Averdson, 2008). Premature infants may present with poor bolus formation and fluid management, and therefore at higher risk of aspiration during oral feeding (Thoyre et al., 2012). Feeding experts across disciplines advocate bottle feeding in an elevated sidelying position to avoid aspiration of liquid not cleared from the posterior oropharynx due to immature swallowing in the preterm infant (Clark, 2007; Garber, 2013).

The principal assumption is that in the elevated sidelying position, the flow of milk to the esophagus may be slowed by gravity, limiting oral transit time (Park et al., 2014; Thoyre et al., 2012). As milk flows into the infant's cheek (rather than directed backward to the pharynx), the elevated sidelying position may provide the infant more time to form and control a milk bolus, thereby facilitating safe and effective swallowing (Park, 2014; Thoyre et al., 2012). The ability to swallow more safely may support breathing and prevent prolonged breathing interruptions and aspiration (Stevens, 2007; Park, 2014).

Though theoretically based on development of oral feeding skills and a preterm infant's inability to effectively coordinate suck, swallowing, and breathing (Gewolb & Vice, 2006), this intervention lacks evidenced based data to support its benefits. However, this hypothesis will be best verified by radiographic studies of swallowing (videoflouroscopic swallow study) during oral feeding in preterm infants rather than indirect measures of cardiopulmonary outcome.

***Position and physiologic stability.*** Optimizing position is cited in the literature as a developmentally supportive strategy to promote oral feeding in preterm infants (Lau, 2013; Thoyre et al., 2012). The theoretical proposition that positioning impacts cardiopulmonary outcomes is based on characteristics of a preterm infant's developing musculoskeletal system and limited capacity for respiration during oral feeding. Factors identified as influencing this physiologic model include: development of the cardiopulmonary system, maturation and mechanics of oral feeding skills, coordination of suck, swallow, breathe pattern, feeding performance and efficiency, and optimal behavioral state for feeding. Along with published research (Clark et al., 2007; Lau, 2013; Park et al., 2014, Thoyre et al., 2012), unpublished PhD dissertations (Daley, 2002; Steven, 2007), the author's dissertation study established the model of physiologic stability as the theoretical framework to examine the effect of position on cardiopulmonary outcomes during oral feeding in preterm infants.

*Positioning to support cardiopulmonary stability*. Coordination of breathing with swallowing presents the greatest challenge for preterm infants as they progress to oral feeding; and respiratory issues are often the basis of feeding problems (Bu'Lock et al., 1990: Gewolb & Vice, 2006; Jadcherla et al., 2012; Mizuno & Uedo, 2003). Inefficient feeding patterns may result in insufficient breathing, physiologic distress, fatigue and early cessation of feeding (Lau et al., 2003; Park et al., 2014; Thoyre et al., 2012). Due to the complexity of oral feeding and cardiorespiratory demands of oral feeding, preterm infants are at risk of aspiration, apnea, desaturations and bradycardia during feeding

(Lau, 2003; Park et al., 2014; Thoyre et al., 2012). Physiologic maturity is required to develop the suck, swallow, and breathe coordination necessary for successful oral feeding (Hallowell & Spatz, 2012). An infant who is physiologically stable will feed more efficiently and transition to full oral feedings (Clark et al., 2007). Therefore, interventions need to support respiration in order to maintain physiologic stability throughout the feeding. Therapeutic positioning is a potential intervention strategy to support breathing during feeding (Clark et al., 2007; Daley, 2002; Dawson et al., 2013; Park et al., 2014; Stevens, 2007; Thoyre et al., 2012).

*Musculoskeletal development of the chest wall and muscles of inspiration.* The immaturity of the preterm respiratory system impacts breathing. Immature muscular development, neurologic processes and cardiopulmonary system can cause immature infants to tire quickly during oral feeding. Respiratory mechanics and pulmonary function may be affected by positioning (Clark et al., 2007; Daley 2002; Stevens 2007; Park et al., 2014; Thoyre et al., 2012). An understanding of the musculoskeletal development of the thorax and muscles of inspiration provides a foundation for evaluating the influence of posture on cardiopulmonary outcomes.

The diaphragm is the primary muscle of respiration in the neonate. Therefore, breathing efforts of the neonate are dependent upon the strength and endurance of the diaphragm (Massery, 1991; Montessero, Kristjanson, & Cole, 2002). The diaphragm inserts on the lower six ribs, the sternum, and the first three lumbar vertebrae. It is innervated bilaterally by the phrenic nerve. The muscles of the rib cage include the external intercostal muscles (inspiration), the internal intercostal muscles (expiration), and the accessory muscles including the sternocleidomastoid, pectoral, and scalene muscles. The major role of these muscles is to fixate the chest wall by contracting tonically during diaphragmatic excursion. If unable to stabilize the thorax, the chest wall is likely to distort during inspiration (Blackburn, 2013; Montessero et al., 2002). Contraction of the intercostal and accessory muscles of the rib cage can contribute to inspiration by elevating the anterior end of each rib (Winn, 2010).

The rib cage of the newborn has nearly equal anteroposterior and transverse diameters and the ribs are more horizontally aligned (Montessero et al., 2002). This reduces the mechanical efficiency of the chest wall excursions in the newborn since most of the tidal volume must be generated by the diaphragm (Blackburn, 2013). To maximize diaphragmatic work, the intercostal muscles must stabilize the rib cage and the internal/external obliques and the rectus and transverse abdominis muscles should stabilize the abdomen. In the term infant, the coordination of these efforts is reduced. Due to immaturity, the preterm infant is even less effective at synchronizing muscular respiratory efforts.

*Chest wall compliance.* The chest wall in the infant is cartilaginous, soft, and pliable. The neonate's diaphragm is attached to a chest wall that is highly compliant. This can lead to distortion of the lower portion of the chest wall during contraction, especially with a forceful contraction (Blackburn, 2013: Ratnovski, Elad, & Halpern, 2008). As a result, the infant must perform more work to move the same amount of Tidal Volume ($V_T$). The decreased efficiency of the contraction and reduced $V_T$ can make ventilation less effective, requiring adjustments in the respiratory pattern (Blackburn, 2013; Ratnovski et al., 2008). Increased diaphragmatic force and the pliable chest wall lead to chest distortion. These characteristics can also alter breathing patterns with increased risk of paradoxical or asynchronous pattern. The increased compliance results in a tendency of the chest wall to collapse and retract as the infant tries to generate negative pressures needed for lung expansion. Retractions are the clinical signs of the degree of inward rib cage collapse during forceful diaphragmatic contractions. This increase in work of breathing can lead to fatigue and eventually apnea (Blackburn, 2013; Ratnovski et al., 2008).

***Clinical implications.*** Immaturity of the neonate is manifested in all aspects of respiratory control. Due to anatomic risk factors, immaturity of the musculoskeletal system, and physiologic constraints, the neonate has limited capacity to respond to cardiopulmonary stress. The infant responds to stress by a decreased response to $CO_2$, inward distortion of the chest during inspiration, and irregular breathing patterns (periodic breathing, apnea, tachypnea) (Martin et al., 2011; Monteresso et al., 2002). Tidal volume is influenced by the strength of the diaphragm and intercostal muscles, resistance to airflow through the upper and lower airways, structural integrity of the thorax, and compliance of the lung tissue (Ratnovsky et al., 2008). Because of these developmental factors, the infant is particularly vulnerable to diaphragmatic muscle fatigue, especially when the work of breathing is increased. This vulnerability increases with lower gestational age.

Knowledge of development of posture and movement is important to promote musculoskeletal alignment and support cardiopulmonary outcomes in preterm infants during bottle feeding. Therapeutic positioning impacts physiologic function and stability by supporting the infant's ability to stabilize the chest, expand the lungs, and maximize diaphragmatic expansion. Infants therefore should be positioned to support musculoskeletal development of the thorax and optimize ease of breathing.

Optimal position for bottle feeding premature infants is orientation toward midline, neutral alignment of the trunk and flexed hips and knees (Daley, 2002). The neck is stabilized in slight capital flexion with the chin tucked inward. Preterm infants lack inherent control therefore they need external support from positioning. Positioning may be assisted by swaddling to provide trunk stability.

Postural stability provides a base for feeding skills. Stability of the head, neck, and trunk is needed to support the fine oral motor movements of feeding (Averdson, 2008). Proper body alignment, containment of the extremities, and a flexed posture decrease work of breathing and promote energy conservation (Garber, 2013). Poor endurance and fatigue limit efficiency of oral feeding, therefore, consistent and appropriate positioning may provide for more regulated heart and respiratory rate and oxygen saturation.

Investigators suggest that infants have less physical support in the semiupright position than in the elevated sidelying position (Clark et al., 2007; Dawson et al, 2013, Thoyre et al., 2012). As infants tire during nipple feeding, it is often difficult for them to maintain trunk alignment and stability making them prone to neck flexion (Garber, 2013; Thoyre et al., 2012). The preterm infant larynx and trachea are less rigid and therefore prone to airway collapse (Dawson, 2013), therefore excessive neck flexion in the semiupright position may interfere with the preterm infant's ability to maintain adequate patency of the airway (Daley, 2002; Park et al., 2014). Cervical posture and pharyngeal airway stability are interconnected and excessive neck flexion can also contribute to inefficient breathing (Park, 2014). As a result, preterm infants may experience adverse physiologic events such as oxygen desaturation, apnea, and bradycardia. However, the risk of airway collapse can be minimized by avoiding excessive neck flexion or hyperextension (Daley, 2002; Garber, 2013). Differently than other investigators, Stevens (2007) proposes that improvements in oxygen saturation in semiupright may be related to improved diaphragmatic function as a result of changes in intra-abdominal pressure. For the infant in the semiupright position, the abdomen lengthens, pressure from the abdominal organs decrease, and diaphragm is able to shift downward (Stevens, 2007). These physiologic changes permit lung volume to increase which may improve oxygen saturation and cardiorespiratory stability in an upright position. This view is consistent with the development and anatomy of the thoracic musculoskeletal system in preterm infants. Semiupright positioning may provide biomechanical support for effective contraction of the diaphragm muscle and accessory muscles stability.

Elevated sidelying position is proposed as a supportive feeding strategy that may allow preterm infants to conserve energy and develop effective feeding techniques (Clark et al., 2007; Park et al., 2014). Thoyre & Carlson (2003) found changes in respiratory control when an infant's level of arousal decreased during feeding. They theorized these changes may be due to loss of muscle tone, decreased muscle activity in the intercostal muscles and in the upper airway; and changes in quality of breathing pattern (shallow breaths, breathing pauses). The elevated sidelying position allows the caregiver to provide support of the neck and trunk alignment in a neutral position (Garber, 2013; Park et al., 2014). To support musculoskeletal changes associated with fatigue, Park (2014) states that the elevated sidelying position reduces the work of breathing by facilitating lung expansion and supporting upper body control.

The physiologic model as a theoretical framework for the relationship between position and cardiopulmonary outcomes, suggests the physiologic benefits of one position over another needs to be identified in order for caregivers to develop sound clinical interventions to improve feeding outcomes (Lau, 2013). Evidence is therefore needed on the optimal feeding method to support cardiopulmonary stability during feeding in preterm infants.

***Nonlinear dynamics analysis***. Respiratory waveform is a measure of thoracic impedance and an indirect measure of respiratory waveform variability. Variability analysis refers to the assessment of patterns of variation over time intervals and is based on the dynamic systems theory. The dynamic systems theory postulates that nonlinear regulatory systems, such as respiration, reveal complex variability whereby variability is the defining feature of healthy function (Bloch-Salisbury, Indic, Bednarek, & Paydarfar, 2009). From this perspective, the complexities of oral feeding would require increased variability to accommodate the multiple tasks of suck, swallow, breathe coordination and various other factors influencing oral feeding (NICU environment, nipple selection, milk flow rate, positioning of the infant, caregiver technique). Goldfield (2007) suggests that the ability to identify variability patterns may provide indication of an infant's readiness to feed.

Dynamic systems is a theoretical approach to the study of development. Two primary tenets are inherent in studying developmental processes in dynamic systems theory: 1) development is understood as the complex, continuous interaction of multiple levels of the developing system and 2) biological systems self organize from the interactions of the components of a complex system (Thelen & Smith, 1994). When applied to oral feeding, the dynamic system theory helps elucidate the complexities of oral feeding and provides support to positioning as a therapeutic intervention (Goldfield, 2007: Park et al., 2014). Successful oral feeding is multifactorial, requiring the interaction and organization of multiple subsystems: oral motor, neurologic, cardiopulmonary and gastrointestional (Goldfield, 2007; Jadcherla et al., 2012; Park, 2014). In a dynamical approach, efficient oral feeding is the cooperative interaction of multiple elements in a system whereby sucking, swallowing and breathing are characterized by a more or less stable coordination pattern (Goldfield, Jadcherla). Variability is part of development and needed for functional skill acquisition. Variability, therefore, may be a hallmark of healthy physiologic control (Goldberger et al., 2002) where as a lack of complexity may be early marker of delay in neuromaturation and oral sensorimotor performance.

Consequently, the purpose of analyzing respiratory waveforms was to evaluate the clinical utility of respiratory variability. This doctoral study assessed whether variability, or the capacity to respond to unpredictable stimuli and stresses during oral feeding in preterm infants is correlated with gestational age and/or postmenstrual age. The application of variability monitoring may be helpful in assisting infants with oral feeding problems by providing interventions, such as positioning, which is based on the process of coordination or variability of wave form pattern to improve clinical outcomes during oral feeding in preterm infants.

# Chapter III

# Methods

## Purpose of Research, Specific Aims and Hypothesis

This study investigated the work of bottle feeding and the effect of positioning and behavioral state associated with feeding, on cardiopulmonary parameters in preterm infants. The target population was healthy premature infants transitioning from gavage feeding to bottle feeding. Outcomes measures were cardiopulmonary physiology (heart rate, respiratory rate, oxygen saturation, respiratory pattern variability), behavioral state and feeding efficiency (volume intake and length of feeding). This study used an intervention crossover design with washout period. The comparison between elevated sidelying position and semiupright position was referred to as a change in feeding method. Subjects were randomly assigned to one of two sequences of feeding methods: elevated sidelying position/ semiupright position or the reverse. Infants were observed across three feeding times with a recovery (gavage feeding) period between oral feedings. Each infant was fed in both feeding positions and served as its own control.

The measured variables were volume consumed (cc), time required to complete feeding (sec); and percentage of total feeding time spent outside of acceptable physiologic range for each of the following variables: hemoglobin oxygen saturation (%SaO2), respiratory rate (rpm), and heart rate (bpm).

**Research question.** The aim of this dissertation research study was to measure infant cardiopulmonary physiology outcomes related to body position during feeding.

- How do heart rate, respiratory rate, and hemoglobin oxygen saturation compare when preterm infants are fed by bottle in elevated semiupright or in elevated sidelying?
- How does the respiratory pattern vary when preterm infants are fed by bottle in elevated semiupright or in elevated sidelying?
- How does behavioral state associated with bottle feeding affect heart rate, respiratory rate, respiratory variability and hemoglobin oxygen saturation in preterm infants?

**Specific Aim 1.** Estimate the differences in infant cardiopulmonary physiology outcomes by body position during feeding.

***Primary hypothesis***. There will be no difference in percentage of total time spent outside of acceptable physiologic range when preterm infants are fed in semiupright compared to elevated sidelying for the following variables:

- Percent hemoglobin oxygen saturation (%SaO2)
- Respiratory rate (rpm)
- Heart rate (bpm)

***Secondary hypothesis***. There will be no difference in respiratory variability as measured by respiratory waveform when preterm infants are fed by bottle in semiupright compared to elevated sidelying.

**Specific Aim 2.** Estimate the differences in infant feeding outcomes by body position during feeding.

***Primary hypothesis***. There will be no difference in volume intake or duration of feeding when infants are fed in semiupright compared to elevated sidelying.

**Specific Aim 3**. Determine the association between infant behavioral state and body position during feeding.

***Primary hypothesis***. There will be no difference in behavioral state when preterm infants are held or fed in semiupright compared to elevated sidelying.

**Specific Aim 4.** Measure differences in infant respiratory waveform variability by body position during feeding.

***Primary hypothesis***. There will be no difference in respiratory variability as measured by respiratory waveform when preterm infants are fed by bottle in semiupright compared to elevated sidelying.

**Directional Hypothesis Prior to the Study**

The difference in respiratory variability as well as infant cardiopulmonary outcomes related to body position during feeding, will be dependent on the stability of the respiratory system, the coordination of oral motor skills, gestational age at birth and postmenstrual age at time of study.

There is an association between cardiopulmonary outcomes and a) gestational age and b) postmenstrual age. Neurodevelopmental and physiologic markers are dependent on perinatal maturation and therefore gestational age at birth. Ventilation and oxygenation are influenced by postmenstrual age as coordination of sucking, swallowing, and breathing improve with maturation. Therefore, it is hypothesized that infants who are born at a younger gestational age (< 30 weeks) and who are younger postmenstrual age at time of testing (< 35 weeks) will demonstrate a larger percentage of total time spent outside of physiologic range for oxygen saturation, heart rate and respiration when positioned in semiupright as compared to sidelying during bottle feeding.

Respiratory rhythms during feeding undergo developmental changes with maturation and postmenstrual age correlates with respiratory pattern stability. Therefore, there will be a difference in respiratory variability when infants are fed in semiupright as compared to elevated sidelying based on postmenstrual age at time of testing.

Infants who are more physiologically stable will feed more efficiently. Therefore, infants who: 1) demonstrate a poor endurance and increased fatigue with feeding as evidenced by increased work of breathing or increased respiratory rate during pauses to breathe and 2) demonstrate immaturity of oral motor skills as evidenced by overfilling of the oral cavity and/or anterior fluid loss; will demonstrate a larger percentage of total time spent outside of acceptable physiologic range for oxygen saturation, heart rate and respiratory rate when infants are fed in semiupright as compared to elevated sidelying.

Measures of infant behavioral state will be related to body position during feeding. Infants who are fed in semiupright will demonstrate increased levels of alertness and have their eyes open, with a score of 6 through 9 as measured by the Anderson Behavioral State Scale, as compared to infants fed in the sidelying position.

There will be a difference between groups based on research design methodology. Infants who require an additional recovery gavage feeding (Alternative 1) will demonstrate a larger percentage of total time spent outside of the acceptable physiologic range for oxygen saturation, heart rate and respiratory rate when infants are fed in either semiupright or elevated sidelying as compared to infants fed without a recovery gavage period (Alternative 2) or infants fed according to the standard research protocol.

**Pilot study**

Prior to initiation of the dissertation study, a protocol for a pilot study was developed to look at feasibility, instrumentation, and to refine methodology. Additionally, the pilot study served as an opportunity to test equipment and analyze data output. Assessment of data from the respiratory waveform was examined to determine if the data was robust enough to use for the PhD dissertation, appropriate for analysis of respiratory variability, and applicable to nonlinear methods of analysis.

**Preliminary data**. Pilot study data was collected on 5 babies. A trend toward an increase in heart rate was noted in the semiupright position as compared to the sidelying position ($p=0.08$). Differences in feeding volume intake were related to postmenstrual age at time of study, previous feeding experience, and position. Higher volumes were consumed by older adjusted gestational age infants and in sidelying position regardless of adjusted gestational age. Infants fed at a younger adjusted gestational age demonstrated decreased endurance at the second feeding trial regardless of position. One baby who was enrolled at >35 weeks took less volume as compared to same aged cohorts and fatigued at second feeding; this baby later went on to develop periventricular leukomalacia.

Sample size calculations were performed both on the average heart rate and respiratory rate. Using desired power of .8, the calculated sample sizes are 14 and 97 respectively. Given the small sample size and high standard deviations for respiratory rate, it was anticipated that this sample size calculation for heart rate and respiratory rate would change with more subjects.

**Respiratory waveform analysis.** An unexpected finding in the pilot study was the realization that respiratory waveforms could be gathered from the bedside monitor via a computer software processing system. This respiratory waveform is an indirect measure of respiratory waveform variability. Changes in impedance due to thoracic movement produce a respiratory waveform (Phillips, 2010).

MatLab was used to determine if the respiratory waveform and the use of nonlinear methods provide clinically relevant data regarding respiratory variability during feeding of preterm infants. Respiratory waveforms were examined to determine the effect of position on respiratory patterns of variability

**Modifications to research protocol.** Analytic synthesis of the literature and completion of the pilot study resulted in refinement of the methodology for the dissertation research study. The patient population was finalized after review of nursing flow sheets to ensure research design was consistent with current nursing care standards. The feeding method procedure was finalized after review and feedback from nursing staff ensuring the process was consistent with current care practices (Appendix A, p. 165). A videotaping procedure was developed to ensure capturing the infant fully while observing infant's behavioral cues, as well as to verify accuracy of goniometeric measurement. Reliability of cardiopulmonary measures was improved by standardizing and verifying neonatal probe placement. Proper placement of ECG leads and pulse oximeter probe was outlined to ensure consistency, limit movement artifact, and improve accuracy of measurement (Appendix B, p. 167). The investigator was trained in the use of the Anderson Behavioral State Scale, a behavioral data collection form was created (Appendix C, p. 168), and a process to test inter-rater reliability was established. Finally, a process was developed to ensure protection of health information including de-identifying patient data for processing/analysis and proper storage of protected data.

Unexpected challenges encountered during the pilot study data collection were related to lack of equipment, staffing, and infant feeding behaviors. Lack of additional RS232 boards resulted in loss of potential subjects due to inability to collect data. A scholarship was granted to purchase of an additional RS232 board which allowed for collection of data in each of the pods within the NICU. Different feeders for recorded feedings crossing day/night shifts and unit policy of using patient care assistances (PMAs) to feed infants impacted consistency in caregiver technique. Standardization of positioning was verified by goniometric measurement and adjusted as needed to be within 5 degrees of defined measure. A detailed feeding protocol with direct instruction by the primary researcher was used to train each feeder prior to data collection to ensure consistency in feeding technique and to enable use of PMAs and different skilled feeders across shifts.

Variable infant feeding readiness cues impacted the ability to feed infants according to research design. Standardization of criteria based on nursing assessment of infant readiness to feed and development of alternatives to research design, allowed infants who needed to rest to be fed through a nasogastric tube for the subsequent feeding; while infants who were ready to feed without a break to feed sequentially.

Documentation of feeding patterns allowed for comparison between groups based on these criteria.

Based on a review of the literature, modification to data analysis included the use of gestational age (GA), postmenstrual age (PMA), days of life (DOL) and neonatal disease severity scores as co-variates. There is much variation in the GA at which preterm neonates attain various oral feeding milestone during early development. Therefore, examining data in relation to GA was essential (Dodrill et al., 2008). Infants are often assessed according to PMA and DOL at time of study entry (Bu'Lock et al., 1990; Hanlon et al, 1990; Jadcherla et al., 2010; Lau & Smith, 2011). According to Jadcherla et al., stratification is supported by the evidence of neurodevelopmental and physiologic markers dependent on perinatal gestational age.

Neonatal disease severity scores are related to initiation and attainment of full volume oral feeding (Dodrill et al., 2008; Jadcherla et al., 2010; Pickler et al., 2005). Infants who had a greater degree of neonatal morbidity took longer to transition from start of oral feeding to attainment of full volume oral feeding.

Gestational age, postmenstrual age, days of life at entry into study and neonatal disease severity scores were analyzed using the Spearman rank correlation coefficient.

To align with current literature and evidenced based practice, modifications to the research protocol included explicit definitions as actual feeding skill and endurance are equally important in determining feeding success (Lau et al., 2003; Lau & Smith, 2011; Park, 2014; Pickler et al., 2005). *Proficiency (Pro)* was defined as the percentage taken during the first five minutes per milliliter prescribed. Proficiency has been described as an index of oral motor skill since its measurement is taken at a time when fatigue is expected to be minimal (Pickler et al., 2005). *Rate of Milk Transfer (RT)* measured as milliliters/minute over an entire feeding was used an index of endurance. *Oral feeding performance (OT)* was the percentage of milliliters taken during the feeding per milliliters prescribed and is a reflection of oral motor skill as well as fatigue.

**Paradigm and Research Design**

The dissertation study was based on a model of physiologic stability as the theoretical framework to examine the effect of position on cardiopulmonary outcomes during oral feeding in preterm infants. The theoretical proposition that positioning impacts cardiopulmonary outcomes was based on characteristics of a preterm infant's developing musculoskeletal system and limited capacity for respiration during feeding. Positioning is designed to support the musculoskeletal system biomechanically and thereby improve work of breathing. The goal of positioning is therefore to stabilize the chest and trunk, support lung expansion, maximize diaphragmatic excursion, maintain neck alignment, and provide postural stability. The head elevated sidelying position is hypothesized to support trunk alignment and stability, prevent excessive neck flexion, and conserve energy. Semiupright positioning is postulated to improve diaphragmatic function by providing biomechanical support for effective contraction of the diaphragm muscles and accessory muscle stability. Quantitatively documenting the effect of position on cardiopulmonary outcomes during oral feeding in preterm infants can provide information that may be used by nursing and neonatal therapists to feed successfully. Results of this study provided information on optimizing infant position during feeding. Benefits for the infant may therefore have included: improved cardiorespiratory response to enteral feeding, reduced fatigue with oral feeding, improved nutritional intake and/or improved behavioral response to handling and position change. In addition, suggestions for positioning the infants were provided to caregivers so they may also assist their infant in making a smooth transition from gavage to bottle feeding during subsequent feedings.

