Comparison of different rhinomanometry methods in the measurement of nasal airway resistance

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“Remember to breathe. It is after all, the secret of life.”
-Gregory Maguire

To my parents Mark and Lily and my sister Sylvia, for their endless love, support and encouragement.

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DECLARATION

This work has not been submitted in substance for any other degree or award at this or any other university or place of learning, nor is being submitted concurrently in candidature for any degree or other award.

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Summary

Various rhinomanometry methods can be used to measure nasal airway resistance, which include the classic method at fixed pressure of 150 Pa or 75 Pa, Broms method at radius of 200 and 4-phase rhinomanometry method.

This thesis compared the unilateral nasal resistance measurements obtained using these methods, when applied across four artificial model noses, to further improve our understanding of their relationship.

The first comparison was made between the classic and 4-phase rhinomanometry method. No statistically significant differences were found between the values obtained from both methods ($U>U_{critical}$, $p>0.05$). Bland-Altman plots also showed good agreement between both methods with narrow limits of agreement.

The second comparison was made between the classic and Broms method. The measurements from the classic (at 75 Pa or 150 Pa) and Broms method gave either statistically significant similarities or differences ($U>U_{critical}$, $p<0.05$) depending on the level of nasal resistances. The magnitude of change in resistance was also dependent on the method used, with bigger changes in resistance observed when using Broms method at certain levels of nasal resistances compared to classic measurements in the same patient.

The last part of the thesis was to evaluate the reproducibility of the rhinomanometry methods and the rhinomanometer used in this study over a 24-hour period. Bland-Altman plots showed high level of agreement between measurements taken in both days and CV value ranges from 0.49-14.3%, which were acceptable levels of reproducibility.

In conclusion, there was a high degree of conformity between resistances measured by the classic and 4-phase rhinomanometry methods. Broms method either gave similar or different measurements to the classic and, by extension of this study, 4-phase rhinomanometry measurements, depending on the level of nasal resistance. Applying the principle of Ockham's razor, the simple classic method is recommended as the method of choice for rhinomanometry.

CHAPTER 1

Introduction

1.1 Rhinomanometer

1.1.1 History and origin of rhinomanometer

1.1.1.1 Historical apparatus for measurement of nasal resistance

In 1889, Zwaardemaker[1] from Netherlands placed a cold mirror beneath the nose to measure the size of resultant condensation spots in his first attempt to measure nasal airflow objectively. Glatzel[2] then improved this method in 1901, using a metal plate instead of a mirror. Even though these hygrometric methods were physiologically ideal because there were no artificial airstream and no nostril deformities involved, they were too dependent on environmental factors like temperature and humidity[3]. Jochims[4] further modified this method with fixation of the condensed pattern using Gummi Arabicum in 1938.

These hygrometric methods were later replaced with new approach using flow and pressure parameters, allowing measurements and calculations to be made instead of estimation[3].

1.1.1.2 Development of rhinomanometry

Seebohm and Hamilton[5] performed the first rhinomanometry in 1958. Kayser (1895)[6] was considered to be the first to have studied passive rhinomanometry where the measurement of pressure difference was made after passing artificial airflow through the nose. This, along with other earlier rhinomanometries were of the passive types[7]. These passive methods were not widely used in clinical setting because of the difficulty for patients to hold their breath and not swallow when the air was being blown through their noses, which sometimes required general anaesthesia[7].

Courtade (1902) invented the first active anterior rhinomanometry[8] which was then developed by Semerak (1958)[9] who recorded the nasopharyngeal pressure through one nostril and airflow through the other nostril during spontaneous breathing. On the other hand, Spiess (1900)[10] performed measurement of nasopharynx pressure perorally in posterior rhinomanometry.

Aschan et al. (1958)[11] was the first to describe the modern principle of rhinomanometry where nasal patency was calculated using a mathematical ratio called resistance, obtained through simultaneous measurement of nasal airflow and transnasal pressure difference. The first active rhinomanometry was used for research purpose initially, followed by application in clinical setting[7]. There have been many developments made since then, for example the flow-regulator by Ingelstedt et al.[12] in 1969, where a predetermined value was given for either pressure (P) or volume (V) in his method.

1.1.1.3 Modern computerized rhinomanometer

Jonson et al. (1983)[13] found a close correlation between nasal resistance data obtained manually with those calculated automatically using a microprocessor in automated rhinomanometer. Lenz et al. (1985)[14] later described connecting rhinomanometer to a mini computer that present the results on the monitor, with the ability to print them via a printer. These computerized rhinomanometers continue to be developed by Stevens et al. (1987)[15] with new software developed by Bachert and Feldmeth (1988)[16] and Vogt et al. (1990)[17].

Computerized rhinomanometers have the advantages of operating automatically with minimal human routine work required in terms of storing information, measurement control, data calculation, result processing and calibration of pneumotachograph and pressure transducers[8].

1.1.2 Technical aspect of airflow and differential pressure measurement

The word rhinomanometry means nose ('rhino') and measurement of pressure ('manometry')[18]. The term 'rhinomanometer' came about in early twentieth century because the earliest measurements of nasal resistance involved subjects breathing through one nostril while nasal pressure of the other nostril being measured with a water manometer[18]. From a technical point of view, rhinomanometry is the simultaneous measurement of the differential pressure required to generate airflow and the measurement of volume of airflow through the nose[19].

1.1.2.1 Measurement of airflow

Most rhinomanometer uses the principle of pneumotachography for measurement of airflow[19]. The introduction of Fleisch pneumotachograph in 1925 with a rise time of 0.018 s and a linear behaviour up to 20 Hz allowed airflow to be recorded in time accurately[20].

This technique requires usage of a defined resistance (referred to as a 'spiroceptor') to the nasal airflow[19], causing a pressure difference[8] or pressure drop which is proportional to the flow velocity (Bernoulli's principle)[19], measured via two tubes at opposite sides of the device connected to a pressure transducer[8].

Two types of spiroceptors have been described where 'lamellar spiroceptor' consists of plastic foils arranged in parallel, whereas a 'diaphragm spiroceptor' contain a diaphragm which functions as curtain blowing in response to airflow changes to such a degree that a linear relationship results between the decrease in pressure and airflow [21]

The International Standardization Committee for Rhinomanometry (ISCR) accepts usage of both lamellar or diaphragm types of pneumotachographs as long as they behave in a linear fashion in 1984[22].

1.1.2.2 Measurement of pressure

Pressure is measured using pressure-sensing tubes, which is either taped to one nostril (anterior rhinomanometry) or placed in the mouth (posterior rhinomanometry)[18]. Both anterior and posterior rhinomanometry measure the pressure at the back of the nose[18]. The sealed nasal passage in anterior rhinomanometry acts as an extension of the nasal tube because there is no airflow through this tube[18].

A pressure transducer is used to measure the pressure difference between the front of the nose and the nasopharynx via the pressure-sensing tubes[8]. The pressure transducers have a thin diaphragm in an airtight chamber with pressure tubes connected to separate sides of the diaphragm[8]. Any pressure difference occurring between the two tubes would cause a deviation in the diaphragm, which then causes a change in the magnetic or optic sensor outside the chamber[8]. This change is detected as electrical currents by the rhinomanometer's computer unit, which is then converted into digital form by an analog/digital (AD) converter[8].

1.1.2.3 Technical set up of rhinomanometer

Figure 1.1.1 illustrates how pressure and airflow are measured in a modern rhinomanometer. There are two pressure transducers in each rhinomanometer (pressure transducer (A) measures pressure difference and pressure transducer (B) measures nasal airflow)[18]. Pressure transducer (A) measures pressure difference in the nose via pressure tubes (1) and (2)[18]. Pressure tube (1) is either taped to the nostril or placed in the mouth[18]. On the other hand, pressure tube (2) is hidden within the rhinomanometer casing and is connected via a 'T-junction' to pressure tube (3) to enable measurement of pressure at the front of the nose, which in turn allows pressure difference across the nose to be obtained via transducer (A)[18].

Nasal airflow is measured using pressure transducer (B) by measuring the pressure difference across the gauze resistance in the flowhead via tubes (3) and (4) connected on either side of the flowhead[18]. The greater the airflow through the flowhead, the greater the pressure difference measured at transducer (B)[18].

This arrangement of pressure tubes (with only three tubes exiting the rhinomanometer) is typical for rhinomanometers such as the GM Instruments rhinomanometer[18]. Data from both pressure transducers (A) and (B) are sent to a computer, which then display the pressure-flow curve[18].

Figure 1.1.1 Illustration of the technical set up of rhinomanometer showing transducers (A) and (B) and pressure tubes (1)-(4), taken from Eccles (2011)[18].

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1.1.3 Calibration of rhinomanometer

The comparability of clinical and research results worldwide depends on reliable calibration methods[19]. In 1984, the ISCR concluded that pressure transducer can be calibrated using simple water manometer[22]. On the other hand, calibration of pneumotachograph for airflow can be performed using a rotameter, which is accurate enough (within 5% limit)[22].

Basic calibration of new rhinomanometers should be carried out by the manufacturers[23]. Rhinomanometers should also be calibrated at least once a day[22] before the start of any measurements[18]. The manufacturers should recommend the maximum time between re-calibrations although this should not exceed 2 years[19].

1.1.3.1 Calibration of pressure

Eccles (2011)[18] described calibration of pressure using a slopping paraffin manometer (Figure 1.1.2) where the pressure scale is extended through usage of paraffin (which is lighter than water) and a sloping scale (rather than a vertical scale)[18]. These features of manometer allow a pressure scale of 5 cm H_2O to be extended to around 25 cm on the slopping paraffin manometer[18]. Calibration of the pressure transducer is performed by connecting the slopping paraffin manometer to a syringe (that alter the pressure by pumping air into the side arm) and the pressure tube of the rhinomanometer[18]. The pressure transducer is usually calibrated at a sample pressure used for anterior and posterior rhinomanometry at 150 Pa and 75 Pa[18].

1.1.3.1 Calibration of airflow

Airflow and flow head (pneumotachograph) is calibrated using a flow meter or ‘rotameter’, which consists of a calibrated vertical glass tube with an air float inside that moves according to the flow rate[18] (Figure 1.1.3). The glass tube is narrower at the bottom than at the top, therefore it requires increasingly greater airflow to move the float as it moves towards the top of the scale[18]. The calibration is performed by moving a known rate of airflow through the flow head, which can be achieved by adjusting the electric voltage (through a transformer) to the electric air pump that generates the airflow in the flow meter[18]. This is then compared with the readings shown on the rhinomanometer monitor in calibration mode. The flow head is usually calibrated at rates achieved at normal breathing, for example at 200 and 300 cm^3/s[18].

Figure 1.1.2 Diagram of calibration of pressure using a slopping paraffin manometer, taken from Eccles (2011)[18].

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Figure 1.1.3 Diagram of calibration of airflow using a rotameter, taken from Eccles (2011)[18].

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1.1.3.3 Standard resistor

Although it is more reliable to calibrate both pressure and airflow separately[18], the calibration status can also be checked quickly with a standard resistance or model nose[17,18]. This can be done by inhaling and exhaling through the model nose and compare the readings obtained with the known fixed resistance of the model nose. A more sophisticated method of calibration using the standard resistance was also described where cyclic flow produced by standard motorized flow pump can be passed through an artificial nose, where a computer will automatically alter the calibration parameters according to the results obtained[8]. The flow value of resistors should be recorded during a differential pressure of 150 Pa and between 100 and 300 cm^3/s, and the rhinomanometric curve of this device should also be documented and filed[17].

In 2005, the International Standardisation Committee on Objective Assessment of the Nasal Airway (ISOANA) also recommended the usage of this standard resistor to compare the pressure and flow difference data with a calibration curve documented on the data file[23]. If there is >5% difference from the original calibration, re-calibration is required by authorized personnel or the manufacturer[23].

1.1.3.4 Other practical aspects of calibration

Vogt et al. (2010)[19] also described other important practical aspects of calibration of rhinomanometers such as resetting to zero-line before calibration and the importance of documenting calibration date and be able to provide proof that calibration was done properly for medico-legal reasons concerning rhinomanometric investigations, such as in a lawsuit, for insurance purposes and for authorities approving nasal medications.

1.1.4 Factors affecting measurements on rhinomanometer

Many papers have described factors that affect nasal airflow in patients such as temperature, humidity, exercise, alcohol, medicines (decongestants, aspirin, steroids) and diseases (infection, allergy, septal deviation, previous nasal surgeries)[18].

Possible technical errors that can occur during rhinomanometry recordings was also identified by Pinkpank (1986)[24] which include incorrect fitting of mask, incomplete mouth closure during recording, non-tight seal around nostril, nostril distortion, humidity in the measuring tubes, unstable temperature and high level of humidity in the room, patient not at rest before recording and patient position not standardized. Besides that, in prolonged testing, the spiroceptor must also be warmed up to prevent water condensation inside[19].

Use of antiviral filter can also add a significant resistance to measurements (around 0.1 Pa/cm^3/s), which may not always be known in the final data[18]. Since the filter does not have the same linear characteristics as the flowhead, this additional resistance will also vary in an unknown way even if this is taken into account during the measurements[18].

1.1.5 Reproducibility of rhinomanometry

The reproducibility of rhinomanometry readings has been a topic of interest since the first rhinomanometric measurements were made[8]. Rhinomanometers are tested and validated by manufacturers to provide stable measurements in laboratory and clinical setting[18]. Factors like characteristics of pressure transducers and fluctuations in humidity and temperature does not usually affect the reproducibility of measurements[18].

In 1979, Kumlien and Shiratzki[25] found that the coefficient of variation (CV) at “short interval” to be 20-25% and the “day-to-day variation” to be 55%, and concluded that rhinomanometry is more suitable for comparisons of groups rather than individuals.

In 1982, Broms[26] found the usage of decongestants produce very good reproducibility of nasal resistance measurements and recommended this method of eliminating random variation in nasal resistance when studying skeletal deformities such as deviated nasal septum. However, it was pointed out that decongested noses were not in their normal state and this technique was of no value when studying conditions like allergic or vasomotor rhinitis which affects nasal mucosa rather than nasal skeleton[27]. However, a study by Jones et al.[27] in 1987 found good repeatability (most measurements agree within 0.1 KPasl) between repeated total nasal airway resistance (NAR), 24 hours apart, on normal subjects without using decongestants. This is further supported by Eccles (2011)[18] who demonstrated a mean variation of measurements over 12 hours to be less than 5% (maximum variation of 11%) in patients with acute rhinitis from common cold receiving placebo nasal spray. This variation represents a combination of inherent variation of rhinomanometer and spontaneous fluctuations of mucosa in common cold without decongestants[18].

In 2011, Thulesius et al[28] tested the short term (same day within 60 minutes) and long term (over 5 months) reproducibility of NAR measurements using Broms method and found the CV value to be 8-17% (acceptable limits for investigation method) and 8-53% (high variability with a mean of 27%) respectively. Therefore, it was concluded that long-term reproducibility of NAR is low[28].

The change in total NAR before and after a nasal operation is expected to be larger, therefore making this random variation in rhinomanometer relatively small and comparisons of NAR can be made in individuals to provide useful information on success or failure of operations[27]. However, when studying subtle changes such as effect of Aspirin on nasal resistance, the error due to random variation can become relatively large, and this can be reduced by studying a population rather than an individual[27].

In 1992, Sipila et al.[29] compared the reproducibility of various methods in rhinomanometry as well as defining the level of clinically significant variation between two repeated recordings of the same nostril to be +/- 20% change from the mean. It was found that classic method at 150 Pa and Broms method at radius of 200 and 300 produced good level of reproducibility in decongested subjects and these methods were recommended for clinical practice[29]. On the other hand, Broms method at radius of 100 and classic method using fixed flow at 150ml/s showed poor reproducibility[29].

In 1988, Sandham[30] found that repeatability can be improved with frequent calibration and visual feedback for the patients where the study reported method error that ranges from 1.4% to 5.2%. In 2000, Carney et al.[31] described the importance of using a protocol involving multiple recordings with identification and exclusion of erroneous data, where they improved the coefficient of variations from 19%-60% to 7%-15%.

1.2 Rhinomanometry methods

1.2.1 Basic principle of rhinomanometry

1.2.1.1 Need for objective test

Nasal obstruction is the most common symptom in rhinology practice[32]. The incidence of nasal obstruction was reported to be as high as 33% in Finnish adults[33]. On the other hand, the prevalence of subjective nasal obstruction was found to be around 13% among Swedish adults[34].

Kayser (1895)[6] described the necessity to determine objective nasal airflow over 100 years ago, stating that "only in this way can we demonstrate any effects of this intervention in an objective way. After all, we measure the acuity of the eye and hearing ability of the ear". Subjective sensation of nasal obstruction is a poor guide to nasal airway patency[35], subject to unpredictable physiologic and pathological changes[20]. There is also poor intra- and inter-observer agreement when it comes to clinical examination with anterior rhinoscopy[36]. Studies have also shown that it is more difficult for patients to detect the more obstructed side of the nose if the difference is subtle[37].

Therefore we need a more reliable and objective way of assessing airway patency[20]. The information from rhinomanometry can be used to substantiate and quantitate symptoms of nasal obstruction[32]. The many uses of objective nasal resistance measurements using rhinomanometry will be discussed in Chapter 1.4.

1.2.1.2 Nasal airflow physics

Nasal airflow occurs along a pressure gradient from area of high pressure to area of low pressure in airway[18]. During inspiration, air moves into the nose due to the work of respiratory muscles which contract to expand the lungs[18] and alter the postnasal pressure, creating a pressure difference between the atmospheric air and nasopharynx, therefore causing airflow through the nose[38].

On the other hand, during expiration, the elastic recoil of lungs and relaxation of respiratory muscles create pressure, which is greater in the lungs than atmospheric pressure at the nostrils, driving airflow in the opposite direction[18].

Besides NAR, the occurrence of turbulences also contribute to the subjective feeling of nasal obstruction[23]. Turbulence is caused by the constrictions[18] and irregularities inside the walls of the nasal cavity, mainly the turbinates[8]. Well-balanced turbulence is important for the exchange between air flowing through the nose and the mucosa[39] to ensure maximal air conditioning, efficient warming and humidification of the air[18], which in turn is important for respiration and olfaction[39].

1.2.1.3 Parameters in rhinomanometry

The original aim of rhinomanometry was to measure the nasal airflow that could pass through the nose at a given pressure, or to determine how much pressure is required to move a given volume of air through the nose during normal breathing[3]. Later, it became apparent that the most important parameter is neither the pressure nor airflow, but the relation between the two parameters[3]. The basis of these relations became the accepted standard for evaluating the degree of nasal obstruction[22].

The consensus meeting in 1984 decided that rhinomanometric values should be expressed in standard international (SI) unit (pressure in Pascal and flow in cm^3/s) and that different companies manufacturing rhinomanometers should apply these units on their equipment[22].

1.2.1.4 Calculation of NAR

Modern rhinomanometry involves measurement of nasal airflow (V°) and the pressure gradient (Δp) required to achieve that flow[41], from which nasal airway resistance (NAR) can then be calculated[42]. Simultaneous recording of both flow and pressure is important to ensure the result is not distorted by any individual variations in the lower airway function[43]. At the same time, any delay between measurements of left and right nasal resistances should also be minimized when measuring total NAR[18].

In 1984, the ISCR[22] accepted the calculation of NAR using the formula adapted from Ohm's law[3]; $R = \Delta p/V°$ (R=nasal airway resistance, Δp=pressure difference, V°=airflow)[22]. NAR is expressed as Pascal per cubic centimetres per second ($Pa/cm^3/sec$)[22]. The total NAR is derived by the formula $1/R = 1/r$ left $+ 1/r$ right[18].

1.2.2 Classic method

1.2.4.1 Need for fixed pressure gradient

During quiet breathing, the pressure-flow curve is almost a straight line but this changes to a curved line at higher pressures and flows[18]. This means the resistance calculated varies according to where the measurements are taken[18]. Over the linear part of the pressure-flow curve all points will calculate the same resistance, but in the curved part of the pressure-flow curve, the calculated resistance increases because the pressure tends to increase more than the flow[18].

With a curvilinear relationship between the nasal pressure and airflow, it is therefore important to standardize the point on the line at which resistance is calculated so that measurements of NAR can be standardized between research centres[22,23] and comparison of results from different studies can be made[3]. Preference should be given to expression of resistance at fixed pressure rather than at a fixed flow[22]. This is because there is no partition at the back of the nose and one driving pressure in the posterior nares causes nasal airflow through both nasal passages. On the other hand, the airflow through both nostrils will always differ due to various anatomical, physiological and pathological factors, therefore using a fixed flow for both nostrils in rhinomanometry measurements was not recommended.

1.2.4.2 Recommendations by the ISCR

In 1984, the International Standardisation Committee for Rhinomanometry (ISCR) recommended that nasal resistance should be calculated at a fixed pressure gradient of 150 Pa[22]. This is because up to 150 Pa, the pressure and flow curve is almost a straight line[18]. At the Committee Meeting in Amsterdam 1988, it was concluded that resistance could be calculated at different pressures of 150, 100 and 75 Pa[23].

Further recommendations was made at the Consensus Meeting in 2005 where the reference pressure of 150 Pa should be used in pathological conditions because this can easily be reached by patients[23]. However, if this pressure level is not reached, for example in physiologic studies, the resistance can be measured at lower pressure of 75 or 100 Pa[23] (Figure 1.2.1). Routinely, NAR should be expressed as resistance calculated at 150 Pa during inspiration[23].

Figure 1.2.1 Pressure-flow curve illustrating the fixed pressure gradient used in the classic method (150 Pa and 75 Pa) and that up to 150 Pa, the curve is almost a straight line, taken from Eccles (2011)[18].

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<u>1.2.3.4 Existing concerns on classic method</u>

One of the main concerns regarding the classic method is that the pressure-flow curve may not reach 150 Pa[44]. Sipila et al. (1991)[8] found that 80% of population could not reach the pressure gradient of 150 Pa in decongested phase, where this could only be reached if asked to breathe more deeply, which was against the physiological principle of rhinomanometry to measure NAR in normal spontaneous breathing. Similarly, Vogt et al. (2010)[19] found that 7.34% to 46% of decongested subjects could not reach 150 Pa, therefore requiring a substitute of 75 Pa to be used, which was argued to be less reliable[45]. The inability to measure 150 Pa greatly reduces the usefulness of this method[8].

Besides that, using a predetermined pressure level only describe one point during acceleration of breathing instead of giving information for the entire breath, for example, information on effects of airstream and inertia, which is possible using modern computerized rhinomanometry[19]. Therefore, there is also a loss of important diagnostic information in this method[19].

Vogt et al. (2010)[19] was also concerned about the usage of the "classic" parameters (flow or resistance at fixed pressure), which does not represent the physical performance of nasal breathing and morphological structures of the inner nose. It was pointed out that there was an important error in the way pressure-flow curve is generated in the classic method where the curve always meet the intersection point of the x and y axis, when Computational Fluid Dynamics (CFD) studies supported the appearance of a loop that does not necessarily run through the intersection point as the true configuration of rhinomanometry curve[19]. Therefore, the pressure-flow curve in the classic method would only be an approximation of the true status of the curve[19].

1.2.3 Broms method

1.2.3.1 Historical origin

In 1982, Broms et al.[46] identified the need to develop a systematic way of measuring airway resistance, which allows inclusion and comparison of all different pressure-flow curves in studies. Various characteristics of the pressure-flow curves were observed, including the fact that all curves have similar shape, reach varying pressures and flow rates, run through the origin and reach a circle with certain radius in the x-y system[46]. Broms et al.[46] proposed a mathematical model on a polar co-ordinate system in 1982.

1.2.3.1.1 The clinical mode (R_2)

Broms et al. (1982)[46] found that all the pressure-flow curves reached and crossed a circle with radius of at least 200 Pa or 200 cm^3/s with a constant quotient between the scale for pressure and flow rate. Therefore, the point of intersection between the curve and a circle with radius of 200 (R_2) (Figure 1.2.2) is considered to represent a "physiological range of flow and pressure" and can be used to define a standardised condition[46]. The flow rate and pressure during spontaneous breathing at rest usually also correspond to radius of 200[46].

R_2 can be calculated using the formula $R = \Delta p/V°$ previously described and it was originally suggested that a scale in calibrated resistance units can be constructed for each point of the circle[46]. This would allow R_2 to be read directly from this circular resistance scale[46].

Since R_2 for patients can be compared with the normal values in clinical evaluation, this measurement is suitable for clinical work ("clinical mode"). The distribution of R_2 values is often very skewed.

1.2.3.1.2 The statistical mode (V_2)

The point of intersection between the curve and the circle with radius of 200 can also be expressed as an angle (V_2) between the flow axis and the line from origin to the point where pressure-flow curve intersects with radius of 200[46] (Figure 1.2.2). This is to overcome the problem with asymmetrical R_2 values resulting in some measurements being very high[46]. The distribution of V_2 has been found to be symmetrical and is therefore appropriate for standard statistical tests based on normal distribution[46].

V_2 can be calculated using the formula R_2=10 tan V_2. Factor 10 is the quotient between pressure and flow scales used for nasal cavity. V_2 can also be read directly from a conventionally graduated scale along the circle, where all curves will have a V_2 value between 0 (no obstruction) and 90° (total obstruction). A greater V_2 corresponds to a greater R_2[46].

Figure 1.2.2 Diagram showing Broms R_2 (resistance at the intersection between the pressure-flow curve and radius of 200) and V_2 (angle between the flow axis and the line from origin to the point of intersection between the pressure-flow curve and radius of 200), taken from Clement and Gordts (2005)[23].

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1.2.3.1.3 The mathematical mode (V_r)

The mathematical mode is used to compare the nonlinearity of inspiratory and expiratory curves in normal and unwell patients using the formula $V_r=V_0+cr$ (V_r is the angle between the flow axis and a line from origin to the point where pressure-flow curve intersects with the circle at radius r, V_0 is the angle at the origin and c is a constant describing the curvature)[46]. This is usually calculated using a programmable calculator[46].

