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Master's Degree in Biomedical Engineering

Direct and Indirect Tidal Volume estimation in Preterm Newborn

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Abstract

Premature birth is one of the major risk factors for infant mortality. This is caused by the incomplete development of the respiratory system. This failure can lead to a series of situations in which the newborn baby is faced with episodes of apnoea and bradycardia.

In order to allow a correct approach and a correct estimation of the seriousness of the situation, it is essential to correctly monitor the respiratory parameters of the preterm newborns. Indeed, the occurrence of apneic episodes is anticipated by an oscillation in the respiratory signal. Timely intervention by hospital personnel could thus be ensured in order to improve the infant's care. Such monitoring is usually performed with instrumentation that is invasive for the newborns and therefore leads to the development of new methodologies for monitoring these parameters.

This study examines the hypothesis of assessing respiration by means of the electrocardiographic signal obtained through the use of electrode already placed on the patient's chest. Of the respiratory signal, the tidal volume was analysed in particular.

The aim of the analysis performed is to verify the correlation between the tidal volume of the respiratory signal measured through the inductive band and the tidal volume of the respiratory signal obtained through the electrocardiogram. For this purpose, the tidal volumes of the two signals mentioned above were calculated using three different methodologies. For each calculation methodology, comparisons were made between the respiratory signal detected by the electrocardiogram and the respiratory signal given by the inductive band measurement.

This may be a step towards becoming revolutionary way of monitoring respiration for preterm infants.

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1 Cardio-respiratory System

The cardio-respiratory system is the system which is responsible for the correct oxygenation and transport of blood throughout the body.

It is made up of the circulatory and respiratory systems. The two systems are connected and work together; this connection is represented by the blood vessels which are able to link the two principal organs: the heart and the lungs.

Thanks to the heart, which acts as a pump to transport the blood, and thanks to the lungs, which are able to oxygenate it, our body receiver around 400 litres of oxygen every day; oxygen that is carried by haemoglobin, a globular protein component of the blood.

1.1 Respiratory System

The body can breathe in oxygen and expel carbon dioxide thanks to the numerous components that make up the respiratory system. It is constituted of the rib cage, the breathing muscles, the lungs and respiratory centres that are found in the brainstem.

Prematurity additionally has sizable outcomes on lung characteristic past the primary 12 months of age. [1]

Preterm infants have better rates of respiratory issues than term-born infants. The resulting pathologies appear like an outcome of ordinary lung structures, such as multiplied bronchial muscle, collagen and elastin. [2]

1.1.1 Lungs

Two organs are in charge of respiration: the lungs. The mediastinum serves as a barrier between them, which are situated in the so-called pulmonary lodge within the thoracic cage.

The intricate bronchial branching, interstitial tissue, blood arteries, nerves and pulmonary lobules make up the lungs. While the left lung only has two lobes (upper and lower), the right lung has three (upper, middle and lower). [Figure 1]

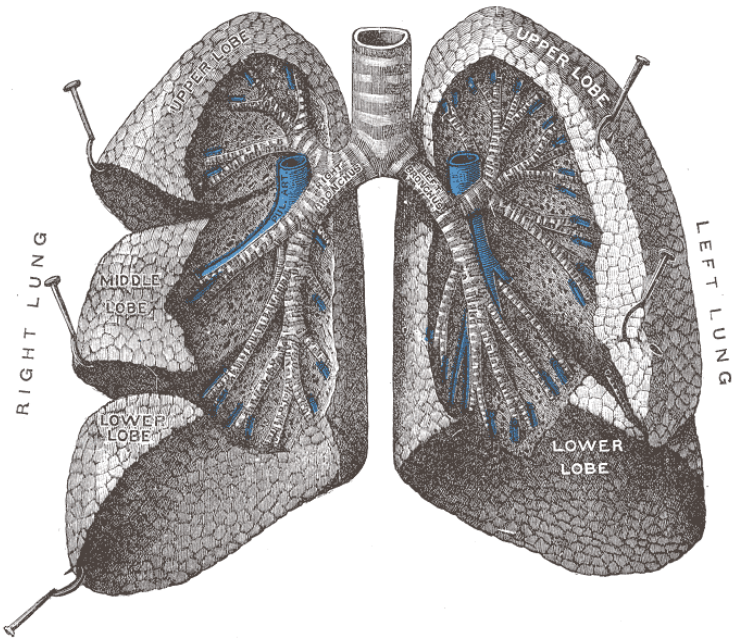

Figure1. Anatomy of lungs.

Pleuras, serous membranes that round the lungs, line them. The parietal and visceral leaflets make up each pleura. Pleural fluid, which is necessary for the respiratory process to function, is located between the two leaflets.

The pulmonary hilum, which is on the medial face of each lung, is where blood vessels and nerves enter and exit; this grouping of arteries and veins is known as the pulmonary peduncle.

The lungs can be divided into two parts: the parenchyma, which facilitates gas exchange, and the airways, which allow the distribution of air.

We have the following branching after the initial ramifications that permit air to move across the two distinct organs. The bronchi divide to create ramifications that eventually enable respiratory exchange by being progressively smaller in width. The vestibule, from which the alveolar ducts branch out and enter the pulmonary alveoli, marks their conclusion. The respiratory component is made up of the pulmonary alveoli. [Figure 2]

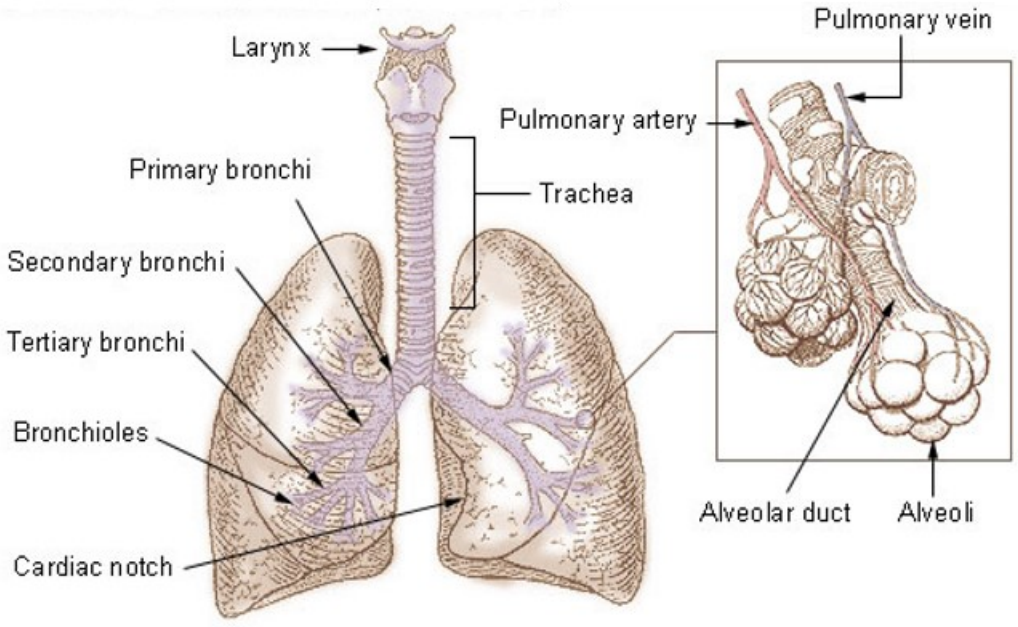

Figure 2. Structure of the intrapulmonary airways.

1.1.2 Respiratory Mechanism

The two phases of breathing are inhalation and expiration. Due to the depression caused by the diaphragm's descent and the contraction of the intercostal muscles, the lungs fill up during the inhaling phase. Then, as a consequence of the intrathoracic pressure dropping, the lungs expand and we inhale air.

On the other hand, exhalation is a passive phenomenon.

Due to the selective action of the epiglottis, air enters through the nose (or mouth), travels through the pharynx, larynx and lastly the trachea. The air then travels through the right and left bronchi and different branches before arriving at the pulmonary alveoli.

1.1.3 Respiratory Development

1. <u>Embryonic period (weeks 0 to 6)</u>

   This is the period while organ formation occurs. The lung seems as a ventral bud of the oesophagus [Figure 3], there may be the increase of a small diverticulum withinside the ventral wall of the anterior intestine, that is known as a primitive breathing diverticulum or pulmonary bud. In some days, the groove among the diverticulum and the anterior intestine closes. Thereafter we have the formation of the number one right and left bronchial buds after which hold with the secondary and tertiary ones [Figure 4].

   Vasculogenesis additionally occurs, the pulmonary vein seems as a small tubule that develops from the left atrial part of the heart.

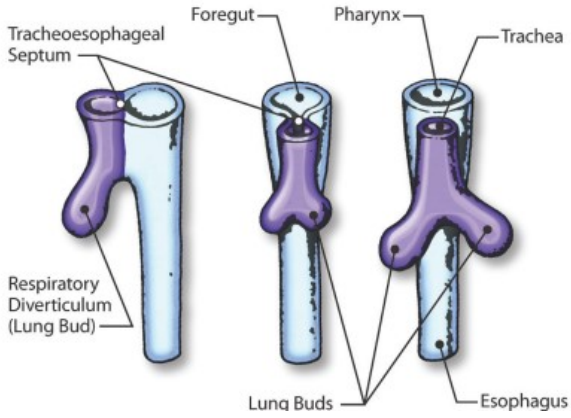

Figure 3. Embryonic period of the respiratory development.

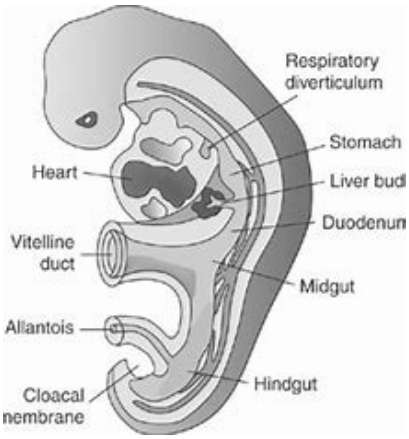

Figure 4. Development of respiratory tract during embryonic period.

2. <u>Pseudoglandular period (weeks 6 to 16)</u>

At this level there is the formation of all conductive airways. By the give up of this period, all vascular improvement is complete. [Figure 5]

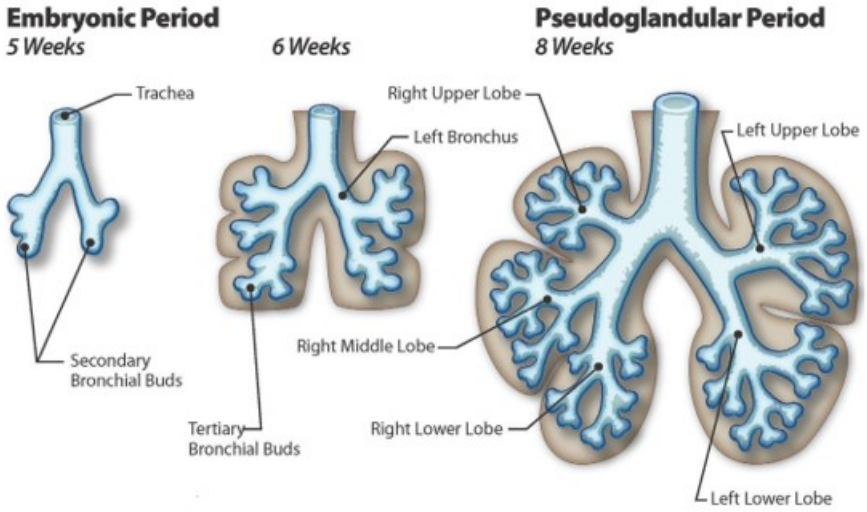

Figure 5. Comparison between the development of embryonic period and pseudoglandular period.

3. <u>Canalicular period (weeks 16 to 24)</u>

During this period, there may be improvement of the lung parenchyma and multiplication of capillaries. There is an elongation of the bronchial branching. As a ways as pulmonary vascular improvement is concerned, there may be a proliferation of vessels and a three-dimensional network is shaped withinside the mesenchyme.

4. Saccular period (weeks 24 to 36)

This phase is the restrict for untimely birth. The airlines lead to cluster of thin-walled terminal saccules; right here the ultimate airlines and alveolar ducts are formed. At 32 weeks the alveoli are already visible. [Figure 6]

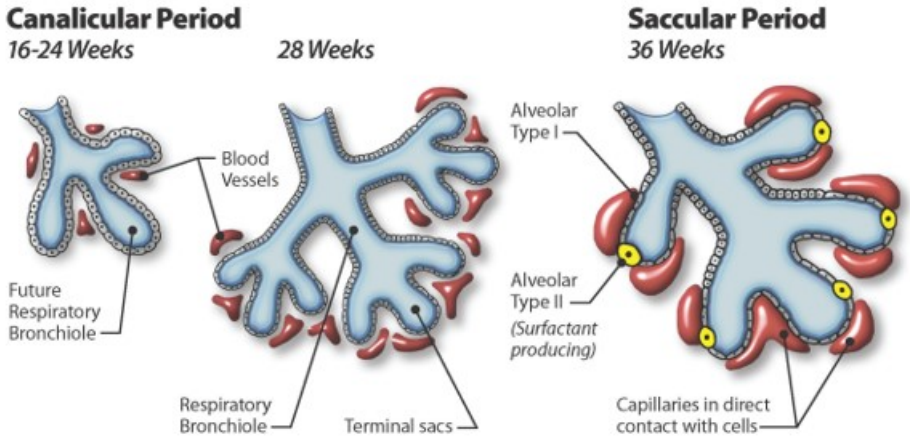

Figure 6. Comparison between the development of canalicular period and saccular period.

