Development and evaluation of a long-term management system for sleep-related breathing disorders

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Preface

This doctor thesis was written at the Heinz Nixdorf-Chair for Medical Electronics at TU München and is based on scientific research conducted between April 2008 and April 2011.

There are many who have supported me in the course of this work and should be mentioned. I would especially like to thank my supervisor Prof. Dr. Bernhard Wolf for supporting the development of the system at his chair, and Johannes Clauss and Hans-Georg Gruber for their guidance, support, and motivation along the way. I am also grateful to Sven Becker, Martin Sattler, and my other colleagues and co-workers at the chair for their tips and for creating an encouraging working atmosphere. And of course, the students Kira Rekovets, Christian Herber, and Weiling Wu, who contributed to the development of the appliance with creative ideas and helpful input.

The help and guidance from sleep physicians and dentists were also essential: Dr. Markus Frantz, Dr. Jürgen Langenan, and Dr. Maximilian Bauer deserve a lot of credit for providing input from a medical point of view and enabling important testing and clinical trials during course of the developing the new technology.

The research conducted would not have been possible without the financial support of Bund der Freunde e.V. I am therefore truly grateful for the 1-year PhD scholarship grant which enabled the initiation of this doctoral work.

The help and support from friends and family have been of great importance, especially from my wife Viviane and my parents.

Munich, May 2011            Dan Anker Hofsøy
Abstract

Snoring disturbs the sleep of millions every night. Heavy snoring is also an indicator for obstructive sleep apnea (OSA), and up to 80% of OSA patients are yet to be diagnosed. Even after a correct diagnosis, a lack of motivation can lead to discontinuation of therapy – especially in snorers and patients with a mild to moderate degree of OSA. More than half of these are so-called positional patients, meaning that they experience snoring and OSA events predominately in the supine position.

In this thesis, an innovative long-term monitoring system for these sleep-related breathing disorders with an integrated positional biofeedback therapy was developed and evaluated. By simply using an accelerometer attached to a headband or in a tooth splint we were able to detect important parameters such as snoring, breathing movement, and sleeping position, as thoroughly verified in this thesis.

The automatic detection of snoring and respiratory disturbances developed in Matlab was tested in a clinical trial: simultaneous measurements with headband and polysomnography (PSG) were conducted on seven patients at a sleep clinic. The results proved that detection of snoring and an indication of the severity of obstructions is possible using an automatic detection system. In addition, it was demonstrated that an envelope of snoring and breathing signals with very low sampling frequencies can be created using a microcontroller with real-time signal processing. In this way, snoring and OSA detection could potentially be achieved with a microcontroller directly, or the data could be transmitted wirelessly to further reduce the size of both hardware and data amount to be processed.

Long-term monitoring of snoring therapy was tested on a snoring patient on multiple nights with and without therapy. A very good approximation of snoring duration was possible with the headband in comparison to the PSG recording, and confirmed a reduction in snoring when using therapy.

A vibration alarm as biofeedback signal was integrated to enable intelligent positional therapy. Experiments on participants also confirmed that when applied with the vibration motor the biofeedback signal can prevent them from sleeping in the supine position without disturbing their sleep.

The work in this thesis has established a basis for reliable and comfortable initial multiple-night screening, as well as regular, on-going follow-ups at home. Those identified as positional patients can initially try the integrated biofeedback therapy as an alternative to, or in conjunction with, CPAP or an oral appliance. In this way, an objective monitoring of positional therapy, but also weight loss, oral appliances, and other therapy approaches, can be undertaken in order to help motivate patients and regularly report on therapy efficiency.
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1 Introduction

“A person awakes from sleep when digestion is complete”
- Aristotle; first known scientific theory of sleep (350 B.C) [1]

1.1 Motivation

Even though we spend a third of our lives sleeping, it was first in the second half of the 19th century that scientists started to investigate this apparent inactive and passive state of body and mind through experiments. However, with the lack of technical advances it was only possible to observe the apparent behavior of the sleeper. In 1863 Köhlerschütter tried to use acoustic signals to find variations in sleep levels throughout the night. The first breakthrough in sleep science came in 1929 with the publication of electroencephalography (EEG) by the psychiatrist Hans Berger [2]. This enabled the measurement of the brain’s electrical activity through electrodes attached to the skin, and led to the first classification of different sleep stages by Loomis in 1937 [3]. In 1968, criteria for the classification of sleep stages based on EEG, EOG (electrooculography), and EMG (electromyography) was published. At first, these were only applicable to healthy humans and not to those with the many sleep disorders discovered at that time and in the following years [4].

