TAMPEREEN TEKNILLINEN YLIOPISTO
TAMPERE UNIVERSITY OF TECHNOLOGY

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VALIDATION OF IMPEDANCE PNEUMOGRAPHY MEASUREMENT FOR ASSESSMENT OF RESPIRATION IN CARDIOTHORACIC SURGERY PATIENTS

Master of Science thesis

Examiners: Assoc. prof. Jari Viik and prof. Jari Hyttinen
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ABSTRACT

MILLA JAUHIAINEN: Validation of Impedance Pneumography Measurement for Assessment of Respiration in Cardiothoracic Surgery Patients
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Impedance pneumography (IP) is an indirect method of assessing respiration by measuring bioimpedance of the thorax. Conventionally respiration is evaluated by measuring the volume of air inhaled and exhaled during forced spirometry manoeuvres: these patterns require skills and cooperation from the patient, and strong guidance from the physician. IP provides a comfortable alternative for the patient, since the results do not depend on the performance of the patient. Purpose of the work was to assess the agreement of IP measurement and pneumotachography (PNT), which was used as a reference method.

Open-chest surgery intrudes chest anatomy and physiology and decreases the functions for several days after the surgery. Pain and medication also complicate respiration, and postoperative complications, such as air leak or pneumothorax are common. Thus, an effective method for measuring respiration with minimal effort from the patient is needed to evaluate the physiotherapy needs and recovery. IP is a promising method for this purpose.

The study population was 136 patients with elective cardiac operations, pulmonary resections and minor pleuropulmonary surgeries. The study was conducted during the normal episode of care in the hospital one day before the operation and for 1–3 days after the operation. Simultaneous IP and PNT measurements were conducted for one minute.

The linearity of IP and PNT was evaluated by calculating the sample-by-sample difference and average deviation from the linearity in different phases of the respiratory cycle. The results showed that there was no difference in linearity in the three surgery groups before and immediately after the operation. Also, difference between the groups in the same measurement day was not detected.

The study indicates that thoracic surgery does not change the linearity properties of IP, thus it can be used to evaluate the recovery of the surgery patients by assessing the lung functions. It should be considered in further studies, whether some changes in the linearity were due to fluid accumulation in cardiac patients, or for some other reasons.

TIIVISTELMÄ

MILLA JAUHIAINEN: Impedanssipneumografian validointi sydän- ja keuhkoleikkauspotilaiden hengitysfunktion arviointia varten
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Impedanssipneumografia (IP) on epäsuora menetelmä hengityksen arviointiin, jossa mitataan rintakehän yli olevaa bioimpedanssia. Tavanomaisesti hengitystä arvioidaan mittaamalla sisään- ja uloshengitetyn ilman tilavuutta keuhkojen toimintakokeen eli spirometrian avulla: hengitysmanööverit vaativat yhteistyökykyä ja osaamista potilaalta sekä kannustavaa ohjausta kokeen valvojalta. IP mahdollistaa potilasmukavuudeltaan paremman vaihtoehdon, sillä mittauksen tulokset eivät riipu potilaan suorituskyvystä tutkimuksen aikana. Työn tarkoituksena oli tarkastella IP-mittauksen ja pneumotakografiamittauksen (PNT) vastaavuutta.

Rintakehän avoleikkaus muuttaa rintakehän anatomiaa ja heikentää keuhkofunktiota usean päivän ajan leikkauksen jälkeen. Kipu ja lääkitys vaikeuttavat hengitystä, mutta myös leikkauksen jälkeiset komplikaatiot, kuten ilmavuoto tai ilmarinta ovat yleisiä. Hengityksen seuraamiseen tarvitaankin tehokas ja potilasta rasittamaton mittausmenetelmä, jotta voidaan arvioida potilaan fysioterapian tarvetta ja paranemisen etenemistä. IP on lupaava menetelmä tähän tarkoitukseen.

Tutkimukseen hyväksyttiin 136 potilasta, jotka saapuivat suunniteltuun sydänleikkaukseen, keuhkolohkon poistoon tai pienempään keuhkoleikkaukseen. Tutkimus toteutettiin potilaan normaalin sairaalassaoloajan aikana leikkausta edeltävänä päivänä sekä 1–3 päivää leikkauksen jälkeen. IP- ja PNT-signaalit mitattiin samanaikaisesti yhden minuutin ajan, ja lisäksi mitattiin 10 minuutin lepohengitysjakso IP-menetelmällä.

IP:n ja PNT:n lineaarisuutta arvioitiin laskemalla mittausten erosignaali näyte näytteeltä sekä keskimääräinen erotus oletetusta lineaarisuudesta hengitysjakson eri vaiheissa. Tulokset osoittivat, että missään kolmesta leikkausryhmässä lineaarisuudessa ei esiintynyt merkittävää muutosta ennen leikkausta ja välittömästi leikkauksen jälkeen. Lineaarisuudessa ei myöskään havaittu eroa eri leikkausryhmien välillä.

Tutkimus osoittaa, että rintakehäkirurgia ei muuta IP-menetelmän ja referenssimenetelmän suhdetta, joten IP-menetelmää voidaan käyttää leikkauspotilaiden hengitysfunktion arvioimiseen. Myöhemmässä tutkimuksessa täytyy kuitenkin arvioida, johtuvatko sydänleikkauspotilaiden muutokset lineaarisuudessa nesteen kertymisestä rintakehään, vai jostain muusta syystä.

PREFACE

I have learned so much in the past one and a half years: to see the scientific world through glasses of healthy criticism, to trust and defend my own opinions and thoughts, and to read and search information more thoroughly than before. I have noticed my strengths, improved my weaknesses and learned to be more creative than ever which I think are the fundamentals of being a Teekkari.

The study would not have been possible without all the support and feedback that I've had. I would like to thank Javier Gracia Tabuenca for enormous effort and support during the whole project. You have taught me critical viewing of scientific world and given me a boost of confidence about believing in my own opinions and research. I also thank Tampere Tuberculosis Foundation for financially supporting the study.

I thank my supervisors, Jari Hyttinen and Jari Viik for support and discussion about the project and research in general. I thank Jari Laurikka and Heidi Mahrberg from Sydänsairaala for medical insights, supportive research environment and all the help. And of course, Ville-Pekka Seppä, whose example I've been trying to follow in the world of novel impedance pneumography research.

I thank my family and friends, who have probably heard more than enough of absurd questions, complains or endless enthusiasm for the topic. Your support is invaluable.

Tampere, 19.5.2017

Milla Jauhiainen

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LIST OF SYMBOLS AND ABBREVIATIONS

AD	Analogue-to-digital transducer
ATS	American Thoracic Society
C	Cardiac surgery patients group
CGO	Cardiogenic oscillation
COPD	Chronic obstructive pulmonary disease
ECG	Electrocardiography
ERS	European Respiratory Society
EVC	Expiratory vital capacity (l)
FEV1	Forced expiratory volume after one second (l)
FIVC	Forced inspiratory vital capacity (l)
FIV1	Forced inspiratory volume after one second (l)
FVC	Forced vital capacity (l)
ICG	Impedance cardiograph
IMT-P	Inspiratory muscle training physiotherapy
IP	Impedance pneumography
IVC	Inspiratory vital capacity (l)
MIP	Maximal inspiratory pressure (cmH_2O)
NASA	National Aeronautics and Space Administration
PEF	Peak expiratory flow (l/s)
PEP-P	Positive expiratory pressure physiotherapy
PIF	Peak inspiratory flow (l/s)
PM	Minor pleuropulmonary surgery patients group
PNT	Pneumotachograph
PR	Pulmonary resection surgery group
PREOP	Preoperative measurement
RR	Respiratory rate (1/min)
SD	Standard deviation
SpO2	Oxygen saturation (%)
VATS	Video-assisted thoracoscopic surgery
VC	Vital capacity (l)
VT	Tidal volume (l)
WHO	World Health Organization
1POP	First postoperative measurement
2POP	Second postoperative measurement
3POP	Third postoperative measurement

1. INTRODUCTION

Respiration is one of the vital functions of the body, essential to sustain life. Respiration is mostly controlled by the autonomous nervous system, but a person can also voluntarily affect breathing rate and deepness. There are many environmental and medical causes for decreased respiratory functions, sense of breathlessness or even respiratory failure.

Medical reasons for decreased breathing are various respiratory diseases. Amongst the top ten causes of death in 2015 were four respiratory diseases: lower respiratory infections, chronic obstructive pulmonary disease (COPD), lung cancers and tuberculosis. For example, deaths caused by tuberculosis have decreased since the year 2000 of about 0.4 million, but lung cancers have increased. [60] These medical conditions cause a variation of respiratory problems, some of them disrupting everyday life, and some of them almost non-noticeable.

Not only the diseases affect breathing, but also the treatment can cause temporary decrease in respiration. Certain pulmonary diseases such as lung cancer and cardiovascular diseases are treated with surgical procedures, which commonly are conducted as open-chest surgeries. Open-chest surgery intrudes breathing physiology and anatomy, which causes difficulties in respiration after the surgery [48]. To achieve effective recovery, physiotherapy is given already before the surgery and continued after it. It is also important to clinically evaluate the patient's respiratory functions and follow the progress of recovery. [52]

Conventionally respiratory functions are evaluated with spirometry and peak expiratory flow (PEF) measurements at rest perioperatively. Spirometry is based on performing forced manoeuvres with the guidance of a doctor, and the measured parameters are compared with reference values according to the patient's sex, age and height. [16] Thus, with large reference value databases and well established measurement procedures, spirometry is considered the golden standard of respiration measurements [25].

However, there are difficulties arising from spirometry and other forced breathing methods. The contraindications of spirometry include air leaks from the lungs or pneumothorax, recent thoracic surgery or acute illnesses. [8] Also the level of patient cooperation needs to be considered. If the patient is not able to cooperate with the clinician due to cognitive or neurological disease or is too sick to perform the test after a surgery, spirometry cannot be performed. In these circumstances, other methods to evaluate respiration are needed.

Impedance pneumography (IP) is an indirect method for measuring respiration. It is clinically used to evaluate the respiration rate (RR), but studies for applying the method for evaluating the respiratory flow profiles have been performed [39]. Previously IP has been studied for healthy children and adults, and for children with obstructive respiratory symptoms [42; 45]. The commercial development of IP technique is considering the overnight assessment of asthmatic children. [56]

Use of IP for diagnosing obstructive respiratory diseases (such as asthma) have been studied especially with young children, but the method could be applied for other target groups as well. IP could provide effective measurements of respiration with minimal effort and discomfort to the patient. This is important to patients in pain or at risk of complications. To avoid air leaks or other complications after a cardiothoracic surgery, tidal breathing could be assessed instead of forced breathing. To achieve this, the agreement of IP to a reference method needs to be assessed first to validate that the IP signal provides similar information than the reference method. Next, it should be studied whether IP can provide useful information to evaluate the recovery after surgery.

This study introduced a new target group for evaluating respiratory functions with IP: adult thoracic surgery patients with various types of elective cardiac and pulmonary operations. Breathing was assessed one day before and for 1–3 days after the surgery amongst normal hospital routines. The patients were provided with physiotherapy throughout the episode of care, and the respiration was measured and evaluated by the patient and the physiotherapist. Three measurement methods were used: conventional spirometry procedure, direct pneumotachography (PNT) flow measurement, and IP measurement during tidal breathing and overlapping with PNT.

The aim of the study was to evaluate IP method for cardiothoracic surgery patients by assessing the agreement of simultaneously measured one-minute signal of IP and PNT. It was expected, that indirect IP measurement of tidal breathing provides similar information of the respiratory functions as the direct PNT measurement. Therefore, IP could be potential methods to evaluate the changes of respiration of thoracic surgery patients.

The study material was collected during 2013–2016 in the Tampere University Hospital Heart Center, Finland. A physiotherapist performed all the measurements and physiotherapy interventions at the Heart Center. Author's contributions in the study were the processing of IP signals with previously developed algorithms. The author implemented and adjusted the algorithms used for signal processing and analysed the results with both visual and statistical methods. Thesis was performed in collaboration with Tampere University Hospital Heart Center.

2. BACKGROUND

Theoretical background introduces the fundamental physiology and anatomy of the respiratory system. The respiratory system is controlled by the autonomous nervous system but also partly voluntarily. Respiratory physiology might change due to disease, intrusive operations or pain. The effect of cardiothoracic surgery and ways to prevent pulmonary complications is presented in Section 2.1.2.

Conventionally respiration is assessed with spirometry, which measures the volume and flow from the mouth. However, spirometry is not a perfect method for patient groups with difficulties in cooperation, such as small children or infants, patients with cognitive diseases or disorientation after an operation due to pain and medication.

IP provides an indirect method to assess respiration via bioelectric measurement from the thorax. The measurement principles are introduced and discussed to provide a general view of respiratory evaluation. Also, the signal processing requirements and tidal breathing parameters are discussed to provide an understanding of the potential of the method. Finally, spirometry and IP are compared to conclude the theoretical background of the study.

2.1 Respiration

2.1.1 Respiratory System

The main function of a respiratory system is to exchange gases between the environment and the body. Effective gas exchange requires the upper airways to moisten, clean and to heat the air before air goes through the lungs. In addition to these the upper airways also affect speaking, swallowing and coughing. [50] The upper airways include nose, nasal cavity, mouth, pharynx and larynx [3].

Lower respiratory system includes trachea, bronchi and lungs. The trachea is supported by cartilage and smooth muscles. The surface of the trachea has epithelial cells and mucus, which help to move inappropriate particles away from the lungs towards the pharynx. [50] The smallest component in the respiratory system is the acinus, the basic ventilator unit [3]. Basic components of the respiratory system are presented in Figure 1.