5. Alveolar period (36 weeks to 8 years)

The secondary alveolar septa are formed, which divide the terminal ducts and saccules into real alveolar ducts and alveoli. The gas exchange floor additionally increases.

[3] [4]

1.2 Cardiac System

The circulatory system, sometimes referred to as the cardiovascular or cardiocirculatory system, is made up of a number of components, including the heart, blood vessels, capillaries and lymphatic vessels. The body's internal fluid transportation is handled by this apparatus.

The heart is the focal point of the cardiovascular system. Veins are blood vessels that deliver blood to the heart, whereas arteries are blood vessels that flow blood away from the muscle. The aorta, which starts in the left ventricle, and the pulmonary artery, which originates in the right ventricle, are the two primary arteries.

1.2.1 Heart

The muscle at the center of all circulation is the heart. It consists of four chambers: two atria and two ventricles, which are independent in pairs. The primary function of the heart is to pump blood to all of the organs via the arteries, and it also has a secondary function of controlling heart bear via the unique conduction tissue.

The cardiac muscle is located in the centre of the thoracic cavity, in the anterior mediastinum between the two pleuropulmonary regions behind the sternum and the costal cartilages. It is located anterior to the vertebral column and above the diaphragm. [Figure 7]

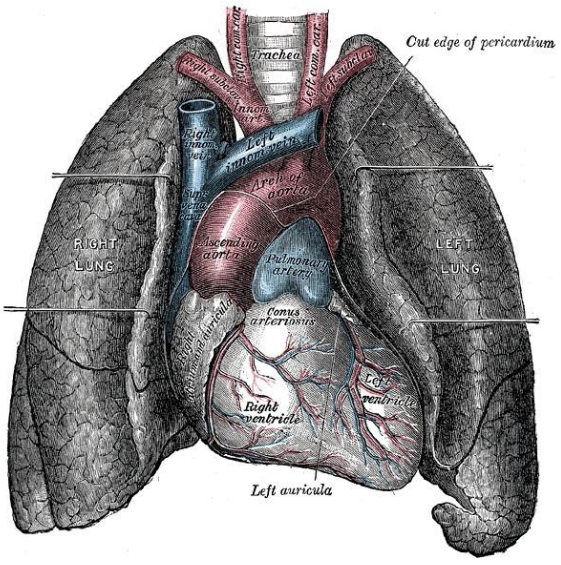

Figure 7. Frontal section of the thorax demonstrating the position of the heart in relation to the lungs.

The heart is contained within a membrane called the pericardial sac. A fibrous layer is also closely affixed to the heart and is called epicardium. A watery fluid fills the incredible small area between the pericardium and the epicardium, acting as a lubricant for the heart's motion inside the sac. Several valves regulate the blood flow. The valves that are located at the exit of the muscle are called the semilunar valves, while between the atria and the ventricles are the bicuspid or mitral valve, relating to the left side of the heart, and the tricuspid valve, relating to the right side. The valves allow blood to move from the atrium to the ventricle but not the other way around. [Figure 8] [Figure 9]

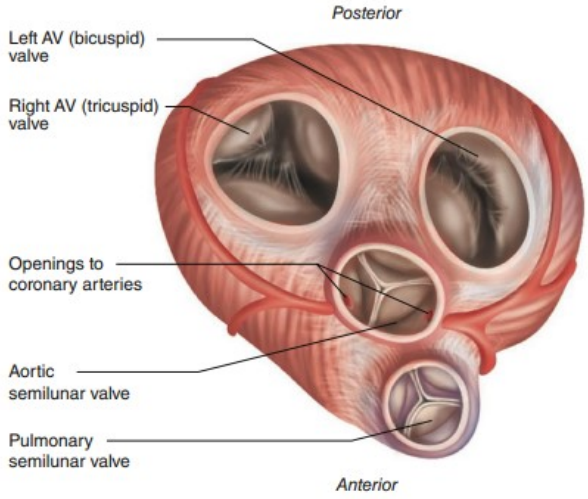

Figure 8. Representation of bicuspid, tricuspid, pulmonary and aortic valves.

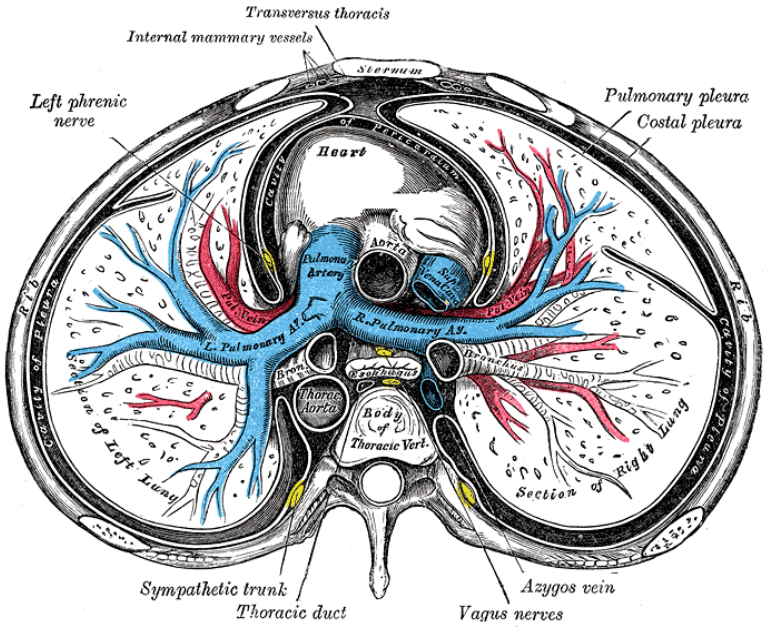

Figure 9. Top-down representation of the position of the valves

Myocardial cells, which are responsible for the muscle's autonomous and rhythmic contraction, and a fibrous framework make up the heart. Due to the activation of sodium channel, a membrane potential is produced, activating the calcium channels and causing the muscle to contract.

Systole and diastole, the two distinct phases of the cardiac cycle, are responsible for the heart pumping function. Systole is the contraction phase of the heart muscle, which then permits the blood flow to be pushed outwards. The diastole phase, on the other hand, is the relaxation phase that permits the atria to fill up. Atrio-ventricular valves are open and semilunar valves are closed during diastole; conversely, during systole, atrio-ventricular valves are closed while semilunar valves are one, allowing blood to flow outside the heart muscle. The atrio-ventricular valves' opening and closing are passive processes brought on by pressure variations across the valves. The atrio-ventricular valves are attached to muscular projections (papillary muscles) of the ventricular walls by fibrous strands (chordae tendinea) to prevent the valves from being forced up and opening backward into the atria when the ventricles are contracting.

1.2.2 Electrocardiogram

An electrocardiogram (ECG) is performed for the diagnosis of numerous diseases; it records the electrical activity of the heart muscle and the changes that arise at some stage in contraction and relaxation of the atria and the ventricles. The electrical activity of the heart and, consequently, its excitability is favoured to the contraction of the heart muscle.

Underlying this mechanism is the sinoatrial node, which acts as a pacemaker for the heart. It is able to determine the heart rate, i.e. the number of contractions occurring per minute. The depolarization of the sinoatrial node is capable to generate the action potential that leads to the depolarization for the remaining heart muscle cells. Starting from the sinoatrial node, the depolarization initially spreads to the right and left atria, whose contraction occurs almost simultaneously. It then spreads to the two ventricles, causing them to contract. Depolarization of the atria and subsequently the ventricles is made possible by the atrioventricular node, part of the conduction system, whose location is at the base of the right atrium. Propagation within the sinoatrial node is relatively slow, allowing

atrial contraction to be completed before the next ventricular contraction. From the atrioventricular node, the excitation propagates along the interventricular septum through the His bundle or atrioventricular bundle. [Figure 10]

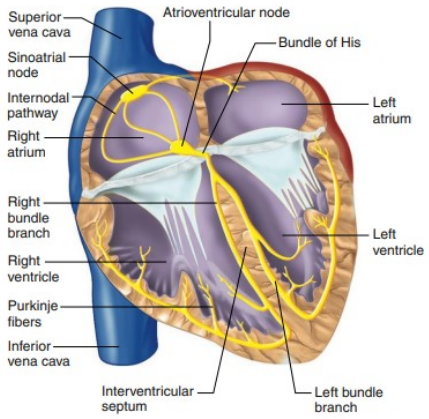

Figure 10. Heart conduction system.

The ECG is represented in form of waves representing the different phases of systole and diastole of the heart muscle. The first deflection corresponds to the P wave, there is depolarization of the atria. Next, we have the QRS complex which occurs approximately 0.15 seconds after the P wave and stands for depolarization of the ventricles. Finally, we have another deflection that matches the T wave, in which ventricular repolarization occurs. Atrial repolarization, on the other hand, occurs simultaneously with the QRS complex and is not always visible. [Figure 11]

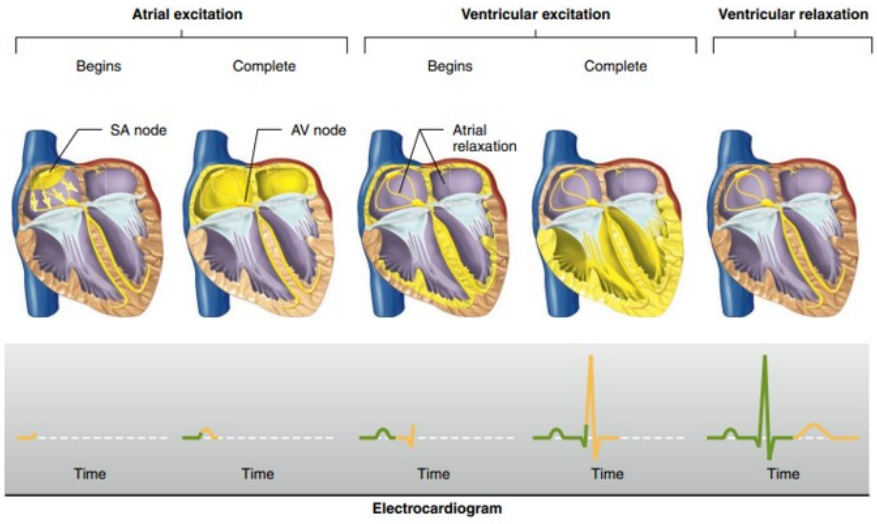

Figure 11. Cardiac conduction phases related to the representation of electrocardiographic waves detected.

1.3 Circulation Mechanism

Blood is circulated throughout the body through the lungs and left atrium as part of the pulmonary circulation. Then, it is carried from the left ventricle to the right atrium via the systemic circulation, passing through every organ and tissue in the body, aside from the lungs. The blood vessels in both circuits are known as arteries and veins, respectively, with arteries delivering blood away from the heart and veins returning blood from body organs and tissues to the heart.

Blood exits the left ventricle through the aorta, a single, sizable artery, as part of the systemic circuit. Offshoots of the aorta are the arteries of the systemic circulation, which separate into progressively smaller vessels. The tiniest arteries divide into arterioles, which divide into a massive number of extremely tiny vessels called capillaries, which combine to form larger-diameter veins called venules.

The systemic circulation's venules subsequently combine to produce the veins, which are bigger vessels. The inferior vena casa, which collects blood from below the heart, at the superior vena cava, which collects blood from above the heart, are produced by the union of the veins from the numerous peripheral organs and tissue. The blood is returned to the right atrium by these two veins.

A comparable circuit makes up the pulmonary circulation. A single, sizable artery, the pulmonary trunk, which splits into two pulmonary arteries, one serving the right lung and the other the left, is how blood exits the right ventricle. The arteries in the lungs continue to branch and link up with arterioles, which in turn lead to capillaries, which finally combine to form venules and veins. Four pulmonary veins empty the blood from the lungs into the left atrium. [Figure 12]

Blood picks up oxygen from the lungs as it passes through the capillaries in the lungs. As a result, the blood in the systemic arteries, left side of the heart, and pulmonary veins contains a lot of oxygen.

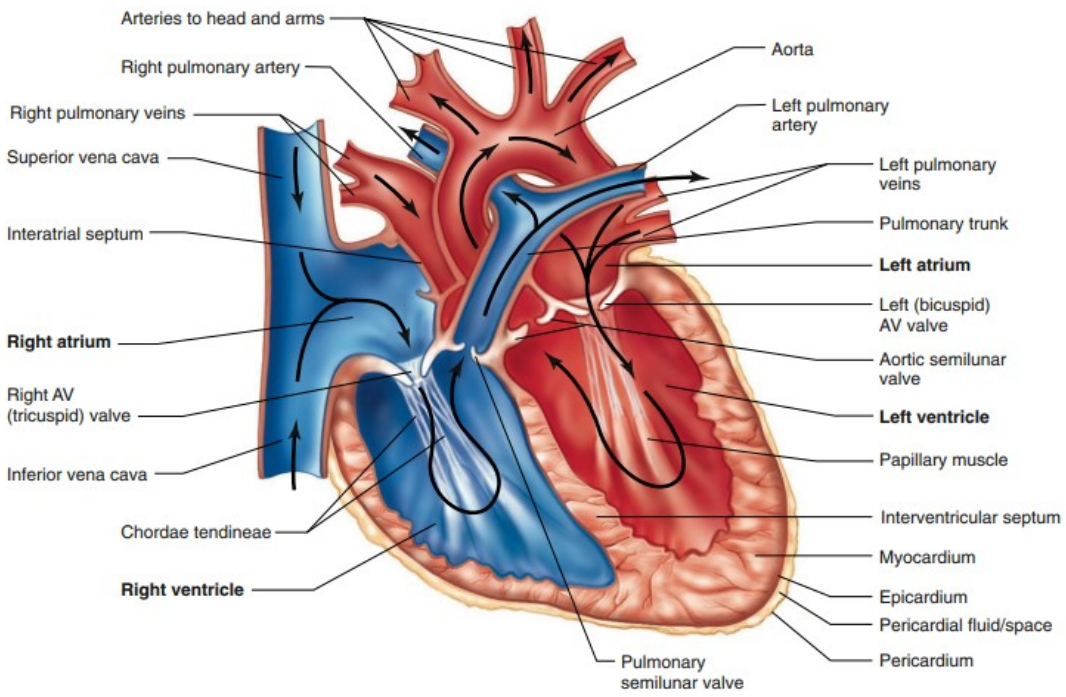

Figure 12. Representation of the circulation mechanism of the heart.