One of these sleep disturbances was the obstructive sleep apnea (OSA), which was reported for the first time in medical literature in 1965 [5]. Charles Sidney Burwell first brought attention to this dysfunction when he considered the association of obesity and sleepiness in 1956. He named it “Pickwickian syndrome”, since the symptoms had already been described in the Charles Dickens’ novel The Pickwick Paper (1837). This novel describes a very fat boy who constantly falls asleep in the middle of tasks [6]. This is common in OSA patients because their sleep is constantly disturbed by obstructed breathing. They are therefore three to seven times more likely to be in a serious car crash involving personal injury [7, 8]. Pickwickian syndrome is today known as obesity hypoventilation syndrome, an advanced form of OSA when the patients are severely obese.

At Dickens’s time the average was 9 hours of sleep every night, which over the decades has been greatly reduced. Now, the average German goes to bed at 23:04, lies awake 15 minutes and then sleeps until 06:18 – which means roughly 7 hours of sleep every day [9]. The reason for this dramatic change is not because the human being needs less sleep nowadays, but rather the increasing demands from the industrial society leading to a hectic lifestyle [10]. Through sleep deprivation experiments it has been demonstrated that the human being needs six hours of sleep to function properly, if this continues the average will soon reach this limit [11].

On top of that, about 25 percent of the German population complain of sleep disturbances, and more than 10 percent, often or always, have trouble getting a good night’s sleep. Most sleep disturbances, like insomnia, can be effectively identified without any measurement
equipment by simply questioning the patients and testing for potential psychiatric or organic
diseases. The rest have to be diagnosed with polysomnography (PSG) in a sleep laboratory.
The number of official sleep laboratories in Germany has risen from 10 to almost 300 over
the last 25 years, but still, there are only about 12 beds per million inhabitants available [12].

A visit to a sleep laboratory is expensive and requires trained personnel to attend the
patients and then analyze eight hours of complex physiologic data from each night. It is also
inconvenient for the patients to spend the night in a sleep laboratory with cables attached
all over their bodies, which often leads to unwanted “first-night” effects [13]. Unnecessary
visits should therefore be avoided.

Approximately 80 percent of sleep laboratory visits are in relation to obstructive sleep apnea
[14], a condition which causes repeated breathing pauses longer than 10 seconds followed
by abrupt awakenings. Still, 70 – 80 percent of OSA patients are not even aware of their
condition and are yet to be diagnosed [13]. Although snoring is not classified as a medical
condition, regular and especially loud snoring is considered a precursor to obstructive sleep
apnea [15] and can disturb the sleep of both the sleeping partner as well as the snorer
themself. Snoring and OSA increases with age and weight – extra fat increases the narrowing
of the upper airway, while the stabilization of muscle tissue decreases with age. With a
demographic change and a constant increase in the number of obese, not just in western
countries [16], these conditions are worldwide increasing: As early as 2003 WHO reported
that more than 1 billion adults are overweight, and more than 300 million, obese [17].

If OSA syndrome is diagnosed, a CPAP (continuous positive airway pressure) machine is
prescribed in most cases. This means sleeping with a breathing mask every night, which only
has a high compliance by those with severe OSA [18]. Those with milder OSA or heavy
snoring can alternatively be referred to a dentist in order to receive a tooth splint, a so-
called mandibular retaining appliance (MRA) that pushes the mandible forward and thereby
increases the airway and reduces the incident of snoring and OSA.