This mathematical mode is also used to calculate total NAR using the formula $R_2=5 \tan V_2$[46].

1.2.3.2 Advantages of Broms method

Broms et al[46] described the importance of having a system that has various modes of application to fulfill different needs in rhinomanometry. The Broms mathematical model can be used to obtain meaningful data for clinical work (R_2), be included in statistical calculation (V_2) and to provide adequate mathematical expression for the pressure-flow curve as well as allowing calculation of total NAR (V_0 and c).

All pressure-flow curves were found to cross the circle at radius 2, therefore can be used to represent a standard condition[46].

1.2.3.2 Recommendations of ISCR

In 1984, the ISCR agreed that NAR measured with Broms method at radius of 200 (R_2) was to be considered as equally good as measurements taken using the classic method[22].

The 2005 Consensus report[23] described the difficulty of turning a "p/V°" recording into numerical values for statistical analysis and recommended Broms method as it described the whole pressure-flow curve. The committee recommended measurement using Broms at V_2[22,23].

1.2.3.4 Existing concerns on Broms method

Vogt et al. (2010)[19] described the Broms model as inaccurate because the resistance is calculated at different pressure levels. This is because usage of the intersection between rhinomanometric curve and a given radius results in high flow values measured at low pressure or low flow values measured at high pressure[19].

Vogt et al. (2010)[19] also criticised that Broms method only generate single values at radius of 200 or 300 but does not give a representation of the entire breath compared to 4-phase rhinomanometry method.

Besides that, Sipila et al. (1992)[29] also found that resistance at radius of 300 could not be measured in 9% of very obstructed subjects because extremely blocked nasal breathing could not reach the radius.

1.2.4 Four-phase rhinomanometry (4PR) method

1.2.4.1 Historical origin

In 1990, Vogt et al.[19] used rhinomanometry software that allowed averaging of data as well as independent, time-related recording of data points for differential pressure and flow. During this, they observed a difference between the aerodynamic conditions of the increasing and decreasing phases of airflow as well as generation of a pressure-flow loop instead of a simple curved line[19].

At the 1994 European Rhinologic Society Conference in Copenhagen, Vogt and Hoffrichter proposed the term "High-Resolution Rhinomanometry" for the analysis of four different phases of breathing in order to underline the difference in the quality of this new method[19]. Vogt claimed that the hysteresis observed due to the phase shift between flow and pressure gradient is caused by inertia of the airstream and elasticity of anatomical structures, rather than due to an artifact of the apparatus[20].

This term was changed to "Four-Phase Rhinomanometry" at the 2005 ISOANA Consensus Conference in Brussels as it was thought to be a more accurate description of this method because "high resolution" refers more to imaging techniques[23]. The Standardisation Committee also concluded that studying the ascending and descending parts of the curves separately during inspiration and expiration in four-phase rhinomanometry could provide useful supplementary information in regards to the movements of the nasal lateral wall and vestibule during respiration[23].

1.2.4.2 Basic principle

In 2010, Vogt et al.[19] published a 50-pages supplement in Rhinology Journal to fully introduce the 4-phase rhinomanometry (4PR) method where emphasis was placed on analysis of the nasal breathing cycle in four different phases and included a factor of time as one of the key parameters on top of intranasal pressure and flow.

1.2.4.2.1 The generation of loop in 4PR

Vogt et al. (2010)[19] described nasal breathing as an alternating ventilation of air in both directions through an irregular cavity with narrowing at both ends, where the rate of change in pressure and the rate of change in corresponding flow are different.

This is because at inspiration, the air stream is swirled to a greater extent than at expiration; therefore at the same level of flow, the corresponding change in pressure differs, resulting in hysteresis[19]. This explains the loop appearance (Figure 1.2.3) rather than a simple line when pressure and flow changes are plotted against each other in an x-y diagram[19].

1.2.4.2.2 Data acquisition

The difference between the classic rhinomanometry and 4PR originate from the differences in data acquisition and method of data averaging[19]. In the classic method, alternating values for flow and pressure are sequentially collected and placed in an x-y Cartesian system where a regression line that starts at the origin of the axis is constructed[19].

On the other hand, in 4PR, the flow and pressure data uptake are separately and visually controlled, and used to construct a “representative breath” as a real-time procedure[19]. This data is then transferred into the Cartesian system to generate an open loop (with greater opening at the inspiratory side) that does not run through the intersection of the flow and pressure axes[19].

1.2.4.2.3 The four phases (Figure 1.2.3)

The four phases in 4PR are:

a) Phase 1: Ascending inspiratory phase (airflow accelerate up to peak inspiratory flow where the relationship between pressure and flow is linear)[19]
b) Phase 2: Descending inspiratory phase (from peak inspiratory flow to end of inspiration with lower flow than Phase 1)[19]

c) Phase 3: Ascending expiratory phase (airflow accelerate up to peak expiratory flow in opposite direction where the pressure-flow relation is linear)[19]
d) Phase 4: Descending expiratory phase (from peak expiratory flow to resting position with higher flow than Phase 3, followed by an expiratory break in physiological conditions)[19]

1.2.4.2.4 ISOANA recommendations

Vogt et al. (2010)[19] described the necessity to carry out 4-phase rhinomanometry according to the recommendations of the ISOANA in the "Consensus report on acoustic rhinometry and rhinomanometry" (2005)[23] which states that "for 4-phase rhinomanometry, resistance is determined for phase 1 (ascending inspiratory phase) and phase 4 (descending expiratory phase) of the four loop rhinomanometry by using the "highest possible flow" at the pressure of 150Pa" (Figure 1.2.3).

The ascending inspiratory and descending expiratory curve parts were chosen because they are much more consistent and reproducible[23].

1.2.4.2.5 New parameters

Two additional new parameters were also introduced in 4-phase rhinomanometry:

1. Vertex resistance (VR), which is the resistance at the point of maximum flow during inspiration or expiration in a normal breath[19]. This is also the steady phase of nasal airstream and the longest part of breathing cycle, where acceleration is not occurring and the pressure- and flow curves run parallel to each other in a linear relationship (Figure 1.2.4)[19].
2. Effective resistance (Reff), which is equivalent to the average of all the resistances during either inspiratory, expiratory or the entire breath[45]. This is calculated using the sum of values of 2000 measurements of flow and pressure gradient from one loop, divided by each other[20].

Figure 1.2.3 Diagram illustrating the loop appearance and the four different phases of 4PR where resistance is determined using phase 1 and phase 4 at fixed pressure of 150 Pa, taken from Vogt et al. (2010)[19] and Clement and Gordts (2005)[23].

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Figure 1.2.4 Diagram illustrating vertex resistance (marked region) where the relationship between pressure and flow is almost linear, taken from Vogt et al. (2010)[19].

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the author for copyright reasons

1.2.4.3 Claimed advantages

Many advantages of 4-phase rhinomanometry over other methods have been claimed and include:

1. Better diagnostic information due to representation of the entire work of breathing rather than measuring resistance at only one point[19].
2. Better correlation of the logarithmic transformation of vertex resistance (LVR) and effective resistance (LER) values with subjective feeling of obstruction on the visual analogue scale (VAS)[45].
3. Better functional diagnosis and surgical planning as it takes into account the 'valve problems' and physiological Bernoulli's effects in breathing[45].
4. Increased sensitivity and specificity of rhinomanometry by allowing practical classification of severity of all degrees of nasal obstruction without losing any data in subjects where 150 Pa cannot be reached by the classic method[45]. This was backed up by studies showing that 150 Pa could not be reached by 7.34% to 46% of decongested subjects in classic method[19], therefore requiring a substitute of 75 Pa to be used which was argued to be less reliable[45]. In such cases, 4PR method is a good compliment to the classic method[19].

1.2.4.4 Existing concerns on 4PR

There were concerns by the ISOANA members in 2005 regarding how far the observed phase shift is due to the equipment used and/or the unphysiologically high pressure generated during the forced respiration necessary to obtain four phases rhinomanometry[23]. Clement et al. (2014)[20] also commented that the loop formation in this method seemed to be very dependent on the level of nasal valve and on the distortion of the mask when these high pressures (600-1000 Pa) are applied. These high pressures during respiration can cause alar collapse in normal subjects[20] as demonstrated by Bridger and Proctor (1970)[48] who found that nasal valves collapse at 600 Pa in normal subjects.

Gross and Peters (2011)[49] described that hysteresis is not inherent to nose flow but primarily dependent on the way rhinomanometric measurements are set up. It was found that hysteresis is not caused by nasal airflow, change in flow regime, inertia or variable resistance but caused by the fluid mechanic "storage effect", which distorts the allocation of flow rate and pressure whenever flow rate is measured remote from the nose[49]. It was therefore concluded that the loops and hysteresis analysed by 4PR are an artifact of the equipment rather than caused by pathological nasal conditions and this reduces considerably the clinical value of 4-phase rhinomanometry[20].

Lastly, Clement et al. (2014)[20] also described problems associated with the new parameters (VR and Reff) introduced in this method. It was pointed out that it is impossible to calculate total NAR using vertex resistance because different pressures are involved in each nostril[20]. Similarly, without a known reference pressure, it is very difficult to compare NAR values between individuals using effective resistance because the relation between flow and pressure gradient is lost[20].

1.2.5 Existing comparison of methods

One of the main obstacles in rhinomanometry has been the existence of various mathematical models used to calculate NAR[8]. This has led to confusion when comparing results from different authors and caused difficulty in adopting the results into clinical practice[8].

Few studies on comparison of different resistance parameters used in rhinomanometry have been carried out in the past[29]. For example, Eichler and Lenz compared different coefficients and units in rhinomanometry in 1985[50] although no patient material was presented[29]. Pallanch et al. (1985)[51] studied 7 different mathematical models on humans, however, these were only performed on normal subjects and no pathological cases were involved.

1.2.5.1 Comparison between classic and Broms method

In 1991, Sipila et al. compared different mathematical models (including classic and Broms method) to investigate their ability to classify different degrees of nasal obstruction as well as their reproducibility of readings[29]. All the mathematical models were able to separate different grades of obstruction, with classic at 150 mls/s, Broms at radius of 200 and W (coefficient of nasal resistance) being the most reliable ones[8].

They also found that Broms at radius 200 was calculable in all cases with better reproducibility compared to the classic method taken at 150 Pa or 150 mls/s[29]. However, Broms at radius 300 was not reached in 9% of very obstructed noses and was therefore not recommended[8].

1.2.5.2 Comparison between classic and 4PR

Comparison of the classic and 4-phase rhinomanometry methods were done by Vogt et al. (2010)[19] where 4PR was found to have better correlation with subjective feeling of obstruction compared to the classic method. They also claimed that all patients were measurable using 4PR as opposed to classic method where the pressure gradient of 150 Pa and 75 Pa were not reached by some patients[19]. However, it is important to note that these comparisons were made between the classic method (at 150 Pa or 75 Pa) and the vertex (VR) and effective (Reff) resistances of 4PR, rather than with 4PR at 150 Pa (as recommended by the Consensus meeting in 2005[23]).

1.2.5.3 Comparison between Broms and 4PR

No studies have been found so far that compared Broms and 4-phase rhinomanometry methods.

1.3 Model noses

1.3.1 Development and usage of model noses in rhinology studies

Various model noses made of different materials have been developed and used in different rhinology studies.

In 1920, Mink[52] introduced the "Mink's boxes" which were made of transparent plastic with inflow and outflow openings. Many more plastinated model noses were then developed for various studies. For example, the Perspex model in 1987[53] (to show involvement of septum in trauma), the plastinated human nose in 1989[54] (to demonstrate aerodynamic effect of nasal obstruction depends on localization of stenosis), a cylindrical model nose with acrylic plates in 1996 (to investigate the correlation between rhinomanometry and acoustic rhinometry)[55], the modified "Mink's boxes" in 2001[39] (to study the influence of nasal morphology on the stream mechanics and nasal airflow) and the transparent acrylic box model with silicone "septum" and "concha" in 2003 (to evaluate paranasal sinus volume and junction using acoustic rhinometry)[56].

In 2011, Durand et al.[57] developed a new plastinated model nose, which was anatomically, geometrically and aerodynamically validated using endoscopy, CT scans, rhinomanometry and acoustic rhinometry, and claimed that this model is suitable for studies on nasal flow, drug delivery and aerosol deposition[57].

Besides using plastinated models and human nasal cast models, animal noses such as rabbits[58], sheeps[59], rats[60] and pigs[61] have also been used to study the efficacy of nasal surgeries and medicines.

In addition, three-dimensional computerized model noses have also been constructed from Computational Fluid Dynamics (CFD) using Computerised Tomography (CT) images[62,63].

1.3.2 Issues with model noses

The main disadvantages of various types of model noses were described by Durand et al. (2011)[57].

For example, there are concern regarding the time stability and biosecurity of nose models made from cadavers[57]. Plastic replicas on the other hand lacks the thin anatomical details[57] as well as having the risk of the casting compound displacing the mucosa and causing local deformities[64].

"Pipe models", for example the one used by Moller et al. (2008)[65] to investigate aerosol deposition, was described to be lacking the real human anatomical structures, where the results can only be partly applied to human noses.

1.3.3 Rhinocal resistance unit

The model nose used in this study was first utilised in 1991 by Sipila et al.[29] to compare different rhinomanometry methods in order to assess whether the various methods could separate different levels of nasal patency. Four straight plastic tubes of 10 cm in length with varying diameters of 9 mm (very patent), 6mm (patent), 4.5 mm (obstructed) and 3 mm (very obstructed) were constructed and connected to the rhinomanometer, where four recordings of quiet respiration was conducted through them via a mask[29] (Figure 1.3.1). This study by Sipila et al. (1991)[29] showed that the rhinomanometer gave similar pressure-flow curves and mathematical data in these model noses compared to human noses across all different rhinomanometric methods[29].

Sipila and Suonpaa[66] used the same set of model noses as "test noses" to study the long term stability of rhinomanometer calibration. These models have inlets for pressure tubes and connections for pneumotachograph and standard anaesthetic mask[66]. In this study, rhinomanometric measurements were performed four times a year over a 7-year period from 1988 to 1994[66]. Even though there were some fluctuation in the recordings made over the 7-year period, four distinct levels of obstruction were clearly separated from each other at all times[66]. Therefore, it was concluded that these model noses are suitable as simple and economical calibration device to check if the flow and pressure signals given by the standard calibration equipment remained stable over a long period ('calibrate the calibrator')[66]. This is to give additional reliability to the results obtained with rhinomanometer[66].

Even though this model nose may not replicate all aspects of human noses, it is important to remember that rhinomanometry is an integral measurement taken across the entire nasal cavity[49] and is simply a method of measuring the patency of a channel through which airflow is conducted[29]. Therefore, this simple model nose is adequate to provide information on rhinomanometry parameters of pressure drop and flow rate across a tube or channel.

The model nose used in this study is marketed as the "Rhinocal" units (GM Instrument, Glasgow UK). The full detail of these units will be described in Chapter 2.

Figure 1.3.1 Diagram showing the model nose used in this study, taken from Sipila et al. (1991)[8].

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1.4 Use of rhinomanometry in practice

1.4.1 Use in human

Rhinomanometry is used to obtain an objective measurement of nasal resistance for many different reasons:

1.4.1.1 Effects of surgery

Rhinomanometry has been widely used to assess objective rhinological benefit of various operations like septoplasty[67], reduction of inferior turbinates[68], surgery of nasal valve[69] and surgery for obstructive sleep apnoea[70].

In these studies, the investigators performed rhinomanometry on their subjects before and after their operations in order to quantify the functional outcome of surgery in terms of changes in flow rate and nasal resistance.

1.4.1.2 Effects of medical treatments

Rhinomanometry has also been used to investigate effects of different medical treatments like hypertonic sodium chloride nasal spray[71], glucan solution nasal spray in chronic rhinosinusitis[72] and oral pseudoephedrine[73].

The nasal airflow and resistance were measured during and after the treatment period to assess any changes to these parameters as a result of the administered interventions.

1.4.1.3. Effects of diseases on nasal resistance

Rhinomanometry can also been used to assess effects of different diseases on nasal resistance, for example, patients with rhinovirus infection[74], allergic rhinitis (seasonal and perennial)[75] and chronic otitis media (COM)[76].

These studies utilised rhinomanometry to measure the nasal resistance in patients with disease and compared the results with those from healthy control group in order to reach a conclusion.

1.4.1.4 Effects of exposure to different environmental factors on nasal resistance

The changes in nasal resistance after exposure to different environmental substances like air pollutants (in city centre runners)[77], chlorinated water (in competitive swimmers)[78] and secondhand smoke[79] were also investigated with rhinomanometry.

The nasal resistances of subjects exposed to these substances were compared with the control group over a period of time and the differences in their nasal resistance were noted.

1.4.1.5 Factors that affect physiological nasal patency

Rhinomanometry has also been used to measure physiological changes in nasal resistance in response to different factors like exercises[80], postural changes[81] and nasal cycle[82]. These are usually performed on healthy subjects.

1.4.1.6 Factors that affect anatomical nasal patency

Factors affecting anatomical nasal patency like sex[83], age[84] and race[85] can also be investigated using rhinomanometry.

These studies are usually carried out in an attempt to find reference values for normal nasal patency in different population groups.

1.4.1.7 Correlation between subjective and objective nasal symptoms

One of the common uses of rhinomanometry is in studying correlations between the subjective feeling of nasal obstruction and objective measurement of nasal resistance, for example, in patients with septal deformities (>10 degrees)[86] and allergic rhinitis[87], as well as studying correlation between the subjective perception and the objective findings of the more obstructed side of nostrils[88].

1.4.2 Use in animals

Rhinomanometry has also been used in animals. For example, Chen et al. (1995)[89] used a modified set up of anterior rhinomanometry (fitted strip in the mask to divide left and right nostril) in anaesthetized ferrets, which were infected with influenza virus, to investigate the effect of various medications to relieve nasal congestion.

Active anterior rhinomanometry was also used in conscious rhesus monkeys (Macaca mulatta) to show an increase in NAR after introduction of intranasal histamine[90].

On the other hand, Wiestner et al. (2007)[91] used modified posterior rhinomanometry in anaesthetized Beagles and Bulldogs to evaluate the repeatability of rhinomanometry. They found that body size plays a role in the transnasal resistance in dogs and is non-linearly associated with airflow[91].

There have also been other studies where measurements of nasal resistance in animals were described. For example, use of modified anterior constant-flow rhinomanometry in dogs[92,93] where the nasal resistance was determined by measuring the air pressure required to achieve a constant flow of humidified air through the nasal passage.

1.4.3 Why has rhinomanometry not been used more commonly in clinical practice

Historically, Broms (1982)[26] identified three obstacles in rhinomanometry measurements, which include inadequacy of methods and equipment used, lack of standard numerical description of the recorded pressure-flow curves and lack of ability to differentiate between skeletal or mucosal cause of nasal obstruction. The first two problems have largely been eliminated with modern rhinomanometry techniques and general consensus on the main principles of measurements and description of recordings[22,26]. The third problem was largely overcome with good decongestants (either with physical exercise or nasal drops)[26].

Clement et al. (2014)[20] recently made an excellent summary of why rhinomanometry is not more widely used in common ENT practice. One of the reasons is that rhinomanometry is difficult to perform and is time consuming[20]. Proper instruction and good protocol is needed for the test and the whole procedure can take up to 30 minutes in total (10 minutes to measure average of five breathing cycles in both nostrils plus time for decongestants to work)[20]. However, it was pointed out that audiometry is even more difficult to perform and also takes time, and yet otologists would not operate without an objective assessment of hearing first[20].

Another reason identified was that rhinomanometry results are difficult to interpret[20]. This could be because rhinomanometry is often used to provide a single measurement of nasal resistance to help guide decision in patient management. However, there is a lack of standard reference values in rhinomanometry for surgeons due to the fact that there is a great variation in nasal resistance secondary to nasal cycle, instability of nasal patency due to direct exposure to external environment, as well as population factors such as age, height, sex, race and nasal shape and size that affects anatomical nasal patency[94]. However, it was pointed out by Clement et al. (2014)[20] that with experience, it is not hard to differentiate a pathological recording from a normal one[20].

The expensive price of rhinomanometry equipment is another reason for its lack of usage in practice, where in many countries, the equipment is not funded by the national health care or insurance company[20]. This could be because most guidelines for septoplasty and septorhinoplasty only regard rhinomanometry as a “complimentary” test when making decision on surgery[20]. It is therefore important to made these organisations aware of the importance of funding this test[20].

There have also been opposing research evidence when it comes to finding the correlation between rhinomanometry measurements and the subjective sensation of nasal airflow, with some studies found poor correlations[95,96] while others found good correlations[97,98] between the two. On top of that, the reliability of rhinomanometry has also been questioned[20]. However, studies have shown that the CV value for NAR measurements are low when properly carried out[20] (as discussed in Chapter 1.1.5) and rhinomanometry is more reliable than subjective sensation of nasal obstruction or rhinoscopy findings which have high inter- and intra-individual deviations and low repeatability[20]. Issue with nasal cycle can also be resolved with usage of nasal decongestants[20].

The lack of ability to perform rhinomanometry could also be a reason for its lack of usage in clinical practice. Prior to the recent article provided by Eccles (2011)[18], there was a lack of simple guide on rhinomanometry to help users understand the basic principles and technique of rhinomanometry, where they had to rely on mainly technical instruction manuals from the manufacturers.

Finally, the existence and availability of a broad range of rhinomanometry methods (as described in Chapter 1.2) made it difficult to compare results obtained by different researchers[99] and add to the confusion of clinicians planning on using rhinomanometry in clinical practice.

1.4.4 Which equipment and methods used in the last 5 years

A literature search using PubMed on 06 June 2014, employing the search term “Rhinomanometry” yielded 322 results within the last 5 years. Of these, information was retrieved regarding the rhinomanometry method and instrument used in 76 papers where 63(82.9%) of the studies used the classic method, 7(9.2%) used Broms, 4(5.3%) used 4-phase rhinomanometry and 2(2.6%) used combination of different methods. Table 1.4.1 illustrates a summary of some of the commonly used methods and rhinomanometers by the authors in these papers.

Table 1.4.1 Summary of the methods and rhinomanometers used in various studies over the last 5 years. This information does not represent the product's ability to measure nasal resistance using other methods.

Company	Country	Name of model	Methods used in study			
			classic	Broms	4PR	Combination
Atmos Medical	Germany	Atmos 300 Rhinomanometer	14			
GM Instruments	UK	NR6 Clinical/Research	6	4		2 (classic and Broms)
RhinoMetrics	Denmark	SRE2000/2100/ Rhinostream	9	1		
Sibelmed Group	Spain	RHINOSPIR-PRO	7			
RhinoLab	Germany	HRR2	2		4	
Nihon Kohden Co	Japan	Rhinorheograph MRP-3100	6			
Allergopharma Joachim Ganzer KG	Germany	Rhinotest MP500	4			
Homoth	Germany	Rhino 4000	3			
Medtronic	Italy	Rhinomanometer SR2000	3			
IBBAB	Sweden	Rhino-Comp		2		
Menfis Biomedica	Italy	Rynozig/Rhino-Kit	2			
ZAN 100	Germany	ZAN Messgeraete	2			
EVG GmBH	Germany	Rhinotest 2000 plus	1			
Euroclinic	Italy	RhinoPocket	1			
Pistone Instruments	Hungary	Pistone Rhinomanometer	1			
MircroTronics Corp	USA	PERCI-SAR System rhinomanometer	1			
Rhinosoft	Germany	Hortmann	1			

1.5 Rationale and aims

Rhinomanometry is an objective way to measure nasal airflow during normal breathing, expressed as the nasal airway resistance (NAR). The clinician and the researcher studying the effects of surgery or other treatments on the nose is interested in obtaining a single numerical value that represents NAR but the problem is that there are various methods of analyzing the pressure-flow curve in order to obtain NAR in rhinomanometry.

The International Standardization Committee for Rhinomanometry recommended that nasal resistance should be calculated at a fixed pressure gradient of 150 Pa or 75 Pa in 1984[22] and 2005[23]. On the other hand, Broms (1982)[46] recommended calculation of resistance at the intersection point between the pressure-flow curve and radius of 200. In 2010, Vogt et al.[19] introduced yet another new method called 4-phase rhinomanometry (4PR) where nasal resistance is calculated by analyzing the four different phases of breathing.

Each author has described his or her own methods as the better way of measuring nasal resistance for various reasons. The Broms method is mainly used where it originated in Scandinavia, and the 4-phase method is now promoted as being superior to the classic method despite the long history of use of the classic method in clinical trials on medicines and nasal surgery.

Modern computerized rhinomanometers like NR6 Rhinomanometer (GM Instruments, Glasgow UK) utilise software that allows nasal resistance to be calculated by all the 3 different methods, which can be confusing to clinicians and researchers. There have been a few clinical studies comparing various mathematical models in rhinomanometry but there has not been any study comparing the actual values calculated from all three methods.

The aim of this study is to compare the unilateral NAR values measured using all three methods across a range of resistances provided by four model noses. This is to further improve our understanding of the relationship between these rhinomanometry methods. The reproducibility of measurements was also investigated.

CHAPTER 2

Methodology

2.1 Study design

This was an in-vitro study comparing the values of nasal airway resistances obtained using different rhinomanometry methods when applied across four model noses of fixed resistances. The study was conducted at the Common Cold Centre and Healthcare Clinical Trials in Cardiff University, Wales.

2.2 Equipment used

<u>2.2.1 Rhinomanometer</u>

An NR6-2 Rhinomanometer Clinical/Research model (GM Instruments, Glasgow UK) was used for all the measurements in this study. It uses NARIS software that allows nasal resistance to be calculated using the classic (at 150 Pa and 75 Pa), 4-phase rhinomanometry (at 150 Pa and 75 Pa including the logarithmic transformation of vertex resistance and effective resistance) and Broms (at radius of 200) methods. All pressure-flow curves and mathematical results were displayed on the monitor and were printed out on A4-size paper (Examples in Appendix 1).