1.3.1 Fetal Circulation

The behaviour of the fetal circulation differs from that of normal circulation; in fact, there is no meaningful distinction between the arterial and venous systems, nor is there a distinction between the systemic and pulmonary circulation.

In actuality, the foetus receives oxygen-rich blood from the mother's placenta rather than breathing with its own lungs. Blood that has been oxygenated enters the inferior pulmonary vein, travels through the right atrium of the heart, the left ventricle, and both the right ventricle and the aorta before being disseminated throughout the body. The blood will only travel to the lungs in a very little quantity. The ducts arteriosus of Botallo, which connects the pulmonary trunk to the descending aortic artery and then closes after birth, enables this procedure.

2 Preterm new-born

The greatest risk factor for neonatal mortality appears to be preterm birth.

The WHO defines a preterm birth as one that takes place prior to 37 weeks of pregnancy.

Preterm birth occurs for a number of reasons, including complications during pregnancy or pre-existing conditions on the mother's side (such as asthma, diabetes and hypertensive disorders (HDP)), but it can also happen as a result of spontaneous birth; so, there are a number of situations that increase the likelihood of it.

The 6.5% of infants are preterm, and the 0.75% have significant issues. Despite significant advantages in paediatrics, 60-70% of infants do not survive. Compared to babies born between 34- and 36-weeks' gestation, risk factors, such as respiratory distress syndrome, are more prevalent in infants born before 34 weeks. Therefore, the gestational period is regarded as an indicator, the evaluation of which greatly affects obstetrical management choices.

The Association of Women's Health, Obstetric and Neonatal Nurses and the National Institute of Child Health and Human Development recently established a research agenda to better understand the short- and long-term medical complication linked to late-preterm births. Understanding the risk of morbidity in late-preterm infant is crucial for both assisting neonatal care providers in anticipating and managing potential morbidity during the hospitalization following birth, as well as possibly assisting in guiding decisions regarding nonemergency obstetric intervention and improving maternal care to reduce the risk for newborn morbidity. [5]

2.1 Classification

A “premature” or “immature” infant was first defined in 1948 by the World Health Assembly as a child who was born with a gestation period of less then 38 weeks or weight less than or equal to 2.5Kg. The definition was ineffective, though, as some infants were mistakenly classified as belonging to this category even though they weighed less than 2.5Kg and were delivered at 38 weeks, or as being “full-term” even through they weighted more than the required amount but were delivered at shorter gestational age. [6]

To determine the severity of mortality risk, a correlation between gestational weeks and infant weight was then made. [Figure 13]

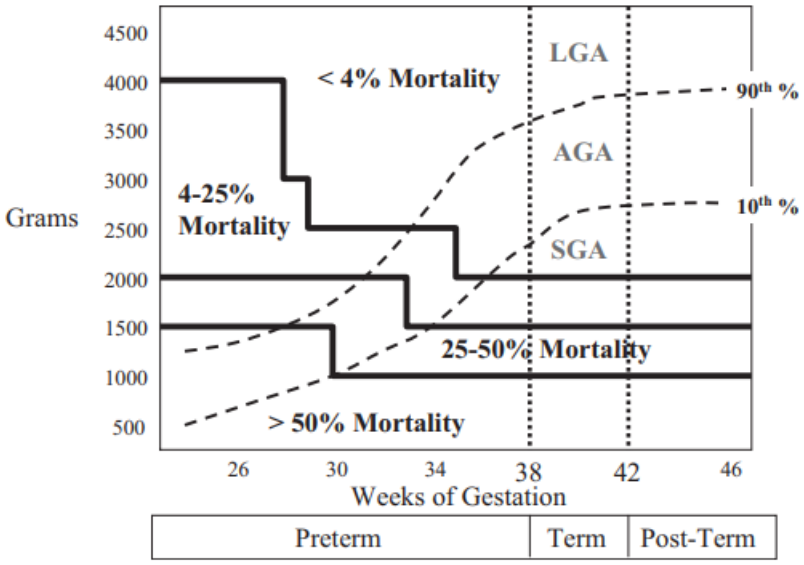

Figure 13. Classification by birth weight and gestational weeks.

The care of the newborn is encouraged by this classification.

According to the American Academy of Paediatrics (AAP) and the American Collage of Obstetrician and Gynaecologists (ACOG), the preterm infant is the baby given within 37 weeks of gestational age. [7]

A child being born prematurely is a risk factor, but this must be compared to the child’s birth weight. Therefore, the terms low birth weight (under 2.5 Kg), very low birth weight (under 1.5 Kg) and extremely low birth weight (under 1 Kg) must be distinguished.

2.2 Apnoea and Bradycardia

Apnoeic episodes are the primary issue brought on by the premature birth. Such occurrences may be so severe as to seriously jeopardize the premature baby's health. When caring for premature infants, the issue of apnoeic episodes is one that is frequently encountered. Early development of the respiratory and nervous systems is the cause of this difficulty.

Such episodes are moved on by immaturity, which causes brainstem neurons to fire incorrectly. The encephalogram flattens as a result of decreased muscle tone and monosynaptic reflex excitability caused on by prolonged apnoea [Figure 14].

Effective ventilation is dependent on two stuffs:

1. The rib cage, diaphragm and abdomen;
2. The upper airways;
3. The chest wall muscles (nostrils, pharynx and larynx).

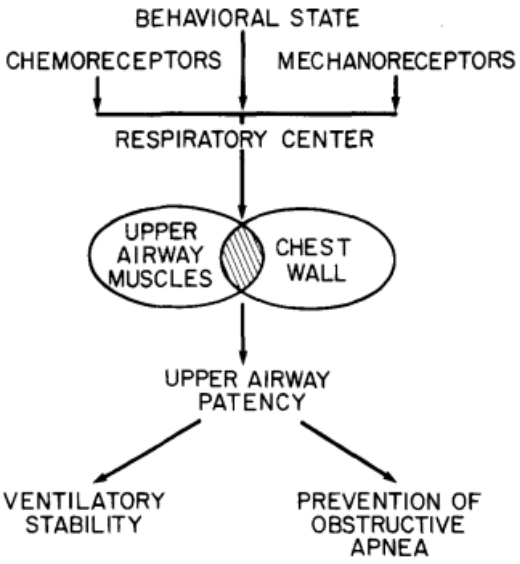

Figure 14. Mechanisms under control of breathing.

[8]

When discussing apneic episodes with premature newborns, it's important to understand that there are various classes and that some occur more frequently than others. Usually,

upper airway obstruction precedes or follows a central respiratory pause that results in neonatal apnoea; leading to central nervous system depression due to hypoxia and acidosis. Over 50% of apnoeic episodes in premature infants are caused by this type of apnoea, known as “mixed apnoea”. Airflow and chest wall movement stop simultaneously during isolated central apnoea, which is also frequent. On the other hand, less frequently, obstructive apnoea episodes occur in which the upper airway is completely blocked for the duration of the episode. [9]

Obviously, apnoeic episodes result from a variety of triggers that the baby has, such as: infections, thermal instability, metabolism disorders, impaired oxygenation etc; however, the newborn baby's premature birth is the main contributing factor. The effects of apnoea, which impair the subject’s oxygenation and heart rate, put the premature infant’s health at risk. [10] Additionally, a large occiput, hypotonic neck muscles, neck flexion, narrow airways, nasal oedema, gastro-oesophageal reflux and other conditions can increase the risk for premature infants. [11]

Some research have been done on the connection between respiratory rate and smells. A pleasant smell has been shown to partially offset respiratory failure. [12]

2.2.1 Pathophysiology

What initiates an apnoea is just as crucial to understand as what terminates one. Because of this, it's critical to understand the pathophysiology of such events and what causes them.

Apnea is a sign of improper respiratory mechanical control. The rhythmogenesis of the respiratory process is regulated by neurons in the bulbopontine area of the brainstem. They are able to direct the respiratory control muscles as a result of the input they receive (signals from peripheral and central chemoreceptors). Infants ‘immaturity affects their input receptors and their ability to control their upper airways. [8]

The improper respiratory mechanical control causes bradycardia and desaturation of it continues for a long time. [8] When an apnoea lasts longer than 20 seconds, or longer that 10 seconds and oxygen desaturation or bradycardia are also present, the apnoea is deemed clinically significant. [11]

The respiratory system disturbances can result in hypoxaemia and bradycardia, which lower cerebral oxygenation levels and reduce blood flow, both of which can cause brain injury.

Apnea, bradycardia and desaturation all have a direct relationship to one another. Recent research suggests that bradycardia results from a reflex reaction to the end of lung inflate, which is known to raise heart rate. Eighty-six percent of bradycardic occurrences are accompanied by a decrease in SpO_2, 83% are accompanied by apnoeas lasting longer than four seconds and in 79% of instances, both of the aforementioned conditions are present. [13]

One hypothesis for the increased bradycardia in preterm newborns is because the heart rate is primarily affected by hypoxia, which Is made worse by the simultaneous halt of lung inflate during apnoea. [13]

A reduction in arterial pO_2 (hypoxaemia) and oxygen saturation is one of the effects of Apnea of Prematurity (AOP). Hypoxic activation of carotid body chemoreceptors is one of the processes through which apnoea and desaturation cause bradycardia. In fact, $PaCO_2$ (partial pressure of carbon dioxide) is reduced and alveolar ventilation is increased by hypoxic stimulation. Bradycardia may result in decreased cardiac output, which could then lead to decreased systemic arterial pressure and cerebral blood flow velocity. Impaired brain flow may result in hypoxic ischemia damage given the subject's immaturity. [11]

Hypoxia (lack of oxygen in the body) and hypercapnia (increased blood carbon dioxide concentration) have both been like to asthma attacks in premature newborns. [11]

Premature newborns who experience hypoxia display a biphasic ventilatory response, first increasing ventilation and then decreasing respiration. This decline, known as "hypoxic ventilatory depression", is typical in preterm newborns. Any anemia issue a baby has can also contribute to hypoxia; red blood cells 'inadequate capacity to carry oxygen might have a negative impact on the respiratory system. [11]

Developing tissues and organs may be permanently damaged by the hypoxia caused by apnoea. Also, infant's condition deteriorates as a result of such hypoxia and hypercapnia events. [14]

In contrast to newborns and adults, the rise of CO_2 in the blood results in a prolonging of the exhalation period. [11]

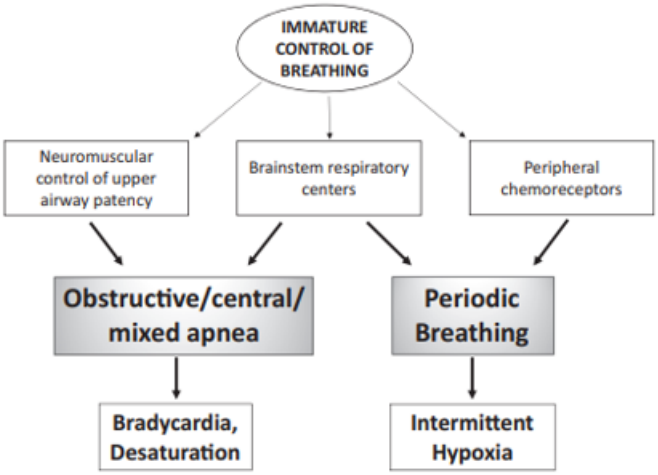

Figure 15. Pathophysiology of apnoea of prematurity.

Apnoeas are influenced also by metabolic health and ambient temperature, maternal administration of meperidine (a substance taken to treat pain) and sleep deprivation. These elements seem to be crucial in the development of apneas. [11] [15]

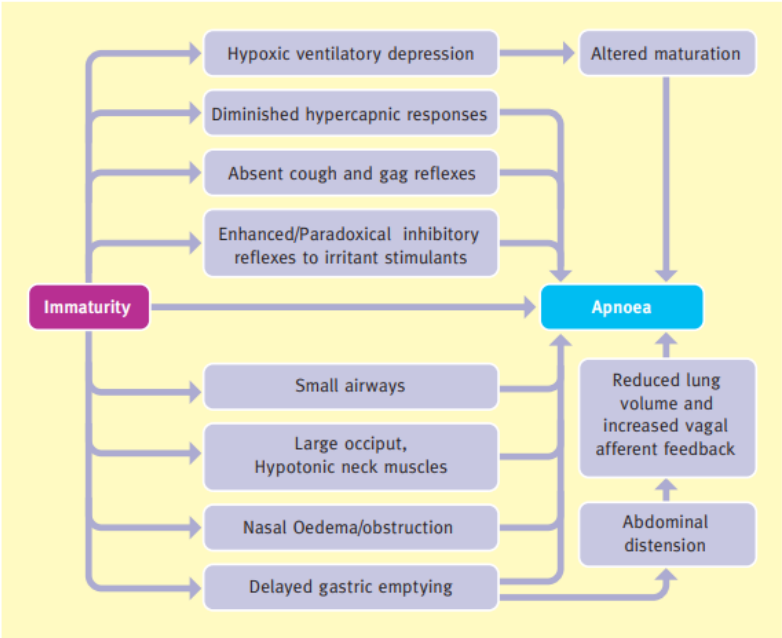

Figure 16. Causes of apnoea in premature infants.