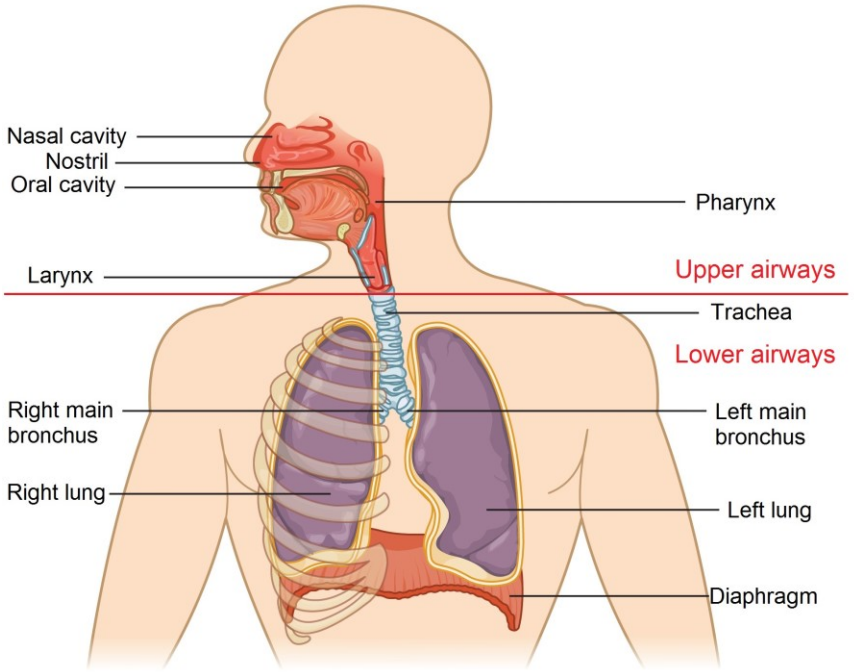

Figure 1. *Structure of the respiratory system divided to upper and lower airways. Modified from figure by OpenStax College [34]*

During tidal breathing, only the inspiratory muscles are working actively. The most important inspiratory muscle is the **diaphragm**. When inspiratory muscles contract, the thoracic cavity is dilating (ribs and the sternum move upward and out) causing a negative pressure and flow of air into the lungs. Tidal expiration is passive and occurs when the thoracic cavity and lungs recover to their initial volume. On the other hand, when respiration is forced the pressure change in the lungs depends on the force used by the expiratory muscles: when creating a forced expiration, the abdominal muscles, intercostal muscles and neck muscles need to work actively. [50]

Pulmonary physiology can be roughly divided into four properties: **mechanics** of the respiratory system, **gas exchange**, **neural control** and **non-respiratory functions**. All of them are vital in achieving normal pulmonary functions. [3]

The **mechanical properties** of the respiratory system determine how much effort is needed to breath and how comfortable it feels. Dyspnea, a sense of uncomfortable breathlessness means that the function is taking more effort than it normally should. The most severe abnormality in breathing is respiratory failure. In this case the lungs cannot function without an assistance of a machine or a person. Respiratory failure can occur because of many abnormalities in the respiratory system, but a change in the mechanical properties of the lungs is the most common reason. [3]

In human respiratory system, the solution for efficient **gas exchange** is the cardiopulmonary system, which uses a very thin blood-gas barrier to exchange gases between the body and the environment. Gas exchange occurs between blood cells travelling from

the right ventricle of the heart to the capillaries surrounding the alveoli of the respiratory units. [50] The blood-gas barrier brings blood and gases into close juxtaposition and causes passive diffusion occur through the barrier [3]. Fresh oxygen from the lungs is transferred to blood cells, and carbon dioxide from the blood cells is transferred to the lungs [50]. Oxygen is transferred with blood through the body and carbon dioxide is released through the lungs to the environment.

Neural control of respiration is in the brainstem. Usually respiration is controlled by the autonomic nervous system, but the respiration can also be modified consciously. Chemoreceptors continuously signal about the amount of oxygen and carbon dioxide in the arterial blood. On the other hand, mechanoreceptors signal about the inflation of the lungs. Thus, the neural control of the respiratory system is based on negative feedback given by the two types of receptors and resulting in appropriate ventilation. [3]

There are several **non-respiratory functions** that are not related to breathing but still necessary for normal human physiology. For example, the amount of blood in the pulmonary vessels is equal to the right ventricular output, but the blood that takes part in gas exchange is only 70–100 ml. The remaining blood is held in the pulmonary vessels as a reservoir and used to optimize the cardiac output. Another example of important non-respiratory functions is the filtration of harmful particles from inspired air. [18]

2.1.2 Effect of Cardiothoracic Surgery to Breathing

Respiration functions may decrease because of an intrusive operation in the thoracic area. Certain cardiovascular diseases and for example lung cancer are treated with open-chest operations, which may cause difficulties in breathing for several days.

Postoperative evaluation of lung function is important, since the surgery decreases the patient's lung functions and exposes the patient to pulmonary complications. To prevent complications after cardiothoracic surgeries, it is important to measure respiration and monitor the oxygen levels of the patient to detect if symptoms of any complications occur. The overall incidence of complications after cardiothoracic surgeries is 15–37.5%, and most of them are caused by pulmonary complications. They are also causing significant number of deaths and morbidity in thoracotomies. [17]

An open-chest surgery causes pain and discomfort for the patient and an invasive operation affects the physiology of the respiratory system. The incision made in the surgery affects the integrity of the respiratory muscles. The contraction of the muscles is also weakened by anaesthetic drugs used in the operation and the effect might continue for a considerable time after the surgery. [48] Increased mechanical load, pain and medications may cause hypoventilation [5].

Respiratory functions are also affected by the cardiopulmonary bypass used in cardiac surgeries. Perfusion causes a risk of inflammation in the thoracic area. Lung ischemia reperfusion injury may be caused by the restricted blood flow from aorta to the heart. Unlike in other organs, where the loss of blood automatically leads to hypoxia, in the lungs the availability of oxygen from alveolar ventilation causes the mechanism of the ischemic injury to be more complicated. [9]

Neely et al. [31] studied the respiratory work before and after an operation of 21 randomly selected patients. They noticed that the respiratory work was increased immediately after the operation and then decreasing slowly on the next day. It was also noticed that the respiratory work more increased on elderly patients with prolonged anaesthesia compared to younger patients. For obese patients, the respiratory work was higher preoperatively, but also more increased postoperatively than for other patients.

However, postoperative evaluation of respiration is challenging for example due to the condition of the patient after the surgery. [17] Postoperative lung function can be assessed with the same methods as preoperatively or in diagnostics, but some factors need to be considered. Air leaks are common in thoracic surgeries, especially in pulmonary resections. Air leak can occur in inspiration, expiration, continuously or in forced expiration. [17] This restricts for example the use of spirometry and expiratory physiotherapy, if air leak occurs during expiration or forced expiration. In this case, other methods need to be used to evaluate respiration. If deep breathing causes a lot of pain for the patient, more comfortable methods of assessing respiration should be considered. Pain might significantly decrease the ability to perform respiratory measurements effectively.

The prevention of complications after thoracic surgery can be improved by paying attention to the preoperative care of the patient. This includes preoperative physiotherapy and education, such as respiratory muscle training and education in coughing and deep breathing. Although the benefit of preoperative education and physiotherapy has been questioned in some studies, it is still part of the episode of care in the hospitals. [17]

Tampere University Hospital Heart Center provides preoperative physiotherapy for elective cardiothoracic surgeries. The initial condition of the patient is evaluated with an interview and measurements. The physiotherapist guides the patient about postoperative training and other important things related to the surgery. The rehabilitation begins as soon as possible after the surgery supported by the nurses and the physiotherapist. The patient is encouraged to take an independent role in the rehabilitation. Physiotherapy and breathing exercises continue throughout the hospital care and at home. Additional physiotherapy or other support can be arranged to ensure the patients mobility and health. [52]

2.2 Spirometry

Spirometry is thoroughly studied and widely used method for assessing lung functions. It measures inhaled and exhaled air from mouth with a flow sensor. To ensure respiration only through the mouth a nose clip is used during the measurements. The flow sensor is connected to the spirometry device to record both the raw signal and parameters related to different forced breathing manoeuvres. [25]

Spirometry is considered the gold standard for measuring respiratory functions. It gives valuable information about the patient's general lung function, but to make a specific diagnosis other methods are needed alongside it. Spirometry can be used for example to measure the effect of a disease to respiration, to assess therapeutic intervention or to evaluate respiratory symptoms before diagnosis. The guidance and encouragement of the patient by the instructor is very important to achieve accurate results. The patient needs to be able to inhale and exhale maximal volume and to produce powerful respiration and voluntarily change breathing frequency. [25]

The standard parameters measured in spirometry test are presented next. The respiratory pattern for the first two parameters, tidal volume (VT) and vital capacity (VC) are in Figure 2.

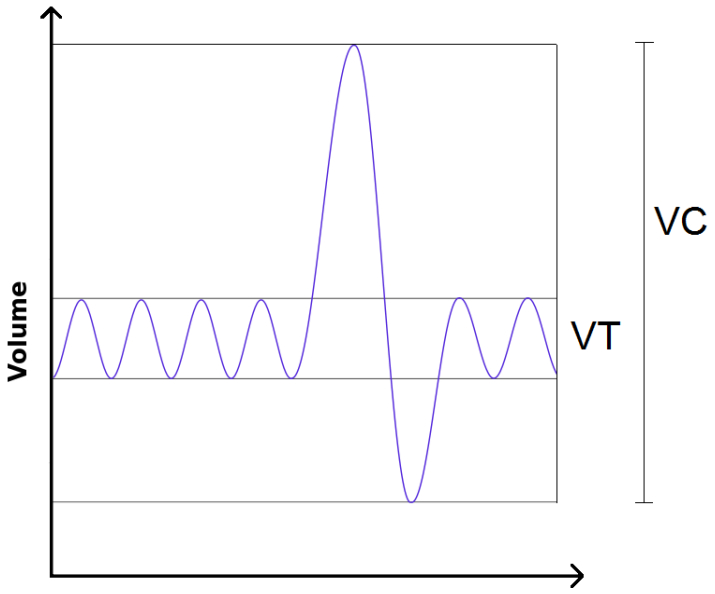

Figure 2. *Respiratory volume pattern for tidal volume (VT) and vital capacity (VC). Modified from [57]*

VC is the maximum volume that the patient can either inhale (IVC) or exhale (EVC). The highest volume of three acceptable manoeuvres is counted. VT is the volume of one respiratory cycle in tidal breathing. [25]

A flow-volume loop presenting the forced vital capacity (FVC), forced expiratory/inspiratory volume in one second (FEV1 and FIV1), forced inspiratory capacity (FIVC) and peak expiratory/inspiratory flow (PEF, PIF) are presented in Figure 3.

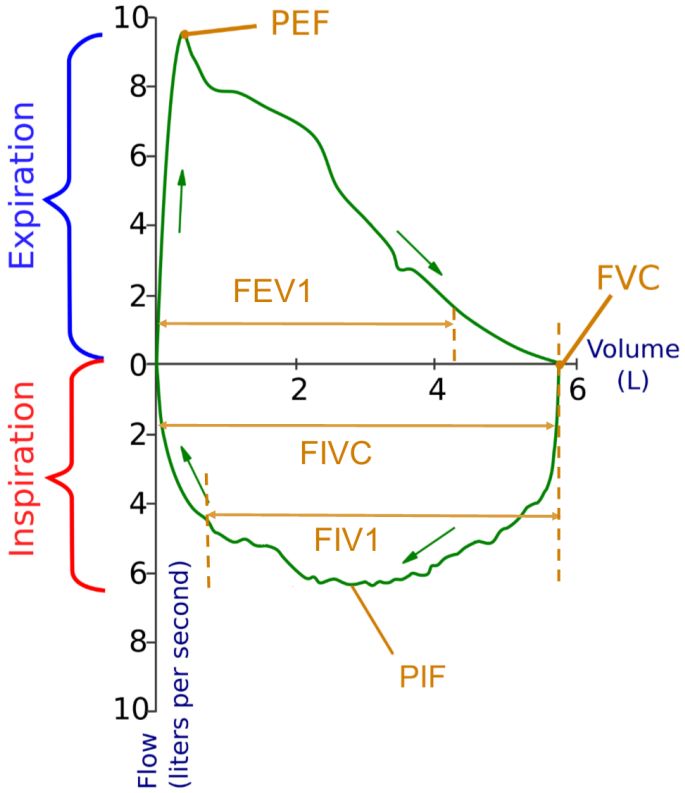

Figure 3. *Flow-volume loop presenting forced vital capacity (FVC), forced expiratory/inspiratory volume in one second (FEV1 and FIV1), forced inspiratory capacity (FIVC) and positive expiratory/inspiratory flow (PEF, PIF). Modified from [51]*

FVC is the maximal volume of expiration after maximal inspiration and conducted with maximal force of expiration. It is measured in litres. PEF is the highest flow achieved in maximum expiration. In flow-volume loop it can be calculated from the highest positive value of the flow in litres per second. [25] PIF has the same principle as PEF, but it is measured from the inspiration.

Forced expiration volume in one second (FEV1) is the volume exhaled during the first second of expiration after a maximum inspiration, also measured in litres. Forced inspiration volume in one second (FIV1) has the same principle as FEV1 but it is measured from the inspiration. [25] Forced inspiratory vital capacity (FIVC) has the same principle as FVC, but the manoeuvre is performed by maximal inspiration after expiration and holding breath. It is used to check the quality of the study to determine whether there are air leaks [1].

Miller et al. [25] discussed the current standardizations of spirometry. They are based on American Thoracic Society (ATS) statement in 1979 and the updates in 1987 and 1994. The European Community for Steel and Coal published the first official statement of the European Respiratory Society (ERS) in 1983 and updated it in 1993. The modern statements of both ATS and ERS are quite similar with some minor differences.

