

Objective measurement of nasal airway dimensions using acoustic rhinometry: methodological and clinical aspects

Ole Hilberg

Department of Environmental and Occupational
Medicine, University of Aarhus, Denmark

Ole Hilberg
Department of Environmental and Occupational
Medicine
University of Aarhus
Vennelyst Boulevard 6
Building 260
DK-8000 Aarhus
Denmark

Fool: Thou canst tell why one's nose stands i' the middle on's face?

King Lear: No.

Fool: Why, to keep one's eyes of either side's nose: that what a
man cannot smell out, he may spy into.

William Shakespeare,
King Lear: Act I, Scene V

Nasal airway patency and nasal function

Introduction

The nasal cavity is the first part of the airway and the nasal mucosa is the first line contact area between the air, gases, suspended elements, and the respiratory tract. The surface area of the nasal mucosa is 150 cm² compared with 100 m² for the lower airways (1). Because of the powerful capacity of the nasal mucosa to humidify and warm the inhaled air, the nasal airway plays a significant role in the normal homeostasis of the body. Nasal breathing conserves humidity in comparison to oral breathing (2–5). During normal breathing through the nose, approximately half the total resistance of the airways is located in the nasal airway, implying that relative small changes in the nasal patency affect the total airway resistance significantly, thereby influencing the total respiratory function (6–9).

The nasal cavity is responsible for filtration of particles larger than 10 µm and a fraction of smaller particles (10, 11). In this process the nasal mucosa, as a part of the immune system, is in contact with specific allergens and other elements from the environment. The nasal mucosa may react to stimulus in a localized process or as an effector organ, e.g. in the immune response in hay fever. The response in

these cases may mirror the reactivity of the immune system with increased risk of a more profound reaction of the airways (12, 14). In contrast, in other diseases, the nasal mucosa is the target organ (e.g. common cold, caused by rhinovirus or certain types of corona virus), although effects also may be seen in other part of the respiratory system, like rhinovirus-induced asthma (15–18).

The advanced position and the relatively direct accessibility of the nasal mucosa offer a possibility to study not only local diseases but also generalized inflammatory reactions, for example, in the respiratory system more easily than in the lower parts of the respiratory system.

The purpose of this thesis is to describe methodological aspects and the clinical use of acoustic reflections in determination of nasal airway patency – acoustic rhinometry – and discuss the variability and sensitivity of the allergic nasal mucosa with regard to nasal patency.

Regulation of nasal airway patency

The turbinates divide the nasal cavity into a slit like formation with a large surface-to-airway area ratio (19, 20). This suggests that even minor changes in the congestion of the mucosal blood vessels may considerably alter the nasal patency and airflow pattern in the nasal cavity (21, 22).

Furthermore, the structure of the nasal mucosa vasculature allows the possibility for complex responses to stimuli (5, 23, 24). The vasculature comprises arterioles, venules and capillaries as well as arterio-venous anastomoses and capacitance vessels such as sinusoids and distensible venules (25, 26).

The regulation of the vascular tone and thereby

patency in the nasal passage is also intricate. The regulation of the congestion and the blood flow in the vessels are affected humorally, nervously, and by local conditions. Both the sympathetic as well as the parasympathetic nervous systems have a major influence on vascular regulation in the nose (27–30) and assigned to a central control (31–35), which is manifested as the nasal cycle. This central control may be influenced by simple external conditions like a light pressure on one side of the body or in the axilla (32, 36, 37).

Both capacitance and resistance vessels possess receptors and are affected by nervous stimulation and humoral influence, e.g. during exercise (27, 38–42).

Numerous other receptors have been found on the vasculature in the nasal mucosa. Serotonin may induce vasodilatation (43–45), although the clinical importance of this has not completely been elucidated yet. Vasoactive effects of a number of mediators, e.g. vasoactive intestinal peptide (VIP), substance P (SP), avian pancreatic polypeptide (APP), prostaglandins, leukotrienes, and kinins (46–51) have been described. The mechanisms of action of other mediators like histamine are better described and specific antagonists against the receptors have been synthesized and are now in use in treatment (52–55). The increasing numbers of mediators known to have a possible effect on nasal airway patency makes it more difficult to achieve a simple comprehensible model of the reactions in the mucosa.

Furthermore, localized effects, local reflexes, and interactions between the cells in the mucosa seem to play an important role in the regulation of the normal mucosa as well as in diseases (56, 57). Renewed interest in the histology of the mucosa, to examine the cellular responses at the site of action, and the possibilities to detect cytokines in very small concentrations give us the opportunity to study the reactions of the mucosa in normal and during pathological conditions (58–61). This will probably lead to an even more complicated conception of the regulation of mucosal integrity but hopefully also a more accessible model (e.g. in allergy; the capability of relevant cells to react to an allergen may be seen as an imbalance between INF- γ and IL-4).

The present summary of some of the mechanisms involved in the regulation of mucosal congestion illustrates the enormous potential of the mucosa to react very diversely and complicatedly to stimuli. Therefore, it is essential to have reliable and sensitive methods to study the outcome – the symptoms – of these reactions. The four major symptoms from the nasal airways: itching, sneezing, secretion, and occlusion may be seen as an exaggerated response, disproportionate or not, to a stimulus. The necessity of objective methods to evaluate these symptoms should

be emphasized both for clinical and investigational purposes because the subjective perception of the different symptoms may interfere with each other.

Nasal airway physiology and function

The functions of the nose are besides being the first part of the respiratory system and thereby a filter and acclimatizer of the inspired air also the seat for smell. The congestion state of the nasal cavity and the sinuses may have a certain impact on phonetics (62–64).

The geometry of the nasal cavity implies that almost all particles larger than 10 μm and a fraction of smaller particles are retained in the anterior part of the nasal cavity (10, 65). These particles are removed from the nasal cavity by the mucociliary clearance. Normally mucous is transported in a posterior direction by the movements of the ciliated epithelium in nasal cavity. The normal velocity is between 3 and 25 mm/min (66, 67). In the very anterior part of the nasal cavity before the anterior end of the ciliated epithelium the clearance rates are prolonged (65, 68). In this way particles and other material deposited on the mucosa are effectively cleared from the nasal mucosa, although water solubility and other physical and chemical characteristics may influence the clearance time (69, 70).

Abnormalities in the nasal cavity, e.g. structural changes as septal deviations may impair the normal mucociliary clearance (71–73). Therefore, at least theoretically a normal nasal patency and mucociliary function tend to promote the clearance of virus and bacterias from the nasal cavity membrane and decrease the risk of viral infections (74, 75) or bacterial infections (76–78).

The heat and humidity conserving capacity of the nasal cavity are important for the normal function of the respiratory system. If the capacity is exceeded, e.g. during exercise in extreme cold circumstances where mouth respiration takes place or pathological conditions in the nasal cavity there is probably increased risk of development of asthma or having attacks of bronchial constriction (2, 4, 79, 80).

Another important function of the nose, which also is closely connected with normal nasal patency, is smell (81). Normal olfaction is dependent on eddies in the inspired air arising in the nasal valve and anterior part of the nasal cavity. Impaired olfaction function may improve during surgery or other therapy if normal nasal patency is affected before treatment (82–85).

Although some controversies exist, normal development of the face is partially dependent on normal nasal breathing (86–90). Normal speech development and phonetics may also be associated with normal conditions in the first part of the airway – the nasal cavity and the pharynx (62–64, 91, 92).

Therefore, impaired nasal patency has not to be considered only as an isolated symptom, but may

affect different aspects of normal nasal function and need to be measured as accurately as possible using objective methods that are easy to implement under a variety of test and disease conditions. Acoustic rhinometry seems well suited to meet these objectives.

Methods to evaluate nasal patency

History

Examination of the nasal cavity has been described more than 3000 years ago (Papyrus Ebers), for instance by Egyptian medical doctors and also in the mummification process of the Pharaohs, where the brain was removed through the nose. Examination of the nose has also been described by Hippocrates in Greece (460–377 B.C.). To improve the view into the nasal cavity different means have been used. Guy de Cehauliac (93, 94) has referred to a nasal speculum in the 13th century.

More systematic evaluation of nasal patency was described in the late 19th century by Zwaardemaker (34, 95, 96) and modified by Glatzel in 1901. Differences in patency of the two sides of the nose was evaluated by the difference in the condensed area of water on a metal plate placed in front of the nasal cavity during expiration. Other, at best semiquantitative methods included the hum-test by Spiess (1902), where external occlusion of the nonoccluded side of the nasal cavity is experienced as a change in the timbre of sound during humming or simply as a difference in the sound during forced expiration for each side of the nasal cavity separately (Bruck, 1901). These qualitative methods, some of which are still in use, are highly dependent on the mode of respiration and the capability of the subjects to carry out the tests. A measurement of the pressure drop over the nasal cavity at a passive flow has been described in 1903 by Courtade (97) and is one of the first descriptions of rhinomanometry. Since then, rhinomanometry has been used in more than 500 studies described in international papers. (A search in the 'Silverplatter Medline system' for the period 1966–99 showed more than 630 references with the keyword 'rhinomanometry'.) The first paper describing acoustic rhinometry was published in 1989 (see I; 483).

Optical methods

The most commonly used optical method for evaluation of the nasal cavity passage is rhinoscopy. Although rhinoscopy should be included in all clinical evaluations of nasal patency, different studies have shown that a clear-cut relation between anterior rhinoscopy, subjective evaluation or other tests (98–101) is not always present.

Using a flexible rhinoscope may improve the results of the examination of nasal pathology and in certain

cases for operations (102), but the results using the endoscopic examination do not necessarily correlate with rhinomanometry for evaluation of nasal patency (103).

Different optic devices have been used to characterize or quantify nasal patency. Rhinostereometry (104, 105) is a method for measurement of the distance between the medial and lateral wall of the nasal cavity. The distance is determined using an inbuilt scale in a microscope, and the head position has to be fixed to assure measurements at the same position during repeated measurements. This gives only limited information of isolated structures and not of the larger part of the nasal airway.

Video recording during flexible endoscopy allows subsequent evaluation of the results (103, 106, 107), but is still an invasive procedure and may not be the optimal method for evaluation of nasal patency.

Quantitative acoustic methods

Methods using sound or analysis of sound in the airways have been used to characterize the size of the airways or an obstruction in the larynx (108), nasal cavity, and paranasal sinuses (64, 92), to determine the location of snoring problems (109, 110), and in the upper airways and epipharynx (111–114). Despite these attempts to use more or less subject generated sound to evaluate the patency of the airways the methods have so far not been very successful.

Flow methods

Flow measurements for the evaluation of the nasal airway passage have been used more or less systematically for the last five decades. The simplest way is to measure the maximum flow – the nasal peakflow. In this case the power of the driving force, the chest wall, and lower airways, have influence on the nasal expiratory or inspiratory peakflow. Different authors have tried to reduce the factor by calculating an index between nasal and oral peakflow (115–120). Despite the fact that correlations between nasal peakflow and other methods to evaluate nasal occlusion have been found, nasal peakflow seems to be most suitable to measure changes in the same subject during repeated measurements (121–123).

In rhinomanometry simultaneous measurements of flow and pressure are performed. Different techniques have been applied using the subjects own respiration flow (active methods) or using an external flow generator (passive methods) (97, 124). The matching flow is measured in the anterior part of the nasal cavity (anterior methods) or in the pharynx (posterior methods).

The active methods are more frequently used than the passive anterior method (125, 126) and the passive posterior method (127). Results may differ between the

anterior and posterior method (128, 129) although others find quite similar results with the methods (130).

Rhinomanometry has also been correlated with other tests normally used for pulmonary function, e.g. body plethysmography and the forced oscillation technique (131–133) and reasonable correlations have been found.

The repeatability in rhinomanometric measurements ranges from 10 to 30% (134–136) and therefore some authors find it unusable for precise evaluation of nasal patency.

One essential problem is the description of the flow–pressure relationship. Because of the nonlinear relationship between flow and pressure, different methods have been adopted, e.g. using an Ohmic resistance at a specified flow or pressure rate, using a power function in the description, or other models (e.g. Rohrer's equation) (137, 138). The angle between the abscissa (flow) and the intercept between the pressure–flow curve and a circle in coordinate system (Brom's system) (139–141) or the relative difference of the two sides; a lateralization index (142), have also been used.

The rhinomanometric resistance may also be expressed as a minimum cross-sectional area of the nasal cavity and some authors find this to be the best way to depict resistance (143). It assumes a complicated model of the flow in the nasal cavity and the models being used (144, 145) may not always give the 'true' area at different flow regimes. The slit like structure demands special requirements of the models since the flow profile in the nasal cavity may be nonuniform and change between laminar and turbulent flow (146–148).

Furthermore, the localization of a deviation affects the resistance evaluated by rhinomanometry (149, 150). A deviation of the septum at the nasal valve affects the resistance more than a deviation in the posterior part of the nasal cavity.

Different attempts have been made to standardize rhinomanometry (151–153) to allow comparison of the results from different studies. Rhinomanometry has been used in different aspects of rhinology, e.g. in the diagnosis of different rhinologic diseases (154), in allergy tests (155, 156), in pharmacological studies (157, 158), and in physiological studies (159, 160). Certain authors have found that rhinomanometry is useful in the selection of treatment, e.g. operation or not (100, 161–164), or as a tool for evaluation of operative procedures (136, 165), whereas others find the present techniques unsuitable for these purposes (134, 166).

In some studies a clear correlation between the subjective feeling of nasal occlusion and rhinomanometry has been found (167–169), in others a poor correlation (170, 171), because other factors than just resistance influence the feeling of nasal obstruction. It

is well known that menthol relieves the feeling of nasal obstruction, whereas the nasal resistance to airflow is unchanged (172).

Some of the drawbacks of rhinomanometry are relatively low reproducibility; low correlation to subjective feeling of nasal obstruction, no uniform way of describing results, different techniques may be used- viz anterior, posterior, active, passive, and it is therefore not used in daily clinic routine, except in a few laboratories (173, 174).

Radiological methods

Radiological methods are seldom used in the investigation of nasal patency, although X-ray examination has been used in relation with evaluation of the paranasal sinuses (88, 175, 176).

Computer aided tomography (CT) is increasingly used instead of X-rays especially in evaluation of the paranasal sinuses (177, 178).

Magnetic resonance scanning (MRI) is also used for evaluation of nasal patency, primarily if pathological changes are suspected, e.g. malignancies in the nasal cavity and paranasal sinuses, and will probably replace CT for evaluation of the mucosa (64, 178–180).

Other methods

Other methods for evaluation of nasal patency have been described, e.g. subjective evaluation of increasing external resistance, measurements of O₂ while breathing pure oxygen, other flow methods than described above. None of these methods have been successful (123, 181–183).

Acoustic reflections

History

The acoustic reflection technique for determining the cross-sectional area as a function of distance in the human airways has developed gradually. The mechano-acoustical properties of the lungs were initially examined 40 years ago (184) and electrical analogues were introduced to facilitate comprehensive modelling of the airways (185). Acoustic reflections have been used in geophysical investigations especially in the United States of America with regard to search for oil (186, 187). The use of acoustic reflections from the airways gained special interest in 1960–70 for determining the geometry of the vocal tract with regard to speech reconstruction. Methods similar to those described later (188, 189) were used to examine the area as a function of distance from the lips to the glottis (190–192). One of the main problems at that time was the computational procedure for recovering successive areas from the coefficients of reflections. A new method (later named 'the Ware–Aki algorithm') for this procedure was

developed (193) and is still one of the most efficient algorithms for solution of the inverse problem – calculation of the impedances from an impulse response (194). In 1970–80 the use of the acoustic reflection technique was introduced for measurements in the pharynx and trachea (188, 189, 195, 196).

Methodological aspects

The method for determining the cross-sectional area as function of distance in the airways is relatively simple. The incident sound impulse or pseudorandom noise in the audible frequency range is compared with the response – the reflections from the airways. Intuitively, if the size of the entrance to the airways is known, the size of the reflections may reflect changes of the airway size. The time between the reflections may give the distance between the changes dependent on the speed of sound. In this way it is possible to determine the area as function of distance in the airways. Given the area–distance function different variables can be determined. In the nose the minimum cross-sectional area, the nasal volume 0–5 cm or 0–7 cm from the nostril estimated by integration of the curve and areas at particular anatomical structures could be of interest (see below).

In a tube system with one-dimensional sound propagation, changes in the acoustic impedance are proportionate to changes in the cross-sectional area. The technological development of microcomputers has made it possible to sample, store, and calculate the reflections. Figure 1 depicts the reflection pattern of an incident pulse from a tube with multiple changes in acoustic impedance (cross-sectional area).

Despite the intuitively simple principle of the acoustic reflection technique, the calculation of the area–distance function from the incident and reflected impulses requires somewhat complicated arithmetic transformations. The original set-up, for the nose and lower airways with a short impulse and a temporal space between incident wave and reflections, make the system relative insensitive to minor changes in the sound impulse and the linearity of the microphone, since the signals of the incident wave and reflected wave are compared in the frequency domain. Therefore, it is also necessary to do the Fourier and inverse Fourier transformations of the data. Figure 2 shows the different steps in the calculation (cf. IV; 486).

Two inputs are used: the calibration of the system and the measurement. The first input (calibration) is the impulse response of the measurement system including the characteristics of the sound source and the microphone. In practice this impulse response is measured as the reflection of the incident pulse from a high impedance (closed tube) connected to the measuring tube. This sets the properties of the 'measuring system', defines the starting point of the measurement and sets up the area size. The second input is the measurement of the

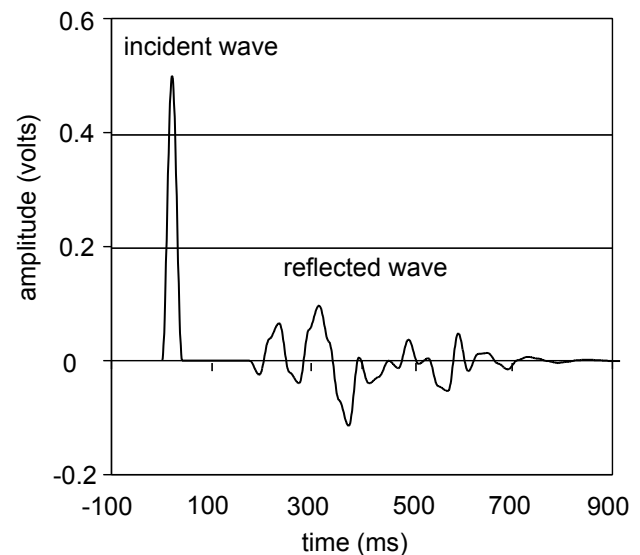


Figure 1. The reflected signal from a nasal cavity.

actual cavity in which the area–distance function (AD-function) is to be estimated by the equipment. After having obtained the reflection from the cavity, the influence of the equipment characteristics on the reflection is suppressed by convolution with the first input. The following deconvolution employs the Hunt's algorithm, which is a frequency domain technique to compensate for amplitude differences. Since the deconvolution is performed in the frequency domain, the algorithm contains two implicit FFT transforms (forward/inverse). The output from the deconvolution is the measured impulse response of the cavity. The last step is to transform the measured impulse response into an AD-function. To solve this inverse problem, as described above, the Ware–Aki algorithm (193) has been implemented.

Theoretically, to obtain reliable measurements with this technique a number of assumptions have to be fulfilled (189, 197) (see also I; 483).

The first assumption is that the sound waves propagate as plane waves to avoid cross-modes, which will make the computations difficult. Based on theory it is possible to calculate the frequency at which cross-modes start to appear. The formula is only valid for a tube and the complex geometry of the nose makes it impossible to predict the frequency limit where cross-modes appear and make the results invalid. During the measurements cross-modes can be recognized as a 'ringing' of the reflected signal. In a normal nose cross-modes seem not to appear below 12 kHz and normally frequencies up to 15 kHz or more can be used. The second assumption is that viscous losses are negligible. If the nose is very narrow at the anterior end, viscous loss in the constriction may induce underestimation of the areas beyond. It is not only the size of the constriction but also the shape that may have an

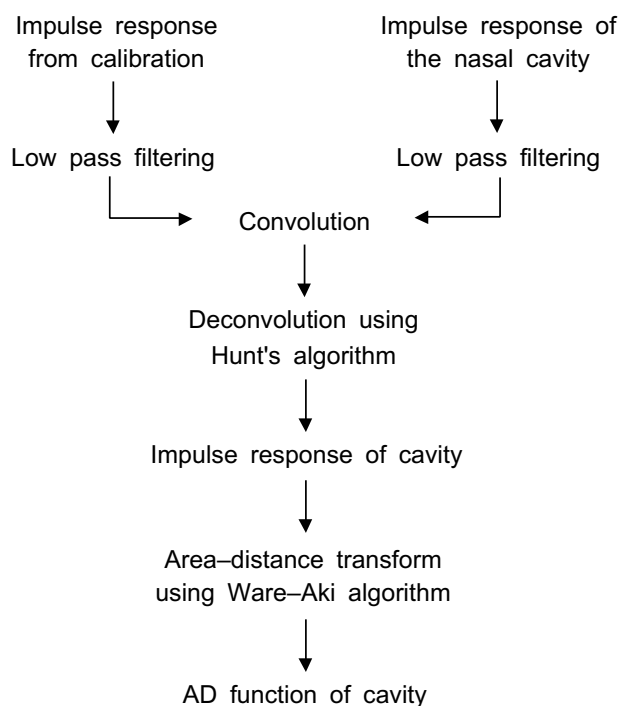


Figure 2. The calculation of the area-distance function for acoustic rhinometry.

influence. Therefore, it is not possible to identify a fixed value below which the results could become unreliable. The actual set-up, especially the low-pass filtering frequency may also influence the results. Results suggest the area of 0.35 cm^2 in some set-ups could be a limit (see I; 483). The third assumption, that any bifurcations are regular (i.e. symmetric), is valid for the distance to the epipharynx where the two nasal cavities join. Model studies and filling one nasal cavity with water (see I and III; 483, 485) suggest that the influence of the other side adding space to the epipharynx is of minor importance and is mainly seen behind the epipharynx. Finally, the walls in the nasal cavity should behave rigidly. The bony part is rather rigid but the mucosa may not be so. For the human tissue (cheek and trachea) results have indicated that the tissue is behaving rigidly at frequencies greater than 120 Hz (188, 198). To examine the effect of the nasal mucosa – its acoustic properties were studied in one male subject who was examined by laser vibrometry (see IV; 486). By this technique the specific acoustic admittance of the nasal mucosa was examined. This value was used in a simulation to study the effect of increasing sound losses (due to nonrigid properties of the nasal mucosa) on the recovered area-distance function. In summary, the sound loss should be increased a 100 times before significant effects are seen (see Fig. 3).

Despite all assumptions having not been completely fulfilled; validation of measurements using the acoustic

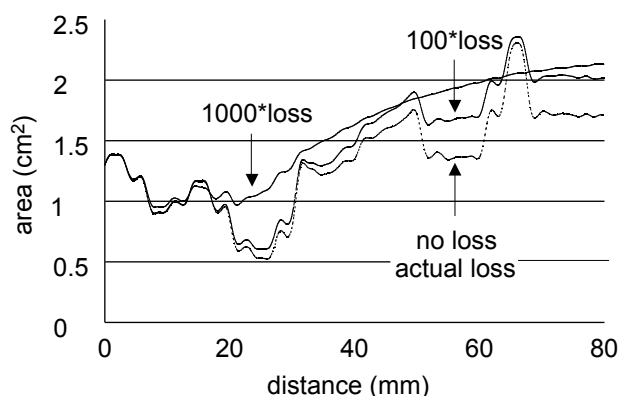


Figure 3. The sound loss due to wall motion, 4 curves are depicted (no loss and actual loss are on top of each other). The error is increased by losses and by increasing distance.

reflection technique in the nose (see the subsection on Validation for use in the nasal cavity) reveals acceptable results.

Use of the acoustic reflection technique for measurements in the pharynx and lower airways has been validated by use of different techniques. In the initial studies of the trachea, models, excised tracheas, and dogs were used and a reasonable correlation was found (196, 199, 200). In humans, comparisons primarily with roentgenographic techniques had acceptable correlations (125, 200–202).

One of the reasons for differences using *in vivo* models and, e.g. cadavers is that the size of the airways increases after death (203). This may increase the influence of the paranasal sinuses considerably. It has been examined whether the assumption of nonrigidity of the walls and limited resolution could partly be overcome using a mixture of 20% O_2 and 80% He instead of atmospheric air in the tube system and in the airways. In this mixture the speed of sound is almost doubled (from 340 m/s to 620 m/s). This provides the opportunity to increase the frequency band before cross-modes start to occur and should increase resolution (197) and improve accuracy (188). The resolution is however, not increased since the wavelength is 'unchanged'. Furthermore, the higher frequencies and the use of He increase the technical demands of the equipment. The ability of the sound generators, in some of the studies using He, to deliver a sufficient energy content at high frequencies has been questioned (204). Although the microphones frequency range increases in He (see Brüel & Kjaer manual) technical problems may arise at this point too. The main effect of He is probably to reduce (relative to air) the lower part of the frequency band where effects of wall motion may influence the measurements, although some authors believe it to be other unspecified factors (205).

In the pharynx no clear improvement in results were found using He (206). Neither was there improvement in

nasal cavity (see IV; 486) where identical results were observed using either air or He (80%), O₂ (20%) in a model and 8 nasal cavities.