A physiological condition known as gastroesophageal reflux (GER) usually affects preterm newborns. Through stimulation of the laryngeal chemoreflexes, it can cause apneic episodes. The widespread usage of anti-reflux medications in infancy is due to the continual prevalence of this syndrome together with apnoea. However, there is still no conclusive evidence linking GER and AOP. In reality, there is no link between the frequency of GER and the number of apneas associated with it; hence, the severity of GER is not a reliable indicator of AOP. [16]

2.2.2 Treatments

Apneic episodes need to be treated for AOP if they happen frequently, do not end on their own, or are accompanied by bradycardia or hypoxemia. [8]

Three macro-categories can be used to group interventions to treat apnoea in premature infants:

1. Interventions aimed to reduce respiratory work;
2. Interventions aimed to increase respiratory drive;
3. Interventions aimed to improve diaphragmatic contractility.

[13]

2.2.2.1 Interventions aimed to reduce respiratory work

The initial intervention looked at is the nursing position or prone head-elevated positioning.

Number of studies have found that nursing positions have a substantial impact on reducing sudden infant death in infants who are at risk. Normally, the supine position is advised to reduce this risk; however, because premature newborns often have respiratory issue, the prone position is more recommended. This decision was made because of greater lung compliance, reduced energy use and improved arterial oxygen tension. The issue of apnoeic episodes in preterm newborns is likewise positively impacted by this stance. [17]

In the pronated position with the head lifted, the chest wall is stabilized, which reduces thoraco-abdominal asynchrony; however, the commencement of apneic and bradycardic episodes does not always seem to benefit from this strategy. [13]

This position seems to be useful as a first-line strategy in preterm newborns. However, it doesn't seem to be significantly more beneficial when individuals are given caffeine or continue positive airway pressure treatment. [14]

When severe apnea manifests itself, one may need to take action with reanimation, mechanical ventilation or continue positive airway pressure (CPAP). Preterm infants now routinely receive CPAP, which is especially beneficial for treating neonatal respiratory distress syndrome (RDS). According to the 2016 European recommendations, CPAP should be administered as soon as possible after a premature birth. The main benefit of this method is that severe ventilation can be avoided; however, the likelihood of success is influenced by the newborn's weight and gestational age. There is an increased risk of pneumothorax, bronchopulmonary dysplasia, etc. among infants who cannot use CPAP. [19]

CPAP lowers the failure rate of extubation in premature newborns. A (bi)nasal needle or a nasopharyngeal tube can be used to administer it. Reintubation rates are lowered by 40% in this approach. Nasal intermittent positive pressure ventilation is a kind of CPAP (NIPPV). The frequency of bradycardia and desaturation is reduced by 50% when NIPPV is used. As a result, we can say that nasal ventilatory assistance is an effective way to enhance AOP. [13]

The (NCPAP) has numerous advantages, including:

- Improved oxygenation;
- Improved pulmonary function;
- Reduction in upper airway resistance;
- Upper airway stenting;
- Lung volume preservation;
- Reduction of respiratory work.

[20]

2.2.2.2 Interventions aimed to increase respiratory drive

The oxygen administration falls within this therapeutic area.

The first instance of oxygen delivery to stabilize a newborn's respiratory system was recorded in 1923. Intermittent hypoxia and apnea ca be diminished thanks to this technique. However, oxygen delivery is rarely employed due to its significant negative effects. [13]

An additional technique is the increased inspiratory CO_2 concentration. Administering a concentration of 0.8 percent CO_2 can be helpful in lowering the length and frequency of apnoeic episodes because apnoea also happens after a decline in CO_2 levels. However, given how fast newborns adjust to a change in CO_2 concentration breathed, this is not true over the long term. [13]

It is natural to immediately take into account also a red blood cell transfusion because preterm infants frequently have anemia issue. Despite this, other studies have not seen any improvement in transfused newborns. [13]

Currently, caffeine is the drug most commonly used to treat preterm infants with apnea.

Up until the 1970s, methylxanthines and continuous nasal positive airway pressure were used to treat apnoea in preterm infants. This treatment's dosage or duration are still not entirely clear. Caffeine is the most widely used of the methylxanthines. [23] Unfortunately, treatments like respiratory support and caffeine are only partially effective in lessening the burden of AOP. [14]

The most popular trimethylaxanthine is caffeine, which has a wider therapeutic range and fewer adverse effects. Additionally, caffeine can only be taken once day. These methyxanthines exerts their effects by activating receptors that promote respiration. Liver enzymes metabolize caffeine. These enzymes are lacking at birth, but they develop ad an individual grows throughout pregnancy and after giving birth. Caffeine is administered orally, thus being fully absorbed by the body. [8]

The initial dose of caffeine is 20 mg/kg, and then smaller daily doses are given after that. Opinions on these amounts are divided; the daily quantity might range from 5 mg/kg to 20 mg/kg. while some research indicate that a high daily dose benefits the neurological system and reduces the frequency of apneic episodes, other studies point to a problem with the prevalence of cerebral hemorrhages. [8]

Methylxanthines affect many different systems, including the digestive, respiratory and circulatory systems, in addition to the neuronal system. As a result, taking these medications may have unwanted consequences such temporary tachycardia, agitation, growth retardation, higher metabolic rate, etc. Therefore, it is advised to provide such treatments carefully. [8]

In addition to easing apnoea-related symptoms, methylxanthines also make extubation easier and minimize the need for mechanical ventilation. A decline in the prevalence of bronchopulmonary dysplasia and a definite improvement is neurological development with regard to motor function are also noted. [8]

Methylxantines boost diaphragmatic contractility as well as chemoreceptor sensitivity and respiratory drive. [13]

Despite being one of the most widely used chemicals, caffeine is regarded as detrimental for infants with recurrent hypoxia since it is an adenosine antagonist and can lower tolerance to hypoxia. [13]

Caffeine-treated infants are able to discontinue CPAP, oxygen and mechanical ventilation roughly a week earlier than caffeine-untreated neonates. [13]

During the first three days of life, there was a decrease in the requirement for ventilatory assistance among newborns given caffeine. These findings suggest that newborns who weigh less than 1.250g in their first three days, who need respiratory support and who have AOP (or are likely to develop it) would be recommended to receive treatment. [13]

Other evaluations have been done on interventions like Kangaroo care. Due to the lack of resources, the Kangaroo care was developed in impoverished countries. In situation when incubation was not an option, remarkable improvements have been discovered. Contact

between the premature baby and the mother's body serves as a source of stimulation, warmth and nutrients. Numerous newborns' lives have been saved thanks to this treatment, which has also facilitated their quick hospital departure.

This technique, known as skin-to-skin care, is periodically employed in industrialized nations to strengthen parental bonds.

There are some mixed benefits to using this approach over AOP. According to certain research, this practice raises the infant's body warmth but decreases regular breathing, which raises the danger of injury. This latter element is likely impacted by the infant's head posture. [22]

2.2.2.3 Interventions aimed to improve diaphragmatic strength

Since muscle exhaustion contributes to apnoea in premature infants, increasing diaphragmatic strength is another possibility. This method is not used since it has not yet undergone enough testing. [13]

Apnoeas are a very common occurrence during active sleep phases, given the physical-excitatory inhibition that occurs during this phase of the infant's sleep. The chest wall of the premature infant is subject to inward movement when the intercostal muscles are inhibited in apnoea during sleep. This thoracic paradox is due to several factors, such as:

- Decrease in lung volume during the final phase of exhalation;
- Decrease in transcutaneous PO_2;
- Increased respiratory work by the diaphragm;
- Inhibition of the intercostal-phrenic reflex.

[15]

3 State of the art

Breathing monitoring has become an increasingly important factor as it reflects the health of patients and is therefore of relevance for the identification of disease that may alter this state of health.

Several techniques can be used to address this issue. Often, reference is made to simple and non-invasive monitoring, such as that provided by wearable devices. However, it is sometimes necessarily to have a reliable continuous measurement rom the electrocardiogram. In fact, some breathing related characteristics can be obtained from the ECG. In order to obtain these parameters, it is sometimes difficult to avoid systematic errors or errors due to noise and artefacts.

When we talk about premature infants, the situation is even more difficult due to the impossibility of introducing numerous probes or electrodes on the infant's body; but, at the same time, continuous and reliable monitoring is indispensable for the correct detection of episodes of apnoea and bradycardia.

Techniques such as spirometry, pneumography or body plethysmography are usually used to record respiratory signals; however, they are difficult to apply in the neonatal field.

Oscultation of the heart is the most commonly used method for monitoring newborns; it has been shown to be inaccurate and therefore unreliable. To ensure a non-invasive measurement, the pulse oximeter is used, which is also considered imprecise when used in the first few minutes of life. The most reliable system is considered to be the ECG, and is therefore highly recommended. [23]

Monitoring of respiration and blood oxygen saturation are used to detect apnoea and bradycardia. Sensors for such monitoring are annoying, but above all they can adversely affect breathing for preterm infants. In contrast, lightweight thoracic electrodes for ECG measurement are non-invasive and do not impact the newborn; consequently, it was investigated how the detection of cardiac electrical activity can be a predictor of apnoea and bradycardia. [23]

3.1 Respiration Signal from Wearable Devices

Wearable devices are considered the feature as they can be non-invasive and easy to use for any kind of patient. They are also devices that can monitor subjects even at a distance, thus enabling more comprehensive and more comfortable monitoring.

Several devices have become part of everyday live over the years, but they are still inaccurate and not perfectly reliable. For this reason, research in recent times has focused on this type of device.

In addition to the lack of confidence in the measurements taken with such instruments, aspect related to data storage, power supply and automated diagnosis must be taken into account.

These devices are able to monitor different vital parameters such as heartbeat; but also several modes can be used to monitor respiration such as electric impedance plethysmography (EIP), respiration induction plethysmography (RIP) or respiration bands and piezoelectric inductive displacement sensors. RIP is rated as more accurate for monitoring respiratory effort and is therefore recommended by the American Academy of Sleep Medicine.

It has been studied how sensitive the ECG can be to the presence of sleep apnoea; in fact, changes have been found due to an increase in R-R intervals, a change in the area of the QRS complex, but there is also heart rate variability.

In the study [25] ECG and Plethysmography signals were recorded with a sampling rate of 100 Hz for 455 and 529 minutes. Both ECG and RIP signals were registered simultaneously thanks to respiration band

From the ECG signal, ECG-Derived-Respiration (EDR) signals and heart rate variability were derived; from which the features were extracted. Subsequently, epoch classification was performed, from which the presence or absence of apnoea was determined.

For the RIP signal, on the other hand, features were extracted directly and then classified to allow the final classification.

In conclusion, an excellent classification of sleep apnoea was obtained with the combination of the RIP signal and the ECG signal using the features of heart rate variability, but also of the cardiopulmonary coupling spectrum.

Another method that has proven to be effective for respiratory monitoring is the use of bioimpedance devices. Bioimpedance devices have been used to monitor lung capacity as they can be related to respiratory volume. Soft electronic devices that can be applied directly to the skin of the subject to be monitored have also been developed.

The study [26] advances a wearable device based on a stethoscope and electromyogram (EMG) measurements that can monitor breathing even from a distance. It adheres to the skin and weighs only 15 g, making it comfortable and manageable for the patient.

A piezoelectric microphone can detect sounds form the heart and lungs, which are then converted into analogue electric signals by the transducer. The biopotential electrons for the EMG sensors acquire the heartbeat and muscle movements and then the collected data are transmitted to the PC where they are processed with special programmes and then classified.

3.2 Respiration Signal from Electrocardiogram

Due to the easy availability of ECGs withing every hospital ward, ways have been found to derive respiratory parameters from this signal. Some studies are based on amplitude of the R wave relative to the baseline or the amplitude of the S wave, or the area of the QRS complex. However, these methods are not very effective due to their sensitivity to noise; therefore, signal analysis in the frequency domain was considered.

A method that has, hence, met with great success is the extraction of the respiratory signal from the ECG by means of empirical mode decomposition techniques; these techniques, however, present problems related to the presence of noise within the derived signal. There are several techniques that can be used for the extraction of the signal of interest and some are more valid than others.

3.2.1 Amplitude-based Method, Slope-Based Method, Frequency-Based Method and Baseline Wander-Based Method

These four methods are the methods that were more commonly used when we talk about the extraction of respiration signal.

The data under study [27] were taken from within the Fantasia database and comprised 120 minutes of ECG recording, but only the first 10 minutes were researched. Sampling was performed at 250 Hz ECG.

The ECG signal was processed through the use of a low-pass filter with 35 Hz cut-off frequency; after Pan & Tompkins algorithm was used for the correct detection of R peaks. After obtaining the respiration signal, a further resample at 5 Hz was performed to eliminate any noise.

The four methods above mentioned were used and compared for the extraction of the respiratory signal: Amplitude-based Methods (AM), Slope-Based Methods (SM), Frequency-Based Method (FM) and Baseline Wander-Based Method (BM).

At the end of the study, it was concluded that the four methods were problematic with regard to the presence of errors and artefacts; for this reason, different approaches have been developed by the researchers to overcome this shortcoming.