Spirometry equipment has a lot of manufacturers and companies over the world. For example, Medikro Oy (Kuopio, Finland) produces three different types of spirometers and additional parts, such as flow sensors. Medikro® Pro is one of the spirometer systems provided by the company. It was also used in this study. [23]

Although spirometry is considered the golden standard of spirometry, it also has some disadvantages. The results from spirometry are strongly influenced both the patient's and the clinician's performance. The patient needs to perform at maximal level and the clinician needs to encourage the patient to perform the with maximal effort to get reliable and comparable results. The calibration of the spirometry device need to be performed correctly to receive accurate relationship of the sensor values and actual volume or flow. Daily or even more frequent calibration is required. [25]

Another disadvantage of spirometry is that commonly the maximum number of performed manoeuvres is eight, depending on the condition of the subject. The results of spirometry are related to very short interval; thus, long-term interpretation of the data is not possible. In obstructive diseases, such as asthma, there are both short-term and long-term triggers and effects to asthma symptoms. The performance and lung functions depend on the environmental changes (allergens or pollutants) but also due to complexity and non-linearity of the respiratory system. Temporal pattern of respiration is difficult to predict, but evaluation of nocturnal respiration should be considered as well. [12] For nocturnal or otherwise long-term measurements, another measurement method is needed.

2.3 Impedance Pneumography

IP is a non-invasive and indirect methods for assessing changes in the respiration. It can be used to assess the flow and volume profiles of tidal breathing by applying a small current and measuring the impedance of the thorax. IP has been proposed as an indirect method for assessing respiration with minimal effort to the patient. In general, the impedance measurement is based on the Ohm's law: the electrical impedance of the thorax can be calculated: $Z = \frac{U}{I}$, when the current I is fed to the body and resulting voltage U is measured [33].

IP is a method that has been actively researched in the 1960s and 70s. One of the first applications of IP was the monitoring of respiration in the manned Apollo missions flown by the National Aeronautics and Space Administration (NASA), which was based

on the research by Geddes et al. [13]. During the Mercury program a heated thermistor was used to detect cooling caused by air flow in and out of the mouth, but it was not detecting respiration accurately enough. Impedance based method was found to be considerably more accurate. [24]

In 1972 Grenvik et al. [15] studied the correlation of transthoracic impedance and respiratory volumes measured with spirometry. They found that IP could be used to measure respiration rate and to detect apnea, but because of variation in the calibration factor the reproducibility of the measurement was poor.

Two years later, in 1974 Freundlich and Erickson [11] applied IP method for continuous monitoring of respiration during surgical anaesthesia. They resulted in mean correlation of 0.89 between impedance waveform amplitude and tidal volume during anaesthesia, and 0.87 in control study. The concluded the method easy and safe to use, and emphasized that the method was especially useful, since electrocardiography (ECG) could be measured simultaneously with same electrodes. They also detected intentional airway obstruction effectively with IP.

Fein et al. [10] suggested two applications for the impedance measurements in pulmonary oedema patients: for measuring the level of oedema with high risk patients in circumstances, where radiographic methods or blood gas analysis is not available or for patients that non-invasive measurement is required if the conventional method is medically contraindicated or technically impossible.

Sim et al [49] used IP for directly assessing pulmonary function test parameters. Their method detected COPD patients from normal patients, when considering the changes of PEF, FEV1 and the ratio of FEV1 and FVC. They found the method useful for periodic monitoring of already diagnosed COPD patients.

Ville-Pekka Seppä developed the modern IP method towards clinical applications in his dissertation in 2014 [39]. So far the method has been validated for healthy adults [47] and children [45] and children with asthmatic symptoms [46]. As it can be concluded from previous paragraphs, most of the IP research has been concentrating on obstructive events in the respiration.

Currently IP is clinically used in intensive care units to measure respiration rate. Other clinical applications have not yet been validated, but the first commercial device for investigational use has been presented in early 2017. Ventica® Lung Function Testing System is developed by Revenio and it is used for overnight lung function testing for young children. [56]

2.3.1 Fundamentals of Bioimpedance

The principle of impedance theory is simple: applied current through the material results in voltage, thus impedance can be calculated. However, when the impedance is measured from the thorax which contains a changing physical volume, several organs, muscles and tissue types, different components affecting the measured impedance signal from the thorax are not as straight-forward. The components affecting the changes in the measured impedance are not self-evident, since the thorax cannot be modelled as a parallel circuit of different organs. The geometry of the thorax is not stable, and the conductivity is different for different tissues. [39]

When the continuous current is fed to the thorax, a volume conductor consisting the distribution of the current forms a spatial distribution, a lead field ($\boldsymbol{J}_{LI}$). Also, the measured voltage forms a lead field ($\boldsymbol{J}_{LE}$) and the dot product of the fields produce a scalar field called the sensitivity field ($\boldsymbol{S}$). [14] Sensitivity field and lead field theory are also the fundamental of impedance cardiograph measurement (ICG). Theoretical lead field approach in bioimpedance measurements was found potential by Kauppinen et al. [19].

Thus, the impedance can also be calculated by integrating the product of the inverse of conductivity and sensitivity over the volume conductor

$$Z = \int_V \frac{1}{\sigma}\boldsymbol{S}\, dv = \int_V \frac{1}{\sigma}\boldsymbol{J}_{LE} \cdot \boldsymbol{J}_{LI}\, dv \quad (1)$$

The sensitivity field can be either positive, negative or zero, depending on the angle of the lead fields, if a tetrapolar electrode configuration is used. Benefit of using tetrapolar electrode configuration is that the tissues close to the surface may be excluded, and the electronics beyond the electrode-tissue interphase do not cause distortive components to the signal, since the lead fields do not meet in the electronics of the measurement system. Impedance changes also occur when the geometry of the thorax changes, for example due to organ movement. Therefore, minimizing the movement artefacts is important when measuring IP. [21]

Biological impedance measurements can be conducted in time domain or in frequency domain. In frequency domain measurements, a sinusoidal current is fed through the body at several frequencies resulting in different voltages depending on the tissue properties: tissues are resistive, but the value of resistivity depends on the tissue type. [22] The method of applying several frequencies is called bioelectrical impedance analysis and it is used for example for detecting the body composition. [20]

In time domain, the current is fed through the body at a constant frequency and the fluctuations of the impedance are evaluated continuously to assess the changes in physiology. The method includes for example the measurement of respiration and cardiac activity (ICG). [39]

2.3.2 Measurement Principle and Signal Processing

IP could be measured with bipolar or tetrapolar electrode configuration with various electrode placements. In IP measurement presented by Seppä et al. [41], four electrodes are attached on both sides of the thorax and the alternating current is fed through the body. The voltage is measured with the other pair of electrodes and the computed impedance signal is stored to the device.

The measured impedance increases during inspiration when the flow of the current is restricted due to changes in the dielectric properties of the tissues in the thorax. Dielectric properties are assumed to be a linear function of the air content in the lungs. Also, the redistribution of blood in the thorax in each heartbeat affects the impedance. [33]

The electrode location needs to be selected in a way that the respiratory signal is strong and motion artefacts are minimized. According to the study of Seppä et al. [41] in 2013 the highest linearity is achieved by placing the current electrodes on the midaxillary line at the height of the fifth intercostal space and the voltage electrodes placed on the arms opposite to the current electrodes. This electrode configuration was used to achieve high linearity on healthy adults and young children with symptoms of respiratory difficulties. The electrode configuration is seen in Figure 4.

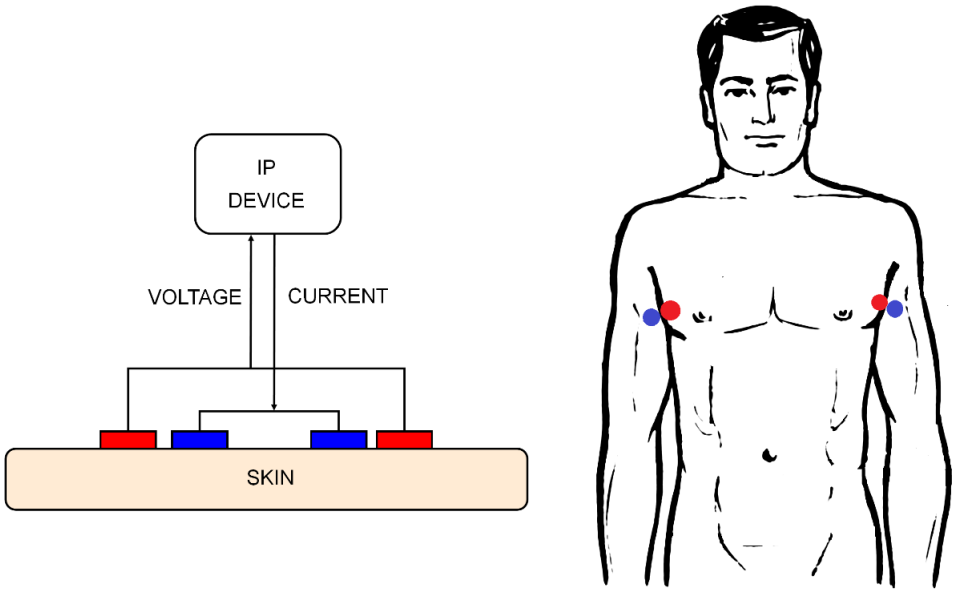

Figure 4. *Sketch of the impedance pneumography measurement setup (left) and tetrapolar electrode configuration (right). Four commonly used electrodes are attached to the skin. Blue electrodes are used for driving a small alternating current to the body and red electrodes measure the resulting voltage. The impedance is calculated in the device and stored. Sketch on the right modified from [35].*

The cardiogenic oscillations (CGO) are the effect of heart muscle pumping blood in the thorax and the pulsatile redistribution of blood. In ICG the impedance related to redis-

tribution of blood is deliberately measured to assess cardiodynamic parameters, such as the stroke volume. In IP, CGO is an artefact which needs to be effectively attenuated to assess the change caused by respiration. [39]

The effect of CGO can be attenuated by using different filtering methods having two main requirements. Firstly, the cardiac part needs to be maximally attenuated and secondly, the filter should have minimal distortion to the respiratory part. Seppä et al. [40] have benchmarked three different filters: a standard low-pass filter, a Savitzky-Golay smoothing filter [37] and a filter of their own design. The Savitzky-Golay filter was already used in the study of Seppä et al. [44] in 2010, because of its ability to preserve high frequencies while having properties of a low-pass filter. Thus, its justifiable to compare Savitzky-Golay filter and own design to low-pass filter, which is the simplest solution.

The difference of the new filter was that CGO waveform model was lung-volume dependent, and it produced excellent results when evaluating CGO attenuation and respiratory signal distortion. [40] A simplified CGO filtering process by Seppä et al. [40] is presented in Figure 5.

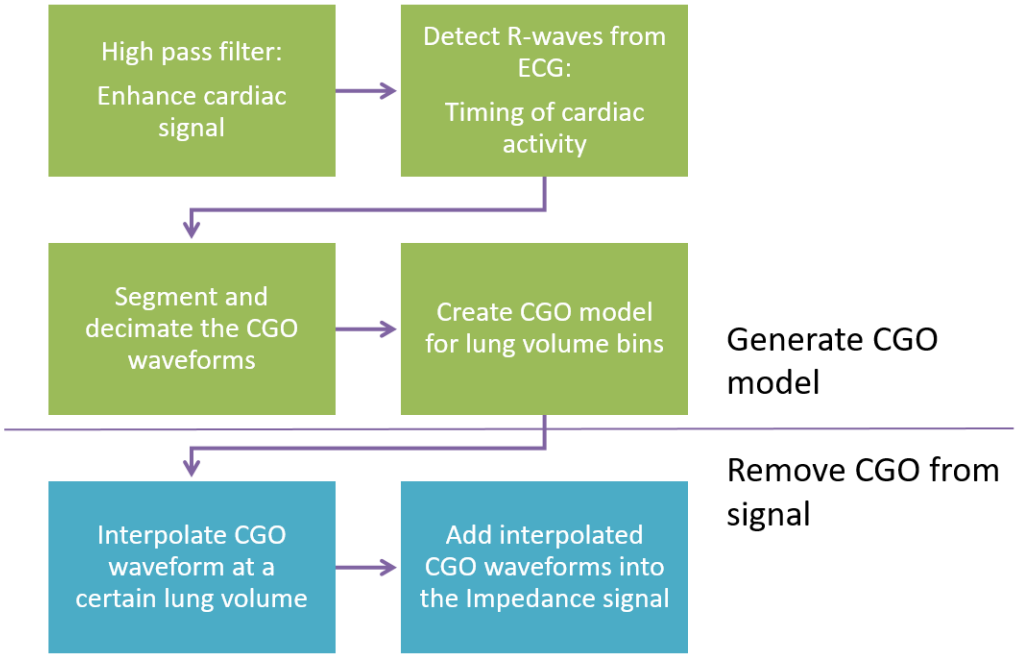

Figure 5. *Visualization of the cardiogenic oscillation (CGO) filtering method based on the method presented by Seppä et al. [40]. Input is raw impedance signal and output is the impedance signal with attenuated CGO.*

The filter designed by Seppä et al. [40] consists of two phases: generating a CGO model and cancellation of the CGO with the designed filter. The impedance signal is filtered with a high pass filter to attenuate respiration and preserve the cardiac component. The

respiratory and cardiac component have some overlap in the frequency spectra, but high-pass filtering attenuates most of the respiratory signal.

Individual CGOs are segmented with timing from R-R intervals of the ECG signal measured by the IP device and decimated to a fixed number of points for a spline fitting process. Decimated CGOs are put into bins according to the relative lung volume and the mean CGO waveform is calculated. When the CGO is attenuated from the original signal, the estimate for each CGO is calculated and the generated waveform is subtracted from the raw impedance signal. [40]

Effective filtering of CGO is important to achieve highly linear $\frac{\Delta Z}{\Delta V}$ ratio. When the distortive effect of blood flow through the thorax is subtracted from the signal, and the electrode configuration is carefully selected, the highest linearity of IP signal is received. [39]

The effect of CGO in IP signal and the filtering result with a filter based on the filter by Seppä et al [40] designed is presented in Figure 6.