Besides the effect of the density of the 'wave-transporting medium' it has been debated whether a different algorithm for the last step in the area–distance calculation would improve the results. Studies have employed different algorithms but, until now (year 2000), no algorithm has shown better recovery than the Ware–Aki algorithm (194, 204, 207). The Ware–Aki algorithm has been considered very time consuming but with new computers this is no longer a problem. Unpublished data from simulation models suggest that simple integration of the reflected signal will give reasonable results in most instances, compared with the Ware–Aki-calculation.

Acoustic rhinometry

The acoustic reflection technique applied in the nasal cavity

The use of the acoustic reflection technique in the nasal cavity was first described in 1989 (see I; 483). As mentioned, the first measurements with the technique in the human airways were done more than 20 years earlier (192). In the meantime, approximately 35 papers were published in which the acoustic reflection technique was used to study the pharynx and trachea. In the period from 1989 to 1999, more than 230 papers have been published where the acoustic reflection technique has been utilized in the nasal cavity. In contrast, in the same period, few studies on the pharynx and lower airways have been reported. The main reason for this is technical aspects. Firstly, the accessibility of the nose is much easier than the lower airways. Secondly, the significant change in cross-sectional area from the mouth to the pharynx and trachea increases the risk of cross-modes to appear, but a special mouth piece was designed to avoid cross-modes and made it possible to use higher frequencies and thereby increase resolution (200, 208, 209). Another study indicates that the mouth piece may not be necessary but the resolution may not have been optimal (210). The clinical application in the nose is wider than in the trachea and the accuracy in the pharynx is debatable due to sound leakage to the mouth if the measurement is done through the nose or to the nose if done through the mouth. Finally, the lowered costs of computers may also be a factor for the increased interest for the method. These factors favour the use in the nasal cavity of the acoustic reflection technique.

Technical aspects for use in the nasal cavity

In principle, use of the acoustic reflection technique in the nasal cavity does not differ significantly from its use in the lower airways (see Fig. 4). As mentioned in the subsection on Methodological aspects, some basic

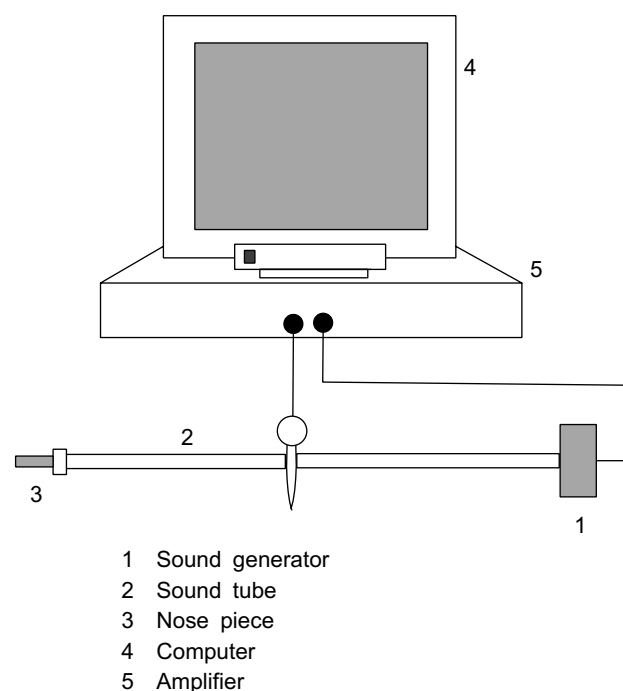


Figure 4. The set-up for acoustic rhinometry.

assumptions (plane waves, negligible viscous loss, regular branching, and rigid walls) have to be fulfilled for optimal results. Special concerns with regard to sound loss have drawn attention since the nasal cavity consists of narrow slits that may induce sound loss due to friction at the walls. The sound loss due to nonrigid walls is negligible as demonstrated by laser vibrometry (see the subsection on Methodological aspects and IV; 487). Sound loss due to special geometry of the nose was also examined in different ways. These included construction of a model with increasing surface but constant cross-sectional area, construction of a model with the same cross-sectional area as the nose but with a circular geometry (see IV; 486) and by evaluating the error of the area–distance function in relation to the circumference determined in subjects by MRI (see II; 484).

No effect of the surface was found comparing both a model made by stereolithography (based on a MRI scanning of the nasal cavity of a subject) and the area equivalent circular model and also the area–distance function in a model with a constant area but increasing circumference (see IV; 486).

In another study (see II; 484) comparing MRI and acoustic rhinometry, the circumference was measured at every single distance in the nasal cavity and the deviation between MRI and acoustic rhinometry was calculated. The circumference was not directly compared with the deviation but is shown in Fig. 5. The maximum error is observed beyond the maximum circumference indicating that large circumference and potentially large sound loss is not important in the measured subjects.

The effect of using He (80%), O₂ (20%) instead of air has already been discussed (see the subsection on Methodological aspects). Figure 6 shows no effect on the area–distance function in the one subject.

The paranasal sinuses may also influence the measurement, although in the first paper on acoustic rhinometry the ostia were considered too small (see I; 483). It has later been demonstrated by model studies (211) (see also III; 485) that especially the ostium size of the maxillary sinus and the size of the sinus may influence the area–distance function. A special technique – stereolithography was employed to make equivalent models of the in vivo nasal cavity including the paranasal sinuses (see III; 485). The models have also been used in other studies (see IV; 486). A MRI scan of a subject is digitally transferred to a CAD system where noise is removed manually. Then the model is built from this data, in a bath with liquid plastic, which solidified when exposed to ultraviolet light. The procedure was validated by comparing a scanning of the model with the subject's MRI.

Very close agreement was seen between the original scanning of the subject and the scanning of the model (see III; 485).

In accordance with these results (see Fig. 7) filling of the maxillary sinus with water significantly changes the area–distance function in vivo (see III; 485).

The conclusion of the study (see III; 485) was that up to 6 cm from the nostril, the volume of the cavity and the area–distance function are measured 'correctly' but thereafter the maxillary sinuses may influence the result at least in the decongested nose.

Based on these studies and as discussed in the subsection on Methodological aspects, many technical

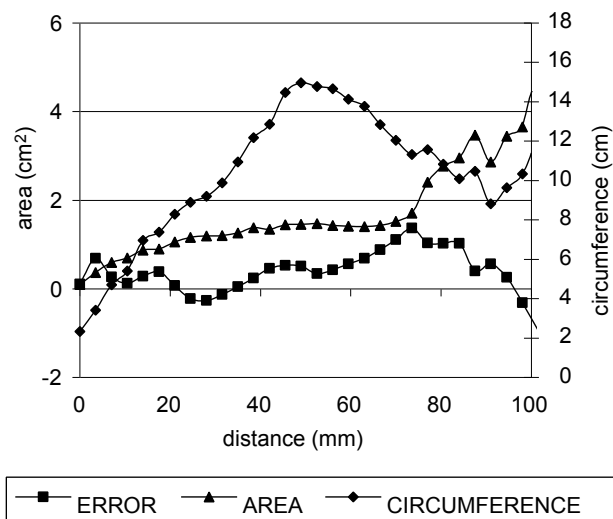


Figure 5. The error in area as a function of the distance in a model. It is seen that the error is not affected by increasing circumference (surface).

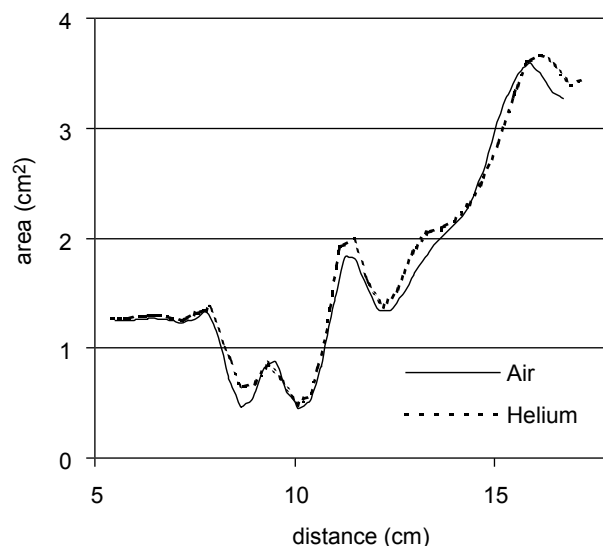


Figure 6. The effect of helium on the area–distance function in a subject.

and physical factors may influence the measurement of the area–distance function in the nose by the acoustic reflection technique.

However these seem to be of minor importance as demonstrated by the validation data for the technique implemented in the nasal cavity (see the subsection on Validation for use in the nasal cavity).

Still, other factors may be important. Some authors have suggested a stand to fix the position of the head during the measurement while others have found that this in fact increases the variability (212, 213).

It has been discussed based on model and in vivo studies whether the normal nasal valve will act as a considerable constriction and affect the measurement and how well these measurements correlate with subjective evaluation (214–217). The influence of a constriction has already been discussed (see the subsection on Methodological aspects) and the correlation between

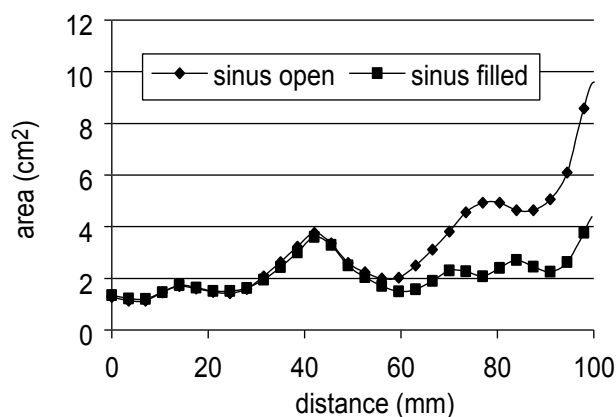


Figure 7. The area–distance function before and after filling the maxillary sinus with water in one subject.

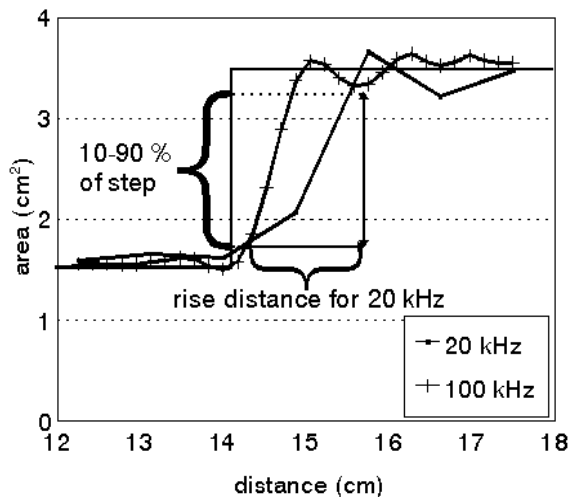


Figure 8. The area–distance function of a step cavity model measured at two different frequencies.

objective evaluation of nasal patency and the subjective evaluation is a general problem, which is not going to be discussed in detail here.

Another important factor is the resolution. Strictly, the resolution in this context is the distance between the data points on the abscissa. The distance between the points is inversely proportional to the sampling frequency of the equipment. Due to low-pass filtering of the signal an increase of the sampling frequency may not increase the information in the results. Therefore, the influence of both sampling frequency and low-pass filtering was tested in a step model (see IV; 486). It was found that the system's ability to recover a step is proportional to the low-pass filtering frequency and that increasing the sampling frequency more than 3–5 times the low-pass filtering frequency did not further improve the accuracy of the area measurement. Figure 8 depicts the effect of different sampling frequencies at a constant low pass filtering (10 kHz) in a step model.

Validation for use in the nasal cavity

Validation of the acoustic reflection technique for use in the nasal cavity has been described in a number of papers (see I–IV (483–486); see also below). In the initial study (see I; 483) a simple technique by filling the nasal cavity with water was employed. The volume entering the nasal cavity was measured together with the pressure at the nostril representing the height of water or distance in the nasal cavity. The cross-sectional areas of the portion of the nose filled by the incremental volume (dV) was estimated from dV/dP and plotted as function of distance. Reasonable correlation was found in both a model and 5 subjects. In the same study a CT-scanning of a cadaver head was compared with acoustic

area–distance function and good correlation was found ($r=0.937$, $N=48$). Here, as in the following study of 10 subjects comparing acoustic rhinometry and MRI (see II; 484) the main problem is the definition of the exact tissue–air boundary. Relatively small changes in the absorption coefficients (contrast in the MRI) may affect the area estimation considerably.

Furthermore, the manual delineation of the border between air and tissue may also influence the results. The results were found to vary up to 10–15% because of these problems.

In another study of a stereolithographic model where the original scanning of a subject was compared with the scanning of a model (and the procedure had to be performed twice), a deviation of only a few percent was seen (see III; 485).

A study (see II; 484) comparing MRI in 10 subjects with the volume of the decongested nasal cavity measured by acoustic rhinometry showed an acoustic volume of 6.47 cm^3 ($SD=1.83$) and MRI volume of 5.65 cm^3 ($SD=1.34$) (Paired t -test $P=0.011$). The regression line (for all 20 cavities, comparing all data points) was $V_{ac} = \text{slope} \times V_{mri} + \text{intercept}$ with a correlation coefficient = 0.70 , $P=0.0007$, intercept = 1.11 , and slope = 0.95 . It was found that there was better correlation in the anterior part of the scanning than in the posterior part. To test the hypothesis that this difference was due to deviation in the axis of the acoustic areas and the MRI areas, a posterior scanning perpendicular to a plane tilted at $45\text{--}50^\circ$ relative to the nasal floor was performed. This gave a better correlation but still a considerable overestimation of the areas by acoustic rhinometry. Correction based on the circumference of the cavity was also tried, but no significant effect was seen. This indicates that the complex geometry in certain parts of the nasal cavity does not significantly influence the results (e.g. in terms of error in the area determination by MRI or sound loss during acoustic rhinometry), see Fig. 6. As an example the effect of decongestion of the nasal cavity evaluated by MRI and acoustic rhinometry is presented in Fig. 9.

In the initial study (see I; 483) 10 subjects were examined in a 'normal congested' state, decongested state after nose drops, and post congestion by histamine. The minimum area obtained by acoustic rhinometry and the minimum area determined by the pressure–flow relationship (rhinomanometry) in the nose were compared. This is based on the assumption that the total pressure difference across the nose is converted to kinetic energy at the minimum cross-sectional area. The results showed that the minimum cross-sectional area determined by rhinomanometry was only one third of the area determined by acoustic rhinometry. Other reasons (e.g. deviations from the expected flow regimen: turbulent vs. laminar) could be possible but unpublished data comparing a stereolithographic model of a subject and circular model with

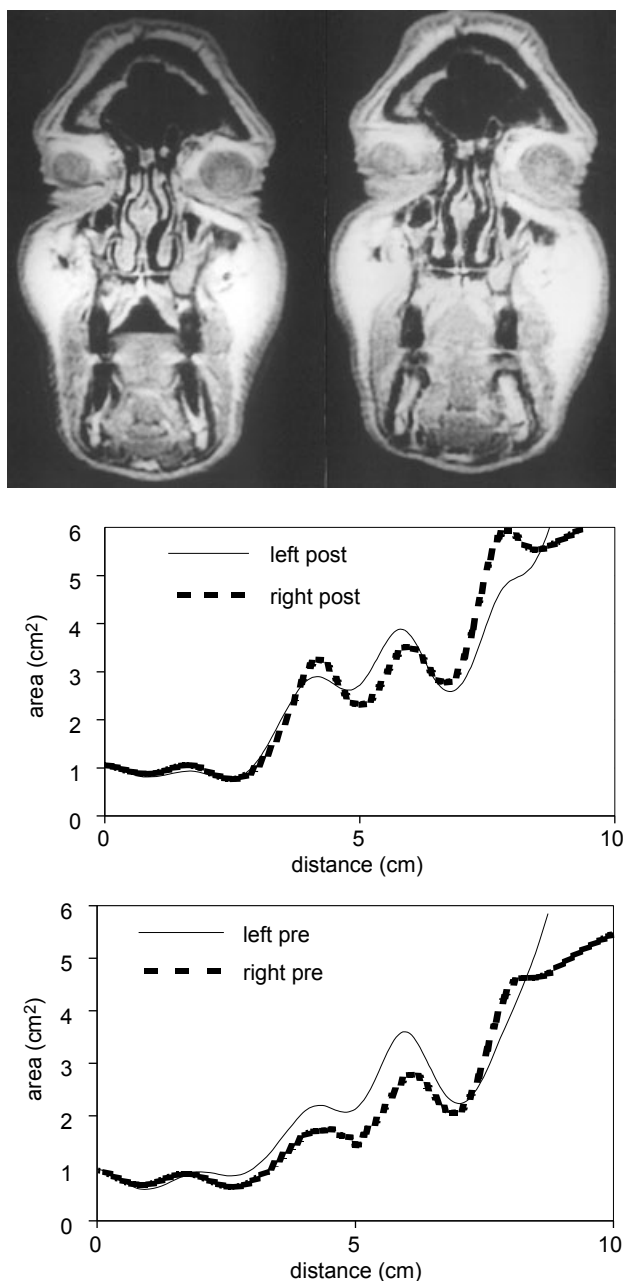


Figure 9. The acoustic area–distance function and MRI before and after decongestion in a subject.

equivalent cross-sectional areas, revealed the same difference indicating that the total pressure loss over the nose is not located at a small segment. This is in contrast with earlier studies (218).

Others have also demonstrated a high correlation between the cross-sectional areas obtained by MRI and by acoustic rhinometry in decongested subjects (0.969) whereas a poorer result was observed in the non-decongested nose (219). In a study, high resolution CT of the nasal cavity and sinuses was compared with a semiautomatic calculation of the area–distance function and acoustic rhinometry in 5 subjects. Comparable

results were found in the anterior part of the nasal cavity but in agreement with other results (see II; 484) the acoustic trace was not so well defined in the posterior end of the nasal cavity (220). Comparable results were also found using the same technique in a study of 14 patients suffering from chronic sinusitis (221). Similar results were seen in a study of nine patients with turbinate hypertrophy who underwent CT-examination and examination with acoustic rhinometry. The cross-sectional areas at the three deflections or minimum notches on the area–distance curve were measured and compared with the 3 narrowest cross-sections in the anterior, middle and posterior part of the nasal cavity determined by CT. High correlation was found for the two first notches ($P < 0.005$) but was poor in the posterior part (222). A recent study comparing the findings by rigid endoscopy and acoustic rhinometry in 85 subjects has confirmed that the first deflection on the area–distance curve reflects the nasal valve and the second the anterior end of the inferior turbinate. The choanae may also in a number of subjects be identified from the area–distance curve as an abrupt change in cross-sectional area (223). Overestimation of the areas in the posterior part of the nasal cavity was also seen in another study comparing acoustic rhinometry and CT-scanning (224). In examining the effect of small spheres introduced into the nasal valve and middle meatus in 3 anaesthetized subjects spheres with a diameter less than 5 mm were not well recovered on the area–distance recording in the middle meatus (225). The reason for this may partly be due to the actual set-up and resolution of the system but also some physical circumstances, e.g. a large middle turbinate hiding the sphere. Others have in similar studies in models and cadavers found better sensitivity for acoustic rhinometry, being able to detect spheres of 0.3 cm^3 (226). Test of the repeatability has shown variation less than 5% in repeated measurements of the nasal cavity volume (227).

As expected, an acoustic leak may affect the measurement considerably (228). It has been described that the area–distance function is affected by breathing and that breath hold is recommended during the measurement (229). It has been shown (unpublished data from the manufacturer) that breathing disturbances are very much dependent on whether the microphone in the equipment is ventilated or not and is insensitive to low frequency pressure changes. In the time scale of an area distance measurement, breathing could be considered as an offset, DC, or constant pressure that may affect the measurement. It has also been questioned whether acoustic rhinometry is reliable if the ambient temperature is changed (230). Unfortunately, it is not clear in that particular study whether the system has been recalibrated at different temperatures and if major changes (more than 10°C) whether the speed of sound setting was corrected. It has

also been discussed in that paper that the measurement in some instances may be unreliable. This may not be due to inherent errors in the system but untrained operators, and the same authors have suggested that standard operating procedures should be used (231–234).

The axis in which sound travels in the nasal cavity may, as already described, affect the area measured, but the axis appears to be parallel with the nasal floor from the nasal valve (235). The terms I-notch and C-notch were introduced to describe the first two deflections (notches) on the area–distance curve. It was hypothesized that the deflections represent the Isthmus nasi and the head of the inferior turbinate (Concha) (235, 236).

Acoustic rhinometry and other methods

Acoustic rhinometry has been compared with rhinomanometry. A study found that the changes in acoustic rhinometry and rhinomanometry were comparable for histamine and bradykinin challenge but acoustic rhinometry was more user-friendly (237). The effect of intranasal levocabastine during allergen challenge could only be demonstrated by subjective methods. Neither acoustic rhinometry nor rhinomanometry or nasal lavage examinations could demonstrate any effect (238). A number of authors find differences between acoustic rhinometry and rhinomanometry, and advocate that the methods are used complementarily (239–241). By nature acoustic rhinometry may measure changes not measured by rhinomanometry and vice versa (242). The resistance of a cross-section may differ considerably depending on the shape despite a constant area. Furthermore, the acoustic axis may also influence the measurement (243). A comparative study of acoustic rhinometry, nasal peak flow, and rhinomanometry found the nosepieces the major drawback of acoustic rhinometry (244), but this was before the discussion of nosepieces and the importance of a correct fitting. Repeated measurements in 6 subjects over a period of two months showed reproducibility for acoustic rhinometry between 5 and 10%, and for rhinomanometry 8–15% (245). In a study of 39 patients with nasal obstruction no significant correlation between subjective scoring and acoustic rhinometry or rhinomanometry could be found (246). As expected not all variables from the rhinomanometric and acoustic rhinometric measurements are equally well correlated with the subjective feeling of obstruction (247). In a number of studies acoustic rhinometry has been compared with other methods: rhinomanometry, manometric rhinometry, nasal peak flow measurements, and similar sensitivity (248, 249) (see also section on Other clinical uses of acoustic rhinometry and acoustic reflections). An investigation has demonstrated qualitatively different effects of tobacco-smoke in subjects complaining of smoke induced rhinitis

compared to nonsufferers. Differences were seen both with regard to symptoms and the dose–response curve from acoustic rhinometry and rhinomanometry (250). Differences in the correlation between the feeling of congestion and acoustic rhinometry and rhinomanometry were found in smoke sensitive and nonsensitive subjects, which made the authors conclude that the two methods are complementary (239). Also when testing for nasal patency in allergy, the methods do not differ from methods used in other cases. Of course, if there is any suspicion of malignancy, visualizing methods like CT and MRI should be used. However, not all studies have it as a primary objective to compare, e.g. sensitivity, variability and reproducibility of the different methods. In general, the user friendliness of acoustic rhinometry is recognized in many of the studies.

Nasal patency in rhinitis: application of acoustic rhinometry and other methods

Rhinitis and hypersensitivity

Rhinitis may be defined as inflammation of the lining of the nose, characterized by one or more of the following symptoms: nasal congestion, rhinorrhoea, sneezing, and itching. Clinically, it may be defined by 2 or more symptoms (nasal discharge, blockage, or sneeze/itch) for more than one hour on most days. These definitions are stated in a consensus report but not further discussed in the report (251). A discussion of the definition is important for epidemiology and monitoring changes in the frequency of the disease, for treatment and for the individual patient. Different classifications of rhinitis have been used based on the precise assumption of causal mechanisms and seasonal variation in frequency of symptoms. Even emotional rhinitis seems to be a special entity. The lack of definitions indicates biological heterogeneity, lack of knowledge of causal mechanisms as well as methods for evaluation. Acoustic rhinometry has been used to differentiate between different types of rhinitis, indicating a higher sensitivity to histamine in allergic rhinitis than in vasomotor rhinitis and a pronounced effect of feet cooling in vasomotor rhinitis (252).

The definition of nasal hypersensitivity or hyperreactivity is even more vague than the definition of rhinitis. Nasal hypersensitivity may be related to any of the common nasal symptoms. Nasal hyperreactivity can be described as a clinical feature characterized by occurrence of nasal symptoms on exposure to stimuli such as dust particles, change of temperature, tobacco smoke, perfumes, and paint smell (253). International guidelines for testing nasal hypersensitivity have not been published but many studies have examined different agents (254) and techniques for testing hypersensitivity. A study of nasal provocation with histamine in allergic rhinitis patients found better reproducibility of nasal

symptoms than nasal airway resistance. The challenge was done using the end-point titration method to obtain a certain level of symptoms (fixed endpoint), e.g. five sneezes or double airway resistance (255). One of the reasons for the poor results could be that hyperreactivity may be multifactorial. Different sites could be involved in hypersensitivity, e.g. the vasculature, receptors, etc. At least some studies seem to indicate increased number of histamine receptors as well as autonomic dysfunction (256). Intrasubject differences in responsiveness to histamine and methacholine do also indicate that hypersensitivity is multifactorial (257). Studies have also shown increased sensitivity to change in posture. Thirty subjects suffering from allergic rhinitis, 25 patients affected by nonspecific rhinitis, and 40 healthy controls underwent positional rhinomanometry. Significant differences in nasal resistance were observed in patients compared with controls a change from seated to supine position (258). A sensitive and specific method could ideally be used to separate healthy from diseased. Numerous studies have reported that histamine challenge may be used (53, 259). A study of sufferers from sick building syndrome found higher sensitivity to histamine measured by rhinostereometry compared to controls (260). The rhinostereometer has been used in many studies of nasal reactivity (261–263). In a study of 60 healthy and 65 patients with allergic rhinitis the authors found it possible to separate the two groups with a specificity of 95%, sensitivity of 86.5%. The test used a derived parameter (nasal airway resistance) and evaluated the dose-response of doubling doses of histamine (264). Other substances have also been used, e.g. distilled water (265) and showed more congestion in patients with rhinitis than controls measured by rhinomanometry. Cold dry air has been used to induce nasal inflammation and congestion (53, 266, 267). A recent small study has shown that intranasal cold dry air is superior to histamine challenge in determining the presence and degree of nasal hyperreactivity in nonallergic, noninfectious perennial rhinitis (268) (see also the section on Physiological reactions and pharmacological studies for study VI (488)). In conclusion, despite many studies, nasal hypersensitivity is still not a clinical entity and the diagnostic procedures are not well defined. Acoustic rhinometry may, in testing hypersensitivity, have a potential advantage compared with other methods since it can ‘focus’ specifically on changes at the inferior turbinate where the major changes during challenge take place.