A problem related to therapy of sleep-related breathing disorders is the low possibility of
measuring compliance and efficiency [19]. Now, CPAP machines have this possibility, but
alternative therapies like tooth splints or the avoidance of certain sleeping positions can only
be evaluated by single-night follow-ups using PSG.
1 Introduction

1.2 Objective

The purpose of this thesis is therefore to analyze the current state-of-the-art techniques, then propose and evaluate an efficient and convenient appliance in order to provide long-term monitoring and follow-up of both diagnosis and therapy of sleep-related breathing disorders.

Figure 1.1: Traditional polysomnography in a sleep laboratory

Current home monitoring systems have multiple sensors and hence multiple cables attached to the patient which are awkward and difficult for the patient himself to deal with correctly, and are therefore not suitable for long-term monitoring. A wireless alternative shall therefore be proposed and evaluated. In short, three important aspects are to be evaluated:

- **Detection of sleep-related breathing disorders**: Patients who snore also potentially have obstructive sleep apnea, but are often undiagnosed. The ability to perform initial screening in snorers and indicate the level of disease is therefore important and part of the objective.
- **Long-term monitoring**: Currently the possibility of regular follow-ups and therapy monitoring is very limited and shall be evaluated.
- **Avoiding the supine sleeping position**: Positional therapy is a simple but effective therapy for positional patients, but available appliances have very low compliance. Therefore, it is important to investigate the integration of an intelligent positional therapy in the long-term monitoring system.

1.3 Overview

Chapter 2 presents the spectrum of sleep-related breathing disorders, followed by an evaluation of current diagnosis and therapy options in chapter 3. Chapter 4 illustrates the development and evaluation of the proposed long-term monitoring and therapy system with a comparison between the results and reference measurements from the sleep laboratory in chapter 5. The discussion in chapter 6 leads to the conclusion in chapter 7 and future prospects in chapter 8.
2 Sleep-related breathing disorders

"Sleep!" said the old gentleman, 'he's always asleep. Goes on errands fast asleep, and snores as he waits at table."

"How very odd!" said Mr. Pickwick.

- Charles Dickens in the The Pickwick Papers (1836); first description of symptoms of a sleep-related breathing disorder

2.1 Publications on sleep-related breathing disorders Journals on sleep-related research

Over the past decade, there has been an explosion of information, and hence it has become increasingly difficult to stay up-to-date on all published work. This also applies to the research field of sleep-related breathing disorders. Up to 1992 there was only one journal dedicated to field of sleep research ("Journal of Sleep"; the official publication of a joint venture of the American Academy of Sleep Medicine and the Sleep Research Society, first published in 1978). By 2004, there were more than 10 dedicated sleep journals and at least 16 others that published sleep studies on a regular basis. Today there are at least 30 journals that must be reviewed to keep track of sleep-related science [20, 21].

Robert et al. have made a good illustration of this trend by investigating the growth and distribution of papers on sleep research in journals over time. They found that in the first two years investigated, 1974 and 1984, the numbers of journals and articles remained stable whereas in the last two last investigated, 1994 and 2004, the numbers increased dramatically. The top 20 journals accounted for 20.3 % in 1984, 16.2 % in 1994 and only 11.6 % in 2004, which means that the articles are increasingly scattered. Hence, more journals must be reviewed in order to obtain coverage on sleep-related literature [22].

2.1.2 Journals and publications on sleep-related breathing disorders

As mentioned in the introduction, sleep-related breathing disorders are a relatively new field of science. OSA was not discovered until 1965, and CPAP was used as treatment for the first time in 1981 (Table 2.1). Snoring, on the other hand, has been known for a long time, but was not taken seriously until the dangers of OSA was revealed and loud snoring was recognized as one of the key symptoms [13, 23].
2 Sleep-related breathing disorders