**Target population.** The target population was premature infants with limited experience in bottle feeding. On the days of observation of the study, all infants were in transition from gavage to bottle feeding. All infants completed at least one oral feeding trial (25-50% of prescribed volume feeding) for no less than 24 hours and no greater than 72 hours prior to initiation of observation.

***Inclusion criteria.*** Healthy preterm infants who had medical order for oral feeding and met the following criteria will were included in the study:

- Admitted to the NICU before 37 weeks gestational age (age of prematurity)
- ≥ 33 weeks postmenstrual age at time of study (adjusted gestational age)
- Breathing room air
- Demonstrate the ability to maintain body temperature out of the isolette for at least thirty minutes on two previous occasions
- Demonstrate cardiorespiratory stability at rest as evidenced by:
    - a respiratory rate of less than 60 rpm
    - a heart rate of 100 to 160 bpm
    - a hemoglobin oxygen saturation of greater than 95%

***Exclusion criteria.*** Infants who demonstrated complex medical conditions that could interfere with the ability to effectively evaluate outcomes were excluded. Specific exclusion criteria included infants with:

- Major congenital anomalies
- Grade III or IV intraventricular hemorrhage
- An Apgar score less than 7 at 10 minutes
- Infant history of positive urine and/or meconium toxicology screen
- Known patent ductus arteriosus at the time of study
- Gastrointestinal complications that interfere with the ability of the infant to progress to full oral feeding
- Craniofacial abnormalities or a diagnosis affecting the ability to safely swallow
- Infants who demonstrate consistent vomiting or bradycardia with oral feeding
- Infants who are exclusively breast feeding

**Setting.** Infants were selected from the NICU at Connecticut Children's Medical Center in Hartford, Connecticut. This is a Level 3 NICU with 32 patient beds. The majority population within this NICU consists of premature infants and infants requiring surgical intervention.

**Sampling.** Subjects were chosen by convenience sampling with a sample size of 12 infants for 24 feedings determined after power analysis based on preliminary data. The researcher identified infants through the electronic patient record and then reviewed the medical record to ensure eligibility. The principal investigator obtained parental/caregiver consent. No parent was contacted for informed consent until the eligibility of the infant for the study was confirmed by chart review.

**Sample size justification.** Data was collected on five babies during the pilot study. As this was an exploratory study, data were collected to look at variability in the statistics to see if a meaningful difference is detected between groups. Collected data on 5 babies allowed for analysis of the change (if any) in cardiopulmonary and feeding outcome measures. This data was then used to calculate the statistical power analysis using SPSS and enabled calculation of the sample size.

## Methodology

### Research design.

***Feeding Sequence A:***

Elevated Sidelying Washout Semiupright

Oral Feeding Position----------Recovery Gavage Feeding---------Oral Feeding Position

T1 T2 T3 T4 T5 T6 T7 T8 T9 T10 T11

Baseline Prefeeding Feeding Postfeeding PostBaseline Recovery Baseline Prefeeding Feeding Postfeeding PostBaseline

***Feeding Sequence B:***

Semi upright Washout Elevated Sidelying

Oral Feeding Position------------Recovery Gavage Feeding-----------Oral Feeding Position

T1 T2 T3 T4 T5 T6 T7 T8 T9 T10 T11

Baseline Prefeeding Feeding Postfeeding PostBaseline Recovery Baseline Prefeeding Feeding Postfeeding PostBaseline

This study used an investigational cross-over design with a washout period. The independent variable was position, and the comparison between elevated sidelying position and semiupright position was referred to as a change in feeding method. Subjects were randomly assigned to one of two sequences of feeding methods: elevated sidelying position/semiupright position or the reverse. Infants were observed across two feedings with a recovery (gavage feeding) period between oral feedings. Feeding position was randomized to Feeding Sequence A or Feeding Sequence B according to a coin toss (Heads semiupright/sidelying; Tails sidelying/semiupright) and counterbalanced across infants.

An infant driven approach to feeding is now standard of care in the NICU at CCMC. Infants' physiological and behavioral cues are assessed prior to each feeding to determine readiness to feed. This care practice inadvertently impacted the ability to feed infants according to the pilot study research design protocol. Therefore, a modification to the research protocol was established to provide standardized criteria for data collection, based on nursing assessment of infant readiness to feed. This adjustment in methodology allowed infants who needed to rest an additional nasogastric feeding; while infants who were ready to feed without a break to feed sequentially. This modification matches the current practice in the NICU.

***Research Design Alternative 1.***

Oral Feeding Position 1------Recovery Gavage-----Recovery Gavage-----Oral Feeding Position 2

| T1 | T2 | T3 | T4 | T5 | T6[1] | T6[2] | T7 | T8 | T9 | T10 | T11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Baseline | Prefeed | Feeding | Post feeding | PostBaseline | Recovery | Recovery | Baseline | Prefeed | Feeding | Post feeding | PostBaseline |

***Research Design Alternative 2.***

Oral Feeding Position 1--------------------*No Recovery Gavage*---------------------Oral Feeding Position 2

| T1 | T2 | T3 | T4 | T5 | T7 | T8 | T9 | T10 | T11 |
|---|---|---|---|---|---|---|---|---|---|
| Baseline | Prefeed | Feeding | Post feeding | PostBaseline | Baseline | Prefeed | Feeding | Post feeding | PostBaseline |

Documentation of feeding patterns and additional data analysis allowed for comparison between groups based on research design methodology.

A NICU healthcare team member (nurse or patient care assistant) fed the infant using the intervention protocol. Each oral feeding was divided into five periods of observation: a two minute prefeeding supine, a two minute prefeeding semiupright/elevated sidelying, bottle feeding in semiupright or elevated sidelying, a two minute post feeding semi- upright/elevated sidelying and a two minute post feeding supine. Data was recorded prior to the feed to obtain baseline measures. A three hour recovery gavage feeding was provided between oral feedings. The three hour washout period is necessary to support cardiopulmonary physiology and provide a rest period between oral feedings.

Each infant was assigned to one sequence, fed in both feeding positions and served as their own control to account for the possible effects of maturation and history. Axillary temperature was taken with an IVAC thermometer by the nurse prior to the prefeeding supine control period to ensure thermoregulation.

**Instruction in feeding protocol.** In-services were held to educate staff about the research prior to the start of the study. Education included a power point presentation to the NICU research team, a verbal presentation to staff about their role and a physical demonstration about each feeding position using a doll. In addition, small posters explaining the study design, methodology, and feeders' role were placed in the nurses' lounge and at each nursing station. The principal investigator coordinated the research schedule with the nurse caring for the enrolled infant and the feeding protocol was reviewed prior to data collection. Any questions and concerns were answered at that time.

## Data Collection Instrumentation

**Heart rate, respiratory and oxygen saturation monitoring.** Heart rate (beats per minute) and respiratory rate (breaths per minute) were sensed by standard ECG leads connected to a Philips Intellivue Monitor MP70. Percent hemoglobin oxygen saturation (%SaO2) was measured by a Masimo Radical-7 pulse oximeter. Heart rate, respiratory rate, and oxygen saturation were monitored and measured across all five periods of observation (baseline, prefeed, during feeding, recovery and post feeding) for both feeding positions.

Utilizing a SatShare™ cable, the Radical-7 pulse oximeter interfaced with the SpO2 input of the Intellivue monitor. This connection instantly upgraded the conventional pulse oximetry of the Intellivue monitor to Masimo SET pulse oximetry. A RS232 board was inserted by a clinical biomedical engineer into the Intellivue neonatal monitor; this was used to export data. The Intellivue monitor was then connected to a laptop computer via a serial connection using a RJ45 to USB connection for data collection.

Software was available to export and store data from the Intellivue monitor. For the Philips monitor, ixTrend is the recommended software package. ixTrend is a software application for data acquisition from patient monitors that acquires, visualizes, and stores vital sign parameters. The software has the ability to export the data in different file-formats (i.e. Excel or Dataport).

**Respiratory waveform**. Cardiorespiratory bedside monitoring and pulse oximetry are commonly used to evaluate cardiopulmonary stability and oxygen saturation in hospitalized preterm infants. Therefore, use of these monitors in this doctoral study to measure the physiologic outcomes (heart rate, respiration rate, oxygen saturation), was clinically sound. However, changes in these parameters may not be substantial enough to demonstrate statistical significance. A more precise method of measuring physiologic stability across time may lead to more precise applications of feeding interventions. This research study therefore extracted respiratory data from the Intellvue monitor using the respiratory waveform· Mat Lab is a computer software program that is capable of analyzing waveforms. Data was examined using MatLab to determine if the wave form via the use of nonlinear methods provided clinically relevant data regarding respiratory variability/rigidity during feeding of preterm infants.

**Behavioral state.** The Anderson Behavioral State Scale (ABSS) is a standard assessment of an infant using a 12 category scale that was used for assessments of behavioral state. Behavioral state at the beginning of the observation was determined and recorded. All changes in state were recorded throughout the observation. Infants were ineligible for feeding if scores on the ABSS are less than a 5 (drowsy) or greater than a 10 (fussing). Inter-observer reliability of the researcher's ability to administer the ABSS was established prior to initiation of study (IRR = 90%).

Physiologic stability and behavioral state were filmed and recorded for the duration of the feeding. The ixTrend software program was time stamped to sync data from video tape recording to monitor output. All equipment was calibrated to a known signal with assistance of the Hartford Hospital Biomedical Engineering Department.

**Neonatal disease severity scoring**. Neonatal disease severity scores (SNAPPE-II) were used to quantity the morbidity of infants in this study. The SNAPPE-II is a neonatal disease scoring system often used in NICUs to predict neonatal mortality (Ramirez, Godoy, & Barrientos, 2014). The period of data collection is the first 12 hours of life and the measured variables include mean blood pressure, lowest temperature, PO/$FiO_2$ ratio, serum pH, seizures, urine output, birth weight and Apgar scores (Darling, Field & Manktelow, 2004). Numbers for each variable are then entered in an online computerized system and risk scores are calculated. SNAPPE-11 scores are correlated to risk of mortality (Appendix D, p. 170).

Neonatal disease severity scores were obtained after data collection on 9 of the 12 infants. After initiation of the study, the hospital where the research was being conducted upgraded to an electronic health records system; and obstetrical data from the original three infants enrolled in the study was lost to follow-up.

**Volume intake and duration of feeding.** Total volume of milk (formula or breast milk) consumed and total time period of feeding were measured at the end of the feeding.

***Volume intake.*** Total amount of feeding consumed were measured in milliliters. Volume intake was measured by subtracting the amount of formula/breast milk remaining in the standard hospital volufeeder at the end of the feeding from the amount of formula/breast milk prescribed at the beginning of the feeding.

*Proficiency (Pro)*. Proficiency was defined as the percentage taken during the first five minutes per milliliter prescribed. Proficiency has been described as an index of oral motor skill since its measurement is take at a time when fatigue is expected to be minimal (Pickler et al., 2005).

*Rate of milk transfer (RT. Rate of milk transfer)* measured as milliliters/minute over an entire feeding and was used an index of endurance.

*Oral feeding performance (OT)*. Oral feeding performance was the percentage of milliliters taken during the feeding per milliliters prescribed as is a reflection of oral motor skill as well as fatigue.

***Duration of feeding.*** Duration of feeding was measured as the time at completion of nutritive sucking minus the time at first presentation of the nipple, measured to the nearest half minute. Time at beginning and at completion of feeding for both oral feeding methods was marked in real time on data collection sheet, and was voice recorded on videotape. Total time of feeding was measured post hoc from the continuously recorded computer record and videotape recording.

***Measure of Feeding Position.*** Feeding position was filmed and recorded for the duration of the oral feeding. Semiupright feeding specified that the preterm infant be held with the trunk and head up to approximately 70 degrees in relation to the feeder's lap. Elevated sidelying feeding specified that preterm infant be held perpendicular to the feeder, with the trunk and head up to approximately 45 degrees in relation to the feeder's lap. A goniometer was used to verify the feeding position angle and adjustments were made by the researcher if position angle varies greater than 5 degrees. A goniometer is a tool commonly used by physical therapists to measure joint angles. The primary investigator is a pediatric physical therapist with over 25 years of clinical experience and skilled in the use of this instrument (Sweeney, Heriza, & Blanchard, 2009).

**Data Collection Management**

Data were collected with data collection tools and entered into a password protected electronic database. The electronic database was maintained by the Principal Investigator. All paper forms were kept in a locked file in the Principal Investigator's office which also was locked. Data collection for this research study was completed by December 2014.

**Roles and Responsibilities.** Research design, data collection, analysis, and interpretation were the responsibility of the Primary Investigator. Research instrumentation and methodology was developed and tested in collaboration with the biomedical engineer from Hartford Hospital. Dr. Phyllis Guarrera-Bowlby, dissertation chair, contributed to research conception, methodology, and overall advisement of the study.

**Human Subjects Protection and Ethical Conduct of Study.** Strict measures were required for respecting and maintaining patient confidentiality. To minimize risk, all medical record review were conducted according to the requirements of the Connecticut Children's Medical Center IRB. Each subject was assigned an anonymous study identifier that was used once they entered the study. The database used for the study is password protected and maintained in a secure fashion by the study PI. In addition to any institutional requirements, identifying health information as defined by HIPAA were not collected or retained on disk other than the minimal amount necessary to ensure that all eligible subjects are included and that data are accurately processed. Collection of a patient identifier such as a medical information number, for example, was necessary to ensure comprehensive inclusion of eligible subjects and accurate linking of data from different data sets. Once data collection was complete and the data set frozen for analysis, the data set was entirely de-identified. For example, medical record numbers were deleted and replaced with a unique identifier created for this study. De-identification of the data set will take place at the time of IRB closure. It is expected that these measures minimize any risk to confidentiality very effectively.

**Data Utilized for Statistical Analysis**

The measured dependent variables were volume consumed (ml), time required to complete feeding (min); respiratory pattern variability and percentage of total feeding time spent outside of acceptable physiologic range for each of the following variables: hemoglobin oxygen saturation (%SaO2); respiratory rate (rpm) and heart rate (bpm). Coefficients of variation were calculated for all variables.

Analysis began by examining the data to assess for normal distribution to determine if variables satisfy assumptions of parametric tests. If these assumptions were not met, then non- parametric tests were used. Data from the Microsoft Excel database was transferred into SPSS for data analysis and summary statistics were calculated. Descriptive statistics were used to characterize the sample and the feeding characteristics of the sample. For Aim #2 (infant feeding outcomes) volume of feeding consumed, overall time of feeding and percentage of prescribed feeding volume were calculated and the means and standard deviations compared.

For Aim #1 (measure infant outcomes related to body position during feeding), Aim #3 (measure infant behavioral state related to body position during feeding) and Aim #4 (measure of respiratory wave pattern related to body position during feeding): these hypotheses were tested using a repeated measures ANOVAs followed with post hoc t-tests, to test if there are any significant differences in dependent variables (heart rate, respiratory rate, respiratory pattern, oxygen saturation and behavioral state) between the two different positions during bottle feeding. No infants were assigned to the alternative research design in the study.

Variables of gestation age, postmenstrual age, days of life at time of study, neonatal morbidity, level of alertness, nursing experience and sequence of feeding, were used in a covariate analysis.

Respiratory waveform was submitted to nonlinear analysis using MatLab to calculate Approximate Entropy (an indicator of rigid versus adaptable behavior). The mathematical equation was correlated to clinical variables to identify the factors that were determining the pattern of the waveform.

**Reliability and Validity**

This study has a number of strengths that contribute to its reliability and validity. The within subject design controls for the potential influence of individual subject characteristics, which decreases threats to internal validity. History and maturation are theoretical limitations but were controlled by using a within-subject design and by making positional comparisons conducted in a short period of time (i.e. one day). Data collection instrumentation was calibrated by biomedical engineering to ensure reliability. Consistency in electrode placement accounted for movement artifact regarding cardiopulmonary monitoring and a process (Masimo Set Technology quality signal indicator) was employed to ensure accuracy of pulse oximeter measures. A detailed protocol and training ensured consistency between feeders. The use of videotaping and a goniometer promoted consistency of positioning.

Study variables were clearly identified and operationally defined, which improve construct validity. The application of theories of the nonlinear properties of respiration and the dynamic systems theoretical framework improve the study's criterion validity. All data analyses meet the assumptions of the statistical tests chosen to measure the intended outcomes. Intervening variables such as different feeders and years of nursing experience, were anticipated and addressed by the pilot study, pretesting instrumentation and through research design. Cardiopulmonary monitors were calibrated by biomedical engineering and interrater reliability was established for the use of the Anderson Behavioral State Scale.

Limitations included generalizability or external validity, due to subject selection as infants selected were a convenience sample. Additionally, this study was limited to a narrow population as only healthy preterm infants were included due to exclusion criteria. The small sample size in this study limits the strength of the findings.

However, the enrollment of 12 infants and 24 feedings was justified based on power analysis.

**Importance of Topic**

This topic is of importance to health care professionals working with high risk infants in the neonatal intensive care unit. Postural stability provides a base for feeding skills. Positioning is designed to support the musculoskeletal system biomechanically and thereby improve work of breathing. Knowledge of therapeutic positioning that promotes musculoskeletal alignment, impacts physiologic function, and is optimal for bottle feeding premature infants is essential. Results of this study provided information on optimizing infant position during feeding. Quantitatively documenting the physiologic response to feeding provided information that may be used by nursing and neonatal therapists to support infants in order to feed successfully. Benefits for the infant may therefore include: improved cardiorespiratory response to enteral feeding, reduced fatigue with oral feeding, improved nutritional intake and/or improved behavioral response to handling and position change. In addition, suggestions for positioning the infant and modifications in response to behavioral state and cardiopulmonary outcome, were provided to caregivers so they may also assist their infant in making a smooth transition from gavage to bottle feeding.

# Chapter IV

## Results and Findings

This chapter presents the findings of the study. Characteristics of the study infants and descriptive statistics are presented first. Following the descriptive statistics, the results of ANOVA tests to address specific aims and related hypothesis are given along with pertinent post hoc t-test comparisons. Correlation analyses are presented last.

### Characteristics of Study Infants

Fourteen infants who were admitted to the Newborn Intensive Care Unit at Connecticut Children's Medical Center (CCMC) were enrolled in the study. Two infants failed to complete the study as they progressed to consecutive bottle feedings. Therefore, the final sample consisted of twelve preterm infants, all of whom were in transition from gavage feeding to bottle feeding at the time of the study. All infants had completed at least one oral feeding trial (25-50% of prescribed volume feeding) for no less than 24 hours and no longer than 72 hours, prior to initiation of the observation. Gestational age at birth ranged from 27. 3 to 34.0 (M= 31.5 +/- 1.9) weeks. Four of the infants were female and most infants were white. Half of the infants were twins (3 sets of twins). Gender and race/ethnicity of the infant sample were closely representative of the demographics of the CCMC NICU. The infants' characteristics are summarized in Table 1.

At the time of the testing, the postmenstrual age of the infants ranged from 34.3 to 35.5 (M= 35.1 +/- .4) weeks and chronological age from 7 to 49 (M= 25 +/- 12) days of life. All infants were medically stable upon entry into the study; breathing room air, off intravenous fluids and on full enteral feeds. None of the infants had documented reflux. Two infants were on caffeine at the time of the study.

**Descriptive Statistics**

The effect of position on cardiopulmonary outcomes and feeding performance during bottle feeding was compared between the elevated sidelying position and semiupright position. Each of the two feedings were divided into five periods of observation: a two minute prefeeding supine, a two minute prefeeding semiupright/elevated sidelying, bottle feeding in semiupright/elevated sidelying, a two minute post feeding semiupright/elevated sidelying and a two minute post feeding supine. Changes in physiologic stability and feeding performance were analyzed across the ten phases of both feedings. Post hoc analyses were performed based on valuation of means.

Cardiopulmonary outcomes (heart rate, respiratory rate and percent hemoglobin oxygen saturation) and feeding performance were then analyzed by sequence of feeding (first feeding versus second feeding) to assess the effect of order of position.

**Cardiopulmonary outcomes.** Heart rate (beats per minute), respiratory rate (breaths per minute) and percent hemoglobin oxygen saturation (%SaO2) were measured continuously across all five periods of observation (baseline, pre-feed, during feeding, recovery and post feeding) for both feeding positions.

**Feeding performance.** Total volume of milk (formula or breast milk) consumed and total time of period of feeding were measured at the end of the feeding. Total volume intake included measures of: 1) proficiency (the percentage taken during the first five minutes), 2) rate of milk transfer (milliliters/minute over an entire feeding) and 3) oral feeding performance (percentage of milliliters during the feeding per milliliters prescribed).

**Respiratory waveform.** Respiratory waveform variability was measured using Approximate Entropy (ApEn), a statistical measure of the change in complexity of physiologic processes. The respiratory waveform is a measure of impedance and an indirect measure of respiratory waveform variability. Variability was calculated for one minute intervals across each of the periods of observation.

## Specific Aims and Hypotheses

The aim of this dissertation study was to measure infant cardiopulmonary physiologic outcomes related to body position during feeding. Analysis began by examining the data to assess for normal distribution to determine if variables satisfy assumptions of parametric tests. When assumptions of normality were not met, nonparametric statistics were used.

**Specific Aim 1.** Measure infant cardiopulmonary physiology outcomes related to body position during feeding. The mean, standard deviation and coefficient of variance were calculated for each physiologic variable (heart rate, respiratory rate, percent hemoglobin oxygen saturation), for each of the feeding phases, for both feedings. Percentage of time outside the acceptable physiologic range for each of these variables was also computed. Post hoc analyses were run to assess the effect of position, before the influence of feeding (baseline supine to prefeeding semiupright/elevated sidelying).

*Heart rate*. There was a statistically significant difference in average heart rate between semiupright and elevated sidelying across the ten phases of feeding (F=2.067, df= 9, p=.040), with an increase in heart rate in sidelying. Post hoc analysis revealed the significance was between baseline semiupright and recovery phase in sidelying; and between prefeeding semiupright and recovery sidelying. These comparisons were unrelated, therefore, there was no clinically significant difference in mean heart rate between the semiupright and sidelying positons across the ten phases of feeding.

Additional post hoc analysis revealed no significant difference in mean heart rate for: a) feeding in semiupright versus sidelying, b) baseline semiupright to post feeding semiupright, c) nor any phase of the feeding observation comparing semiupright to sidelying. There was trend toward a significant increase in mean heart rate from baseline sidelying to post feeding sidelying (t=1.855, df=11, p=.091). Assessment of the effect of change of position reveal no significant difference from supine baseline to prefeeding for semiupright nor sidelying.

*Respiratory rate*. There was a trend toward a difference in mean respiratory rate between semiupright and sidelying (F=1.768, df=9, p= 0.084). Post hoc analysis revealed a significant difference in mean respiratory rate, increasing from baseline to post feeding in sidelying (t= -2.180, df=11, p= 0.052) but not from baseline to post feeding in semiupright (t= -1.303, df= 11, p= 0.219).

There was a significant increase in mean respiratory rate in response to change in position from baseline in supine (M=43.3 bpm +/- 6.2) to sidelying (M=52.0 bpm +/- 12.3), (t=2.561, df=11, p= 0.026) without the effect of feeding; but not for change in position from supine (baseline) to semiupright (t=.138, df=11, p= 0.892).

*Percent hemoglobin oxygen saturation.* There was no significant difference in mean percentage of oxygen saturation between the semiupright and sidelying positions across the ten phases of feeding.

*Coefficient of Variance*. Coefficient of variances were calculated to measure relative variability. Heart rate, respiratory rate and percent hemoglobin oxygen saturation did not vary significantly between semiupright and sidelying across the ten phases; and did not vary significantly by sequence of feeding (first feeding versus second feeding).

*Sequence of Feeding.* The effect of sequence of feeding, first feeding versus second feeding regardless of position, was analyzed. No significant difference was found between the first feeding as compared to the second feeding for the heart rate, respiratory rate and percent hemoglobin oxygen saturation.

Post hoc analysis based on means revealed a significant difference in mean respiratory rate from baseline to post feeding after the second feeding ($t=2.258$, $df=11$, $p= 0.045$). This increase in average respiratory rate (53 bpm to 64 bpm) may be due to increased work of breathing and fatigue.

*Percentage of time outside of acceptable physiologic range*. There was no significant difference in percentage of time outside of acceptable physiologic range for heart rate, respiratory rate, and percent hemoglobin oxygen saturation regardless of position or sequence of feeding.

Post hoc analysis based on means revealed a significant percentage of time spent with respiratory rate greater than 60 bpm during the post feeding phase of the second feeding compared to baseline ($t=2.527$, $df=11$, $p= 0.028$).