Evaluation of symptoms in nasal allergy

Nasal symptoms in allergy do not differ from the symptoms in other nasal conditions. The methods for evaluation are the same in all nasal conditions – subjective or objective. All the symptoms can be

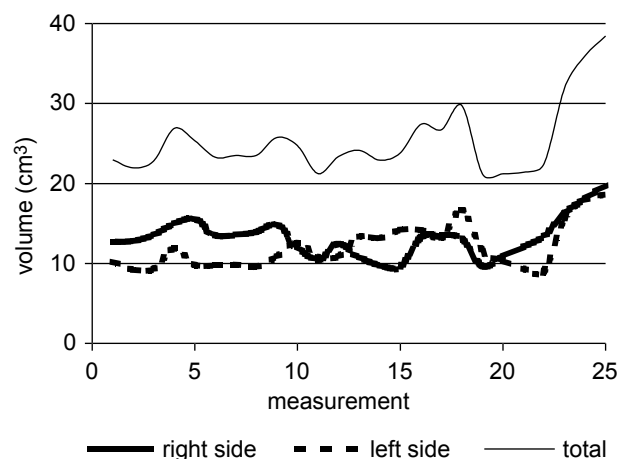


Figure 10. The variability of the nasal mucosa in one subject over 6 h. Nasal volume (0–7 cm) measured by acoustic rhinometry.

‘subjectively’ recorded by more or less complicated scoring systems, e.g. visual analogue scales (VAS). Reviews have described the different methods for examination of normal nasal function and patency (269). Nasal congestion is probably the most complex symptom and its measurement has already been discussed (see the section on Acoustic rhinometry). Secretion can be weighed or number of used handkerchiefs can be counted. Sneezing can be counted (or scored). Sneezing and itching are usually closely linked though itching is often a less prominent symptom.

Normal nasal patency and the variability of the nasal mucosa

Different synonyms have been used for nasal obstruction. In one review, congestion is defined as the swollen mucosa seen during clinical examination, obstruction is the subjective discomfort because of insufficient airflow during breathing and decreased patency, and is determined by objective measurements (270). Normal values measured by acoustic rhinometry have been reported from different countries (271, 272).

In a study from America 106 subjects were examined by acoustic rhinometry and analysed with regard to race and height, indicating racial differences between Anglo-Saxon, Chinese, and Negroid noses (273, 274). No differences could be demonstrated between Anglo-Saxon and Indian noses (275). In a Swedish study of 334 normal individuals the MCA (minimum cross-sectional area) correlated weakly to weight, height, age, and body mass index (276). In the normal nose the minimum area is located at the nasal valve or at the head of the inferior turbinate and moves anteriorly during decongestion (277). In the normal population 10–20% suffer from nasal obstruction to such an extent that it is noticed in daily life but did not cause professional attention. Based on a history of nasal hypersensitivity or allergy, septal deviation or small nasal dimensions measured by acoustic rhinometry, it is possible to predict a

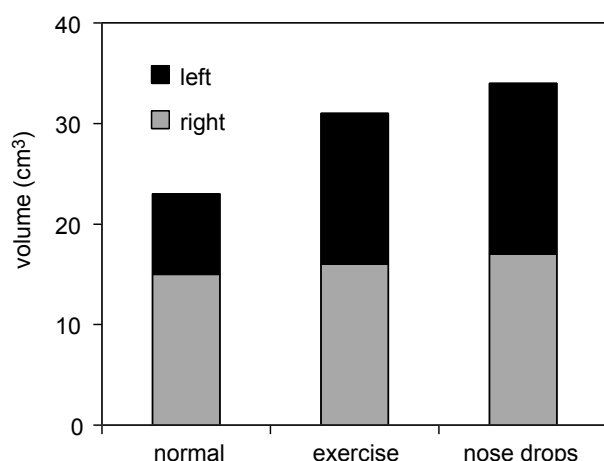


Figure 11. The nasal volume (0–7 cm) during exercise in a nonallergic subject compared with decongestion by nose drops.

considerably increased risk of the feeling of nasal obstruction (278). Subjects with apparently normal nasal patency may feel nasal obstruction; probably due to increased vasomotor activity but in 36% of 67 patients the feeling of obstruction disappeared over a period of 11 years (279). When evaluating normal nasal patency it is important to have an estimate of the normal or spontaneous variation in nasal mucosa congestion. Studies have shown that an acclimatization period reduces mucosa variability during the measurements (280). The nasal cycle may also contribute to the variation of the nasal mucosa but in case of a bilateral (classical) cycle the total 'congestion', sum of the two sides, is usually constant. In a study (see V; 487) of 12 nonallergic subjects measurement of the nasal volume, minimum cross-sectional area as well as the area at the anterior end of the inferior turbinate, a typical nasal cycle was found in 4 out of 12 subjects. The measurements were done every 15 min for 6 h. The variability of the nasal mucosa determined as the coefficient of variation for the entire was 9.4% for the total nasal volume, 11.3% for the minimum area and 17.8% at 3.3 cm from the nostril which usually represents the head of the inferior turbinate. Figure 10 shows the variation and nasal cycle in a subject in this study.

During exercise (e.g. 15 min exercise at 75% of maximum expected heart rate), the nasal mucosa decongests almost to the same level as after using topical decongestant (α -agonist, xylometazoline hydrochloride nose drops), see Fig. 11. The effect of exercise indicates the potential of large variability of the mucosa to external stimulation.

Variability in congestion of the nasal mucosa in allergy

The minimum cross-sectional area is located at the inferior turbinate in patients suffering from allergic or vasomotor rhinitis in contrast to nonallergic subjects

where it more often is located at the internal ostium (281). The spontaneous variation of the nasal mucosa was found to be larger in allergic subjects than in nonallergic subjects (see V; 487). The coefficient of variation for the nasal volume (0–7.2 cm in the nasal cavity) was 14% in allergic and 9.4% in nonallergic subjects ($P=0.004$). After exercise a decrease in the variability of the nasal mucosa in allergic subjects compared with a tendency to increase in nonallergic subjects was seen. The reason for this is unknown but may indicate that increased adrenergic tone for a period of time may stabilize the vasculature in allergic subjects and destabilize in nonallergic subjects.

The volume before decongestion did also tend to be smaller in allergic subjects than in nonallergic subjects making the effect of decongestion larger in the allergic subjects ($P=0.08$, 56% vs. 42% for the nonallergic subjects; see Fig. 12) (see V; 487).

Similarly, in a study of the response of normal and allergic subjects to a topical decongestant, the normal subjects showed an average total (right + left) percent area change at the minimum cross-section of 15.6%, and the allergic subjects had a percent change of 24.6% ($P=0.04$) (282). Another study of the decongestant tramazoline also showed a more congested mucosa in severe perennial allergy than in controls (nasal volume) and subjectively a more pronounced effect of decongestion (283).

Nasal challenge and acoustic rhinometry

Nasal challenge may be used to test hypersensitivity (see the subsection on Rhinitis and hypersensitivity), allergy, or to investigate effects of drugs, etc. In the first study using acoustic rhinometry to examine nasal airway challenge (see VI; 488), 12 allergic and 12 nonallergic subjects were challenged with histamine. Nasal airway volume and the minimum area were measured. Different dose-response curves for histamine

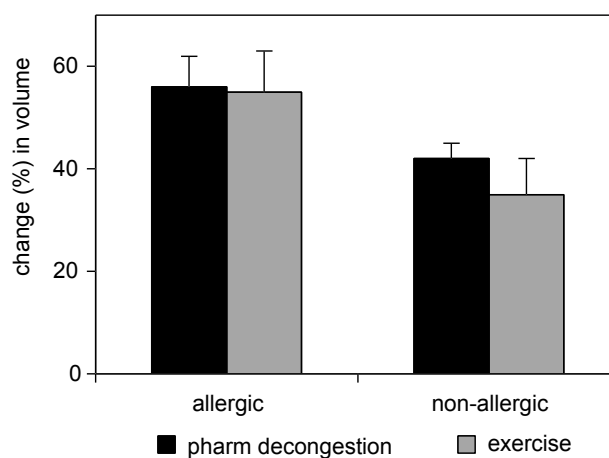


Figure 12. Nasal volume in allergic and nonallergic subjects before and after decongestion.

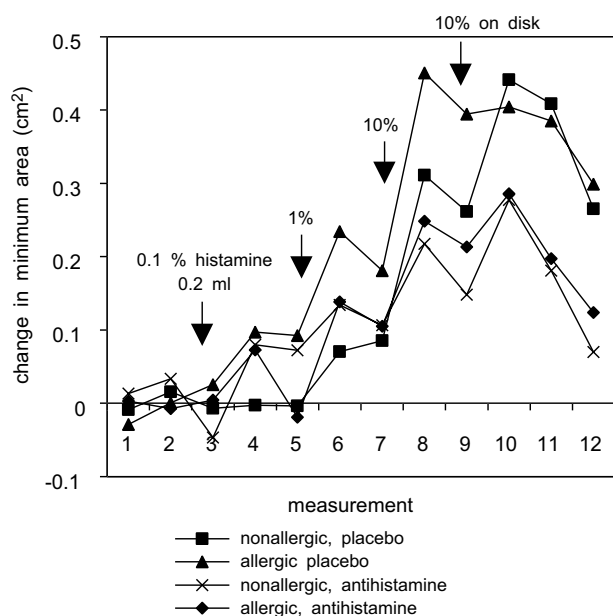


Figure 13. The dose-response curve for histamine challenge in allergic and nonallergic subjects.

were obtained showing a shift to the left in allergic compared with nonallergic subjects. No difference was seen after pretreatment with antihistamine (Fig. 13).

In an increasing number of reports it has been claimed that topical nasal decongestant may have a rebound effect. The rebound effect is, according to some authors, synonymous with the term rhinitis medicamentosa. The phenomenon has especially been examined by rhinostereometry in nasal challenge tests and it has been claimed that the rebound effect may be seen after only 7 days of treatment with decongestant nose drops. The phenomenon has been attributed to increased sensitivity of the nasal mucosa induced by the active substance itself (agonist) or the preservative benzalkonium chloride (261).

In the most recent study by the same authors, acoustic rhinometry and rhinostereometry was used to evaluate two parallel groups receiving decongestant nose drops with and without benzalkonium chloride. The previous results could not be confirmed and in fact this study showed that the group who received the preserved nose drops had decreased reactivity to histamine after 10 days of treatment (284). Treatment with a nasal steroid in patients suffering from rhinitis medicamentosa induced increased histamine sensitivity measured by acoustic rhinometry and rhinostereometry, which should indicate that interstitial oedema is an important factor in rhinitis medicamentosa (285). The reduction in swelling was faster than with placebo (286). In another study benzalkonium chloride caused a slight prolongation of mucociliary clearance shortly after application but had no detectable effect on nasal mucosal function after 2 weeks of regular use (287).

In a study, 10 patients with allergic rhinitis under-

went a unilateral nasal provocation test with 1000 biological units of specific allergen. Acoustic rhinometry was performed at 10, 20, 30, 45 and 60 min, and 2 and 8 h after exposure to allergen. The minimum cross-sectional area and nasal volume were measured and showed a unilateral early response and a symmetrical late phase response (288). In a study of 8 patients suffering from either grass pollen or house dust mite allergy, congestion in the contralateral nostril to the challenge side was interpreted as a late-phase reaction (289). Azelastine showed efficacy in a study of 28 subjects suffering from hay fever after histamine and pollen challenge measured by acoustic rhinometry and rhinomanometry (290).

Acoustic rhinometry evaluating treatment of rhinitis

This section covers only studies VI and VII (488, 489) and other studies concerning the treatment of rhinitis are mentioned in the subsection on Allergy and asthma. In the study of 12 allergic subjects (see VI; 488), it was found that antihistamine (cetirizine) did not have significant effect on mucosal swelling measured by acoustic rhinometry during allergen challenge. The effect was quite clear during histamine challenge. During both allergen challenge and histamine challenge there was a clear effect of antihistamine on the subjective evaluation (VAS) of the histamine-mediated symptoms sneezing and itching. Therefore, another double blind placebo-controlled study (see VII; 489)

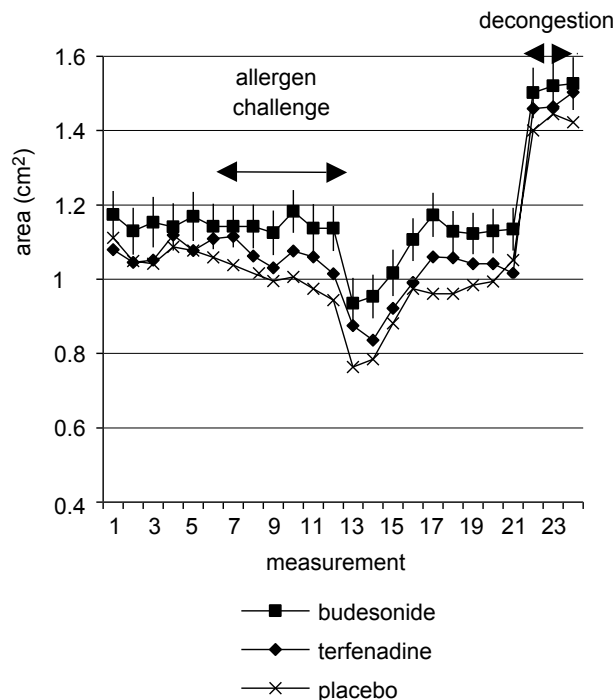


Figure 14. The total minimum cross-sectional area during pollen challenge in 17 allergic subjects pretreated with placebo, terfenadine or budesonide. Decongestion was performed before the last 3 measurements.

was performed in 17 patients suffering from hay fever to evaluate the effect of nasal steroid (budesonide) and antihistamine (terfenadine) during allergen exposure. The minimum cross-sectional area and nasal volume were measured by acoustic rhinometry and the subjective evaluation by a questionnaire (VAS), every 15 min for 6 h. Olfaction was also evaluated (see the subsection on Rhinitis and olfaction). The results showed a significant effect of budesonide on nasal congestion during pollen challenge. There was a tendency to an effect for terfenadine for the objective variables. Furthermore, a tendency to decrease nasal congestion during budesonide treatment before nasal challenge was found. This and the findings in studies V and VI (487, 488), and (282, 283) indicate a tendency to increased effect of decongestion in allergic subjects, and that inflammation and hypersensitivity is present in hay fever patients out of the season. Figure 14 depicts the results of the challenges.

In the same study a high correlation between the total minimum area and the subjective occlusion score was found in some subjects exposed to increasing doses of pollen whereas in others no correlation was seen. Especially in subjects with 'small' noses a good correlation was found, see Fig. 15.

Rhinitis and olfaction

Impaired olfaction may be an important symptom in 10–15% of patients suffering from hay fever (291). Until study VII (489) the correlation between nasal patency and olfactory function or the effect of nasal steroid on olfaction had not been studied. Later, another study also found some effect on the olfactory function in hay fever patients by treatment with local steroid (292). In study VII (489), the olfactory function was measured by a triangle olfactometer determining the olfactory threshold for butanol. The threshold was determined before, immediately after, and 1.5 h after allergen challenge. A correlation between nasal cavity dimensions and the olfactory threshold was found in 7/17 subjects. In these subjects, benefit of budesonide treatment on olfactory function was seen during challenge. Another study also showed correlation between the change in olfaction and change in nasal dimensions measured by acoustic rhinometry during corona virus induced common cold (293). Others using olfactory and event-related potentials (ERPs) to assess olfaction could not demonstrate a significant effect of decongestion on olfaction in acute rhinitis due to common cold despite a clear effect on the nasal dimensions evaluated by acoustic rhinometry (294, 295). Similarly, no significant correlation was found between olfaction and nasal patency during allergen challenge (296). A study of healthy men across the diurnal cycle showed a weak but statistically significant negative correlation

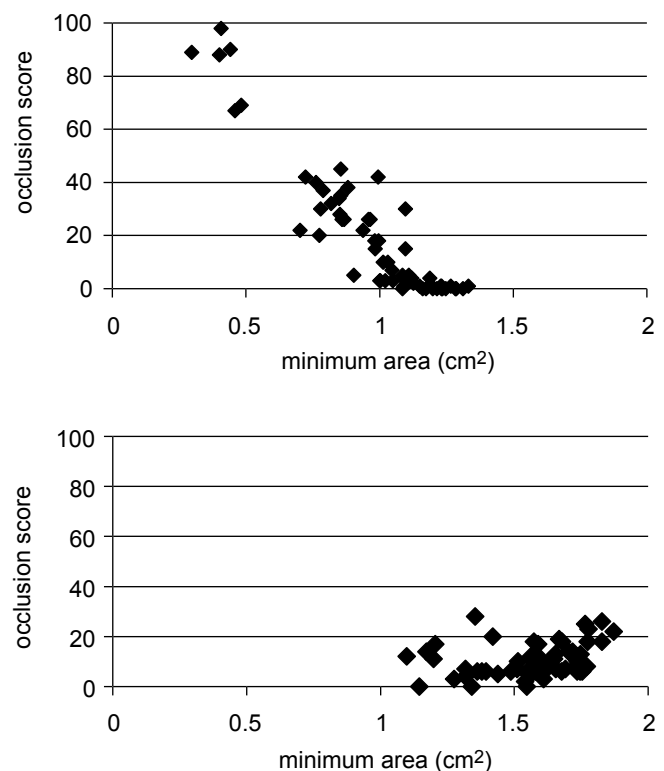


Figure 15. The correlation between subjective evaluation of nasal occlusion and the total minimum area in two subjects with different ranges of minimum cross-sectional area.

between nasal volume and odour threshold (297). A study of paired phenylethyl methyl ethyl carbinol olfactory detection thresholds in 102 patients operated for chronic rhinosinusitis showed a correlation between olfaction and increase in nasal volume measured by acoustic rhinometry ($P < 0.005$) (298). In conclusion, the olfactory function in hay fever and other forms of rhinitis may partly be dependent on the nasal dimensions but inflammation in the nasal mucosa may be a more prominent factor.

Other clinical uses of acoustic rhinometry and acoustic reflections

Clinical application

The acoustic reflection technique for determining the cross-sectional area as function of distance has been used to investigate different aspects of physiology, anatomy, and pathology in the upper airways. The main interest so far has been in surgical procedures in the nose, and pathological changes in the pharynx and trachea including snoring, see reviews (299–301). Acoustic rhinometry seems to have established its value for different clinical applications in the upper airways (302).

Normal anatomy and nasal obstruction

The use of acoustic rhinometry has confirmed the observation that the minimum cross-sectional area in the nasal cavity is located anteriorly, in agreement with pressure measurements which indicate that the resistive segment of nasal cavity is located in the first few centimetres of the nasal cavity (218, 303). In some subjects the minimum cross-sectional area is located at the nasal valve, in others especially in cases of turbinate hypertrophy it is the anterior part of the inferior turbinate (277, 281). Correlation has been found between the dimensions of the external nose and the minimum cross-sectional area (304).

Physiological reactions and pharmacological studies

Acoustic rhinometry has been recognized as a method to study nasal physiology and vascular reactions in the nose (305). The effect of localized skin cooling has been studied by acoustic rhinometry. An immediate reflex shrinkage of the nasal mucosa followed by a tendency to congest was observed (306). The same nasal reaction to whole body cooling is seen (307).

The nasal cycle has been examined, but in contrast to the original studies where a typical reciprocating cycle was found in 80% of subjects (34); acoustic studies in a limited number of subjects showed only 25–50% with a typical cycle (see I; 484) and (308, 309). In another study of the nasal cycle the subjective feeling of patency was not related to the volume and cross-sectional area changes measured simultaneously (310).

The nasal mucosa is affected by posture (311). It has been shown that the mucosa swells when the posture is changed from upright to supine position and by reflexes producing congestion in the ipsilateral nasal cavity if a lateral pressure is applied to the body (312–316). It is still discussed whether the patency of one side influences the other (317, 318).

The concentration of intranasal nitric oxide seems independent of nasal cavity volume (319). On the other hand a study using acoustic rhinometry showed that nasal nitric oxide is not the principal substance controlling basal nasal patency or acute congestion following allergen challenge in allergic rhinitis (320).

In the lower airways a tracheobronchial dilatation is seen during isocapnic hypoxia (321). Nasal decongestants have been evaluated by acoustic rhinometry, as a simple method to assess the effect of different compounds, dosages, and dosage forms (284, 314, 318, 322). In a dose–response study of oxymetazoline, acoustic rhinometry was found to be more sensitive than rhinomanometry (323). Differences between conventional imidazoline-containing nasal drops were found with regard to duration of action (324). Another study also showed equivalent effects on nasal patency of a single dose of oxymetazoline nasal spray evaluated by acoustic rhinometry, rhinomanometry, and VAS, in

normals. The day-to-day baseline variability was less than 10% in this study (325). A single 60 mg dose of pseudoephedrine produced significant increases in the dimensions of the nasal cavity compared to placebo using acoustic rhinometry, and this is associated with a reduction in the symptoms of congestion in common cold (326).

The influence of other compounds delivered through the nasal mucosa, like octreotide or starch microspheres (327, 328), has also been examined. The effect of different neurotransmitters has been studied (305, 329) and both substance P and calcitonin gene-related peptide were found to congest the mucosa. A study found comparable results during nasal challenge with histamine and bradykinin evaluated by rhinomanometry and acoustic rhinometry (237). The efficacy of antihistamines for nasal congestion has been measured by acoustic rhinometry in a number of studies (330, 331). In one study using acoustic rhinometry and rhinoscopy, topical treatment with furosemide after polypectomy has been described to effectively hinder reoccurrence (332). The effect of antibiotics on congestion due to nasal infection has also been studied by acoustic rhinometry (333). Findings suggest that a thromboxane A antagonist ramatroban may inhibit the increase in nasal mucosal swelling measured by acoustic rhinometry during allergen challenge, but has no effect on nasal mucosal hemodynamics measured by Laser Doppler (334). A study examining 4 different antiallergic drugs found good correlation between acoustic rhinometry and symptom score (VAS) (335). In conclusion, acoustic rhinometry seems to be a valuable tool in examination of physiological reactions and pharmacological effects in the nose. Still, nasal congestion is only one of the complex responses of the mucosa and is not always directly related to the feeling of obstruction.

Pharynx

The cross-sectional areas of the pharynx have been shown to be dependent on lung volume (336–339) and posture with decreasing size in supine compared with the upright position (340, 341). Changes in the pharynx have also been observed after methacholine challenge although the reasons for this are unknown (342). Most of the studies with the acoustic reflection technique in the pharynx have been related to snoring.

Snoring

It has been found that the cross-sectional area of the pharynx and glottis is smaller in subjects with obstructive sleep apnoea than in controls, and that the size of the airway correlates with the frequency of apnoeas (343–345). In another group of patients with sleep apnoea syndrome, smaller passage in the nasal cavities was found (107). Similarly, other studies have found a correlation between change in the cross-

sectional area of the airways during negative pressure load or at different lung volumes and the number of apnoea periods. This suggests a clinical use for acoustic rhinometry in the examination of subjects with snoring and sleep apnoea syndromes (346–350). In snorers with obstructive sleep apnoea compared to subjects without apnoea, increased compliance of the pharynx was found and an effect of weight loss in obese patients has been demonstrated by the acoustic reflection technique (351–354). In a study of female snorers, there were no differences in nasal cavity volume compared with controls, whereas differences were observed in the body mass index and nasal flow volume curves (355). After uvulo-palato-pharyngoplasty (340) a decrease in compliance is related to reduction in number of apnoeas. The effect of continuous positive airway pressure ventilation has also been examined (356). In an evaluation of uvulopalatopharyngoplasty using acoustic rhinometry the authors concluded that no effect was seen in the epipharynx but was observed in the turbinate region. This may be due to sound transmission from one side through the epipharynx to the other side (357). No correlation between the sleep apnoea index and nasal dimensions could be found in a study of 76 patients with sleep apnoea syndrome but without any nasal complaints (358). Acoustic rhinometry can be used to exclude major abnormalities in the nose, which may lead to sleep disorders. The acoustic reflection technique in its present form has some limitations for measurements during sleep but modified techniques, e.g. measuring inside a catheter may show to be useful.

Application in larynx and trachea

One of the first clinical applications of acoustic reflections has been the examination of the trachea. Both the glottic area and the cross-sectional areas of the trachea may change during respiration and measurements should be done at a fixed lung volume (201, 209). A positive correlation between tracheal cross-sections and lung volume has been found and so also to different flow variables in some subjects (208, 359). Tracheal stenoses have been measured with acoustic reflections and the results were in agreement with radiographic evaluation (202). The effect of laryngotracheoplasty has also been examined (360). Different mechanical properties or bronchomotor tone of the trachea has been demonstrated by different relative hysteresis of the upper and lower part of the trachea (361). Positive and negative pressure seems to have approximately the same effect on the extra thoracic and intra thoracic parts of the trachea (362). The changes in the cross-sectional areas of the bronchi during apnoea were found to be more pronounced in asthmatic subjects than controls, and

smallest in double lung transplanted subjects. This could be abolished by ipratropium in asthmatic subjects indicating a higher airway tone in these subjects (363). The tracheal distensibility in patients with cystic fibrosis is probably increased whereas the size does not differ from normals (364).