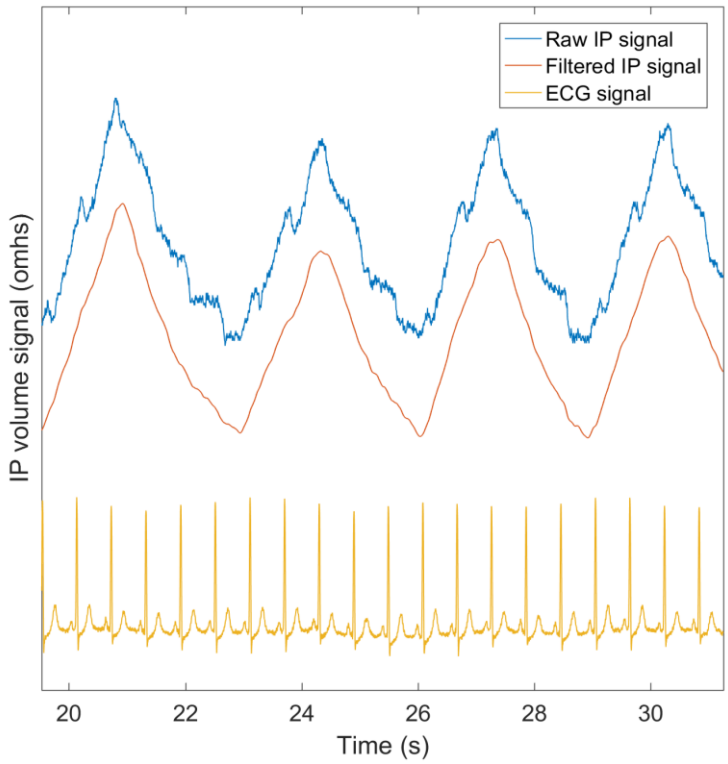

Figure 6. *Raw volume related signal measured with impedance pneumography, before any filters are applied (blue signal). Red signal denotes the impedance signal after CGO filtering and the yellow signal denotes the ECG signal visualizing the effect of CGO.*

In the raw IP signal inspiration and expiration are visible (signal increasing and decreasing, respectively), but the CGO artefact is visible throughout the signal. When examin-

ing the raw signal and ECG, it can be noted that increases in impedance occur during R-peaks of the ECG. The filtered signal is considerably smoother than before filtering and the effect of the CGO has been effectively attenuated, but the respiratory pattern is still visible in the signal.

2.3.3 Calibration and Reproducibility

The unit of impedance is ohms (Ω), but the absolute signal received from the IP device is an arbitrary unit by the analogue-to-digital (AD) transducer. AD transducer has some device-to-device variation, which needs to be considered when comparing the signals measured with different devices. The unit of spirometry signal is either litres (volume) or litres/second (flow), thus the IP signal needs to be calibrated before receiving absolute volume or flow signals. This can be done by measuring a calibration signal of simultaneous IP and direct flow measurement, and calculating a calibration factor between the signals (Ω/l) [39].

The calibration period could be feasible in static patients, but for mobile patients the changes of posture also change the $\frac{\Delta Z}{\Delta V}$ ratio. Fein et al. [10] studied normal 27 normal subjects and 33 patients with severe pulmonary oedema by measuring the transthoracic impedance by impedance plethysmograph. Results showed that in normal subjects the impedance increased from supine to standing posture and when lung volume was increased. Impedance varied between four measurement days (± 2.7 Ω) but was quite constant with multiple measurements on the same day without removing the electrodes (± 0.7 Ω).

Amongst pulmonary oedema patients the impedance did change according to the severity of the oedema measured either with clinical indexes or radiographic indexes. However, all the oedema patients did not have impedance values outside of the normal range, thus it was concluded that a single impedance measurement was not diagnostically useful, but the variation in impedance related to the level of pulmonary oedema was more significant. The study concluded that the $\frac{\Delta Z}{\Delta V}$ ratio might change even with static intensive care unit patients due to accumulation of fluids in the thorax. [10]

Młyńczak et al. [28] assessed the effect of four properties on the slope values of linear regression and the coefficient of determinations (R^2) calculated from simultaneous IP and PNT measurement under static conditions. The quantitative impact of respiratory rate, depth of breathing, body posture and subject (sex and body mass index (BMI)) was determined. They resulted in high values of average R^2, thus the agreement of the methods for both volume and flow was sufficient. They also discovered that the subject variability and body posture had the greatest impact on the results.

In another study Młyńczak et al. [27] assessed the calibration methods and reproducibility of IP on three sessions. The second and third measurement were conducted approximately two months after the first one, and there were 1–3 days between the second and third measurement. They discovered that the VT values did no change considerably, if only body posture was considered in the calibration (depth of breathing and respiratory rate were discarded). The reproducibility of the measurement was best, if the calibration was conducted on the same day before the measurement, but also short term reproducibility was quite similar (calibration from the 2nd measurement applied on 3rd measurement).

If absolute volume or flow values are assessed IP should be calibrated before analysis. Also, the difference of the AD transducer readings should be considered. However, if only relative parameters are assessed, the calibration is not necessary. The parameters are discussed in the next Section.

2.3.4 Tidal Breathing Parameters

IP signal can be used to calculate and plot a flow-volume loop for one or more respiratory cycles. An example of the flow-volume loop averaged from 1 minute IP signal is in Figure 7.

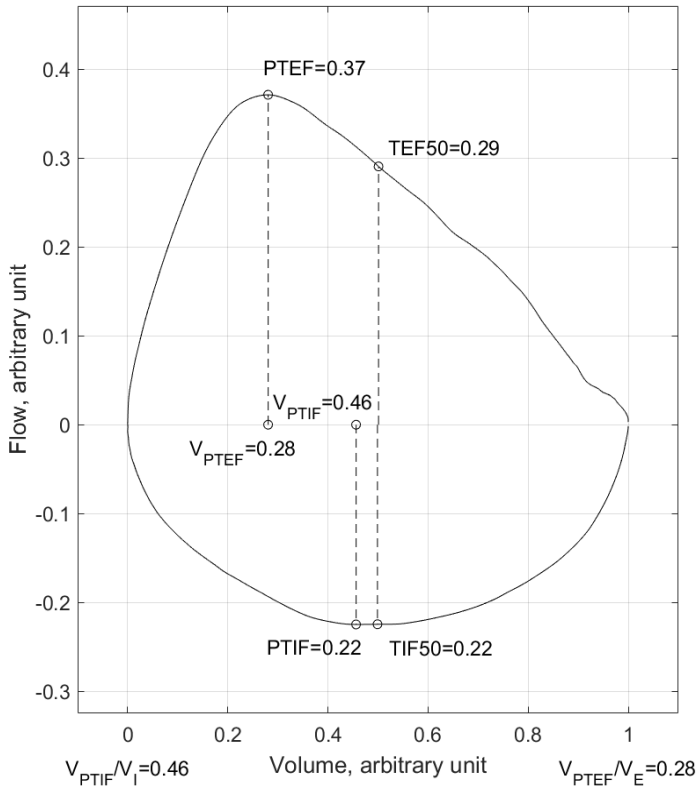

Figure 7. *Flow-volume loop from 1 minute impedance pneumography signal (measured while also breathing through a pneumotachograph).*

The flow-volume loop can be used to calculate tidal breathing parameters, some of them similar than the conventional spirometry parameters. The figure visualizes how to determine six parameters from the flow-volume loop. Peak tidal expiratory / inspiratory flow (PTEF and PTIF) are measured similarly than PEF and PIF in spirometry, but the values are related to tidal breathing, not forced manoeuvres. Volume at PTEF or PTIF (V_{PTEF}, V_{PTIF}) is the volume inhaled or exhaled at the time of the peak flow. These can be used to determine the percentage of volume at tidal peak flow (V_{PTEF}/V_E and V_{PTIF}/V_I).

Tidal expiratory / inspiratory flow at 50% of the expiration / inspiration (TEF50, TIF50) are measuring the tidal flow at the halfway of the expiration or inspiration. TEF50 and TIF50 have been studied for example by Schmalisch et al. [38] in 2005, who found that there was a difference in the results between healthy infants and infants with chronic lung disease. They also resulted a difference in PTIF, V_{PTEF}, PTEF between the two groups.

In 1981, Morris and Lane [30] studied the tidal expiratory flow pattern measured by PNT of 99 subjects with normal respiration, obstructive and restrictive symptoms. They studied three parameters: PTEF, VPTEF/VE and percentage of expiratory time to tidal peak flow (tPTEF/tE). The percentage parameters correlated with airways obstruction

detected with the conventional methods, but PTEF did not correlate with the airway obstruction.

Seppä et al. [42; 45] found that the IP method can accurately measure tidal breathing parameters in adults and children. Despite induced airway obstruction and irregularity of breathing, IP could successfully measure tidal breathing parameters and flow signal. Flow signals were also obtained during expiratory loading on healthy adults, when an appropriate electrode configuration and cardiac filtering was used.

Tidal breathing parameters have been studied in many age groups (adults, adolescents and infants), but most of the studies are related to determining the airway obstruction of the subjects. Therefore, no literature of tidal breathing parameters measured before and after thoracic surgeries were found.

2.3.5 Impedance Pneumography Wearables

IP can be measured with almost any device producing bioelectric physiological measurements. For example, Biopac Systems [6] was used in various studies by Seppä et al. [40; 41; 44; 47]. However, wearable devices have been proposed specially to enable ambulatory measurements.

In his doctoral dissertation Timo Vuorela [58] produced five prototypes of the wearable bioimpedance measurement device. The device size varied between 63–85 cm^3 (weight 66–102 g), and it was encapsulated with commercial plastics and one waterproof epoxy and silicone solution. However, the waterproof device was not functioning after encapsulation, and since the encapsulation was almost impossible to remove, the failed device was not repaired. The data was stored into a µSD memory card and transferred to the computer either by a radio link, with data transfer cable or my applying the memory card into an external card reader. The device was powered with a rechargeable lithium-polymer battery.

All prototypes included bioimpedance and ECG measurement, and the functions were validated both by Vuorela et al. [59] and Seppä et al. [43]. The measurements with the fifth prototype resulted relatively good correlation of the impedance and respiration measured with a pneumotachograph attached to a Biopac [6], when the subject was not moving. According to preliminary tests by Seppä et al. [43] the respiration was still accurately measured despite the motion artefacts, when a robust movement artefact reduction algorithm was developed.

Młyńczak et al. [26; 29] designed three of their own prototype of ambulatory IP monitor "Pneumonitor". The Pneumonitor consisted of the current feeding block, receiver, voltage supply for electronics and the control for AD converter and storing of the data to an SD card. Pneumonitor 1 was studied in a group of 12 healthy volunteers by deriving the

tidal volume with three breathing rates, two depths and three body postures. The average determination coefficients (R^2) was 0.985 (range 0.934–0.997). Some subjects had higher relative difference to the reference method (PNT), but it was concluded that Pneumonitor produces signals related to respiratory and cardiac activities. [26]

Pneumonitor 2 was an improved version of Pneumonitor 1: they added ECG and motion sensors and improved the power management. The most power consuming devices were replaced, and the battery was changed to rechargeable one. Pneumonitor 3 had the previous properties, but a wireless pulse oximetry was added. Pneumonitor 2 weighted 160 g, but Pneumonitor 3 was 330 g. Whereas Pneumonitor 2 had seven leads, Pneumonitor 3 was reduced to five leads by combining the IP input leads and two ECG leads. [29]

Both devices were used with two electrode configurations: the one presented by Seppä et al [41] and a "classical configuration", in which all the electrodes are placed in the 5th and 6th rib level because of better resilience to motion artefacts. A pilot test of 10 subjects resulted in 86.5% accuracy in tidal volume estimation and 97.3% agreement in heart rate estimation compared to the ECG signal. [29]

2.4 Comparison of Impedance Pneumography and Spirometry

Despite both IP and spirometry are measuring respiration, there are a lot of differences in the measurement procedures, analysing methods and results. The properties of IP and spirometry are collected and compared in Table 1.

Table 1. *Comparison of impedance pneumography and spirometry properties, current state in research and commercial use.*

Property	Impedance pneumography	Spirometry
Measurement method	Indirect, measures electrical impedance Z	Direct, measures air flow Q
Posture	Supine (also others studied)	Sitting
Procedure	Tidal breathing, can be measured awake or during sleep	Carefully instructed manoeuvres
Results	Research devices: Processing with MATLAB or other software, commercial devices: RR detection automatically	Automatic parameter calculation
Reference values	No comparable clinical values or guidelines for diagnostics in tidal breathing parameters, RR clinically validated	Variety of reference values and literature
Calibration	Manual calibration needed for accurate volume measurements	Automated calibration
Target group	Suitable also for measurements with infants or non-cooperative patients, RR measurement for all patient groups	Adults and children can be measured but requires awareness and commitment from the patient
Commercial devices*	Ventica® ADAS1000 (Analog devices) ADS1298R (Texas Instruments)	Many, for example Medikro® Pro

* Ventica® [56] currently for investigational use only, ADAS1000 [2], ADS1298R [53] Medikro® Pro [23]

The comparison shows that two different measurement methods are potential in expanding the variety of patients. IP enables the method to be used in various patient groups, since the method itself is not depending on the posture although movement should be limited. Therefore, the method is potential for use in ICU, patients with diseases weakening the overall condition or during recovery from a surgery, when extensive physical activity is not recommended or possible.