There was a trend toward an increased percentage of time spent with $SaO_2$ <95% during the second feeding as compared to the first feeding (1.99% vs. 10.39%, $p=.087$).

**Specific Aim 2.** Measure infant feeding outcomes related to body position during feeding.

There was no significant difference in feeding performance measures: proficiency, rate of milk transfer, or oral feeding performance between semiupright and sidelying during bottle feeding. There was a significant difference in duration of feeding ($t=2.632$, $df=11$, $p= 0.023$). Infants fed longer in the semiupright position (M=15.7 minutes +/- 3.2) as compared to the sidelying position (M= 12.0 minutes +/- 3.2). Feeding outcomes related to body position during feeding are presented in Table 2.

**Specific Aim 3.** Measure infant behavioral state related to body position during feeding. There was no significant difference in level of alertness in the semiupright position compared to the sidelying position. The effect of sequence of feeding on behavioral state was analyzed. There was a significant difference in level of alertness between the first feeding and the second feeding regardless of position ($t=2.191$, $df=11$, $p=0.051$). Infants were more alert during the first feeding as compared to the second.

**Specific Aim 4.** Measure infant respiratory waveform variability related to body position during feeding. Since the overall variability was not significant, Approximate Entropy, a measure of complexity, was used to look more carefully at variability and how the waveform changes when the infants were fed in semiupright versus sidelying. Respiratory waveform characteristics were measured continuously across all five periods of observation for both feedings. Respiratory waveform variability was calculated for one minute of each of four phases (baseline, prefeeding, post feeding, recovery) and for one minute intervals at the beginning, middle and end of the feeding phase; and analyzed across the phases of both feedings. There was no significant difference in respiratory waveform variability between the semiupright and sidelying positions across the phases of feeding ($F=.572$, $df=13$, $p= 0.872$). However, as this was an exploratory study, power for respiratory variability was low (power = 0.325) and may mean that the available evidence is not strong enough to demonstrate statistical significance. Therefore, infants' respiratory waveforms were examined based on valuation of means and characteristics of variability.

**Directional Hypotheses**

Correlation analyses were performed to address three directional hypotheses.

**Directional hypotheses 1.** Infants who were more physiologically stable would feed more efficiently. The Spearman rank correlation coefficient ($r_s$) was used to test the correlation between cardiopulmonary outcomes and: gestational age, postmenstrual age, days of life, measures of feeding performance, sequence of feeding, neonatal morbidity and level of alertness. Correlation was significant at the 0.05 level (1-tailed). This nonparametric statistic was appropriate to use with ordinal data and the best choice for a small sample set (Portney & Watkins, 2009). Results of analyses correlating coefficient of variance were presented as this study hypothesized that there would be differences in the variability, reflected in the CV as opposed to the overall mean.

*Coefficient of variance heart rate (CV HR).* CV for heart rate was negatively correlated with gestational age ($r_s$= -.334, p= 0.032), rate of milk transfer ($r_s$= -.448, p= 0.014) and oral feeding performance ($r_s$= -.587, p= 0.001); and positively correlated with days of life ($r_s$= .446, p= 0.014). There was a trend toward an association between CV HR and neonatal morbidity ($r_s$= -.344, p=.081). Babies who were born younger and who were chronologically older at the time of the study had a higher heart rate across phases of feeding. Heart rate is associated with rate of milk transfer and oral feeding performance.

Infants who had higher neonatal morbidity scores tended to have lower variance in heart rates across phases of feeding.

*Coefficient of variance respiratory rate (CV RR)*. There was an association between CV RR and age of time of study ($r_s$= .353, p= 0.046). There was a trend toward a negative correlation between CV RR and 1) gestation age ($r_s$= -.320, p= 0 .064) and 2) rate of milk transfer ($r_s$= -.319, p= 0.064). There was no significant association between CV RR and neonatal morbidity.

Babies who were chronologically older at the time of the study had a higher respiratory rate across the phases of feeding. Babies who were born younger tended to have a higher respiratory rate. The higher the respiratory rate, the trend toward lower rate of milk transfer.

**Directional hypotheses 2.** Infants at a younger gestational age and younger postmenstrual age would demonstrate a larger percentage of time outside of the physiologic range for heart rate, respiratory rate and percent hemoglobin oxygen saturation when positioned in semiupright as compared to sidelying. The Pearson correlation coefficient (r) was used to test the association between percentage of time outside of the acceptable physiologic range during feeding and: gestational age, postmenstrual age and days of life at the time of the study.

*Percentage of time spent outside of acceptable physiologic range*. Percentage of time outside of the acceptable physiologic range during feeding, was compared between the semiupright and elevated sidelying position based on gestational age, postmenstrual age and days of life at time of the study.

*Respiratory rate less than 30 breaths per minute(bpm)*. The younger the gestational age the more time spent with the respiratory rate (RR) less than <30 bpm in sidelying (r=-.488, p= 0.054). The younger the postmenstrual age, there was a trend toward more time with RR <30 bpm in sidelying (r=-.432, p= 0.080). The greater the number of days of life the more time spent with RR <30bpm in sidelying (r=.679, p= 0.008). There was no significant correlation between gestational age, postmenstrual age nor days of life for RR<30 bpm during feeding in semiupright.

*Respiratory rate greater than 60 bpm*. Days of life was negatively correlated with RR >60 bpm in sidelying (r=-.490, p= 0.053). The greater the DOL the less likely to increase RR; more likely to become apneic. There was no correlation between gestational age or postmenstrual age and the percentage of time spent with RR >60 bpm in sidelying. There was no correlation between gestational age, postmenstrual age nor days of life and percentage of time spent with RR >60 bpm in semiupright.

*Heart rate greater than 160 bpm.* There was no correlation between gestational age or postmenstrual age or days of life at time of study and percentage of time spent with HR >160bpm during feeding in sidelying. There is no correlation between postmenstrual age nor days of life and percentage of time spent with HR >160 during feeding in semiupright. The younger the gestational age, there was a trend toward a greater percentage time spent with HR >160 during feeding in semiupright ($r=-.444$, $P= 0.074$)

*Heart rate greater than 180 bpm.* There was no correlation between gestational age or days of life and percentage of time spent with HR >180 bpm during feeding in either the sidelying or semiupright position. The younger the postmenstrual age, there is a trend toward a greater percentage of time spent with HR >180 bpm in both sidelying and semiupright.

*Percent hemoglobin oxygen saturation less than 95%.* There was no correlation between gestational age, postmenstrual age and days of life at time of study and percentage of time spent with $SaO_2$ <95% in either sidelying or semiupright.

**Directional hypothesis 3**. There will be a difference in respiratory variability when infants are fed in semiupright versus sidelying based on postmenstrual age. The Pearson correlation coefficient (r) was used to test the association between respiratory variability during feeding and: gestational age, postmenstrual age and days of life at the time of the study. The Spearman rank correlation coefficient ($r_s$) was used to assess the effect of sequence of feeding. There was no significant association between respiratory waveform variability and gestational age, postmenstrual age, days of life or sequence of feeding.

**Secondary correlation analyses.** Secondary analyses was done to measure the association between covariates: gestational age, postmenstrual age, days of life, measures of feeding performance, sequence of feeding, level of alertness and years of nursing experience) using the Spearman rank correlation coefficient ($r_s$). Gestational age, postmenstrual age and day of life are interdependent and were all positively correlated.

*Gestational age*: Gestational age was negatively correlated with duration ($r_s$= -.441, p= 0.016) and positively correlated with rate of milk transfer ($r_s$= .473, p= 0.010). There was a trend toward an association between gestational age and proficiency ($r_s$= .378, p= 0.061). The younger the baby at birth the less time spent orally feeding.

The younger the baby at birth the faster the rate of milk transfer (or more endurance) and there is a trend toward more proficiency.

*Postmenstrual age.* There was a trend toward an association between babies' age at the time of the study and rate of milk transfer ($r_s$= .293, p= 0.083. Babies who are older at the time of the study tended to have a higher rate of milk transfer (endurance).

*Days of Life.* Chronological age was negatively correlated with proficiency ($r_s$= -.527, p= 0.012), rate of milk transfer ($r_s$= -.521, p= 0.005) and oral feeding performance ($r_s$= -.363, p= 0.041. Babies who were chronologically older at the time of the study were less proficient (less oral motor skills), had less endurance and less overall volume intake.

*Oral Feeding Performance.* Oral feeding performance was positively correlate with proficiency ($r_s$=.589, p= 0.012), rate of milk transfer ($r_s$= .794, p= 0.000) and duration of feeding ($r_s$= .484, p= 0.008). There was an association between proficiency and rate of milk transfer ($r_s$= .863, p= 0.000).

*Duration.* Duration was positively correlated with oral feeding performance ($r_s$= .484, p= 0.008). The longer a baby orally fed the more overall volume intake.

*Sequence of feeding.* Sequence of feeding was significantly associated with oral feeding success. Sequence of feeding was negatively correlated with proficiency ($r_s$= -.529, p= 0.012), rate of milk transfer ($r_s$=-. 521, p= 0.029) with a trend toward oral feeding performance ($r_s$= -.363, p= 0.072). Infants demonstrated less oral motor skills (less proficiency) and a lower rate of milk transfer (less endurance) with a trend toward lower volume intake after the second feeding as compared to the first. Feeding outcomes related to sequence of feeding are presented in Table 3.

*Level of alertness.* There was no significant correlation between behavioral state scores on the ABSS and oral feeding outcomes (proficiency, rate or milk transfer, oral feeding performance nor duration).

*Nursing experience*. Years of nursing experience and years of neonatal nursing experience were both associated with oral feeding success. Years of nursing experience was positively correlated with proficiency ($r_s$= .788, p= 0.000), rate of milk transfer ($r_s$= .691, p= 0.000) and oral feeding performance ($r_s$= .454, p= 0.013). Neonatal nursing experience was positively correlated with proficiency ($r_s$= .712, p= 0.000) and rate of milk transfer ($r_s$= .458, p= 0.012) with a trend toward improved oral feeding performance ($r_s$= .330, p= 0.057). Duration of feeding was not associated with years of nursing or neonatal nursing experience.

**Respiratory Waveform Variability: An Exploratory Analysis**

Respiratory waveform is a measure of thoracic impedance and an indirect measure of respiratory variability. Transthoracic electrical Impedance is a measure of resistance and the signal is obtained by two electrocardiogram electrodes placed on the surface an infant's chest. The electrodes are measuring the electric potential generated by electrical activity in the cardiac tissue. The monitor uses the values to calculate the relative change in impedance based on chest movement that occurs during inspiration and expiration. This measurement is based on the knowledge that air has a much higher level of impedance than tissue (Di Fiore, 2004). The electrodes detect increases in impedance as the air-to-tissue ratio changes with air entering the lungs during an inspiratory effort. Since the waveform is a reflection of impedance, as the chest expands during inspiration there is an increase in impedance (positive slope). The more air inhaled the higher the impedance as the air-tissue ratio is higher. The changes in numeric value equate to the rise in impedance until a maximum impedance level is reached, and then there is a drop toward negative numbers as exhalation occurs (Figure 1). The change in impedance during respiration can be very small in relation to the baseline thoracic impedance (Martin, Fanaroff & Walsh, 2011).

Figure 1. Electrophysiologic Anatomy of a Single Breath

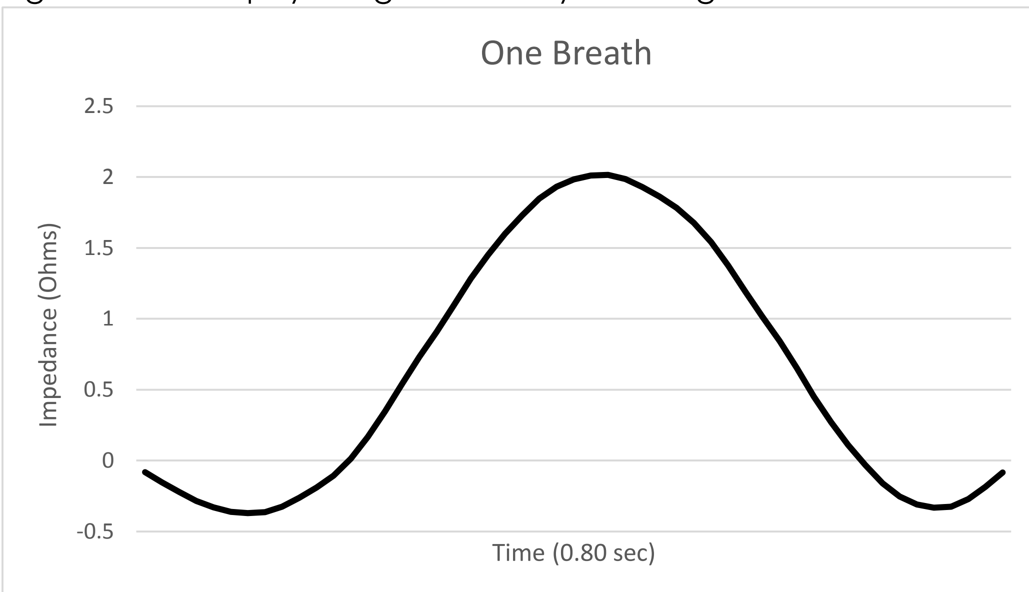



Figure 1. One breath (full inspiration to full expiration)
The positive slope of the graph indicates inspiration. The maximum value of impedance is the peak of inspiration (2.016 Ohms), then the values drop as the infant exhales until the impedance reaches a minimum which is the peak of expiration (-.085 Ohms) $V_I$= .4 seconds RR= 49 bpm

**Approximate Entropy (ApEn)**. Approximate Entropy (ApEn) was used to determine if nonlinear methods of analyses of respiratory waveforms, would provide clinically relevant data regarding respiratory variability.

The formula for ApEn used was $ApEn = \Phi^{m}(r) - {}^{m+1}(r)$. Two input parameters, m and r, must be fixed to compute ApEn: m is the “length” of compared runs, and r is effectively a filter. For fixed m and r, both the parameter (the true number, expressed as a limit) ApEn (m,r), and the statistical estimate ApEn (m,r,N) were defined. ApEn was calculated with m=2 and r= 0.6 beats /min and N samples typically ranging from 1000 to 7000 sample points for the analysis. The values were chosen to be consistent with guidelines for implementation of ApEn formula on heart rate tracing of infants (Lake et al., 2002; Pincus & Goldberger, 1994; Seeley & Macklem, 2004). ApEn values of complexity range from 0 to 1, whereby reduced values are associated with rigidity or less variability and values closer to one represent more adaptability in the system.

Respiratory waveform variability was calculated on ten of the twelve subject infants. Two infants were on caffeine and Approximate Entropy was zero. Therefore these infants were considered outliers and data was disregarded for analysis.

**Approximate Entropy means across phases**. Approximate Entropy means across all the phases of feeding ranged from (ApEn= 0.005 to 0.01). The most rigid phase was during the change from baseline to prefeeding in sidelying. The most variability in respiration was noted during the recovery phase after feeding in semiupright. Approximate Entropy across phases is depicted in Figure 2.

Figure 2. Comparison of Approximate Entropy across Phases

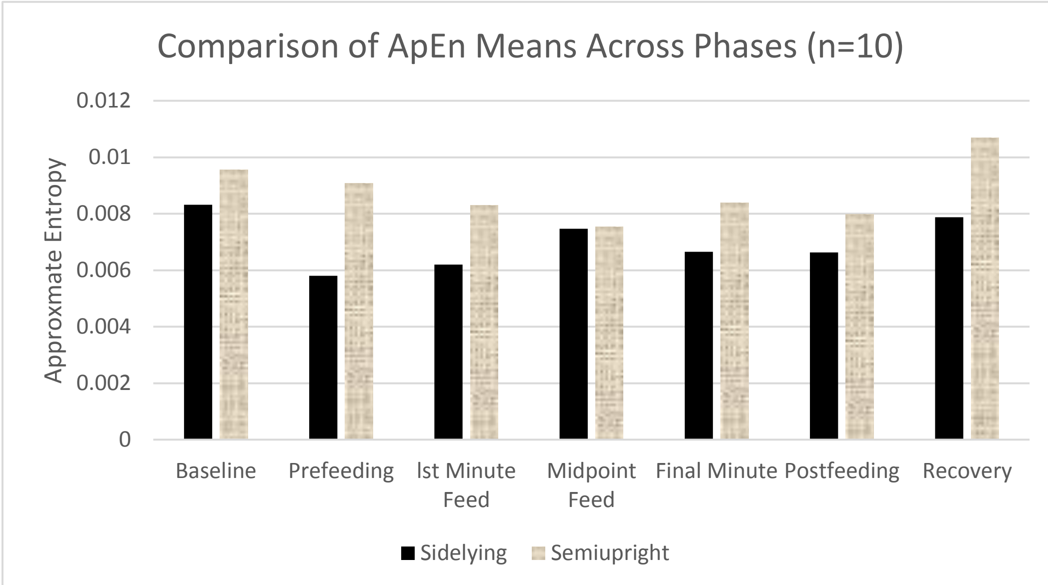
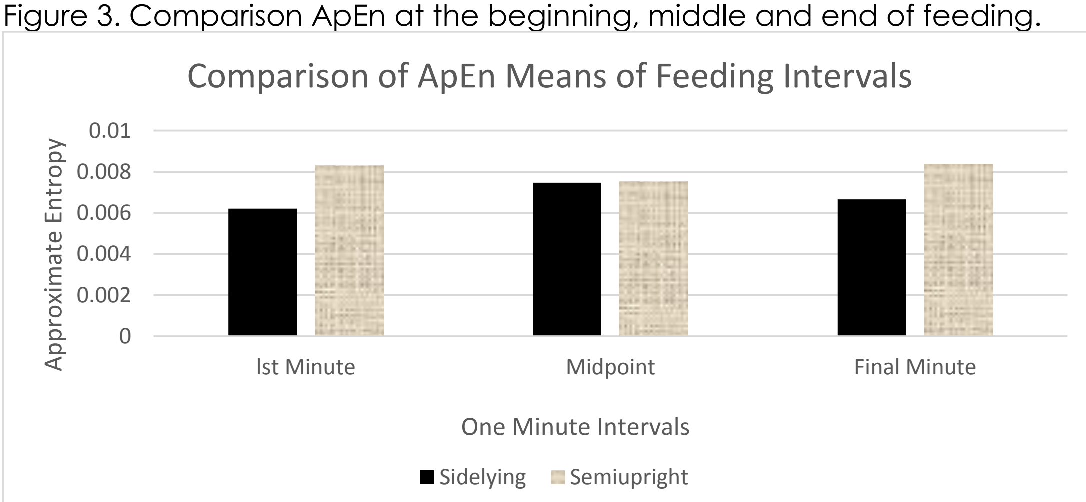



Figure 2. Approximate Entropy means compared between sidelying and semiupright across all the phases of feeding.

**Approximate Entropy between feeding positions**. There was no significant difference in respiratory variability between the beginning, midpoint or end of the feeding; nor in feeding intervals between sidelying and semiupright (Figure 3).

Figure 3. Comparison ApEn at the beginning, middle and end of feeding.



**Fidelity of one minute intervals**. Fidelity of Approximate Entropy values for one minute intervals at the beginning, middle and end of the feeding was validated as accurately representing the mean respiratory variability across the full duration of the feeding phase (Figure 4).

Figure 4. Comparison of Feeding Minute Intervals and Full Feeding

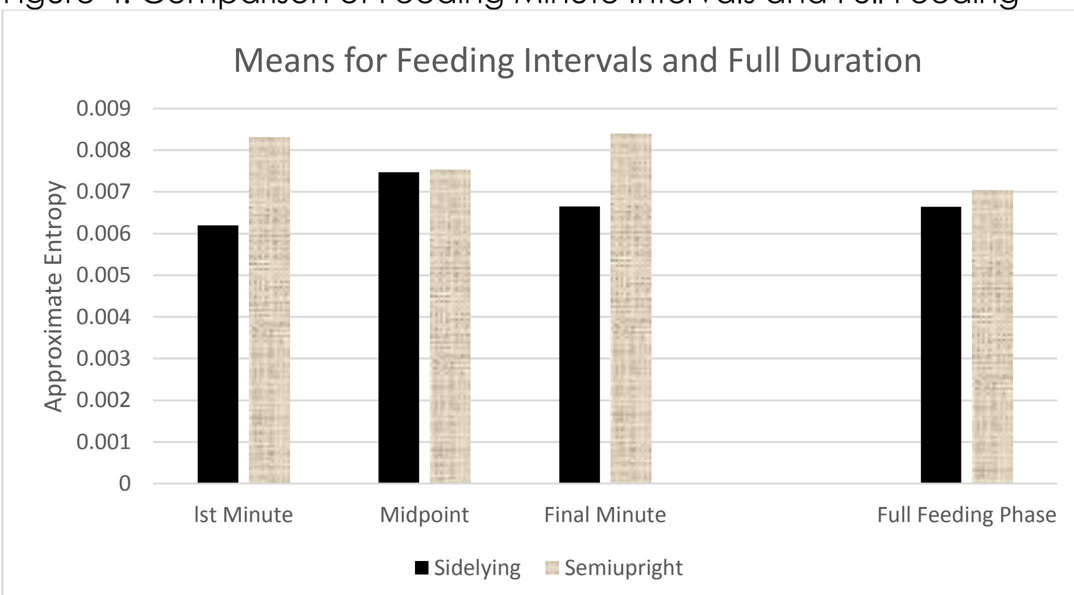



Figure 4. Measures of feeding at one minute intervals was validated as accurately representing the mean respiratory variability across the full duration of the feeding phase.

**Variability during feeding between positions.** Infants' respiratory variability was compared between sidelying and semiupright during the full duration of the feeding. The mean Approximate entropy value was comparable between the elevated sidelying (M= 0.0066) and semiupright positions (M=0.0070), with a trend toward more variability in semiupright (Figure 5).

Figure 5. Respiratory Wave Variability Range by Position

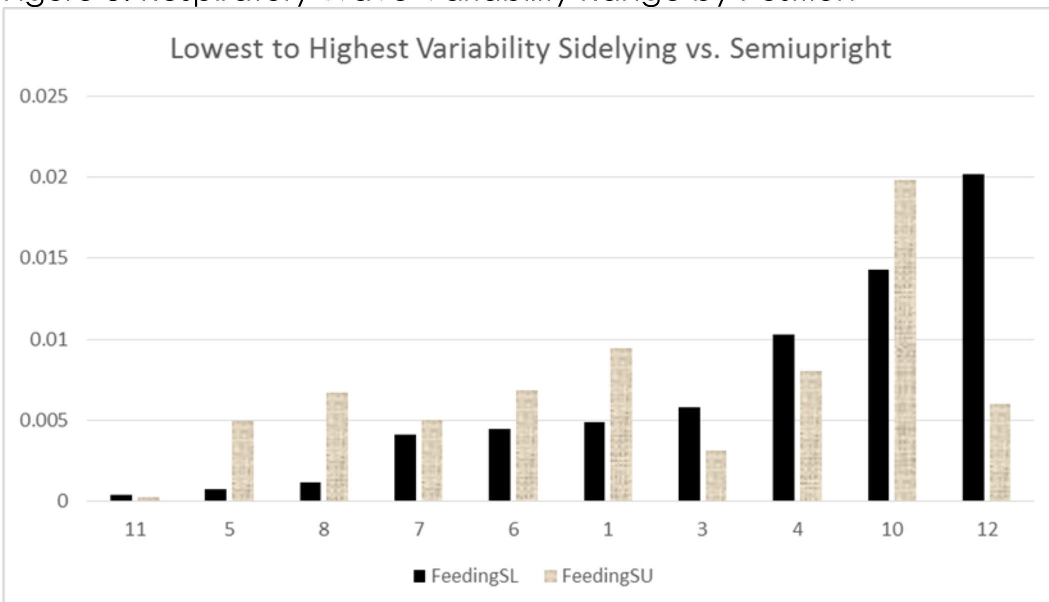
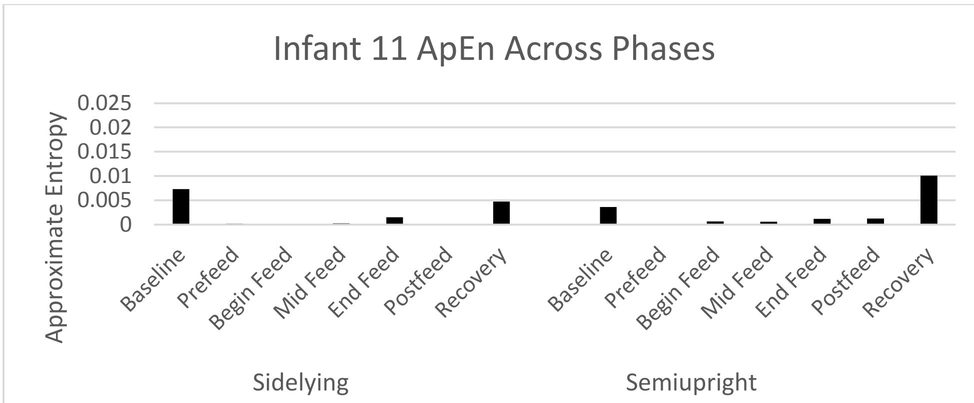
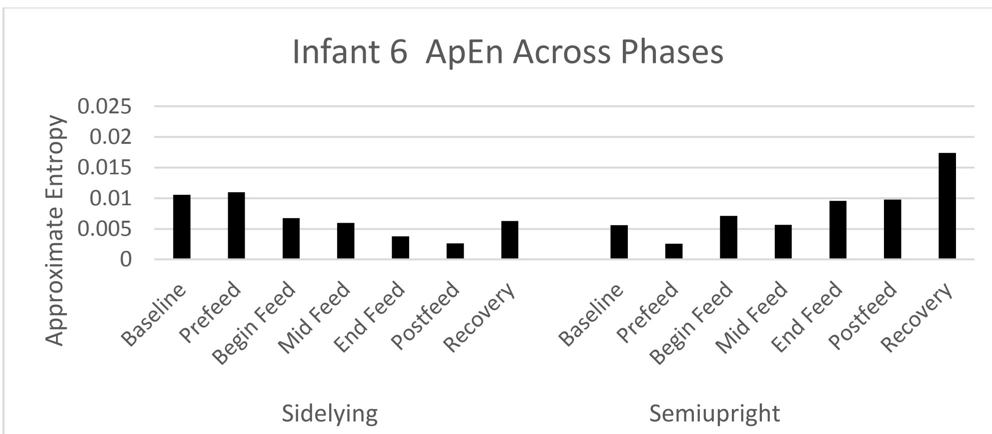



Figure 5. Respiratory variability compared between sidelying and semiupright during the full duration of the feeding revealed a trend toward more variability in semiupright.