Nasal surgery and acoustic rhinometry

Acoustic rhinometry has been employed to evaluate the effect of different kinds of nose surgery (365, 366). The effect of septoplasty has been demonstrated (367–371). Results suggest that patients with the smallest preoperative minimum cross-sectional areas have the subjectively best effect of the operation (367). Despite this, large-scale studies should be performed to test the ability of acoustic rhinometry in the preoperative evaluation of the patients to anticipate the results of an operation. A new laser-assisted septoplasty technique has been evaluated in 120 patients (372). Both acoustic rhinometry and nasal peak flow are recommended for evaluation in relation to septoplasty (373). Turbinoplasty seems to induce a reduction of tissue or a scarring in the mucosa that normally can be decongested (281, 368, 374, 375) which can be seen as a reduction of the decongestant capacity of the mucosa evaluated by acoustic rhinometry. Acoustic rhinometry has been used complementary with other methods to examine different surgical procedures for turbinate hypertrophy (376, 377). A follow-up examination 5 years after septoplasty and turbinoplasty showed significantly reduced dimensions in the nasal cavity and that only 40% of the patients were satisfied with the result (378). Another study concluded that the value of acoustic rhinometry is limited because negative effects were seen after septoplasty and there was a lack of correlation between symptoms and objective measures in this selected group of patients (379). On the contrary, others have found acoustic rhinometry useful. They show that postrhinoplasty obstructed patients still have smaller nasal dimensions than normals despite an increase in cross-sectional area (380). A good correlation was found between objective and subjective results in a study of 24 patients operated for septal deviations (381). A study of 50 patients with septal deviations and 15 controls showed that both rhinomanometry and acoustic rhinometry were able to detect anterior deviations but more uncertainty appears in the posterior part of the nasal cavity (382).

In postoperative care, acoustic rhinometry has been used to study the effect of different nasal packings (383). An important finding by acoustic rhinometry is that reduction rhinoplasty also reduces the nasal valve area with the risk of inducing breathing problems (384). This has also been shown in a

cadaver study and seems to be related to the detachment of the bony vault from the surrounding structures (385). Lateral rhinotomy has been shown to have negative effects on the nasal patency (386). Some authors find acoustic rhinometry very useful in maxillary osteotomy to relieve obstructive sleep apnoea and in cleft palate patients to identify obstructions and evaluate operative results (387–392). As expected, rhinomanometry was more sensitive than acoustic rhinometry to demonstrate changes due to operation for nasal valve collapse (393).

Occupational medicine and acoustic rhinometry

Inhalation of pollutants, gases, and particles may affect the congestion of the nasal mucosa, which can be monitored by acoustic rhinometry. Inhalation of diethylamine had no acute congestion effect on the nasal mucosa evaluated by acoustic rhinometry and rhinomanometry (394). The deposition of particles in the nasal cavity in relation to nasal cavity dimensions has also been described (65). Acoustic rhinometry was employed to study the effect of an increasingly used solvent, N-methyl-2-pyrrolidone (NMP). No significant effect was found neither on the nasal airway nor on the eyes or lower airways examined by other methods (395). A dose–response study of N,N-dimethylbenzylamine (DMBA) showed no significant symptoms or nasal congestion evaluated by acoustic rhinometry but an increase of eosinophils in the nasal lavage (396). Similarly, a study of methyl tertiary butyl ether (MTBE) and related compounds did not cause any dose–response effect measured by nasal lavage, acoustic rhinometry, tear film break up time, etc., although a minor effect was seen simply due to challenge (397–399). A study of nitrous acid (HONO) did not show any effect detectable by acoustic rhinometry (400). Swine dust challenge clearly induced mucosal swelling measured by acoustic rhinometry and the response correlated with an increase in IL-8 in nasal lavage fluid (401). No effect using acoustic rhinometry measures, nasal lavage or lung function was seen by the use of active charcoal filters, and a particle filter, though there was clear reduction of the intensity of symptoms induced by diesel exhaust (402). In Swedish schools with poor indoor environment due to low ventilation and higher bacterial counts in air samples, nasal lavage from personnel showed higher cytokine activity and acoustic rhinometry revealed swollen nasal mucosa (381, 403, 404). Acoustic rhinometry has also been used in similar studies of hospitals (405). Exposure to passive smoking and increased body mass were predictors of reduced nasal volume in children 7–12 years old (406).

Measurements in children

Acoustic rhinometry has been used in newborns (407) and preschool children (408) to evaluate the normal nasal cavity dimensions. A study of 183 Asian children 1–11 years old found a correlation between age and the size of the minimum cross-sectional area (409). The dimensions in the nasal cavity have been examined in 12-year-old children with congenital deviation of the nasal septum indicating that the septum may straighten during growth (410). Decreased nasal volume was found in children with oral breathing (411). Acoustic rhinometry has also been used in preliminary studies to demonstrate changes in the volume of the nasopharynx after adenoidectomy (412) and the response of the nasal mucosa to histamine challenge (413). Some 101 patients aged 2–13 years were examined preoperatively prior to adenoidectomy, to evaluate the predictive value of acoustic rhinometry. As a single examination it had a low but significant predictive value of the severity of obstruction due to adenoids evaluated by the surgeon intraoperatively. Using logistic regression and combining the parents' scores of obstruction, snoring, and mouth breathing, a high predictive value with regard to the decision to operate was found (414). Another study showed reduction of congestion in the nasal cavity after adenoidectomy indicating a sustained effect of the adenoids on inflammation in the upper airways (415). Some authors find that acoustic rhinometry is a sensitive method to detect adenoids (416) while others are unable to separate subjects with adenoids and controls (417). Acoustic rhinometry may also be a useful nonendoscopic technique to evaluate the nasal airway in the stridorous child (418).

Acoustic rhinometry has been compared with rhino hygrometry (a method for determining the size of condensed air on a cold plate in front of the nose) in 15 children to examine the nasal cycle. In children with a regular classical cycle (80%) high correlation was found between the two methods, which was lower looking at all data. It was concluded that acoustic rhinometry is the method of choice to investigate physiological changes in nasal congestion in children and that the nasal cycle has equivalent patterns in children and adults (419). Due to the uncomplicated and noninvasive nature of the technique, it may prove to be a useful tool in examination of the airways in children although the equipment has to be adjusted to obtain optimal results (420, 421). Some artefacts may occur, but model examinations provide the means to optimize the system (421, 422), keeping in mind that the results may only be valid for the specific set-up. The application of acoustic rhinometry in children has especially been examined by Djupesland (423). The continuous acoustic method was used but the results of this technique do principally not differ from the

results of other techniques like the one described in the section on Acoustic rhinometry. The modified method for use in children has been validated in model studies and in a CT examination of 5 children with congenital malformation (choanal atresia) (424–426). In a study of 94 newborn infants correlation between the nasal dimensions and the circumference of the head was found (427). The results confirmed what has been found earlier (407). Re-examination of 39 of the 94 infants showed that the total minimum cross-sectional area increased by 67% (0.21 to $>0.35 \text{ cm}^2$) during the first year of life. A significant difference in nasal volume in a subgroup of children with nasal congestion compared to the rest was found (428). No effects were seen on respiratory mechanics by closure of one nostril measured as the compliance and resistance of the total respiratory system (closure of one nostril reduced the total minimum cross-sectional area in the nose by more than 50% measured by acoustic rhinometry) (429).

Measurements in laboratory animals

Previously, assessment of changes in congestion of the nasal cavity in guinea pigs was primarily done by passive rhinomanometry or other flow methods. Guinea pigs are used in development of drugs and acoustic rhinometry, as a noninvasive method for objective assessment of the nasal passage, seems to be valuable (430, 431). Examinations in models and correlations with rhinomanometry confirm a reasonable accuracy if the equipment is modified and optimized for measurement of the small dimensions (432). The effect of an antiallergic drug has been examined (433). Based on a receptor binding assay and measurements by acoustic rhinometry, it is suggested that sensitization with allergen increases the number of histamine H1 receptors. The increased number of H1 receptors in the nasal mucosa of sensitized guinea pigs may be one of the causes of nasal hyperresponsiveness to antigen (434, 435). The vascular effects of sensory peptides have also been examined (436).

The paranasal sinus and acoustic rhinometry

The paranasal sinuses may influence the evaluation of the nasal cavity by acoustic rhinometry (see IV; 486) (211). Acoustic rhinometry has been used to describe the effect of various fenestrating operations (365, 438) although one study did not find acoustic rhinometry able to detect any effect of inferior meatal antrostomy (438). Acoustic rhinometry has also been recommended along with other methods for evaluation of the nasal function in relation to sinus disorders (439, 440). Here, a modification of the technique may give valuable information about the ostia and sinuses but further research is necessary.

Polyps

The effect of medical and surgical treatment of nasal polyps are easily demonstrated by acoustic rhinometry (441–444). A reasonable correlation between the amount of polyp tissue during polypectomy and the change in acoustic volume has been found in 20 subjects (445). In a study, 20 patients with recurrent nasal polyposis but without any history of aspirin sensitivity were examined. 2000 micrograms of intranasal lysine aspirin was administered to one nostril and saline to the other, once a week for periods of up to 15 months. This had a preventive effect on reoccurrence of the polyps evaluated by acoustic rhinometry and rhinoscopy (446).

Allergy and asthma

An expiratory glottic widening has been demonstrated in asthmatic subjects during exercise-induced bronchoconstriction (447). In exercise-induced asthma the expected reduction in bronchial areas could be detected, whereas an intrathoracic tracheal dilatation was seen in both asthmatic and normal subjects during exercise (448). Changes in pulmonary function evaluated by, e.g. FEV1, may not necessarily reflect the change in all segments of the airways. Histamine does not seem to affect the trachea whereas LTC4 and methacholine induce a constriction (449). Differences have also been found between various bronchodilators (450) and among asthma patients (451).

Acoustic reflections have been used to evaluate the allergen challenge effect (see VI and VII; 488, 489) and a late phase reaction in the nasal cavity has been described. However, the interpretation of the results of the study (289) can be discussed because of the influence of the nasal cycle during unilateral challenge. A study of 5 allergen challenged subjects concluded that acoustic rhinometry can quantitatively assess congestion during immediate and late-phase reactions without significant correlation to the degree of individual inflammatory events assessed (452).

Acoustic rhinometry and anterior rhinomanometry showed significant correlation in an allergen challenge study, but acoustic rhinometry was found superior to rhinomanometry especially in the evaluation of initial nasal blockage (453). Acoustic rhinometry was compared with nasal inspiratory peakflow in a nasal provocation test with allergen and was found equally sensitive though acoustic rhinometry was superior because it is less dependent on the subject's cooperation (454). In another study, nasal peakflow measurements were found to be more sensitive than acoustic rhinometry and rhinomanometry (455). The specifications of the acoustic rhinometer used in that study would probably not fulfil later requirements. Also a combination of measurements of nasal secretion and acoustic rhinometry or rhinomanometry has been recommended (456). A study found that changes

measured by acoustic rhinometry and rhinomanometry were comparable in histamine and bradykinin challenge but acoustic rhinometry was more user-friendly (237, 457). Other studies find acoustic rhinometry very suitable for histamine and allergen challenge (458–461) and along with rhinomanometry to monitor the effect of local nasal immunotherapy (462).

Others had less success in using acoustic rhinometry in a cat allergen challenge (463) but the way of dosing the allergen may also be an important factor here. A study found that hypertonic saline nasal provocation stimulates nociceptive nerves, substance P release, and glandular mucous exocytosis in normal humans but no effect was seen on the nasal cavity volume measured by acoustic rhinometry (464). The timing between nasal congestion during allergen challenge and the presence of the high-affinity IgE receptor (Fc epsilon RI) has also been examined (465). Rhinitis during pregnancy has been described in a number of studies but no single factor has been established as responsible for increased rhinitis symptoms during pregnancy. A study showed increased presence of house dust mite allergy but no significant difference from (pregnant) controls measured by the susceptibility to histamine (rhinostereometry and acoustic rhinometry) (466). This is similar to earlier reports (467). Furthermore, neither nasal peakflow measurements nor acoustic rhinometry could prove any correlation between the menstrual cycle and nasal congestion (468). Acoustic rhinometry was used to show that capsaicin de-sensitization of the human nasal mucosa reduces vascular effects of lactic acid and hypertonic saline (469). Capsaicin desensitization of the nasal mucosa reduces symptoms after allergen challenge in patients with allergic rhinitis, but no effect was found on nasal swelling measured by acoustic rhinometry or eosinophilic migration (470). Acoustic rhinometry has been used in a number of experimental studies in allergy but until now, similar to other methods for evaluation of the nasal passage in allergy, acoustic rhinometry is not used routinely in daily clinical work.

Other applications

Acoustic reflections have been used to test the longitudinal area profile of endotracheal tubes (471) and also to test musical instruments (204).

In a pilot study (cross-over) of 13 patients suffering from nonallergic rhinitis treated with acupuncture, and two placebo controls (sham acupuncture and mock electrical nerve stimulation), an improvement was found on the minimum cross-sectional area (472). The effects of the Breathe Right nasal strips and other dilators (Airplus), which are used to decrease the nasal resistance, were examined by rhinomanometry and acoustic rhinometry. They showed equivalent significant

increases in conductance and minimum cross-sectional area (473–476). Similar results were seen in 53 athletes where an increase in the nasal valve area by means of the nasal strip was demonstrated using acoustic rhinometry (477). Acoustic rhinometry has been used in a case report to examine the facial development in a pair of twins, one of them suffering from trauma to the nose (478).

The nasal pressure-volume relationship has been evaluated after congestion with histamine and decongestion with oxymetazoline. The compliance of the nasal mucosa is changed during decongestion especially at the anterior part to the turbinates but seems to be unaffected by congestion due to histamine (479). It has been correctly stressed in a paper that follow-up after surgery for nasal tumours is not an area where acoustic rhinometry should be used (480). A study indicates that acoustic rhinometry is capable of detecting changes in velar positioning during 'silent' speech (481). Other applications of acoustic rhinometry are of course possible but further validation may be necessary.

Conclusion and future aspects of acoustic rhinometry

Acoustic rhinometry was introduced in 1989 after the technique for measuring the area–distance function by acoustic reflections in the lower airways had been known for more than 20 years. During the first decade of the nasal application more than 250 papers have been published indicating increasing interest in the technique. This may also be due to increasing demands from patients, doctors, and authorities to objectively document the effects of treatment and ensure correct diagnosis.

Our own validation of the acoustic reflection technique for use in the nasal cavity (see I–IV; 483–486) has demonstrated reasonably good correlation of the area–distance function obtained by acoustic rhinometry with the area–distance function obtained by other methods, e.g. CT and MRI. Despite theoretical assumptions not being completely fulfilled, acoustic rhinometry will in most instances give a valid result at least for the first 5–6 cm into the nasal cavity. The concerns of errors due to a constriction in the anterior part of the nasal cavity do not seem to be a problem at least in normal subjects. In the posterior part of the nasal cavity and the epipharynx, the paranasal sinuses may influence the measurement. Further studies are necessary to clarify the problems of 'sound loss' to the paranasal sinuses and the contralateral side. It may be possible to compensate for these losses and probably also get valuable information of the function of the sinus ostia. In this thesis the importance of calibration and checking the equipment has not been discussed particularly but it is worthwhile stressing

that calibration and checking the set-up are necessary for satisfactory results. Fundamental rules, applicable to almost every measuring technique, such as daily checks of the equipment and training of operators are also important factors despite the simplicity of use of the equipment. Since congestion of the nasal mucosa shows considerable variation and is easily influenced by numerous factors, a standardized operating procedure that includes an acclimatization period will also enhance the 'quality' of measurements.

Guidelines for system usage and methods to obtain optimal results have recently been published (272, 482). The present equipment can technically be further improved and lead to better results. In conclusion, validation of the acoustic reflection technique for use in the nasal cavity – acoustic rhinometry – has proved that area-distance functions in the nose can be obtained with acceptable accuracy (5–10%) and reproducibility (5–10%) with the present technique (272). Further validation and improvement of the equipment are needed to ensure better results from the posterior part of the nasal cavity and epipharynx. Revision and improvement of guidelines are also a natural part of a continuous process.

Despite acoustic rhinometry having been used in many different aspects of rhinology, major studies or meta-analyses are still needed to establish 'normal values' in the population and confidence limits to assess values from individuals. These confidence limits may not be able to very strictly divide subjects into two groups: healthy and diseased, since the feeling of nasal obstruction depends on other factors than nasal cavity dimensions alone. It is affected by different factors, e.g. pressure receptors, thermal receptors, pain receptors, and other symptoms like secretions. Even a relatively low correlation between objective and subjective evaluation is no reason for omitting objective testing in diagnostics as well as evaluation of treatment effects.

Though current clinical use is still limited, some centres use acoustic rhinometry in all rhinologic patients.

In the allergic patient (see V–VII; 487–489), larger spontaneous variations in nasal mucosal congestion out of the season have been found compared to normals. Furthermore, allergic subjects were also found more sensitive to histamine than nonallergic subjects and treatment with nasal steroid inhibited a nonspecific inflammation. Increased histamine sensitivity seems to be only a part of nasal hypersensitivity, and the nasal histamine challenge test cannot be used as a stand-alone test for nasal hypersensitivity.

Nasal cavity dimensions may affect olfaction in hay fever patients during allergen challenge but inflammation is also an important factor. Still, many aspects of nasal hypersensitivity and especially the relation to olfaction are unknown. Acoustic rhinometry will most

likely continue to prove its value in the future as a tool in rhinology and upper airway diagnostics, research, in evaluation of treatment effects and not only as a tool for article writers.

Summary in English

Introduction: Nasal congestion is an important symptom in many diseases of the upper airways. Nasal congestion may also affect personal well-being and quality of life. Furthermore, as the nasal mucosa is the first part of the airways in contact with the environment, objective evaluation of nasal congestion or nasal patency is important. Systematic evaluation of nasal patency was described in the last part of the 19th century by Zwaardemaker. Measurement of the pressure drop over the nasal cavity at a passive flow has been described in 1903 by Courtade and is one of the first descriptions of rhinomanometry. The technique is still in use and computer technology has made the measurements much easier but the method has not yet been accepted for wide clinical use.

Methodology: Acoustic methods have also been used for evaluation of nasal patency. A qualitative method was the hum-test by Spiess (1902), where external occlusion of the nonoccluded side of the nasal cavity is experienced as a change in the timbre of the sound during humming. Acoustic reflections have been used in geophysical investigations especially with regard to search for oil. The use of acoustic reflections from the airways gained special interest in 1960–70 for determining the geometry of the vocal tract shape with regard to speech reconstruction. A method described by A. Jackson (1977) was adopted and for the first time applied to the nasal cavity. The method for determining the cross-sectional area as function of distance in the airways by acoustic reflections is relatively simple. The incident sound impulse or pseudorandom noise in the audible frequency range is compared with the response – the reflections from the airways. Intuitively, if the size of the entrance to the airways is known, the size of the reflections may represent changes of the airway size and the time between reflections may give the distance between the changes, dependent on the speed of sound. In this way it is possible to determine the area as function of distance in the airways. The technique has some assumptions and the major effort has been to validate use in the nose and elucidate aspects with regard to sound loss in the airways and resolution. Therefore, the acoustic reflection technique – named acoustic rhinometry – was compared with other methods like MRI, CT, and rhinomanometry. Allergic and nonallergic subjects were also compared.

Results: Acoustic rhinometry showed reasonable correlation with CT in a cadaver and in 10 subjects in comparison with MRI for the first 6 cm of the nasal cavity. Models based on MRI scannings of subjects also showed good correlation for the first 6 cm of the nasal cavity. Posteriorly in the nasal cavity and the epipharynx, differences were found mainly due to 'sound loss' to the paranasal sinuses. Sound loss due to viscous loss or friction at increasing surface/area ratio (the complex geometry in the nose) and loss due to nonrigidity of the nasal mucosa were also examined. Neither of these factors affected the area-distance function significantly. Acoustic rhinometry seems to reflect the area-distance function in the nose reasonably accurately. In allergic subjects acoustic rhinometry has been used to evaluate hypersensitivity. More pronounced spontaneous variation in nasal mucosa congestion was found in patients suffering from hay fever compared to nonallergic subjects. Furthermore, a tendency to a more swollen mucosa in the allergic subjects compared to the normal state, and increased sensitivity to histamine was found. This and reduction in swelling of the mucosa in allergic subjects during nasal steroid treatment out of the pollen season indicate an ongoing inflammatory process or hypersensitivity in allergic subjects out of the pollen season. During allergen challenge the change in nasal cavity dimension as well as inflammation may affect olfaction in hay fever patients.

Discussion: Acoustic rhinometry has not only been used to examine hay fever patients but in many different aspects of rhinology. Since the introduction of the acoustic reflection technique in the nose more than 250 papers using the technique have been published. Most of the papers find the technique valuable for evaluation of nasal patency. Fortunately, some critical papers have drawn attention to some practical aspects of the technique. Standard operating procedures, and calibration checks as well as training of operators will enhance the accuracy and reproducibility of results.

Conclusion and perspectives: A decade after its introduction acoustic rhinometry is a well-established method for evaluation of nasal patency, but further improvement can be obtained by continued validation and adjustments of the technique.

Summary in Danish

Introduktion: 'Tilstoppet næse' er et vigtigt symptom ved mange sygdomme i de øvre luftveje. Tilstoppet næse kan også påvirke det personlige velvære og

livskvaliteten. Desuden er næseslimhinden luftvejenes første kontakt med omgivelserne, hvorfor en objektiv vurdering af tilstoppethed eller nasal passagen er vigtig. Systematisk vurdering af nasal passagen er beskrevet af Zwaardemaker i den sidste del af det nittende århundrede. Målinger af trykfaldet over næsehulen ved et passivt flow er beskrevet i 1903 af Courtade og er den første beskrivelse af rhinomanometri. Denne teknik anvendes stadig og den moderne computerteknologi har gjort målingerne nemmere, men metoden anvendes dog ikke klinisk i særlig vid udtrækning.

Metoder: Akustiske metoder har også været anvendt til vurdering nasalpassagen. En semikvantitativ metode er beskrevet af Spiess i 1902. Ved udvendig obstruktion af et næsebor vil lyden fra det modsatte næsebor ændre kvalitet, når personen nynn timer, afhængig af i hvor høj grad næseboret er obstrueret. Akustisk refleksion har været anvendt til geofysiske undersøgelser, specielt olieforekomster. Brugen af akustisk refleksion i luftvejene samlede opmærksomhed i årene 1960–70 hvad angår strubehovedets bevægelser i forbindelse med talegenkendelse. En metode beskrevet af A. Jackson i 1977, blev i 1989 for første gang anvendt på næsehulen. Metoden, der kan bestemme tværsnitsarealet som funktion af afstanden ind i næsehulen ved hjælp af akustiske refleksioner er relativ simpel. Et hørbart lydsignal sendes ind i luftvejene og sammenlignes med det reflekterede signal. Intuitivt, vil størrelsen af det reflekterede signal være et mål for ændringer i størrelsen af luftvejen og tiden vil være et mål for afstanden til ændringen, når lydhastigheden kendes. Hermed er det muligt at bestemme tværsnitsarealet som funktion af afstande i luftvejene. Teknikken har visse forudsætninger og den største indsats ved nærværende arbejde har været at validere brugen af teknikken i næsen og klarlægge lydtab og metodens opløsningsevne. Derfor blev den akustiske refleksions teknik, for anvendelse i næsen, sammenlignet med andre metoder så som MRI, CT, og rhinomanometri. Allergiske personer blev sammenlignet med ikke-allergiske personer.

Resultater: Akustisk rhinometri viste rimelig korrelation med CT i et kadaver og hos 10 personer med MRI i de første 6 cm af næsehulen. Modeller baseret på MRI-scanninger af personer viste også god korrelation for de første 6 cm. Bagtil i næsehulen og i næsesvælget blev der fundet afvigelser primært på grund af lydtab til bihulerne. Lydtab på grund af viskøst tab eller friktion ved tiltagende omkreds/areal ratio (kompleks geometri i næsehulen) og lydtab som følge af, at næseslimhinden ikke opfører sig som en hård væg synes ikke at have væsentlig betydning.

Akustisk rhinometri synes at reflektere areal-afstands funktionen i næsen rimeligt nøjagtigt. Hos allergiske personer har akustisk rhinometri været anvendt til at vurdere en øget følsomhed af slimhinden. Større spontan variation blev fundet hos personer med høfeber i forhold til normale. Desuden var der tendens til at slimhinden var mere hævet og der var øget histamin følsomhed ved provokationstest. Dette og en afsvulmende effekt af lokal steroid behandling indikerer en igangværende inflammatorisk proces og hyperreaktivitet hos allergikere uden for pollensæsonen. Ved allergenprovokation kan såvel ændrede dimensioner som den inflammatoriske proces påvirke lugtesansen hos høfeberpatienter.

Diskussion: Akustisk rhinometri har ikke kun været anvendt til at undersøge høfeberpatienter men også i en række andre sammenhænge i rhinologien. Siden introduktionen af akustisk rhinometri er der i løbet af en dekade publiceret mere end 250 artikler hvor metoden har været anvendt. Mange finder metoden værdifuld ved undersøgelse af nasalpassagen. I kritiske artikler er der gjort opmærksom på nogle praktiske betydningsfulde aspekter. Selvom metoden er ganske simpel at anvende vil faste procedurer ved måling og check af systemets funktioner, samt oplæring af brugere i målingerne øge nøjagtigheden og reproducerbarheden.