<u>2.2.2 Model noses</u>

The model noses used in this study were developed in 1997[66] and have been used over 16 years as standard calibrating devices for rhinomanometers. They are marketed as ‘Rhinocal’ units (GM instruments, Glasgow UK) and consist of cylindrical tubes of different diameters (fixed resistances) with inlets for pressure tube and airflow as well as attachments for flowhead as illustrated in Figures 2.2.1 and 2.2.2

Figure 2.2.1 Example of model nose used in this study.

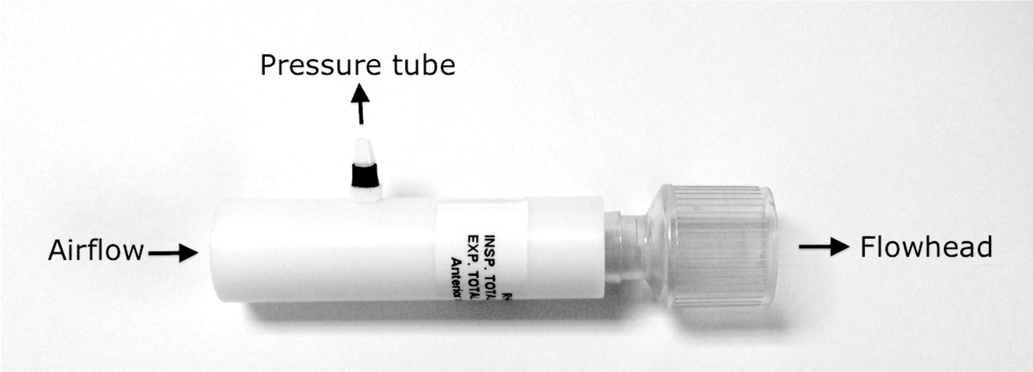
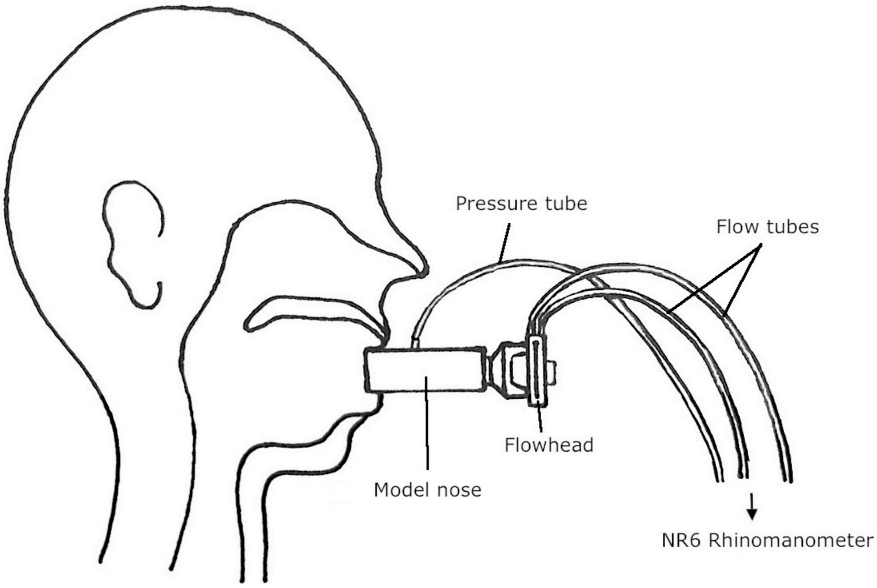


Figure 2.2.2 Illustration of the set up of model nose.



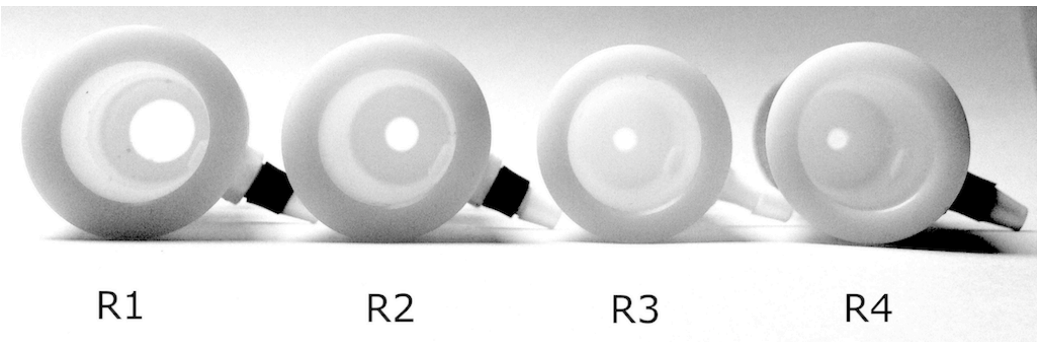
Model noses were used instead of human volunteers in order to eliminate the variability and instability of human nasal resistance that is associated with environmental factors such as temperature, humidity and dust, as well as physiological factors like the nasal cycle[94] when comparing different methods used in rhinomanometry. The real nose will introduce uncontrolled variability of resistance into the measurements whereas the model nose will provide a stable resistance.

Even though human nose is not a simple tube, the principle of measuring resistance with a rhinomanometer is the same for a simple tube model nose and a complex nasal airway. If the flow through each and the pressure drop across each is the same, then each will have the same resistance value because a rhinomanometer only measures the flow and the pressure drop. For example, if a complex nasal structure has a pressure drop of 75 Pa and a flow of 100 cm^3/s then its resistance will be measured as 0.75 $Pa/cm^3/s$. Similarly if a model nose has a pressure drop of 75 Pa and a flow of 100 cm^3/s the rhinomanometer will measure the resistance as 0.75 $Pa/cm^3/s$. The various clinical conditions that may affect the nose are irrelevant when considering measurement of resistance with a rhinomanometer.

Therefore it is acceptable to use a model nose to calibrate a rhinomanometer and this is the method of calibration recommended by the 2005 Consensus report on rhinomanometry[23].

In this study, four different model noses (Figure 2.2.3) with decreasing diameters (increasing resistances) were used to represent a wide range of human nasal resistances. The unilateral fixed resistances of the units were approximately 0.18 $Pa/cm^3/s$ (R1), 0.54 $Pa/cm^3/s$ (R2), 1.10 $Pa/cm^3/s$ (R3) and 1.29 $Pa/cm^3/s$ (R4) when measured at 150 Pa using the classic method.

Figure 2.2.3 Four model noses showing progressive increase in resistance (decrease in diameter).



2.3 Measurement of nasal airway resistances

The rhinomanometer was calibrated at the beginning of each study day using a rotameter (Fisher KDG 2000) for calibration of airflow and a slopping paraffin manometer (Airflow 504) for calibration of pressure.

Measurements of NAR were taken using active rhinomanometry where airflow was provided by normal quiet inhalation and exhalation from the mouth through the model noses to mimic human respiration in a normal rhinomanometry study. This method was supported by Sipila et al[66] who found that it was not necessary to use an automatic flow pump in model noses because any alterations in human breathing pattern (change in frequency and amplitude) would have similar effect on both pressure and flow changes, therefore would not affect the final calculated NAR values.

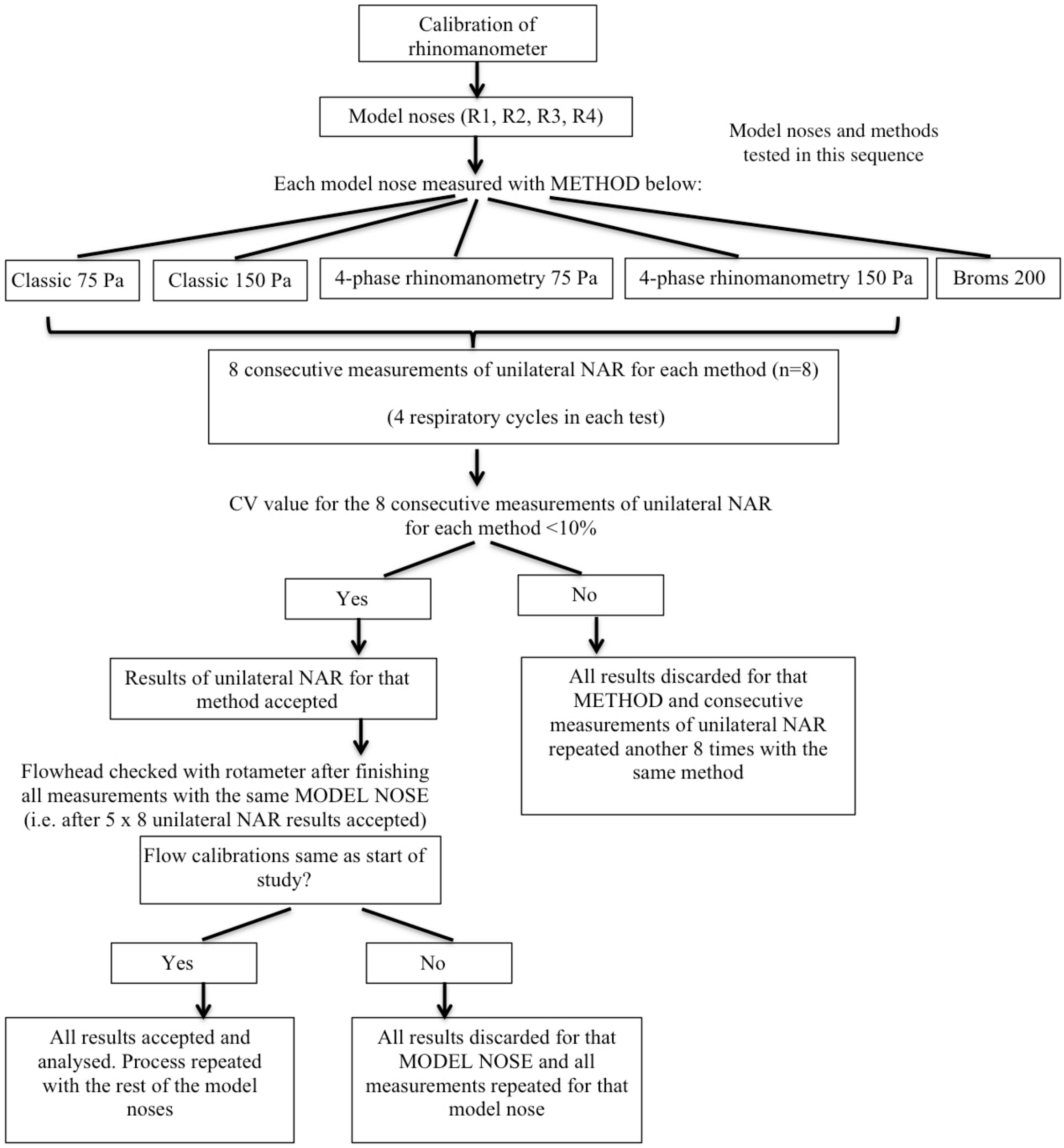
For each model nose, NAR was measured using the classic (at 75 Pa and 150 Pa), 4-phase rhinomanometry (at 75 Pa and 150 Pa) and Broms (at radius 200) method. The measurements were taken according to the same sequence, starting with R1, followed by R2, R3 and R4 each time (for the model noses), with each model noses first tested with classic (at 75 Pa and 150 Pa), followed by 4-phase rhinomanometry (at 75 Pa and 150 Pa) and finally with Broms (at radius 200) method. The model noses and rhinomanometry methods were not randomized when measurements were taken in this study.

For each method, eight consecutive sets of unilateral NAR measurements were obtained and the coefficient of variation (CV) was calculated. In our daily usage of rhinomanometry, a CV of less than 10% for repeated measurements is used to validate the measurements.

The flowheads were calibrated again using the rotameter at the end of each series of measurements with each model nose. All the results from a series were to be discarded if there were any discrepancies in airflow calibration between the start and finish of use of each model nose, which may be the result of condensation or accumulation of moisture in the flowhead from the expired air. Figure 2.3.1 illustrates our study protocol in a flowchart.

All measurements and calibration of the rhinomanometer were standardised according to the study site Standard Operating Procedures (SOP) (Appendix 2 and 3) in a quiet laboratory room.

Figure 2.3.1 Flowchart illustrating our study protocol.



2.4 Reproducibility of NAR measurements

Two rhinomanometric recordings were made on two separate occasions with at least 24 hours apart in R1 and R4 model noses. The 24 hours interval was chosen because the original study was conducted over 2 days period. R1 (lowest resistance model) was used because some studies[66,100] have found that the highest variation of NAR measurements occurred in noses with higher flows or lower resistances. However, other studies[101,102] have found that the variation of NAR increases at higher resistances due to the airflow becoming more turbulent, therefore R4 (highest resistance model) was also included in this experiment. Both of these model noses were also chosen to cover the full extremes of nasal resistances used in the initial study.

The NR6-2 rhinomanometer was again calibrated at the beginning of each study day and each of the model noses were used to measure NAR using the classic (at 150 Pa and 75 Pa), 4-phase rhinomanometry (at 150 Pa and 75 Pa) and Broms (at radius 200) methods. This is then repeated on the second day. The study protocol is the same as initial study (Figure 2.3.1) except that the same model noses (R1 and R4) were re-tested using all methods 24 hours later.

2.5 Statistical analysis

The Statistical Package for the Social Sciences version 20 (IBM SPSS Statistics 20) and the Microsoft Excel 2011 version 14.1.2 for the Macintosh platform was utilised for statistical analysis.

Comparisons of NAR values were made separately between the classic and 4-phase rhinomanometry methods; and between classic and Broms method. Only the inspiratory measurements were presented in the result sections, as this is the data used in calculation of NAR in practice. The correlation between the NAR measurements of different methods were analysed with Mann-Whitney U test and the strength of correlations was tested with Spearman's Rank Order correlation method. A value of $p<0.05$ was considered significant. The extent of agreement between the methods were also investigated using the Bland-Altman[103] method with limits of agreement (+/- 2SD).

Reproducibility of the measurements was also analyzed using the Bland-Altman method with calculation of the Coefficient of Repeatability (CR). We expect 95% of differences to be less than two standard deviations as per definition of repeatability coefficient by British Standards Institution[103]. The coefficient of variation (CV) was also calculated for the repeated measurements.

CHAPTER 3

Comparison of the classic and 4PR methods

3.1 Introduction

In 2010, Vogt et al.[19] introduced 4-phase rhinomanometry as a revolutionary way of obtaining data on nasal resistances by using data analysis of the entire pressure-flow curve, and claimed that this new method was superior to the classic method in many ways as discussed in Chapter 1.2.4.

Since modern rhinomanometers allow NAR to be obtained using various different methods, clinicians and researchers studying the effects of surgery or other treatments on the nose may be confused by the choices available to them especially when the 4-phase rhinomanometry is now being overstated in literature as the better method and so far, there has not been any study comparing the more complex 4-phase rhinomanometry method with the simple classic method.

The objective for this part of the study is to determine if there is any difference between the actual NAR measurements obtained by both methods. The data obtained would give rhinomanometry users a more informed decision when choosing the parameters to be used for their study.

3.2 Methods

3.2.1 Rhinomanometry

Unilateral nasal airway resistances for each of the four model noses were measured using the classic method at 150 Pa and 75 Pa, followed by 4-phase rhinomanometry method at 150 Pa and 75 Pa. The rhinomanometer and model noses used as well as the study protocol for measuring of NAR was performed as described in Chapter 2.

3.2.2 Results analysis and statistics

Data of unilateral nasal airway resistance (Pa/cm^3/s) at 150 Pa and 75 Pa for both methods were expressed as the means ± S.D. The correlation between the results obtained from both methods were analysed with Mann-Whitney U test ($U_{critical}$=13, H_0=no significant difference between the two methods) and the strength of correlations was tested with Spearman's Rank Order correlation method. A value of $p<0.05$ was considered significant. The extent of agreement between both methods was also investigated using the Bland-Altman method with limits of agreement (+/- 2SD) to assess whether both methods can be used interchangeably.

3.3 Results

3.3.1 Flowhead calibration

There were no discrepancies in airflow calibration found between the start and finish of usage of each model nose. Therefore, no measurement series were discarded.

3.3.2 Coefficient of variation (CV)

The CV value for all the eight consecutive measurements for each method and model nose was less than 10% therefore, no measurements needed to be repeated.

3.3.3 Comparison of actual unilateral NAR values

Only inspiratory measurements were presented, as this is the data used in calculation of NAR in practice. Figures 3.3.1 and 3.3.2 illustrate the comparison of unilateral NAR values obtained using both the classic and 4-phase rhinomanometry method at 150 Pa and 75 Pa, along with their standard deviations.

Mann-Whitney U test showed no statistically significant difference for all the values compared ($U>U_{critical}$ for sample size, $p>0.05$) (Table 3.3.1). The null hypothesis was therefore accepted that there were no statistically significant differences between the results obtained using the two different mathematical models at 150 Pa and 75 Pa.

A Spearman's Rank Order correlation was also run to determine the relationship between the nasal resistance values obtained using the classic and 4-phase rhinomanometry. There was a strong, positive correlation between the results measured using both methods at 150 Pa and 75 Pa, which was statistically significant (Spearman's Correlation Coefficient, r_s =1.000, $p<0.001$ for all comparisons).

Figure 3.3.1 Rhinomanometry reading from both methods at 150 Pa. Error bars (± 2 standard deviations) are shown.

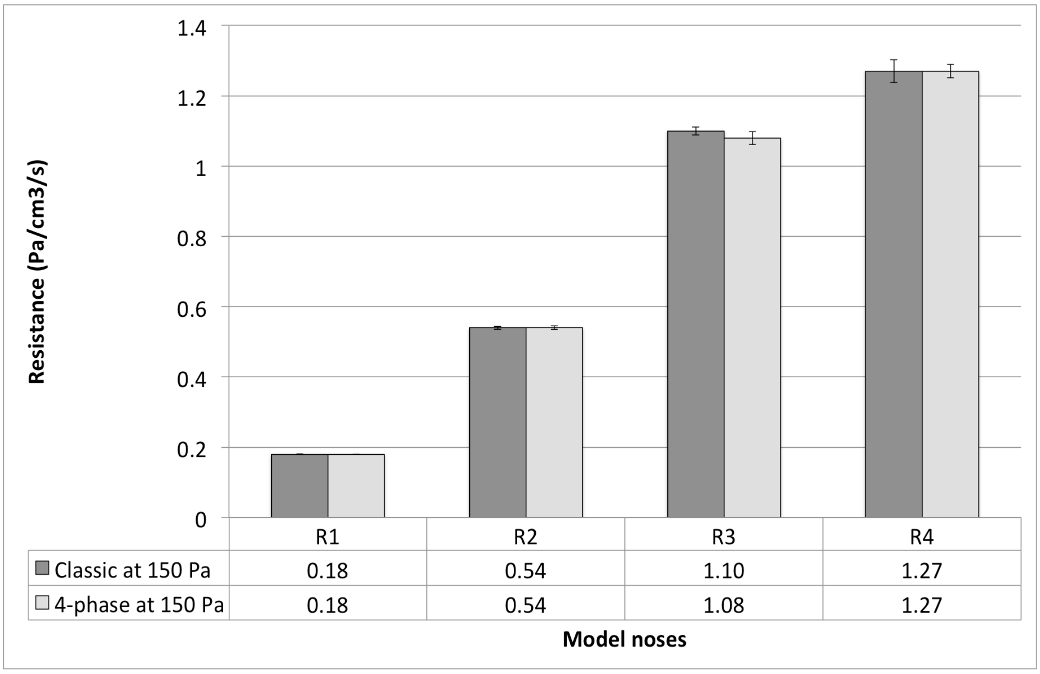


Figure 3.3.2 Rhinomanometry reading from both methods at 75 Pa. Error bars (± 2 standard deviations) are shown.

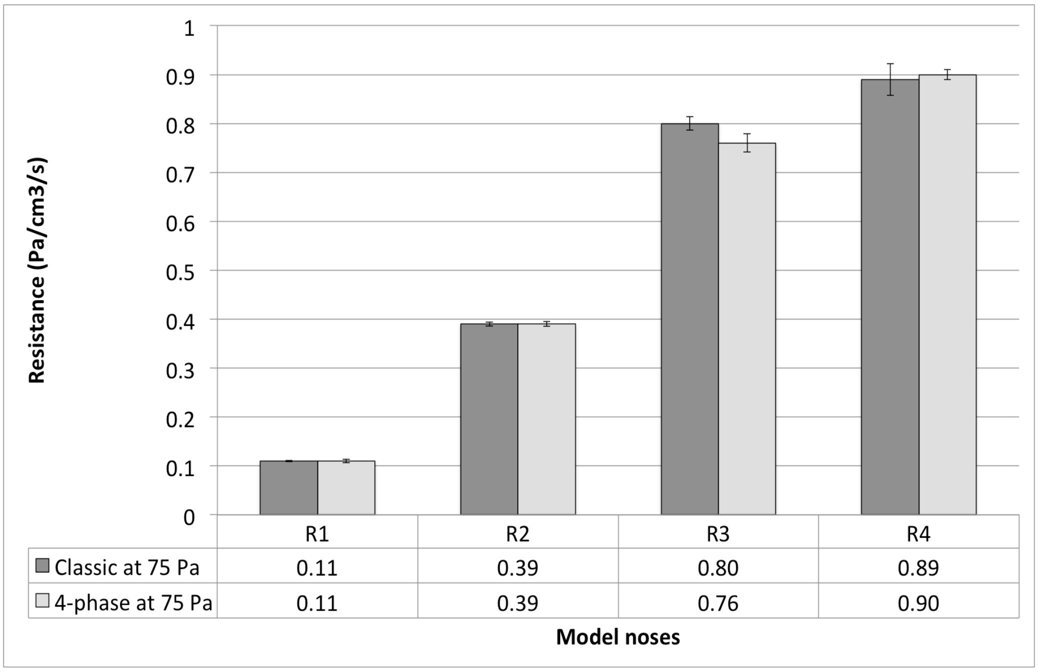


Table 3.3.1 Results of Mann-Whitney U test comparing values obtained using both methods across different resistances.

	150 Pa				75 Pa			
	R1	R2	R3	R4	R1	R2	R3	R4
U value	32	32	32	28	32	32	24	24
p value	1.000	1.000	1.000	0.721	1.000	1.000	0.442	0.442
Conclusion (A/R)	A	A	A	A	A	A	A	A

A=accept H_0 (not statistically significant difference)

R=reject H_0 (there is statistically significant difference)

Figures 3.3.3 and 3.3.4 shows scatter plots of NAR measurements using classic method against NAR measurements using 4-phase rhinomanometry method at 150 Pa and 75 Pa across all four model noses. It demonstrates a very close agreement between values obtained from both methods on the line of equality.

The Bland-Altman plots for all the model noses at both 150 Pa and 75 Pa have scatter points within the limit of agreements of +/- 2SD, which suggest good agreement between both methods. The intervals for limits of agreement were so small (range of +/- 2SD was 0.001-0.078 Pa/cm3 for 150 Pa and 0.008-0.076 Pa/cm3 for 75 Pa) that we are confident that it would not be clinically significant or affect decisions on patient management, allowing both methods to be used interchangeably. Figures 3.3.5-3.3.8 show some of the Bland-Altman plots (R1 and R4 at 150 Pa and 75 Pa) to cover the two extremes of nasal resistances.

Figure 3.3.3 Scatter plot showing close agreements between NAR measured using both methods at 150 Pa on the line of equality.

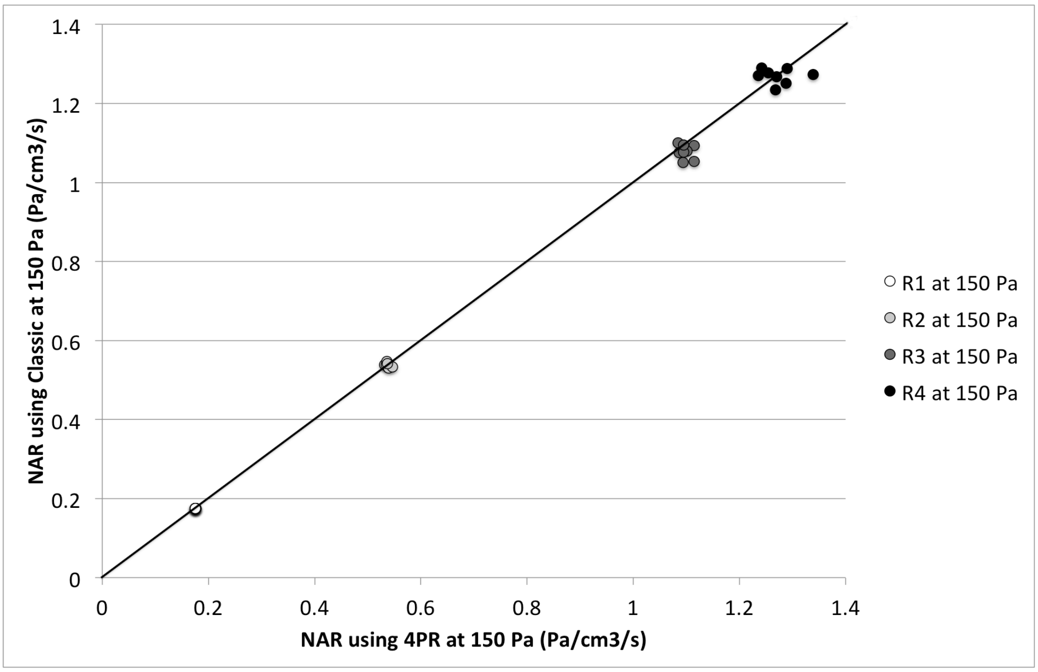


Figure 3.3.4 Scatter plot showing close agreements between NAR measured using both methods at 75 Pa on the line of equality.