**Approximate Entropy means between infants.** Respiratory waveform characteristics were further explored comparing the infant with the least (infant 11), average (infant 6) and most (infant 10) variability across phases of observation (Figure 6). Appendix E (p. 172) graphically depicts the variability in waveform between the least, average and most variable infants for the first feeding.

Figure 6. Comparison of Sample Infants' Approximate Entropy across Phases



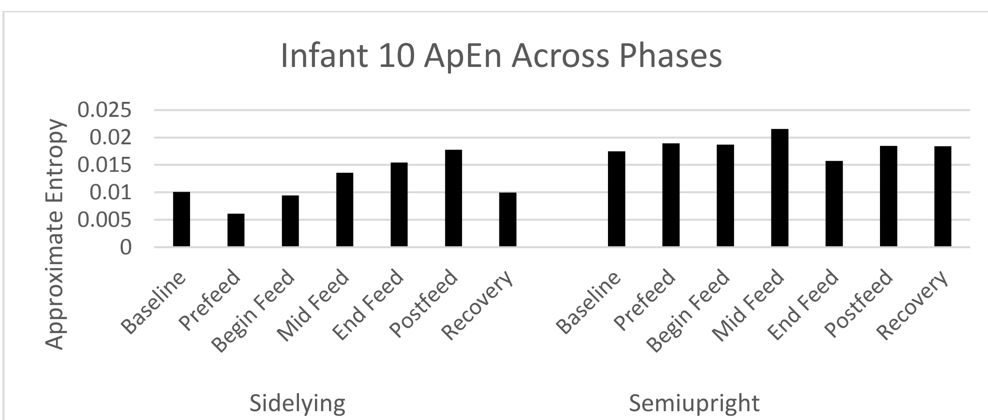




Figure 6. Respiratory waveform characteristics comparing the infant with the least (infant 11), average (infant 6) and most (infant 10) variability across phases of observation.

# Chapter V

## Discussions, Conclusions and Recommendations

This final chapter presents an interpretation of the results in relation to the theoretical framework and purpose of the study. Findings are examined in relation to prior research. The importance of the results, limitations of the study, clinical implications and suggestions for future research are discussed.

### Interpretation of the Results

The effect of position (semiupright and elevated sidelying) on cardiopulmonary outcomes and oral feeding performance during bottle feeding in preterm infants was investigated during this research study. The theoretical framework proposed that positioning impacts cardiopulmonary outcomes based on characteristics of a preterm infant's developing musculoskeletal system and limited capacity for respiration during oral feeding. Due to the immaturity of the preterm infant's musculoskeletal and cardiorespiratory systems, infants demonstrate decreased efficiency of ventilation and often fatigue, limiting efficiency during oral feeding. Therapeutic positioning was suggested as a potential intervention strategy to support respiration during feeding.

**Cardiopulmonary outcomes**. Measures of infant cardiopulmonary outcomes related to body position during feeding (heart rate, respiratory rate and percent hemoglobin oxygen saturation) examined the concept that infants' respiratory mechanics and cardiopulmonary function may be affected by positioning. However, the principle findings related to cardiopulmonary physiology revealed no significant difference in heart rate, respiratory rate or percent hemoglobin oxygen saturation between the semiupright and elevated sidelying position during oral feeding in healthy preterm infants. The infants' respiratory waveform did not vary significantly between positions during bottle feeding. Additionally, heart rate, respiratory rate and percent hemoglobin oxygen saturation did not vary significantly by sequence of feeding (first feeding versus second feeding).

In contrast, respiratory rate increased significantly in response to change in position from supine to sidelying prior to feeding; but not for change in position from supine to semiupright. Also, the average respiratory rate and percentage of time spent with respiratory rate greater than 60 bpm increased from baseline to post feeding after the second feeding. This increase in respiratory rate may be due to increased work of breathing and fatigue. A trend toward an increased percentage of time spent with SaO2 <95% during the second feeding was found and may be attributed to fatigue as well.

Further analyses supported the relationship between cardiopulmonary outcomes and infant age (gestational age, postmenstrual age and days of life at time of study). Infants who were born at a younger gestational age and who were chronologically older at the time of the study (more days of life before initiation of oral feeding) had on average a higher heart rate and respiratory rate across the phases of feeding. Also younger infants (GA and PMA) and those with more days of life before initiation of feeding, spent more time with their respiratory rate less than 30 bpm in sidelying.

**Oral feeding outcomes**. Feeding outcomes (proficiency, rate of milk transfer and oral feeding performance) did not differ significantly between the semiupright and elevated sidelying position. However, infants fed longer in the semiupright position as compared to the sidelying position. The duration of feeding may have been longer in semiupright because this is a more alerting position than elevated sidelying.

Oral feeding outcomes were associated with GA, PMA and DOL at the time of the study. Babies who were older (PMA) at the time of the study tended to have more endurance. Infants who were born at a younger GA spent less time orally feeding as compared to infants born at a later GA. Infants who were chronologically older (more DOL at the time of the study) demonstrated less oral motor skill, endurance and overall volume intake.

Sequence of feeding and years of nursing experience were related to feeding performance. Order of feeding was significantly associated with successful oral feeding. Infants demonstrated less proficiency in oral motor skills, decreased endurance and a trend toward lower volume intake after the second feeding as compared to the first. Though not associated with feeding outcomes, level of alertness was decreased in the second feeding as compared to the first suggesting fatigue and decreasing endurance related to order of feeding. More years of both nursing experience and neonatal nursing experience were correlated with oral feeding success (proficiency, endurance and oral feeding performance).

The physiologic model as a theoretical framework for the relationship between position and cardiopulmonary outcomes, suggests that either position (semiupright or elevated sidelying) may be beneficial for healthy preterm infants learning to bottle feed.

**Respiratory variability**. As there was no significant difference in mean respiration between semiupright and elevated sidelying during feeding, mean Approximate Entropy values were also comparable between positions during feeding. Approximate Entropy revealed the most rigid phase of feeding was during the change from baseline to prefeeding in sidelying. This corresponds to the finding of a significant increase in mean respiratory rate during the same periods. Therefore, the change of position from supine to sidelying (before the influence of feeding) appears to be physiologically stressful for infants. Respiratory variability was highest during the recovery phase after feeding in semiupright and almost returned to baseline; suggesting that infants fed in semiupright recover cardiopulmonary stability more easily after being feed in semiupright.

### Findings Related to Prior Studies

**Cardiopulmonary outcomes.** Similar to Daley (2002), Dawson et al. (2013) and Stevens (2007), the results of this study suggest no significant difference in cardiopulmonary outcomes comparing feeding positions. In contrast, the findings by Clark et al. (2007), Park et al. (2014) and Thoyre et al. (2012) suggest improvements in cardiopulmonary outcomes in the elevated sidelying position.

Clark (2007) found improved physiologic stability in the elevated sidelying position during the midpoint of feeding. Thoyre et al. (2012) reported physiologic stability (less SaO2 variability, less heart rate decline, less increased work of breathing) in the head elevated side lying position. In the study by Park et al. (2014), infants fed in the head elevated sidelying position showed significantly less variability in heart rate, less severe and fewer decreases in heart rate. Additionally, heart rate was more stable over time and regulated breathing improved over time in the head elevated sidelying position. No significant findings for SpO2 were found.

Inconsistences between findings of this research study and the related research studies, were differences in research design or methodology, differences in infant characteristics of sample enrolled in the study and/or limitations of the other research studies.

Infants enrolled in the study by Clark et al. (2007) were all very preterm (< or equal to 29 weeks gestation at birth) and one of the six infants was on supplemental oxygen. The study period for each of the infants ranged from one to three weeks, therefore maturation could have impacted the cardiopulmonary findings.

In the study by Thoyre et al. (2012), multiple components comprised the co-regulated approach to feeding, therefore it is difficult ascertain which component of the feeding protocol was beneficial. Additionally, infants in the control group were positioned in either semiupright or elevated sidelying at the discretion of nursing, limiting comparison of position as the factor effecting cardiopulmonary outcomes.

Infants enrolled in the study by Park et al. (2014) differed from those enrolled in the dissertation study. Like Clark et al. (2007), in the study by Park et al. (2014), all infants were very preterm (<30 weeks gestation at birth). Infants orally fed 50% of their prescribed volume for three consecutive days prior to the study observation. Therefore these infants had more experience in feeding as compared to this research study. Additionally, Park's research was a pilot study with a small sample (n=6) and therefore insufficiently powered to detect statistically significant differences at the conventional 0.05 alpha level.

Dawson et al. (2013) found no significant difference in mean heart rate, respiratory rate or oxygen saturation between the semiupright cradle hold and sidelying position. Although findings were similar, there are marked differences in methodology between the study by Dawson et al. and this dissertation study. Unlike Park et al. (2014) but similar to Daley (2002), Dawson positioned the infants cradled in the caregivers' arms in the semiupright position. Infants enrolled in the study differed significantly in level of respiratory support both within this study and as compared to the dissertation study. Eight infants were receiving respiratory support (low flow oxygen, nasal continuous positive airway pressure, or high flow oxygen greater than 4L/min) at the time of the study. All infants were breathing room air at the time of entry into the dissertation study. Differences in need for respiratory support can significantly impact cardiopulmonary outcomes.

Stevens (2007) results also revealed no significant difference in cardiopulmonary outcomes between feeding positions. However, this study compared two different semiupright positions, cradle (15 degree head up) and upright (45 degree head up).

**Respiratory wave outcomes**. The only other related study to examine respiratory wave patterns was Park et al. (2014). The methodology for data collection differed significantly between the study by Park and the dissertation study. Park collected a respiratory wave form using elastic straps around the infant's chest and measured the intervals between breaths, pauses greater than three seconds, amplitude of breaths and respirations per minute. In the elevated sidelying position, Park found shorter and more regular intervals between breaths, breathing frequency closer to prefeeding state, and more variation in breath duration.

Differences in methodology to assess respiratory variability make comparison in outcomes difficult. Respiratory inductance plethysmography as used in the study by Park et al. (2014) measures the quantity of chest wall expansion; whereas analysis of respiratory waveform impedance using nonlinear methods of analysis, analyzes the quality or variability of the waveform. Respiratory waveform analysis is noninvasive as data is collected from bedside cardiopulmonary monitor, demonstrating the clinical utility of this measure as compared to respiratory inductance plethysmography.

Also, in the study by Park et al. (2014), two of the six infants required supplemental oxygen at the time of the study and four infants had a diagnosis of bronchopulmonary dysplasia at discharge. These differences in neonatal respiratory morbidity can significantly impact analyses of breathing patterns.

**Feeding performance outcomes**. Six of the seven related studies examined feeding performance (Daley, 2002; Dawson, 2013; Lau 2013; Park et al., 2014; Stevens, 2007; Thoyre et al., 2012). Like the dissertation study, no significant difference was found in feeding outcomes between feeding positions.

**Relationship between oral feeding performance and age**. The relationship between oral feeding performance and age of the infant is consistent with research by Lau and Smith (2011), Dodrill, Donovan, Gleghorn, McMahon and Devies (2008), Jadcherla et al. (2010) and Pickler et al. (2005). Similar to the dissertation study, these researchers found differences in oral feeding skills related to infant age. The relationship between feeding performance and age is consistent with the knowledge that infants undergo developmental changes with maturation that impact oral feeding outcomes.

**Relationship between oral feeding performance and behavioral state.** The lack of an association between oral feeding performance and behavioral state is inconsistent with the literature on cue based feeding (Brown & Ross, 2011; Jadcherla et al., 2012; Kirk, Alder & King, 2007; Pickler et al., 2005; Puckett, Grover & Sankaran, 2008; Thoyre et al., 2012). Feeding readiness indicates the developmental maturation of an infant who starts to show feeding cues. Current research emphasizes the importance of feeding readiness cues in initiating and progressing oral feeding ( Brown & Ross, 2011; Kirk et al., 2007; Puckett et al., 2008) and the relationship between level of alertness and successful oral feeding performance (Jadcherla et al., 2012; Thoyre et al., 2012). The use of the Anderson Behavioral State Score may have been limiting in capturing the infants' readiness for and capability of feeding.

**Clinical Implications**

The implications of this research were to advance clinical care. The primary results of this study suggest that either the semiupright position or the elevated sidelying may be beneficial for healthy preterm infants transitioning to oral feeding; elucidating the importance of an individualized approach to oral feeding. Feeding in the head elevated sidelying positon may support young preterm infants with decreased stamina by providing an opportunity for the milk bolus to clear from the posterior oropharynx when swallowing is immature. Supportive positioning in semiupright may encourage infants to remain more alert to sustain adequate respiration and efficient sucking patterns. Other factors affecting successful feeding outcomes: age of the infant (gestational age, postmenstrual age and days of life), the experience of the nurse feeding the infant and sequence of feeding are important considerations. These influences should therefore be considered when assessing an infant's oral feeding skills, setting expectations for progression of oral feeding and designing therapeutic interventions to support oral feeding.

More precise measures of infant feeding success (proficiency, rate of milk transfer, oral feeding performance) may provide a more accurate representation of infant skill than percentage of prescribed volume taken over the past 24 hours as is typically used in NICUS. Calculation of these measures is relatively simple and only requires the caregiver to note volume intake at 5 minutes along with the standard measure of volume intake at the end of the feeding. These measures are more indicative of actual infant progress in oral feeding and conversely may help health care providers identify whether feeding issues are related to immaturity, oral motor skill difficulties and/or endurance.

The purpose of investigating respiratory waveforms was to evaluate the clinical utility of respiratory variability. The exploratory analysis of respiratory waveforms and nonlinear methods of analysis, Approximate Entropy, proved useful in assessing variability in respiratory patterns in healthy preterm infants beginning to bottle feed. Examination of the characteristics of waveforms allowed comparison of infant respiratory patterns.

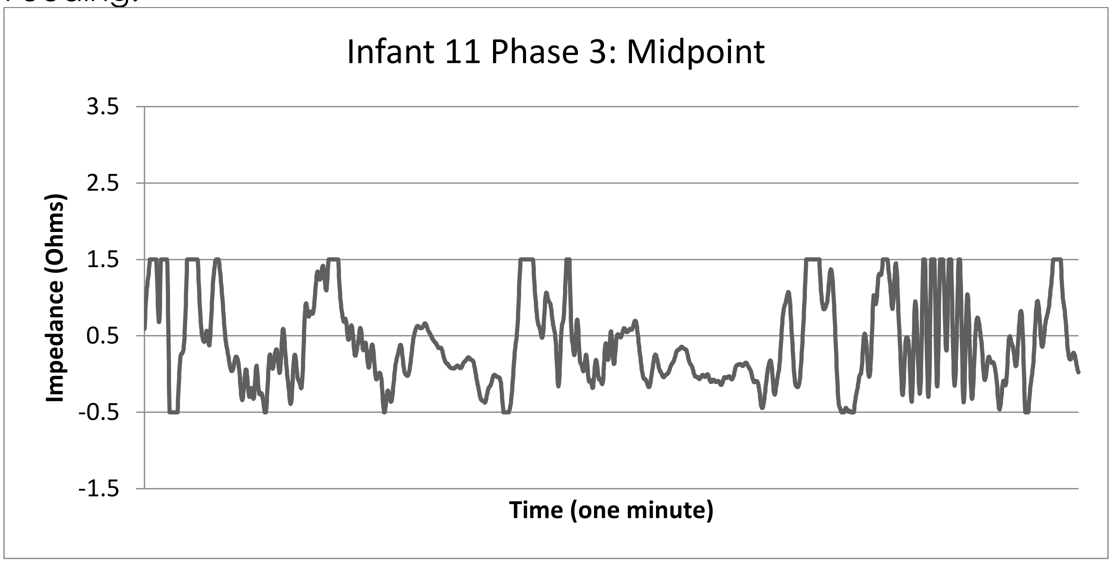
**Dynamics systems theory and respiratory variability**. The dynamic systems approach to oral feeding hypothesizes that interactions among various subsystems organize to establish coordinated functional behaviors. The dynamics of oral feeding are driven by the infant's goal to satisfy hunger while coordinating breathing and swallowing. Successful oral feeding requires the organization of multiple subsystems: oral motor, neurologic, cardiopulmonary, musculoskeletal and gastrointestinal. Proficient feeding requires the simultaneous coordination of various muscle groups with protection of the airway while sustaining respiration.

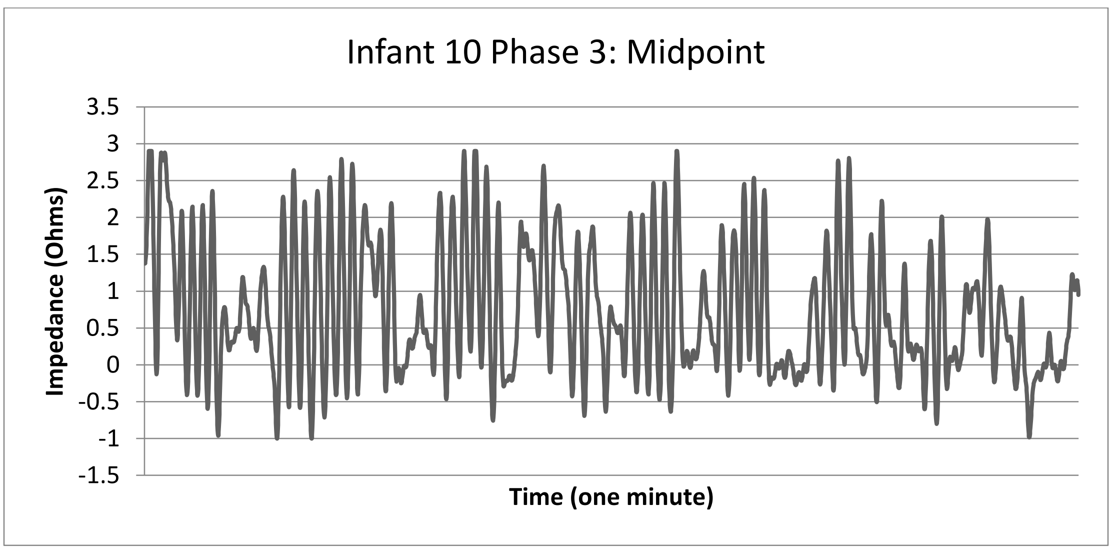
The dynamic systems theory proposes that healthy nonlinear systems such as respiration demonstrate complex variability. From this theoretical premise, the complexities of oral feeding would require increased variability to coordinate the multiple tasks of suck, swallow breathe coordination. Immature respiratory control may limit the breathing pattern variability, interfere with suck, swallow breathe coordination and decrease feeding efficiency.

**Comparison of two infant respiratory waveforms**. Respiratory waveforms were analyzed comparing infant 11 with the most rigid respiratory waveform and infant 10 with the most variable waveform across phases of observation. Infants 10 and 11 were male twins born at 32.5 weeks gestation and were 35.4 weeks postmenstrual age (19 days of life) at the time of the study. Infant 10 was twin A and infant 11 twin B. Birth weight was average for gestational age for both infants with infant 10 weighing slightly less than infant 11 at birth and at the time of the study. Apgar scores were $9^1$, $9^5$ (infant 10) and $4^1$, $8^5$ (infant 11). Prior to initiation of the study, vital sign stability (heart rate, respiratory rate and percent hemoglobin oxygen saturation) at rest were comparable. Twenty hours prior to the observation infant 10 had 5 full volume gavage feedings and 3 partial oral feeding (nipple/gavage); infant 11 had 6 full volume gavage feeding and 2 partial oral feedings (breast/gavage). Infant level of alertness/feeding readiness scores were comparable and the same at both feedings for both infants. Infant 10 was fed in sidelying first and infant 11 was fed in first in semiupright. Infant 10 was fed by two different nurses while Infant 11 was fed by the same nurse (who was also the nurse who fed infant 10 for the second feeding). Both nurses had minimal NICU nursing experience (0-5 years) but the first nurse who fed infant 10 had more overall years of nursing experience. Total percent prescribed volume intake for both infants was the same for the first feeding with both infants demonstrating a decrease in volume intake during the second feeding regardless of position.

Despite the similarities in birth history and neonatal course, both infants presented with markedly different respiratory wave patterns (Figure 7).

Figure 7. Comparison of Least and Most Variable Infant Midpoint of Feeding.




**Caffeine and respiratory waveforms**. Analysis of an infant on caffeine at the time of the study revealed Approximate Entropy values of zero across all phases of observation. The waveform for this infant appears so rigid that perhaps the MatLab software program designed to measure ApEN reached a calculation limit. Examination of the waveform characteristics reveals less complexity and multiple square peaks at both the maximum for inspiration and expiration. The range of impedance measures for this infant are -0.3 and 0.8 Ohms, a much small range than the average infant (-0.5 to 2.5 Ohms) (Figure 8). Caffeine is a central nervous system stimulate acting to increase respiratory drive. Theoretically, the caffeine should not affect the respiratory waveform but it is uncertain whether the caffeine makes the respiratory response more vigorous. Instead, perhaps the infant's baseline respiration is so rigid, the monitor learned that baby's rigid respiration and set a smaller range of impedance. This begs the clinical question of whether infants who require caffeine have less complex respiratory patterns at baseline and requires further study.

Figure 8. Comparison of Approximate Entropy Infant 9 on Caffeine

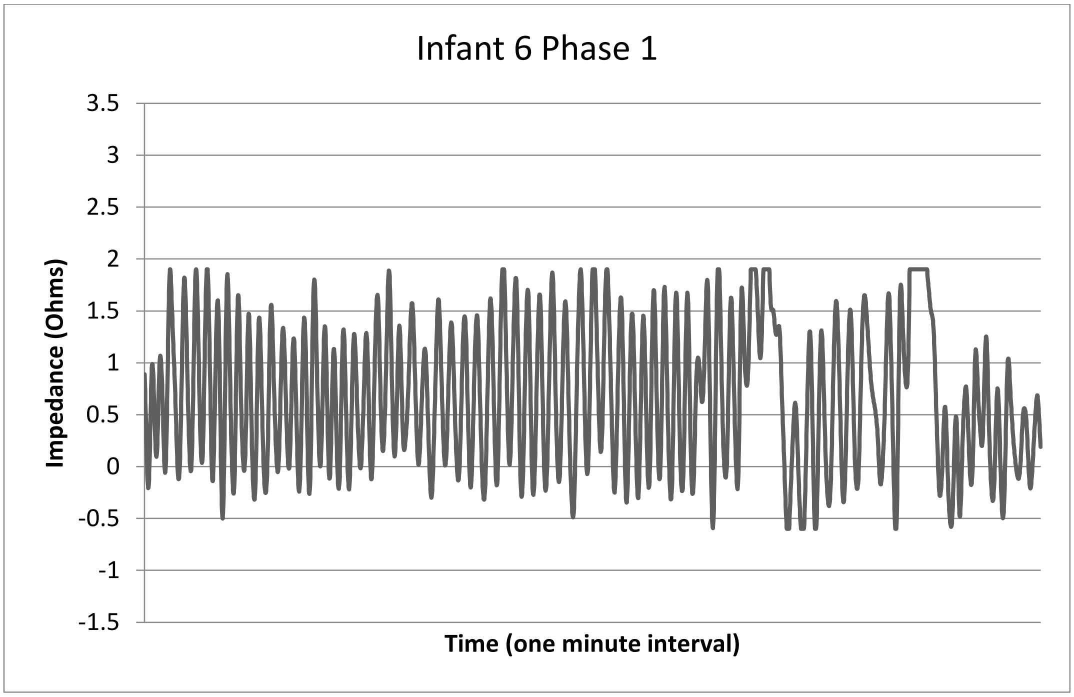



Figure 8a. Prefeeding baseline (supine), infant not on caffeine.