Konklusion: En dekade efter introduktionen er akustisk rhinometri en veletableret metode til vurdering af nasal passagen men yderligere forbedringer kan opnås ved fortsat validering og justering af teknikken.

Acknowledgments

The first study of this thesis was initiated in 1987 and carried out at the Department of Environmental and Occupational Medicine, University of Aarhus. At the department Ole F. Pedersen was interested in measurements of nasal airway resistance as a part of the total airway resistance. In 1985, as medical student, I was employed to examine different methods for determination of nasal airway resistance. The initial experiments showed that it was difficult to get reproducible and consistent results with different

available methods. Therefore, we started doing experiments with sound applied at the mouth and measuring the attenuation in the nostrils. Correlation was found to one of the established methods for evaluation of nasal airway resistance – rhinomanometry. Literature studies revealed different methods applied to the pharynx and lower airways using sound to evaluate the geometry of the airway. Ole F. Pedersen contacted Andrew Jackson in Boston, who had used acoustic reflections to describe the cross-sectional areas in the trachea as function of distance. Together with the late David Swift from Baltimore, he stayed for two weeks at the department. We succeeded using the acoustic reflection technique in the nasal cavity and did the first simple validation of the measurements by filling water into the nasal cavity and comparing the volume of water with the volume measured by the acoustic reflection technique. Here an incident happened, which will stay in our minds forever as a part of the history of acoustic rhinometry. Andrew Jackson went to rent car and suddenly several millilitres of water flushed out of his nose all over the documents and he had to apologize!

First I would like to express my gratitude to my chief and teacher in medical science Ole F. Pedersen for his invaluable support and criticism during the work, as advisor, and for providing the opportunities for me to work in his laboratories. Andrew Jackson adapted the acoustic reflections technique to measurements in the nose and brought the prototype equipment, which made it easy to start measurements in the nose. Andrew Jackson and David Swift are appreciated for their great contribution to the process that has lead to this thesis. The late Ole Elbrønd and Luisa Grymer from the ENT-department, Aarhus University Hospital, are acknowledged for enthusiasm and belief, from the very beginning, in the clinical applicability of the acoustic reflection technique in the nasal airway. Torben Riis Rasmussen, Søren K. Kjærgaard, Gunnar R. Lundqvist department of Environmental and Occupational Medicine, University of Aarhus, and Kurt Pfeiffer Petersen, Astra Danmark A/S, are thanked for inspiring discussions and collaboration. Special thanks to Niels Trolle Andersen, Institute of Biostatistics, University of Aarhus, for his willingness, day and night, to discuss results and design of experiments.

I am indebted to Axel Michelsen, Institute of Biology, Odense University, the master of laser vibrometry, Oluf Jacobsen, the former chief of the Engineering School of Aarhus, responsible for the electrical analog simulation of vibration of the nasal mucosa, and Benny Lyholm who all participated in complex description of sound dissipation in the nasal airway.

To my other colleagues I want to express my gratitude for their encouragement and collaboration in the past. The William Demant foundation is thanked for financial support and University of Aarhus for a postgraduate fellowship. The Danish Medical Association Research Fund, Schering-Plough, and Astra-Zeneca kindly supported the publication of this thesis.

References

1. MYGIND N, PIPCORN U, DAHL R, editors. Rhinitis and asthma: similarities and differences. Copenhagen: Munksgaard, 1990.
2. DRETTNER B, FALCK B, SIMON H. Measurements of the air conditioning capacity of the nose during normal and pathological conditions and pharmacological influence. Acta Otolaryngol (Stockh) 1977;**84**:266–277.
3. SCHMIDT-NIELSEN K, HAINSWORTH FR, Murrish DE. Counter-current heat exchange in the respiratory passages: Effect on water and heat balance. Respir Physiol 1970;**9**:263–376.
4. INGELSTEDT S. Humidifying capacity of the nose. Ann Otol Rhinol Laryngol 1970;**79**:475–480.

5. GEURKINK N. Nasal anatomy, physiology, and function. *J Allergy Clin Immunol* 1983;**72**:123–128.
6. DE WIT G. The function of the nose in the aerodynamics of respiration. *Rhinology* 1973;**11**:59–67.
7. FERRIS BG. Partitioning of respiratory flow resistance in man. *J Appl Physiol* 1964;**19**:653–658.
8. COHEN BM. Nasal airway resistance and the effects of bronchodilator drugs in expiratory airflow disorders. *Respiration* 1969;**26**:35–46.
9. CRAIG AB, DVORAK M, MCILREATH FJ. Resistance of airflow through the nose. *Ann Otol Rhinol Laryngol* 1965;**74**:589–603.
10. PATTLE RE. The retention of gases and particles in the human nose. In: DAVIES CN, editor. *Inhaled particles and vapours*. Oxford, Pergamon, 1961;302–311.
11. LIPPMANN M. Deposition and clearance of inhaled particles in the human nose. *Ann Otol Rhinol Laryngol* 1970;**79**:520–528.
12. BRAMAN SS, BARROWS AA, DECOTIS BA, SETTIPANE GA, CORRAO WM. Airway hyperresponsiveness in allergic rhinitis. A risk factor for asthma. *Chest* 1987;**91**:671–674.
13. KAUFFMANN F, NEUKIRCH F, ANNESI I, KOROBAEFF M, DORE MF, LELLOUCH J. Relation of perceived nasal and bronchial hyperresponsiveness to FEV1, basophil counts, and methacholine response. *Thorax* 1988;**43**:456–461.
14. WRIGHT AL, HOLBERG CJ, MARTINEZ FD, HALONEN M, MORGAN W, TAUSSIG LM. Epidemiology of physician-diagnosed allergic rhinitis in childhood. *Pediatrics* 1994;**94**:895–901.
15. MESCHIEVITZ CK, SCHULTZ SB, DICK EC. A model for obtaining predictable natural transmission of rhinoviruses in human volunteers. *J Infect Dis* 1984;**150**:195–201.
16. CALLOW KA, PARRY HF, SERGEANT M, TYRRELL DA. The time course of the immune response to experimental coronavirus infection of man. *Epidemiol Infect* 1990;**105**:435–446.
17. LEMANSKE RFJ, DICK EC, SWENSON CA, VRTIS RF, BUSSE WW. Rhinovirus upper respiratory infection increases airway hyperreactivity and late asthmatic reactions. *J Clin Invest* 1989;**83**:1–10.
18. WINTHER B. Effects on the nasal mucosa of upper respiratory viruses (common cold). *Dan Med* 1994;**41**:193–204.
19. WALIKE JW. Anatomy of the Nasal Cavities. *Otolaryngologic Clinics North Am* 1973;**6**:609–621.
20. HAMILTON WJ, HARRISON RJ. Anatomy of the nose, nasal cavity and paranasal sinuses. Unpublished, 1977.
21. COLE P. Upper respiratory airflow. In: PROCTER DF, ANDERSEN I, editors. *The Nose*. Amsterdam, Elsevier, 1982; 177–189.
22. INGELSTEDT S, TOREMALM NG. Air flow patterns and heat transfer within the respiratory tract – A new methods for experimental studies on models. *Acta Physiol Scand* 1961;**51**:204–217.
23. WIDDICOMBE J. Physiologic control. Anatomy and physiology of the airway circulation. *Am Rev Respir Dis* 1992;**146**:S3–S7.
24. DANKMEIJER J. Applied anatomy, vascularisation and innervation of the nose. *Int Rhinol* 1992;**2**:37–43.
25. RITTER FN. The vasculature of the nose. *Ann Otol Rhinol Laryngol* 1970;**79**:469–474.
26. WIDDICOMBE JG. The physiology of the nose. *Clin Chest Med* 1986;**7**:159–170.
27. ÄNGGÅRD A. Autonomic nervous control of blood circulation and secretion in the nasal mucosa. Stockholm: Thesis, 1974.
28. ÄNGGÅRD A. Parasympathetic control of blood circulation and secretion in the nasal mucosa. *Rhinology* 1975;**13**:147–153.
29. ÄNGGÅRD A, EDWALL L. The effects of sympathetic nerve stimulation on the tracer disappearance rate and local blood content in the nasal mucosa of the cat. *Acta Otolaryngol (Stockh)* 1974;**77**:131–139.
30. LUNG MA, PHIPPS RJ, WANG JC, WIDDICOMBE JG. Control of nasal vasculature and airflow resistance in the dog. *J Physiol Lond* 1984;**349**:535–551.
31. ECCLES R, LEE RL. The influence of the hypothalamus on the sympathetic innervation of the nasal vasculature of the cat. *Acta Otolaryngol (Stockh)* 1981;**91**:127–134.
32. ECCLES R. Sympathetic control of nasal erectile tissue. *Eur J Respir Dis Suppl* 1983;**128**:150–154.
33. ECCLES R. The central rhythm of the nasal cycle. *Acta Otolaryngol (Stockh)* 1978;**86**:464–468.
34. KEUNING J. On the nasal cycle. Thesis. Leiden, 1967.
35. GALIOTO GB, MEVIO E, GALIOTO P, LORINI R, CISTERNINO M. [Central regulation of the nasal cycle. Studies on hypothalamic pathology]. *Acta Otorhinolaryngol Ital* 1986;**6**:99–106.
36. BURROW A, DAVIES AM, ECCLES R, GREEN SM. The effect of pressure applied to the axilla on human nasal resistance airflow. *J Physiol* 1984;**350**:40–40.
37. DAVIES AM, ECCLES R. Reciprocal changes in nasal resistance to airflow caused by pressure applied to the axilla. *Acta Otolaryngol (Stockh)* 1985;**99**:154–159.
38. MALM L. Vascular and secretory effect of adrenoceptor agonists and peptides in the nose. *Eur J Respir Dis Suppl* 1983;**128**:139–142.
39. MALM L. Resistance and capacitance vessels in the nasal mucosa. *Rhinology* 1975;**13**:84–89.
40. JUTO JE, LUNDBERG C. Nasal mucosa reaction, catecholamines and lactate during physical exercise. *Acta Otolaryngol (Stockh)* 1984;**98**:533–542.
41. OLSON LG, STROHL KP. The response of the nasal airway to exercise. *Am Rev Respir Dis* 1987;**135**:356–359.
42. KONNO A, TOGAWA K, ITASAKA Y. Neurophysiological mechanism of shrinkage of nasal mucosa induced by exercise. *Auris Nasus Larynx* 1982;**9**:81–90.
43. TONNESEN P, MYGIND N. Nasal challenge with serotonin and histamine in normal persons. *Allergy* 1985;**40**:350–353.
44. HOWARTH PH. Histamine and asthma: an appraisal based on specific H1-receptor antagonism. *Clin Exp Allergy* 1990;**20**(Suppl. 2):31–41.
45. VARGAFTIG BB, LEFORT J. Pharmacological evidence for a vasodilator receptor to serotonin in the nasal vessels of the dog. *Eur J Pharmacol* 1974;**25**:216–225.
46. UDDMAN R, MALM L, SUNDLER F. Peptide containing nerves in the nasal mucosa. *Rhinology* 1981;**19**:75–79.
47. NACLERIO RM, MEIER HL, ADKINSON NFJ et al. In vivo demonstration of inflammatory mediator release following nasal challenge with antigen. *Eur J Respir Dis Suppl* 1983;**128**:26–32.
48. NACLERIO RM, BAROODY FM, TOGIAS AG. The role of leukotrienes in allergic rhinitis: a review. *Am Rev Respir Dis* 1991;**143**:S91–S95.
49. PROUD D, REYNOLDS CJ, LACAPRA S, KAGEY SOBOTKA A, LICHTENSTEIN LM, NACLERIO RM. Nasal provocation with bradykinin induces symptoms of rhinitis and a sore throat. *Am Rev Respir Dis* 1988;**137**:613–616.
50. BRUNNEE T, NIGAM S, KUNKEL G, BAUMGARTEN CR. Nasal challenge studies with bradykinin: influence upon mediator generation. *Clin Exp Allergy* 1991;**21**:425–431.
51. RAPHAEL GD, IGARASHI Y, WHITE MV, KALINER MA. The pathophysiology of rhinitis. V. Sources of protein in allergen-induced nasal secretions. *J Allergy Clin Immunol* 1991;**88**:33–42.

52. MYGIND N, SECHER C, KIRKEGAARD J. Role of histamine and antihistamines in the nose. *Eur J Respir Dis Suppl* 1983;**128**:16–20.
53. CLEMENT PA, STOOP AP, KAUFMAN L. Histamine threshold and nasal hyperreactivity in non specific allergic rhinopathy. *Rhinology* 1985;**23**:35–42.
54. NACLERIO RM, KAGEY SOBOTKA A, LICHTENSTEIN LM, FREIDHOFF L, PROUD D. Terfenadine, an H1 antihistamine, inhibits histamine release in vivo in the human. *Am Rev Respir Dis* 1990;**142**:167–171.
55. NACLERIO RM, TOGIAS AG. The nasal allergic reaction. observations on the role of histamine. *Clin Exp Allergy* 1991;**21**(Suppl. 2):13–19.
56. ALVING K. Airways vasodilatation in the immediate allergic reaction. Involvement of inflammatory mediators and sensory nerves. *Acta Physiol Scand Suppl* 1991;**597**:1–64.
57. LUNDBERG JM, ALVING K, LACROIX JS, MATRAN R. Local and central reflex mechanisms in the neural control of airway microcirculation. *Eur Respir J Suppl* 1990;**12**:624s–628s.
58. DURHAM SR, YING S, VARNEY VA, et al. Cytokine messenger RNA expression for IL-3, IL-4, IL-5, and granulocyte/macrophage-colony-stimulating factor in the nasal mucosa after local allergen provocation: relationship to tissue eosinophilia. *J Immunol* 1992;**148**:2390–2394.
59. MASUYAMA K, JACOBSON MR, RAK S, et al. Topical glucocorticosteroid (fluticasone propionate) inhibits cells expressing cytokine mRNA for interleukin-4 in the nasal mucosa in allergen-induced rhinitis. *Immunology* 1994;**82**:192–199.
60. HOWARTH PH, BRADDING P, QUINT D, REDINGTON AE, HOLGATE ST. Cytokines and airway inflammation. *Ann N Y Acad Sci* 1994;**725**:69–82.
61. BRADDING P, FEATHER IH, WILSON S, et al. Immunolocalization of cytokines in the nasal mucosa of normal and perennial rhinitic subjects. The mast cell as a source of IL-4, IL-5, and IL-6 in human allergic mucosal inflammation. *J Immunol* 1993;**151**:3853–3865.
62. ANDREASSEN ML, LEEPER HA, MACRAE DL. Changes in vocal resonance and nasalization following adenoidectomy in normal children: preliminary findings. *J Otolaryngol* 1991;**20**:237–242.
63. DALSTON RM, VIG PS. Effects of orthognathic surgery on speech: a prospective study. *Am J Orthod* 1984;**86**:291–298.
64. DANG J, HONDA K, SUZUKI H. Morphological and acoustical analysis of the nasal and the paranasal cavities. *J Acoust Soc Am* 1994;**96**:2088–2100.
65. RASMUSSEN TR, SWIFT DL, HILBERG O, PEDERSEN OF. Influence of nasal passage geometry on aerosol particle deposition in the nose. *J Aerosol Med* 1990;**3**:16–25.
66. ANDERSEN I, LUNDQVIST GR, PROCTOR DF. Human nasal mucosal. *Arch Environ Health* 1971;**23**:408–420.
67. PROCTOR DF, ANDERSEN I, LUNDQVIST G. Clearance of inhaled particles from the human nose. *Arch Intern Med* 1973;**131**:132–139.
68. MCLEAN JA, BACON JR, MATHEWS KP, et al. Distribution and clearance of radioactive aerosol on the nasal mucosa. *Rhinology* 1984;**22**:65–75.
69. SLEIGH MA, BLAKE JR, LIRON N. The propulsion of mucus by cilia. *Am Rev Respir Dis* 1988;**137**:726–741.
70. GIROD S, ZAHM JM, PLOTKOWSKI C, BECK G, PUCHELLE E. Role of the physiochemical properties of mucus in the protection of the respiratory epithelium. *Eur Respir J* 1992;**5**:477–487.
71. GINZEL A, ILLUM P. Nasal mucociliary clearance in patients with septal deviation. *Rhinology* 1980;**18**:177–181.
72. MAURIZI M, PALUDETTI G, OTTAVIANI F, ALMADORI G, FALCETTI S. Mucociliary function and nasal resistance evaluation before and after adenoidectomy. *Int J Pediatr Otorhinolaryngol* 1986;**11**:295–300.
73. MCNICHOLAS WT, COFFEY M, McDONNELL T, O'REGAN R, FITZGERALD MX. Upper airway obstruction during sleep in normal subjects after selective topical oropharyngeal anesthesia. *Am Rev Respir Dis* 1987;**135**:1316–1319.
74. ANDERSON PJ. Factors promoting pathogenicity of influenza virus. *Semin Respir Infect* 1991;**6**:3–10.
75. UKAI K, SAKAKURA Y. [Effect of mucociliary dysfunction on nasal viral infection]. *Nippon Jibiinkoka Gakkai Kaiho* 1990;**93**:762–771.
76. MASAKI H, AHMED K, FUJISHITA M et al. [A case of Kartagener's syndrome with S. pneumoniae lung abscess]. *Kansenshogaku Zasshi* 1993;**67**:355–360.
77. BOUCHER RC, KNOWLES MR, JOHNSON LG et al. Gene therapy for cystic fibrosis using E1-deleted adenovirus: a phase I trial in the nasal cavity. The University of North Carolina at Chapel Hill. *Hum Gene Ther* 1994;**5**:615–639.
78. READ RC, WILSON R, RUTMAN A, et al. Interaction of nontypable *Haemophilus influenzae* with human respiratory mucosa in vitro. *J Infect Dis* 1991;**163**:549–558.
79. MELON J. [Physiopathology of nasal respiration]. *Rev Belge Med Dent* 1991;**46**:13–20.
80. STROHL KP, DECKER MJ, OLSON LG, FLAK TA, HOEKJE PL. The nasal response to exercise and exercise induced bronchoconstriction in normal and asthmatic subjects. *Thorax* 1988;**43**:890–895.
81. ELWANY S, HARRISON R. Inferior turbinectomy: comparison of four techniques. *J Laryngol Otol* 1990;**104**:206–209.
82. LELONG M, HENARD J, VANDEPUTTE H. [Chronic rhinopathies of childhood (apropos of 265 cases)]. *Allerg Immunol Paris* 1989;**21**:33–38.
83. STEVENS CN, STEVENS MH. Quantitative effects of nasal surgery on olfaction. *Am J Otolaryngol* 1985;**6**:264–267.
84. JANKOWSKI R, GOETZ R, Moneret Vautrin DA, Daures P, Lallemand JG, Wayoff M. [Insufficiency of ethmoidectomy in the treatment of nasal polyposis]. *Ann Otolaryngol Chir Cervicofac* 1991;**108**:298–306.
85. LILDHOLDT T, FOGSTRUP J, GAMMELGAARD N, KORTHOLM B, ULSOE C. Surgical versus medical treatment of nasal polyps. *Acta Otolaryngol (Stockh)* 1988;**105**:140–143.
86. KLEIN JC. Nasal respiratory function and craniofacial growth. *Arch Otolaryngol Head Neck Surg* 1986;**112**:843–849.
87. SMITH RM, GONZALEZ C. The relationship between nasal obstruction and craniofacial growth. *Pediatr Clin North Am* 1989;**36**:1423–1434.
88. SHAPIRO GG. The role of nasal airway obstruction in sinus disease and facial development. *J Allergy Clin Immunol* 1988;**82**:935–940.
89. TRASK GM, SHAPIRO GG, SHAPIRO PA. The effects of perennial allergic rhinitis on dental and skeletal development: a comparison of sibling pairs. *Am J Orthod Dentofacial Orthop* 1987;**92**:286–293.
90. BRESOLIN D, SHAPIRO PA, SHAPIRO GG, CHAPKO MK, DASSEL S. Mouth breathing in allergic children: its relationship to dentofacial development. *Am J Orthod* 1983;**83**:334–340.
91. LAINE T, WARREN DW, DALSTON RM, MORR KE. Effects of velar resistance on speech aerodynamics. *Eur J Orthod* 1989;**11**:52–58.

92. PARKER AJ, CLARKE PM, DAWES PJ, MAW AR. A comparison of active anterior rhinomanometry and nasometry in the objective assessment of nasal obstruction. *Rhinology* 1990;**28**:47–53.
93. RAUCHFUSS A. [The nasal speculum. Its historical development and remarks on the history of rhinoscopy]. *Laryngol Rhinol Otol Stuttg* 1985;**64**:551–558.
94. TANGE RA. Some historical aspects of the surgical treatment of the infected maxillary sinus. *Rhinology* 1991;**29**:155–162.
95. DRETTNER B. Vascular reactions of the human nasal mucosa on exposure to cold. *Acta Otolaryngol (Stockh)* 1961;Suppl. 166:1–144.
96. GROBLER NJ. Reactivity of the nasal respiratory mucosa (a clinical and epidemiological study). Unpublished, 1966.
97. MELON J, DAELE J. Les explorations fonctionnelles et endoscopiques en rhinologie. *Acta Otorhinolaryngol Belg* 1979;**33**:639–721.
98. PINKPANK A. [Relation of self evaluation of nasal respiration to rhinoscopy and rhinomanometry]. *HNO* 1986;**34**:194–197.
99. HUYGEN PL, KLAASSEN AB, DE LEEUW TJ, WENTGES RT. Rhinomanometric detection rate of rhinoscopically-assessed septal deviations. *Rhinology* 1992;**30**:177–181.
100. HOLMSTROM M, KUMLIEN J. A clinical follow-up of septal surgery with special attention to the value of preoperative rhinomanometric examination in the decision concerning operation. *Clin Otolaryngol* 1988;**13**:115–120.
101. HARALDSSON PO, NORDEMAR H, ANGGARD A. Long-term results after septal surgery – submucous resection versus septoplasty. *ORL J Otorhinolaryngol Relat Spec* 1987;**49**:218–222.
102. STAMMBERGER H, POSAWETZ W. Functional endoscopic sinus surgery. Concept, indications and results of the Messerklinger technique. *Eur Arch Otorhinolaryngol* 1990;**247**:63–76.
103. ZEDALIS D, DOLEN WK, GLOVER GC, WIENER MB, SELNER JC, WEBER RW. Evaluation of nasal patency by fiberoptic rhinoscopy. *J Allergy Clin Immunol* 1989;**83**:973–978.
104. JUTO JE, LUNDBERG C. Methods for standardization of nasal mucosa decongestion in man. *Rhinology* 1983;**21**:361–368.
105. JUTO JE, LUNDBERG C. Human nasal mucosa reaction during chilling of the feet. *Rhinology* 1985;**23**:131–136.
106. WANG D, CLEMENT P, KAUFMAN L, DERDE MP. Fiberoptic examination of the nasal cavity and nasopharynx in children. *Int J Pediatr Otorhinolaryngol* 1992;**24**:35–44.
107. LENDERS H, SCHAEFER J, PIRSIG W. Turbinate hypertrophy in habitual snorers and patients with obstructive sleep apnea: findings of acoustic rhinometry. *Laryngoscope* 1991;**101**:614–618.
108. SEKIZAWA K, SHINDOH C, HIDA W, et al. Noninvasive method for detecting laryngeal narrowing with low-frequency sound. *J Appl Physiol* 1983;**55**:591–597.
109. LEIBERMAN A, COHEN A, TAL A. Digital signal processing of stridor and snoring in children. *Int J Pediatr Otorhinolaryngol* 1986;**12**:173–185.
110. SCHAFER J, PIRSIG W. Digital signal analysis of snoring sounds in children. *Int J Pediatr Otorhinolaryngol* 1990;**20**:193–202.
111. SLAWINSKI EB, DUBANOWICZ KOSSOWSKA E. The assessment of hypertrophy of nasopharyngeal tonsil by acoustical methods. *Int J Pediatr Otorhinolaryngol* 1993;**27**:229–244.
112. SHI Y. [Lung sound analysis of upper airway obstruction]. *Chung Hua Chieh Ho Ho Hu Hsi Tsa Chih* 1992;**15**:228–230,256.
113. PASTERKAMP H, SANCHEZ I. Tracheal sounds in upper airway obstruction. *Chest* 1992;**102**:963–965.
114. COLEMAN RF, SCHECHTER GL. A basic model to study acoustic evaluation of airway obstruction. *Arch Otolaryngol Head Neck Surg* 1991;**117**:1144–1149.
115. GRONBORG H, WINTHER B, BROFELDT S, BORUM P, MYGIND N. Effects of oral norephedrine on common cold symptoms. *Rhinology* 1983;**21**:3–12.
116. LARSEN K, KRISTENSEN S. Peak flow nasal patency indices and self-assessment in septoplasty. *Clin Otolaryngol* 1990;**15**:327–334.
117. PERTUZE J, WATSON A, PRIDE NB. Maximum airflow through the nose in humans. *J Appl Physiol* 1991;**70**:1369–1376.
118. LARSEN K, OXHOJ H. Spirometric forced Volume measurements in the assessment of nasal patency after septoplasty. A prospective clinical study. *Rhinology* 1988;**26**:203–208.
119. TAYLOR G, PATH D, MACNEIL AR, FREED DLJ. Assessing degree of nasal patency by measuring peak expiratory flow rate through the nose. *J Allergy Clin Immunol* 1972;**52**:193–198.
120. HOLMSTROM M, SCADDING GK, LUND VJ, DARBY YC. Assessment of nasal obstruction. A comparison between rhinomanometry and nasal inspiratory peak flow. *Rhinology* 1990;**28**:191–196.
121. SAKAI S. [Use of nasal flowmeter to measure nasal patency]. *Nippon Jibiinkoka Gakkai Kaiho* 1989;**92**:253–259.
122. WIHL JA, MALM L. Rhinomanometry and nasal peak expiratory and inspiratory flow rate. *Ann Allergy* 1988;**61**:50–55.
123. FROLUND L, MADSEN F, MYGIND N, NIELSEN NH, SVENDSEN UG, WEEKE B. Comparison between different techniques for measuring nasal patency in a group of unselected patients. *Acta Otolaryngol (Stockh)* 1987;**104**:175–179.
124. MASING H. Rhinomanometry, different techniques and results. *Acta Otorhinolaryngol Belg* 1979;**33**:566–571.
125. CLEMENT PA, VAN DISHOECK A, VAN DE WAL J, STOOP P, HOEK T, VAN STRICK R. Nasal provocation and passive anterior rhinomanometry (PAR). *Clin Allergy* 1981;**11**:293–301.
126. GROSCLAUDE M, BALLAND S, BALLANDRAS A, PERRIN FAYOLLE M. [Diagnostic value of passive anterior rhinomanometry in everyday allergological practice. 4 years' experience]. *Rev Pneumol Clin* 1985;**41**:9–16.
127. VAN DISHOECK EA. Passive anterior rhinomanometry and inhalation provocation through the nose. *Rhinology* 1973;**11**:103–108.
128. KORTEKANGAS AE. Significance of anterior and posterior technique in rhinomanometry. *Acta Otolaryngol (Stockh)* 1972;**73**:218–221.
129. JONES AS, LANCER JM, STEVENS JC, BECKINGHAM E. Rhinomanometry: do the anterior and posterior methods give equivalent results? *Clin Otolaryngol* 1987;**12**:109–114.
130. DVORACEK JE, HILLIS A, ROSSING RG. Comparison of sequential anterior and posterior rhinomanometry. *J Allergy Clin Immunol* 1985;**76**:577–582.
131. NOLTE D, LÜDER-LÜHR I. Comparing measurements of nasal resistance by body plethysmography and by rhinomanometry. *Respiration* 1973;**30**:31–38.
132. PETRO W, BIRKENBIHL P. [Measurement of nasal oscillatory resistance]. *Pneumologie* 1989;**43**:387–391.
133. SHELTON DM, PERTUZE J, GLEESON MJ, et al. Comparison of oscillation with three other methods for measuring nasal airways resistance. *Respir Med* 1990;**84**:101–106.
134. KUMLIEN J, SCHIRATZKI H. Methodological aspects of rhinomanometry. *Rhinology* 1979;**17**:107–114.