More clinical research is required to achieve more literature values from IP measurements and to prove the reproducibility of the results. The quality of IP as a stand-alone method needs to be determined, but also how to efficiently calibrate it in everyday use. Guidelines for different parameters and the to standardise the measurement method need to be made. The measurements from this project can be used to analyse the feasibility of IP in cardiothoracic surgery patients.

3. MATERIALS AND METHODS

The study material was divided to two major surgery types: cardiac surgeries and pulmonary surgeries. The study groups have various backgrounds and conditions, thus some basic medical information about the patients are discussed. All patient information is presented in a way, that the patients cannot be individualized. The author did not handle any personal information, such as names or social security numbers.

First part of the study consisted the clinical measurements performed by the physiotherapist of the Heart Center. The material was collected in Tampere University Hospital, Finland during the years 2013 to 2016 in two phases. The signal processing was performed by the author in 2016. Two medical students from University of Tampere started to study the effect of intervention in 2016 and are still ongoing. Signal analysis of IP data was performed by the author between Fall 2016 and Spring 2017. The study of physiotherapy methods and care will start in 2017, although preliminary studies have been made already.

The statistical analysis of the measurements was based on assessing the agreement between IP and PNT: first preliminary tests contained simple visualization and correlation, but the second phase consisted statistical analysis based on the study by Seppä et al. [45]. The concept of linearity was studied by assuming the reference method to be true and comparing the agreement of IP to it.

3.1 Materials

A pilot study consisted of 12 patients measured between May and June 2013. The second phase of the study started in September 2013 and ended in Spring 2016. In total of 136 patients were recruited from elective routine cardiothoracic surgeries in the hospital. The participation to the study was voluntary, and based on informed consent. The study was approved by the institutional ethics committee of the Pirkanmaa Hospital District, Finland.

Patients were excluded from the study if there was a neurological or other type of condition significantly lowering the ability to cooperate, the patient was intoxicated when entering the hospital or he/she had BMI over 40 kg/m^2. Also, a danger of contagious lung or other type of infection, severe respiratory difficulty or high breathing frequency and a preoperative pacemaker were exclusion criteria. Most of the reasons are related to ensured patient safety. It was important to ensure that the patients could perform the

spirometry test. Patients with preoperative pacemaker were excluded to avoid any electrical safety risks, even though IP should not affect the function of the pacemaker.

Some studies were interrupted due to postoperative complications and second operations. The patients were not excluded from the study unless there was an increased risk for the patient or he / she wanted to discontinue.

Descriptive characteristics of the patients selected to the study are in Table 2.

Table 2. *Descriptive characteristics of the total study population (N = 136). Due to length of the study and combined pilot group and official study, some parameters have not been measured from all the patients.*

Variable	Value (Mean ± SD)	N
Age	63.4 ± 12.8 years	136
Gender (male / female)	84 / 52	136
Weight (PREOP)	81.0 ± 16.8 kg	132
Smoking	25 (9*)	136
Oxygen saturation, PREOP**	95.96 ± 1.71 %	136
Oxygen saturation, 1POP	91.32 ± 3.41 %	134
Oxygen saturation, 2POP	91.17 ± 4.20 %	136
Oxygen saturation, 3POP***	90.90 ± 3.82 %	49

*Recently quit smoking;
**PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. postoperative measurement
*** Only cardiac surgery patients were measured in 3POP

The age of the study population varied; the range of age was 19–79 years. 18% of the patients were smoking at the time of the study, and many of the patients reported to have smoked in the past. The starting weight of the patients varied (Table 2), but in cardiac patients the relative difference in weight was greater than in pulmonary patients. The change of weight during the episode of care in cardiac patients is related to fluid accumulation in the thorax. This can be seen from Table 3.

Table 3. *Mean weight of cardiac surgery patients (N = 46) on different measurement days. The weight difference (Δ) is the difference to PREOP measurement (e.g. weight (1POP) – weight (PREOP)).*

Measurement	Mean (kg)	SD (kg)	Δ (mean ± SD, kg)
PREOP	81.72	14.24	
1POP	87.54	14.05	7.36 ± 3.80
2POP	88.25	14.26	7.73 ± 4.08
3POP	87.25	14.15	6.32 ± 4.09

*PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. postoperative measurement

It can be seen from the cardiac patients that the mean weight increases until 2POP, and slowly starts to decrease after that. There is variance in the weight, since the starting weight of the patients also varied. The difference in weight shows that the mean gain was 7.73 kg after the surgery. All cardiac patients gained weight after surgery, whereas some of the pulmonary patients lost weight after surgery for example due to lobectomy, where tissue was removed or due to natural day-to-day fluctuation of weight.

The patients were divided into three groups based on the type of surgery they had. These three groups were **cardiac surgery patients** (C), **minor pulmonary surgery patients without resection** (PM) and **pulmonary surgery patients with resection** (PR). Group C included different types of open heart surgeries. Both PM and PR type surgeries were done by using either thoracotomy or video-assisted thoracoscopic surgery (VATS), but the vital difference between PM and PR is that in PM a surgical biopsy was performed whereas in PR a section of the lung or even the complete lung was removed.

The patients in these three surgery type groups were randomized into to equally sized subgroups. The control group (A) trained with positive expiratory pressure physiotherapy (PEP-P) whereas the study group (B) trained with inspiratory muscle training physiotherapy (IMT-P). The fundamental difference between these methods is that the method has resistance either for expiration or inspiration, respectively. Both groups received otherwise similar physiotherapy before and after the surgery.

All the measurements and physiotherapy related to the study was conducted amongst the normal hospital routines of the patient and the nurse, and the episode of care was not prolonged due to the study. The studies were conducted one day before the surgery (PREOP) and for 1–3 days after the surgery (1POP, 2POP and 3POP, respectively). 3POP was only measured in group C.

3.2 Measurement Procedure

The measurements were done by a physiotherapist amongst her and the patient's other routines at the hospital. The planned measurement procedure was similar on the days before and after the surgery but the condition of the patient effected the execution of the measurement. Measurements were cancelled if the condition of the patient was very unstable after the surgery, or if the patient was not willing to conduct the measurement.

The measurements were done preferably during one session, but sometimes in two separate sessions. The planned measurement procedure was following:

1. Spirometry and IP devices were applied and turned on
2. Three respiration cycles with restful pace but deep breathing
3. Three times forced breathing manoeuvre:

   a. Relaxed full inhale
   b. Explosive exhale
   c. Explosive inhale
4. Tidal breathing recording for one minute (IP + PNT)
5. Spirometry mouth piece removed and tidal breathing recording was continued for 19 minutes (the patient was left alone)

The beginning and the end of the one-minute recording was marked to the IP file by an attention button in the IP device. This was later used to find the simultaneous measurements of IP and direct flow signal for assessing the agreement of two methods.

In PREOP the physiotherapy with PEP-P and IMT-P was given after the measurement, to evaluate the true baseline of the patients before any breathing education. In postoperative measurements, the physiotherapy was given before the measurement.

3.3 Measurement Devices

IP was measured with a small portable device similar than the one described by Vuorela et al. [59]. The sampling frequency of IP was 256 Hz. Four electrodes were connected to the midaxillary line at the height of the fifth intercostal space and to the arms opposite to the first two electrodes. The data was stored to the device memory card and transferred to a computer after each measurement. [45]

IP was measured with one of the two available devices. The same device was used for the patient throughout the study if it was working at the time of the measurement. If it was not (for example due to empty battery), the other device was used. Devices were similar, but the reading of the AD transducer might vary between devices.

Medikro® Pro -spirometer and disposable Medikro® Spirosafe flow sensors were used in the study [23]. The sampling frequency of the spirometer was 100 Hz and it was later oversampled to match the IP sampling frequency.

In addition to the respiratory measurements, a Nonin Wrist Ox_2 wrist oximeter [32] was used to measure the oxygen saturation (Sp02) of the patient. BD MicroRPM [4] device was used to measure maximal inspiratory mouth pressure (MIP). MIP was used to determine the starting resistance of the inspiratory muscle training device in the study groups. These devices are not further discussed in this thesis.

3.4 Signal Processing

Both IP and PNT data was processed with MATLAB R2016a software. The signal processing flow for both IP and PNT is presented in Figure 8.

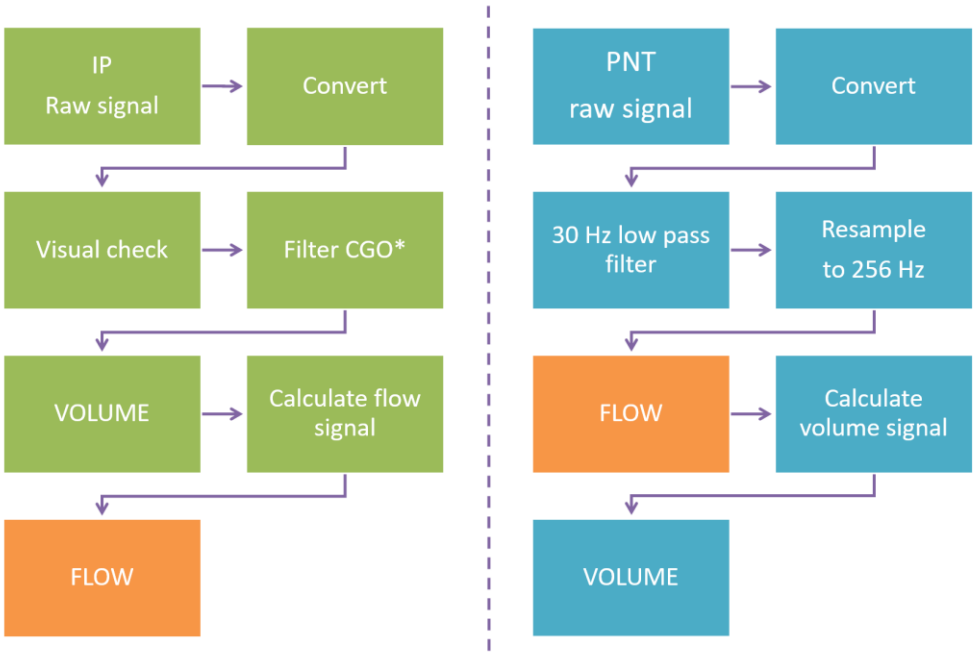

Figure 8. *Impedance pneumography signal processing scheme is presented on the left (green) and pneumotachography signal processing scheme is presented on the right (blue). Flow signal (orange) was used in the analysis in later phases. *Cardiogenic oscillation (CGO) filtering was presented in Figure 5.*

The first step of the processing was to visually check all the IP signals, and to select a 10-minute interval from the section of tidal breathing without the spirometry device on the mouth (step 5 in the measurement procedure). If tidal breathing for ten minutes was not found, the measurement was rejected from all further analysis.

Next, CGO was filtered from the IP signal by a filter based on the one presented by Seppä et al [40]. After filtering the CGO from the signal, the flow signal can be computed by differentiating the volume-related signal over time with a Savitzky-Golay filter using second-order fitting [44]. Flow signal was used in the further linearity analysis; thus it is highlighted in Figure 8.

PNT was measuring direct flow signal from the mouth. The raw signal was converted into MATLAB format. The PNT was filtered with 30 Hz low pass filter and resampled to 256 Hz. Volume signal was calculated from the flow signal with the same but inverted principle as IP flow signal was calculated from volume signal.

One-minute recording of IP measured simultaneously with PNT (Step 4 in measurement procedure, Chapter 3.2) was extracted from the whole signal. The attention button pushed before and after the one minute of recording with simultaneous IP and PNT was automatically detected and the interval was automatically selected. If the interval was not found automatically, it was visually checked and added.

Flow signals from IP and PNT for each measurement were aligned in time scale in a way, that the cross-correlation function had the highest value. In practise, this was done automatically by moving the PNT signal through the IP signal and the correlation was calculated in every step. When the highest cross-correlation was found, the signals were cut to same length. One-minute signals were used to study the agreement between IP and PNT methods.

Additionally, the selected 10-minute IP signal was used to calculate tidal breathing parameters. The signal was filtered with the same CGO filter than the one-minute signal. Tidal breathing parameters were calculated from 10-minute interval by averaging all the respiratory cycles of the signal into one cycle and by calculating the parameters automatically from the flow-volume loop. The parameters are not reported or analysed in this thesis, but they were derived for later use in the project.

In total of 459 measurements were planned, but 15 of them were cancelled due to the patient's condition after the surgery. 97 of the measurements were unsuccessful: either the IP was rejected (10-minute interval was not selected), or PNT file or the ECG measured with the IP device were corrupted. Thus, 347 measurements were processed by using MATLAB R2016 -software. A visualization of accepted and rejected measurements is in Figure 9.

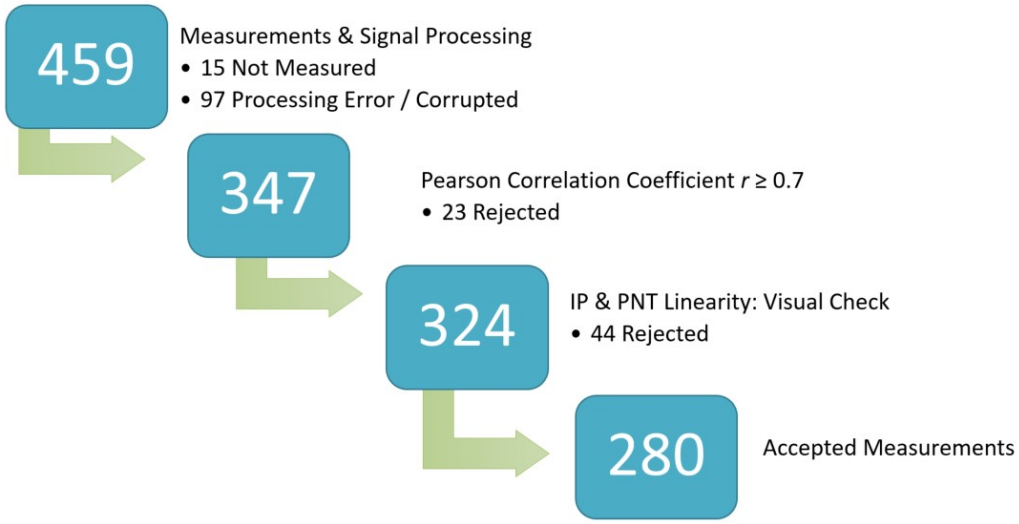

Figure 9. *Chart of accepted and rejected measurements in the processing order. In total of 459 measurements were planned, and in the end 280 measurements were accepted for the analysis.*

The Figure includes also the correlation coefficient and visual inspection based rejection, which are discussed more in the following Chapters. The number of rejected measurements is analysed in the Discussion.