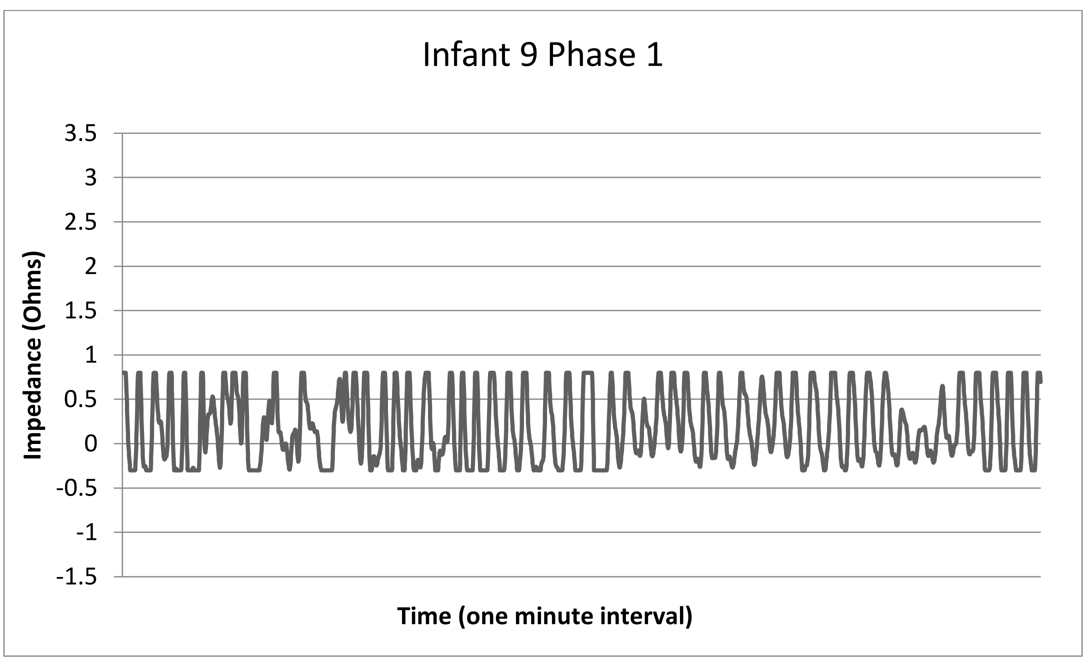



Figure 8b. Prefeeding baseline (supine), infant on caffeine.

**Limitations of the Study**

Limitations of the study include generalizability due to subject selection as infants selected were a convenience sample and findings are only applicable to healthy preterm infants with similar characteristics. The findings should be interpreted with appropriate caution given the small sample size.

**Neonatal disease severity scoring.** The SNAPPE II is a measure of the risk of infant mortality based on assessment in the first 12 hours of life, limiting valuation as a measure of the relationship between infant morbidity and feeding outcomes. A different neonatal disease severity scoring system such as the CRIB II or the nursery Neurobiologic Risk Score (NBRS) may better capture an infant's morbidity and the impact on oral feeding skills. Both the CRIB II and NBRS have been cited as predictive of neurodevelopmental outcomes (Darling, Field & Manktelow, 2004)

**Behavioral state scoring.** The Anderson Behavioral State Score may have limited assessment of infant cues and readiness for oral feeding. Though a measure of behavioral of state, infants whose eyes are closed score low on levels of alertness and are considered to be in a sleep state even if feeding. In addition, the ABSS does not provide information on quality of oral feeding. Other cue based feeding scales

(Ludwig & Waitzman, 2007; Newland, L'Huiller & Pretrey, 2003) may provide a more complete assessment of feeding readiness. Moreover, the Early Feeding Skills Assessment for Preterm Infants (Thoyre, Shaker & Pridham, 2005) is a comprehensive assessment of infant feeding readiness and feeding capabilities. This scale may therefore, more accurately capture the relationship between level of alertness and oral feeding outcomes in preterm infants than the ABSS.

**Respiratory Waveforms**. Waveform data output revealed an intermittent flat line or square peak at the maximum or minimum impedance range within respiratory waveforms. These values varied from infant to infant and sometimes within individual infants based on phase of observation. This threshold in ability to capture data at end range values appears a limitation in the Phillips monitoring recording system (Figure 9). When initially connected to an infant, the monitor is designed to analyze, for 12-15 seconds, the general characteristics of the infant based on electrocardiograph measures. The monitor then calculates and sets the baseline zero point based on the infants' representative vital signs. The monitoring system appears to have a maximum capability to collect data, with a distinctive limit for each infant imposed at initial configuration during monitoring set up.

This limitation in the monitoring system restricted the ability to collect data outside the specified ranges, therefore reduced accuracy of the Approximate Entropy values. However, as this constraint was inherent in the data collection process across all infants studied, comparison of the quality of waveforms and relative ApEn (variability) across infants and between phases of observation was valid.

There is a need to define relative waveform complexity based on ApEn values. ApEn values typically range from 0 to 1. Values closer to 0 are consistent less complex (more rigidity) while values closer to 1 represent greater complexity or more variability. As all of the infants ApEn values were close to zero and the range of values is limited (ApEn= 0.0002 to 0.0201), there is a need define relative variability (i.e. how variable is the respiratory pattern of an infant with ApEn= 0.0001 compared to an infant with ApEn= 0.0005).

Figure 9. Comparison of Flat Line (Square) Peaks in Recording Systems


Figure 9a. NICU central monitor print out of waveforms

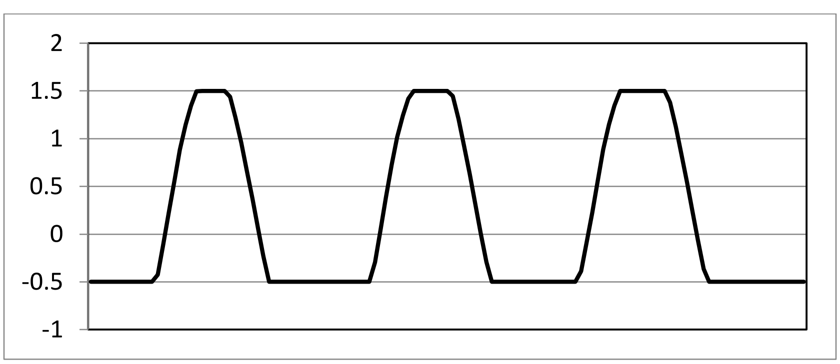



Figure 9b. IxTrend to Excel print out of waveforms

## Suggestions for Future Research

Respiratory waveform variability and nonlinear methods of analysis can be used for clinical research within the NICU as data collection is performed using the clinical bedside monitoring system with minor adaptations. Data collection is noninvasive providing the opportunity to study infants in clinical situations. The ability to change the limits in data collection capabilities within the monitoring system need to be explored to define specific ApEN values of respiratory variability. A future study with a larger sample increase confidence in the findings of variability. A longitudinal study could examine changes in respiratory pattern variability over time and evaluate ApEN as a marker of neuromaturation. The applicability of respiratory variability to clinical situations provide the opportunity to study infant respiratory patterns while breast feeding without interfering with the feeding pattern or mother/infant dyad. Studies of infants on caffeine or infants diagnosed with chronic lung disease, may provide information regarding respiratory pattern variability in infants with comorbidities and the impact on oral feeding performance.

## Conclusion

Premature infants typically attain full volume feedings by 36-37 weeks postmenstrual age. However, respiratory control and coordination of the suck, swallow and breathe pattern during oral feeding may mature at different rates in preterm infants. Analysis of respiratory waveform variability may be a more sensitive measure of cardiopulmonary physiology than heart rate, respiratory rate and percent hemoglobin oxygen saturation. The clinical application of monitoring respiratory wave patterns may be helpful in identifying infant's readiness to initiate and progress feeds orally. This measure of variability may be used as screening tool clinically to identify coordination patterns in infants with oral feeding challenges. Individualized therapeutic interventions integrating an infant's unique respiratory pattern may assist preterm infants in transitioning from gavage to full volume oral feeding and foster improved feeding outcomes.

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Appendix A

**Feeding Method Procedure**

Infants will be swaddled in receiving blankets and held by nurse/therapist for oral feedings (semiupright and elevated sidelying). Semiupright feeding specifies that the preterm infant is resting on the feeder's lap and is held in one hand, with the trunk and head up to approximately 70 degrees in relation to the feeder's lap. Elevated sidelying feeding specifies that preterm infant is resting on the feeder's lap and is held in one hand, perpendicular to the feeder, with the trunk and head up to approximately 45 degrees in relation to the feeder's lap. Feeder will avoid the gaze of the infant and talking will kept to a minimum to avoid over stimulating the infant. Prior to initiation of oral feeding, nursing will verify tube position in the stomach and checked for residual formula left in stomach from the last feeding. If residual formula was obtained, researcher will note amount, color and appearance of contents. If aspirates appear bloody or heme positive, green, yellow, or fecal, study will be discontinued.

Infants will be provided with two minutes of non-nutritive sucking on a pacifier prior to each bottle feeding during the prefeeding recording in semiupright/elevated sidelying. Researcher will continuously assess the infant throughout the feeding for signs of cardiorespiratory distress evidenced by crying, oxygen desaturation, apnea or bradycardia that may require nursing/therapist to interrupt or discontinue feeding. The criteria for stopping a feeding includes: persistent oxygen desaturation < 80%, repeated bradycardia for more than two times, repeated apnea more than two times, persistent cyanosis accompanied by oxygen desaturation, vomiting or other as deemed necessary by nursing/therapist discretion to ensure safety of infant.

Feeding will begin by nursing/therapist eliciting a rooting response to stimulate mouth opening and then gently inserting nipple into the infant's mouth. Infants will be encouraged to maintain a quiet alert state throughout feeding. Feeding will continue until the total prescribed volume is consumed by mouth. Termination before full volume is consumed will occur when the infant ceases sucking, cannot not maintain an alert state, thirty minutes of sucking has elapsed or the infant demonstrates cardiopulmonary stress. If oral feeding is terminated prior to completion of full prescribed volume, remainder of feeding will be given through the gavage tube. Pauses to burp the infant will occur as needed, at 5-l0cc before the end of the feeding and at the end of the feeding.

Appendix B

## Optimal EKG Lead Placement

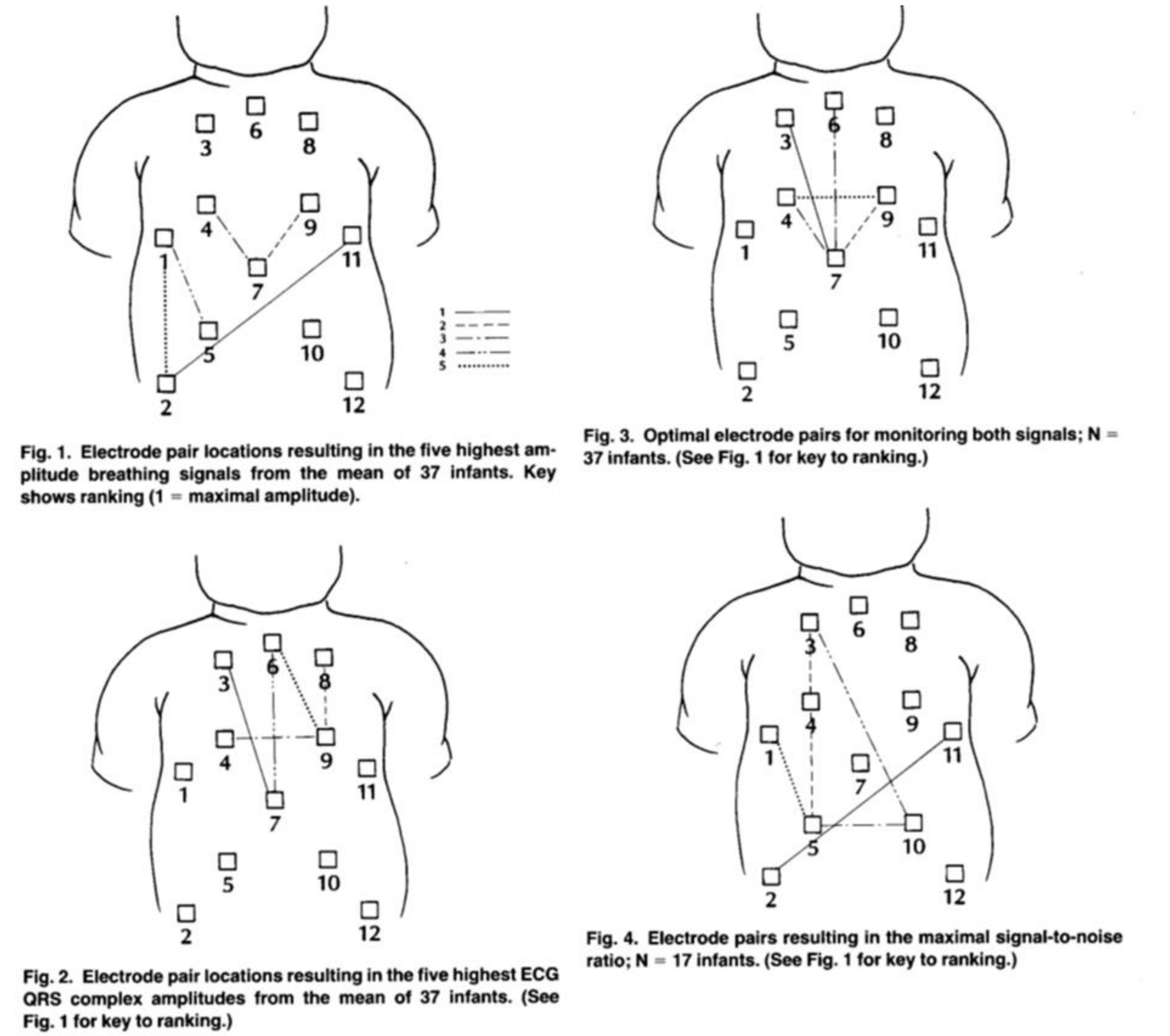


Fig. 1. Electrode pair locations resulting in the five highest amplitude breathing signals from the mean of 37 infants. Key shows ranking (1 = maximal amplitude).

Fig. 3. Optimal electrode pairs for monitoring both signals; N = 37 infants. (See Fig. 1 for key to ranking.)

Fig. 2. Electrode pair locations resulting in the five highest ECG QRS complex amplitudes from the mean of 37 infants. (See Fig. 1 for key to ranking.)

Fig. 4. Electrode pairs resulting in the maximal signal-to-noise ratio; N = 17 infants. (See Fig. 1 for key to ranking.)

Optimal EKG lead placement (Figure 1)
From Baird et al. (1992). Optimal electrode location for monitoring the ECG and breath in neonates. *Pediatric pulmonology, 12* (4), 247-250

Appendix C **Anderson Behavioral State Scale Scoring Sheet**

| TIME | Baseline | Prefeeding | TIME | Feeding | TIME | Post feeding | Recovery |
|---|---|---|---|---|---|---|---|
| 0 sec | | | 0 sec | | 0 sec | | |
| 30 sec | | | 2 min | | 30 sec | | |
| 60 sec | | | 4 min | | 60 sec | | |
| 90 sec | | | 6 min | | 90 sec | | |
| | | | 8 min | | | | |
| | | | 10 min | | | | |
| | | | 12 min | | | | |
| | | | 14 min | | | | |
| | | | 16 min | | | | |
| | | | 18 min | | | | |
| | | | 20 min | | | | |
| | | | 22 min | | | | |
| | | | 24 min | | | | |
| | | | 26 min | | | | |
| | | | 28 min | | | | |
| | | | 30 min | | | | |

Comments:________________________________________

## Anderson Behavioral State Scale (ABSS)

EYES OPEN OR CLOSED
12 Hard Crying: very red face; clinched fists; very prolonged exhalation' audible or silent cry; entire body very tense
11 Crying: red face; prolonged exhalation; audible or silent cry; general body tension
10 Fussing: normal color; slightly prolonged exhalation; whimpers; (precry grimace; snorts)

EYES OPEN
9 Very active: total body movement; twisting or lifting trunk
8 Active: whole limb movement
7 Awake, quiet: eyes don't fix and follow; same movement as 6
6 Alert inactivity: eyes fix and follow; no movement or slight slow movement of face, hand, foot, head, forearm, or lower leg; (eye contact)

EYES OPENING AND CLOSING
5 Drowsy: quiet or some movement; dull glazed appearance to eyes

EYES CLOSED
4 Very active sleep: total body movement; twisting trunk
3 Active sleep: irregular respiration; whole limb movement; (rapid eye movement; facial grimaces)
2 Irregular quiet sleep: irregular respiration; no movement or slight slow movement of face, hand, foot, head, forearm, or lower leg; (brief apnea)
1 Regular quiet sleep: regular respirations: faint or no mouthing; (movement of fingers and toes)

Sucking: hand = H; finger - F: thumb - T; pacifier = P; object = O;
Behaviors: hiccoughs = C; yawn = Y; twitch = W; mouthing = M.
Use only one letter

**Rules for Scoring ABSS**

1. Score the highest number that occurs during a 30-second interval.

2. If the baby has eye patches on, assume the eyes are closed, unless they are seen to be open.

3. If someone is working with the infant, wait until 1 min. after the intervention; then score arousal for 30 sec.

4. If State 6 occurs at any time during the observation, score the arousal level as 6, even if a higher number occurs.

5. If one eye is open and one eye is closed, score this a State 5.

6. Items in parentheses need not be present.

Appendix D

**Neonatal Disease Severity Scores (SNAPPE II)**

| Neonatal Infant Morbidity SNAPPE II Scores (n=9) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| Subject | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| | | | | | | | | | |
| | | | | | | | | | |
| Mean BP | 30 | 31 | 35 | 30 | 39 | 37 | 44 | 37 | 37 |
| | | | | | | | | | |
| Lowest Temperature | 36.4 | 35.6 | 35.6 | 36.4 | 36.4 | 36.7 | 35.5 | 36.6 | 34.5 |
| | | | | | | | | | |
| PO2/FiO2% | 0.21 | 0.21 | 0.5 | 0.21 | 0.21 | 0.38 | 0.21 | 0.21 | 0.25 |
| | | | | | | | | | |
| Lowest Serum Ph | 7.31 | 7.23 | 7.32 | 7.31 | 7.35 | 7.2 | 7.38 | 7.31 | 7.33 |
| | | | | | | | | | |
| Multiple Seizures | No | No | No | No | No | No | No | No | No |
| | | | | | | | | | |
| Urine Output | 3.62 | 1.97 | 2.97 | 3.89 | 1.46 | 1.78 | 1.22 | 1.04 | 2.5 |
| | | | | | | | | | |
| Apgar Scores | 9,9 | 4,8 | 7,8 | 7,8 | 7,8 | 7,7,7 | 9,9 | 4,8 | 1,9 |
| | | | | | | | | | |
| BW | 1450 | 2415 | 1965 | 1810 | 1086 | 1545 | 1507 | 1610 | 1733 |
| | | | | | | | | | |
| SGA | No | No | No | No | No | No | No | No | No |
| | | | | | | | | | |
| GA | 30.1 | 34 | 33.4 | 33.4 | 27.3 | 29.5 | 32.5 | 32.6 | 32.3 |

Risk of Mortality based on SNAPPE-II Score

## Calibration of mortality risk model, by birth weight category

| | | Observed deaths | | Expected deaths | |
|---|---|---|---|---|---|
| **SNAPPE-II** | Total | No. | % | No. | % |
| | | **For all birth weights** | | | |
| **0-9** | 16,274 | 48 | 0.3% | 51 | 0.3% |
| **10-19** | 3,923 | 61 | 1.6% | 61 | 1.6% |
| **20-29** | 1,952 | 74 | 3.8% | 71 | 3.6% |
| **30-39** | 1,262 | 93 | 7.4% | 101 | 8.0% |
| **40-49** | 790 | 124 | 15.7% | 116 | 14.7% |
| **50-59** | 476 | 105 | 22.1% | 102 | 21.4% |
| **60-69** | 310 | 101 | 32.6% | 100 | 32.3% |
| **70-79** | 142 | 55 | 38.7% | 63 | 44.4% |
| > = **80** | 141 | 94 | 66.7% | 90 | 63.8% |

Appendix E

**Comparison of Waveform Variability in Three Infants**

Infant 6 Semiupright Across All Five Phase of Feeding Observation

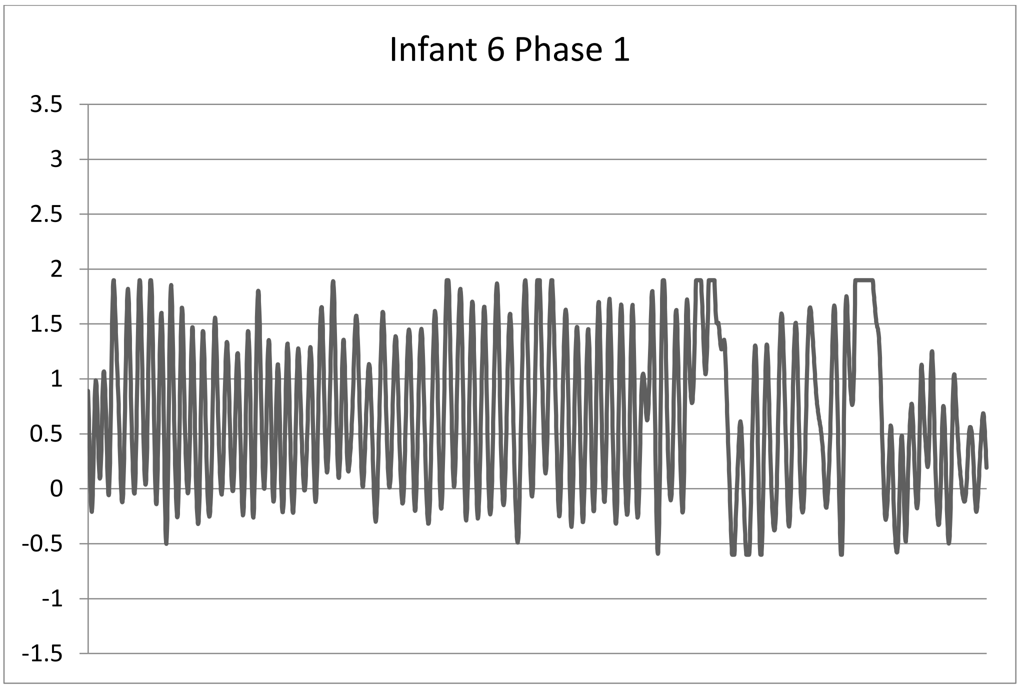



Figure 6a. Pre-feeding Baseline (Supine)