135. CORRADO OJ, OLLIER S, PHILLIPS MJ, THOMAS JM, DAVIES RJ. Histamine and allergen induced changes in nasal airways resistance measured by anterior rhinomanometry. reproducibility of the technique and the effect of topically administered antihistaminic and anti-allergic drugs. *Br J Clin Pharmacol* 1987;**24**:283–292.
136. SHELTON DM, EISER NM. Evaluation of active anterior and posterior rhinomanometry in normal subjects. *Clin Otolaryngol* 1992;**17**:178–182.
137. EICHLER J, LENZ H. Comparison of different coefficients and units in rhinomanometry. *Rhinology* 1985;**23**:149–157.
138. GHAEM A, MARTINEAUD JP. [Determination of nasal resistance in healthy subjects using two techniques of rhinomanometry]. *Bull Eur Physiopathol Respir* 1985;**21**:11–16.
139. BROMS P, JONSON B, LAMM CJ. A universal way to evaluate the curve in rhinomanometry. *Acta Otolaryngol Suppl* (Stockh) 1979;**360**:22–23.
140. CLEMENT P, MARIEN J. The use of a mathematical model in rhinomanometry. *Rhinology* 1980;**18**:197–207.
141. BROMS P, IVARSSON A, JONSON B. Rhinomanometry. I. Simple equipment. *Acta Otolaryngol* (Stockh) 1982;**93**:455–460.
142. POSTEMA CA, HUYGEN PL, LECLUSE RG, WENTGES RT. The lateralization percentage as a measure of nasal flow asymmetry in active anterior rhinomanometry. *Clin Otolaryngol* 1980;**5**:165–170.
143. RIVRON RP. Cross-sectional area as a measure of nasal resistance. *Rhinology* 1990;**28**:257–264.
144. WARREN DW. A quantitative technique for assessing nasal airway impairment. *Am J Orthod* 1984;**86**:306–314.
145. WARREN DW, HAIRFIELD WM, DALSTON ET. Effect of age on nasal cross-sectional area and respiratory mode in children. *Laryngoscope* 1990;**100**:89–93.
146. ARBOUR P, BILGEN E, GIRARDIN M. Experimental study of velocity fields in a human nasal fossa by laser anemometry. *Rhinology* 1985;**23**:201–207.
147. GIRARDIN M, BILGEN E, ARBOUR P. Experimental study of velocity fields in a human nasal fossa by laser anemometry. *Ann Otol Rhinol Laryngol* 1983;**92**:231–236.
148. SCHERER PW, HAHN II, MOZELL MM. The biophysics of nasal airflow. *Otolaryngol Clin North Am* 1989;**22**:265–278.
149. COLE P, CHABAN R, NAITO K, OPRYSK D. The obstructive nasal septum. Effect of simulated deviations on nasal airflow resistance. *Arch Otolaryngol Head Neck Surg* 1988;**114**:410–412.
150. CHABAN R, COLE P, NAITO K. Simulated septal deviations. *Arch Otolaryngol Head Neck Surg* 1988;**114**:413–415.
151. KERN EB. Committee report on standardization of rhinomanometry. *Rhinology* 1981;**19**:231–236.
152. CLEMENT PA. Committee report on standardization of rhinomanometry. *Rhinology* 1984;**22**:151–155.
153. KERN EB. Standardization of rhinomanometry. *Rhinology* 1977;**15**:115–119.
154. OGURA JH, STOKSTED P. Rhinomanometry in some rhinologic diseases. *Laryngoscope* 1958;**68**:2001–2014.
155. PELIKAN Z, FEENSTRA L, BARREE GOF. Response of the nasal mucosa to allergen challenge measured by two different methods of rhinomanometry. *Ann Allergy* 1977;**38**:263–267.
156. OLIVE PEREZ A. Nasal provocation test (NPT) through previously active rhinomanometry: physical and mathematical reasons. *Allergol Immunopathol Madr* 1989;**17**:291–299.
157. SVENSSON G, HEGARDT B, LOFKVIST T. Effects of topical use of beta-adrenoceptor stimulants of nasal mucosa. Rhinomanometric evaluations in experiments with terbutaline and KWD 2131. *Acta Otolaryngol* (Stockh) 1980;**90**:297–303.
158. BENDE M, ANDERSSON KE, JOHANSSON CJ, SJOGREN C, SVENSSON G. Dose–response relationship of a topical nasal decongestant: phenylpropanolamine. *Acta Otolaryngol* (Stockh) 1984;**98**:543–547.
159. HASEGAWA M, KERN EB. The effect of breath holding, hyperventilation, and exercise on nasal resistance. *Rhinology* 1978;**16**:243–249.
160. STROHL KP, ARNOLD JL, DECKER MJ, HOEKJE PL, McFADDEN ER. Nasal flow-resistive responses to challenge with cold dry air. *J Appl Physiol* 1992;**72**:1243–1246.
161. BACHMANN W, NIEDER T. [The clinical value of rhinomanometry. An analysis of the discrepancy between anamnesis, clinical state and rhinomanometry (author's transl)]. *Laryngol Rhinol Otol Stuttg* 1978;**57**:379–383.
162. JESSEN M, MALM L. The importance of nasal airway resistance and nasal symptoms in the selection of patients for septoplasty. *Rhinology* 1984;**22**:157–164.
163. GORDON AS, McCAFFREY TV, KERN EB, PALLANCH JF. Rhinomanometry for preoperative and postoperative assessment of nasal obstruction. *Otolaryngol Head Neck Surg* 1989;**101**:20–26.
164. JESSEN M, JACOBSSON S, MALM L. On rhinomanometry in rhinoplasty. *Plast Reconstr Surg* 1988;**81**:506–511.
165. CLEMENT PA, KAUFMAN L, ROUSSEUW P. Active anterior rhinomanometry in pre- and postoperative evaluation, use of Broms' mathematical model. *Rhinology* 1983;**21**:121–133.
166. THOMAS PL, JOHN DG, CARLIN WV. The effect of inferior turbinate outfracture on nasal resistance to airflow in vasomotor rhinitis assessed by rhinomanometry. *J Laryngol Otol* 1988;**102**:144–145.
167. ORGEL HA, MELTZER EO, KEMP JP, WELCH MJ. Clinical, rhinomanometric, and cytologic evaluation of seasonal allergic rhinitis treated with beclomethasone dipropionate as aqueous nasal spray or pressurized aerosol. *J Allergy Clin Immunol* 1986;**77**:858–864.
168. MYERS T, LONDON SJ, RANKELL AS, POETSCH CE. A system of rhinomanometry in the clinical evaluation of nasal decongestants. *Ann Otol Rhinol Laryngol* 1977;**86**:310–317.
169. JONSON B, MALM L, IVARSSON A, BENTHIN M, LAMM CJ. Automated rhinomanometry. *Rhinology* 1983;**21**:265–272.
170. GLEESON MJ, YOULTEN LJ, SHELTON DM, SIODLAK MZ, EISER NM, WENGRAF CL. Assessment of nasal airway patency: a comparison of four methods. *Clin Otolaryngol* 1986;**11**:99–107.
171. JONES AS, WILLATT DJ, DURHAM LM. Nasal airflow: resistance and sensation. *J Laryngol Otol* 1989;**103**:909–911.
172. ECCLES R, JAWAD MS, MORRIS S. The effects of oral administration of menthol on nasal resistance to airflow and nasal sensation of airflow in subjects suffering from nasal congestion associated with the common cold. *J Pharm Pharmacol* 1990;**42**:652–654.
173. LUND VJ. Objective assessment of nasal obstruction. *Otolaryngol Clin North Am* 1989;**22**:279–290.
174. COLE P. Toronto rhinomanometry: laboratory, field and clinical studies. *J Otolaryngol* 1988;**17**:331–335.
175. BINDER E, HOLOPAINEN E, MALMBERG H, SALO OP. Clinical findings in patients with allergic rhinitis. *Rhinology* 1984;**22**:255–260.

176. FILIACI F, LUCARELLI N, ZARDO F, RALLI G. Incidence of allergic rhinitis in children. *Rhinology* 1983;**21**:13–19.
177. GODLEY FA. Chronic sinusitis: an update. *Am Fam Physician* 1992;**45**:2190–2199.
178. DRUCE HM. Imaging techniques in the diagnosis of sinusitis. *Ann Allergy* 1991;**66**:132–136.
179. LLOYD GA, LUND VJ, PHELPS PD, HOWARD DJ. Magnetic resonance imaging in the evaluation of nose and paranasal sinus disease. *Br J Radiol* 1987;**60**:957–968.
180. WASICKO MJ, LEITER JC, ERLICHMAN JS, STROBEL RJ, BARTLETT DJ. Nasal and pharyngeal resistance after topical mucosal vasoconstriction in normal humans. *Am Rev Respir Dis* 1991;**144**:1048–1052.
181. OPHIR D, ELAD Y, DOLEV Z, GELLER BERNSTEIN C. Effects of inhaled humidified warm air on nasal patency and nasal symptoms in allergic rhinitis. *Ann Allergy* 1988;**60**:239–242.
182. CHOWANETZ W, SCHOTT J, JANY B. Nasal admixture during mouth breathing in awake normal subjects. *Bull Eur Physiopathol Respir* 1987;**23**:125–130.
183. DIAMOND L, CANESTRARI DA, DRESSLER WE. A technique for measuring the perception of added resistive loads during nasal breathing. *J Pharmacol Meth* 1983;**10**:255–261.
184. DUBOIS AB, BRODY AW, LEWIS DH, BURGESS BF. Oscillation mechanics of lung and chest wall in man. *J Appl Physiol* 1956;**8**:587–594.
185. VAN DEN BERG JW. An electrical analogue of the trachea, lungs and tissue. *Acta Physiol Pharmacol Neerl* 1960;**9**:361–385.
186. CLAERBOUT JF. Synthesis of a layered medium from its acoustic transmission response. *Geophys* 1968;**33**:264–269.
187. GOUPIILLAUD PL. An approach to inverse filtering of near-surface layer effects from seismic records. *Geophys* 1961;**26**:754–760.
188. FREDBERG JJ, WOHL ME, GLASS GM, DORKIN HL. Airway area by acoustic reflections measured at the mouth. *J Appl Physiol* 1980;**48**:749–758.
189. JACKSON AC, BUTLER J, MILLET EJ, HOPPIN FG, DAWSON SV. Airway geometry by analysis of acoustic pulse response measurements. *J Appl Physiol* 1977;**43**:523–536.
190. SONDHII MM, GOPINATH B. Determination of vocal-tract shape from impulse response at the lips. *J Acoust Soc Am* 1971;**49**:1867–1873.
191. MERMELSTEIN P. Determination of the vocal-tract shape from measured formant frequencies. *J Acoust Soc Am* 1995;**41**:1283–1294.
192. SCHROEDER ME. Determination of the geometry of the human vocal tract by acoustic measurements. *J Acoust Soc Am* 1967;**41**:1002–1010.
193. WARE JA, AKI K. Continuous and discrete inverse scattering problems in a stratified elastic medium. I. Plane waves at normal incidence. *J Acoust Soc Am* 1969;**45**:911–921.
194. MARSHALL I. Impedance reconstruction methods for pulse reflectometry. *Acustica* 1992;**76**:118–128.
195. SIDELL RS, FREDBERG JJ. Non-invasive inference of airway network geometry from broadband lung reflection data. *J Biomech Eng* 1978;**100**:469–479.
196. JACKSON AC, OLSON DE. Comparison of direct and acoustical area measurements in physical models of human central airways. *J Appl Physiol* 1980;**48**:896–902.
197. FREDBERG JJ. Acoustic determinants of respiratory system properties. *Ann Biomed Engineering* 1981;**9**:463–473.
198. ISHIZAKA K, FRENCH JH, FLANAGAN JM. Direct determination of vocal tract wall impedance. *IEEE Trans Acoust Speech Signal Process* 1975;**ASSP-23**:370–373.
199. JACKSON AC, KREVANS JRJ. Tracheal cross-sectional areas from acoustic reflections in dogs. *J Appl Physiol* 1984;**57**:351–353.
200. BROOKS LJ, CASTILE RG, GLASS GM, GRISCOM NT, WOHL ME, FREDBERG JJ. Reproducibility and accuracy of airway area by acoustic reflection. *J Appl Physiol* 1984;**57**:777–787.
201. D'URZO AD, LAWSON VG, VASSAL KP, REBUCK AS, SLUTSKY AS, HOFFSTEIN V. Airway area by acoustic response measurements and computerized tomography. *Am Rev Respir Dis* 1987;**135**:392–395.
202. HOFFSTEIN V, ZAMEL N. Tracheal stenosis measured by the acoustic reflection technique. *Am Rev Respir Dis* 1984;**130**:472–475.
203. GUILMETTE RA, WICKS JD, WOLFF RK, MAUDERLY JL. In vivo measurement of human nasal airway dimensions. *ITRI Annual Report*. Albuquerque, NM: ITRI, 1992;101–104.
204. MARSHALL I, ROGERS M, DRUMMOND G. Acoustic reflectometry for airway measurements. Principles, limitations and previous work. *Clin Phys Physiol Meas* 1991;**12**:131–141.
205. LOUIS B, GLASS GM, FREDBERG JJ. Pulmonary airway area by the two-microphone acoustic reflection method. *J Appl Physiol* 1994;**76**:2234–2240.
206. SHEN H, HUANG J, KITAGAWA S, et al. [Pharyngeal area measured by acoustic reflection technique while breathing room-air]. *Nippon Kyobu Shikkan Gakkai Zasshi* 1990;**28**:1593–1598.
207. STROWBRIDGE CM. Investigation of the limitations of acoustic airway measurement. Unpublished, 1988.
208. BROOKS LJ, BYARD PJ, HELMS RC, FOUKE JM, STROHL KP. Relationship between lung volume and tracheal area as assessed by acoustic reflection. *J Appl Physiol* 1988;**64**:1050–1054.
209. D'URZO AD, RUBINSTEIN I, LAWSON VG, et al. Comparison of glottic areas measured by acoustic reflections vs. computerized tomography. *J Appl Physiol* 1988;**64**:367–370.
210. RUBINSTEIN I, MCCLEAN PA, BOUCHER R, ZAMEL N, FREDBERG JJ, HOFFSTEIN V. Effect of mouthpiece, noseclips, and head position on airway area measured by acoustic reflections. *J Appl Physiol* 1987;**63**:1469–1474.
211. KASE Y, ITIMURA K, IINUMA T. [Acoustic rhinometry as method for evaluating paranasal sinuses – experimental studies]. *Nippon Jibiinkoka Gakkai Kaiho* 1993;**96**:626–636.
212. FISHER EW, BOREHAM AB. Improving the reproducibility of acoustic rhinometry: a customized stand giving control of height and angle. *J Laryngol Otol* 1995;**109**:536–537.
213. PASSALI D, BIAGINI C, DI GIROLAMO S, BELLUSSI L. Acoustic rhinometry. practical aspects of measurement. *Acta Otorhinolaryngol Belg* 1996;**50**:41–45.
214. HAMILTON JW, COOK JA, PHILLIPS DE, JONES AS. Limitations of acoustic rhinometry determined by a simple model. *Acta Otolaryngol (Stockh)* 1995;**115**:811–814.
215. HAMILTON JW, MCRAE RD, PHILLIPS DE, JONES AS. The accuracy of acoustic rhinometry using a pulse train signal. *Clin Otolaryngol* 1995;**20**:279–282.
216. TOLEDANO A, GALINDO A, GAVILAN J. [Reliability of determining minimal cross section by acoustic rhinometry]. *Acta Otorrinolaringol Esp* 1999;**50**:435–437.
217. TOLEDANO A, GALINDO A, GAVILAN J. [Relation between minimal cross section and subjective nasal obstruction]. *Acta Otorrinolaringol Esp* 1999;**50**:439–442.
218. HAIGHT JS, COLE P. The site and function of the nasal valve. *Laryngoscope* 1983;**93**:49–55.
219. COREY JP, GUNGOR A, NELSON R, FREDBERG J, LAI V. A comparison of the nasal cross-sectional areas and volumes obtained with acoustic rhinometry and magnetic resonance imaging. *Otolaryngol Head Neck Surg* 1997;**117**:349–354.

220. DASTIDAR P, HEINONEN T, NUMMINEN J, RAUTIAINEN M, LAASONEN E. Semi-automatic segmentation of computed tomographic images in volume tric estimation of nasal airway. *Eur Arch Otorhinolaryngol* 1999;**256**:192–198.
221. PRASUN D, JURA N, TOMI H, PERTTI R, MARKUS R, ERKKI L. Nasal airway volume tric measurement using segmented HRCT images and acoustic rhinometry. *Am J Rhinol* 1999;**13**:97–103.
222. GILAIN L, COSTE A, RICOLFI F, et al. Nasal cavity geometry measured by acoustic rhinometry and computed tomography. *Arch Otolaryngol Head Neck Surg* 1997;**123**:401–405.
223. COREY JP, NALBONE VP, NG BA. Anatomic correlates of acoustic rhinometry as measured by rigid nasal endoscopy. *Otolaryngol Head Neck Surg* 1999;**121**:572–576.
224. MIN YG, JANG YJ. Measurements of cross-sectional area of the nasal cavity by acoustic rhinometry and CT scanning. *Laryngoscope* 1995;**105**:757–759.
225. FISHER EW, DALY NJ, MORRIS DP, LUND VJ. Experimental studies of the resolution of acoustic rhinometry in vivo. *Acta Otolaryngol (Stockh)* 1994;**114**:647–650.
226. KASE Y, MASATO N, ABE K, TANAKA T. [Precision and problems in interpretation of acoustic rhinometry in cases of nasal mass lesion]. *Nippon Jibiinkoka Gakkai Kaiho* 1995;**98**:813–819.
227. MAYHEW TM, O'FLYNN P. Validation of acoustic rhinometry by using the Cavalieri principle to estimate nasal cavity volume in cadavers. *Clin Otolaryngol* 1993;**18**:220–225.
228. HAMILTON JW, McRAE RD, JONES AS. The magnitude of random errors in acoustic rhinometry and re-interpretation of the acoustic profile. *Clin Otolaryngol* 1997;**22**:408–413.
229. TOMKINSON A, ECCLES R. Errors arising in cross-sectional area estimation by acoustic rhinometry produced by breathing during measurement. *Rhinology* 1995;**33**:138–140.
230. TOMKINSON A, ECCLES R. The effect of changes in ambient temperature on the reliability of acoustic rhinometry data. *Rhinology* 1996;**34**:75–77.
231. TOMKINSON A. The reliability of acoustic rhinometry [letter; comment]. *J Laryngol Otol* 1995;**109**:1234–1234.
232. TOMKINSON A. Acoustic rhinometry: its place in rhinology [editorial]. *Clin Otolaryngol* 1997;**22**:189–191.
233. TOMKINSON A, ECCLES R. Acoustic rhinometry: do we need a standardized operating procedure? *Clin Otolaryngol* 1996;**21**:284–287.
234. TOMKINSON A, ECCLES R. Acoustic rhinometry: an explanation of some common artefacts associated with nasal decongestion. *Clin Otolaryngol* 1998;**23**:20–26.
235. LENDERS H, SCHOLL R, BRUNNER M. [Acoustic rhinometry: the bat principle of the nose]. *HNO* 1992;**40**:239–247.
236. LENDERS H, PIRSIG W. Diagnostic value of acoustic rhinometry: patients with allergic and vasomotor rhinitis compared with normal controls. *Rhinology* 1990;**28**:5–16.
237. AUSTIN CE, FOREMAN JC. Acoustic rhinometry compared with posterior rhinomanometry in the measurement of histamine- and bradykinin-induced changes in nasal airway patency. *Br J Clin Pharmacol* 1994;**37**:33–37.
238. BACHERT C, WAGENMANN M, VOSSEN HOLZENKAMP S. Intranasal levocabastine provides fast and effective protection from nasal allergen challenge. *Rhinology* 1996;**34**:140–143.
239. KESAVANATHAN J, SWIFT DL, FITZGERALD TK, PERMUTT T, BASCOM R. Evaluation of acoustic rhinometry and posterior rhinomanometry as tools for inhalation challenge studies. *J Toxicol Environ Health* 1996;**48**:295–307.
240. KROTOV AI. [The current methodological approaches in assessing nasal breathing function]. *Vestn Otorinolaryngol* 1998;**4**:51–52.
241. ROITHMANN R, COLE P, CHAPNIK J, BARRETO SM, SZALAI JP, ZAMEL N. Acoustic rhinometry, rhinomanometry, and the sensation of nasal patency: a correlative study. *J Otolaryngol* 1994;**23**:454–458.
242. OHKI M, SATA Y, KAWANO K, USUI N. [Evaluation of nasal obstruction with acoustic rhinometry: a simulated study with a nasal model]. *Nippon Jibiinkoka Gakkai Kaiho* 1998;**101**:1022–1028.
243. TANIDA M, NONAKA S, YOKOYAMA T, HORIKAWA H, UNNO T. [A fundamental study of relationships between rhinomanometry and acoustic rhinometry]. *Nippon Jibiinkoka Gakkai Kaiho* 1996;**99**:601–610.
244. SCHMAL F, DEITMER T. [Evaluation of nasal patency]. *Laryngorhinootologie* 1993;**72**:611–613.
245. SILKOFF PE, CHAKRAVORTY S, CHAPNIK J, COLE P, ZAMEL N. Reproducibility of acoustic rhinometry and rhinomanometry in normal subjects. *Am J Rhinol* 1999;**13**:131–135.
246. TAI CF, HO KY, HASEGAWA M. Evaluating the sensation of nasal obstruction with acoustic rhinometry and rhinomanometry. *Kao Hsiung I Hsueh Ko Hsueh Tsa Chih* 1998;**14**:548–553.
247. ZHENG C, POCHON N, LACROIX JS. [Acoustic rhinometry. comparison of pre- and post-septoplasty]. *Chung Hua Erh Pi Yen Hou Ko Tsa Chih* 1995;**30**:343–346.
248. PORTER MJ, WILLIAMSON IG, KERRIDGE DH, MAW AR. A comparison of the sensitivity of manometric rhinometry, acoustic rhinometry, rhinomanometry and nasal peak flow to detect the decongestant effect of xylometazoline. *Clin Otolaryngol* 1996;**21**:218–221.
249. PORTER MJ, MAW AR, KERRIDGE DH, WILLIAMSON IM. Manometric rhinometry: a new method of measuring the Volume of the air in the nasal cavity. *Acta Otolaryngol (Stockh)* 1997;**117**:298–301.
250. BASCOM R, KESAVANATHAN J, PERMUTT T, FITZGERALD TK, SAUDER L, SWIFT DL. Tobacco smoke upper respiratory response relationships in healthy nonsmokers. *Fundam Appl Toxicol* 1996;**29**:86–93.
251. International Rhinitis Management Working Group. International consensus report on the diagnosis and management of rhinitis. *Allergy* 1994;**49**(Suppl. 19):1–34.
252. NUMATA T, KONNO A, HASEGAWA S, et al. Pathophysiological features of the nasal mucosa in patients with idiopathic rhinitis compared to allergic rhinitis. *Int Arch Allergy Immunol* 1999;**119**:304–313.
253. GERTH V W. Nasal hyperreactivity: its pathogenesis and clinical significance. *Clin Exp Allergy* 1991;**21**:661–667.
254. DOYLE WJ, BOEHM S, SKONER DP. Physiologic responses to intranasal dose-response challenges with histamine, methacholine, bradykinin, and prostaglandin in adult volunteers with and without nasal allergy. *J Allergy Clin Immunol* 1990;**86**:924–935.
255. VAN WIJK RG, MULDER PG, DIEGES PH. Nasal provocation with histamine in allergic rhinitis patients. clinical significance and reproducibility. *Clin Exp Allergy* 1989;**19**:293–298.
256. OKUDA M, OHTSUKA H, SAKAGUCHI K, WATASE T. Nasal histamine sensitivity in allergic rhinitis. *Ann Allergy* 1983;**51**:51–55.
257. GERTH V W, DIEGES PH. Nasal reactivity to histamine and methacholine: two different forms of upper airway responsiveness. *Rhinology* 1994;**32**:119–122.
258. ALTISSIMI G, GALLUCCI L, ROSSETTI M, SIMONCELLI C. Diagnosing nasal hyperreactivity with positional rhinomanometry. *Ann Otol Rhinol Laryngol* 1996;**105**:901–904.