<table>
<thead>
<tr>
<th>Year</th>
<th>Sleep research milestones related to SDB and snoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1956</td>
<td>Burwell et al. describe the Pickwickian syndrome in the first medical description of obesity hypoventilation which lays the groundwork for the discovery of obstructive sleep apnea [24]</td>
</tr>
<tr>
<td>1965</td>
<td>Obstructive sleep apnea (OSA) is discovered and published almost simultaneously by Gastaut and colleagues in France [5] and Jung and Kuhlo in Germany [25]</td>
</tr>
<tr>
<td>1974</td>
<td>The name “polysomnography” is proposed by Holland to describe an overnight sleep study [26]</td>
</tr>
<tr>
<td>1976</td>
<td>Carskadon presents sleep latency as an objective measurement of sleepiness [27]</td>
</tr>
<tr>
<td>1981</td>
<td>Continuous positive airway pressure (CPAP) as OSA treatment is introduced by Sullivan and colleagues [28]</td>
</tr>
<tr>
<td>1991</td>
<td>Epworth Sleepiness Scale to diagnose sleep disorders is developed by Johns [29]</td>
</tr>
<tr>
<td>2008</td>
<td>High mortality risk for untreated sleep-disordered breathing is reported by Young and colleagues [30]</td>
</tr>
<tr>
<td>2010</td>
<td>OSA is associated with increased stroke risk for men according to Redline et al. [31]</td>
</tr>
</tbody>
</table>

Table 2.1: Sleep research timeline with milestones associated with SBD and snoring. Excerpts from overview by American Sleep Medicine Foundation [32]

Since the discovery of OSA, there has been a steady growth in the number of research articles produced, it has become one of the major topics in sleep medicine, and is even currently the most written about topic [33].

This was documented by Lavie et al. in a bibliometric analysis on sleep-related topics. They found 66,343 research articles from 1965 to 2006 related to sleep, from which 15,064 were directly related to sleep-related breathing disorders, that is snoring, sleep apnea, upper airway occlusion or obesity-hypoventilation syndrome. Figure 2.1 shows that it now makes up for almost one-third of sleep-related publications [34].

Figure 2.1: Annual numbers of “sleep” versus “sleep apnea”-related research articles, and percentage of research articles published on sleep apnea-related according to country in the period 1965 to 2006 [34]

This illustrates the turn sleep-related research has taken since the discovery of OSA in 1965; first driven by dream-related, then insomnia-related research and hence dominated by psychiatrics, this field is now becoming increasingly dominated by the expert sleep clinician. Unlike insomnia, which can be self-diagnosed, OSA requires the intervention and interpretation of such an expert because even those who suffer from it are aware of it [35]. This and its status as a public-health problem have fueled an increase in public interest and
provided an impressive amount of research articles and in-depth knowledge across the whole spectrum of sleep-related breathing disorders, which will be presented in the rest of this chapter.

### 2.2 International classification

#### 2.2.1 Classification of sleep disorders

It was not until 1979 that an organized effort for the classification of sleep disorders was published in the “Journal of Sleep” under the title “Diagnostic classification of sleep and arousal”, short DCASD[36]. The classification was further improved and revised by major international sleep societies, which has resulted in the most recent classification from 2005 called “International Classification of Sleep Disorders: Diagnostic and Coding Manual”, short ICSD-2 [37]. ICSD-2 now classifies sleep disorders in eight groups.

![Figure 2.2: Classification of sleep disorders according to the ICSD-2 [37]](image)

#### 2.2.2 Classification of sleep-related breathing disorders

1. Central apnea syndromes
   1.1. Primary central apnea
   1.2. Cheyne–Stokes respiration
   1.3. Periodic respiration of high altitude
   1.4. Central apneas without Cheyne-Stokes respiration secondary to other disorders
   1.5. Central apneas caused by medicine or other substances
   1.6. Primary sleep apnea of newborn

2. Obstructive apnea syndromes
   2.1. Obstructive apnea in adults
   2.2. Obstructive apnea in children

3. Hypoventilation/hypoxemia syndromes associated with sleep
   3.1. Non-obstructive alveolar hypoventilation, idiopathic
   3.2. Congenital central hypoventilation
   3.3. Hypoventilation/hypoxemia secondary to other disorders: lung parenchymal, airway (e.g., COPD), or vascular (e.g., pulmonary hypertension) disorders; neuromuscular disorders; thoracic wall abnormalities; obesity.