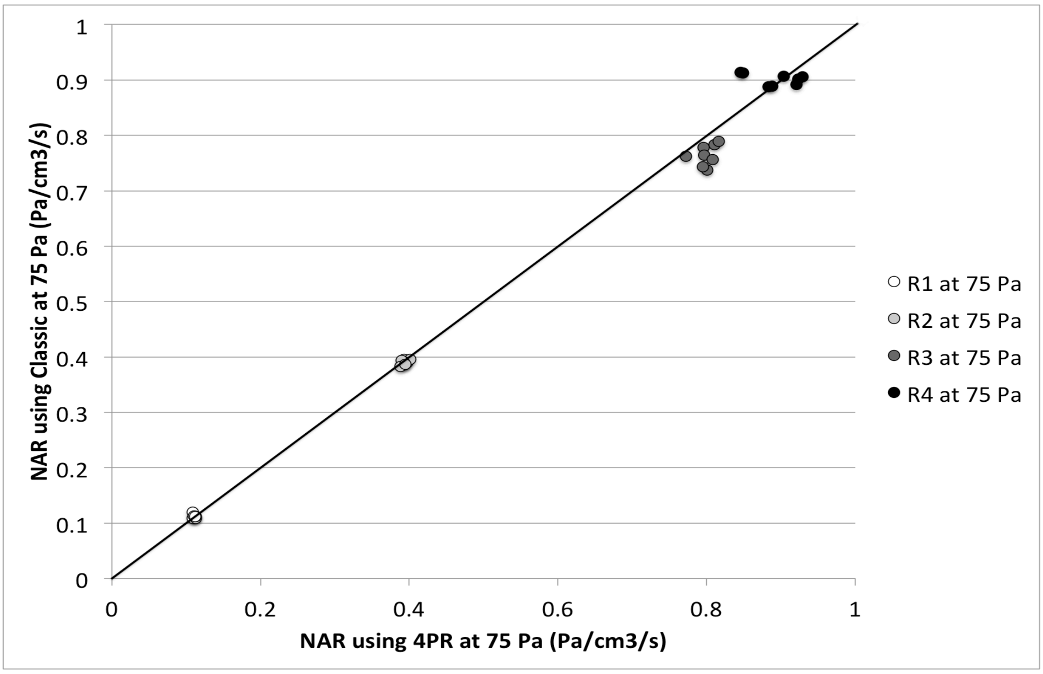


Figure 3.3.5 Bland-Altman plot for model nose R1 (lowest resistance) at 150 Pa.

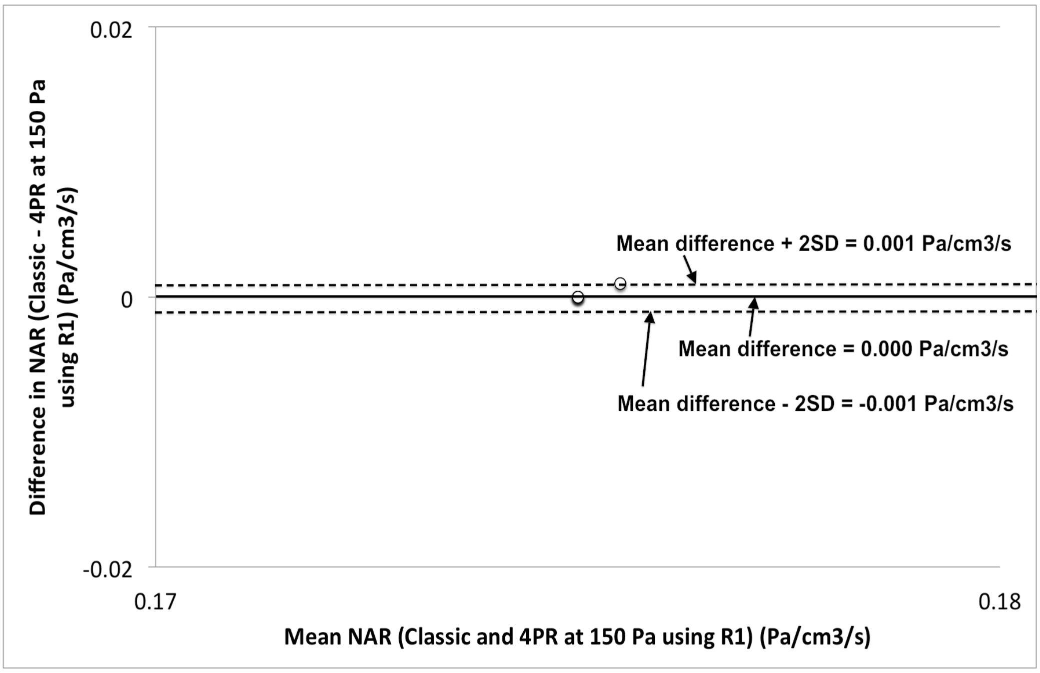


Figure 3.3.6 Bland-Altman plot for model nose R4 (highest resistance) at 150 Pa.

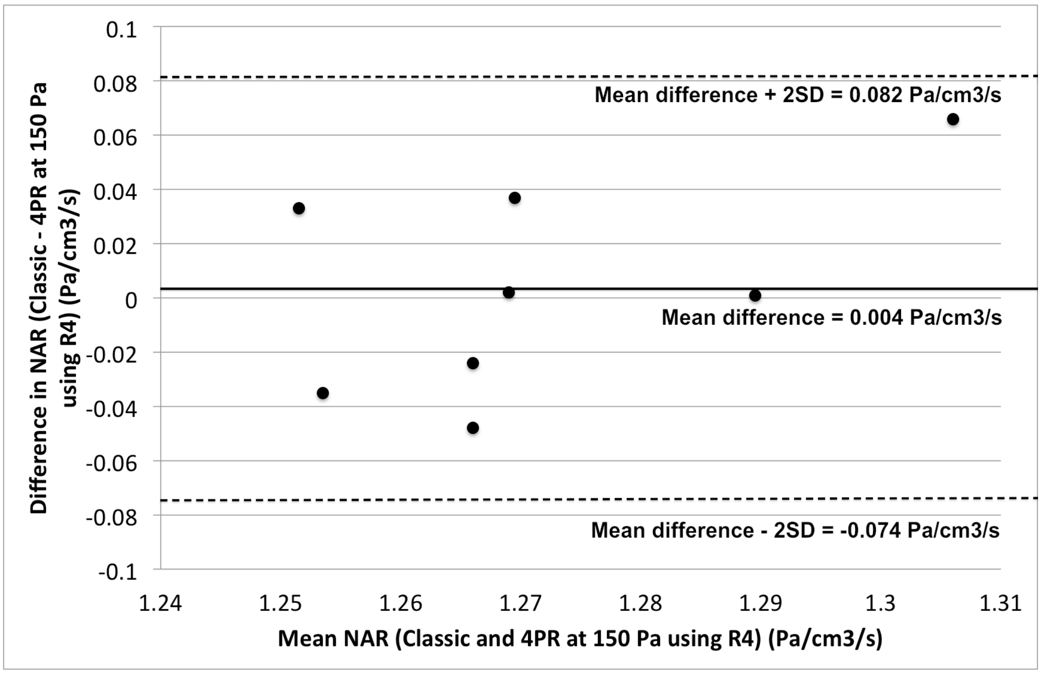


Figure 3.3.7 Bland-Altman plot for model nose R1 (lowest resistance) at 75 Pa.

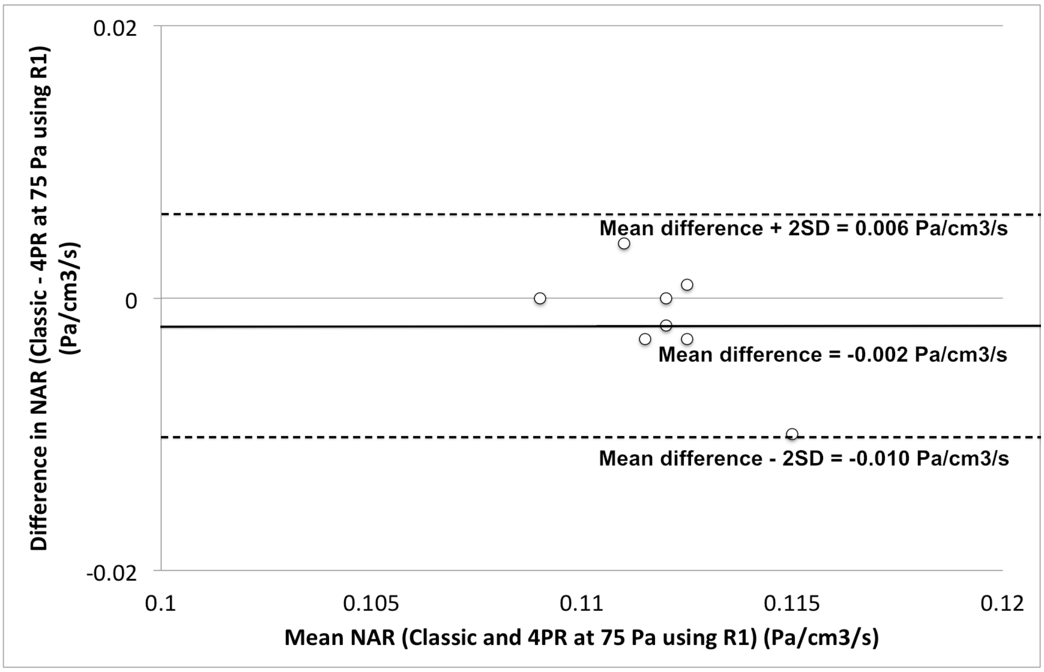
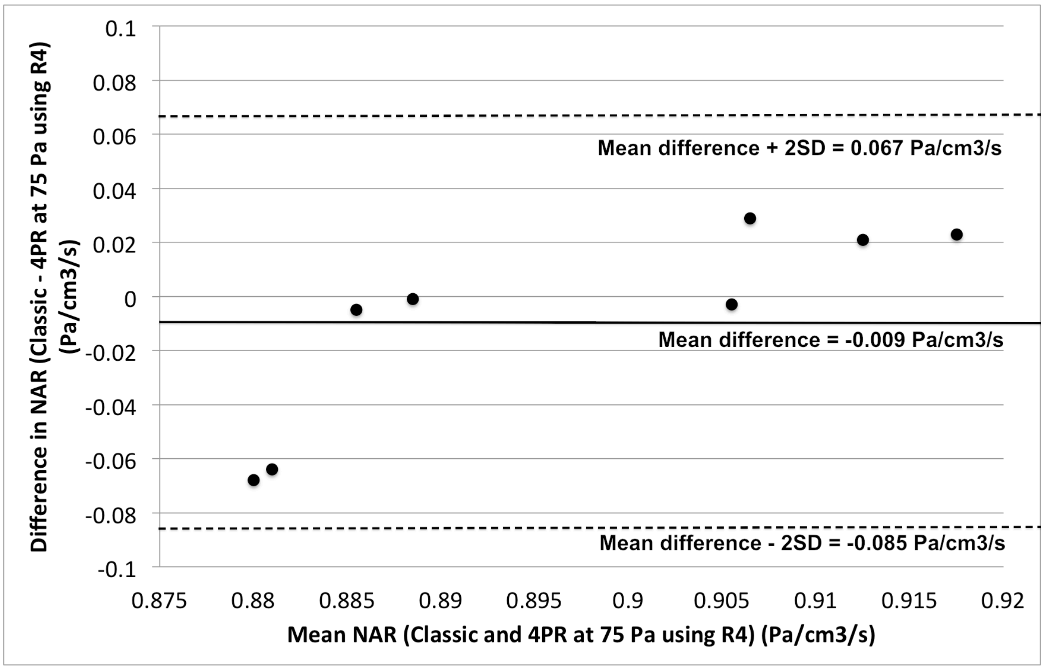


Figure 3.3.8 Bland-Altman plot for model nose R4 (highest resistance) at 75 Pa.



3.4 Discussion

3.4.1 Data acquisition of nasal airway resistance in rhinomanometry

Vogt et al. (2010)[19] explained the differences in data acquisition and method of data averaging between the classic and 4-phase rhinomanometry methods as described in Chapter 1.2.4.2.2. Modern computerized rhinomanometers have the ability to measure NAR using classic and 4-phase rhinomanometry methods. It was pointed out by Vogt et al. (2010)[19] that some computer programs however, either depict the loops as the flow for 150 Pa in phase 1 or describe flow as an averaged value between phase 1 and phase 2.

The NR6 Rhinomanometer (GM Instruments, Glasgow UK) used in this study uses NARIS software that generates NAR measurements according to the correct method of data acquisition and data averaging described in Chapter 1.2.4.2.2, depending on which parameters were chosen in the setting.

3.4.2 Recommendations for measurements of NAR in 4PR

According to the consensus report in 2005[23], "for 4-phase rhinomanometry, resistance is determined for phase 1 (ascending inspiratory phase) and phase 4 (descending expiratory phase) of the four loop rhinomanometry by using the "highest possible flow" at the pressure of 150Pa"[23].

Therefore, it makes sense to compare both methods in this study at the fixed pressure of 150 Pa. Comparison of both methods at 75 Pa were also made to enable a more complete evaluation of the two methods.

3.4.3 The "unreachable" 150 Pa

One of the advantages claimed by Vogt et al. (2010) was that 4-phase rhinomanometry method increases the sensitivity and specificity of rhinomanometry, by allowing practical classification of severity of all degrees of nasal obstruction without losing any data in subjects where 150 Pa cannot be reached using the classic method[45]. This was backed up by studies showing that 150 Pa could not be reached by 7.34% to 46% of decongested subjects in classic method[19], therefore requiring a substitute of 75 Pa to be used which was argued to be less reliable[45], and therefore in such cases, 4-phase rhinomanometry method is a good compliment to the classic method[19].

This claim appears contradictory since recommendation for usage of 4PR (as described in Chapter 1.2.4.2.4) requires the pressure of 150 Pa to be reached in this method as well. There were certainly no differences observed (understandably) regarding the respiratory force needed to reach the recommended 150 Pa in both methods during this study using the model noses.

This shared obstacle of reaching 150 Pa in both methods are further supported by the fact that even though the ISOANA agreed that 4-phase rhinomanometry method is useful in providing supplementary information to rhinomanometry, there were concerns regarding how far the observed phase shift is due to the equipment used and/or the unphysiologically high pressure generated during the forced respiration necessary to obtain measurements in 4-phase rhinomanometry[23].

3.4.4 Comparison of the NAR values measured using both methods

4-phase rhinomanometry was also promoted as being superior to the classic method as it gives better diagnostic information due to representation of the entire work of breathing[19], provides better functional diagnosis and surgical planning[45] as well as better correlation of its parameters with subjective feeling of obstruction on the VAS scale[19].

However, the results of this study clearly demonstrate that the simple classic and the more complex 4-phase rhinomanometry method give the same nasal airway resistance values at both 150 Pa and 75 Pa, when measured across a wide range of resistances. There were strong, positive correlations between the values obtained with both methods, which were statistically significant for all comparisons at 150 Pa and 75 Pa.

The scatter plots also showed a linear relationship across the range of resistances used in this study and only at the higher resistances is there any slight spread of the results, which is to be expected as the airflow becomes more turbulent at the higher resistances[101,102]. Bland-Altman analysis further demonstrates good agreement between both methods with small intervals for limits of agreement, that we are confident both methods can be used interchangeably.

Therefore, all the advantages of 4-phase rhinomanometry described became irrelevant in both research and clinical setting when both methods give the same end values of NAR.

Furthermore, the validity of 4-phase rhinomanometry has recently been questioned by Clement et al. 2014[20] (as described in Chapter 1.2.4.4) who state that the loops and hysteresis analysed by this method are an artifact of the equipment rather than caused by pathological nasal conditions and that this reduces considerably the clinical value of 4-phase rhinomanometry.

3.4.5 Vertex and Effective resistance

No comparisons were made between the classic method and the two new parameters introduced in 4-phase rhinomanometry (vertex and effective resistance) as described in Chapter 1.2.4.2.5 because there are no equivalent data generated from the classic method.

Vertex resistance is the resistance calculated at the point of maximum flow. It is not possible to obtain the resistance at maximum flow in classic method because in order to maintain normal quiet respiration, the pressure-flow curves would end in their ascending phases, rather than plateauing (i.e. maximal flow), therefore making it impossible to obtain that value even through extrapolation of the curve.

Effective resistance is the mean overall NAR, calculated using values of 2000 measurements of flow and pressure gradient summed up and divided by each other. Similarly, this information is not generated in the classic method and therefore not compared in this study.

3.5 Conclusion

Despite using different parameters and methods of data acquisition, it came as a surprise that there is such a high degree of conformity between resistances measured by the classic and 4-phase rhinomanometry methods. Applying the principle of “lex parsimoniae” or Ockham’s razor, the simpler the method or hypothesis the better, the complexity of four-phase rhinomanometry does not provide any benefit over the simpler classic measurements, as both methods give the same resistance values.

CHAPTER 4

Comparison of the classic and Broms methods

4.1 Introduction

In rhinomanometry, the classic method measures NAR on a usual coordinate system at a fixed pressure of 150 Pa[22] or 75 Pa[23]. On the other hand, Broms method measures NAR on a polar coordinate system using the point of intersection between the pressure-flow curve and a circle drawn at radius of 200[7] as described in Chapter 1.2.3. Since these two methods are the most commonly used ones in rhinomanometry, it is important for clinicians and researchers to understand their relationship especially when interpreting results of rhinology studies performed using different rhinomanometry methods.

Sipila et al. (1992)[29] compared the classic method with the Broms method to investigate their ability to classify different degrees of nasal obstruction and the reproducibility of results. However, there has not been any study comparing the actual NAR values obtained from both methods.

The objective for this part of the thesis is to compare the unilateral NAR values measured using both the classic and Broms method across a range of resistances provided by four model noses. This is to further improve our understanding of the relationship between these two most commonly used methods in rhinomanometry.

4.2 Methods

4.2.1 Rhinomanometry

Unilateral nasal airway resistances for each of the four model noses (Rhinocal resistance units) were measured using the classic method at 150 Pa and 75 Pa, followed by Broms method at radius of 200. The rhinomanometer and model noses used as well as the study protocol for measuring of NAR was performed as described in Chapter 2.

4.2.2 Results analysis and statistics

Data of unilateral nasal airway resistance ($Pa/cm^3/s$) measured with classic method at 150 Pa and 75 Pa and with Broms method at radius of 200 were expressed as the means ± S.D. The correlation between the results obtained from both methods were analysed with Mann-Whitney U test ($U_{critical}$=13, H_0=no significant difference between the two methods) and the strength of correlations was tested with Spearman's Rank Order correlation method. A value of $p<0.05$ was considered significant. The extent of agreement between both methods was also investigated using the Bland-Altman method with limits of agreement (+/- 2SD) to assess whether both methods can be used interchangeably.

4.3 Results

4.3.1 Flowhead calibration

There were no discrepancies in airflow calibration found between the start and finish of usage of each model nose. Therefore, no measurement series were discarded.

4.3.2 Coefficient of variation (CV)

The CV value for all the eight consecutive measurements for each method and model nose was less than 10% therefore, no measurements needed to be repeated.

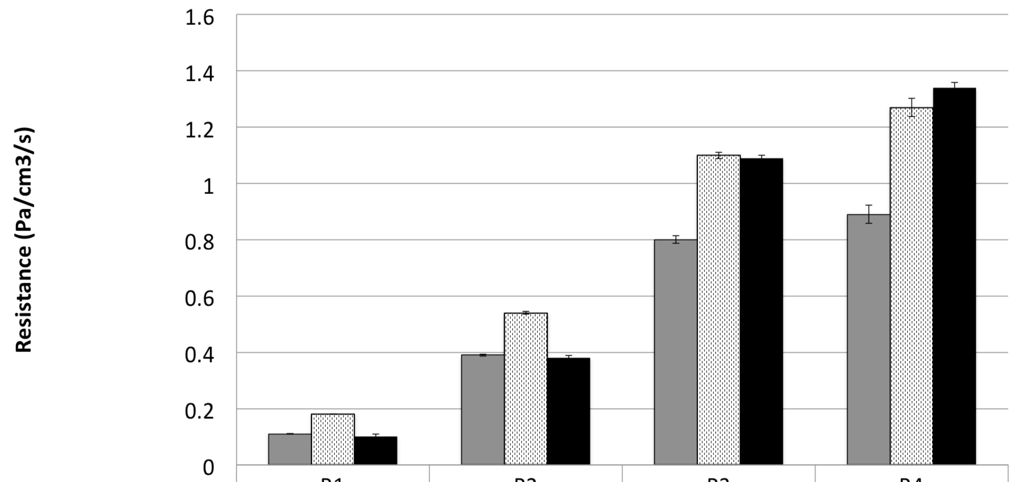
4.3.3 Comparison of actual unilateral NAR values

Only inspiratory measurements were presented, as this is the data used in calculation of NAR in practice. Figures 4.3.1 and 4.3.2 illustrate the comparison of unilateral NAR values obtained using both the classic and Broms method.

Mann-Whitney U test (Table 4.3.1) confirmed the observations from the line graphs and bar charts, showing no significant difference between the NAR values obtained from Broms 200 and classic at 75 Pa at lower resistances (R1 and R2); and between NAR values of Broms 200 and classic at 150 Pa at higher resistances (R3 and R4). On the other hand, there were significant differences shown between NAR values obtained from Broms 200 and classic at 150 Pa at lower resistances (R1 and R2); and between NAR values of Broms 200 and classic at 75 Pa at higher resistances (R3 and R4).

The Spearman's Rank Order correlation test showed a strong, positive correlation between the results measured using both methods as a whole, which was statistically significant (Spearman's correlation coefficient, r_s =1.000, p <0.001 for all comparisons).

Figure 4.3.1 Rhinomanometry readings from classic (at 75 Pa and 150 Pa) and Broms 200 in a bar chart. Error bars (± 2 standard deviations) are shown.



	R1	R2	R3	R4
Classic at 75 Pa	0.11	0.39	0.80	0.89
Classic at 150 Pa	0.18	0.54	1.10	1.27
Broms at radius 200	0.10	0.38	1.09	1.34

Model noses

Figure 4.3.2 Rhinomanometry readings from classic (at 75 Pa and 150 Pa) and Broms 200 method in a line graph. The model nose resistances given on the x-axis were calculated using the classic method at 150 Pa on inspiration.

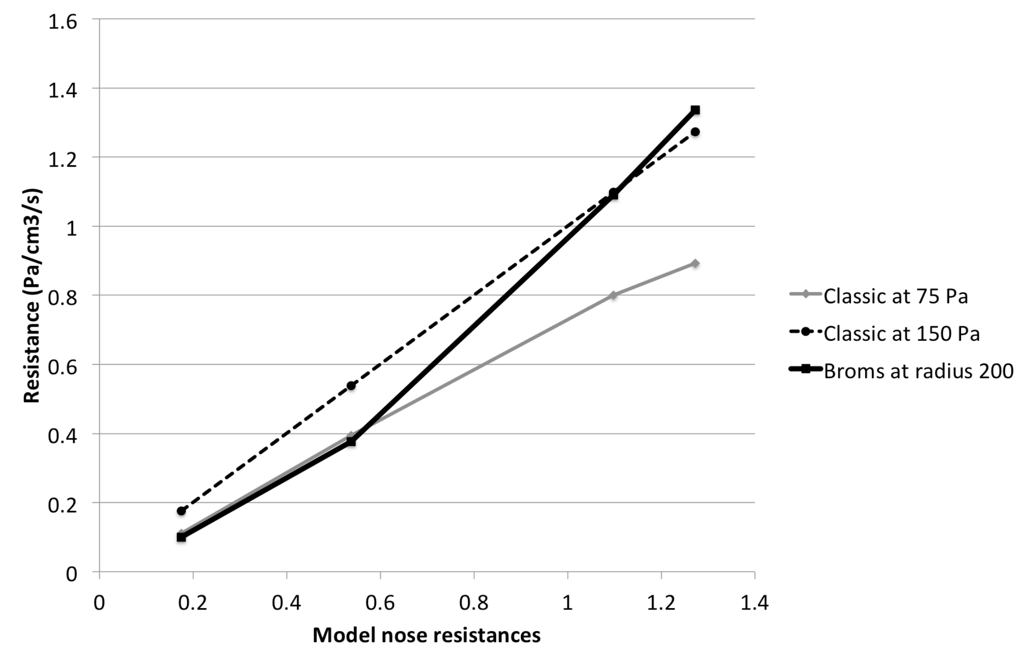


Table 4.3.1 Results of Mann-Whitney U test comparing values obtained using both methods across different resistances.

Mann-Whitney U test	**Broms 200 vs classic at 75 Pa**				**Broms 200 vs classic at 150 Pa**			
	R1	R2	R3	R4	R1	R2	R3	R4
U value	32	32	0	0	0	0	32	21
p value	1.00	1.00	0.01	0.01	0.01	0.01	1.00	0.28
Conclusion (A/R)	A	A	R	R	R	R	A	A

A=accept H_0 (no statistically significant difference)
R=reject H_0 (there is statistically significant difference)

Figures 4.3.3 and 4.3.4 show scatter plots of NAR measurements using Broms method at radius 200 against NAR measurements using classic method at 150 Pa and 75 Pa across all four model noses. Again, they demonstrate either close or weak agreements between values obtained from both methods depending on the level of nasal resistances.

The Bland-Altman plots were used to investigate the degree of agreements between both methods. When compared between Broms 200 and classic at 150 Pa, the Bland-Altman plots showed that at lower resistances (R1 and R2), all the scatter points were above the line of no difference (0), indicating that the measurements of NAR in classic at 150 Pa is higher than that of Broms 200 by an average of 0.080 Pa/cm3/s (R1) and 0.162 Pa/cm3/s (R2). At higher resistance (R3), the mean difference between both methods was very close to zero (0.007 Pa/cm3/s). On the other hand, at the highest resistance (R4), the scatter points were below 0, indicating that the measurements of NAR in Broms 200 has now become higher than that of classic at 150 Pa by an average of 0.064 Pa/cm3/s. This is in keeping with the observation of Figure 4.3.2, where the line for Broms 200 and classic at 150 Pa begins to diverge at highest resistance (R4) with Broms 200 producing higher NAR values. Even though the plots are still within +/- 2SD of the mean difference, both methods cannot be used interchangeably at R1, R2 and R4 because one method produces significantly higher values than the other.