3.5 Preliminary Agreement of Impedance Pneumography and Pneumotachography

Pearson's correlation coefficient was used as one indicator of the agreement between simultaneous IP and PNT measurements. Correlation is represented by *r* and calculated by using formula

$$r = \frac{cov(X,Y)}{\sigma_X \, \sigma_Y}, \tag{2}$$

where cov(X, Y) is the covariance and σ is the standard deviation. The formula of covariance is

$$cov(X,Y) = E[(X - \mu_X)(Y - \mu_Y)], \tag{3}$$

where E is the expectation and μ is the mean. [36] If $r < 0.7$ the correlation was too low and the signals were rejected. If $r > 0.7$ the measurement was accepted. After calculating the Pearson's correlation coefficients, a visual check was performed to all aligned signals. In the visual check, each aligned flow signal pair was plotted and four questions were answered:

1. Are the signals visually correlating?
2. Is there noise in the IP signals?
3. Is there noise in the spirometry signal?
4. Does either of the signals have individual high peaks?

The results from the Pearson's correlation test and visual check were compared to check whether the limit of the correlation coefficient was appropriate, and if there were motion artefacts affecting the correlation. The mean ± standard deviation (SD) was calculated of the accepted measurements.

If there were motion artefacts in the beginning or at the end of the one-minute IP signal affecting the correlation, a small section of less than five seconds was rejected from the signal. If this was done, also the PNT was cut to the same length.

Another way to decrease the effect of individual spikes was to normalize the IP signal by assuming good signal in the middle of the measurement. The signal was standardized with the following equation:

$$z(n) = \frac{x(n) - \mu_{AB}}{\sigma_{AB}}, n = 1,2, \dots, m \tag{4}$$

where *x(n)* is the original signal, *n* is the sample number and *m* the length of the signal, μ_{AB} is the mean of the signal from A to B and σ_{AB} is the standard deviation of the signal from A to B.

3.6 Linearity of Simultaneous Impedance Pneumography and Pneumotachography

When assessing the agreement of two methods, spirometry or PNT measurement is considered the reference method and the relationship with IP measurement is studied. However, direct flow measurement from the mouth has its own disadvantages and artefacts and therefore, the reference method cannot be considered the perfect method. The term "linearity" usually refers to the evaluation, whether the study method successfully performs similar measures than the perfect method.

Although direct flow measurement was not considered perfect, it is clinically accepted method and can be used as a guide to evaluate the feasibility of IP. Thus, PNT was assumed to be the true measurement method. Linearity was studied from the IP-PNT value pairs sample-by-sample and in different phases of the respiratory cycle according to the study by Seppä et al [45]. Sample-by-sample difference is random, and it could be considered as noise in the measurement.

First, the absolute difference signal was calculated

$$D(n) = |Q_{PNT}(n) - Q_{IP}(n)|, n = 1,2, \dots m \quad (5)$$

where $Q(n)$ is the flow signal for PNT and IP, respectively, n is the sample number and m is the length of the signal. The flow signal as normalized to the PTIF of each measurement. [45]

By calculating the median of $D(n)$ for each patient the D_{SS} was determined. The results were represented as mean ± SD of all the patients in the surgery group. D_{SS} gives information of the average difference in the signal, but it cannot specify whether the differences are random or related to some specific phase of the respiration. [45]

Secondly, it was determined whether the signals represent respiratory phase-dependent disagreement. To determine if the difference from the linearity is related to some specific phase, the average deviation from the linearity (D_L) was calculated. IP-PNT value pairs for one measurement were plotted cycle-by-cycle and a line was fitted to the distribution. [45] An example of the IP-PNT value pair plot for 10 respiratory cycles is in Figure 10.

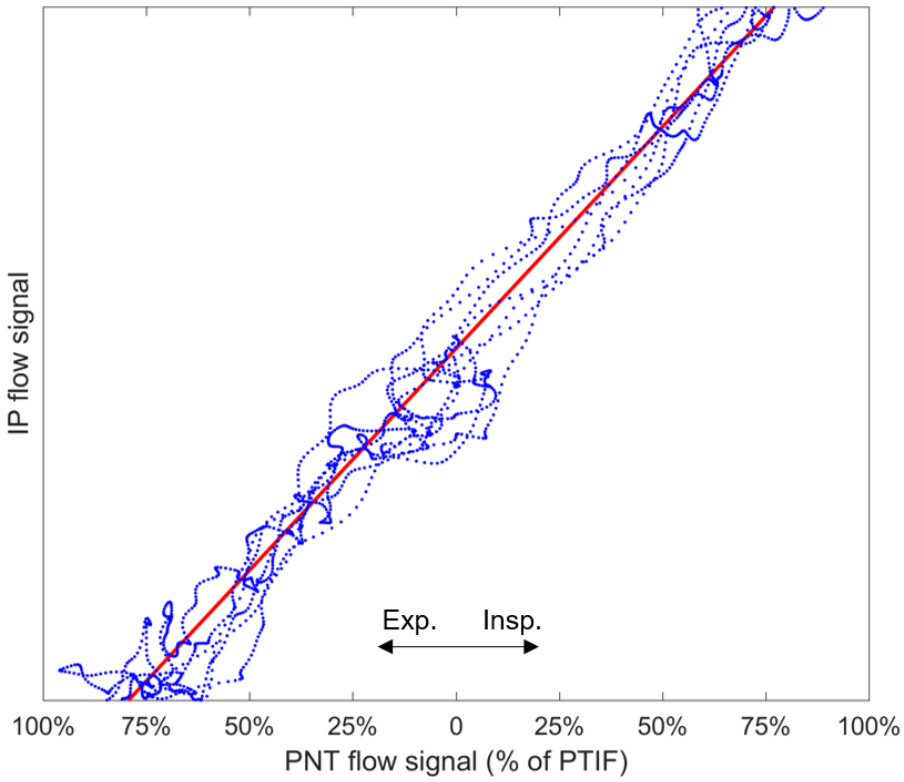

Figure 10. *Simultaneously measured impedance pneumography and pneumotachography signals plotted as value pairs and cycle-by-cycle. The figure contains approximately ten cycles without rejecting any outlier values. Red line denotes the estimated linearity of the measurements, left side is the expiration (exp.) and right side inspiration (insp.).*

It can be seen from Figure 10 that the cycles follow the estimated line, but there is a lot of variation in the signals. The form is not as clear as in the study by Seppä et al. [45], but in this visualization, any individual cycles or outlier values have not been rejected. Altogether, the purpose of the Figure is to demonstrate the procedure of the analysis.

A visual check was performed to reject any extreme outliers from the measurements. Individual breathing cycles or value pairs were not rejected, but if the whole measurement was distorted, it was rejected. At this stage, 44 measurements were rejected from further analysis. Accepted and rejected measurements were visualized in Figure 9.

The overlapping respiratory cycles were divided into ten bins with respect to the respiratory phase. This was performed individually for each measurement. The median distance of the sample pairs from the fitted line was calculated for all the bins. The median of the differences for one measurement is D_L. [45] The results were presented as mean ± SD of all the patients in the surgery group.

Box plot was constructed individually for three surgery groups. The patient-by-patient values of D_L were plotted in different respiratory phases and divided in measurement days.

3.7 Statistical Analysis

The normality was tested on the studied parameters (D_{SS} and D_L) and normal distribution was not confirmed. Therefore, non-parametric tests were used for all the statistical analysis.

Wilcoxon signed-rank test is used to study, whether the distribution of differences has a median of zero. In this study the pairs are observations of the same patient on two different measurement days, thus the samples are not independent. The null hypothesis was that there is no difference between the two distributions. Null hypothesis was rejected with significance level $p < 0.05$. Wilcoxon signed-rank test was chosen, since it is a non-parametric test for paired observations. [36]

Mann-Whitney U test, also known as the Wilcoxon rank-sum test is a method to study, whether the two distributions have the same median. In this case, the tested distributions are independent, since the samples are the parameter values measured on the same day but different groups. [36]

When testing multiple comparisons, for example different group combinations on the same data, it must be considered that the probability of finding something significant increases, when repeated tests are made. Therefore, a Bonferroni correction is presented to provide one solution for multiple comparisons. In Bonferroni correction, the standard significance level (for example $p < 0.05$) is divided by a factor that is the number of comparisons made in the study. The correction decreases the probability of false positive in the statistical test. [7]

By combining the Mann-Whitney U test and the Bonferroni correction, the statistical difference between surgery groups on the same measurement days was tested with significance level of $p < 0.017$, since the amount of comparisons was three (C vs PR, C vs PM, PR vs PM in PREOP, 1POP and 2POP, respectively).

4. RESULTS

The results of the study are presented in two parts. Firstly, the initial agreement of the methods was assessed visually and with Pearson correlation coefficient. Secondly, the linearity of simultaneous IP and PNT signal was evaluated based on the study by Seppä et al. [45]. The results were analysed by dividing the patients into three surgery groups.

4.1 Agreement of the Two Methods

The agreement of successfully processed IP and PNT signals was first evaluated with the Pearson correlation coefficient and visual check. The results from the correlation test and the distribution of rejected measurements are in Table 4.

Table 4. *Results from data processing and Pearson correlation coefficient. Measurements with ρ > 0.7 were accepted and measurements under the limit rejected. Error denotes and error during signal processing (e.g. corrupted signal) and Not measured denotes that the condition of the patient was too low to participate in the study.*

Processing Result	PREOP	1POP	2POP	3POP	Total
$r \geq 0.7$	94	96	100	34	324
$r < 0.7$	9	4	7	3	23
Error	33	28	25	11	97
Not measured	0	8	4	3	15
Total	136	136	136	51	459

*PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. postoperative measurement

Table 4 presents the correlation coefficient results (accepted and rejected) on different measurement days and the distribution of signal errors and unsuccessful measurements. The bottom row defines the total number of measurements in certain measurement day, and the right-most column the total number of measurements accepted, rejected or with errors. An example of acceptable and rejected signal is in Figure 11.

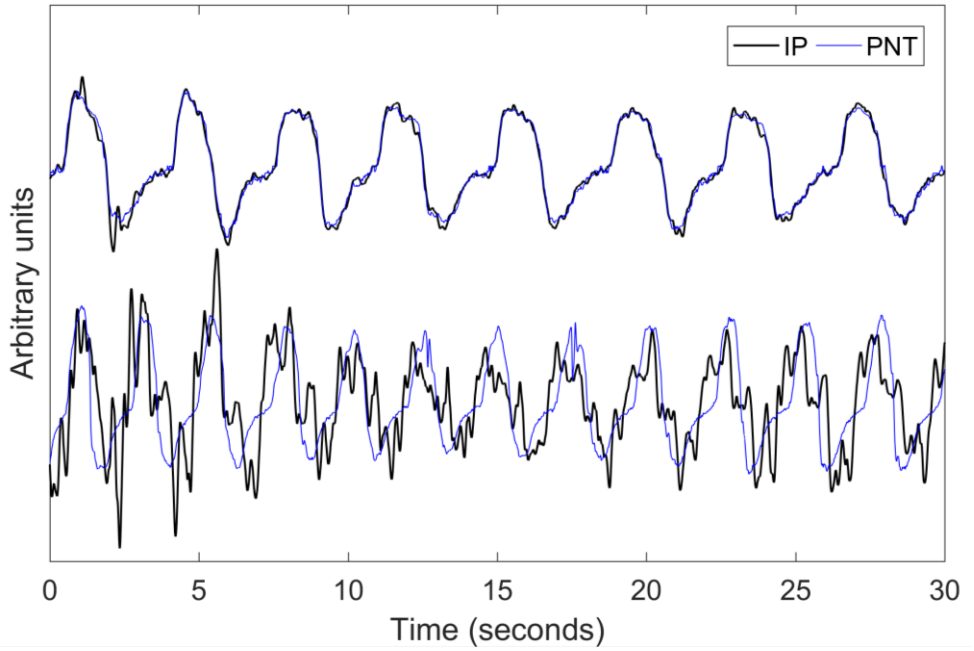

Figure 11. *Two aligned flow signals with accepted and rejected correlation: upper one was accepted (r = 0.991) and the lower one rejected (r = 0.645). Y-axis of the figure has arbitrary units and x-axis denotes the measurement time scale.*

Figure 11 shows the difference of accepted and rejected measurements. In the accepted measurement, the signals are overlapping successfully and there is no noise in the signal. On the other hand, the rejected measurement has very noisy IP signal, thus the CGO filter has not functioned properly. In some parts the signals seem to be in different phases, which might indicate that the IP and PNT signals are not truly simultaneously measured.

The average correlation coefficient (mean ± SD) of accepted measurements was 0.924 ± 0.069 and the average correlation coefficient of all the processed measurements was 0.845 ± 0.172 (range 0.132–0.995). In total, 70.6% of the measurements had correlation coefficient that indicates high or very high correlation. 5.0% of the measurements had lower correlation and 24.4% of the measurements were unsuccessful: either due to error during processing or measurement, or due to cancelled measurement.

In this part, the measurements were not yet divided to groups based on the surgery. In the next Section, the results are presented for groups C, PR and PM individually, and the results between groups are compared.