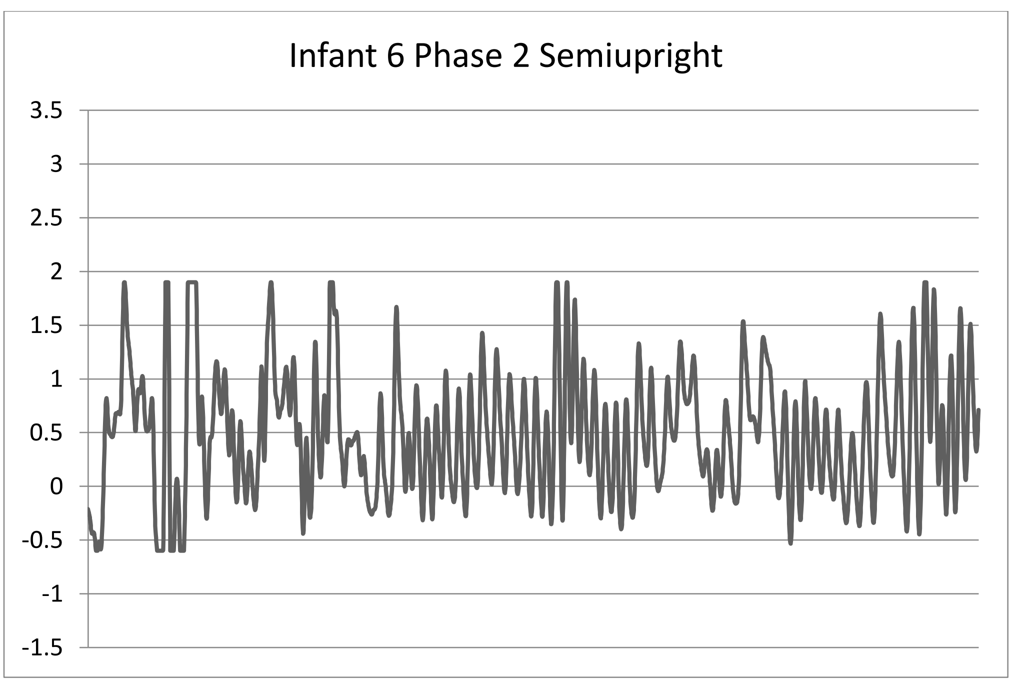


Figure 6b. Prefeeding Phase in Semiupright

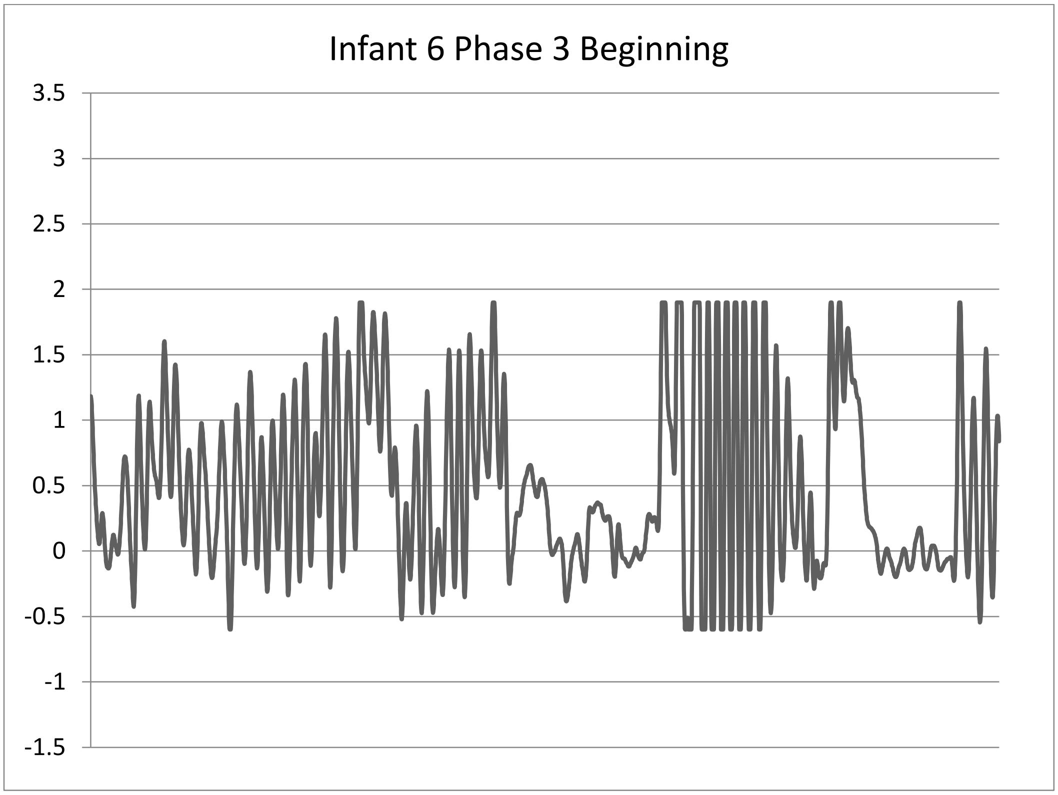



Figure 6c. Feeding Phase in Semiupright (first minute)

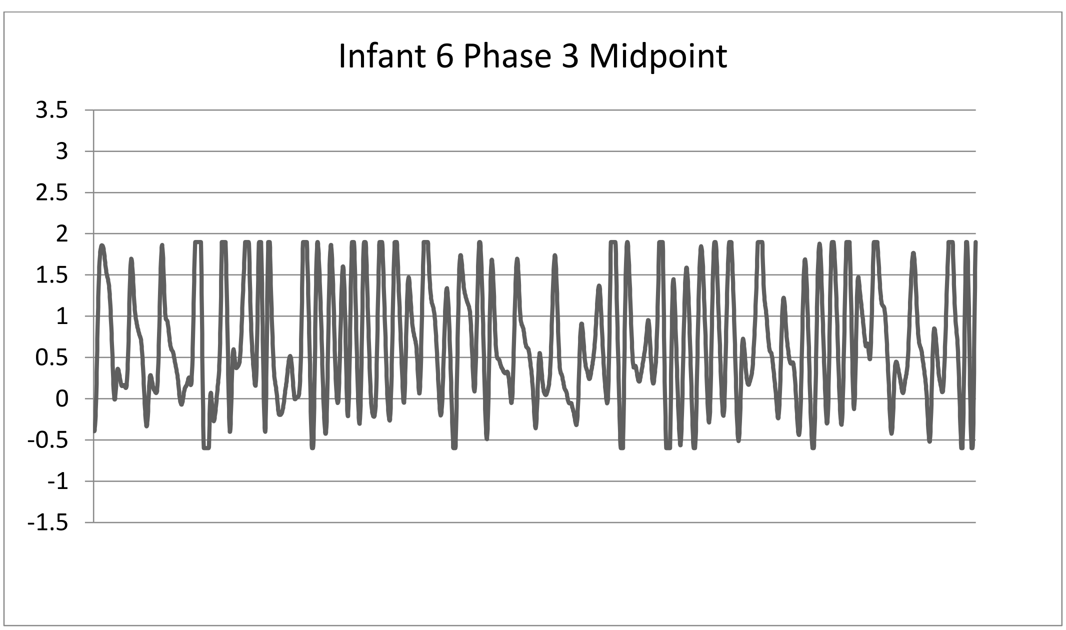


Figure 6d. Feeding Phase in Semiupright (middle minute)

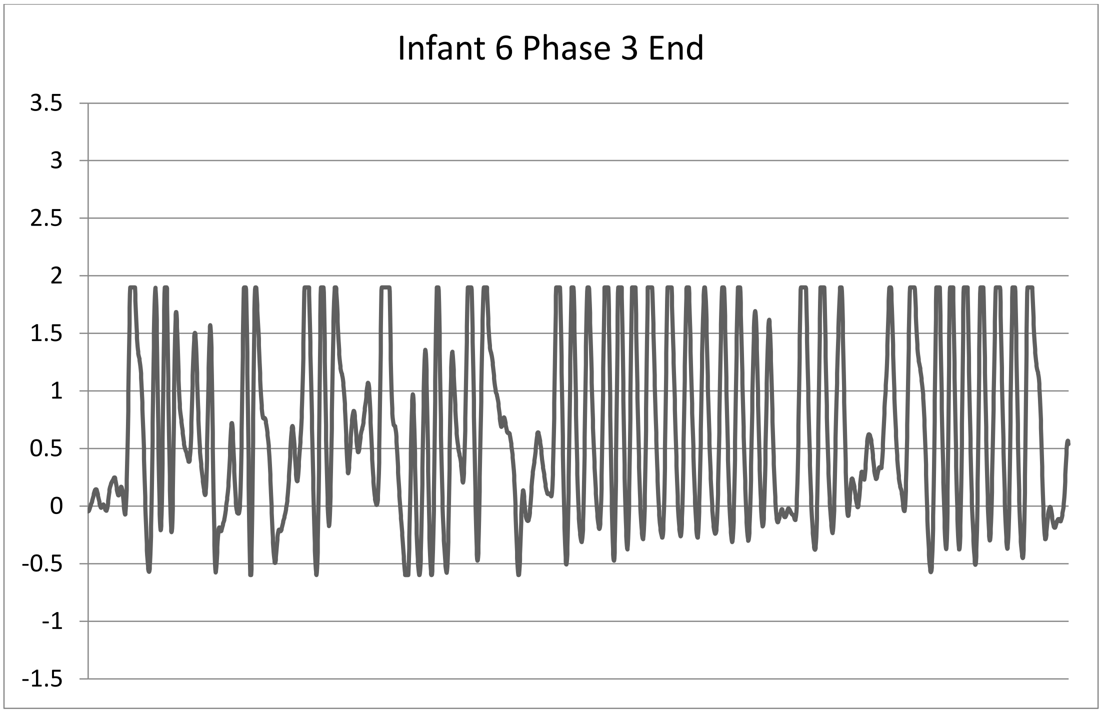



Figure 6e. Feeding Phase in Semiupright (final minute)

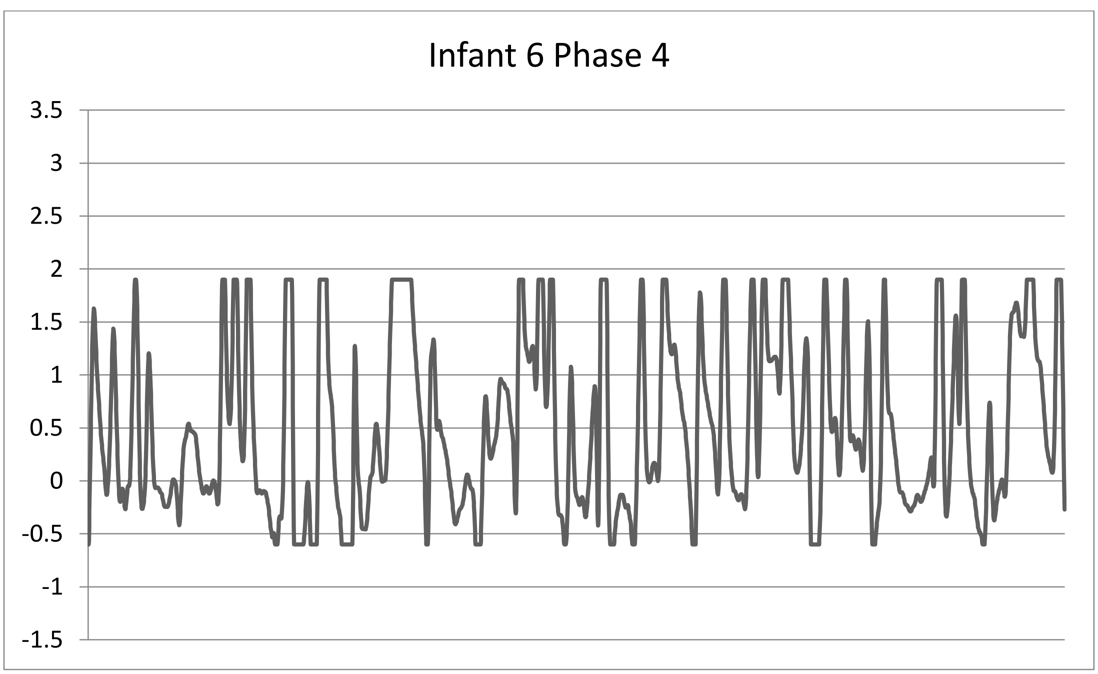



Figure 6f. Post feeding Phase (Semiupright)

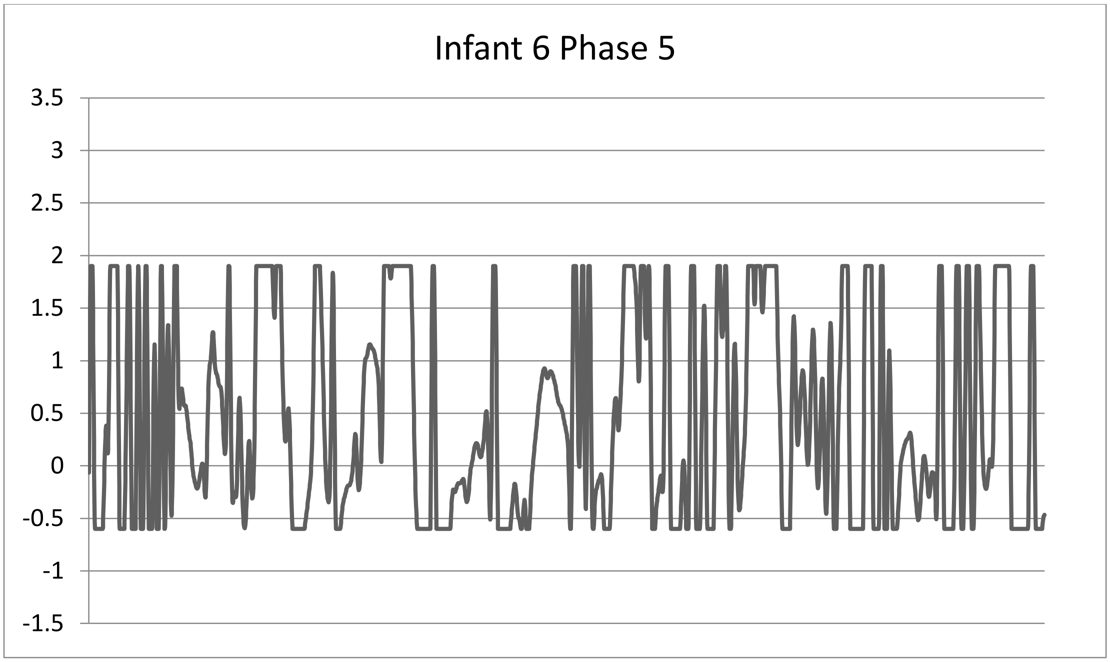


Figure 6g. Post feeding Recovery (Supine)

Infant 10 Sidelying Across all Five Phases of Feeding Observation

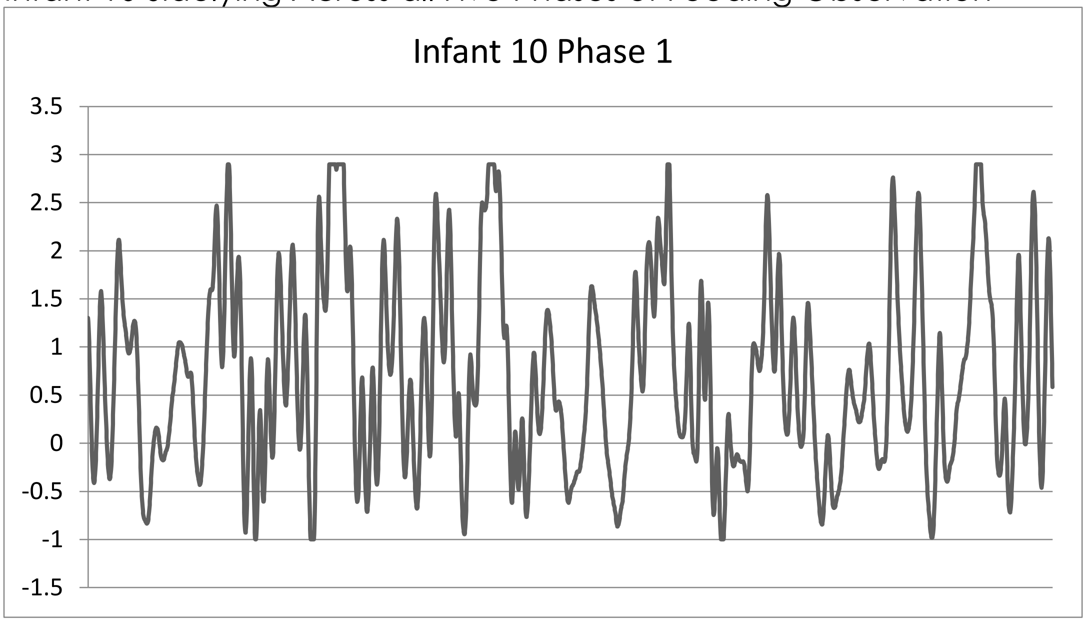



Figure 10a. Pre-feeding Baseline (Supine)

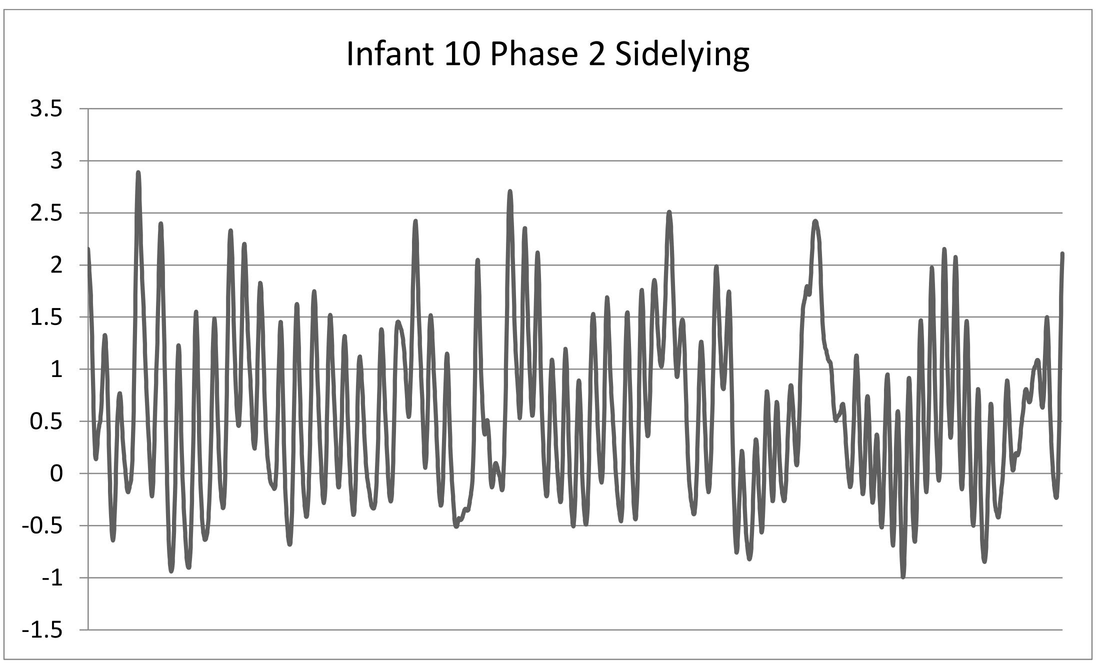



Figure 10b. Pre-feeding Phase in Sidelying

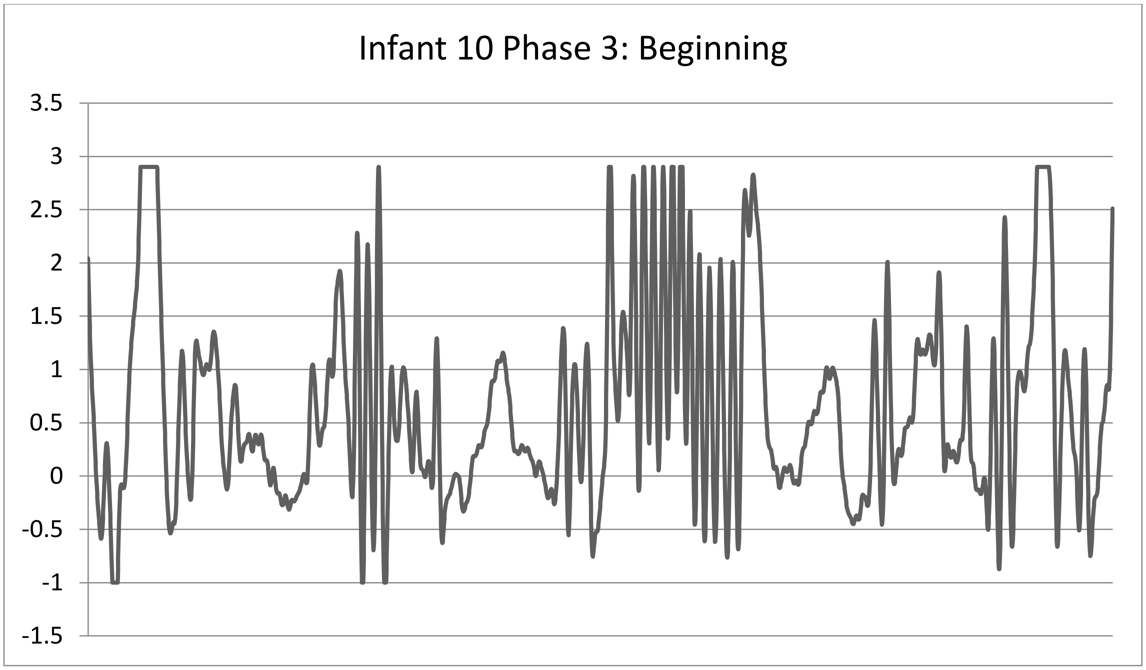


Figure 10c. Feeding Phase in Sidelying (first minute)

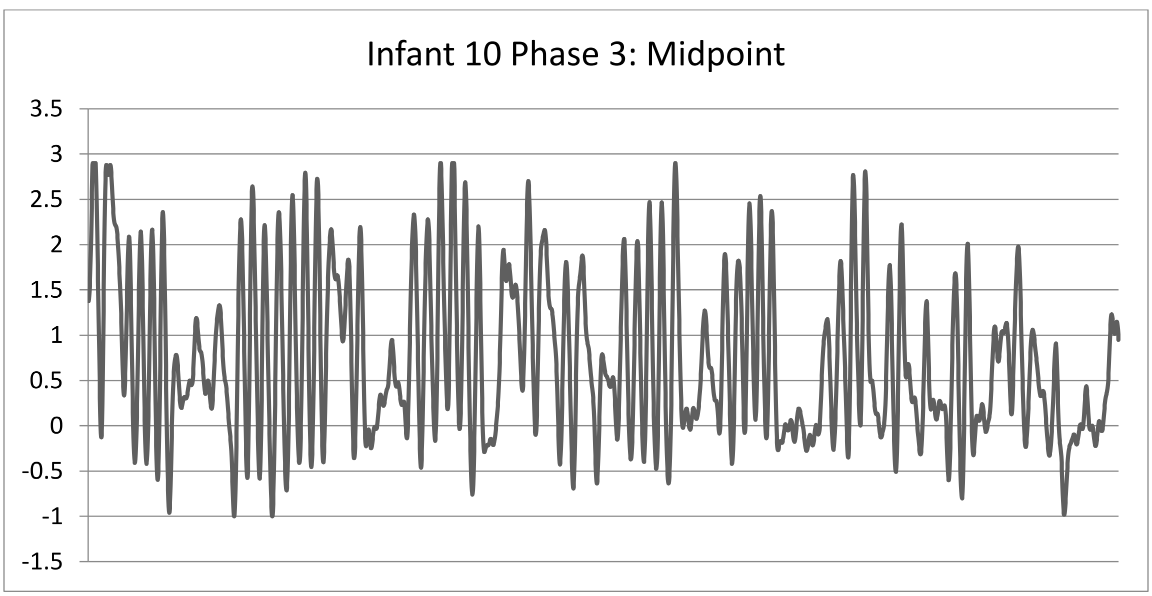


Figure 10d. Feeding Phase in Sidelying (middle minute)

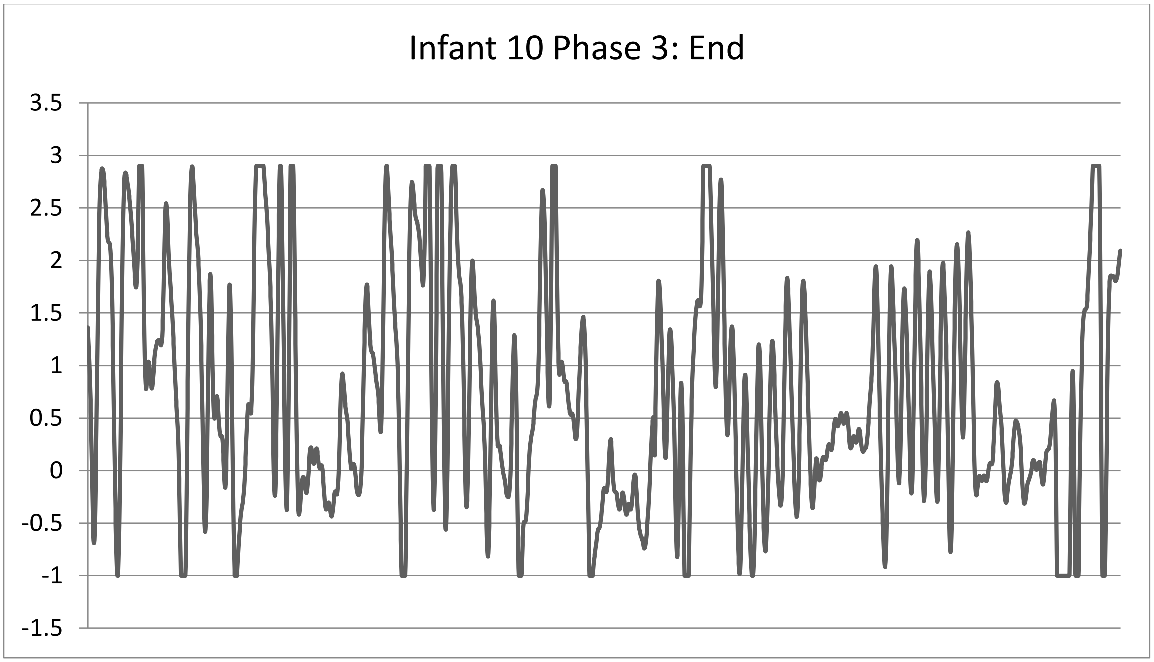


Figure 10e. Feeding Phase in Sidelying (final minute)