3.2.2 Empirical Mode Decomposition

The Empirical Mode Decomposition (EMD) is a data-driven signal processing techniques that decompose a signal into a sum of intrinsic mode functions, each of which represents an oscillatory mode. At the end of the process, the signal can be expressed as the sum of the number of intrinsic mode function and the residue of the signal. [28]

In order to be able to solve the problem concerning the presence of noise, the method including Noise-Assisted Multivariate EMD (NA-MEMD) was evaluated. [29]

3.2.3 Variational Mode Decomposition

The Variational Mode Decomposition (VMD) methos performs the decomposition of all modes of a signal in such a way that they are compact around a central frequency, but allow the original signal to be obtained by summing them up. The critical step in this method is the choice of the number of modes, which must be made taking into account that small or too large numbers cannot be considered. [29]

3.2.4 Variational Mode Extraction

The Variational Mode Extraction (VME) is based on mathematical concepts; this method is in line with VMD, but takes as its focus a mode that turns out to be independent of the other modes, so that we can overcome the problem of stabilising the number of modes.

The mean and standard deviation were then performed for: EMD, NA-MEMD, VMD and VME. The results obtained are summarised in Table 1.

METHOD	EMD	NA-MEMD	BAND-PASS FILTERING	VMD	VME
MEAN	0.267	27.333	0.182	31.527	0.749
SD	0.097	12.104	0.035	9.829	0.121

Table 1. Results of EMD, NA-MED, band-pass filtering, VMD and VME methos taking into account mean and standard deviation.[29]

3.3 Respiration Signal from Electrocardiogram and Photoplethysmogram

Important from a clinical and diagnostic point of view is the knowledge of the respiratory rate (RR). This parameter turns out to be the focus of many studies that are faced with the need to extract it efficiently, i.e., with the absence of noise, in order to be able to subsequently assess it.

To accommodate this requirement, ECG and photoplethysmogram (PPG) signals are usually taken into account. The PPG is used to determine changes in blood volume in the microvascular bed of tissue. To determine the RR with these two signals, several techniques can be used, such as amplitude modulation (AM), frequency modulation (FM) and baseline oscillation (BW). Each of these methods, however, are dependent on several parameters such as the age and the healthy status of the patient; a pre-processing is then performed that is able to determine the presence of a respiratory signal and its strength among the noise components of the signal. A respiratory quality index (RQI) is then assigned.

This study [30] is based on data obtained by CapnoBae and MIMIC and performed on adult and non-adult subjects. Through peak detection is the time domain, AM, FM and BW were derived from ECG and PPG. These modulations were obtained for each 8 minutes data sample by segmenting the sample into 15 non-overlapping windows of 32 seconds length. Each modulation was extracted for every 32 seconds window resulting in 3 respiratory waveforms (AM, FM and BW) for each window of the original data. Each respiratory waveform was then filtered with a 5^{th} order Butterworth IIR bandpass filter between 0.83 and 1 Hz and subsequently down sampled to 4 Hz.

Considering the respiratory signal as stationary, the four RQIs were derived: Fast Fourier Transform RQI, Autocorrelation RQI, Autoregression RQI and Hjorth Complexity RQI. The performance of each RQI was then evaluated according two parameters: mean absolute error and standard error.

At the end of the analysis, it was established that the importance of pre-processing is better that subsequent signal processing and extraction. The RQI indices are able to give

excellent help in dealing with the difficulty of the presence of artefacts and noise within the respiratory signal.

In this investigation [31], 15 respiratory signals extracted from ECG and 11 from photoplethysmogram (PPG) signals were compered. The results were then matched with the reference respiratory signal at oral-nasal pressure by using Pearson's correlation coefficient.

Regarding the PPG probes, they can be located at different sites, such as finger, ear, forearm, shoulder or forehead; but usually the finger and ear are most commonly used. Depending on the position, we have a different systolic pressure and this must be carefully taken into account.

Important for the extraction of the respiratory signal from the ECG is the sampling rate. With high sampling rates, it is possible to have respiratory modulations captured as accurately as possible. Many devices, in fact, sample ECGs and PPG down to 1 kHz.

As we have previously ascertained, a physiological factor such as age can affect the quality of the respiratory signal acquired. As a matter of fact, this factor influences respiratory sinus arrythmia and chest wall expansion. It has been studied dhow an analysis of respiration by means of the FM techniques has a worse outcome in older subjects.

In this research, finger and ear PPG-extracted signals were compered, but a comparative of ECG and PPG was also made. The influence of physiological factors on the extracted respiratory signals was also evaluated.

In conclusion, PPG extracted from the finger was found to be superior to PPG taken from the ear; but the ECG provided more accurate data than PPG. With regard to the influence of the physiological factors of the subjects, there was a negative finding with regard to frequency modulation analysis for elderly subjects; but differences regarding gender were not found.

With the pulse oximeter, it is possible to obtain the PPG signal, which is capable of monitoring respiratory activity. As the pulse oximeter is readily available and can be used anywhere and by any type of subject, it is interesting to find a way of obtaining vital parameters with such an instrument.

Respiratory functions can be obtained either directly by means of spirometric measurements, or indirectly such as with an abdominal belt.

In the study [32] study was carried out on a sample of 121 recordings all sampled at a frequency of 125 Hz. A total of 45 epochs of 30 seconds each were subsequently extracted. An algorithm based on ensemble empirical mode decomposition with principal component analysis (EEMD-PCA) was used to estimate heart rate, respiration rate and respiration activity. The process was carried out in three distinct steps: the EEMD decomposition of the data, the selection of intrinsic modes and the extraction of the parameters under study.

This algorithm was found to be optimal for the estimation of parameters related to respiration.

4 Materials and Methods

This chapter describes the methods used to analyse the data taken from the database [33].

This chapter has been divided into three different parts. The first part concerning the pre-processing of the electrocardiographic and respiratory signal. The second part describing the segmented-beat modulation method, a method used to extrapolate the respiratory signal from the electrocardiographic ones. Finally, the third part presented the calculation of the tidal volume according to three different methodologies.

4.1 Clinical Data

The data used for this study were taken from the “Preterm Infant Cardio-Respiratory Signal Database” [33]. It contains both ECG and respiratory measurement data from ten preterm infants. These data were measured in the Neonatal Intensive Care Unit (NICU) of the University of Massachusetts Memorial Healthcare.

The ten infants examined had a postconceptional age in the range between 29 3/7 and 34 2/7 weeks and weighed between 843 grams and 2100 grams.

The newborns were in healthy condition with no congenital or perinatal infections of the central nervous system, hypoxic-ischemic encephalopathy or intraventricular haemorrhage grade II or higher. They also breathed spontaneously.

When present, a three-lead electrocardiographic signal at 500 Hz was recorded from the patient monitor for approximately 20-70 hours. Due to the absence of such and ECG signal in patients 1 and 5, a 250 Hz compound ECG signal was used.

Respiratory signals were recorded at 50 Hz using an external inductance band placed around the patient’s chest and abdomen; only the first patient was recorded at 500 Hz. The data were recorded and synchronised with a system developed by the Wyss Institute at Harvard University.

The biological signals have been analysed in Matlab® computing environment.

The procedure expects normalization, which permits subjects’ inter-personality to be removed and the data to be objectified.

Furthermore, since physiological signals are collected using different kind of device and with different modalities, data are necessarily characterized by noise. For this reason, ECG signals have been filtered using a second-order pass-band Butterworth filter with a cut-off frequency of 45 Hertz; while, in order to reduce noise in Respiration signal, a fifth-order low-pass filter with a cut-off frequency of 1.5 Hertz has been applied.

4.2 Segmented-Beat Modulation Method

The Electrocardiogram can be thought of as a periodic signal, as the waveforms that characterise the cardiac cycle are repeated over time. However, it can only be regarded as a pseudo-periodic signal as no cardiac wave can be considered the same as the previous or the next one; it can vary morphologically or even change in duration. This variability is due to the workings of the autonomic nervous system, which regulates cardiac activity to stabilise blood circulation according to the subject's physiological and emotional changes.

The Segmented-Beat Modulation Method is a procedure capable of segmenting each heartbeat within the recorded ECG signal into QRS and TUP segments (Figure 17). In this way, it is able to modulate and demodulate the TUP segments by adapting each heartbeat to its starting length [34]. In this manner, it is possible to obtain a uniform electrocardiogram without noise or artefacts.

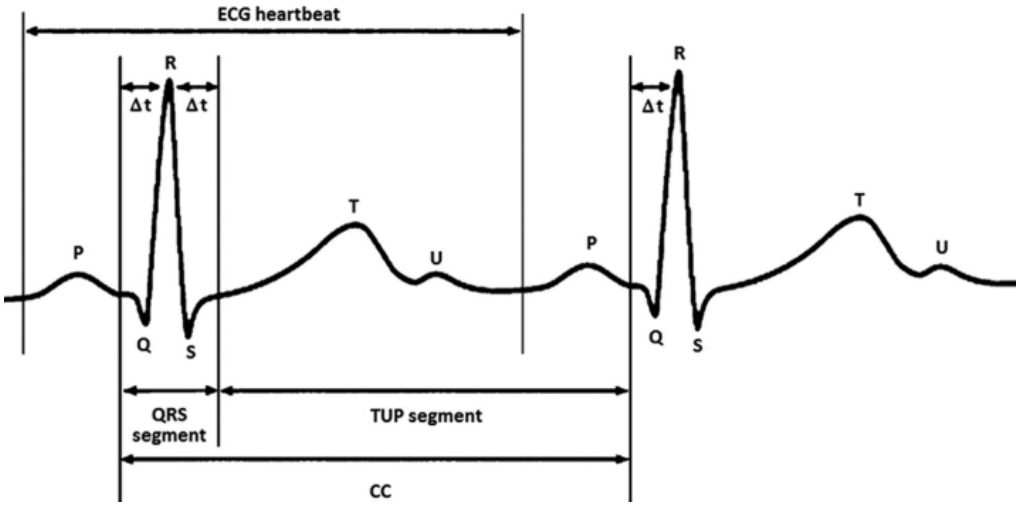

Figure 17. Representation of the electrocardiogram with the different segments related to the cardiac cycle highlighted.

The application of the Segmented-Beat Modulation Method allows an evaluation of the EDR to be derived. This method makes it possible to extract a clean response form the ECG. It is therefore possible to obtain an estimate of the electrocardiogram-derived respiratory signal by means of the difference made between the original ECG signal, which is influenced

by the respiratory signal, and the clean ECG signal, which no longer has the characteristics of the respiratory response [35].

In order to apply the Segmented-Beat Modulation Method, it is necessary to have the position of the R-peaks and the ECG signal. Important for correct prediction by this method is a proper sequence of the R-peaks.

4.3 Tidal Volume

Respiratory monitoring is crucially important for the knowledge of lung disease, as has already been seen in the previous chapters. One of the significant parameters to be taken into account is the Tidal Volume (symbol TV or VT). This is defined as the volume of air moved into or out of the lungs during a normal breath [36].

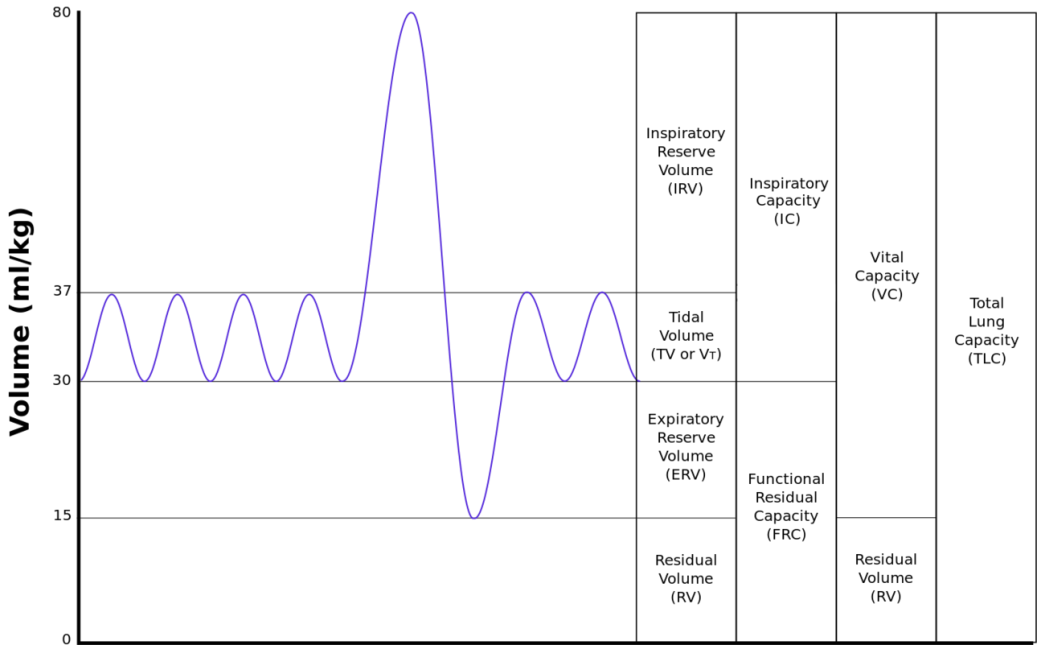

Figure 18. Representation of Tidal Volume.

Considering a healthy young adult, the Tidal Volume is around 500 ml per inhalation or 6/8 ml/kg of body mass [37]. This parameter is very useful for monitoring sleep apnoea, as well as for monitoring other disease of the respiratory system. [38]

Proper monitoring of tidal volume is very important for infants undergoing mechanical ventilation. Information on tidal volume is crucial as incorrect ventilation, whether underventilation or overventilation, can cause problems in the infant's airway. [39]

In the present study, three different methods for calculating tidal volume were compared.

The first method (TV1) consists of the difference between the maximum and minimum of the respiratory signal.

$$TV1 = \max(Resp) - \min(Resp) \quad (1)$$

The second method (TV2) takes the standard deviation into consideration. The standard deviation is a statistic that measures the dispersion of a dataset relative to its mean. Of the standard deviation is low, we have a set of data close to the mean of the set, instead if the standard deviation is high, the values are spread out over a wider range.

$$TV2 = 4 \times std(Resp) \quad (2)$$

Finally, the third method (TV3) takes the percentile into account. In statistics, the percentile is the score below which a given percentage of points in its frequency distribution drops, or a score at which a given percentage of points falls.

$$TV3 = prctile\,(Resp, 75) - prctile\,(Resp, 25) \quad (3)$$

5 Results

This chapter reports the results of the tidal volume analysis performed on the ten preterm infants.