259. MULLINS RJ, OLSON LG, SUTHERLAND DC. Nasal histamine challenges in symptomatic allergic rhinitis. *J Allergy Clin Immunol* 1989;**83**:955-959.
260. OHM M, JUTO JE, ANDERSSON K, BODIN L. Nasal histamine provocation of tenants in a sick-building residential area. *Am J Rhinol* 1997;**11**:167-175.
261. GRAF P, HALLEN H, JUTO JE. Benzalkonium chloride in a decongestant nasal spray aggravates rhinitis medicamentosa in healthy volunteers. *Clin Exp Allergy* 1995;**25**:395-400.
262. HALLEN H, JUTO JE. A test for objective diagnosis of nasal hyperreactivity. *Rhinology* 1993;**31**:23-25.
263. KOLBECK KG, EHNHAGE A, JUTO JE. Nasal and bronchial histamine reactivity in patients with allergic rhinitis out of season. *Ann Allergy Asthma Immunol* 1999;**82**:55-60.
264. PLAVEC D, SOMOGYI-ZALUD E, GODNIC-CVAR J. Modified method of nonspecific nasal provocation with histamine for routine use. *Ann Allergy* 1994;**72**:321-328.
265. BAUDOUIN T, ANZIC SA, KALOGJERA L. Distilled water nasal provocation in hyperreactive patients. *Am J Rhinol* 1999;**13**:229-233.
266. WORTSMAN J, FRANK S, CRYER PE. Adrenomedullary response to maximal stress in humans. *Am J Medical* 1984;**77**:779-784.
267. ILIOPOULOS O, PROUD D, NORMAN PS, LICHTENSTEIN LM, KAGEY SOBOTKA A, NACLERIO RM. Nasal challenge with cold, dry air induces a late-phase reaction. *Am Rev Respir Dis* 1988;**138**:400-405.
268. BRAAT JP, MULDER PG, FOKKENS WJ, VAN WIJK RG, RIJNTJES E. Intranasal cold dry air is superior to histamine challenge in determining the presence and degree of nasal hyperreactivity in nonallergic noninfectious perennial rhinitis. *Am J Respir Crit Care Med* 1998;**157**:1748-1755.
269. SERRANO E, DIDIER A, SNOUSKI K, DILEM S, PESSEY JJ, LACOMME Y. [Diagnostic perspectives in rhinology]. *Ann Otolaryngol Chir Cervicofac* 1993;**110**:92-97.
270. JESSEN M, MALM L. Definition, prevalence and development of nasal obstruction. *Allergy* 1997;**52**:3-6.
271. MARQUEZ DORSCH F, CENJOR ESPANOL C, GUTIERREZ FONSECA R. [Acoustic rhinometry in a normal population]. *Acta Otorrinolaringol Esp* 1996;**47**:121-124.
272. HILBERG O, PEDERSEN OF. Acoustic rhinometry: recommendation for technical specification and standard operating procedures. *Rhinol Suppl.* 2000;**16**:3-17.
273. MORGAN NJ, MACGREGOR FB, BIRCHALL MA, LUND VJ, SITTAMPALAM Y. Racial differences in nasal fossa dimensions determined by acoustic rhinometry. *Rhinology* 1995;**33**:224-228.
274. COREY JP, GUNGOR A, NELSON R, LIU X, FREDBERG J. Normative standards for nasal cross-sectional areas by race as measured by acoustic rhinometry. *Otolaryngol Head Neck Surg* 1998;**119**:389-393.
275. GURR P, DIVER J, MORGAN N, MACGREGOR F, LUND V. Acoustic rhinometry of the Indian and Anglo-Saxon nose. *Rhinology* 1996;**34**:156-159.
276. MILLQVIST E, BENDE M. Reference values for acoustic rhinometry in subjects without nasal symptoms. *Am J Rhinol* 1998;**12**:341-343.
277. GRYMER LF, HILBERG O, PEDERSEN OF, RASMUSSEN TR. Acoustic rhinometry: values from adults with subjective normal nasal patency. *Rhinology* 1991;**29**:35-47.
278. GRYMER LF, HILBERG O, PEDERSEN OF. Prediction of nasal obstruction based on clinical examination and acoustic rhinometry. *Rhinology* 1997;**35**:53-57.
279. JESSEN M, MALM L. The spontaneous course of nasal obstruction in patients with normal nasal airway resistance. *Clin Otolaryngol* 1991;**16**:302-304.
280. SIPILA J, NYBERG-SIMOLA S, SUONPAA J, LAIPPALA P. Some fundamental studies on clinical measurement conditions in acoustic rhinometry. *Rhinology* 1996;**34**:206-209.
281. LENDERS H, PIRSIG W. [How can hyperreactive rhinopathy be modified surgically? II. Acoustic rhinometry and anterior turbinoplasty]. *Laryngorhinootologie* 1990;**69**:291-297.
282. COREY JP, KEMKER BJ, NELSON R, GUNGOR A. Evaluation of the nasal cavity by acoustic rhinometry in normal and allergic subjects. *Otolaryngol Head Neck Surg* 1997;**117**:22-28.
283. TAKENO S, KAWAMOTO H, HIRATA S, FUKUSHIMA N, YAZIN K. [Decongesting effect of tramazoline on nasal airway patency and nasal symptoms as evaluated by acoustic rhinometry. an objective study in 30 allergic and six non-allergic subjects]. *Nippon Jibiinkoka Gakkai Kaiho* 1998;**101**:900-907.
284. GRAF P, ENERDAL J, HALLEN H. Ten days' use of oxymetazoline nasal spray with or without benzalkonium chloride in patients with vasomotor rhinitis [In Process Citation]. *Arch Otolaryngol Head Neck Surg* 1999;**125**:1128-1132.
285. GRAF PM, HALLEN H. Changes in nasal reactivity in patients with rhinitis medicamentosa after treatment with fluticasone propionate and placebo nasal spray. *ORL J Otorhinolaryngol Relat Spec* 1998;**60**:334-338.
286. HALLEN H, ENERDAL J, GRAF P. Fluticasone propionate nasal spray is more effective and has a faster onset of action than placebo in treatment of rhinitis medicamentosa. *Clin Exp Allergy* 1997;**27**:552-558.
287. MCMAHON C, DARBY Y, RYAN R, SCADDING G. Immediate and short-term effects of benzalkonium chloride on the human nasal mucosa in vivo. *Clin Otolaryngol* 1997;**22**:318-322.
288. BUJIA J, RASP G. [Acoustic rhinometry: determination of early and late-phase reactions in allergic rhinitis]. *Acta Otorrinolaringol Esp* 1997;**48**:31-35.
289. RASP G. [Acoustic rhinometry: measuring the early and late phase of allergic immediate reaction in allergic rhinitis]. *Laryngorhinootologie* 1993;**72**:125-130.
290. SPAETH J, SCHULTZE V, KLIMEK L, LENGERSDORF A, MOSGES R. Azelastine reduces histamine-induced swelling of nasal mucosa. *ORL J Otorhinolaryngol Relat Spec* 1996;**58**:157-163.
291. HERBERHOLD C. Funktionsprüfungen und störungen des geruchssinnes. *Arch Otorhinolaryngol* 1995;**210**:67-164.
292. MELTZER EO, JALOWAYSKI AA, ORGEL HA, HARRIS AG. Subjective and objective assessments in patients with seasonal allergic rhinitis: effects of therapy with mometasone furoate nasal spray. *J Allergy Clin Immunol* 1998;**102**:39-49.
293. AKERLUND A, BENDE M, MURPHY C. Olfactory threshold and nasal mucosal changes in experimentally induced common cold. *Acta Otolaryngol (Stockh)* 1995;**115**:88-92.
294. HUMMEL T, ROTHBAUER C, BARZ S, GROSSER K, PAULI E, KOBAL G. Olfactory function in acute rhinitis. *Ann N Y Acad Sci* 1998;**855**:616-624.
295. HUMMEL T, ROTHBAUER C, PAULI E, KOBAL G. Effects of the nasal decongestant oxymetazoline on human olfactory and intranasal trigeminal function in acute rhinitis. *Eur J Clin Pharmacol* 1998;**54**:521-528.
296. LANE AP, ZWEIMAN B, LANZA DC, et al. Acoustic rhinometry in the study of the acute nasal allergic response. *Ann Otol Rhinol Laryngol* 1996;**105**:811-818.
297. NORDIN S, LOTSCH J, KOBAL G, MURPHY C. Effects of nasal-airway Volume and body temperature on intranasal chemosensitivity. *Physiol Behav* 1998;**63**:463-466.

298. ROWE JONES JM, MACKAY IS. A prospective study of olfaction following endoscopic sinus surgery with adjuvant medical treatment. *Clin Otolaryngol* 1997;**22**:377–381.
299. HOFFSTEIN V, FREDBERG JJ. The acoustic reflection technique for non-invasive assessment of upper airway area. *Eur Respir J* 1991;**4**:602–611.
300. FISHER EW, LUND VJ, SCADDING GK. Acoustic rhinometry in rhinological practice: discussion paper. *J R Soc Med* 1994;**87**:411–413.
301. FISHER EW. Acoustic rhinometry. *Clin Otolaryngol* 1997;**22**:307–317.
302. LA ROSA R, MIANI C. [The actual problems in functional and aesthetic nasal surgery]. *Acta Otorhinolaryngol Ital* 1996;**16**:238–244.
303. ROITHMANN R, COLE P, CHAPNIK J, SHPIRER I, HOFFSTEIN V. Acoustic rhinometry in the evaluation of nasal obstruction. *Laryngoscope* 1995;**105**:275–281.
304. TOMKINSON A, ECCLES R. External facial dimensions and minimum nasal cross-sectional area. *Clin Otolaryngol* 1995;**20**:557–560.
305. LUND VJ. Nasal physiology: neurochemical receptors, nasal cycle, and ciliary action. *Allergy Asthma Proc* 1996;**17**:179–184.
306. YAMAGIWA M, HILBERG O, PEDERSEN OF, LUNDQVIST GR. Evaluation of the effect of localized skin cooling on nasal airway Volume by acoustic rhinometry. *Am Rev Respir Dis* 1990;**141**:1050–1054.
307. LUNDQVIST GR, PEDERSEN OF, HILBERG O, NIELSEN B. Nasal reaction to changes in whole body temperature. *Acta Otolaryngol (Stockh)* 1993;**113**:783–788.
308. FISHER EW, SCADDING GK, LUND VJ. The role of acoustic rhinometry in studying the nasal cycle. *Rhinology* 1993;**31**:57–61.
309. FISHER EW, LIU M, LUND VJ. The nasal cycle after deprivation of airflow: a study of laryngectomy patients using acoustic rhinometry. *Acta Otolaryngol (Stockh)* 1994;**114**:443–446.
310. GUNGOR A, MOINUDDIN R, NELSON RH, COREY JP. Detection of the nasal cycle with acoustic rhinometry: techniques and applications. *Otolaryngol Head Neck Surg* 1999;**120**:238–247.
311. RUNCRCANTZ H. Postural variations of nasal patency. *Acta Otolaryngol (Stockh)* 1969;**68**:435–443.
312. HAIGHT JJ, COLE P. Reciprocating nasal airflow resistances. *Acta Otolaryngol (Stockh)* 1984;**97**:93–98.
313. O'FLYNN P. Posture and nasal geometry. *Acta Otolaryngol (Stockh)* 1993;**113**:530–532.
314. FOUKE JM, JACKSON AC. Acoustic rhinometry: effects of decongestants and posture on nasal patency. *J Laboratoryclin Med* 1992;**119**:371–376.
315. JAN MA, MARSHALL I, DOUGLAS NJ. Effect of posture on upper airway dimensions in normal human. *Am J Respir Crit Care Med* 1994;**149**:145–148.
316. KASE Y, HILBERG O, PEDERSEN OF. Posture and nasal patency: evaluation by acoustic rhinometry. *Acta Otolaryngol (Stockh)* 1994;**114**:70–74.
317. KASE Y, TANAKA T, IINUMA T. [The effect of unilateral nasal patency on the contralateral side]. *Nippon Jibiinkoka Gakkai Kaiho* 1993;**96**:1073–1078.
318. NAGANO E, NONAKA S. [Nasal decongestion evaluated by acoustic rhinometry]. *Nippon Jibiinkoka Gakkai Kaiho* 1994;**97**:2075–2084.
319. CHATKIN JM, DJUPESLAND PG, QIAN W, et al. Nasal nitric oxide is independent of nasal cavity Volume. *Am. J Rhinol* 1999;**13**:179–184.
320. SILKOFF PE, ROTH Y, MCCLEAN P, COLE P, CHAPNIK J, ZAMEL N. Nasal nitric oxide does not control basal nasal patency or acute congestion following allergen challenge in allergic rhinitis. *Ann Otol Rhinol Laryngol* 1999;**108**:368–372.
321. JULIA SERDA G, MOLFINO NA, FURLOTT HG, et al. Tracheobronchial dilation during isocapnic hypoxia in conscious humans. *J Appl Physiol* 1993;**75**:1728–1733.
322. TANAKA T, OKITA W, KASE Y, IINUMA T. [Evaluation of the effects of nasal decongestants with acoustic rhinometry]. *Nippon Jibiinkoka Gakkai Kaiho* 1994;**97**:207–212.
323. TAVERNER D, BICKFORD L, SHAKIB S, TONKIN A. Evaluation of the dose-response relationship for intra-nasal oxymetazoline hydrochloride in normal adults [In Process Citation]. *Eur J Clin Pharmacol* 1999;**55**:509–513.
324. HOCHBAN W, ALTHOFF H, ZIEGLER A. Nasal decongestion with imidazoline derivatives: acoustic rhinometry measurements. *Eur J Clin Pharmacol* 1999;**55**:7–12.
325. BICKFORD L, SHAKIB S, TAVERNER D. The nasal airways response in normal subjects to oxymetazoline spray: randomized double-blind placebo-controlled trial. *Br J Clin Pharmacol* 1999;**48**:53–56.
326. TAVERNER D, DANZ C, ECONOMOS D. The effects of oral pseudoephedrine on nasal patency in the common cold: a double-blind single-dose placebo-controlled trial. *Clin Otolaryngol* 1999;**24**:47–51.
327. WEEKE J, CHRISTENSEN SE, ORSKOV H, et al. A randomized comparison of intranasal and injectable octreotide administration in patients with acromegaly. *J Clin Endocrinol Metab* 1992;**75**:163–169.
328. HOLMBERG K, BJORK E, BAKE B, EDMAN P. Influence of degradable starch microspheres on the human nasal mucosa. *Rhinology* 1994;**32**:74–77.
329. TANAKA T, KASE Y, OKITA W, ICHIMURA K, IINUMA T. [Vasoactivity of human nasal mucosa in response to sensory neurotransmitters (a study of nasal geometrical change with acoustic rhinometry)]. *Nippon Jibiinkoka Gakkai Kaiho* 1994;**97**:1211–1218.
330. ENZMANN H, MATHE F. [Acoustic rhinometry for evaluating the effectiveness of antihistaminics]. *H* 1998;**46**:529–533.
331. TERRIEN MH, RAHM F, FELLRATH JM, SPERTINI F. Comparison of the effects of terfenadine with fexofenadine on nasal provocation tests with allergen. *J Allergy Clin Immunol* 1999;**103**:1025–1030.
332. PASSALI D, BELLUSSI L, LAURIELLO M, FERRARA A. [Can the recurrence of nasal polyposis be prevented? A new therapeutic approach]. *Acta Otorhinolaryngol Ital* 1995;**15**:91–100.
333. SAMOLINSKI B, GRZANKA A, ZAWISZA E, ARCIMOWICZ M. [Acoustic rhinometry in the assessment of the topical treatment of upper respiratory infections with fusafungin]. *Otolaryngol Pol* 1998;**52**:327–334.
334. TERADA N, YAMAKOSHI T, HASEGAWA M, et al. The effect of ramatroban (BAY u 3405), a thromboxane A2 receptor antagonist, on nasal cavity Volume and minimum cross-sectional area and nasal mucosal hemodynamics after nasal mucosal allergen challenge in patients with perennial allergic rhinitis. *Acta Otolaryngol Suppl (Stockh)* 1998;**537**:32–37.
335. YAMAGIWA M. Acoustic evaluation of the efficacy of medical therapy for allergic nasal obstruction. *Eur Arch Otorhinolaryngol Suppl* 1997;**1**:S82–S84.
336. HOFFSTEIN V, ZAMEL N, PHILLIPSON EA. Lung volume dependence of pharyngeal cross-sectional area in patients with obstructive sleep apnea. *Am Rev Respir Dis* 1984;**130**:175–178.
337. FOUKE JM, STROHL KP. Effect of position and lung volume on upper airway geometry. *J Appl Physiol* 1987;**63**:375–380.
338. BROWN IG, ZAMEL N, HOFFSTEIN V. Pharyngeal cross-sectional area in normal men and women. *J Appl Physiol* 1986;**61**:890–895.

339. SHEN H. [Pharyngeal cross-sectional area and pharyngeal compliance in normal Japanese males and females]. *Nippon Kyobu Shikkan Gakkai Zasshi* 1993;**31**:1432–1440.
340. BROWN IB, McCLEAN PA, BOUCHER R, ZAMEL N, HOFFSTEIN V. Changes in pharyngeal cross-sectional area with posture and application of continuous positive airway pressure in patients with obstructive sleep apnea. *Am Rev Respir Dis* 1987;**136**:628–632.
341. SHEN H, HUANG J, YAMANOUCHI K, et al. [Effect of posture on pharyngeal area measured by acoustic reflection technique]. *Nippon Kyobu Shikkan Gakkai Zasshi* 1991;**29**:554–559.
342. BROWN IG, ZAMEL N, HOFFSTEIN V. Pharyngeal and glottic changes following methacholine challenge in normal subjects. *Bull Eur Physiopathol Respir* 1986;**22**:251–256.
343. RIVLIN J, HOFFSTEIN V, KALBFLEISCH J, McNICHOLAS W, ZAMEL N, BRYAN AC. Upper airway morphology in patients with idiopathic obstructive sleep apnea. *Am Rev Respir Dis* 1984;**129**:355–360.
344. KATZ I, STRADLING J, SLUTSKY AS, ZAMEL N, HOFFSTEIN V. Do patients with obstructive sleep apnea have thick necks?. *Am Rev Respir Dis* 1990;**141**:1228–1231.
345. BRADLEY TD, BROWN IG, GROSSMAN RF, et al. Pharyngeal size in snorers, nonsnorers, and patients with obstructive sleep apnea. *N Engl J Medical* 1986;**315**:1327–1331.
346. HOCHBAN W, KUNKEL M, BRANDENBURG U. [Functional anatomy of the upper airway: cephalometric and reflective acoustic studies]. *Pneumologie* 1993;**47**(Suppl. 4):766–772.
347. SHEPARD JWJ, GEFTER WB, GUILLEMINAULT C, et al. Evaluation of the upper airway in patients with obstructive sleep apnea. *Sleep* 1991;**14**:361–371.
348. LENDERS H, PIRSIG W. Acoustic rhinometry: a diagnostic tool for patients with chronic rhonchopathies. *Rhinol Suppl* 1992;**14**:101–105.
349. HOFFSTEIN V, WRIGHT S, ZAMEL N, BRADLEY TD. Pharyngeal function and snoring characteristics in apneic and nonapneic snorers. *Am Rev Respir Dis* 1991;**143**:1294–1299.
350. RASCHKE F, FISCHER J. [Use of acoustic rhinometry for determining segmental airway geometry with nasal positive or negative pressure]. *Pneumologie* 1993;**47**(Suppl. 4):735–737.
351. BRADLEY TD, BROWN IG, ZAMEL N, PHILLIPSON EA, HOFFSTEIN V. Differences in pharyngeal properties between snorers with predominantly central sleep apnea and those without sleep apnea. *Am Rev Respir Dis* 1987;**135**:387–391.
352. BROWN IG, BRADLEY TD, PHILLIPSON EA, ZAMEL N, HOFFSTEIN V. Pharyngeal compliance in snoring subjects with and without obstructive sleep apnea. *Am Rev Respir Dis* 1985;**132**:211–215.
353. RUBINSTEIN I, HOFFSTEIN V, BRADLEY TD. Lung volume-related changes in the pharyngeal area of obese females with and without obstructive sleep apnoea. *Eur Respir J* 1989;**2**:344–351.
354. RUBINSTEIN I, COLAPINTO N, ROTSTEIN LE, BROWN IG, HOFFSTEIN V. Improvement in upper airway function after weight loss in patients with obstructive sleep apnea. *Am Rev Respir Dis* 1988;**138**:1192–1195.
355. AH-SEE KW, STEWART M, BANHAM SW, ROBINSON K, CARTER R, WILSON JA. Systematic analysis of snoring in women. *Ann Otol Rhinol Laryngol* 1998;**107**:227–231.
356. FURST G, RIECHELMANN H, SCHLEGEL J. [Measuring pharyngeal pressure in patients with nCPAP ventilation]. *Pneumologie* 1994;**48**:835–836.
357. ANTILA J, SIPILA J, TSHUSHIMA Y, POLO O, LAURIKAINEN E, SUONPAA J. The effect of laser-uvulopalatopharyngoplasty on the nasal and nasopharyngeal Volume measured with acoustic rhinometry. *Acta Otolaryngol Suppl (Stockh)* 1997;**529**:202–205.
358. SCHECHTER GL, WARE JC, PERLSTROM J, McBRAYER RH. Nasal patency and the effectiveness of nasal continuous positive air pressure in obstructive sleep apnea. *Otolaryngol Head Neck Surg* 1998;**118**:643–647.
359. HOFFSTEIN V. Relationship between lung volume, maximal expiratory flow, forced expiratory volume in one second, and tracheal area in normal men and women. *Am Rev Respir Dis* 1986;**134**:956–961.
360. DAVIDSON J, GULLANE P, HAVAS T, BRYCE DP. Functional assessment after laryngotracheoplasty. *Otolaryngol Head Neck Surg* 1987;**97**:294–299.
361. KATZ I, ZAMEL N, SLUTSKY AS, REBUCK AS, HOFFSTEIN V. Relative hysteresis of the airways and lung parenchyma in normal subjects. *J Appl Physiol* 1988;**65**:2390–2394.
362. BROWN IG, WEBSTER PM, ZAMEL N, HOFFSTEIN V. Changes in tracheal cross-sectional area during Mueller and Valsalva maneuvers in humans. *J Appl Physiol* 1986;**60**:1865–1870.
363. MOLFINO NA, SLUTSKY AS, JULIA SERDA G, et al. Assessment of airway tone in asthma. Comparison between double lung transplant patients and healthy subjects. *Am Rev Respir Dis* 1993;**148**:1238–1243.
364. BROOKS LJ. Tracheal size and distensibility in patients with cystic fibrosis. *Am Rev Respir Dis* 1990;**141**:513–516.
365. KASE Y, ITIMURA K, IINUMA T. [An evaluation of nasal patency with acoustic rhinometry – preop. and postop comparisons]. *Nippon Jibiinkoka Gakkai Kaiho* 1993;**96**:197–202.
366. OHNISHI T, KITA H, WEILER D, et al. IL-5 is the predominant eosinophil-active cytokine in the antigen-induced pulmonary late-phase reaction. *Am Rev Respir Dis* 1993;**147**:901–907.
367. GRYMER LF, HILBERG O, ELBROND O, PEDERSEN OF. Acoustic rhinometry: evaluation of the nasal cavity with septal deviations, before and after septoplasty. *Laryngoscope* 1989;**99**:1180–1187.
368. GRYMER LF, ILLUM P, HILBERG O. Septoplasty and compensatory inferior turbinate hypertrophy: a randomized study evaluated by acoustic rhinometry. *J Laryngol Otol* 1993;**107**:413–417.
369. KEMKER B, LIU X, GUNGOR A, MOINUDDIN R, COREY JP. Effect of nasal surgery on the nasal cavity as determined by acoustic rhinometry. *Otolaryngol Head Neck Surg* 1999;**121**:567–571.
370. MANN WJ, RIECHELMANN H, HINNI ML. Acoustic rhinometry – predictive value in septal and turbinate surgery. *Adv Otorhinolaryngol* 1997;**51**:61–67.
371. URPEGUI AM, VALLES H, MILLAN J, ROYO J. [Evaluation with acoustic rhinometry of surgical results in patients undergoing septoplasty]. *Acta Otorrinolaringol Esp* 1999;**50**:34–39.
372. KAMAMI YV. Laser-assisted outpatient septoplasty results on 120 patients. *J Clin Laser Med* 1997;**15**:123–129.
373. MARAIS J, MURRAY JA, MARSHALL I, DOUGLAS N, MARTIN S. Minimal cross-sectional areas, nasal peak flow and patients' satisfaction in septoplasty and inferior turbinectomy. *Rhinology* 1994;**32**:145–147.
374. HILBERG O, GRYMER LF, PEDERSEN OF, ELBROND O. Turbinate hypertrophy. Evaluation of the nasal cavity by acoustic rhinometry. *Arch Otolaryngol Head Neck Surg* 1990;**116**:283–289.
375. GRYMER LF, ILLUM P, HILBERG O. Bilateral inferior turbinoplasty in chronic nasal obstruction. *Rhinology* 1996;**34**:50–53.