4.2 Linearity

Linearity results contain box plots of D_L and numerical results of D_{SS} and D_L. The structure of the box plots in Figures 12–14 is similar. The x-axis is the different phases of the respiration; negative values denote expiration and positive values denote inspiration.

The y-axis presents the deviation from the linearity. Both are measured in % of the PTIF. The boxes denote the 25th and 75th percentiles of the data, the whiskers extend to 99% of the values and extreme outliers are marked with crosses. The colours of the boxes are different measurement days: from the lightest to the darkest the boxes denote PREOP, 1POP, 2POP and 3POP, respectively.

The box plots were constructed individually for the three groups C, PR and PM. The box plot for C is in Figure 12.

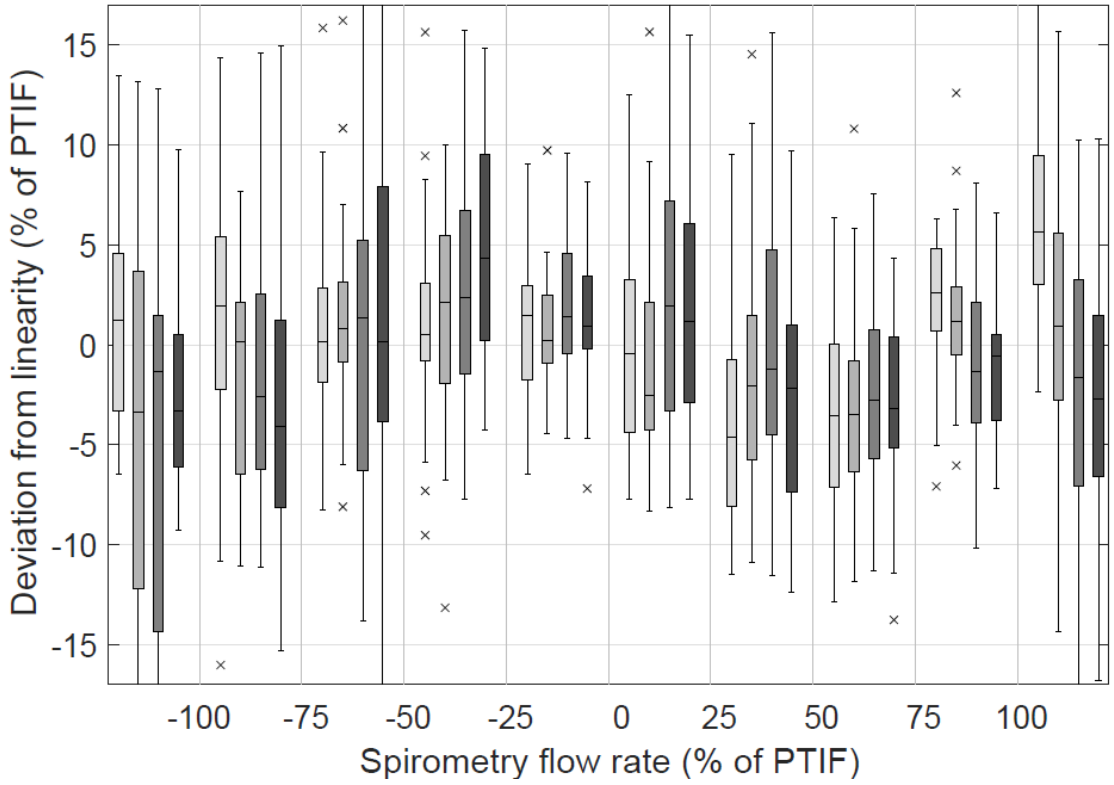

Figure 12. *The deviation from the linearity of impedance pneumography and pneumotachography for cardiac surgery patients (group C, 16–33 patients) is presented as a box plot on four measurement days.*

The deviation from the linearity is mostly ±10% of the PTIF (50% of the results). 99% of the results are between ±15% of the PTIF. The linearity is not dependent on the respiratory phase, but some deviation is present in all the phases. IP-PNT signals are most linear in the end of expiration.

The box plot for PR is in Figure 13.

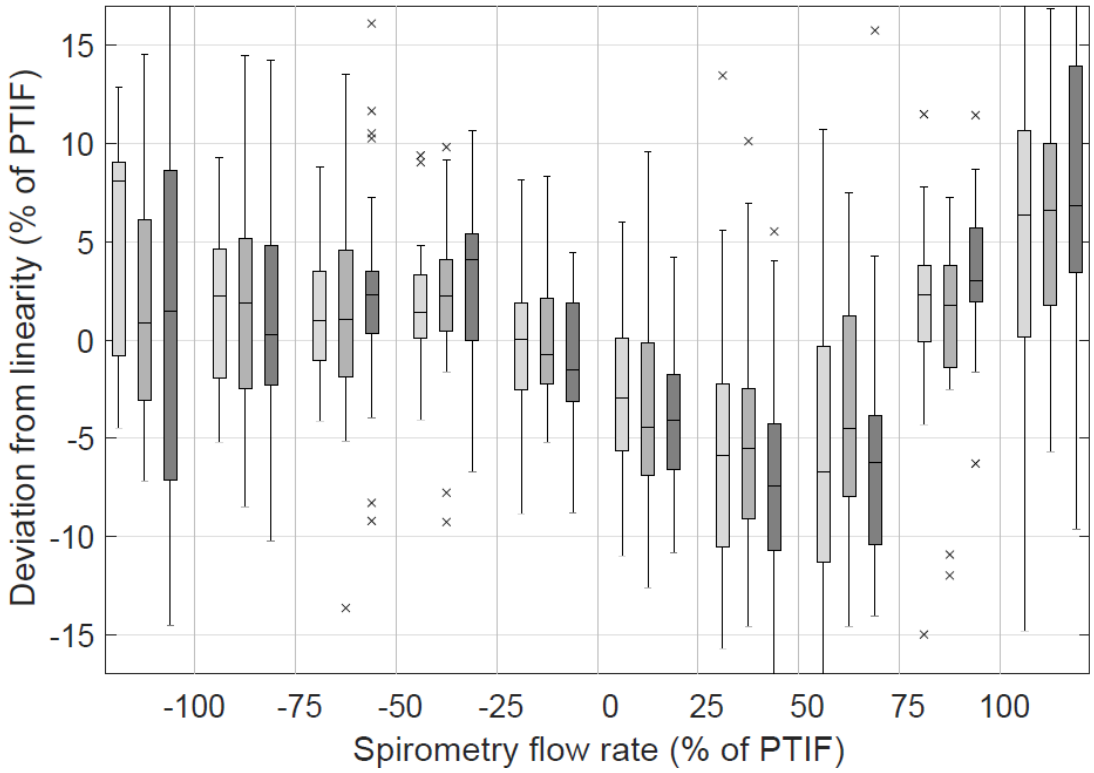

Figure 13. *The deviation from the linearity of impedance pneumography and pneumotachography for pulmonary resection surgery patients (group PR, 25–30 patients) is presented as a box plot on three measurement days.*

PR has only three colours, since 3POP was only measured for group C. The deviation between the patients was less than 10% (50% of the results) but the deviation from the linearity varied more during inspiration than for group C. Especially during 25% and 50% of the inspiration the median deviation was more than -5%, whereas in other phases the median was closer to 0.

The results for PM were similar than for PR. There was more deviation from the linearity during the inspiration (25% and 50%) than in other phases. Otherwise, the linearity is quite stable over the respiratory cycle. The box plot for PM is in Figure 14.

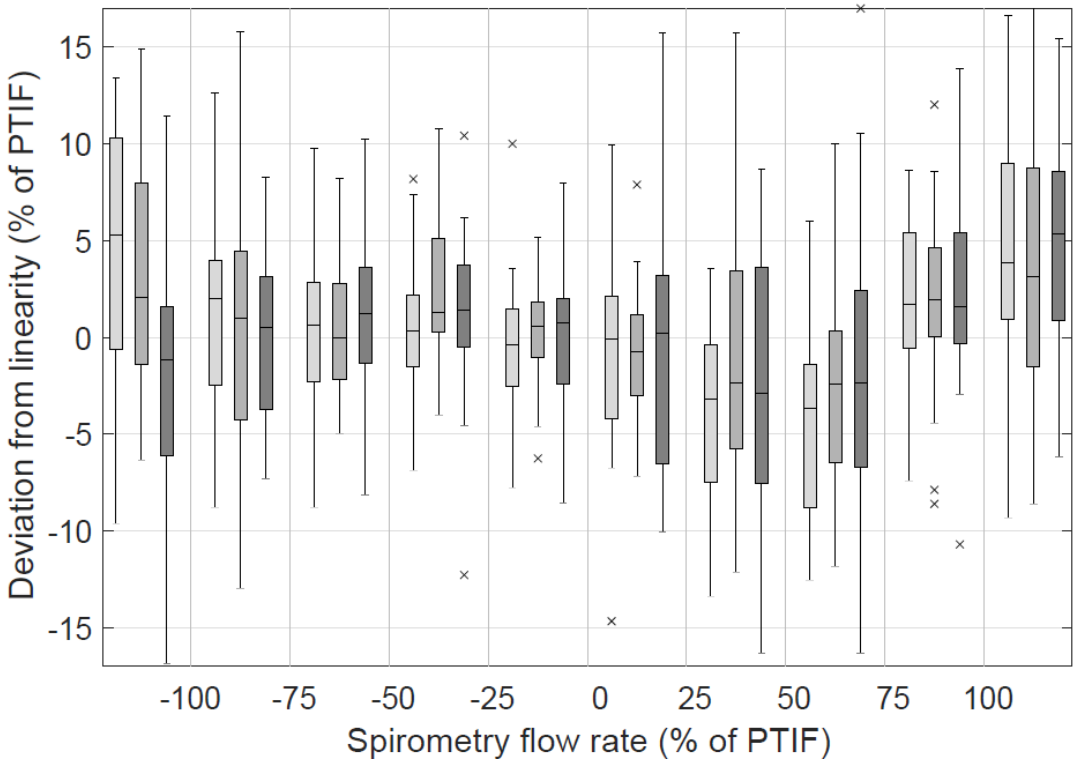

Figure 14. *The deviation from the linearity of impedance pneumography and pneumotachography for minor pleurapulmonary surgery patients (group PM, 32–33 patients) is presented as a box plot on three measurement days.*

In addition to the visualization, two parameters were studied to determine the difference of the IP-PNT value pairs from the linearity: D_{ss} and D_L. The results of D_{SS} and D_L are in Table 5.

Table 5. *The median of sample-by-sample differences (D_{ss}) and the average deviation from linearity (D_L) presented as mean ± SD for three surgery groups and all measurement days.*

Parameter	Group	D_{ss} (mean ± SD %)			
		PREOP	1POP	2POP	3POP
D_{SS}	C	10.4 ± 3.8	9.0 ± 2.7	9.5±2.7	9.0±2.2
	PR	9.2 ± 3.0	8.6 ± 2.2	9.2±1.8	
	PM	8.9 ± 2.0	9.6 ± 3.2	9.9±2.9	
D_L	C	4.6 ± 2.2	4.8 ± 2.7	5.6±2.6	5.2±2.2
	PR	5.0 ± 2.0	4.8 ± 1.8	5.7±2.7	
	PM	4.1 ± 1.6	4.0 ± 1.4	4.5±1.7	

*PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. post-operative measurement

** C = cardiac surgery, PR = pulmonary resection, PM = minor pleuropulmonary surgery

*** PR and PM groups were not measured in 3POP

The D_{SS} results were similar within the surgery group, but also between groups on the same measurement day. Thus, the average difference from the linearity between IP and PNT did not seem to vary due to the surgery. This is proved by using to statistical non-parametric tests. The Wilcoxon signed rank test results are in Table 6.

Table 6. *Wilcoxon signed rank test between different measurement days on three surgery groups for sample-by-sample difference (D_{SS}) and the average deviation (D_L)*

Parameter	Comparison	p-value (*: p < 0.05)		
		C	PR	PM
D_{SS}	PRE vs 1POP	0.0526	0.6580	0.0675
	PRE vs 2POP	* 0.0051	0.7439	0.0768
	1POP vs 2POP	0.3271	0.0727	0.5449
	PRE vs 3POP	* 0.0137		
	1POP vs 3POP	0.2659		
	2POP vs 3POP	0.2015		
D_L	PRE vs 1POP	0.7439	0.3981	0.6682
	PRE vs 2POP	0.5430	0.8405	0.3382
	1POP vs 2POP	0.3720	0.1451	0.5272
	PRE vs 3POP	0.6813		
	1POP vs 3POP	* 0.0277		
	2POP vs 3POP	0.7151		

**PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. post-operative measurement

*** C = cardiac surgery, PR = pulmonary resection, PM = minor pleuropulmonary surgery

**** PR and PM groups were not measured in 3POP

The Wilcoxon rank test shows that there was no significant difference in the linearity between measurement days, except in group C for three pairs (PREOP–2POP, PREOP–3POP and 1POP–3POP).

The Mann-Whitney U test results are collected in Table 7. The justification for Bonferroni correction in the significance level was presented in Section 3.7.

Table 7. *Mann-Whitney U test with Bonferroni correction for the significance level on different surgery groups for sample-by-sample signal difference (D_{SS}) and the average deviation (D_L)*

Parameter	Comparison	p-value (*: p < 0.017)		
		PRE	1POP	2POP
D_{SS}	C vs PR	0.2505	0.7458	0.2737
	C vs PM	0.1992	0.6866	0.9127
	PR vs PM	0.5712	0.3619	0.5164
D_L	C vs PR	0.0957	0.5976	0.9764
	C vs PM	0.9318	0.5416	0.0405
	PR vs PM	0.1484	0.1506	0.0535

**PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. post-operative measurement

*** C = cardiac surgery, PR = pulmonary resection, PM = minor pleuropulmonary surgery

Mann-Whitney U test shows, that there was no difference in the linearity between the surgery groups on different measurement days. None of the combinations reached the determined significance level and only one (C vs PM on 2POP) would have been considered significant, if the common significance value without correcting the multiple comparisons had been used.