The results of the comparison of the tidal volume calculation with the three methods mentioned in the previous chapter, have been summarised in the table below (Table 2). The results were divided according to the type of signal used.

	EDR			RESPIRATION		
	TV1[µL/kg]	**TV2[µL/kg]**	**TV3[µL/kg]**	**TV1[µL/kg]**	**TV2[µL/kg]**	**TV3[µL/kg]**
Infant 1	3,2 [2,1;4,9]	7,1 [1,7;4,2]	3,1 [0,6;1,3]	8,9 [61,5;142,5]	2,1 [54,2;102,3]	0,03 [22,1;29,4]
Infant 2	11,7 [3,8;28,5]	5,7 [2,7;14,0]	2,1 [0,7;2,1]	16,7 [26,1;87,7]	24,1 [27,7;81,8]	8,7 [8,0;20,6]
Infant 3	2,5 [1,2;6,2]	1,6 [0,9;3,1]	0,6 [0,3;0,5]	3,6 [23,1;60,0]	3,5 [24,8;53,9]	1,01 [6,7;16,4]
Infant 4	9,7 [7,2;12,5]	1,3 [5;8,0]	0,4 [1,4;2,1]	15,7 [29,1;78,9]	16,8 [30,8;74,2]	4,2 [9,5;18,9]
Infant 5	2,1 [1,7;2,8]	4,3 [1,3;2,0]	1,5 [0,4;0,6]	1,8 [2,4E-06;3,9E-07]	1,4 [2,3E-05;3,6E-07]	0,4 [7,5E-07;0,014]
Infant 6	7,5 [4,2;18,2]	6,8 [2,9;8,9]	1,8 [0,8;1,4]	11,3 [24,7;61,3]	17,7 [22,0;52,7]	9,2 [5,7;14,5]
Infant 7	11,9 [8,7;15,1]	5,7 [5,7;11,3]	2,3 [1,4;3,6]	685,7 [27,6;116,9]	645,4 [27,9;107,3]	46,2 [9,5;37,1]
Infant 8	8,6 [5,4;12,3]	2,2 [3,6;6,6]	0,8 [1;1,7]	97,5 [22,3;49,9]	73,7 [21,8;47,4]	27,6 [6,8;15,4]
Infant 9	8,9 [5;14,3]	1,4 [3,6;6,6]	0,5 [1;1,5]	71,8 [23,5;84,8]	65,9 [22,6;82,2]	28,8 [5,5;16,5]

Infant 10	13,7 [7,5;21,1]	1,4 [4,3;12,5]	0,5 [1;2,9]	124,9 [53,8;107,2]	97,0 [51,4;110,5]	30,7 [13,8;36,8]

Table 2. Comparison the three different methods of calculating the tidal volume of EDR and Respiration signals by computing median, 25th percentile and 75th percentile respectively.

Correlation coefficients were placed in the table below (Table 3). They were obtained by comparing the tidal volumes for the EDR signal and the respiratory signal. The comparison was made for all preterm infants.

	TV1 vs TV_R1	**TV2 vs TV_R2**	**TV3 vs TV_R3**
Infant 1	0,62	0,62	0,22
Infant 2	0,41	0,39	0,31
Infant 3	0,45	0,53	0,57
Infant 4	0,63	0,62	0,43
Infant 5	-0,09	-0.09	-0.15
Infant 6	0,52	0,44	0,41
Infant 7	0.64	0.57	0.48
Infant 8	0,24	0,26	0,45
Infant 9	0,15	0,18	0,02
Infant 10	0,47	0,38	0,41

Table 3. Correlation coefficients comparing the three different methodologies for calculating tidal volume with regard to the EDR and Respiratory signal.

In order to assess the effectiveness of the relationship between the tidal volumes of the two signals considered, Table 4 was complied. Correlation is considered high if the value testing the hypothesis is less than 0.05.

	TV1 vs TV_R1	**TV2 vs TV_R2**	**TV3 vs TV_R3**
Infant 1	2,96E-19	2,15E-19	0,004
Infant 2	1,27E-07	4,91E-07	6,95E-05

Infant 3	2,45E-09	3,91E-13	1,94E-15
Infant 4	3,33E-21	5,54E-20	2,22E-09
Infant 5	0,33	0,31	0,09
Infant 6	1,07E-13	7,02E-10	1,16E-08
Infant 7	1,54E-09	1,88E-07	2,05E-05
Infant 8	0,03	0,02	1,32E-05
Infant 9	0,01	0,002	0,77
Infant 10	1,08E-10	3,87E-07	1,84E-08

Table 4. Values testing the hypothesis of a relationship between the tidal volume parameters, according to the three different methods, related to the EDR signal and the Respiratory signal.

	TV1 vs TV_R1	**TV2 vs TV_R2**	**TV3 vs TV_R3**
Correlation Coefficients	0.24	0.24	0.21
Test of Hypothesis	4E-22	1.1E-22	2E-17

Table 5. Values of correlation coefficient and values of testing the hypothesis between the tidal volume parameters of the three different methodologies related to the EDR signal and the Respiratory signal.

The pictures below, the values for the tidal volume calculated by the three different methods are shown. The x-axis shows the values for the EDR, while the y-axis shows the values for the respiratory signal. The comparison of the three different methods was carried out for all infants.

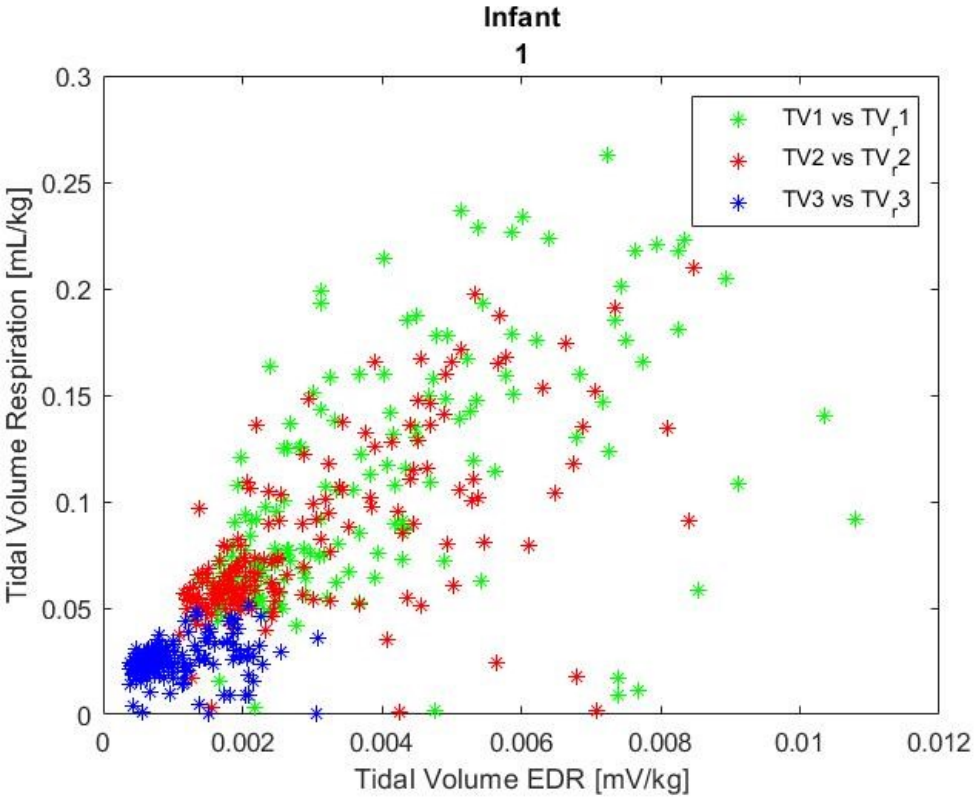

Figure 19. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 1.

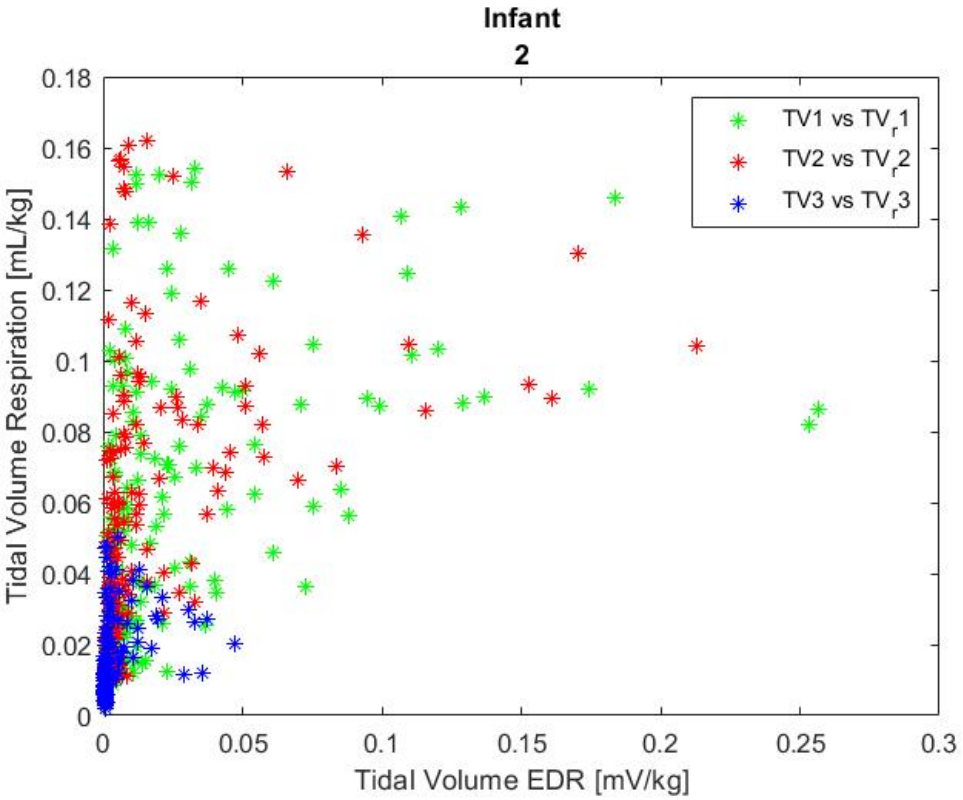

Figure 20. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 2.

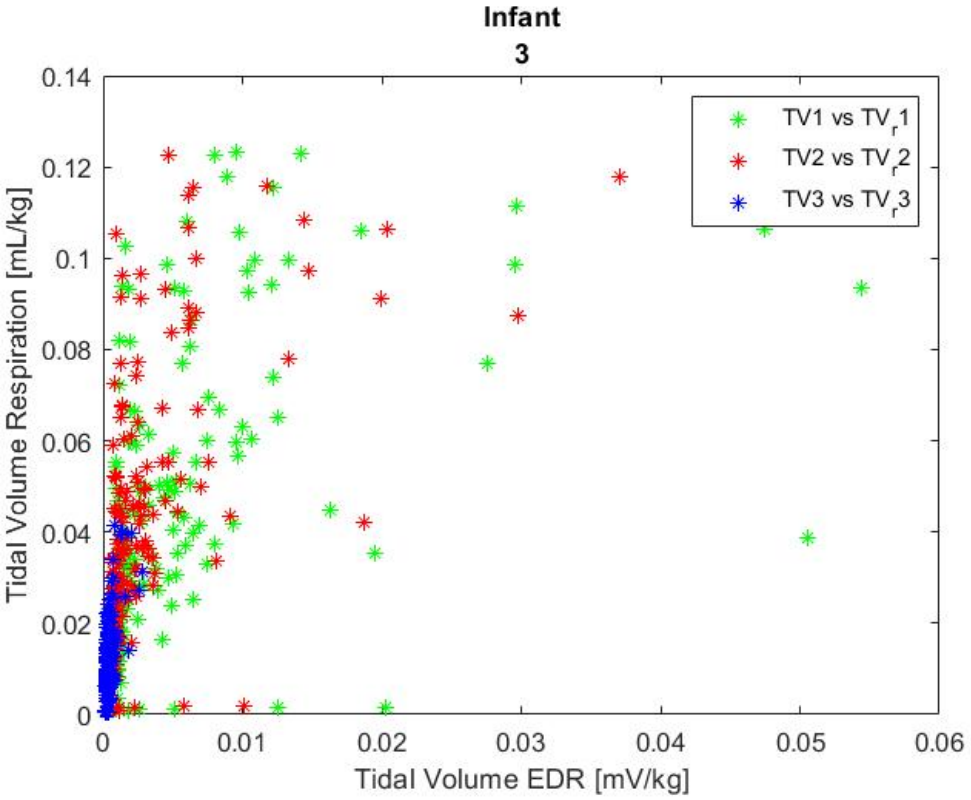

Figure 21. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 3.