On the other hand, when comparing between Broms 200 and classic at 75 Pa, the Bland-Altman plots showed that at lower resistances (R1 and R2), the mean differences were very close to zero (0.015 Pa/cm3/s for R1 and 0.018 Pa/cm3/s for R2). On the other hand, at higher resistances (R3 and R4), the scatter points were below 0, indicating that the measurements of NAR in Broms 200 were higher than that of classic at 75 Pa by an average of 0.292 Pa/cm3/s (R3) and 0.534 Pa/cm3/s (R4). Again, both methods cannot be used interchangeably at R3 and R4 because one method produces higher values than the other.

Figures 4.3.5-4.3.12 showed the Bland-Altman plots for the comparisons of nasal resistances across all model noses.

Figure 4.3.3 Scatter plot showing closer agreements at high resistances (R3 and R4) between Broms 200 and classic at 150 Pa on the line of equality. At lower resistances (R1 and R2), there is poor agreement between both methods.

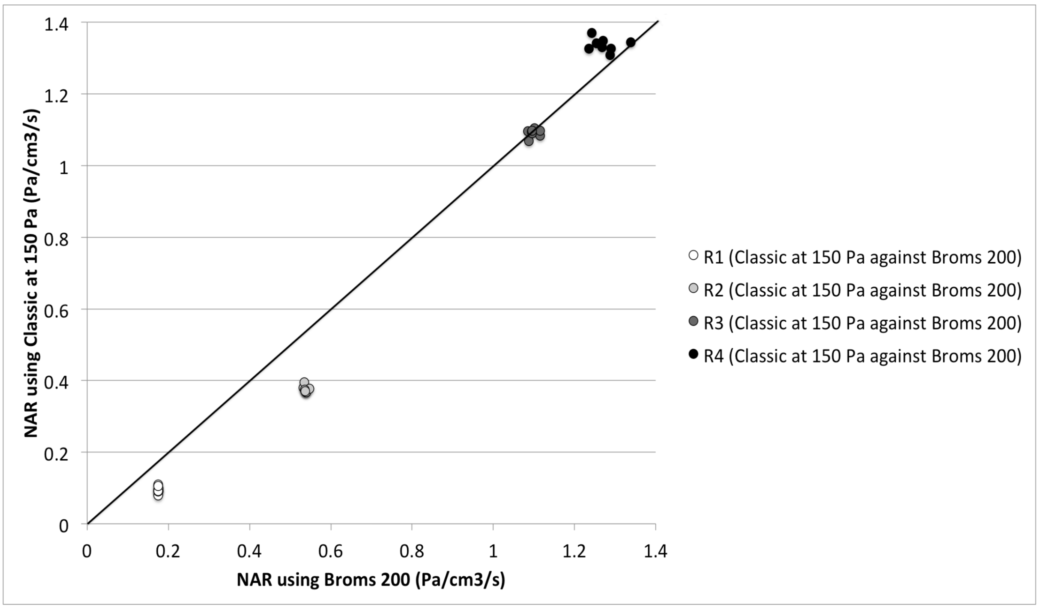


Figure 4.3.4 Scatter plot showing close agreements at low resistances (R1 and R2) between Broms 200 and classic at 75 Pa on the line of equality. At higher resistances (R3 and R4), there is poor agreement between both methods.

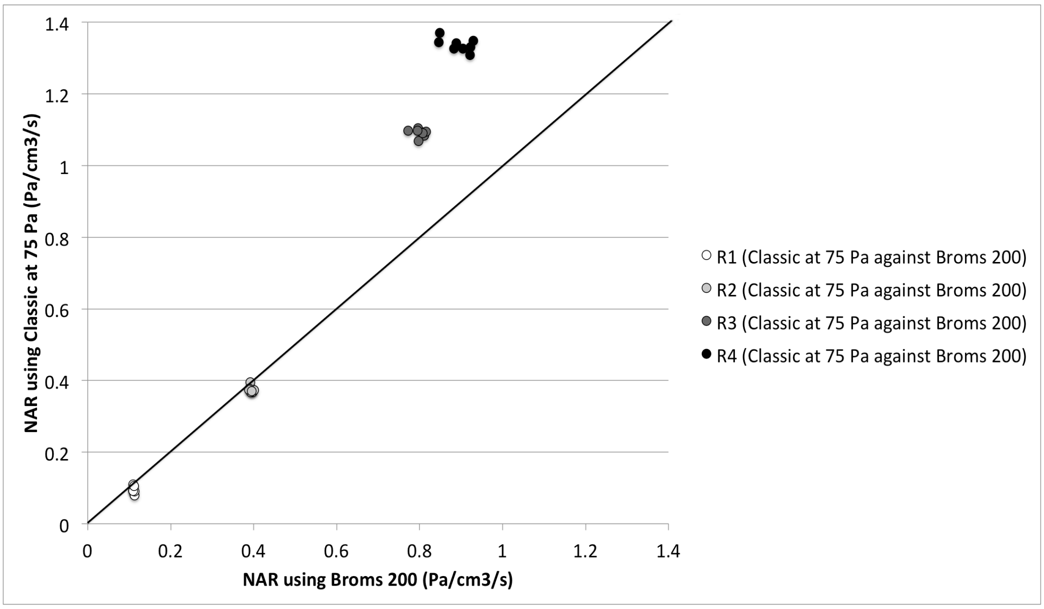


Figure 4.3.5 Bland-Altman plot for classic at 150 Pa and Broms 200 using model nose R1 (lowest resistance).

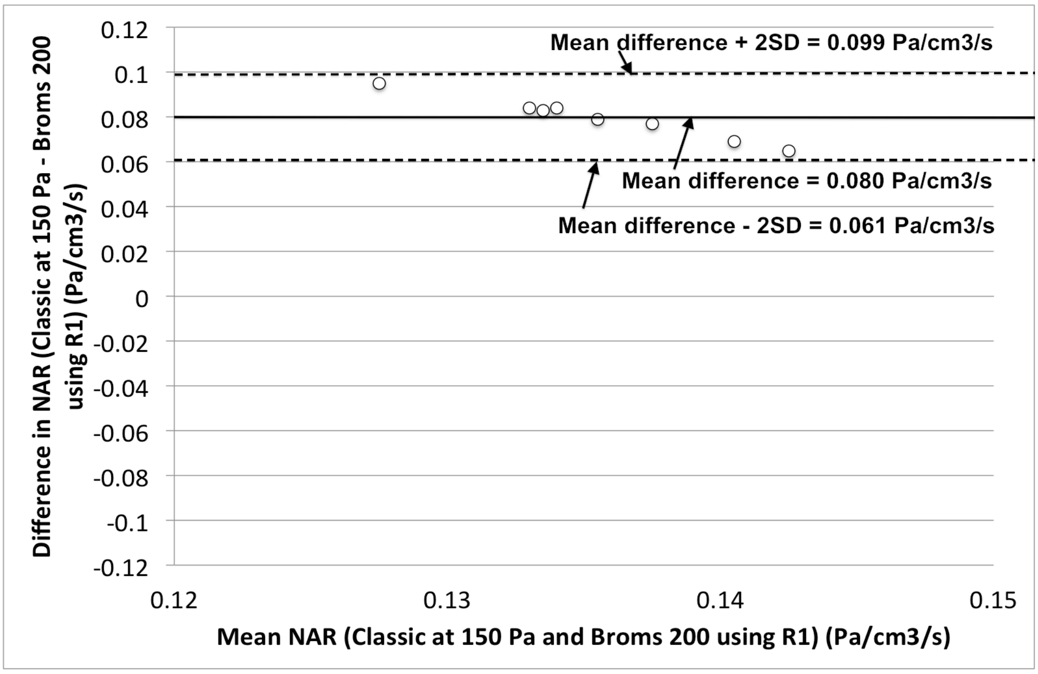


Figure 4.3.6 Bland-Altman plot for classic at 150 Pa and Broms 200 using model nose R2 (low resistance).

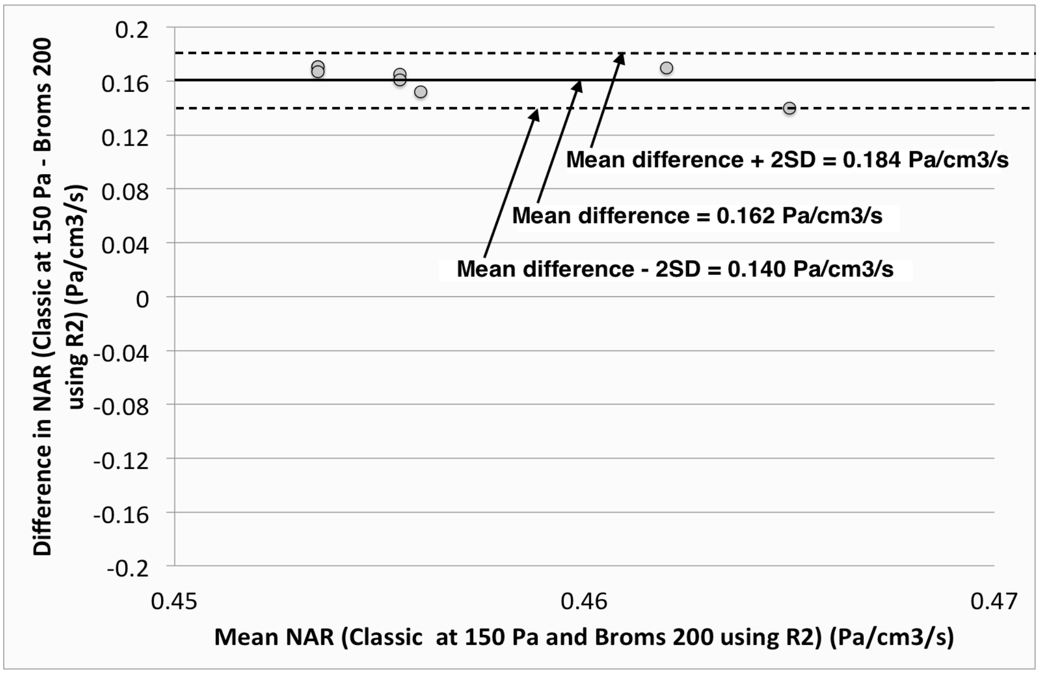


Figure 4.3.7 Bland-Altman plot for classic at 150 Pa and Broms 200 using model nose R3 (high resistance).

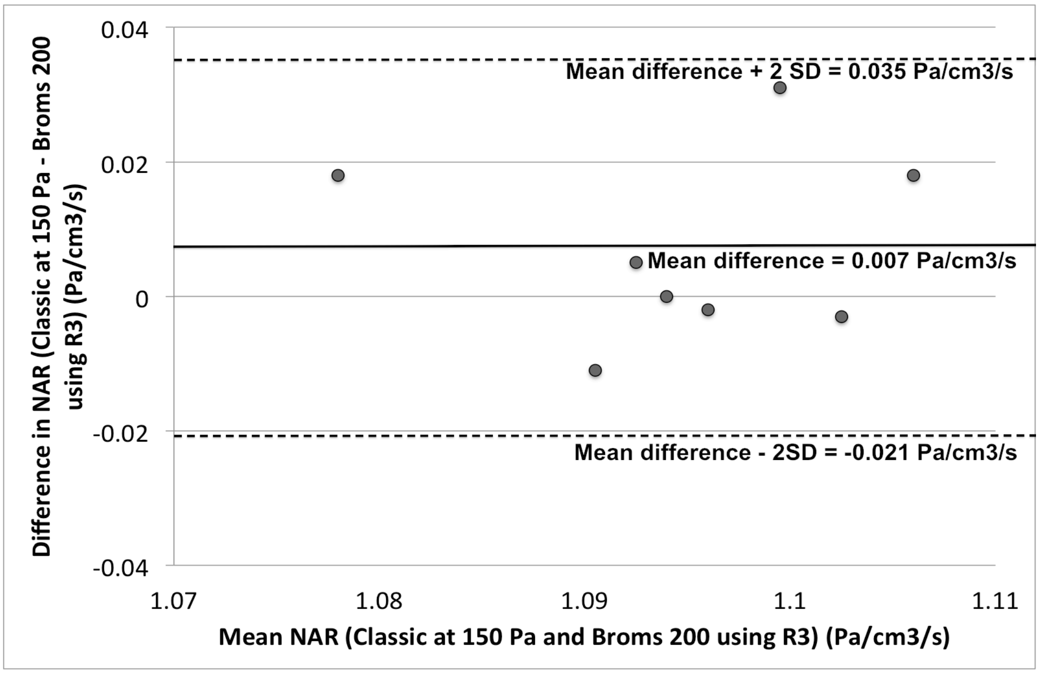


Figure 4.3.8 Bland-Altman plot for classic at 150 Pa and Broms 200 using model nose R4 (highest resistance).

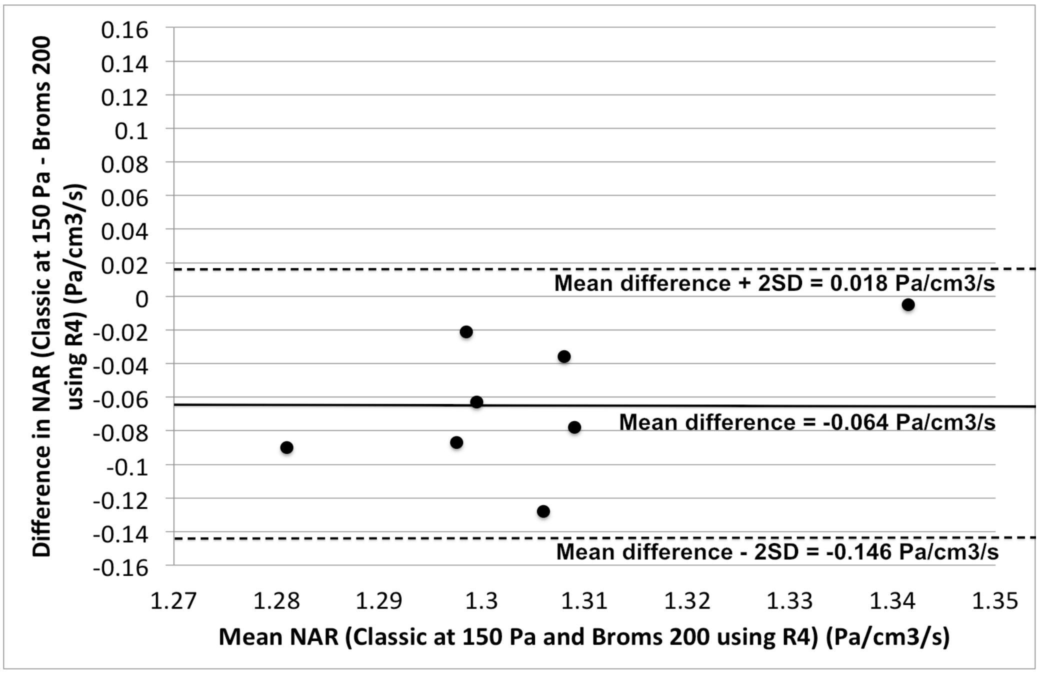


Figure 4.3.9 Bland-Altman plot for classic at 75 Pa and Broms 200 using model nose R1 (lowest resistance).

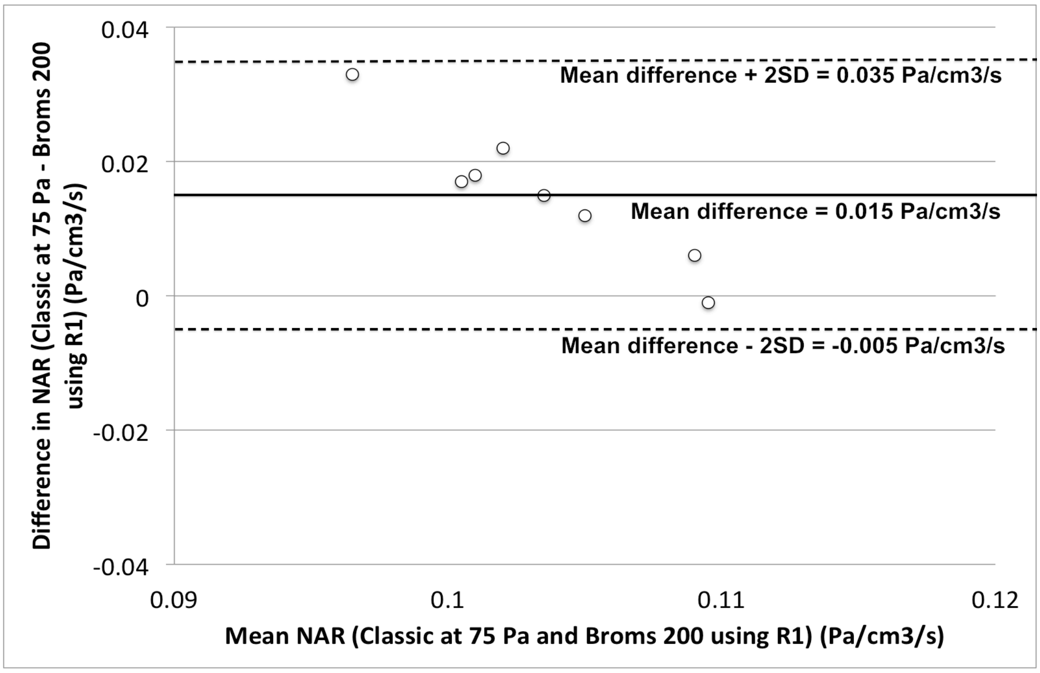


Figure 4.3.10 Bland-Altman plot for classic at 75 Pa and Broms 200 using model nose R2 (low resistance).

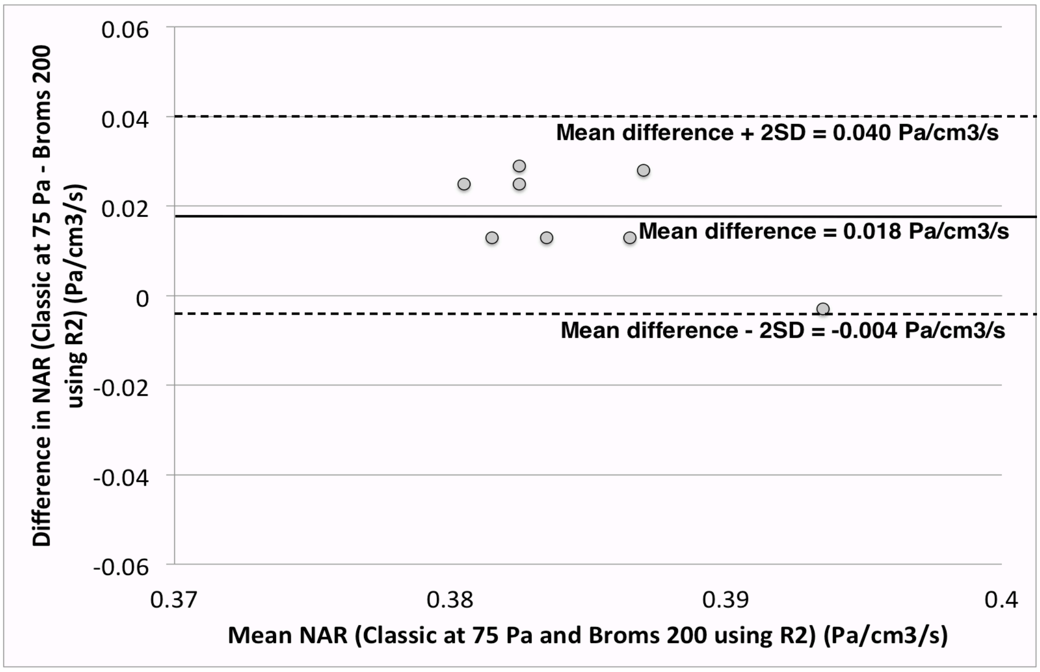


Figure 4.3.11 Bland-Altman plot for classic at 75 Pa and Broms 200 using model nose R3 (high resistance).

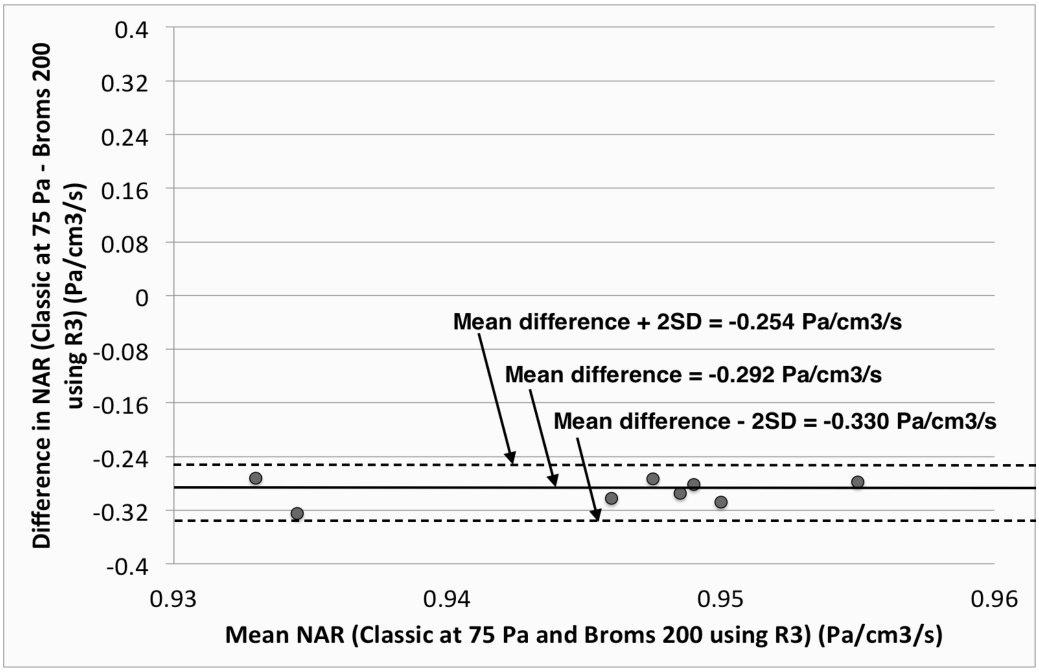
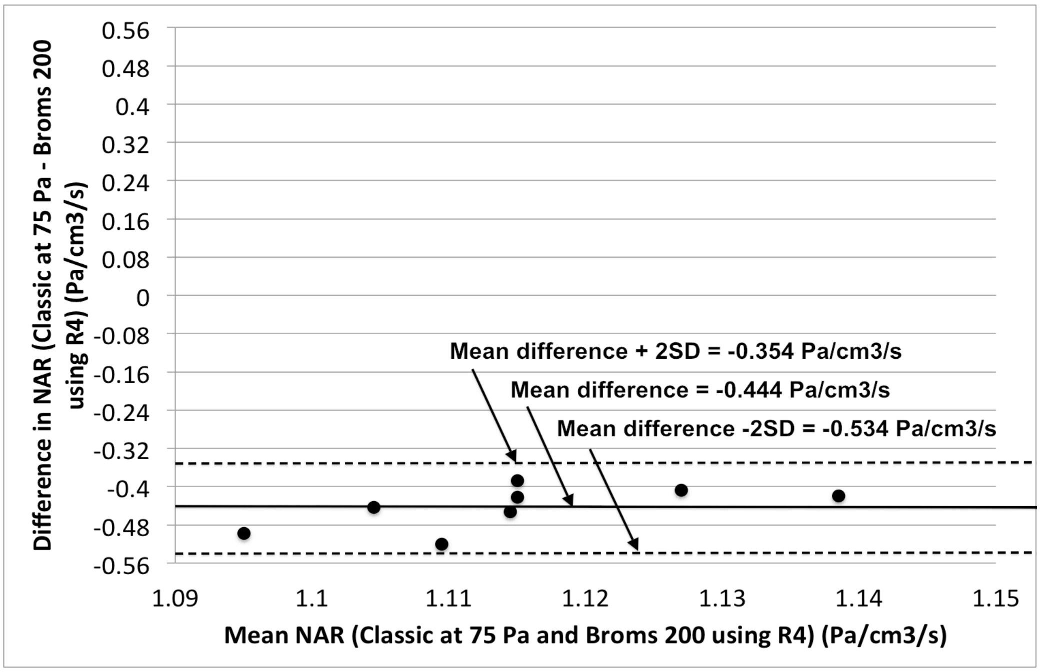


Figure 4.3.12 Bland-Altman plot for classic at 75 Pa and Broms 200 using model nose R4 (highest resistance).



4.4 Discussion

4.4.1 Comparison of the NAR values measured using both methods

Our study showed that when measuring low resistances (R1 and R2), the unilateral NAR calculated from Broms at radius 200 are not significantly different from those calculated with the classic method at 75 Pa. Also, when measuring higher resistances (R3 and R4), the resistances calculated from Broms at radius 200 are not significantly different from those calculated with the classic method at the higher sample pressure of 150 Pa. Both methods can also differentiate all four degrees of nasal resistances, which is in line with what was shown by Sipila et al.[29] in 1992.