5. DISCUSSION

IP measurement was accepted by the clinicians, and the measurement procedure was easy to conduct amongst normal patient care. Only some patients refused to participate in the study. Since the whole study procedure included a 30-minute measurement session with IP and spirometry, other individual measurements and physiotherapy lesson each day, the scheduling amongst the patient's and physiotherapist's routines was difficult from time to time. Thus, not all measurements have been conducted during one session and in static conditions, as it would have been preferable.

The results and identified error sources are discussed and compared to previous studies. Also, an earlier preliminary study by Tuomisto et al. [54] about the effect of intervention in the breathing physiology is discussed.

5.1 Quality of the Measurement Data

Approximately 71% of the measurements were successful and accepted to the analysis. The amount of rejected measurements was small, only 5% of the planned measurements due to extremely poor correlation ($r < 0.7$). 21% of the measurements were rejected due to errors during signal processing or measurement, such as corrupted signals.

There might be several reasons for poor correlation. If the algorithm filtering the CGO was not functioning properly, the result signal might be too noisy for detecting the correlation between very noisy signal and good PNT. The PNT signal might have been noisy as well, for example due to some air leak from the spirometry mouth piece or from nose.

Another reason of poor correlation is related to the timing of the IP signal. The one minute signal was manually marked by the physiotherapist by pressing an annotation button in the IP device. However, there were several cases, in which errors in the timing occurred. The error sources are further discussed in Section 5.3.

Grenvik et al. [15] studied the correlation between transthoracic impedance and respiratory volumes in 11 healthy subjects. They resulted in average correlation of 0.964 (range 0.898–0.989). In our study the average correlation coefficient of accepted IP and PNT flow signal was very similar, although there was more variation. The average correlation coefficient of all measurements was also considerably close, but little lower caused by the errors described previously.

5.2 Linearity of the Methods

The assessment of linearity between IP and a conventional method has been considered the most generalizable method in comparing two measurement modalities, when compared to calculating the power of the difference, or a difference in a parameter derived from both signals [39]. If IP provides similar information than PNT, then IP could be used to evaluate the respiration first alongside with conventional methods, but possibly later to compensate for spirometry or PNT. The general evaluation of the nurse and oxygen level measurements would still be important to support IP results.

It was found that the agreement of IP and PNT is acceptable and stable when considering different patient groups. The deviation from the linearity remained similar between measurement days in individual phases of the respiratory cycle and between different phases. Group C results were visually the most compact, whereas group PR had more deviation from the linearity in 25% and 50% of the inspiration. Groups PR and PM had visually small differences in linearity between different measurement days. The perioperatively preserving linearity was also visible in the average D_{SS} and D_L. The results are very similar in different measurement days, and the standard deviation of the parameters is under 4% throughout the results.

The deviation from linearity was not varying between PREOP and 1POP in group C. In groups PR and PM statistical difference was not found in any of the measurement day combinations. The results indicated that linearity of IP and PNT was not affected by the surgery, thus the changes in the thoracic area were not changing the bioimpedance measurement. Thus, no significant change occurred in the linearity before and immediately after the surgery.

In group C, some statistical difference was found between PREOP and 2POP in D_{SS} and between 1POP and 3POP in D_L. If Figure 12 is reviewed more closely comparing the D_L from 1POP and 3POP, there were four phases with same median values and six phases with median values differing 1–4.5%. There were also differences in the distribution of D_L between 1POP and 3POP: 50% of the values varied from < 5% deviation to ~10%, thus some measurement days and phases were sparser than the others.

More study is needed to determine more exactly, where these differences arose from. One theory is related to the fluid accumulation of cardiac patients. The study of Fein et al. [10] concluded that the patients with severe pulmonary oedema had variety in the impedance measurement. Fluid accumulation is common because of the nature of cardiac surgery and because of cardiopulmonary bypass. In the study the fluid accumulation was measured by weighting the patient on each measurement day. Also, radiologic thorax images were taken and analysed to determine fluid accumulation and the amount of atelectasis. When examining the change of weight in Table 3, it can be noted that the

weight slowly started to decrease between 1POP and 3POP. This could change the dielectric properties of the thorax, and cause more deviation in the linearity.

5.3 Error Sources in the Measurement Setup

The number of unsuccessful measurements was relatively high (~20%) but it was considered acceptable in this study. This is because the study was conducted amongst normal hospital routines, thus redoing the measurements or checking the IP recordings was not usually possible. Also, if the IP device was not functioning correctly, an engineer was not available to fix it immediately.

Timing of IP during the simultaneous measurements was one cause for rejecting the measurements or resulting in poor correlation. Following errors were noticed during the signal analysis: the physiotherapist

- Forgot to push the button for start / stop / both
- Pressed the button more than twice
- Pressed the button too late
- Pressed the button but no time was registered
- Pressed the button but the device registered several annotations

Some of these errors were successfully fixed manually by using the notes given by the physiotherapist. If no recording of the start and stop time of the one minute existed, it was impossible to detect the exact time of the recording. Therefore, the correlation of IP and PNT is obviously poor if the recordings were not simultaneous.

Motion artefacts were one of the most common reasons to reject a measurement in the study. This was already performed in the beginning of the study, when all the IP signals were visually checked. If the patient was moving excessively, the IP signal was very distorted and a normal breathing pattern was not visible at all. The physiotherapist's notes also confirmed excessive movements if it was detected.

Freundlich and Erickson [11] also noted movement artefacts in the IP measurements performed for seven patients in the recovery room after surgery and control group of normal patients. No reference method for measuring tidal volume could be used, but movement artefacts caused by holding hands on the chest, movement of abdomen near the diaphragm and general body movement were detected visually.

Młyńczak et al. [27] stated that the electrode configuration validated by Seppä et al. [41] is suitable under static conditions, but for ambulatory measurements the configuration should be less sensitive for motion artefacts. Also, in ambulatory conditions the linearity of IP and PNT could be compromised for less motion artefacts. [27]

In our study the electrode configuration by Seppä et al. [41] was used, and the patients were instructed to rest quietly in supine position. However, the physiotherapist was not present during the whole IP measurement, as we considered that the patient would be more relaxed when they are not being monitored. This caused that some patients were talking to a doctor / neighbour / on the phone, changed the position of the bed or even left the bed to go to a restroom when they were left alone. This obviously caused motion artefacts to the measurement and changed the entire respiration profile of some patients.

Another reason for relatively high number of rejected measurements was the corrupted IP, PNT or ECG signals. In ECG, this caused the signal to have rapid changes in the signal amplitude, constant signal of zero amplitude and slowly decreasing ECG signal waveform. These signals could not be processed, since the ECG was needed to filter the CGO. Raw PNT signals had errors with timing, thus there may have been an error while recording the data or transferring it to the database. IP signal corruption was shown for example as distorted or not visible time scale.

These signal errors should be carefully considered, when improving the measurement setup. More accurate reasons for the errors should be found to determine, if the cause was due to researcher's or patient's actions, and whether the errors could be avoided in further studies.

5.4 The Effect of Intervention to Breathing

All patients were randomized into two subgroups: a control group (A) and study group (B). These groups received different physiotherapy interventions: group A received conventional PEP-P physiotherapy focusing on the expiration, and group B received IMT-P focusing on inspiration. Although these groups are not further analysed in this thesis, preliminary analysis of the difference caused by the intervention in cardiac surgery group was presented by Lassi Tuomisto et al. in 2016 [54].

The preliminary randomized controlled clinical study shows, that there is significant difference in recovery between intervention methods in cardiac patients when respiration is evaluated using spirometry. In both A and B groups the operation caused considerable decrease in inspiratory and expiratory volumes and flow. On 3POP the relative values of FVC and FEV1 were increased more in group B than in group A, indicating that the physiotherapy methods are equally effective immediately after the surgery (1POP, 2POP), but the recovery after that is faster with patients using IMT-P. The study group recovered better with inspiratory physiotherapy than the control group with expiratory physiotherapy. [54]

The change of respiration is not completely straightforward with three different surgery types. Difficulties in the patients' breathing may be due to different reasons. The diagnosis being treated may interfere breathing already before the operation, or the general

wellbeing of the patient may be decreased. The surgery affects breathing physiology, as discussed in Section 2.1.2. Thus, for some patients the surgery might make breathing significantly more difficult but for some patients the surgery might improve the respiration since the cause of the disease is removed. Another thing to consider is, that pain is a subjective opinion of the patient, some patients might perform very well despite severe pain.

In further studies, the effect of intervention should be studied from IP parameters as well. For example, the changes in tPTEF/tE and tPTIF/tI and their relation to the used physiotherapy can be evaluated. Also, PTEF and PTIF could be studied but without calibrating the AD converter values from the IP devices (two different devices were used), it should be considered in the results. Also, the nonlinear properties of respiration could be studied to determine, whether the amount of chaos changes due to intrusive surgery or differs with the intervention method [55].

6. CONCLUSIONS

Respiration changes due to intrusive operations and pain. However, as pain is a subjective measure of the individuals, it is difficult to generalise the effect of cardiothoracic surgery to breathing. The patients had various diagnoses and overall conditions perioperatively, and the performance during the tests was depending on the actual condition of the patient as well as the subjective view of pain or the medications effecting the orientation.

This thesis was a small part of a bigger research project, which aims to analyse the recovery of cardiothoracic surgery patients treated with two physiotherapy intervention methods. The effect of the intervention and physiotherapy care on the recovery is analysed from the doctor's and physiotherapist's perspective. The objective of the thesis was to study simultaneous one-minute signal measured with IP and PNT in cardiothoracic surgery patients. The main properties and findings of the thesis study are concluded in Table 8.

Table 8. *Conclusion of the main properties and findings of the thesis*

Property	Key property / finding
Measurement setup	1-minute simultaneous IP + PNT signal
Target group	Cardiothoracic surgery patients
Preliminary Correlation	71% accepted, 5% rejected, limit $r \geq 0.7$
Rejected measurements	20% rejected: processing errors, artefacts 3% cancelled due to patient condition 44 measurements rejected visually
Linearity: measurement days	No difference in linearity PREOP-1POP No difference perioperatively in PR and PM (limit $p < 0.05$)
Linearity: surgery groups	No difference between groups (limit $p < 0.017$)
Nonlinearity in group C	May be caused by fluid accumulation due to surgery or cardiac bypass
Artefacts	- Movement artefacts due to patient (moving and talking during measurement) - Corrupted signal - Timing error in IP
Future analysis	- Tidal breathing parameters - Nonlinear properties and complexity - Intervention

* IP = impedance pneumography, PNT = pneumotachography

** PREOP = preoperative, 1POP = 1. postoperative, 2POP = 2. Postoperative, 3POP = 3. postoperative measurement

***C = cardiac surgery, PR = pulmonary resection, PM = minor pleuropulmonary surgery

Preliminary correlation studies concluded, that most of the successful data was also accepted to the analysis. Only about 5% of the measurements were rejected due to low correlation. Other rejected measurements were related to unsuccessful measurements, processing errors or not visible tidal breathing due to excessive movement artefacts. Cancelled measurements were related to patient condition to perform the reference measurements, or willingness to participate in due to pain or disorientation.

The hypothesis of the study was that IP measurement agrees with the reference method throughout the episode of care. The linearity did not change significantly before surgery and immediately after the surgery in any of the surgery groups. This indicates that the change in anatomy did not affect the relationship of bioimpedance measured from the thorax and air flow measured from the mouth. In PR and PM the linearity did not change throughout the episode of care.

Some difference in linearity occurred between PREOP and 2POP in D_{SS} and between 1POP and 3POP in D_L. This might be due to fluid accumulation caused by cardiac surgery or cardiac bypass, but more analysis of the data is required to provide evidence to support or reject the theory. The results indicate that IP could be potential for assessing the respiration of cardiothoracic surgery patients. It can be concluded that the measured data can be used for further analysis in the project.

In overall, IP measurements were successful during the episode of care. It was reported by the clinicians that the IP method was easy to perform in the clinical environment, and the study was accepted amongst patients and nurses. Some difficulties were present due to simple user interface of the device; it was reported that sometimes it was difficult to ensure that the device was functioning correctly. Also, the time-consuming measurement setup with various measured parameters was difficult to fit into the patient's and nurse's daily schedule. In some measurements, this was compromised by dividing the measurement into two sessions.

Movement artefacts were one of the biggest cause of rejecting a measurement. Excessive artefacts were noted during for the tidal breathing measurement for 10 minutes. The patient might have talked or even walked during the measurement, as he / she was not monitored but left alone to create more relaxed environment. In further studies this could be improved by emphasizing the importance of rest to the patient, or not to leave the patient alone during the recording. It should be considered, whether it is more important to reduce artefacts or acquire signals when the patient is alone and more relaxed.

To improve the amount of accepted and successful data some things could be considered in further studies. If the data quality was visually checked after every measurement, it could be possible to redo unsuccessful measurements on the same day. On the other hand, in clinical environment a perfect setup cannot be ensured, and seldom a

technician is always available. Some of the timing issues with IP and PNT alignment could be fixed by measuring the calibration recording into a separate file. Then, the recordings would be equally long and simultaneous.

Further analysis of the data should include analysis of tidal breathing parameters. It could be studied whether the parameters indicate otherwise measured clinical events or difference between intervention methods. Additionally, nonlinear analysis of the parameters should be made. Nonlinearity of the respiratory system is related to the change in complexity due to intrusive operation. When breathing is more painful and anatomy has changed, the respiration needs to be controlled more, thus complexity decreases. [55] This hypothesis could be tested on the study population.

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