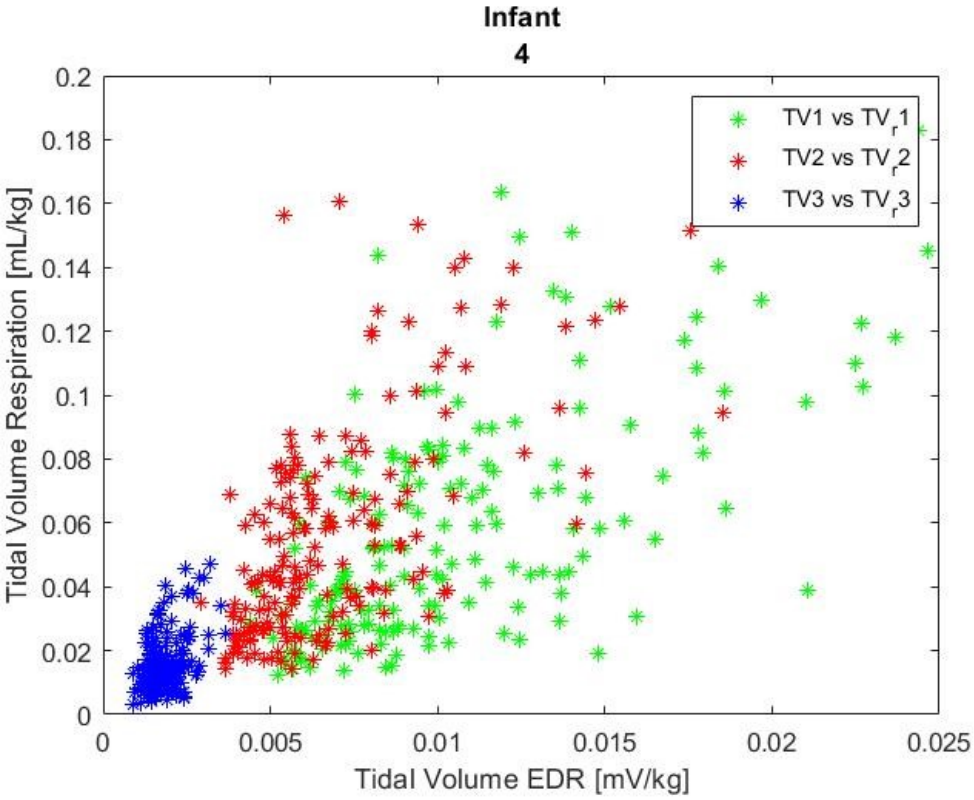

Figure 22. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 4.

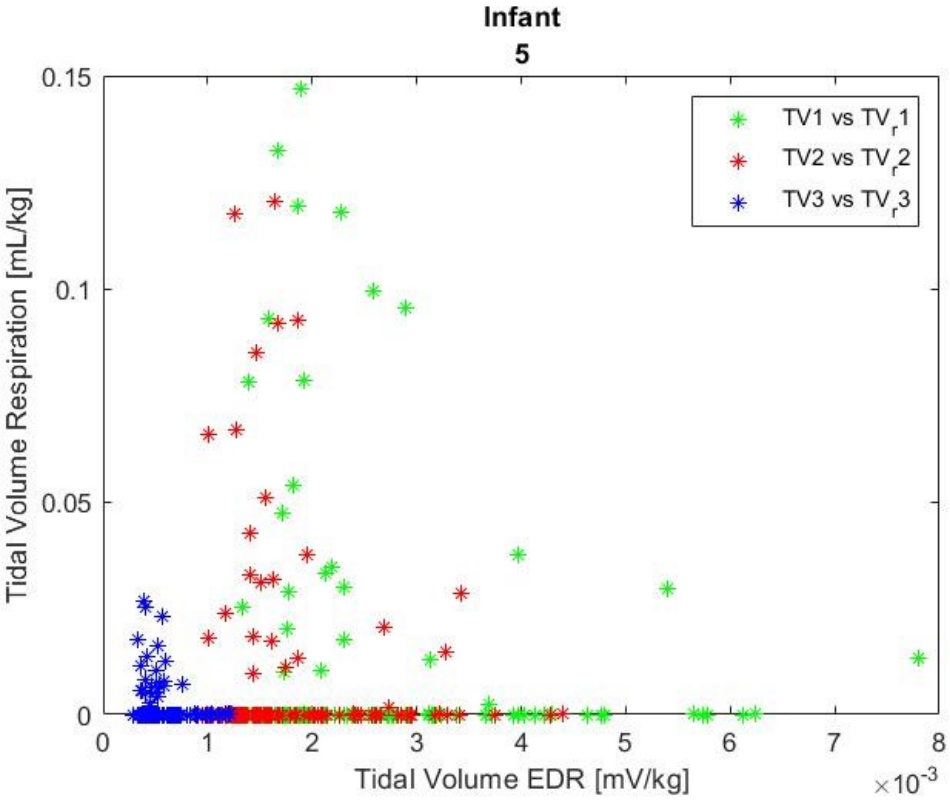

Figure 23. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 5.

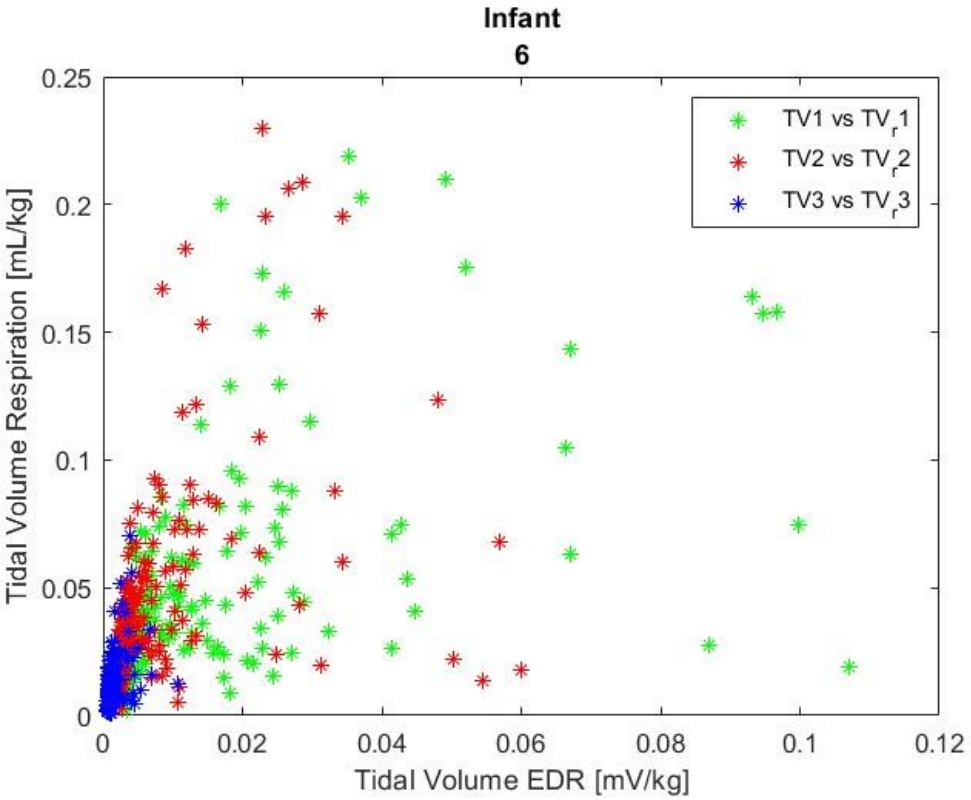

Figure 24. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 6.

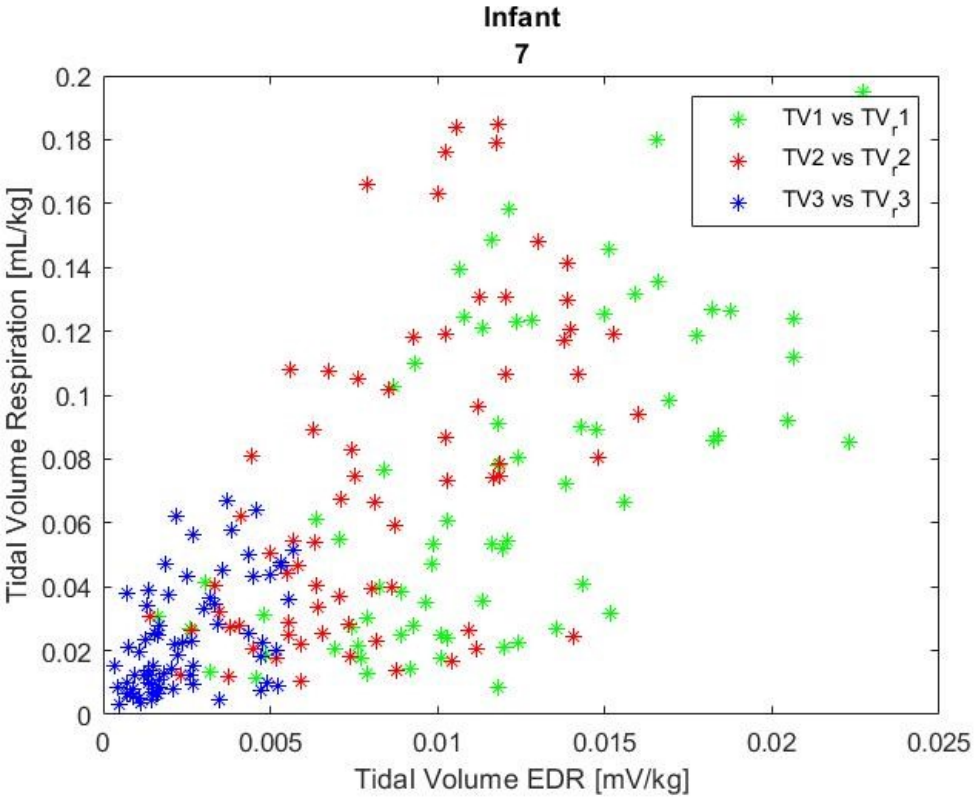

Figure 25. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 7.

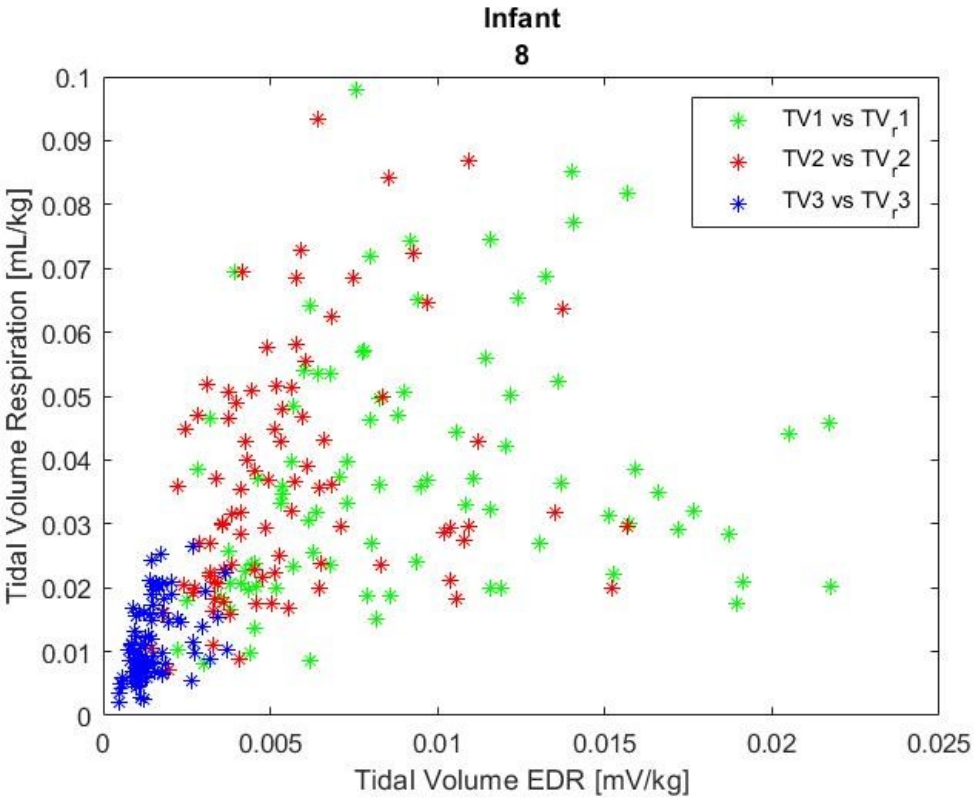

Figure 26. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 8.

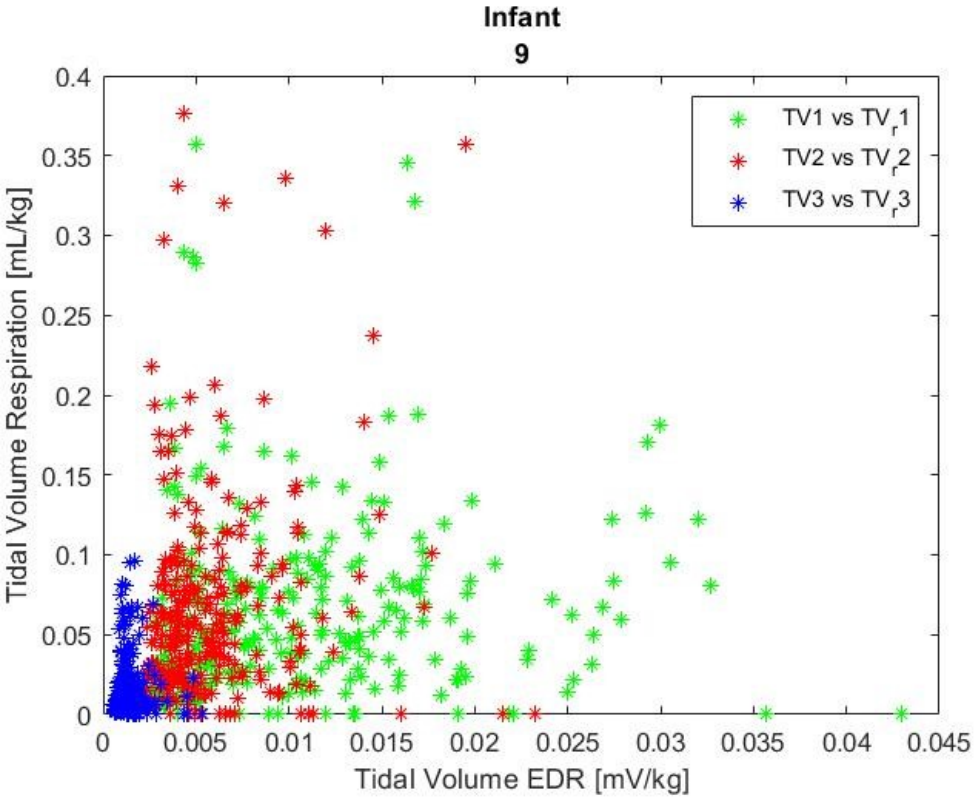

Figure 27. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 9.