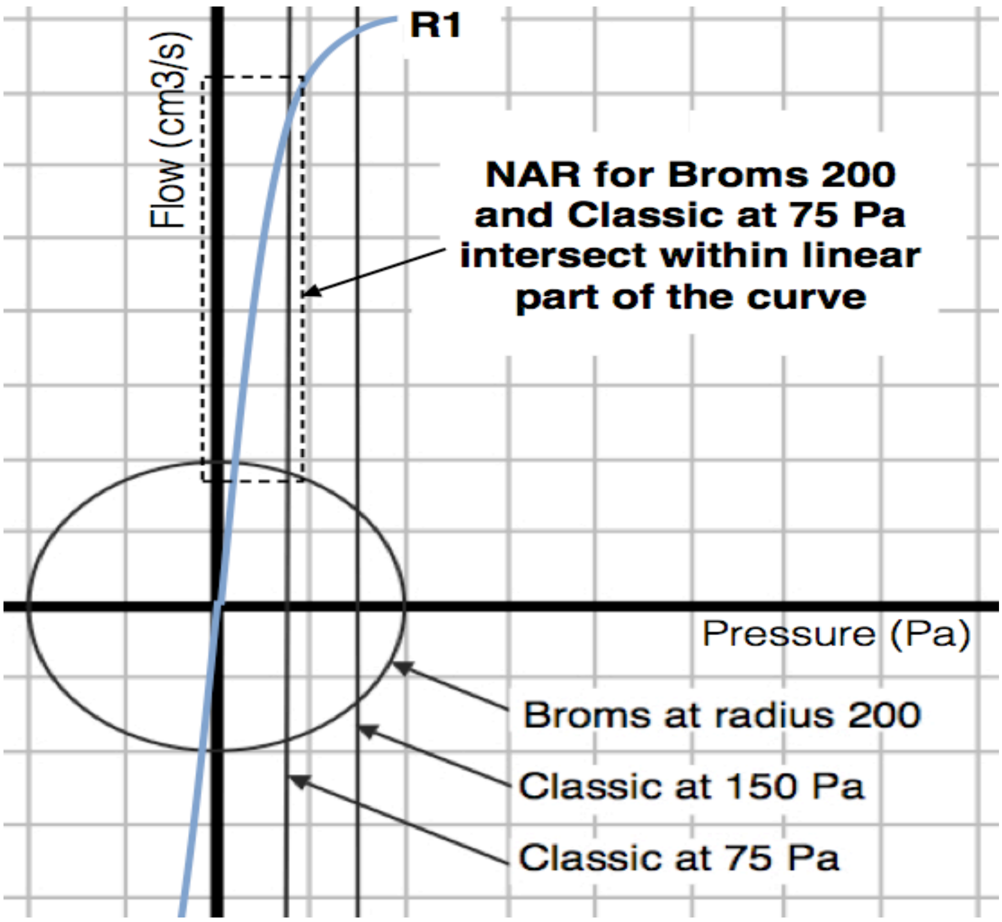
The relationship between the classic and Broms methods can best be seen by illustrating both calculations on the same pressure-flow curve as illustrated in Figures 4.4.1-4.4.5. One point to consider is that the calculated resistance varies along the length of the pressure-flow curve[18]. Over the linear part of the pressure-flow curve all points will calculate the same resistance, but in the curved part of the pressure-flow curve the calculated resistance increases because the pressure tends to increase more than the flow[18].

As the resistance increases from R1 to R4, the resultant pressure-flow curves intersect with Broms radius at 200 and the sample line for classic method (at 150 Pa and 75 Pa) at different points.

4.4.1.1 Model nose R1

One explanation for similarities of NAR values obtained from Broms 200 and classic method at 75 Pa with low resistance model nose (R1) may be due to the fact that the pressure-flow curve is almost a straight line from 0 to 75 Pa (Figure 4.4.1) before it starts to become curved. The intersections (where NAR values are calculated) with Broms radius at 200 and the classic at 75 Pa lie within this straight line of linear relationships at low resistances, therefore producing similar results of NAR values (Broms=0.10 Pa/cm^3/s, classic 75 Pa=0.11 Pa/cm^3/s). However, note that the line for classic method at 150 Pa intersects the pressure-flow curve out of this area of linearity and therefore gives a significantly different resistance from the Broms method (classic 150 Pa=0.18 Pa/cm^3/s).

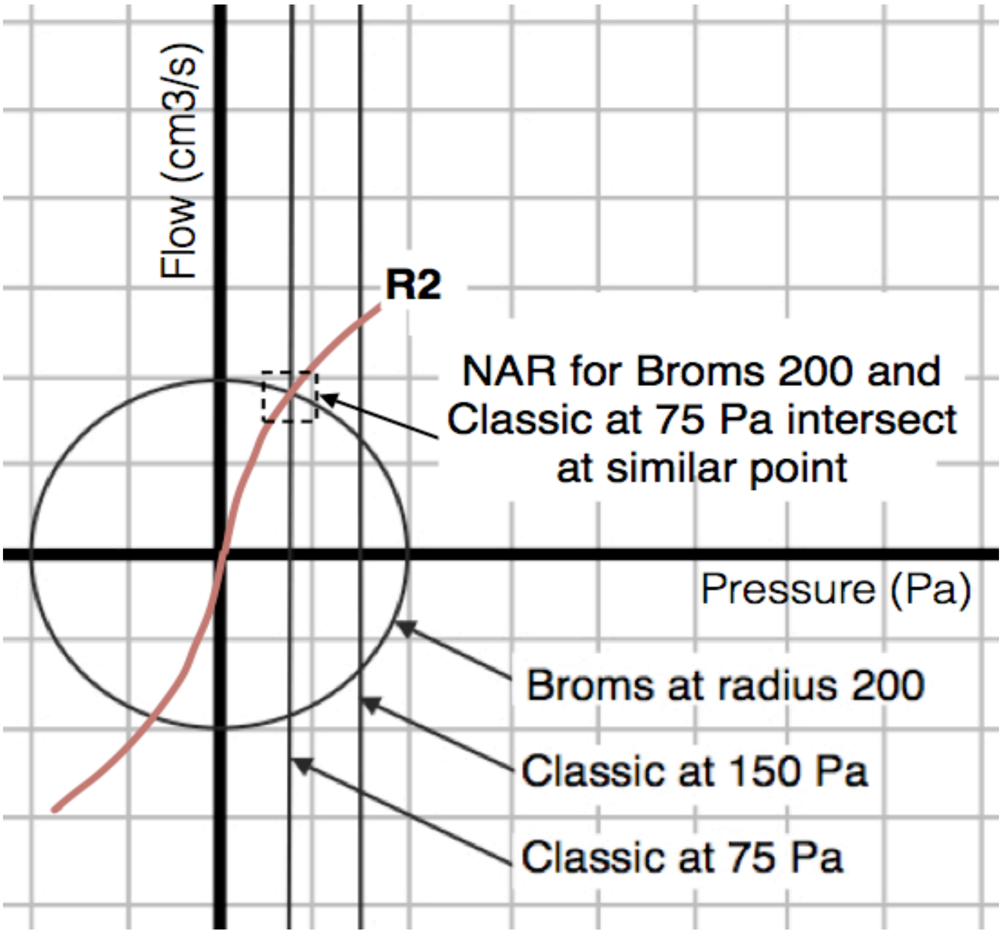
Figure 4.4.1 Illustration of the point of intersections of the pressure-flow curves in both methods when using model nose R1.



4.4.1.2 Model nose R2

With R2, the pressure-flow curve intersects with Broms radius at 200 and the sample line for classic method at 75 Pa at almost the same point (Figure 4.4.2), which explains the closely related NAR values, obtained with both methods at this point (Broms=0.38 Pa/cm^3/s, classic 75 Pa=0.39 Pa/cm^3/s). However, note that the line for classic method at 150 Pa intersects the pressure-flow curve at a different point and therefore gives a significantly different resistance from the Broms method (classic 150 Pa=0.54 Pa/cm^3/s).

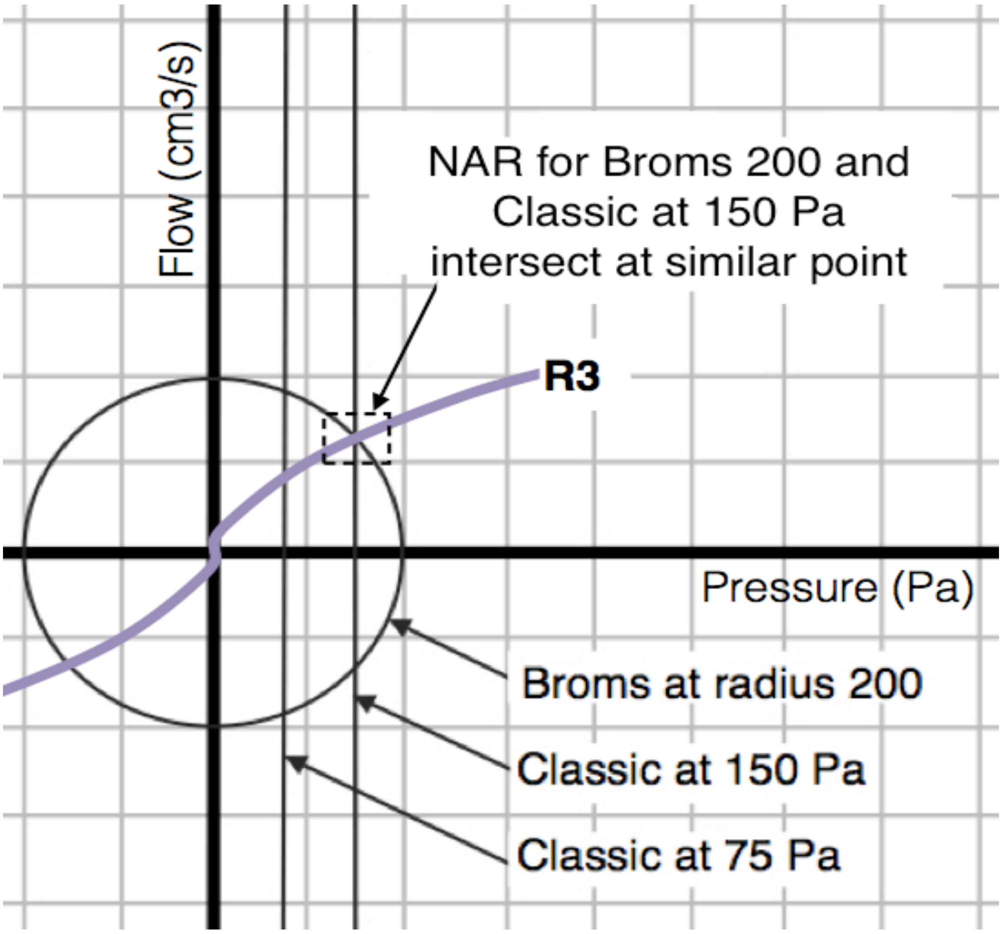
Figure 4.4.2 Illustration of the point of intersections of the pressure-flow curves in both methods when using model nose R2.



4.4.1.3 Model nose R3

With R3, the pressure-flow curve intersects with Broms radius at 200 and the line for classic method at 150 Pa at almost the same point (Figure 4.4.3), which explains the closely related NAR values, obtained with both methods at this point (Broms=1.09 Pa/cm^3/s, classic 150 Pa=1.10 Pa/cm^3/s). However, note that the line for classic method at 75 Pa intersects the pressure-flow curve at a different point and therefore gives a different resistance value (classic 75 Pa=0.80 Pa/cm^3/s).

Figure 4.4.3 Illustration of the point of intersections of the pressure-flow curves in both methods when using model nose R3.



4.4.1.4 Model nose R4

In high resistance model nose (R4), the pressure-flow curve intersects with Broms radius at 200 at a slightly higher pressure point compared to the intersection of the pressure-flow curve with the classic method at 150 Pa (Figure 4.4.4). Even though Mann-Whitney U test showed no significant difference between the two (Broms 200=1.34 Pa/cm^3/s, classic 150 Pa=1.27 Pa/cm^3/s), we can see from the line graph (Figure 4.3.2) that the lines for Broms 200 and classic 150 Pa begin to diverge with Broms 200 producing higher resistance values as confirmed in Bland-Altman plot (Figure 4.3.7). It is likely that if the study is repeated with bigger sample, a significant difference would be found between both measurements in high resistances, as indicated by simple extrapolation of the line graphs. Note that the line for classic method at 75 Pa intersects the pressure-flow curve at a different point and therefore gives a significantly different resistance value (classic 75 Pa=0.89 Pa/cm^3/s).

Figure 4.4.4 Illustration of the point of intersections of the pressure-flow curves in both methods when using model nose R4.

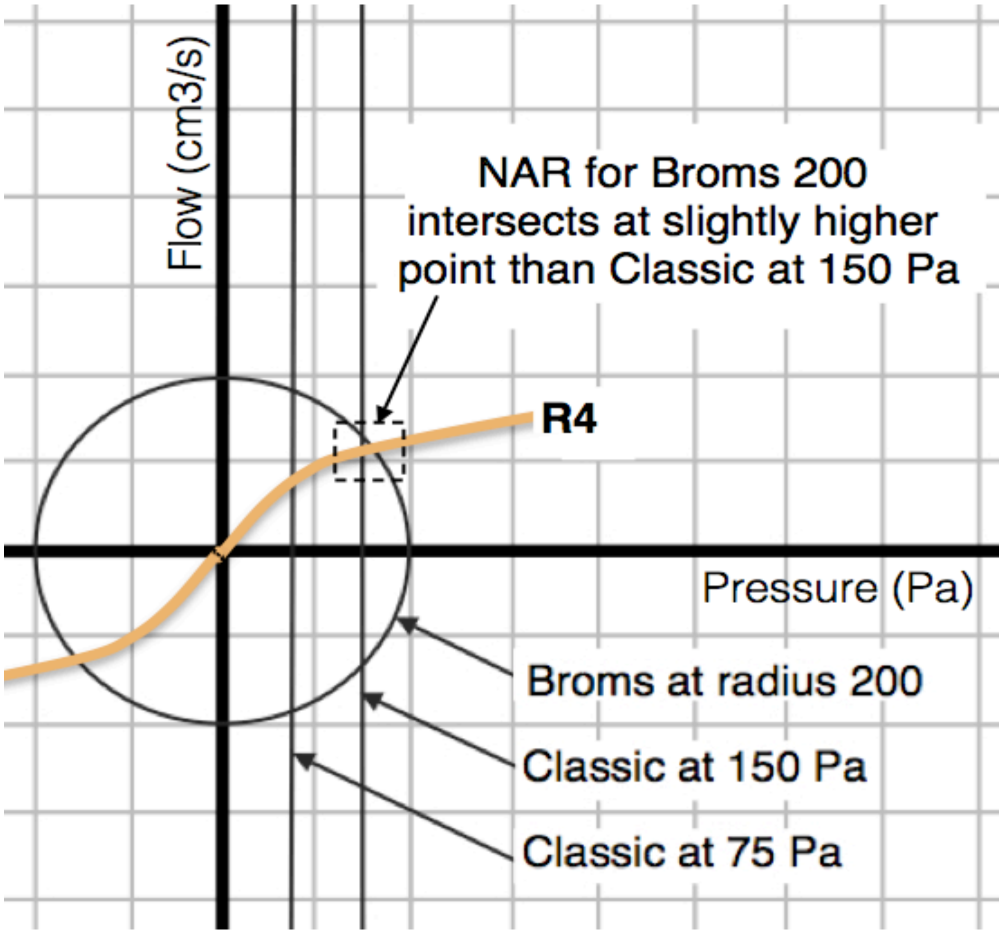
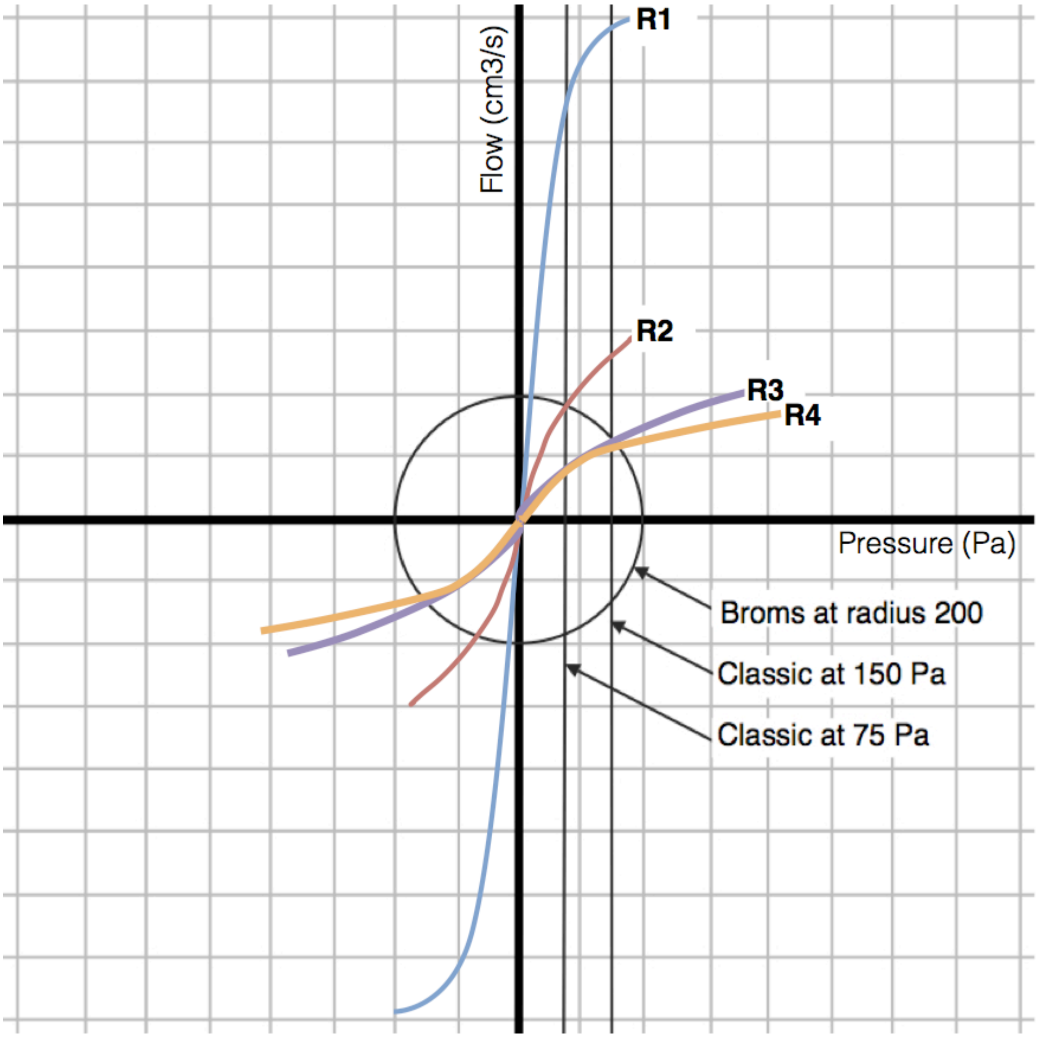


Figure 4.4.5 Illustration of the relationship for all the pressure-flow curves for the four resistances (R1-R4) when plotted onto a single graph.



4.4.2 Implications on study results

4.4.2.1 Magnitude of change in resistance after intervention

When using rhinomanometry to assess the efficacy of nasal surgery or medical procedures for treatment of nasal obstruction, the researcher will recruit patients suffering from nasal obstruction, and may expect that the treatment will decrease nasal resistance. The results of this study demonstrate that the resistance value measured in the patient and the magnitude of any change in resistance due to surgery or medical intervention is dependent on the method used to analyse the pressure-flow curve.

This is best illustrated by comparing the changes in resistance from R4 representing an obstructed nose to R2 representing a nose after some intervention such as nasal surgery. The changes in resistance can be compared in Figure 4.3.1 and 4.3.2. The change in resistance from R4 – R2, measured by Broms is from 1.34 Pa/cm^3/s to 0.38 Pa/cm^3/s (72% reduction in resistance); classic at 150 Pa from 1.27 Pa/cm^3/s to 0.54 Pa/cm^3/s (57% reduction in resistance); and for classic at 75 Pa from 0.89 Pa/cm^3/s to 0.39 Pa/cm^3/s (57% reduction in resistance). For the obstructed nose with a high resistance (represented by R4) the Broms method will tend to exaggerate any reduction in resistance (R4 - R2) due to an intervention such as surgery or medical treatment. Therefore, in this example a 72% reduction in nasal resistance as measured by the Broms method is equivalent to a 57% reduction in resistance measured by the classic method.

4.4.2.2 Measurement of total NAR

In active anterior rhinomanometry, flow is measured through the open nostril and narinochoanal pressure difference is measured from the contralateral occluded nostril[23]. Total resistance is then calculated using the formula[18]:

$$\frac{1}{R} = \frac{1}{r(\text{left})} + \frac{1}{r(\text{right})}$$

On the other hand, active posterior rhinomanometry measures airflow through both nostrils and measures both the narinochoanal and nasopharyngeal pressure difference through the pressure sensor placed at the back of the mouth[23]. This method measures total NAR without the need for further calculation[18].

The flow of air through both nostrils will always differ due to various anatomical, physiological and pathological factors. However, it is important to note that there is no partition at the back of the nose and one driving pressure in the posterior nares causes nasal airflow through both nasal passages. Therefore, in both anterior and posterior rhinomanometry, the same pressure difference should be used for both nostrils when measuring the total NAR. In fact, ISOANA also recommended that “preference should be given to the expression of the resistance at a fixed pressure rather than at a fixed flow” in 1984[22].

Calculation of total NAR using the classic method is more physiological because this fundamental principal is adhered where each side of the nose is measured at the same sample pressure either at 150 Pa or 75 Pa.

With the Broms method, the sample pressure can vary from just above zero to a maximum of 200 Pa in the most obstructed nose with airflow close to zero. Therefore left and right unilateral measurements with Broms may be made at two different pressures and this cannot occur with normal physiological airflow in the nose.

For example, using the results from our model noses, when combining two unilateral measurements like R4 (high resistance) and R2 (low resistance), there is a significant difference in total NAR calculated when using classic method at 150 Pa (0.378 Pa/cm^3/s), classic at 75 Pa (0.273 Pa/cm^3/s) and Broms 200 (0.293 Pa/cm^3/s).

For classic method, as long as the study uses the same fixed pressure gradient (150 Pa or 75 Pa) when measuring total NAR before and after intervention, the basic principle of rhinomanometry is followed. On the other hand, in Broms method, a different pressure gradient is used for each nostril even though they are of the same nose with the same driving pressure. This is not physiological, and this makes standardization and comparison difficult and is fundamentally flawed.

4.4.3 Comparison of the Broms and 4PR methods

A separate study comparing the NAR values of Broms and 4PR methods were not performed because Chapter 3 of this thesis have shown that the classic and 4PR methods produce the same NAR measurements. Therefore, a similar relationship between the classic and Broms method is expected for comparison of Broms and 4PR methods as well.

4.5 Conclusion

This study showed that the NAR measurements of Broms and classic method could either be similar or different depending on the level of nasal resistance and the fixed resistance gradient used in the classic method. Therefore, both methods cannot be used interchangeably for all patients in a study. Only one of the methods should be used consistently throughout the whole study and the method chosen should be taken into account when comparing results between different studies using different methods of measurements. When it comes to comparing total NAR values, Broms method does not adhere to the basic principle of rhinomanometry where the same pressure gradient drives the air flow through both nostrils and is therefore fundamentally flawed as a method of measuring total NAR.

CHAPTER 5

Reproducibility of rhinomanometry readings

5.1 Introduction

Rhinomanometers are tested and validated to provide stable measurements in laboratory and clinical setting[18]. Many studies have been conducted to investigate the reproducibility of rhinomanometry, looking at the coefficient of variation (CV) of repeated measurements[25,28] as described in Chapter 2.4.

The objective for this part of the study is to investigate the reproducibility of the NAR measurements obtained in this study to further evaluate the validity of the comparative results in Chapter 3 and Chapter 4.

5.2 Methods

5.2.1 Rhinomanometry

The unilateral NAR for nose models R1 and R4 were measured using the classic (at 150 Pa and 75 Pa), 4-phase rhinomanometry (at 150 Pa and 75 Pa) and Broms (at radius 200) method. The rhinomanometer and model noses used as well as the study protocol for measuring NAR was performed as described in Chapter 2. R1 and R4 were chosen to cover the full extremes of nasal resistances used in the initial study as described in Chapter 2.

5.2.2 Results analysis and statistics

Reproducibility of the measurements were analyzed using method suggested by Bland and Altman[103] with Bland-Altman plots and calculation of the Coefficient of Repeatability (CR). We expect 95% of differences to be less than two standard deviations as per definition of repeatability coefficient by British Standards Institution[103]. The coefficient of variation (CV) was also calculated.

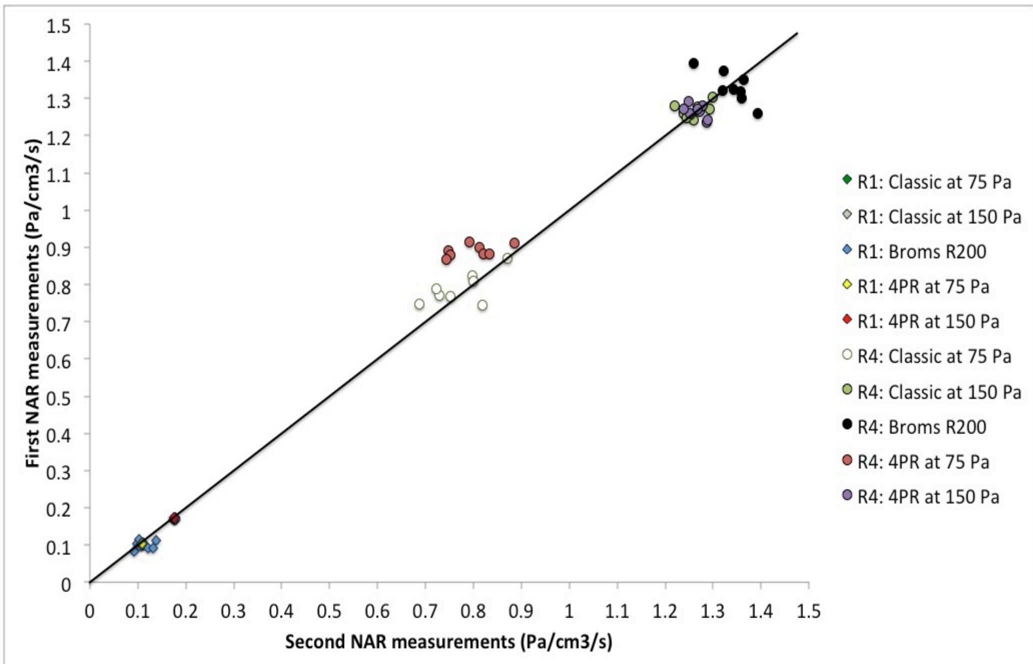
5.3 Results

5.3.1 Comparison of repeated NAR measurements

5.3.1.1 Scatter plot of agreement on the line of equality

When the results from day 1 and day 2 were plotted against each other (Figure 5.3.1), there was a high level of agreement between values obtained on both days on the line of equality.