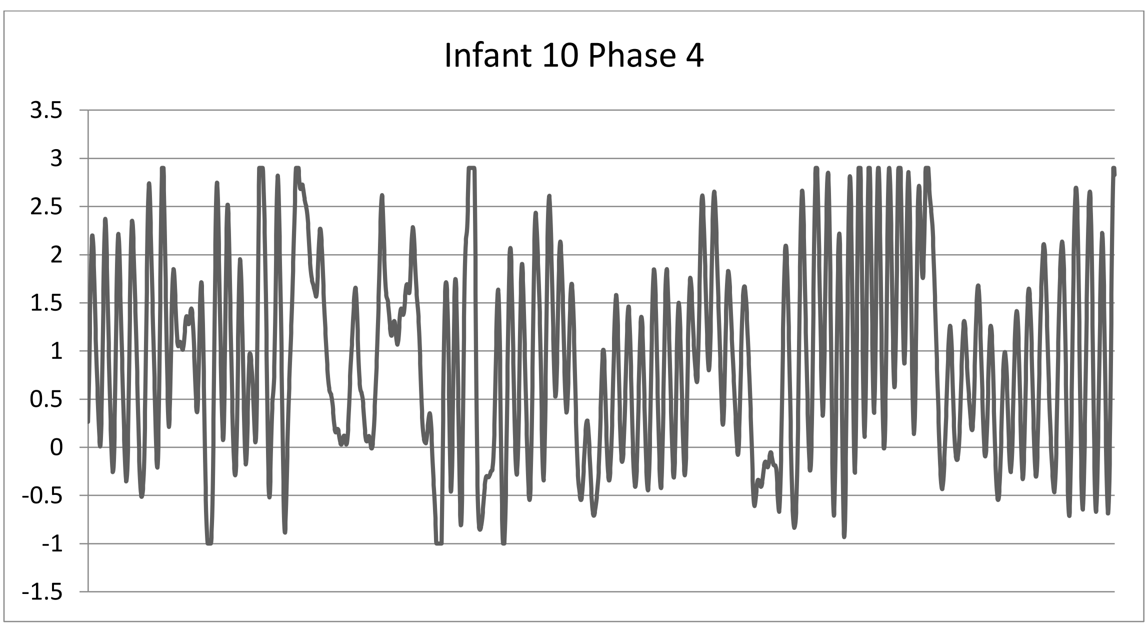


Figure 10f. Post feeding Phase in Sidelying

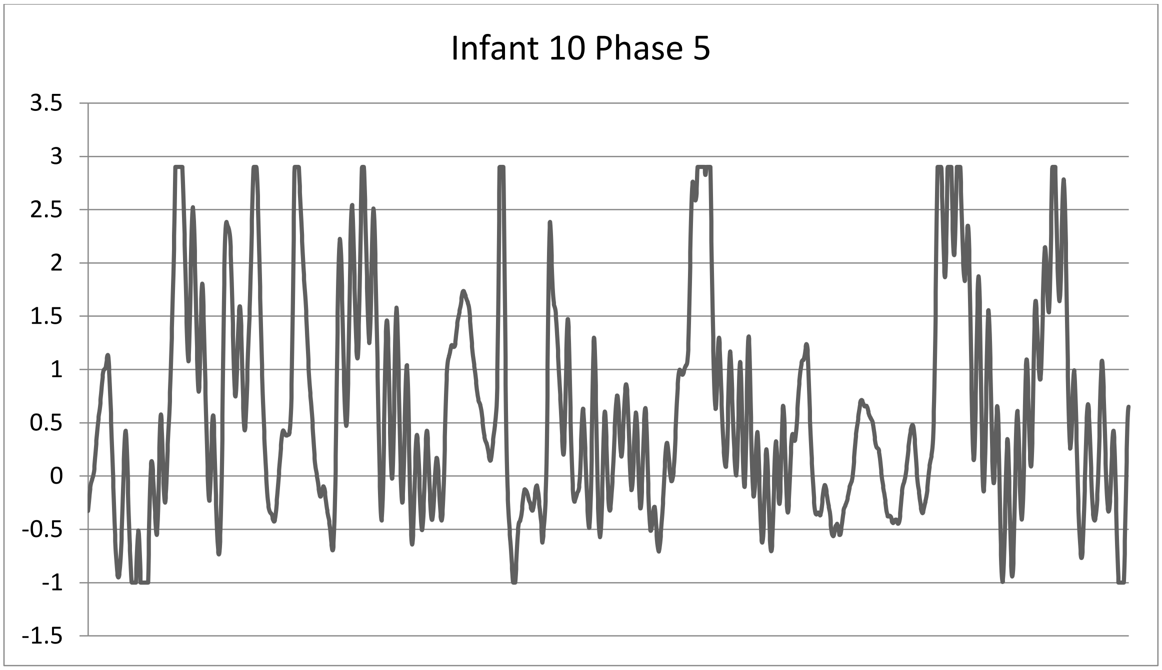


Figure 10g. Post feeding Recovery (Supine)

Infant 11 Semiupright Across all Five Phases of Feeding Observation

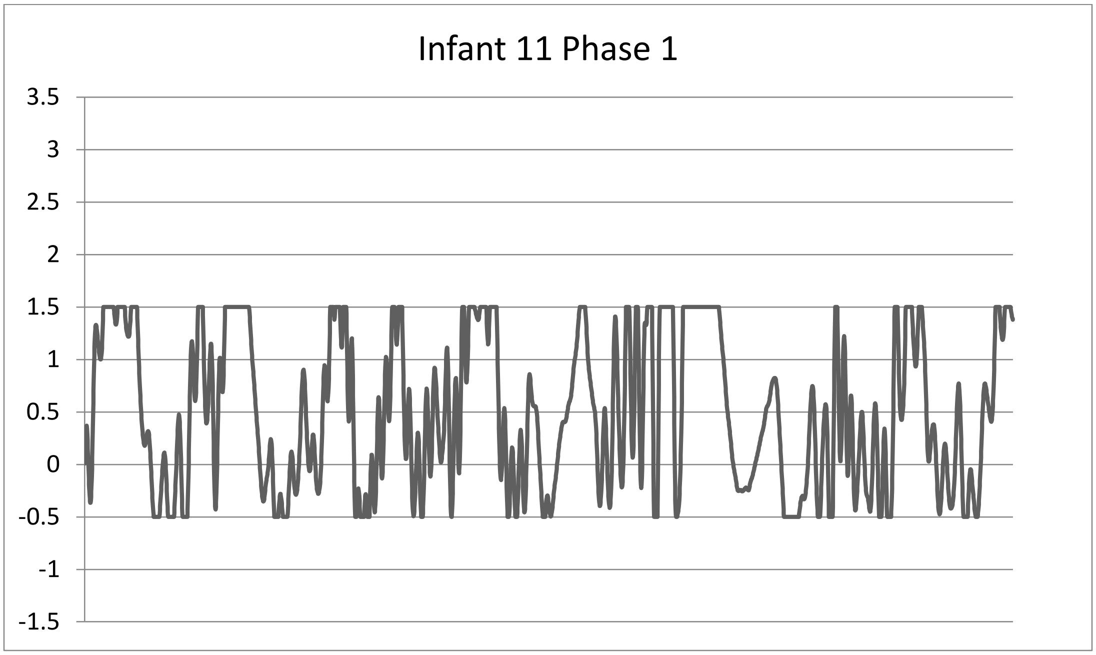



Figure 11a. Pre-feeding Baseline (Supine)

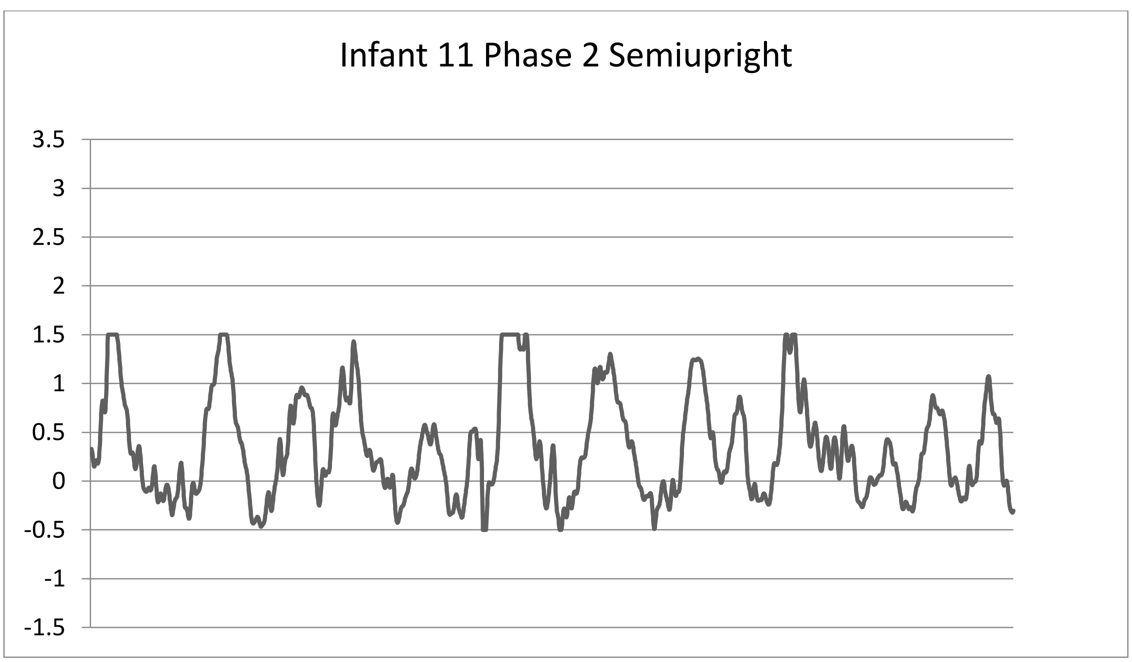



Figure 11b. Prefeeding Phase in Semiupright

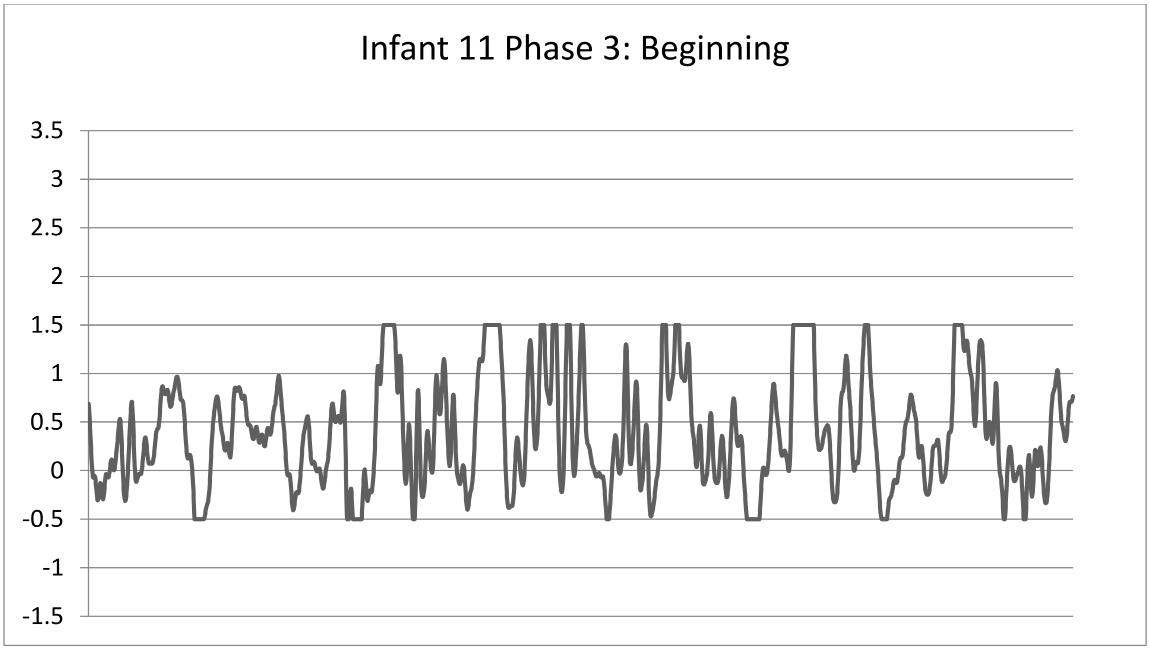


Figure 11c. Feeding Phase in Semiupright (first minute)

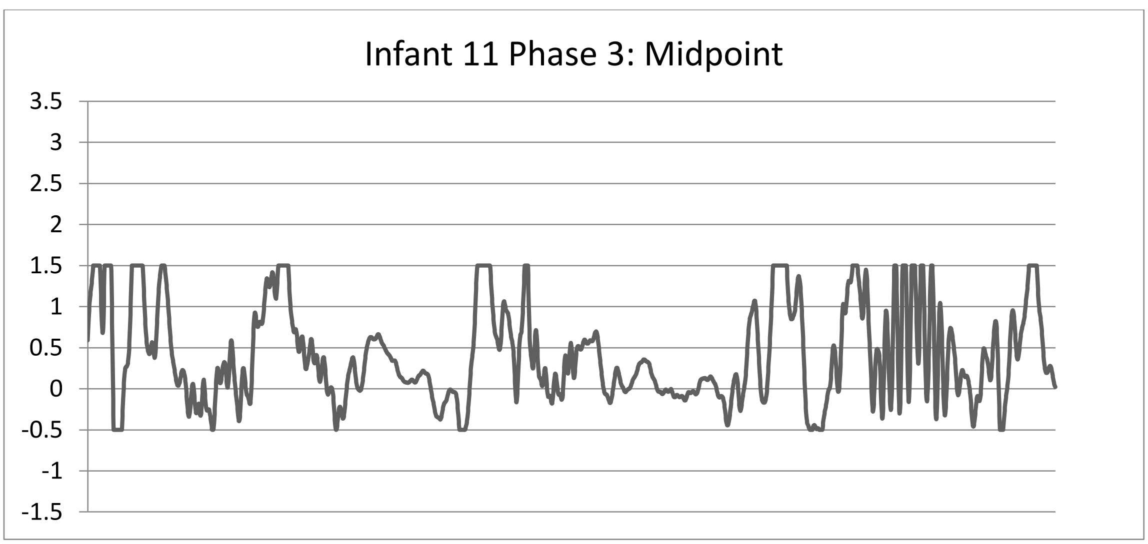


Figure 11d. Feeding Phase in Semiupright (middle minute)

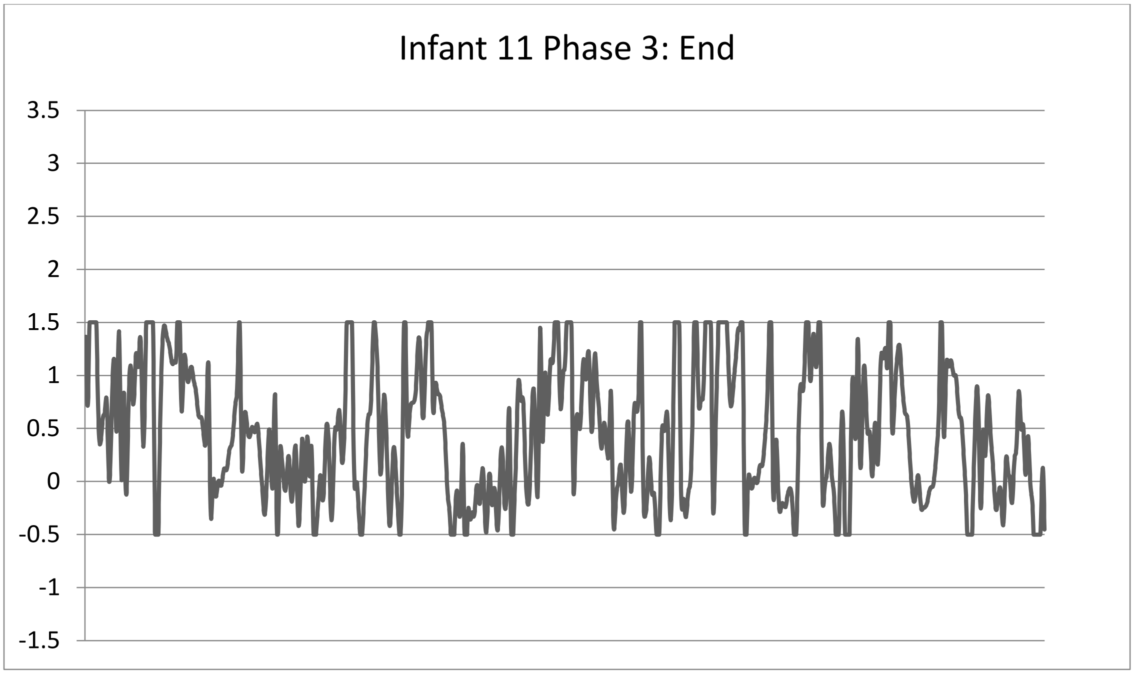


Figure 11e. Feeding Phase in Semiupright (final minute)

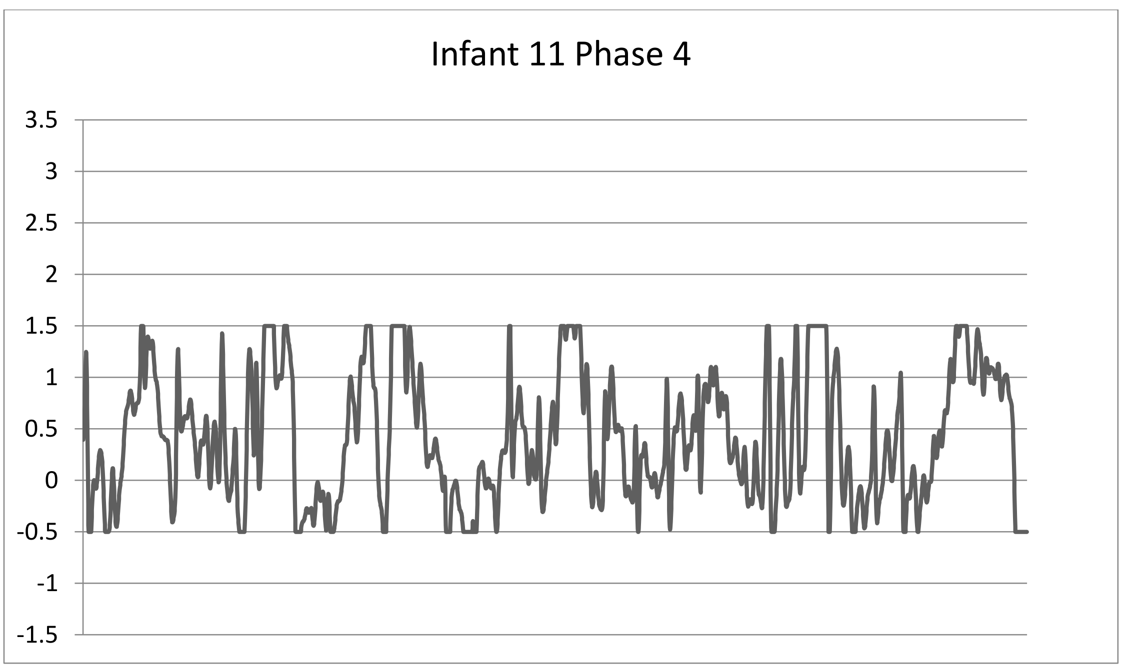


Figure 11f. Post feeding Phase (Semiupright)

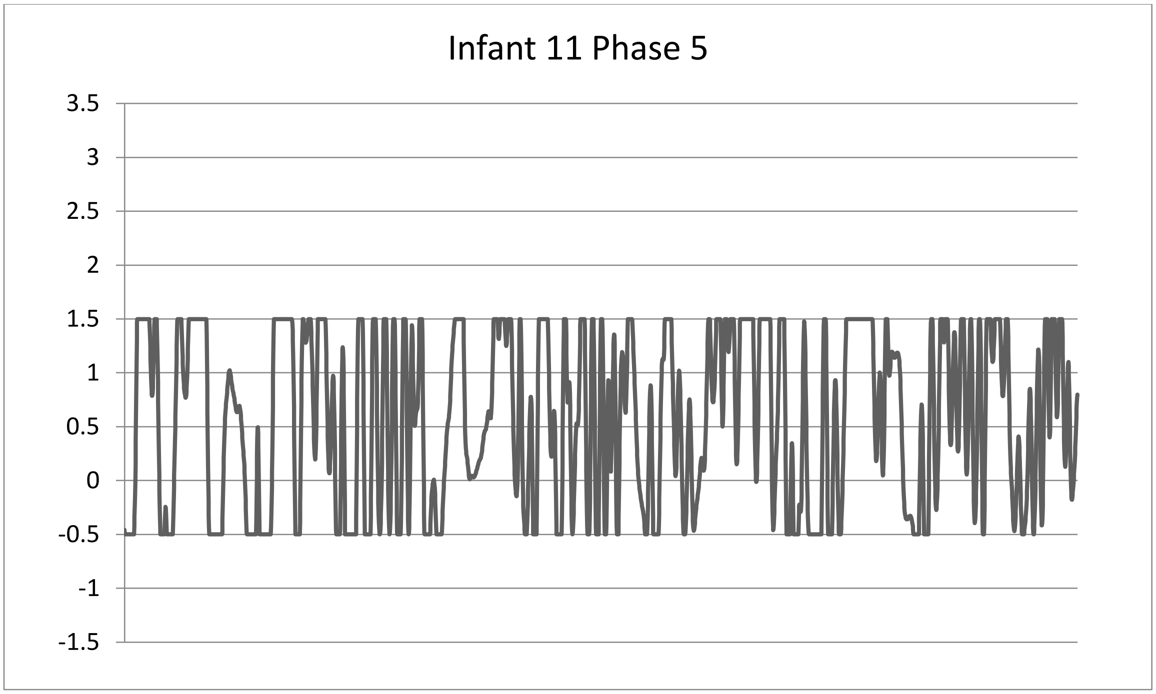
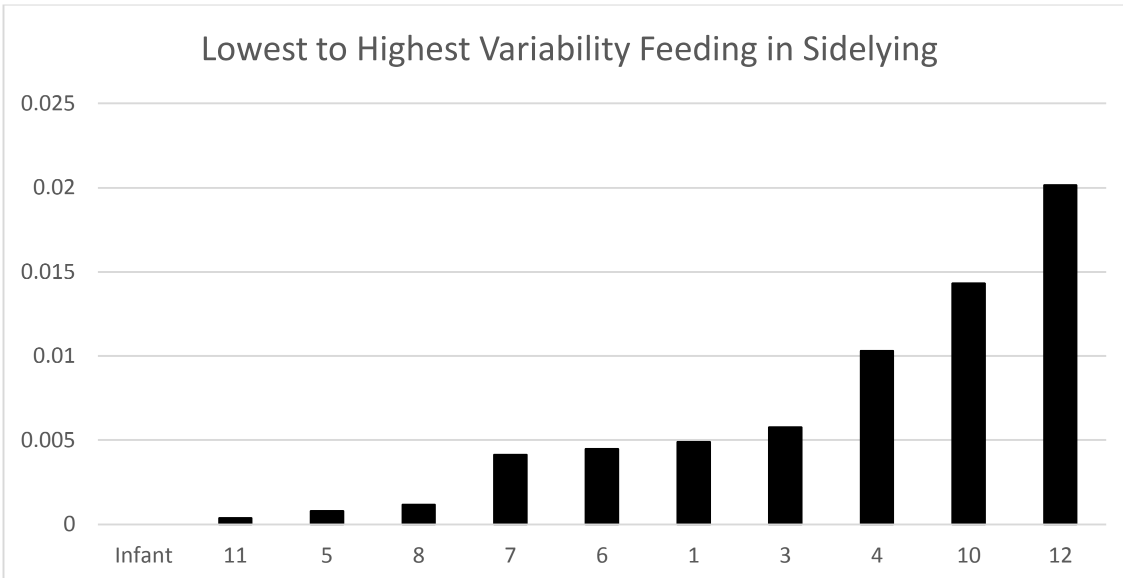
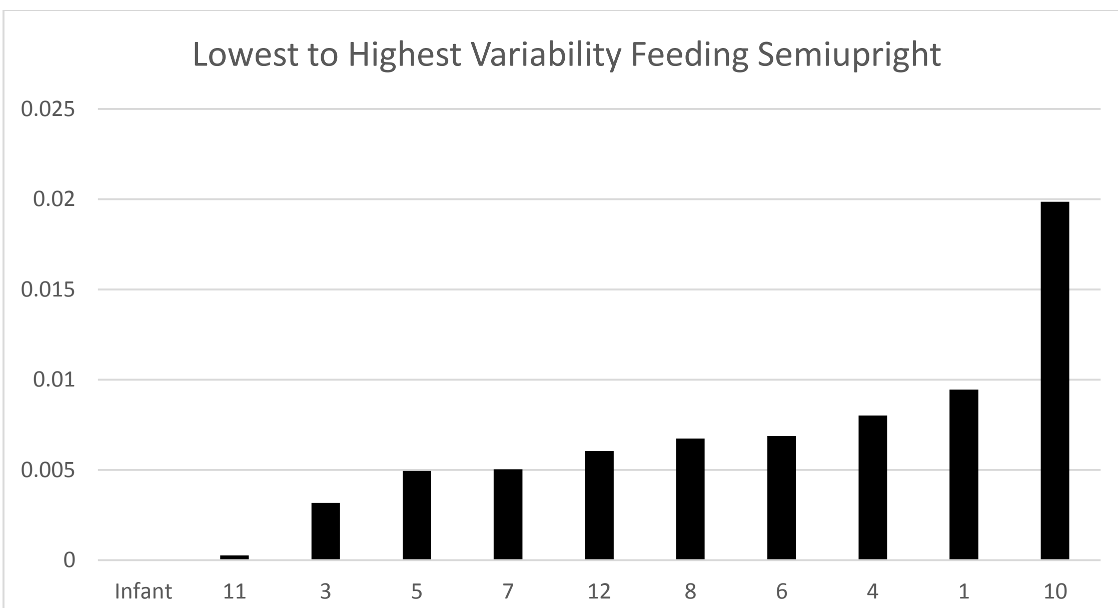


Figure 11g. Post feeding Recovery (Supine)

Appendix F

**Comparison of Approximate Entropy Variability Sidelying vs. Semiupright**



## Appendix G. **Letter of Explanation to Parents**

Dear

Your baby has been chosen to participate in research studying the effects of two different methods of feeding used to help premature infants. Bottle feeding is often difficult for premature infants. I am very interested in studying the way babies respond to feeding so I can assist them in progressing from tube feeding to bottle feeding

I request your permission for your infant to participate in the research. If you agree for your baby to participate, your baby will be fed three times on one day using the same techniques currently used in the nursery, while being observed by me. Your baby will be studied at his/her regular feeding time as determined by nursing. Your baby will be fed the normal type and amount of formula or breast milk prescribed by your doctor. He/she will be fed using a standard slow flow nursery nipple and bottle. Your baby will be carefully monitored using the same bedside monitor and oxygen sensing equipment that you have already seen used with your baby in the nursery. The only difference will be a video tape recorder and lap top computer at the bedside during the feeding observation. The videotaping and computer will allow me to study the information in detail.