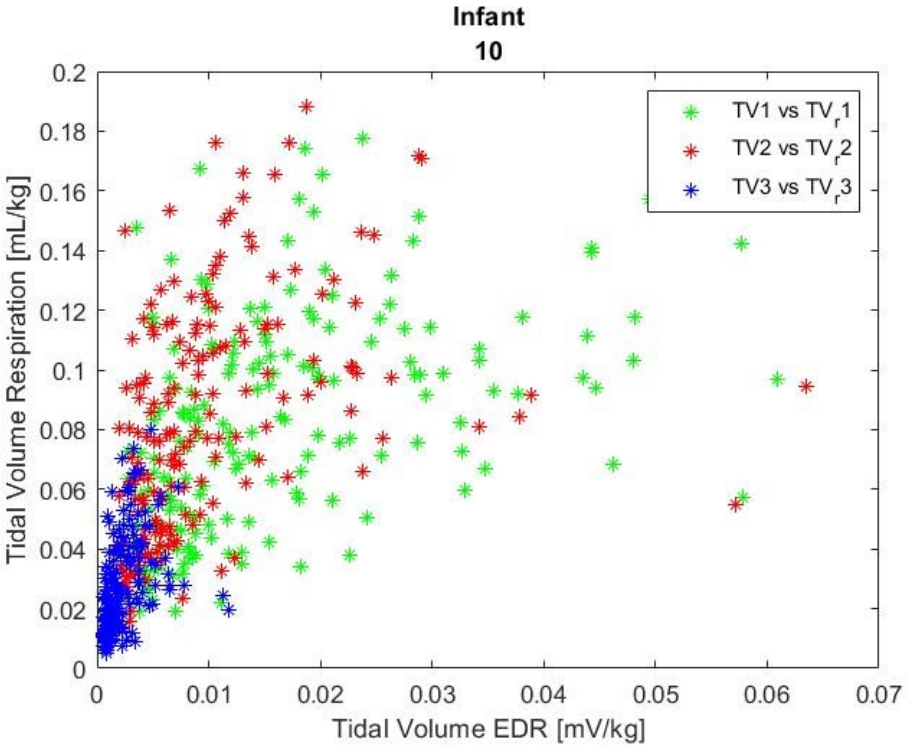

Figure 28. Comparison of the three different methodologies for calculating tidal volume in relation to EDR and Respiratory signal of the infant 10.

Pictures 29, 30 and 31 show the ten subjects comparing the three different methodologies for calculating the tidal volume.

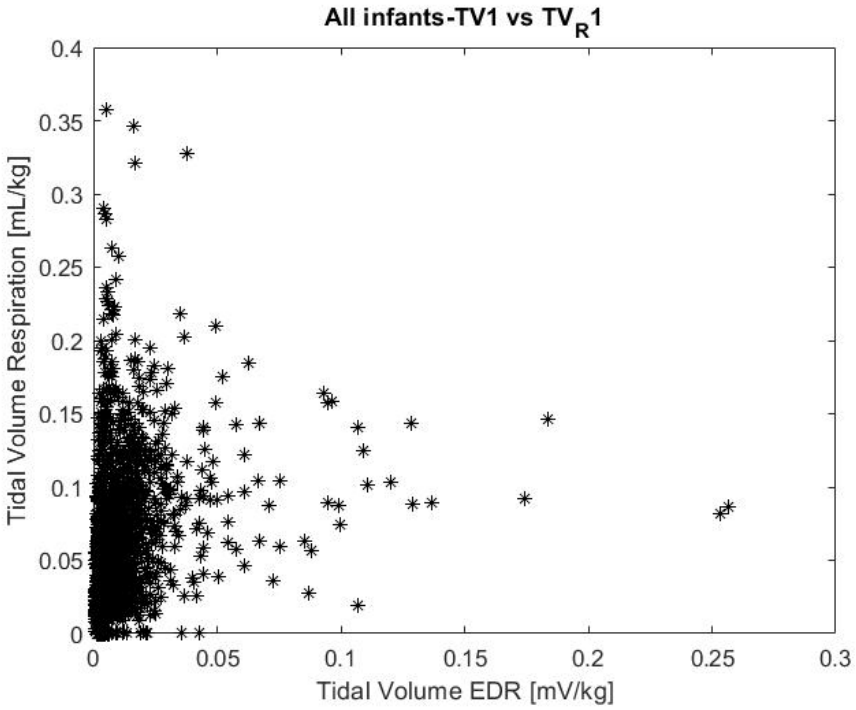

Figure 29. Comparison of the ten patients of the first tidal volume calculation methodology between EDR signal and Respiratory signal.

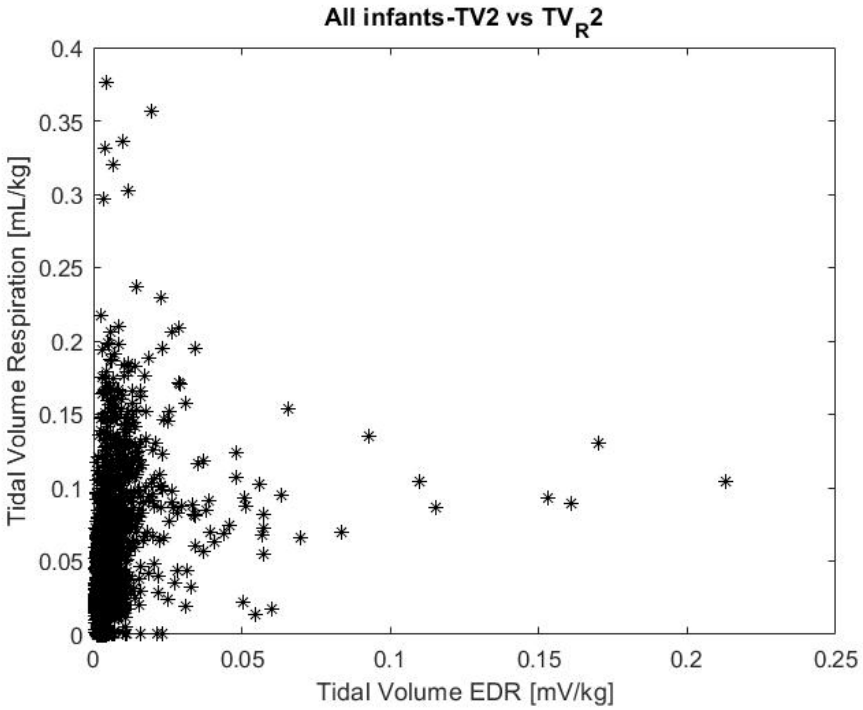

Figure 30. Comparison of the ten patients of the second tidal volume calculation methodology between EDR signal and Respiratory signal.

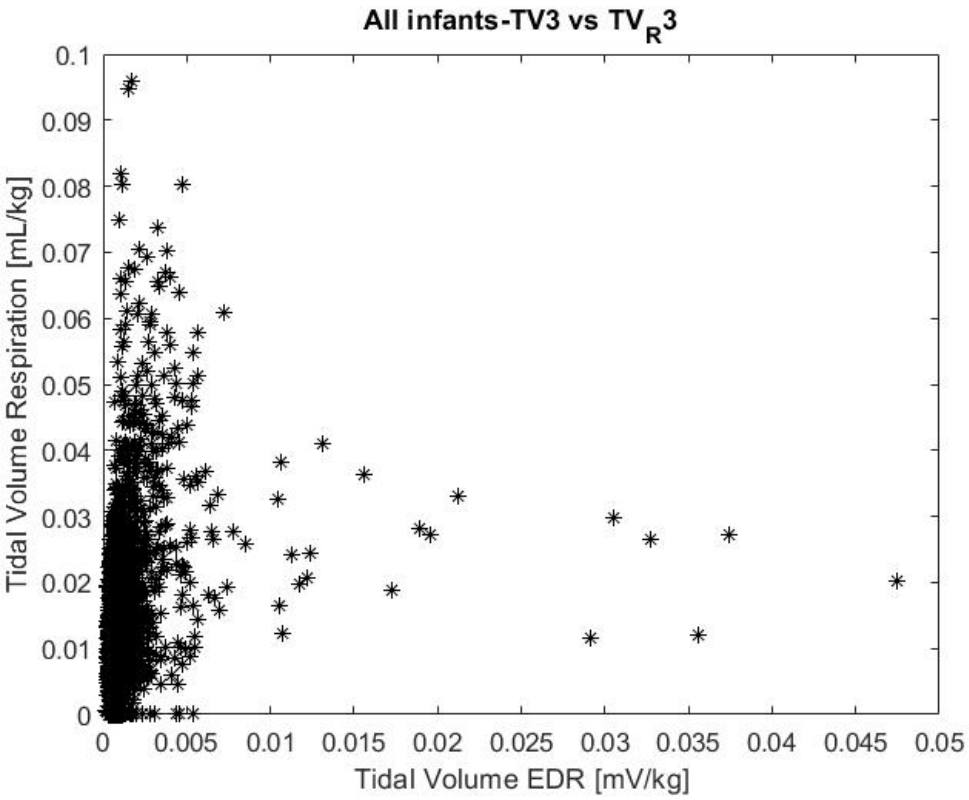

Figure 31. Comparison of the ten patients of the third tidal volume calculation methodology between EDR signal and Respiratory signal.

6 Discussion

Premature birth of newborns is one of the main risk factors for the subject's life. Premature birth results in a lack of finite development with regard to the respiratory system, which is why it is important to conceive the infant no earlier than the 38th weeks. Failure of the lungs to develop results in respiratory difficulty, which can lead to complications such as apnoea and bradycardia; monitoring is therefore essential for the survival of such individuals. A change in the respiratory signal is a warning sign to be taken into account in such infants, it is essential to find methods that allow for proper monitoring while minimising the invasiveness of machines and sensors.

For this reason, the aim of this study is to extrapolate the respiratory signal, usually detected by inductive band placed on the patient's chest and abdomen, through the use of electrodes already placed on the subject's body in order to detect the cardiac signal. From the extrapolation of this respiratory signal, it is considered of fundamental relevance to study the tidal volume, a parameter indicating the amount of air introduced into and emitted from the infant's lungs.

The computation of the tidal volume was performed for both the EDR signal, obtained from the analysis of the electrocardiographic signal, and the respiratory signal taken from the database. The estimated tidal volume for all ten preterm infants is summarised in Table 2. From this table, it can be seen that the calculation of the tidal volume for the EDR signal differs from that for the respiratory signal; in fact, the respiratory signal from the electrocardiogram turns out to be underestimated.

In order to ascertain the interrelation between the two signals, the correlation coefficients shown in Table 3 were derived. These coefficients were estimated for each preterm neonate with reference to the three different methods of calculating tidal volume. The correlation results to be almost homogenous for the ten subjects, with the exception of the fifth and ninth neonate.

In order to evaluate the correlation hypothesis, the values testing its effectiveness are tabulated in Table 4. The interrelation seems to be optimal for values less than 0.05. This condition appears to be verified for approximately all subjects except for the fifth and ninth patient.

In order to obtain a general appraisal of the correlation and the validity of this hypothesis, all ten patients were correlated, thus showing the difference in the three methods of assessing tidal volume. This comparison has been reported in Table 5, through which it is possible to note that the correlation is almost the same for all three calculation methods; furthermore, the validity of this association is verified in that the values obtained in testing this hypothesis are all lower than of the threshold value of 0.05.

From Figure 19 to Figure 28, it is possible to visualise, by plotting the tidal volume calculated with the EDR signal and the tidal volume calculated with the respiratory signal, the relationship that links the two signals. As described before, the relationship is also evident graphically. Some problems also result in this being evident in some subjects. In each figure, the valued of the tidal volume calculated by the three different methods are shown in different colours.

Images 29, 30 and 31 show the trends of all ten preterm subjects divided according the methodology used to calculate the tidal volume.

In this last three images, as in the previous figures, a trend in a specific direction can be seen. This trend is the observation of a correlation between the tidal volumes of the two signals taken into consideration.

7 Conclusion

In conclusion, it is possible to state that the estimation of the respiratory signal by means of the electrocardiographic signal appears to be a viable choice, both form the point of view of the results obtained and the low invasiveness involved. In fact, by calculating respiratory parameters through the electrocardiogram, it is possible to eliminate one of the instruments that are placed on the body of premature infants. This study aims to highlight how this method od estimating the respiratory signal is optimal in order to eliminate instruments that can irritate the infant's skin and restrict its movements.

The tidal volume, a parameter relating to the newborn's breathing, is effective in determining the breathing pattern, this enabling timely intervention by hospital personnel and preventing the occurrence of apneic and bradycardic episodes.

In the present study, the validity of tidal volume calculation was found to be effective for the majority of preterm infants. It is, however, necessary to investigate the subjects who did not have acceptable results. Further analysis should therefore be carried out of ascertain whether gestational week and subject weight are parameters that should be taken into account for the study of the respiratory signal.

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