Figure 5.3.1 Scatter plot of agreement for NAR values measured on both days on the line of equality showing high level of agreement.



5.3.1.2 Bland-Altman plot with Coefficient of Repeatability (CR) and coefficient of variation (CV)

The mean differences for both days (systematic error) in all measurements were very close to zero (mean of 0.005 Pa/cm^3/s for R1 and mean of -0.011 Pa/cm^3/s for R4); therefore repeatability can be assessed using this method.

Bland-Altman plot shows that all the scatter points lie within the 95% limits of agreement (random error) with no outliers. Figures 5.3.2 and 5.3.3 illustrates some examples of the Bland-Altman plots for methods that appeared most widely scattered on Figure 5.3.1 (R1 using Broms 200 and R4 using Broms 200)

The mean difference (systematic error) and Coefficient of Repeatability (CR) for all studies is presented in Table 5.3.1.

Figure 5.3.2 Bland-Altman plot for repeated measurements of R1 using Broms method at radius of 200.

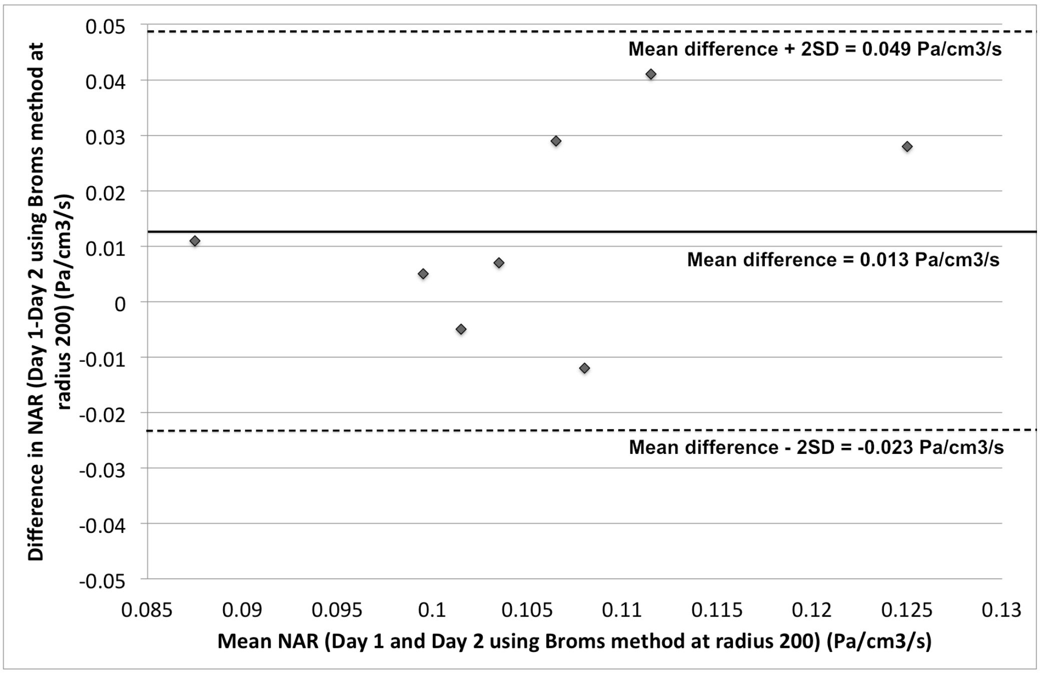


Figure 5.3.3 Bland-Altman plot for repeated measurements of R4 using Broms method at radius 200.

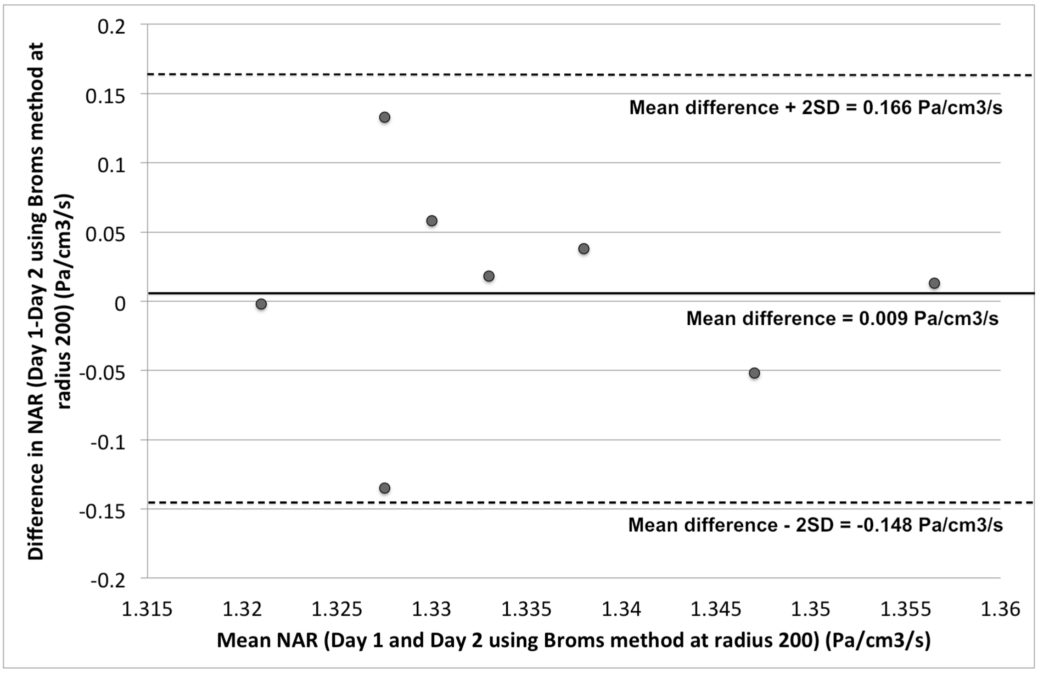


Table 5.3.1 Mean difference, Coefficient of Repeatability (CR) and coefficient of variation (CV) for all the studies using R1 and R4.

Method		Mean difference	Coefficient of Repeatability	Coefficient of variation
R1	classic 75 Pa	0.003	0.004	1.80%
	classic 150 Pa	0.002	0.002	0.74%
	Broms 200	0.013	0.036	14.37%
	4PR 75 Pa	0.003	0.002	1.88%
	4PR 150 Pa	0.002	0.001	0.49%
R4	classic 75 Pa	-0.018	0.089	6.51%
	classic 150 Pa	-0.009	0.051	1.85%
	Broms 200	0.009	0.157	2.99%
	4PR 75 Pa	-0.093	0.086	7.06%
	4PR 150 Pa	0.002	0.067	1.41%

5.4 Discussion

5.4.1 Coefficient of Repeatability (CR)

The relative reliability of the measurements was illustrated on the scatter plot of agreement (Figure 5.3.1) showing a high level of agreement between values obtained on both days on the line of equality.

The Bland-Altman plots for all the repeated measurements have all the scatter points lying within the 95% limit of agreement with no outliers. The absolute reliability was quantified using the Coefficient of Repeatability (CR), below which 95% of test-retest measurement should lie, and represent the smallest change required to represent a true change.

For example, at R1 using classic method at 150 Pa, a change of at least 0.002 Pa/cm^3/s at repeated measurement (for example, after a nasal surgery) is required for the investigator to be 95% confident that it was a true change. If the change in nasal airway resistance is less than 0.002 Pa/cm^3/s, it might simply be due to measurement noise[104] or inherent mechanical inaccuracy[105].

5.4.1 Coefficient of variation (CV)

The "acceptable" CV values for reproducibility has been described in various studies and ranges from 5-17%[18,28,31]. In this study, the coefficient of variation for repeated measurements ranges from 0.49-14.37%, therefore, further validate the reliability of the measurements in this study.

5.5 Conclusion

This study showed that the repeated NAR measurements 24 hours apart have high level of agreement (low mean difference, CR and CV values). Therefore, it further validates the comparative results presented in Chapter 3 and Chapter 4.

CHAPTER 6

Conclusions

This thesis compared the actual unilateral nasal airway resistance (NAR) measurements obtained from three different rhinomanometry methods in order to further improve our understanding of their relationship.

The first study comparing the classic and 4-phase rhinomanometry methods showed that there was no statistically significant difference ($U>U_{critical}$ for sample size, $p>0.05$; r_s =1.000, $p<0.001$; Bland-Altman plots: good agreement with narrow limits of agreement) between the readings obtained from both methods at 150 Pa and 75 Pa, despite using different parameters and methods of generating data. Therefore, both methods can be used interchangeably, although the simpler classic method is preferred based on the principle of Ockham's razor.

The second study comparing the classic and Broms 200 method showed that at lower resistances (R1 and R2 model noses), the Broms 200 and classic at 75 Pa produce similar results. On the other hand, at higher resistances, Broms 200 and classic at 150 Pa generate similar NAR measurements. Therefore, both methods cannot be used interchangeably for all patients in a study. The magnitude of change in NAR differs between classic and Broms, depending on the level of nasal resistances. Therefore, the rhinomanometry method chosen should also be taken into account when comparing results between different studies using different rhinomanometry methods.

Lastly, to validate the results of the studies in this thesis, the reproducibility of measurements was also evaluated. Bland-Altman plots showed high level of agreement between measurements taken in both days and CV value ranges from 0.49-14.3%, which were acceptable levels of reproducibility.

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Publications

Publications of this research study:

1. Wong EH, Eccles R. Comparison of classic and 4-phase rhinomanometry methods, is there any difference? *Rhinology 2014;* **(In print)**

2. Wong EH, Eccles R. Comparison of the classic and Broms methods of rhinomanometry using model noses. *Eur Arch Otorhinolaryngol* 2014; **(Published online, awaiting printed version)**

Eur Arch Otorhinolaryngol
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RHINOLOGY

Comparison of the classic and Broms methods of rhinomanometry using model noses

Eugene H C Wong · Ron Eccles

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Abstract Calculation of nasal airway resistance (NAR) using rhinomanometry can be obtained using different methods of analysis of the pressure–flow curve. The two commonest methods for measuring NAR in rhinomanometry are the classic method at 75 and 150 Pa and the Broms method at radius 200. The objective of this study was to compare the unilateral NAR values measured using both classic and Broms method over four artificial model noses (R1, R2, R3 and R4). The study found that at low resistances (R1 and R2), NAR measurements of Broms were not significantly different from measurements of classic method at 75 Pa but were significantly different from measurements of classic method at 150 Pa. At high resistances (R3 and R4), NAR measurements of Broms were not significantly different from measurements of classic method at 150 Pa but were significantly different from measurements of classic method at 75 Pa. The magnitude of any change in resistance due to surgery or medical intervention is therefore also dependent on the method used to analyze the pressure–flow curves, with bigger change observed in Broms method at certain level of nasal resistances compared to classic measurements in the same patient. In conclusion, nasal airway resistance is not a standardized measurement like blood pressure. Clinicians need to be careful when comparing unilateral measurements of resistance from the classic and Broms methods because the two methods can give either similar or different measurements depending on the level of nasal resistance.

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Keywords Classic · Broms · Comparison · Rhinomanometry

Introduction

Rhinomanometry is an objective way to measure nasal airflow during normal breathing, expressed as the nasal airway resistance (NAR) [1]. The clinician and the researcher studying the effects of surgery or other treatments on the nose are interested in obtaining a single numerical value that represents NAR but the problem is that there are various methods of analyzing the pressure–flow curve to obtain NAR in rhinomanometry.

Classically, NAR is calculated using the formula $R = \Delta p/V°$ (R = resistance, Δp = pressure difference, $V°$ = airflow) [2]. This is based on the fact that during quiet breathing, the pressure–flow curve is almost a straight line but this changes to a curved line at higher pressures and flows [1]. This means the resistance calculated varies according to where the measurements are taken [1]. The International Standardization Committee on Objective Assessment of the Nasal Airway (ISOANA) recommended that NAR should be calculated at a reference pressure of 150 or 75 Pa in 1984 [3] and 2005 [2].

The other commonly used method in rhinomanometry is the Broms method where resistance is measured on a polar coordinate system using the point of intersection between the pressure–flow curve and a circle drawn at radius of 200 [4]. This is based on Broms' finding that all curves reached and crossed the circle with that radius ("physiological range of flow and pressure"), making it possible to define a standardized condition using this intersection point [4]. The ISOANA also agreed that NAR measured with Broms method was to be considered as equally good as measurements taken using the classic method in 1984 [3].

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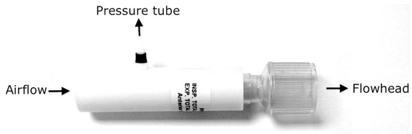

Fig. 1 Example of model nose used in this study

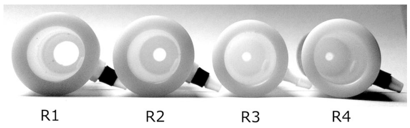

Fig. 2 Four model noses of different resistances (decreasing diameter)

Few studies on comparison of different resistance parameters used in rhinomanometry have been carried out in the past [5]. For example, Eichler and Lenz compared different coefficients and units in rhinomanometry in 1985 [6] although no patient material was presented [5]. In 1991, Sipila et al. compared different mathematical models (including classic and Broms) to investigate their ability to classify different degrees of nasal obstruction as well as their reproducibility of readings [5]. They found that Broms at radius 200 was calculable in all cases with better reproducibility compared to the classic method taken at 150 Pa or 150 mls/s [5].

The aim of this study is to compare the unilateral NAR values measured using both the classic and Broms methods across a range of resistances provided by four model noses. This is to further improve our understanding of the relationship between the two most commonly used methods.

Materials and methods

Artificial model noses

The model noses used in this study were developed in 1997 [7] and have been used since then as calibration devices for rhinomanometers, and are marketed as 'Rhinocal' units (GM instruments, Glasgow, UK). They consist of cylindrical bodies of different fixed resistances (diameters) and attachments for pressure tube, flowhead and airflow as illustrated in Fig. 1.

Model noses were used instead of human volunteers to eliminate the variability in human nasal resistance that is associated with many factors such as the nasal cycle. Four different model noses were used in this study with increasing resistances (decreasing diameters) to represent a wide range of human nasal resistances as illustrated in Fig. 2. The fixed resistances of the units were approximately 0.18 Pa/cm^3/s (R1), 0.54 Pa/cm^3/s (R2), 1.10 Pa/cm^3/s (R3) and 1.29 Pa/cm^3/s (R4) when measured at 150 Pa using the classic method.

Rhinomanometry

An NR6-2 Rhinomanometer Clinical/Research model (GM Instruments, Glasgow UK) was used for all the measurements

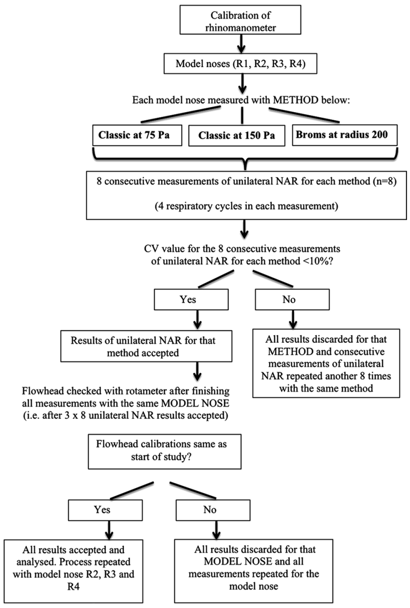

Fig. 3 Flowchart illustrating the study protocol

in this study. It uses NARIS software that allows nasal resistance to be calculated using the classic (at 150 and 75 Pa), Broms (at radius 200) and four-phase rhinomanometry methods. Only the first two methods were used in this study.

The rhinomanometer was calibrated at the beginning of each study day using a flow meter (or rotameter) for calibration of airflow and a slopping paraffin manometer for calibration of pressure. Measurements of NAR were taken using active rhinomanometry where airflow was provided by normal quiet inhalation and exhalation from the mouth through the model noses to mimic human respiration in a

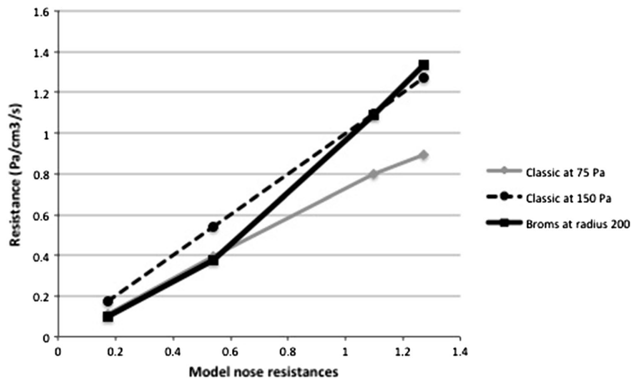

Fig. 4 Mean NAR values obtained using classic (at 75 and 150 Pa) and Broms method. The model nose resistances given on the *X*-axis were calculated using the classic method at 150 Pa

normal rhinomanometry study. The rhinomanometer is programmed so that each measurement of NAR consists of the mean value obtained from four respiratory cycles.

For each model nose, unilateral NAR was measured using the classic (at 75 and 150 Pa) and Broms method (at radius 200). For each of the method, eight consecutive sets of unilateral NAR measurements were obtained and the coefficient of variation (CV) was calculated. In our daily usage of rhinomanometry, a CV of <10 % for repeated measurements is used to validate the measurements.

The flowheads were calibrated using the flow meter at the end of each series of measurements with each model nose. All the results obtained from the same model nose were to be discarded if there were any discrepancies in airflow calibration between the start and finish of use of each model nose, which may be the result of condensation or accumulation of moisture in the flowhead from the expired air. Figure 3 illustrates our study protocol in a flowchart.

All measurements and calibration of the rhinomanometer were standardized according to the study site standard operating procedures (SOP) in a quiet laboratory room at room temperature of 25 ± 1 °C.

Results analysis and statistics

The statistical package for the Social Sciences version 20 (IBM SPSS statistics 20) and the Microsoft Excel 2011 version 14.1.2 for the Macintosh platform were utilized for statistical analysis. Each NAR value consisted of eight measurements ($n = 8$) and mean ± SD was used as a summary measure for illustrations. As NAR usually has a skewed non-parametric distribution, Mann–Whitney *U* test was used to determine statistical significance and a value of $p < 0.05$ was considered significant.

Results

Flowhead calibration

There were no discrepancies in airflow calibration found between the start and finish of usage of each model nose. Therefore, no measurement series were discarded.

Coefficient of variation

The CV value for all the measurements of resistance was <10 %; therefore, no measurements need to be repeated.

Comparison of both methods

We only present the inspiratory measurements, as this is the data used in calculation of NAR in practice.

Figures 4 and 5 illustrate the comparison of NAR values obtained using both the classic and Broms method in each category. Both the line graphs and bar charts showed that the NAR values obtained with Broms method at radius 200 were very similar to the values obtained with classic method at 75 Pa at lower resistances. This correlation changed at higher resistances where the NAR values calculated from Broms became similar to values obtained with classic method at 150 Pa.

Mann–Whitney *U* test confirmed the observations from the line graphs and bar charts, showing no significant difference between the NAR values obtained from Broms and classic at 75 Pa at lower resistances (R1 and R2); and between NAR values of Broms and classic at 150 Pa at higher resistances (R3 and R4). On the other hand, there was significant difference shown between NAR values obtained from Broms and classic at 150 Pa at lower

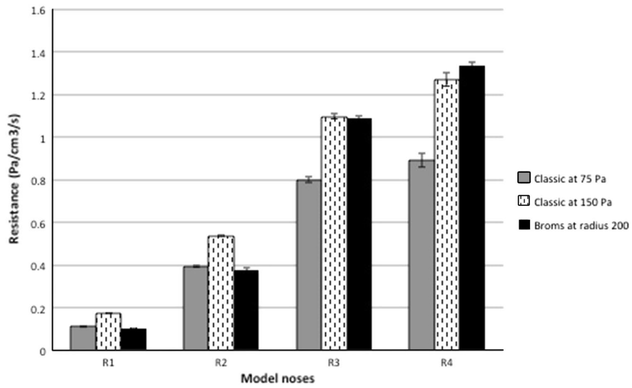

Fig. 5 Mean NAR values obtained using classic (at 75 and 150 Pa) and Broms method. *Error bars* (±2 standard deviations) are shown

Table 1 Mann–Whitney *U* values ($U_{critical} = 13$ for sample size) and *p* values for each comparison for the four model nose resistances R1–R4

Mann–Whitney	Classic 75 Pa vs Broms 200				Classic 150 Pa vs Broms 200			
U test	R1	R2	R3	R4	R1	R2	R3	R4
U value	32	32	0	0	0	0	32	21
p value	1.00	1.00	0.01	0.01	0.01	0.01	1.00	0.28
Conclusion (A/R)	A	A	R	R	R	R	A	A

A accept H0 (no statistically significant difference), *R* reject H0 (there is statistically significant difference)

resistances (R1 and R2); and between NAR values of Broms and classic at 75 Pa at higher resistances (R3 and R4) (Table 1).

Discussion

Our study showed that when measuring low resistances (R1 and R2), the unilateral NAR calculated from Broms at radius 200 is not significantly different from those calculated with the classic method at 75 Pa. Also, when measuring higher resistances (R3 and R4), the resistances calculated from Broms at radius 200 are not significantly different from those calculated with the classic method at the higher sample pressure of 150 Pa.

The relationship between the classic and Broms methods can best be seen by illustrating both calculations on the same pressure–flow curve as illustrated in Fig. 6. One point to consider is that the calculated resistance varies along the length of the pressure–flow curve [1]. Over the linear part of the pressure–flow curve all points will calculate the same resistance, but in the curved part of the pressure–flow curve the calculated resistance increases because the pressure tends to increase more than the flow due to the fact that as airflow becomes more turbulent, it eventually reaches a maximum flow that cannot be exceeded even with greater pressures [1].

One explanation for similarities of NAR values obtained from Broms 200 and classic method at 75 Pa with low resistance model nose (R1) may be due to the fact that the pressure–flow curve is almost a straight line from 0 to 75 Pa (Fig. 6 R1 curve) before it starts to become curved. The intersections (where NAR values are calculated) with Broms' radius at 200 and the classic at 75 Pa lie within this straight line of linear relationships at low resistances, therefore, producing similar results of NAR values (Broms = 0.10 Pa/cm^3/s, Classic 75 Pa = 0.11 Pa/cm^3/s). However, note that the line for classic method at 150 Pa intersects the pressure–flow curve out of this area of linearity and therefore gives a significantly different resistance from the Broms method (Classic 150 Pa = 0.18 Pa/cm^3/s).

With R2, the pressure–flow curve intersects with Broms' radius at 200 and the sample line for classic method at 75 Pa at almost the same point (Fig. 6 R2 curve), which explains the closely related NAR values, obtained with both methods at this point (Broms = 0.38 Pa/cm^3/s,

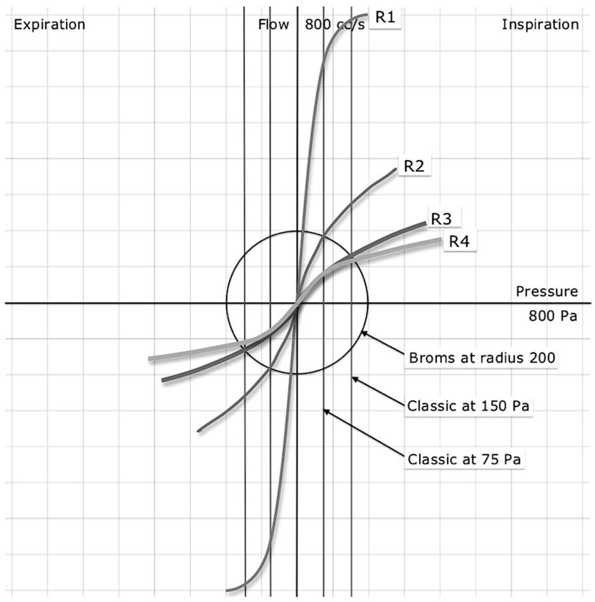

Fig. 6 Illustration of the relationships for all the pressure–flow curves for the four resistances R1–R4 when plotted onto a single graph

Classic 75 Pa = 0.39 Pa/cm^3/s). However, note that the line for classic method at 150 Pa intersects the pressure–flow curve at a different point and therefore gives a significantly different resistance from the Broms method (Classic 150 Pa = 0.54 Pa/cm^3/s).

With R3, the pressure–flow curve intersects with Broms' radius at 200 Pa and the line for classic method at 150 Pa at almost the same point (Fig. 6 R3 curve), which explains the closely related NAR values, obtained with both methods at this point (Broms = 1.09 Pa/cm^3/s, Classic 150 Pa = 1.10 Pa/cm^3/s). However, note that the line for classic method at 75 Pa intersects the pressure–flow curve at a different point and therefore gives a different resistance value (Classic 75 Pa = 0.80 Pa/cm^3/s).

In high resistance model nose (R4), the pressure–flow curve intersects with Broms' radius at 200 at a slightly higher pressure point compared to the intersection of the pressure–flow curve with the classic method at 150 Pa (Fig. 6 R4 curve). Even though our study results show no significant difference between the two (Broms 200 = 1.34 Pa/cm^3/s, Classic 150 Pa = 1.27 Pa/cm^3/s), we can see from the line graph (Fig. 4) that at higher resistances, the lines for Broms 200 and Classic 150 Pa begin to diverge with Broms 200 producing higher resistance values. We believe that if we repeat the study with a bigger sample, we may find a significant difference between both measurements in high resistance noses, as indicated by simple extrapolation of the line graphs. Note that the line for classic method at 75 Pa intersects the pressure–flow curve at a different point and therefore gives a significantly different resistance value (Classic 75 Pa = 0.89 Pa/cm^3/s).