4. Undefined/non-specific sleep-related breathing disorders
   Disorders without specific characteristics to allow their classification in any of the previous categories. Further investigation is required.

![Figure 2.3: Classification of sleep-related breathing disorders (SBD) according to the ICSD-2 [37]](image)
Sleep-related breathing disorders (SBD) are currently divided into three main groups shown in Figure 2.3. The central sleep apnea (CSA) syndromes including Cheyne-Stokes-Breathing (CSB) are caused by imbalance in the brain’s respiratory center while sleeping, whereas obstructive sleep apnea syndromes are caused by a narrowing or blockade of the airway. The difference is demonstrated in Figure 2.4; central sleep apnea syndromes cause periodic alterations in airflow and respiratory effort whereas obstructive sleep apnea syndromes cause periodic alterations in airflow while respiratory effort continues. The lack of oxygen is accompanied by a corresponding decrease in blood oxygen saturation in both cases [37].

<table>
<thead>
<tr>
<th>Obstructive apnea</th>
<th>Mixed apnea</th>
<th>Central apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airflow</td>
<td>Airflow</td>
<td>Airflow</td>
</tr>
<tr>
<td>Wake</td>
<td>Sleep</td>
<td>Sleep</td>
</tr>
<tr>
<td>Obstructive apnea is characterized by complete (apneic) or partial (hyponaptic) obstruction of the upper airway lasting more than 10 seconds. Evidence of respiratory effort during respiratory events.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed apnea is characterized by a mixture of central and obstructive apnea; the apnea begins as a central apnea without respiratory effort, but towards the end of the respiratory event there is an effort to breath without airflow.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central apnea is characterized by cessation of airflow lasting more than 10 seconds without any obstruction and hence no respiratory effort. Cheyne-Stokes is similar, but with a crescendo-decrescendo pattern of breathing.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hypopnea is a reduction in airflow or respiratory effort. It has no official definition, but is normally set to a 30% reduction in airflow or respiratory effort for more than 10 seconds together with a 4% or more blood oxygen desaturation.

Figure 2.4: Demonstration of the differences between obstructive and central sleep apnea, as well as mixed apnea and hypopnea. Adapted from Bailey et al. [38]. Definitions from ICSD-2 [37].

The last group, hypoventilation (decreased respiration) and hypoxemia (decreased partial pressure of blood oxygen) syndromes can be distinguished from central and obstructive sleep apnea syndromes by the length of the events because oxygen desaturation can last several minutes or longer [37]. This could for example be caused by extreme obesity (obesity-hypoventilation syndrome, formerly known as Pickwickian syndrome) or COPD (chronic obstructive pulmonary disease), which has a worsening effect on gas exchange during sleep.

In this thesis, the differentiation between these three groups of sleep-related breathing disorders will be important. For this reason the exact definition of the relevant diseases in these groups are listed in Table 2.2 together with the definition of primary snoring (also known as habitual snoring), which is currently listed under “Isolated symptoms, apparently normal variants and unresolved issues” in the ICSD-2 [37].
2 Sleep-related breathing disorders

Table 2.2: Classification of primary snoring, central sleep apnea, obstructive sleep apnea and obesity-hypoventilation syndrome according to ICSD-2 [37]
2.3 The spectrum of obstructive sleep-related breathing disorders

Snoring is not listed as a sleep-related breathing disorder in the ICSD-2 classification, even though it is established as a precursor to OSA [23] and also one of the main symptoms of the obstructive sleep-related breathing disorders [13].

Hence, the normal perception of the obstructive part of the sleep-related breathing that has been established in literature is shown in Figure 2.5; starting with normal breathing without obstruction, the level of disease goes from snoring via increased airway resistance to obstructive sleep apnea and ending at obesity-hypventilation syndrome [39-43]. Central sleep apnea is not caused by obstructions and is therefore left out of the obstructive branch of SBD, which will be the focus in this thesis.