You are welcome to observe the feeding interventions. On the one day of the study, I will make every attempt to create a schedule that is convenient for you. I will be available to provide you with information regarding your baby's feeding following the observation. This research is being done in partial fulfillment of the requirements for a Doctor of Philosophy Degree in Health Sciences at Rutgers University in New Jersey. The research is approved by the Internal Review Board at Connecticut Children's Medical Center and Rutgers University.

Please feel free to contact me with any questions that you may have about your baby's involvement in the study. The nurses will help you contact me. I will contact you about the scheduling of the feeding observations and will be pleased to talk to you about your baby.

Thank you,
Caryn Bradley PT, MMSc.
Neonatal Physical Therapist

## Appendix H

**INFORMED CONSENT FOR PARTICIPATION IN RESEARCH ACTIVITIES**
Connecticut Children's Medical Center

**CCMC Investigator:** Caryn Bradley PT, MMSc
**Collaborators:** James Hagadorn, MD; Phyllis Guarrera-Bowlby PT,
**Department:** Neonatology **Phone:** 860 545 9720

**Title of Research:** The Effect of Position on Bottle Feeding in Preterm Infants

**Purpose of Research:**
You are being asked to volunteer your infant in a research project that evaluates the effects of two different methods of feeding premature infants. Progressing from tube feeding to bottle feeding is often difficult for infants who are born prematurely. The purpose of this study is to determine whether the positioning of preterm infants during bottle feedings affect the heart rate, breathing rate, breathing pattern and amount of oxygen in the blood during the time of feeding. This study will also examine your baby's alertness during feeding, the time required to complete the feeding and the total amount of formula or breast milk your baby consumed during the feeding.
Your baby was identified as a potential subject because he/she was born prematurely and is learning to transition from tube feeding to bottle feeding. We hope to enroll 10 infants in this study.

**Procedures:**
If you agree to your baby's participation in this project, your baby will be observed across three consecutive feedings for one day. Your baby will be fed every three hours either by tube or bottle feeding. Your baby will be studied at his/her regular feeding time as determined by nursing. Your baby will be fed the normal type and amount of formula or breast milk prescribed by your doctor. Your baby will be fed using a standard slow flow nursery nipple and bottle.

The following is an overview of the sequence of events and procedures that are planned for this study:

1. Your baby will be assigned to one of two sequences of feeding methods: bottle feeding in semiupright then bottle feeding in elevated sidelying or bottle feeding in elevated sidelying then bottle feeding in semiupright.

- Your baby will be fed by bottle two times during the day of observation by a trained nurse or developmental specialist.
- Each feeding will be divided into five periods of observation: a two minute prefeeding recording when your baby is on his/her back in bed, a two minute prefeeding recording when your baby is held in the nurse or therapist's arms, a recording during bottle feeding when your baby is held

in the nurse or therapist's arms in semiupright or elevated sidelying, a two minute postfeeding recording when your baby is held in the nurse or the therapist's arms and a two minute postfeeding recording when your baby is placed back on his back in bed.

- This feeding method is part of standard nursing care, the timing of the phases of feeding and recording of data are part of the research protocol.



2. Your baby's heart rate, breathing rate, breathing pattern and the amount of oxygen in

his/her blood will be carefully monitored using the same bedside monitor and oxygen sensing equipment that you have already seen used with your baby in the nursery. The only difference will be the use of a video camera and a lap top computer at bedside during the feeding observation. The computer will allow us to record the information from the monitors and the video camera will allow us to record your infant's response to feeding in order to study the information in detail.

**Risk and Inconveniences:**
The procedures used in this study are the same as standard care for transitioning premature infants from gavage to bottle feeding. Your infant will be intensely monitored during feedings. The only inconvenience to you will be that you will not be able to hold or feed your baby during the feedings being studied. Observation of your baby across three feeding will last approximately seven hours. You may want to schedule your visits for another time of day so that you can hold and play with your infant when you come to the hospital. You may observe the research if you wish. The physical therapist conducting the study will be available to provide you with information regarding your baby's feeding following the observation. The physical therapist will inform you of the

observation schedule and will work with you on schedule that is convenient for everyone. There is a slight risk of breach/loss of confidentiality.

**Benefits:**
Your infant may or may not benefit from this study. However, results from this study may contribute to the clinical care and standard practice for feeding premature infants. Any information obtained regarding your baby's feeding competencies and/or problems will be shared with your infant's nurse and with the medical staff. Results of this study may provide information on optimizing infant position during feeding. Benefits for your infant may therefore include: improved heart rate and breathing response to bottle feeding, reduced fatigue with oral feeding, improved nutritional intake and/or improved behavioral response to handling and position change. In addition, suggestions for positioning your infant may be provided to his/her caregivers so they may assist your infant in making a smooth transition from gavage to bottle feeding. If you do not wish to participate, your infant will receive the standard nursing care without data collection.

**Voluntariness and Right to Withdraw:**
Your decision for your infant's participation is voluntary. You may refuse to allow your infant to participate, and you may withdraw your consent and discontinue your infant's enrollment in the study at any time. Your decision whether or not to allow your infant to participate will not affect your infant's future medical care at Connecticut Children's Medical Center or any other benefits to which you are entitled.

**Questions:**
The Principal Investigator, Caryn Bradley PT, MMSc., is willing to answer any questions you may have about the study, or address any concerns or complaints, and may be reached at
(860) 545-8378. Further concerns or questions about this study may be directed to Dr. James Hagadorn, Attending Neonatologist. If you have questions about your infant's rights as a research subject, or if you would like to discuss problems, concerns, or questions, obtain information, or offer input about a particular research study, you may call the Institutional Review Board Office at Connecticut Children's Medical Center at (860) 545-9980. In the event of a research-related injury, please contact Dr. James Hagadorn (860) 535-9720.

**Confidentiality:**
The confidentiality of your infant's records will be maintained in accordance with applicable state and federal laws. De-identified data collected (videotapes, recordings of heart rate, breathing rate, breathing pattern and the amount of oxygen in the your baby's blood) will be maintained for future analysis. Neither your baby's name nor any other identifiers (name tag, wrist band) will be on the videotape. The videotaping and data collected with be identified by a subject identification number only. Only the principal investigator has access to the identification key that links the code to your baby's name. This identification key will be password protected and stored in a locked cabinet in a locked office.

You may request that your infant's records be released to your personal physician. However, no information that would reveal your child's identity will be released or published without your permission. The CCMC Institutional Review Board, and individuals designated by the Connecticut Children's Medical Center Institutional Review Board or the Human Research Protection Program Office to monitor research may view the study related medical records. Please note, for the purposes of CCMC, "study related medical records" shall be defined as "research and pertinent clinical medical records".

**Economic Considerations:**
There will be no cost to you by being part of this study and there is no compensation to your infant for being in this study.

Significant new findings developed during the course of the research which may relate to your willingness to continue to participate will be provided to you.

Please read the above information carefully and discuss this study with the principal investigator (or designee) and her staff. You may obtain information about the results of this study when it is completed, by contacting the principal investigator.

Based on the information provided, you agree to allow your child to participate in this study. Upon signing, you will receive a copy of this form. All the questions you have at this time have been answered.

As the parent/guardian, I have legal responsibility for the care and custody of __________________.
I willingly agree to allow my infant, to participate in this investigation, The Effect of Bottle Feeding on Preterm Infants. The purpose, procedures, and length of my infant's involvement have been explained to me.

_________________________________________ ____________________

Parent/Guardian Date

_________________________________________ ____________________

Second parent signature Date

I have fully explained to the parent/guardian the nature and purpose of the above described research and the risks involved in its performance. I have answered and will answer all questions to the best of my ability. I will inform the participant of any changes in the procedure or the risks and benefits, if any should occur during or after the course of this study.

_________________________________________ ____________________

Investigator/Person Obtaining Consent Date

_________________________________________ ____________________

Witness Date

Appendix I

**Research Study Check List**

| | Date: | Person Completing Form: |
|---|---|---|
| Subject Data Collection Form Complete | | |
| Letter of Explanation to Parents Given | | |
| Research Protocol Given to RN | | |
| Consent Form Given | | |
| HIPPA Form Given | | |
| Consent Form Signed | | |
| HIPPA Form Signed | | |
| Feeding Method Procedure Given to RN | | |
| Feeding Method Reviewed with RN | | |
| Observational Data Form Complete | | |

Name: ________________

Appendix J

## Subject Observational Data Form

**SUBJECT #: ________________** **DATE: ____________________**

**FEEDING METHOD SEQUENCE**: A or B

**FEEDING HISTORY:**

FORMULA/BREAST MILK:_____ RX VOLUME OF FEEDING:______________
FEEDING SCHEDULE:___________ TYPE OF NIPPLE:_________________________
MEDICATIONS:______________ MEDICATION SCHEDULE:_________________
CAFFEINE Y N REFLUX MEDS Y N DIURETICS Y N

**FEEDING OBSERVATION 1:**

**VITAL SIGN STABILITY AT REST:**

HEART RATE _______bpm
RESPIRATORY RATE ______rpm
OXYGEN SATURATION_______%
DOCUMENTED REFLUX Y N

**POSITION FEEDING ONE: ______**

AMOUNT OF FEED RESIDUALS ____cc
FEEDING READINESS SCORE: _______
QUALITY OF FEEDING SCORE:______

**ORAL FEEDING :**

START TIME:___________
STOP TIME: ____________
TOTAL VOLUME OF FEEDING:____cc
TOTAL TIME OF FEEDING:____________

**TEMPERATURE:**

PREFEEDING:_____________
POSTFEEDING:____________

**BEHAVIORAL STATE:**

AT INITIAL OBS:___________
AT FINAL OBS:_____________

**FEEDING OBSERVATION 2:**

**VITAL SIGN STABILITY AT REST:**

HEART RATE _______bpm
RESPIRATORY RATE _____rpm
OXYGEN SATURATION______%
DOCUMENTED REFLUX Y N

**POSITION FEEDING TWO: ___________**

AMOUNT OF FEED RESIDUALS ____cc
FEEDING READINESS SCORE:_______
QUALITY OF FEEDING SCORE:______

**ORAL FEEDING:**

START TIME:__________
STOP TIME:____________
TOTAL VOLUME OF FEEDING:___cc
TOTAL TIME OF FEEDING:_________

**TEMPERATURE:**

PREFEEDING:______________
POSTFEEDING:_____________

**BEHAVIORAL STATE:**

AT INITIAL OBS:___________
AT FINAL OBS:_____________

Appendix K

## Subject Data Collection Form

**Subject Number: ________**

NAME: _________________________________ SEX: M/ F

RACE: Asian Black Caucasian Hispanic Other

DATE OF BIRTH:_______________ AGE OF PREMATURITY:_______

POSTNATAL AGE:______________ ADJUSTED GESTATIONAL AGE:_________

BIRTHWEIGHT:__________ IUGR/SGA/AGA

CURRENT WEIGHT:_______________________

MEDICAL HISTORY

MAJOR CONGENITAL ANOMALIES Y N

IVH GRADE III OR IV Y N

PDA MURMURS IN LAST 3 DAYS Y N

SUPPLEMENTAL O2 (CURRENTLY) Y N

INFANT OF SUBS. ABUSING MOTHER Y N

DOCUMENTED REFLUX Y N

MAINTAIN TEMP OOB FOR 30 MIN ON TWO OCCASION Y N

APGAR SCORES 1min. _____ 5min._____ 10min._____

MEDICATIONS:_________ MEDICATION SCHEDULE:_________________

CAFFEINE Y N REFLUX MEDS Y N

DIURETICS Y N

VITAL SIGN STABILITY AT REST:

HEART RATE _______bpm

RESPIRATORY RATE _______rpm

OXYGEN SATURATION _______%

**NAME**:________________________________________

FEEDING HISTORY (FOR DATA COLLECTION) :

FORMULA/BREAST MILK:_________RX VOLUME OF FEEDING:________________
FEEDING SCHEDULE:____________ TYPE OF NIPPLE:_________________________

FEEDINGS 24 HOURS PRIOR TO OBS: OBSERVATION DAY:

AMOUNT OF FEED RESIDUALS ____cc AMOUNT OF FEED RESIDUALS ____cc
FEEDING READINESS SCORES: FEEDING READINESS SCORES:
___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ __ ___

QUALITY OF FEEDING SCORES: QUALITY OF FEEDING SCORES:
___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

#FULL VOLUME GAVAGE _________ #FULL VOLUME GAVAGE _________
# NIPPLE/GAVAGE _________ # NIPPLE/GAVAGE _________

#FULL VOLUME BOTTLE _________ #FULL VOLUME BOTTLE _________

| >24 Hrs 25-50% RxVolume | **PMA** | **Day** | **Feeding 1** | **Feeding 2** | **Feeding 3** | **Feeding 4** | **Feeding 5** | **Feeding 6** | **Feeding 7** | **Feeding 8** |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 0200 | 0500 | 0800 | 1100 | 1400 | 1700 | 2000 | 2300 |
| Readiness Score | | | | | | | | | | |
| Quality Score | | | | | | | | | | |
| Rx/Intake Volume | | | | | | | | | | |
| | | | | | | | | | | |
| 48 Hrs 25-50% Rx Volume | **PMA** | **Day** | **Feeding 1** | **Feeding 2** | **Feeding 3** | **Feeding 4** | **Feeding 5** | **Feeding 6** | **Feeding 7** | **Feeding 8** |
| | | 2 | 0200 | 0500 | 0800 | 1100 | 1400 | 1700 | 2000 | 2300 |
| Readiness Score | | | | | | | | | | |
| Quality Score | | | | | | | | | | |
| Rx/Intake Volume | | | | | | | | | | |
| | | | | | | | | | | |
| <72 Hrs 25-50% RxVolume | **PMA** | **Day** | **Feeding 1** | **Feeding 2** | **Feeding 3** | **Feeding 4** | **Feeding 5** | **Feeding 6** | **Feeding 7** | **Feeding 8** |
| | | 3 | 0200 | 0500 | 0800 | 1100 | 1400 | 1700 | 2000 | 2300 |
| Readiness Score | | | | | | | | | | |
| Quality Score | | | | | | | | | | |
| Rx/Intake Volume | | | | | | | | | | |

Appendix L

# Procedure for Data Collection

Connection of the Patient Monitor to PC

1. Insert RS232 Board into monitor.

Turn monitor off and back on to initiation reading by RS232 board.

2. Serial Connection by using a connector cable (RJ45-USB).

Attach green plug into top port and grey USB inserts in to front left port on laptop computer

3. Ensure blue dongle is plugged into USB port on right

Creating a Patient Record

1. Turn computer on and enter password
2. IxTrend can be accessed from icon or desktop setting ixTrend icon
3. Once ixTrend is open, chose one patient monitor and right click to open and start the connection by clicking Connect.
4. A wizard will open. Now you can choose or create a patient.
5. Create a new patient or select an existing patient from list on left.
    a. A window will open. For creating a new patient record complete unidentified patient information. Click Next, Next and Finish. New patient will be listed on left side.
    b. For an existing patient, the patient record will be displayed in the patient record view on the left side. Here is the master data of the patient. These data can be displayed and changed.

Configuration of Storage Profiles

1. To configure storage profiles, select the session view (double-click on a session).
2. Choose all signals which to be recorded at the same time.
3. Left click on the storage create profile button (top right) to store the profile.
4. Storage profile will be displayed under “Available Resources”.
5. Select the storage profile before beginning data acquisition.

Recording Signals

1. The patient monitor is connected and the patient is chosen. The patient monitor and all data sent (also markers) are listed below the label "Not started session".
2. Double click on "Not started session" and the session view will open.
3. The recording time starts by clicking on the green play arrow (top right) and finishes by clicking on the red stop bottom (top right).
4. Start date and time should be visible in profile fields.
5. Recorded session will appear under the patient name on the left.
6. Expand out to see data collected

Display Signals

1. All available signals are listed in the patient record view.
2. Right click on the favorite signal (vital sign parameter) and a menu will be opened.
3. Choose between different views. The diagram opens on the right side.
4. To scale the y-axis scroll the mouse. When the left mouse button is pressed it is possible to move the y-axis up and down.
5. With the drag-and-drop the numeric signals can be displayed as numeric in the right column of the diagram view.

Configuration of Diagram Profiles

1. To display signals always in the same way, configure the diagram profiles.
2. Drag all signals in to the diagram view and scale them. With left click on the diagram profile button (bottom row top right) you can store the profile.
3. The diagram profile will be displayed under "Available Resources".
4. When connecting the patient monitor again, the diagram profile is available.

Table1

Characteristics of the Study Infants (n=12)

| | Gestation Age (weeks) | Birth Weight (gram) | Postmenstrual Age (weeks) | Chronologic Age (days) | Study weight (grams) | Gender*/ Ethnicity | Apgar Score 1, 5, 10 minutes | Meds |
|---|---|---|---|---|---|---|---|---|
| Infant 1 | 30.1 | 1005 | 34.5 | 32 | 1588 | F/Hispanic | 5, 6, 9 | Ferinsol |
| Infant 2 | 31.4 | 1928 | 34.5 | 22 | 2100 | F/White | 7, 8 | Ferinsol Caffeine |
| Infant 3 | 31.4 | 2215 | 35.1 | 25 | 2215 | F/White | 7, 8 | Ferinsol |
| Infant 4 | 30.1 | 1450 | 35.3 | 37 | 2568 | M/White | 9, 9 | Iron/Vit D |
| Infant 5 | 34.0 | 2415 | 35.0 | 7 | 2335 | F/Hispanic | 4, 8 | None |
| Infant 6 | 33.4 | 1965 | 35.5 | 14 | 2143 | M/White | 7, 8 | None |
| Infant 7 | 33.4 | 1810 | 35.5 | 14 | 2128 | M/White | 7, 8 | None |
| Infant 8 | 27.3 | 1086 | 34.3 | 49 | 2331 | M/White | 7, 8 | Iron/Vit D |
| Infant 9 | 29.5 | 1545 | 35.3 | 40 | 2387 | M/Hispanic | 7, 7, 7 | Caffeine |
| Infant 10 | 32.5 | 1570 | 35.4 | 20 | 1941 | M/White | 9, 9 | None |
| Infant 11 | 32.6 | 1610 | 35.4 | 21 | 2023 | M/White | 4, 8 | Iron/VitD |
| Infant 12 | 32.3 | 1733 | 35.0 | 18 | 2067 | M/Black | 1, 9 | None |

*F= Female M=Male

Table 2
Feeding Outcomes Related to Body Position during Feeding (n=12)

| | Prescribed Volume (mls) | Type of Milk*(calories) | Proficiency** (%) | | Rate of Milk Transfer (ml/min) | | Oral Feeding Performance (%) | | Duration (minutes) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Semiupright | Sidelying | Semiupright | Sidelying | Semiupright | Sidelying | Semiupright | Sidelying |
| Infant 1 | 29 | MOM 25.5 | ** | ** | 0.21 | 1.47 | 10.30% | 75.90% | 14.1 | 15 |
| Infant 2 | 42 | MOM 24 | ** | ** | 1.19 | 0.09 | 40.50% | 2.40% | 14.32 | 11 |
| Infant 3 | 44 | MOM 24 | ** | ** | 1.12 | 0.28 | 45.50% | 6.80% | 17.78 | 10.82 |
| Infant 4 | 44 | MOM 24 | 11.36 | 11.36 | 1.05 | 1.04 | 34.09 | 34.09 | 14.28 | 14.48 |
| Infant 5 | 48 | Enfamil 20 | 29.16 | 45.8 | 1.39 | 3.123 | 29.2 | 62.5 | 10.1 | 9.58 |
| Infant 6 | 43 | Enfamil 20 | 32.6 | 46.5 | 2.57 | 3.35 | 100 | 53.5 | 16.72 | 6.87 |
| Infant 7 | 43 | Enfamil 22 | 34.9 | 34.9 | 2.19 | 2.79 | 69.8 | 90.7 | 13.7 | 13.97 |
| Infant 8 | 44 | MOM 20 | 22.7 | 20.5 | 1.74 | 1.61 | 68.2 | 54.5 | 17.2 | 14.92 |
| Infant 9 | 45 | Elecare 22 | 22 | 20 | 1.35 | 1.19 | 71 | 31 | 23.73 | 11.75 |
| Infant 10 | 40 | MOM 24 | 15 | 37.5 | 0.74 | 2.58 | 30 | 70 | 16.15 | 10.85 |
| Infant 11 | 40 | MOM 24 | 15 | 12.5 | 1.74 | 0.66 | 70 | 12.5 | 16.08 | 7.55 |
| Infant 12 | 40 | MOM 22 | 50 | 50 | 2.59 | 1.78 | 95 | 80 | 14.67 | 18 |

*MOM= Mothers Own Breast Milk

**Data not available on infants 1-3, Proficiency n=9

Table 3

Feeding Outcomes Related to Sequence of Feeding (n=12) **Data not available on infants 1-3, Proficiency (n=9)

| | Prescribed Volume (mls) | Type of Milk*(calories) | Proficiency** (%) | | Rate of Milk Transfer (ml/min) | | Oral Feeding Performance (%) | | Duration (minutes) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Order of Feeding | | Order of Feeding | | Order of Feeding | | Order of Feeding | |
| | | | First | Second | First | Second | First | Second | First | Second |
| Infant 1 | 29 | MOM 25.5 | ** | ** | 1.47 | 0.21 | 75.90% | 10.30% | 15 | 14.1 |
| Infant 2 | 42 | MOM 24 | ** | ** | 1.19 | 0.09 | 40.50% | 2.40% | 14.32 | 11 |
| Infant 3 | 44 | MOM 24 | ** | ** | 1.12 | 0.28 | 45.50% | 6.80% | 17.78 | 10.82 |
| Infant 4 | 44 | MOM 24 | 11.36 | 11.36 | 1.05 | 1.04 | 34.09 | 34.09 | 14.28 | 14.48 |
| Infant 5 | 48 | Enfamil 20 | 45.8 | 29.16 | 3.123 | 1.39 | 62.5 | 29.2 | 9.58 | 10.1 |
| Infant 6 | 43 | Enfamil 20 | 32.6 | 46.5 | 2.57 | 3.35 | 100 | 53.5 | 16.72 | 6.87 |
| Infant 7 | 43 | Enfamil 22 | 34.9 | 34.9 | 2.79 | 2.19 | 90.7 | 69.8 | 13.97 | 13.7 |
| Infant 8 | 44 | MOM 20 | 20.5 | 22.7 | 1.61 | 1.74 | 54.5 | 68.2 | 14.92 | 17.2 |
| Infant 9 | 45 | Elecare 22 | 22 | 20 | 1.35 | 1.19 | 71 | 31 | 23.73 | 11.75 |
| Infant 10 | 40 | MOM 24 | 37.5 | 15 | 2.58 | 0.74 | 70 | 30 | 10.85 | 16.15 |
| Infant 11 | 40 | MOM 24 | 15 | 12.5 | 1.74 | 0.66 | 70 | 12.5 | 16.08 | 7.55 |
| Infant 12 | 40 | MOM 22 | 50 | 50 | 1.78 | 2.59 | 80 | 95 | 18 | 14.67 |