376. PASSALI D, LAURIELLO M, DE FILIPPI A, BELLUSSI L. [Comparative study of most recent surgical techniques for the treatment of the hypertrophy of inferior turbinates]. *Acta Otorhinolaryngol Ital* 1995;**15**:219–228.
377. PASSALI D, LAURIELLO M, ANSELMINI M, BELLUSSI L. Treatment of hypertrophy of the inferior turbinate: long-term results in 382 patients randomly assigned to therapy. *Ann Otol Rhinol Laryngol* 1999;**108**:569–575.
378. ILLUM P. Septoplasty and compensatory inferior turbinate hypertrophy: long-term results after randomized turbinoplasty. *Eur Arch Otorhinolaryngol Suppl* 1997;**1**:S89–S92.
379. REBER M, RAHM F, MONNIER P. The role of acoustic rhinometry in the pre- and postoperative evaluation of surgery for nasal obstruction. *Rhinology* 1998;**36**:184–187.
380. ROITHMANN R, CHAPNIK J, ZAMEL N, BARRETO SM, COLE P. Acoustic rhinometric assessment of the nasal valve. *Am J Rhinol* 1997;**11**:379–385.
381. SHEMEN L, HAMBURG R. Preoperative and postoperative nasal septal surgery assessment with acoustic rhinometry. *Otolaryngol Head Neck Surg* 1997;**117**:338–342.
382. SZUCS E, CLEMENT PA. Acoustic rhinometry and rhinomanometry in the evaluation of nasal patency of patients with nasal septal deviation. *Am J Rhinol* 1998;**12**:345–352.
383. ILLUM P, GRZYMER L, HILBERG O. Nasal packing after septoplasty. *Clin Otolaryngol* 1992;**17**:158–162.
384. GRZYMER LF. Reduction rhinoplasty and nasal patency: change in the cross-sectional area of the nose evaluated by acoustic rhinometry. *Laryngoscope* 1995;**105**:429–431.
385. GRZYMER LF, GREGERS-PETERSEN C, BAYMLER PH. Influence of lateral osteotomies in the dimensions of the nasal cavity. *Laryngoscope* 1999;**109**:936–938.
386. LUEG EA, IRISH JC, ROTH Y, et al. An objective analysis of the impact of lateral rhinotomy and medial maxillectomy on nasal airway function. *Laryngoscope* 1998;**108**:1320–1324.
387. KUNKEL M, HOCHBAN W. Acoustic rhinometry: a new diagnostic procedure – experimental and clinical experience. *Int J Oral Maxillofac Surg* 1994;**23**:409–412.
388. KUNKEL M, HOCHBAN W. Acoustic rhinometry: rationale and perspectives. *J Craniomaxillofac Surg* 1994;**22**:244–249.
389. KUNKEL M, HOCHBAN W. The influence of maxillary osteotomy on nasal airway patency and geometry. *Mund Kiefer Gesichtschir* 1997;**1**:194–198.
390. KUNKEL M, WAHLMANN U, WAGNER W. Nasal airway in cleft-palate patients: acoustic rhinometric data. *J Craniomaxillofac Surg* 1997;**25**:270–274.
391. KUNKEL M, WAHLMANN U, WAGNER W. Acoustic airway profiles in unilateral cleft palate patients [In Process Citation]. *Cleft Palate Craniofac J* 1999;**36**:434–440.
392. WAHLMANN U, KUNKEL M, WAGNER W. Preoperative assessment of airway patency in the planning of corrective cleft nose surgery. *Mund Kiefer Gesichtschir* 1998;**2**(Suppl. 1):S153–S157.
393. PANIELLO RC. Nasal valve suspension. An effective treatment for nasal valve collapse. *Arch Otolaryngol Head Neck Surg* 1996;**122**:1342–1346.
394. LUNDQVIST GR, YAMAGIWA M, PEDERSEN OF, NIELSEN GD. Inhalation of diethylamine – acute nasal effects and subjective response. *Am Ind Hyg Assoc J* 1992;**53**:181–185.
395. AKESSON B, PAULSSON K. Experimental exposure of male volunteers to N-methyl-2-pyrrolidone (NMP). Acute effects and pharmacokinetics of NMP in plasma and urine. *Occup Environ Med* 1997;**54**:236–240.
396. IRANDER K, STAHLBOM B, WELINDER H, AKESSON B. Metachromatic cells and eosinophils in the nasal mucosa and N,N-dimethylbenzylamine exposure. *Acta Otolaryngol (Stockh)* 1997;**117**:433–436.
397. JOHANSON G, NIHLIN A, LOF A. Toxicokinetics and acute effects of MTBE and ETBE in male volunteers. *Toxicol Lett* 1995;**82–83**(713–8):713–718.
398. NIHLIN A, WALINDER R, LOF A, JOHANSON G. Experimental exposure to methyl tertiary-butyl ether. II. Acute effects in humans. *Toxicol Appl Pharmacol* 1998;**148**:281–287.
399. NIHLIN A, LOF A, JOHANSON G. Controlled ethyl tert-butyl ether (ETBE) exposure of male volunteers. II. Acute effects. *Toxicol Sci* 1998;**46**:143–150.
400. RASMUSSEN TR, BRAUER M, KJAERGAARD S. Effects of nitrous acid exposure on human mucous membranes. *Am J Respir Crit Care Med* 1995;**151**:1504–1511.
401. LARSSON BM, PALMBERG L, MALMBERG PO, LARSSON K. Effect of exposure to swine dust on levels of IL-8 in airway lavage fluid. *Thorax* 1997;**52**:638–642.
402. RUDELL B, WASS U, HORSTEDT P, et al. Efficiency of automotive cabin air filters to reduce acute health effects of diesel exhaust in human subjects. *Occup Environ Med* 1999;**56**:222–231.
403. WALINDER R, NORBACK D, WIESLANDER G, SMEDJE G, ERWALL C, VENGE P. Nasal patency and biomarkers in nasal lavage – the significance of air exchange rate and type of ventilation in schools. *Int Arch Occup Environ Health* 1998;**71**:479–486.
404. WALINDER R, NORBACK D, WIESLANDER G, SMEDJE G, ERWALL C, VENGE P. Nasal patency and lavage biomarkers in relation to settled dust and cleaning routines in schools. *Scand J Work Environ Health* 1999;**25**:137–143.
405. WIESLANDER G, NORBACK D, NORDSTROM K, WALINDER R, VENGE P. Nasal and ocular symptoms, tear film stability and biomarkers in nasal lavage, in relation to building-dampness and building design in hospitals. *Int Arch Occup Environ Health* 1999;**72**:451–461.
406. ZAVRAS AI, AL-BULTAN T, JACKSON A, WHITE G. Exposure to passive smoking and other predictors of reduced nasal volume in children 7–12 years old. *J Clin Pediatr Dent* 1997;**21**:295–303.
407. PEDERSEN OF, BERKOWITZ R, YAMAGIWA M, HILBERG O. Nasal cavity dimensions in the newborn measured by acoustic reflections. *Laryngoscope* 1994;**104**:1023–1028.
408. RIECHELMANN H, RHEINHEIMER MC, WOLFENBERGER M. Acoustic rhinometry in pre-school children. *Clin Otolaryngol* 1993;**18**:272–277.
409. HO WK, WEI WI, YUEN AP, CHAN KL, HUI Y. Measurement of nasal geometry by acoustic rhinometry in normal-breathing Asian children [In Process Citation]. *J Otolaryngol* 1999;**28**:232–237.
410. PENTZ S, PIRSIG W, LENDERS H. Long-term results of neonates with nasal deviation: a prospective study over 12 years. *Int J Pediatr Otorhinolaryngol* 1994;**28**:183–191.
411. ZAVRAS AI, WHITE GE, RICH A, JACKSON AC. Acoustic rhinometry in the evaluation of children with nasal or oral respiration. *J Clin Pediatr Dent* 1994;**18**:203–210.
412. ELBROND O, HILBERG O, FELDING JU, BLEGVAD ANDERSEN O. Acoustic rhinometry, used as a method to demonstrate changes in the Volume of the nasopharynx after adenoidectomy. *Clin Otolaryngol* 1991;**16**:84–86.
413. KANO S, PEDERSEN OF, SLY PD. Nasal response to inhaled histamine measured by acoustic rhinometry in infants. *Pediatr Pulmonol* 1994;**17**:312–319.

414. FISHER EW, PALMER CR, DALY NJ, LUND VJ. Acoustic rhinometry in the pre-operative assessment of adenoidectomy candidates. *Acta Otolaryngol* (Stockh) 1995;**115**:815–822.
415. KIM YK, KANG JH, YOON KS. Acoustic rhinometric evaluation of nasal cavity and nasopharynx after adenoidectomy and tonsillectomy. *Int J Pediatr Otorhinolaryngol* 1998;**44**:215–220.
416. MOSTAFA BE. Detection of adenoidal hypertrophy using acoustic rhinomanometry. *Eur Arch Otorhinolaryngol Suppl* 1997;**1**:S27–S29.
417. RIECHELMANN H, O'CONNELL JM, RHEINHEIMER MC, WOLFENBERGER M, MANN WJ. The role of acoustic rhinometry in the diagnosis of adenoidal hypertrophy in pre-school children. *Eur J Pediatr* 1999;**158**:38–41.
418. CONTENCIN P, GUMPERT LC, DE GAUDEMAR I, CHAUSSAIN M, DUPONT C. Non-endoscopic techniques for the evaluation of the pediatric airway. *Int J Pediatr Otorhinolaryngol* 1997;**41**:347–352.
419. FISHER EW, PALMER CR, LUND VJ. Monitoring fluctuations in nasal patency in children: acoustic rhinometry versus rhinohygmometry. *J Laryngol Otol* 1995;**109**:503–508.
420. BUENTING JE, DALSTON RM, DRAKE RF. The acoustic assessment of nasal area in infants. *Am J Rhin* 1994;**8**:305–310.
421. BUENTING JE, DALSTON RM, SMITH TL, DRAKE AF. Artifacts associated with acoustic rhinometric assessment of infants and young children: a model study. *J Appl Physiol* 1994;**77**:2558–2563.
422. BUENTING JE, DALSTON RM, DRAKE AF. Nasal cavity area in term infants determined by acoustic rhinometry. *Laryngoscope* 1994;**104**:1439–1445.
423. DJUPESLAND P. [Acoustic rhinometry. A new method for objective assessment of the nasal airway dimensions]. *Tidsskr Nor Laegeforen* 1996;**116**:3111–3114.
424. DJUPESLAND PG, LYHOLM B. Technical abilities and limitations of acoustic rhinometry optimised for infants. *Rhinology* 1998;**36**:104–113.
425. DJUPESLAND PG, QIAN W, FURLOTT H, ROTNES JS, COLE P, ZAMEL N. Acoustic rhinometry: a study of transient and continuous noise techniques with nasal models [In Process Citation]. *Am J Rhinol* 1999;**13**:323–329.
426. DJUPESLAND P, KAASTAD E, FRANZEN G. Acoustic rhinometry in the evaluation of congenital choanal malformations. *Int J Pediatr Otorhinolaryngol* 1997;**41**:319–337.
427. DJUPESLAND PG, LYHOLM B. Nasal airway dimensions in term neonates measured by continuous wide-band noise acoustic rhinometry. *Acta Otolaryngol* (Stockh) 1997;**117**:424–432.
428. DJUPESLAND PG, LYHOLM B. Changes in nasal airway dimensions in infancy. *Acta Otolaryngol* (Stockh) 1998;**118**:852–858.
429. DJUPESLAND PG, LODRUP CK. Nasal airway dimensions and lung function in awake, healthy neonates. *Pediatr Pulmonol* 1998;**25**:99–106.
430. PEDERSEN OF, YAMAGIWA M, MIYAHARA Y, SAKAKURA Y. Nasal cavity dimensions in guinea pigs measured by acoustic reflections. *Am J Rhin* 1995;**8**:299–304.
431. NAKAMOTO S, SAKAKURA Y, PEDERSEN OF, UKAI K. Evaluation of nasal passage patency after antigen and histamine challenge in guinea pigs by acoustic rhinometry. *Am J Rhinol* 1997;**11**:85–89.
432. KAISE T, UKAI K, PEDERSEN OF, SAKAKURA Y. Accuracy of measurement of acoustic rhinometry applied to small experimental animals. *Am J Rhinol* 1999;**13**:125–129.
433. KAISE T, OHMORI K, SAKAKURA Y, UKAI K. The effect of KW-4679, an antiallergic drug, on experimental allergic rhinitis in guinea pigs: effects on nasal blockage. *Jpn J Pharmacol* 1995;**69**:435–438.
434. OHKAWA C, UKAI K, MIYAHARA Y, SAKAKURA Y. Acoustic rhinometry evaluation of nasal response to histamine and antigen in guinea pigs. *Am J Rhinol* 1999;**13**:67–71.
435. OHKAWA C, UKAI K, MIYAHARA Y, TAKEUCHI K, SAKAKURA Y. Histamine H1 receptor and reactivity of the nasal mucosa in sensitized guinea pigs. *Auris Nasus Larynx* 1999;**26**:293–298.
436. RINDER J. Sensory neuropeptides and nitric oxide in nasal vascular regulation. *Acta Physiol Scand Suppl* 1996;**632**:1–45.
437. LUND VJ, SCADDING GK. Objective assessment of endoscopic sinus surgery in the management of chronic rhinosinusitis: an update. *J Laryngol Otol* 1994;**108**:749–753.
438. MARAIS J, MARAN AG. Nasoantral window assessment by acoustic rhinometry. *J Laryngol Otol* 1994;**108**:567–568.
439. LUND V. Allergic rhinitis – making the correct diagnosis. *Clin Exp Allergy* 1998;**28**(Suppl. 6):25–28.
440. SHIN SH, PARK JY, SOHN JH. Clinical value of olfactory function tests after endoscopic sinus surgery: a short-term result. *Am J Rhinol* 1999;**13**:63–66.
441. LILDHOLDT T. Surgical versus medical treatment of nasal polyps. *Rhinol Suppl* 1989;**8**:31–33.
442. ELBROND O, FELDING JU, GUSTAVSEN KM. Acoustic rhinometry used as a method to monitor the effect of intramuscular injection of steroid in the treatment of nasal polyps. *J Laryngol Otol* 1991;**105**:178–180.
443. LUND VJ, FLOOD J, SYKES AP, RICHARDS DH. Effect of fluticasone in severe polyposis. *Arch Otolaryngol Head Neck Surg* 1998;**124**:513–518.
444. MALM L. Assessment and staging of nasal polyposis. *Acta Otolaryngol* (Stockh) 1997;**117**:465–467.
445. O'FLYNN P. Acoustic rhinometry. validation of Volume changes following intra-nasal polypectomy. *Clin Otolaryngol* 1993;**18**:423–425.
446. SCADDING GK, HASSAB M, DARBY YC, LUND VJ, FREEDMAN A. Intranasal lysine aspirin in recurrent nasal polyposis. *Clin Otolaryngol* 1995;**20**:561–563.
447. RUBINSTEIN I, ZAMEL N, SLUTSKY AS, REBUCK AS, HOFFSTEIN V. Expiratory glottic widening in asthmatic subjects during exercise-induced bronchoconstriction. *Am Rev Respir Dis* 1989;**140**:606–609.
448. RUBINSTEIN I, ZAMEL N, REBUCK AS, HOFFSTEIN V, D'URZO AD, SLUTSKY AS. Dichotomous airway response to exercise in asthmatic patients. *Am Rev Respir Dis* 1988;**138**:1164–1168.
449. MOLFINO NA, SLUTSKY AS, HOFFSTEIN V, et al. Changes in cross-sectional airway areas induced by methacholine, histamine, and LTC4 in asthmatic subjects. *Am Rev Respir Dis* 1992;**146**:577–580.
450. HOFFSTEIN V, ZAMEL N, MCCLEAN P, CHAPMAN KR. Changes in pulmonary function and cross-sectional area of trachea and bronchi in asthmatics following inhalation of procaterol hydrochloride and ipratropium bromide. *Am J Respir Crit Care Med* 1994;**149**:81–85.
451. JULIA SERDA G, MOLFINO NA, CHAPMAN KR, et al. Heterogeneous airway tone in asthmatic subjects. *J Appl Physiol* 1992;**73**:2328–2332.
452. ZWEIMAN B, GETSY J, KALENIAN M, et al. Nasal airway changes assessed by acoustic rhinometry and mediator release during immediate and late reactions to allergen challenge. *J Allergy Clin Immunol* 1997;**100**:624–631.

453. SCADDING GK, DARBY YC, AUSTIN CE. Acoustic rhinometry compared with anterior rhinomanometry in the assessment of the response to nasal allergen challenge. *Clin Otolaryngol* 1994;**19**:451–454.
454. GANSLMAYER M, SPERTINI F, RAHM F, TERRIEN MH, MOSIMANN B, LEIMGRUBER A. Evaluation of acoustic rhinometry in a nasal provocation test with allergen [In Process Citation]. *Allergy* 1999;**54**:974–979.
455. HELLGREN J, JARLSTEDT J, DIMBERG L, TOREN K, KARLSSON G. A study of some current methods for assessment of nasal histamine reactivity. *Clin Otolaryngol* 1997;**22**:536–541.
456. PIRILA T, NUUTINEN J. Acoustic rhinometry, rhinomanometry and the amount of nasal secretion in the clinical monitoring of the nasal provocation test. *Clin Exp Allergy* 1998;**28**:468–477.
457. ROITHMANN R, SHPIRER I, COLE P, CHAPNIK J, SZALAI JP, ZAMEL N. The role of acoustic rhinometry in nasal provocation testing. *Ear Nose Throat J* 1997;**76**:747–750, 752.
458. MIYAHARA Y, UKAI K, YAMAGIWA M, OHKAWA C, SAKAKURA Y. Nasal passage patency in patients with allergic rhinitis measured by acoustic rhinometry: nasal responses after allergen and histamine provocation. *Auris Nasus Larynx* 1998;**25**:261–267.
459. MYGIND N, DAHL R. Challenge tests in nose and bronchi: pharmacological modulation of rhinitis and asthma. *Clin Exp Allergy* 1996;**26**(Suppl. 3):39–43.
460. MYGIND N, DAHL R, NIELSEN LP, HILBERG O, BJERKE T. Effect of corticosteroids on nasal blockage in rhinitis measured by objective methods. *Allergy* 1997;**52**:39–44.
461. NIELSEN LP, BJERKE T, CHRISTENSEN MB, PEDERSEN B, RASMUSSEN TR, DAHL R. Assessment of the allergic reaction in seasonal rhinitis: acoustic rhinometry is a sensitive and objective method. *Clin Exp Allergy* 1996;**26**:1268–1275.
462. PASSALI D, BELLUSSI L. Monitoring methods for local nasal immunotherapy. *Allergy* 1997;**52**:22–25.
463. PHIPATANAKUL W, KESAVANATHAN J, EGGLESTON PA, JOHNSON EF, WOOD RA. The value of acoustic rhinometry in assessing nasal responses to cat exposure. *J Allergy Clin Immunol* 1998;**102**:896–901.
464. BARANIUK JN, ALI M, YUTA A, FANG SY, NARANCH K. Hypertonic saline nasal provocation stimulates nociceptive nerves, substance P release, and glandular mucous exocytosis in normal humans. *Am J Respir Crit Care Med* 1999;**160**:655–662.
465. RAJAKULASINGAM K, DURHAM SR, O'BRIEN F et al. Enhanced expression of high-affinity IgE receptor (Fc epsilon RI) alpha chain in human allergen-induced rhinitis with co-localization to mast cells, macrophages, eosinophils, and dendritic cells. *J Allergy Clin Immunol* 1997;**100**:78–86.
466. ELLEGARD E, KARLSSON G. IgE-mediated reactions and hyperreactivity in pregnancy rhinitis [In Process Citation]. *Arch Otolaryngol Head Neck Surg* 1999;**125**:1121–1125.
467. MABRY RL. Rhinitis of pregnancy. *South Med J* 1986;**79**:965–971.
468. PAULSSON B, GREDMARK T, BURIAN P, BENDE M. Nasal mucosal congestion during the menstrual cycle. *J Laryngol Otol* 1997;**111**:337–339.
469. RINDER J, STJARNE P, LUNDBERG JM. Capsaicin de-sensitization of the human nasal mucosa reduces pain and vascular effects of lactic acid and hypertonic saline. *Rhinology* 1994;**32**:173–178.
470. STJARNE P, RINDER J, HEDEN-BLOMQUIST E, et al. Capsaicin desensitization of the nasal mucosa reduces symptoms upon allergen challenge in patients with allergic rhinitis. *Acta Otolaryngol (Stockh)* 1998;**118**:235–239.
471. VAN SURELL C, LOUIS B, LOFASO F, et al. Acoustic method to estimate the longitudinal area profile of endotracheal tubes. *Am J Respir Crit Care Med* 1994;**149**:28–33.
472. DAVIES A, LEWTH G, GODDARD J, HOWARTH P. The effect of acupuncture on nonallergic rhinitis: a controlled pilot study. *Altern Ther Health Med* 1998;**4**:70–74.
473. GOSEPATH J, MANN WJ, AMEDEE RG. Effects of the Breathe Right nasal strips on nasal ventilation. *Am J Rhinol* 1997;**11**:399–402.
474. NG BA, MAMIKOGLU B, AHMED MS, COREY JP. The effect of external nasal dilators as measured by acoustic rhinometry. *Ear Nose Throat J* 1998;**77**:840–844.
475. NIELSEN H, ORNTOFT S, NIELSEN TG. Change in minimal cross sectional area using the new nasal dilator, 'Airplus'. *Acta Otolaryngol Suppl (Stockh)* 1997;**529**:130–132.
476. PORTUGAL LG, MEHTA RH, SMITH BE, SABNANI JB, MATAVA MJ. Objective assessment of the breathe-right device during exercise in adult males. *Am J Rhinol* 1997;**11**:393–397.
477. GRIFFIN JW, HUNTER G, FERGUSON D, SILLERS MJ. Physiologic effects of an external nasal dilator. *Laryngoscope* 1997;**107**:1235–1238.
478. GRYMER LF, BOSCH C. The nasal septum and the development of the midface. A longitudinal study of a pair of monozygotic twins. *Rhinology* 1997;**35**:6–10.
479. KESAVANATHAN J, SWIFT DL, BASCOM R. Nasal pressure-volume relationships determined with acoustic rhinometry. *J Appl Physiol* 1995;**79**:547–553.
480. LENDERS H, PENTZ S, BRUNNER M, PIRSIG W. Follow-up of patients with inverted papilloma of the nasal cavities: computer tomography, video-endoscopy, acoustic rhinometry? *Rhinology* 1994;**32**:167–172.
481. SEAVER EJ, KARNELL MP, GASPARAITIS A, COREY J. Acoustic rhinometric measurements of changes in velar positioning. *Cleft Palate Craniofac J* 1995;**32**:49–54.
482. PARVEZ L, ERSALA G, NORONHA A. Novel techniques, standardization tools to enhance reliability of acoustic rhinometry measurements. *Rhinol Suppl* 2000;**16**:18–28.
483. HILBERG O, JACKSON AC, SWIFT DL, PEDERSEN OF. Acoustic rhinometry: evaluation of nasal cavity geometry by acoustic reflection. *J Appl Physiol* 1989;**66**:295–303.
484. HILBERG O, JENSEN FT, PEDERSEN OF. Nasal airway geometry: comparison between acoustic reflections and magnetic resonance scanning. *J Appl Physiol* 1993;**75**:2811–2819.
485. HILBERG O, PEDERSEN OF. Acoustic rhinometry: influence of paranasal sinuses. *J Appl Physiol* 1996;**80**:1589–1594.
486. HILBERG O, LYHOLM B, MICHELSEN A, PEDERSEN OF, JACOBSEN O. Acoustic reflections during rhinometry: spatial resolution and sound loss. *J Appl Physiol* 1998;**84**:1030–1039.
487. HILBERG O, GRYMER LF, PEDERSEN OF. Spontaneous variation of the nasal mucosa. *Ann Allergy Asthma Immunol* 1995;**74**:516–521.
488. HILBERG O, GRYMER LF, PEDERSEN OF. Nasal hypersensitivity evaluated by histamine challenge. *Allergy* 1995;**50**:166–173.
489. HILBERG O. Effect of terfenadine and budesonide on nasal symptoms, olfaction and nasal airway patency after allergen challenge. *Allergy* 1995;**50**:683–688.