![Figure 2.5: Simplified spectrum of (obstructive) sleep-related breathing disorders [39-43]](image)

The level of disease can go up and down depending on a number of factors and even change from night to night [39]. These factors like weight gain and sleeping position will be thoroughly described in chapter 2.4, whilst the anatomical influence on the different stages of the disease will be explained in the following pages.

2.3.1 Normal airway during sleep

The upper airway is a complex structure whose purpose is to transport air from the nose to the lungs. At the same time it participates in other physiological functions such as the production of sound (phonation) and swallowing (deglutition). Hence, there is a complicated system of muscles at work in order to provide all functions, for example to ensure that the airway stays open during breathing and closed during swallowing.

![Figure 2.6: Anatomy of the upper airway (left) and muscles supporting the upper airway (right). From Benumof et al. [44]](image)
The upper airway in relation to sleep is usually divided into three anatomical subsegments:

- The **nasopharynx** is the segment between the nares and the hard palate, i.e. the passage to the nose. The **velopharynx** (or retropalatal oropharynx) is the next segment between the hard palate and the soft palate, but is often included in the definition of nasopharynx when related to sleep.
- The **oropharynx** is the oral part of the airway (visible when the mouth is open) from the soft palate to the epiglottis, followed by
- The **laryngopharynx** or **hypopharynx** is the segment from the base of the tongue to the larynx [44, 45].

There are more than 20 muscles supporting the upper airway, which can be divided in four groups; namely, muscles regulating:

- the **position of the soft palate** (levator palatine, tensor palatine),
- the **tongue** (genioglossus),
- the **hyoid apparatus** (geniohyoid) and
- the **posterolateral pharyngeal walls**.

These muscles are precisely controlled in order to maintain an open airway during wakefulness. During sleep there are other forces at work such as gravity, which pushes the tongue and soft tissue structures backwards so that the oropharyngeal area is reduced, especially when sleeping in the supine sleeping position. Still, the muscles are able to maintain an open airway under normal conditions [44].

### 2.3.2 Snoring

A common consequence of the changes of the upper airway that occur during sleep is the sound of snoring, resulting from the vibrations of soft tissues of the soft palate, pharynx and uvula. The origin of snoring is hence in the oral part of the airway: the oropharynx [46]. One of the first investigations made by Lugaresi et al. demonstrated that snoring is associated with increased esophageal pressure swings during inspiration with partial pharyngeal obstruction [47]. Subsequent studies have shown that snorers have increased pulmonary resistance, negative inspiratory pressure and flow limitation in comparison to non-snorers. However, these are all considered to be normal consequences of sleep; snoring is therefore not considered to be a disease [45]. However, the fact that the increased airway resistance lies between normal and obstructive breathing has led to snoring being considered as part of the spectrum of sleep-related breathing disorders, as seen in Figure 2.5 on page 9.

#### 2.3.2.1 The sound of snoring

The sound of snoring is produced, similarly to speech, in the vocal tract. An objective assessment of snoring is difficult. In most cases, it is reported by the bed partner which is simply a subjective assessment based on his or her sensitivity to the snoring sound [48]. Although there is no exact definition, there have been some approaches to classify snoring sound objectively. Pevernagie et al. used the analogy of speech and applied speech analysis in order to evaluate snoring events. The found the pitch of the snoring sound to be in the
lower-frequency range of below 500 Hz consisting of a fundamental frequency with associated harmonics.

![Figure 2.7: Vibrations of the vocal cords. From Pevernagie et al. [49]](image)

According to their model in Figure 2.7, starting with a fundamental frequency $F_0$, the vibration of the vocal folds produces a varying airflow producing a spectrum of equally-spaced frequency peaks (i.e. harmonics) that correspond to a periodic signal (A).

This periodic source signal is input to the vocal tract which can be seen as a variable filter (B). It is variable according to frequency, and its response depends on such factors as the position of the tongue and jaw. The resonance peaks $R_1$ and $R_2$ add gain to the frequencies of the harmonic spectrum.