When using rhinomanometry to assess the efficacy of nasal surgery or medical procedures for treatment of nasal obstruction, the researcher will recruit patients suffering from nasal obstruction, and may expect that the treatment will decrease nasal resistance. The results of this study demonstrate that the resistance value measured in the patient and the magnitude of any change in resistance due to surgery or medical intervention is dependent on the method used to analyze the pressure–flow curve. This is best illustrated by comparing the changes in resistance from R4 representing an obstructed nose to R2 representing a nose after some intervention such as nasal surgery. The changes in resistance can be compared in Figs. 4 and 5. The change in resistance from R4–R2, measured by Broms is from 1.34 to 0.38 Pa/cm^3/s (72 % reduction in resistance), classic at 150 Pa from 1.27 to 0.54 Pa/cm^3/s (57 % reduction in resistance), and for classic at 75 Pa from 0.89 to 0.39 Pa/cm^3/s (57 % reduction in resistance). For the obstructed nose with a high resistance (represented by R4) the Broms method will tend to exaggerate any reduction in resistance (R4–R2) due to an intervention such as surgery or medical treatment. Therefore, in this example a 72 % reduction in nasal resistance as measured by the Broms method is equivalent to a 57 % reduction in resistance measured by the classic method.

Conclusion

Nasal airway resistance is not a standardized measurement like blood pressure. Clinicians need to be careful when comparing unilateral measurements of resistance from the classic and Broms methods because the two methods can give either similar or different measurements depending on the level of nasal resistance.

Acknowledgments We would like to thank Eric Greig (GM Instruments, UK) for providing us with the model noses (Rhinocal resistance units) for this study.

Conflict of interest None.

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1. Eccles R (2011) A guide to practical aspects of measurement of human nasal airflow by rhinomanometry. Rhinology 49:2–10
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Appendices

Appendix 1: Examples of rhinomanometry result sheets

1.1 Classic method

NARIS NR6 - 2

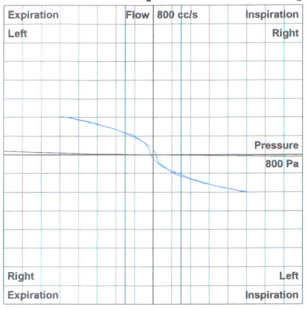
R4
CLASSIC P150 1

gm instruments

Date: 20/09/2013 13:33:07

Initials
Study Number
Subject Number
Time Point
Operators Initials

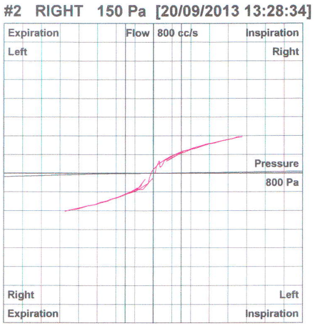
#1 LEFT 150 Pa [20/09/2013 13:28:25]



Standard	Inspiration	Expiration
Mean Flow	118.2	120.7
Mean Resistance	1.270	1.243
Max deviation	0.040	0.043
Respirations	4	4

Rohrer	Inspiration	Expiration
K1	0.230	0.186
K2*1000	13.361	12.375
SDres	13	12

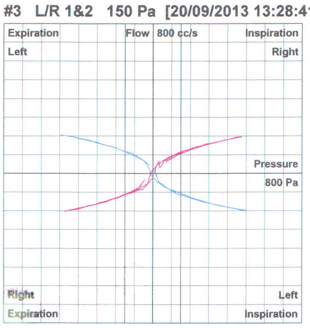
#2 RIGHT 150 Pa [20/09/2013 13:28:34]



Standard	Inspiration	Expiration
Mean Flow	116.5	119.0
Mean Resistance	1.288	1.261
Max deviation	0.028	0.041
Respirations	4	4

Rohrer	Inspiration	Expiration
K1	0.183	0.138
K2*1000	13.125	12.108
SDres	11	11

#3 L/R 1&2 150 Pa [20/09/2013 13:28:41]



Standard	Insp L	Exp L	Insp R	Exp R	Insp Total	Exp Total
Mean Flow	118.2	120.7	116.5	119.0	234.7	239.8
Mean Resistance	1.270	1.243	1.288	1.261	0.639	0.626
Max deviation	0.040	0.043	0.028	0.041		
Respirations	4	4	4	4		
Right > Left by	1%				LAP 0.7%	LAP 0.7%

Diagnostic		75 Pa	% Inc.	150 Pa	% Inc.	300 Pa
Flow [cc/s]	L	90	31%	118	35%	159
	R	86	35%	116	37%	159
	L+R	176		234		318
	L/R	1.047		1.017		1.000
Resistance	L	0.835	52%	1.270	48%	1.881
	R	0.868	48%	1.288	46%	1.883
	Total	0.426		0.639		0.941

Common Cold Research Centre - NARIS-32E - 1 - V3.0.0.968

1.2 4-phase rhinomanometry method

NARIS NR6 - 2

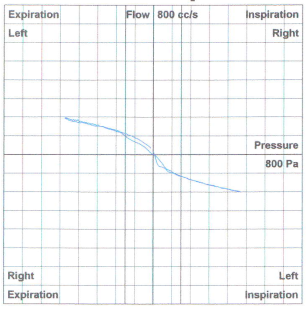
R4
4-PHASE P150 ①

gm instruments

Date: 20/09/2013 13:56:29

Initials
Study Number
Subject Number
Time Point
Operators Initials

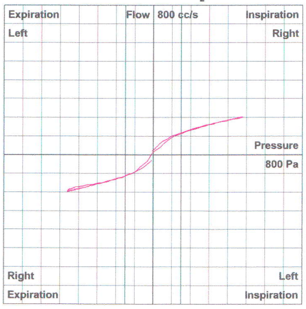
#13 LEFT 150 Pa 4PR [20/09/2013 13:53:11]



4PR	Inspiration	Expiration	Total
Log Vertex Resistance	1.362	1.378	-
Log Effective Resistance	1.321	1.335	1.328

Standard	Inspiration	Expiration
Mean Flow	118.3	115.8
Mean Resistance	1.268	1.296
Max deviation	0.018	0.027
Respirations	4	4

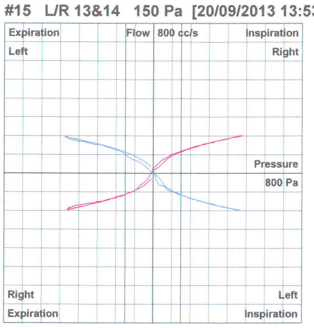
#14 RIGHT 150 Pa 4PR [20/09/2013 13:53:21]



4PR	Inspiration	Expiration	Total
Log Vertex Resistance	1.372	1.368	-
Log Effective Resistance	1.330	1.337	1.334

Standard	Inspiration	Expiration
Mean Flow	118.0	113.0
Mean Resistance	1.271	1.327
Max deviation	0.007	0.023
Respirations	4	4

#15 L/R 13&14 150 Pa [20/09/2013 13:53:28]



Standard	Insp L	Exp L	Insp R	Exp R	Insp Total	Exp Total
Mean Flow	118.3	115.8	118.0	113.0	236.3	228.8
Mean Resistance	1.268	1.296	1.271	1.327	0.635	0.656
Max deviation	0.018	0.027	0.007	0.023		
Respirations	4	4	4	4		
Right > Left by	1%				LAP 0.1%	LAP 1.2%

Diagnostic		75 Pa	% Inc.	150 Pa	% Inc.	300 Pa
Flow [cc/s]	L	83	42%	118	37%	162
	R	84	40%	118	38%	163
	L+R	167		236		325
	L/R	0.988		1.000		0.994
Resistance	L	0.899	41%	1.268	46%	1.850
	R	0.897	42%	1.271	45%	1.845
	Total	0.449		0.635		0.924

1.3 Broms method

~~N~~ARIS NR6 - 2

R4

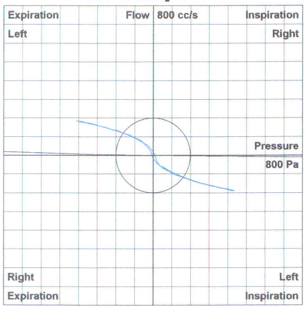
BROMS 200 (I)

gm instruments

Date: 20/09/2013 13:39:08

Initials
Study Number
Subject Number
Time Point
Operators Initials

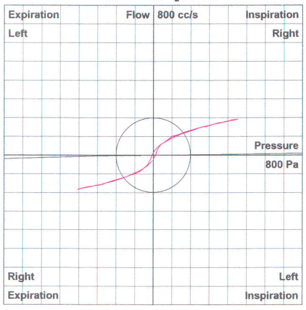
#1 LEFT 200 units [20/09/2013 13:36:14]



Standard (Broms)	Inspiration	Expiration
Mean Resistance	1.348	1.355
Angle	53.4°	53.6°
Max deviation	0.058	0.037
Respirations	4	4

Rohrer	Inspiration	Expiration
K1	0.175	0.201
K2*1000	12.873	12.861
SDres	8	9

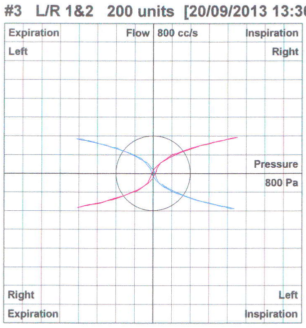
#2 RIGHT 200 units [20/09/2013 13:36:24]



Standard (Broms)	Inspiration	Expiration
Mean Resistance	1.309	1.340
Angle	52.6°	53.3°
Max deviation	0.077	0.043
Respirations	4	4

Rohrer	Inspiration	Expiration
K1	0.196	0.299
K2*1000	13.032	13.701
SDres	10	10

#3 L/R 1&2 200 units [20/09/2013 13:36:31]



Standard (Broms)	Insp L	Exp L	Insp R	Exp R	Insp Total	Exp Total
Mean Resistance	1.348	1.355	1.309	1.340	0.664	0.674
Angle	53.4°	53.6°	52.6°	53.3°	33.6°	34.0°
Max deviation	0.058	0.037	0.077	0.043		
Respirations	4	4	4	4		
Left > Right by	2%				LAP -1.5%	LAP -0.5%

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Appendix 2: Standard Operating Procedure for measurement of nasal airway resistance

SOP No. 2

Procedure for Measurement of Nasal Airway Resistance by Posterior Rhinomanometry. (GM Instruments NR6-2) (Revised 01/02/08, 03/07/09)

Introduction
The purpose of this SOP is to explain the measurement of total and unilateral nasal airway resistance using posterior rhinomanometry with the GM Instruments NR6-2 Rhinomanometer.

It should be used as an introductory aid for people unfamiliar with this technique.

In this Centre inspiratory nasal airway resistance is used to describe nasal airway resistance values.

Procedure
1.0 Preparation of Equipment

1.1 Before attempting any measurements, you must first ensure that the instrument has been correctly calibrated and the results documented according to the procedure described in the SOP 'Calibration of Rhinomanometer (GM Instruments NR6-2) '.

1.2 Always check the printer at the start of each day. Ensure that there is at least one spare ink cartridge available for the printer. Always make sure the printer is switched on and supplied with paper before any measurements are attempted. To check the printer load the test file from the rhinomanometry directory. This can be done by clicking the open file icon button, highlighting the file 'AATEST.rhd' and clicking open. Click on output tab and tick both boxes 1 and 2, on the left hand side press the print button. Check this printout before attempting any measurements.

1.3 All equipment must have been cleaned according to the procedures described in section 4 before attempting any measurements.

1.4 Cut a piece of Portex tubing (inner diameter 3mm, outer diameter 5mm) approximately 5cm long. One end of this curved tube should be cut obliquely, so that the longer edge is on the convex side of the tube. The straight end of this tube is then attached to the connector on the inside of the face mask. Attach the pressure tube (marked black) from the rhinomanometer to the connector on the outside of the face mask.

1.5 Connect the pneumotachograph to the face mask. The flow tubes from the rhinomanometer (marked green and red) should be attached to the pneumotachograph (red nearest the mask).

2.0 <u>Acquisition of data</u>

2.1 Double click on the ‘Naris / Rhinomanometer NR6’ icon on the screen. For a new patient enter the Trial Number, Time point, Patient Initials, Screening Number and/or Treatment Number and the Operator Initials.

2.2 Open the Data Screen by clicking on ‘Tests’. Click on ‘NR6’ icon on the top of the screen. Axes will appear on the screen. This is the ‘Acquisition box’. By default the computer should select Std75 Pa in the ‘test’ box and posterior rhinomanometry in the side box. Remember to change these if required by the trial protocol.

2.3 Click on ‘Zero’ to zero the cursor position, ensuring that no flow or pressure is being applied.

2.4 Ensure that the ‘Batch Mode’ is selected by ticking the box by the ‘Batch Mode’.

2.5 If you are recording unilateral nasal resistance, tape one nostril with surgical tape to form an airtight seal. You will be measuring the resistance of the open nostril. Before taking any measurements instruct the subject to gently blow their nose. Ask the subject to place the mask against the face surrounding the mouth and nose, forming a seal all the way around the mask. Avoid pressing the mask too hard on the bridge of the nose, as this will increase nasal airway resistance. Instruct the subject to close their lips gently around the Portex tube, forming a good seal and to breathe normally through the nose. Ask the subject not to suck or blow into the portex tube. The position of the tongue is very important for the successful performance of posterior rhinomanometry. The tongue should be positioned in such a manner that it does not obstruct the tube, remains stable and is comfortable for the subject. The primary positions of the tongue to attain this standard are as follows:-

a) Tongue pushed down behind and against the bottom teeth.
b) Tongue pushed over the side of the teeth and down into the cheek.
c) Tongue pushed over the bottom teeth and down into the lip.

2.6 When the subject is performing the technique correctly, the cursor will move in a series of reproducible S-shaped curves. This may take some time and practise to achieve (see section 6 ‘Trouble Shooting’).

2.7 When the subject is performing the technique correctly, click on the ‘Record Red button’. The computer will automatically acquire data for 4 complete breaths. If you need to stop data acquisition before this (for example, if the subject is unable to produce four similar curves), click on ‘Stop Recording Black square button’ and click ‘Clear’ to delete the batch results before continuing.

2.8 When four breaths have been completed the computer will automatically stop recording. Ask the subject to remove the face mask. Click on ‘Zero’ before asking the subject to replace the face mask. Repeat from step 2.7.

2.9 After two recordings read the coefficient of variation (C.V.) of the data. This will be displayed at the bottom right hand corner of the Acquisition box. It will be displayed as 'Change'

(i) If measuring total NAR, if the C.V. is greater than 10% delete the readings by clicking 'clear' and make another two measurements. Repeat this procedure until you have two measurements with a C.V. equal to or less than 10%.

(ii) If measuring unilateral NAR, if the C.V. is greater than 15% delete the readings by clicking 'clear' and make another two measurements. Repeat this procedure until you have two measurements with a C.V. equal to or less than 15%.

(iii) If after repeating the measurement of NAR five times the C.V. still exceeds 10% for total NAR or 15 % for unilateral NAR then the NAR measurement can be either documented as 'N.A.' (not available) or as 'TOBS' (totally obstructed).

(iv) If you suspect that the high C.V. is due to some technical problem rather than complete obstruction then document the measurement as not 'N.A.' (not available).

(v) If you suspect that the high C.V. is due to complete obstruction or nearly complete obstruction of the nose or nasal passage, this can be confirmed by asking the patient to breathe in whilst you listen to the nasal airflow sounds. If the patient requires considerable respiratory effort to breathe through the nose and the airflow sounds are loud and restricted then the NAR can be documented as 'TOBS' (totally obstructed).

3.0 Printing

3.1 Before attempting to print the results, ensure the printer is turned on and attached to the computer, and that there is enough paper available.

3.2 When the appropriate C.V has been achieved, press the 'Print' option under the 'batch results' box.

3.3 Click 'OK' when the 'print batch tests' box appears.

3.4 a) If the printout fails to print you must save the results as a file to printout later. Firstly ensure that you record the mean resistance value in the CRF as this will not appear when the file is reloaded. Also remember to document the date, trial number, screening number, patient's initials, timepoint, batch mean, batch standard deviation and batch C.V in a document to be kept with the CRF. These are not automatically printed later and will have to be transcribed to the later printout. Click on [Close] to leave the 'Acquisition Box' screen. Click on the save icon to save the measurements. The filename must consist of the patient initials, screening number, timepoint of measurement followed by the standard file extension for rhinomanometry data (.rhd), i.e. PA001060.rhd

This would be a patient with the initials PA, screening number 001 and timepoint 060. Check the filename has been typed correctly before typing [return] to save the file. To reload the file click on 'file open' icon on top of the screen and double click the appropriate filename. Highlight the last two measurements of the file and select print to print these tests.
b) Check the finished printout to ensure it is correct. The printout must state the patient information, time and date of measurement, and the batch mean and C.V. If the patient details are not correct then you must alter these details in black ink and initial and date the correction. Sign and date the bottom of the printout to indicate completeness. Remember to record whether you have measured Left (L), Right(R) or Total (T) nasal airway resistance.

3.5 Once the printout is complete transcribe the results to the patient CRF. Take care that the time of measurement recorded in the CRF is the time displayed above the second curve on the printout - not the time of printing displayed at the top of the page.

3.6 Printouts will be filed in the CRF which will be kept in a locked cabinet in the laboratory area during the conduct of the trial and will be archived with the trial data on completion of the trial.

3.7 Clear the batch results by clicking 'Clear'. Click on 'Close' in the 'Acquisition Box'. Highlight the tests on the left hand side and delete by clicking the right hand mouse button and then delete with the left hand button. Click 'Yes' to delete test data.

3.8 If performing a measurement on a different subject. Click on 'New' Icon in the top left and enter the correct patient information before acquiring any data. Repeat from 2.3 - 3.7.

3.9 If measuring the same patient, do not change the patient information.
Simply click 'NR6' icon and repeat from step 2.3-3.7.

4.0 Hygiene and Cleaning of Equipment

4.1 A clean mask must be used for each patient.

4.2 The masks should be cleaned with a non-fragrance washing up liquid, then with Virkon and then rinsed with cold water at the end of each day.

4.3 A clean pneumotachograph must be used for each patient and clearly labelled with the patient initials and the registration number.

4.4 The pneumotachograph must be sonicated in Virkon solution and then rinsed in cold water at the end of each day.

4.5 The pneumotachographs must be dried using warm air only, i.e radiator. The pneumotachograph will perish if subjected to high temperatures.

5.0 Sample Page of Printout

6.0 Trouble Shooting

6.1 Inability to produce a small S-shaped curve when performing rhinomanometry technique:- This may be due to several reasons, disruption of the pressure reading may occur if the pressure tube in the mouth is partly or completely blocked by the tongue, due to the movement of the tongue or due to the subject inadvertently sucking on the tube. The latter occurs particularly in subjects who have a high nasal airway resistance. Curves are often improved by asking the subject to reposition the tongue as described in section 2.5.

6.2 A line vertically up and down the screen instead of forming a curve:- This indicates a flow reading but no pressure reading and is usually due to the subject having their mouth open. Ask the subject to close the mouth and ensure the tongue is out of the way as described in section 2.5.

6.3 High coefficient of variation (i.e. wide differences between consecutive resistance measurements):- This may be due to a leak around the mask; ask the subject to press the mask more tightly onto the face and ensure the mask is positioned correctly.

Checklist

a) Ensure instruments are calibrated and in good working order.
b) Ensure that the printer is functioning properly and has a suitable supply of paper.
c) Ensure that the subject is correctly trained and can perform rhinomanometry.
d) Ensure that the correct patient information is recorded before taking any measurements.
e) Always check for mask leaks.
f) The Coefficient of Variation must not be higher than 10% for measurements of total NAR and 15% for measurements of unilateral NAR.
g) The mean value of two nasal airway resistance measurements is calculated by the computer.
h) Printout the completed test and ensure that the data is recorded correctly. If the printout fails record the mean and C.V. in the CRF and save results as a file for printing later. In the back of the calibration log book, remember to record the date, trial number, screening number, patient initials, timepoint, batch mean, batch standard deviation and batch C.V.. This is to be retained for later transcription to the final printout.
i) Sign and date printout and indicate Left (L), Right (R), or Total (T).
j) Transcribe the results into the CRF and place the printout in the CRF. This should at all times be kept in the laboratory cabinet relating to the appropriate trial.

Appendix 3: Standard Operating Procedure for calibration of rhinomanometer

SOP NO. 8

Calibration of Rhinomanometers (GM Instruments NR6 - 2) (Revised 26/02/2007, 23/09/10)

Introduction
This Standard Operating Procedure (SOP) has been written so that calibration of the rhinomanometer equipment can be carried out by different personnel to the same acceptable standard. Calibration must be carried out every day. The SOP is intended for use by persons unfamiliar with the calibration techniques and as a guide to those who can already calibrate the equipment.

1.0 Calibration Equipment.

1.1 Check that you have the following equipment before attempting to calibrate the rhinomanometer:-

Calibration book - should be kept next to the rhinomanometer and labelled accordingly i.e. book no. = 1, rhinomanometer = 1, Sloping manometer, Flowmeter

1.2 Check that the calibration book is formatted as follows:-

Date		P75*	P150	F200	F300*	Status	Initials
08/07/09	Pressure calib.	75	150	-	-	OK	SJ
	Flow calib.	Pneumo.No. 18		200	300	OK	SJ

(* = Values of pressure (P) in Pascal and flow (F) in cm^3/sec that rhinomanometer is calibrated on.)

1.3 Check that the sloping manometer has sufficient fluid to allow correct zeroing of the instrument. If the level is too low then top up the manometer fluid level using the appropriate fluid.

1.4 The units of pressure used by the rhinomanometer are Pascal. 1mmH_2O = 10 Pascal, so the instrument may be calibrated using a manometer with a pressure scale in mmH_2O but care must be taken to ensure calibration at the correct pressures,

i.e. 75 Pa = 7.5 mmH_2O
150 Pa = 15 mmH_2O.

2.0 Procedure for Pressure Calibration using Sloping Manometer

2.1 Choose 'Tools' from the options at the top of the screen and select calibrate.

2.2 Let the equipment settle for approx. 5 minutes or until the values no longer fluctuate greatly. Press zero to clear any offset.

2.3 Make sure that the manometer spirit level is correctly aligned. If not, turn the black knob on the side of the manometer until the spirit level is correctly aligned. Now remove the cap from the screw on the top right of the manometer. Turn the base of this screw until the manometer reading returns to zero.

2.4 Remove the black coloured tube from the rhinomanometer and attach one end of the manometer 't' tubing to the rhinomanometer pressure port. Attach the other end of this tubing to the syringe provided.

2.5 Depress the plunger of the syringe until the manometer reads 75 Pa.

2.6 Note the computer reading at this point. The software reads the applied pressure value. Therefore, the computer should now read 75 Pa.

If the final reading is incorrect then alter the reading using a screwdriver on the pressure calibration screw at the back of the rhinomanometer. Disconnect the manometer tube from the rhinomanometer pressure port and allow the equipment to return to zero.

2.7 Reconnect the manometer pressure tube. Depress the plunger until the manometer reads 150 Pa pressure. Note this second reading. If this reading is within $^{+}/-$ 5 Pa of the required amount then documentation should be completed and the pressure calibration is finished. If this is not the case then you must repeat steps 2.2 - 2.7 inclusive until these criteria are fulfilled.

2.8 The calibration book should be documented as follows:-

a) Enter the date in the column provided.
b) Enter the actual value for the calibration value of 75 Pa.
c) Enter the actual value for the value of 150 Pa.
d) Enter the status of calibration as OK and write your initials in the column provided.

Remove the manometer tube from the rhinomanometer and replace the black coloured tube.

3.0 Procedure for Flow Calibration

3.1 Allow the machine to settle and then press the Zero button. Check that the pneumotachograph is clean and dry. The pneumotachograph should be cleaned after each subject and will need to be recalibrated after cleaning. Attach the narrow end of the pneumotachograph to the flowmeter. Attach the pneumotachograph to the rhinomanometer following the red/green labelling for pressure tubing.

3.2 Turn on the flowmeter and turn the dial at the side until the top of the float is level with the 18 litres/min indicator. This is equivalent to 300cm^3/sec of flow.

3.3 Read the new reading from the computer. It should now read 300 cm^3/sec

3.4 If this reading is incorrect then it must be altered using a screwdriver on the flow calibration screw at the back of the rhinomanometer.

3.5 Once the correct reading has been maintained reduce the flow indicator to the 12 litres/min level. This is equivalent to 200 cm^3/sec. Check the new reading on the computer. If this reading is within $^+$/-5 cm^3/sec of its required amount then calibration is complete. Go to step 3.8.

3.6 If the reading at 200cm^3/sec is not correct then the calibration must be repeated from steps 3.0-3.4 inclusive until the criteria are fulfilled.

3.7 When calibration is completed write all documentation in the calibration book provided. This should be done as follows:-

a) Enter the actual value for flow for the calibration value of 300 cm^3/sec.
b) Enter the actual value for flow for the value of 200 cm^3/sec.
c) Enter the status as OK and write your initials in the columns provided.

3.8 Turn the dial completely back and wait for the flow to drop to zero. Turn off the flowmeter and reconnect the mask and the pneumotachograph.

3.9 Click 'OK' at the bottom of the screen. The rhinomanometer is now calibrated.

<u>Checklists</u>

a) Make sure that the pneumotachograph is clean and dry and that it is cleaned after each subject.

b) Make sure that offsets are zeroed and stable before attempting any calibrations.

c) Make sure that the manometer is correctly levelled and zeroed before attempting calibration. Check if the manometer scale is in Pascal or mmH_2O and calibrate accordingly.

d) Be careful that you are reading stable values, i.e. pressure or flow on the manometer or flowmeter do not alter when you check the reading on the computer.

e) Always check that your documentation in the calibration books is correct and up to date.