The sound output (C) is a result of A and B together with the radiation properties of the mouth and face. From the sound output spectrum it is possible to determine the resonance peaks $R_1$ and $R_2$ approximately, which are then called formants ($F_1$ and $F_2$) [49].

Fiz et al. conducted a spectral analysis on seven simple snorers (without respiratory disturbances) and 10 OSA patients and found the acoustic characteristics of snoring to be different in simple snorers and OSA patients. A pattern corresponding to the model from Pervenagie et al., described above, was found in all of the simple snorers and in two of the OSA patients; the pattern was characterized by a fundamental frequency followed by several harmonics as displayed in Figure 2.8 (left) [50].

![Figure 2.8: Snoring signal from a snorer (a) and an OSA patient (c) with corresponding power spectrum (b and d) in arbitrary units (au). From Fiz et al. [50]](image)
In the rest of the OSA patients, they found another power spectrum pattern characterized by a low frequency peak with sound energy spread on a narrower band of frequencies without any considerable harmonics (Figure 2.8 right). The peak frequency in OSA patients (157 ± 136 Hz) was also significantly lower than in the simple snorers (264 ± 107 Hz). The mean and max frequency were 325 ± 58 Hz and 462 ± 85 Hz in snorers, and 223 ± 147 Hz and 455 ± 199 Hz in OSA patients [50].

2.3.2.2 The annoyance of snoring
Even though there is no objective definition of the snoring sound, it is easily recognizable and when exposed to this sound the normal subjective sensation is annoyance. Dreher et al. investigated the annoyance of snoring by presenting 550 snoring sequences from 11 snorers to ten examiners for the evaluation of their annoyance (from 0 to 100). The average rating of all sequences was 63.9 ± 23. The most acceptable snoring sequence rating was 49.2 ± 28.0 and the most annoying 77.7 ± 16.4, revealing that the listeners noise sensitivity is at least equally relevant for the snoring annoyance as the sound of snoring itself [48].

2.3.3 Upper airway resistance syndrome
Upper airway resistance syndrome (UARS) is a mild form of sleep-related breathing disorder, located on the scale between snoring and obstructive sleep apnea. UARS was not thoroughly described and defined until 1993 by Guilleminault et al [51]. Since then, whether it should be classified as an independent disease or as a part of OSA [52, 53] has been discussed. However, UARS is also called “obstructive snoring” or “heavy snorer’s disease”, which emphasizes the problem of a correct definition of UARS in the transition region between primary snoring and OSA [54].

Hence, UARS does not have a separate classification in the ICSD-2 as OSA does (Table 2.2), but a description of how to distinguish it from OSA is provided: like snoring it is characterized by increased respiratory effort and snoring sound – but in addition, although not accompanied by blood oxygen desaturation like in the case of apneas or hypopneas [37], these are accompanied by arousals (brief change of sleep state). Arousals associated with UARS are called respiratory effort related arousals (RERAs). The definition developed by Guilleminault can be seen in Table 2.3. In other words, a UARS patient has only RERAs but an OSA patient can also have RERAs in addition to apneas and hypopneas [37].

<table>
<thead>
<tr>
<th>Upper airway resistance syndrome (UARS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. An apnea-hypopnea index (AHI) ≤ 5.</td>
</tr>
<tr>
<td>B. A nadir of SpO2 ≥ 92%.</td>
</tr>
<tr>
<td>C. The occurrence of episodes of nasal cannula flow limitation.</td>
</tr>
<tr>
<td>D. At least one of a collection of symptoms that include fatigue, excessive daytime sleepiness (EDS), sleep fragmentation, insomnia, “pseudofibromialgia”, parasomnia, morning headache, and parasympathetic manifestation.</td>
</tr>
</tbody>
</table>

Table 2.3: Classification of upper airway resistance syndrome according to Bao & Guilleminault [55]
2.3.4 Obstructive sleep apnea

Obstructive sleep apnea (OSA) is triggered by an imbalance in the forces at work in the upper airway during sleep favoring an airway collapse. This could be caused by anatomical abnormalities in soft tissue or skeletal morphology [56]. In addition there are a number of other factors which promote an airway collapse which will be discussed in the next section.

Figure 2.9: Anatomical features promoting abnormal breathing in the night. From Fairbanks et al. [57]

OSA is thus characterized by recurring episodes of obstruction of the upper airway, caused by this imbalance of forces; the negative airway pressure generated by diaphragmatic contraction during inspiration exceeds the force produced by the upper airway dilating muscles, which are activated 100-200 ms ahead of inspiration in order to keep the airway open and stable [58]. This could be compared to what happens when trying to suck air from an empty balloon.

Since narrowing of the upper airway requires an increase in upper airway dilator muscle contraction to maintain an open airway, it has been proven that OSA patients have a more forceful contraction of these muscles during wakefulness, but a larger decrease during sleep, than normal subjects [59]. This could be caused by the sustained increase in dilator muscle contraction leading to a fatigue of these muscles and thus cause an increased tendency of obstruction [58].

Figure 2.10: Forces with influence on upper airway collapsibility. From Malhorta et al. [60]

An obstruction is terminated by an arousal, which is a response to the blocked airway and the lack of oxygen. It leads to a shift from a deeper sleep stage to a lighter sleep stage, sometimes even complete awakening, depending on the degree of obstruction. These recurrent changes in sleep stage lead to sleep fragmentation, a major factor in daytime sleepiness. In addition, it can also intensify the OSA since the arousal is normally followed by hyperventilation causing a fall in partial pressure of carbon dioxide in the blood (PaCO₂) and hence also reduced respiratory drive, which can lead to further apneas [58]. All in all, it creates a “vicious cycle”, as seen in Figure 2.11, induced by upper airway narrowing.
influencing the upper airway dilating muscle activity and causing airway obstructions, which triggers arousals and maintains the pattern again and again.

Figure 2.11: Schematic diagram of the forces with influence on upper airway collapsibility. Adapted from McNicholas et al. [58]

2.3.5 Obesity-hypoventilation syndrome

Obesity-hypoventilation syndrome (OHS) was previously known as Pickwickian syndrome and discovered long before obstructive sleep apnea as the symptoms are more obvious; the patients are obese with a body mass index (BMI) > 30 and hypercapnia occurs (PaCO\(_2\) > 45 mmHg) even when awake. In other words, it is a combination of obesity and inadequate ventilation leading to a high concentration of carbon dioxide in the blood, known as hypercapnia and low oxygen concentration in the blood known as hypoxia.

Figure 2.12: The vicious cycle of OHS as described by Olson et al. [61]

There is a strong link between OSA and OHS, which is explained in Figure 2.12 by Olson et al. where 10 to 20 % of OSA patients develop obesity-hypoventilation syndrome [62]: it is believed that OSA, which starts the vicious cycle, triggers depressed ventilator response and hypoventilation. This chronic exposure to hypoxemia and sleep fragmentation may lead to decreased ventilatory drive and hypoventilation. The decreased ventilatory drive, together
with the weaker lung capacity caused by obesity, could prevent a restoration of normal blood gas levels after apneic events in the night, leading to even more severe hypoxemia and hypercapnia and decreased ventilatory response [61]. The severity of hypercapnia has been correlated with the degree of sleep-induced respiratory abnormalities, mechanical impairment of the respiratory system, and the degree of daytime hypoxemia [61, 63].

In other words, those with obesity-hypoventilation syndrome lack a ventilatory response after apneic events, causing hypoxemia and hypercapnia to continue until the next apneic event, and hence over longer periods of time in the night, whereas those with normal obstructive sleep apnea are able to restore gas levels in the blood after apnea events. OHS is therefore also sometimes called *hypercapnic OSA*.

### 2.4 Prevalence and risk factors

It is extremely difficult to provide correct statistics for obstructive sleep-related breathing disorders. Snoring does not have an exact definition and there is no standardized method of objective assessment [64], UARS does not yet have an official separate definition according to ICSD-2 and, as mentioned in the introduction, for OSA, 70 – 80 % of suffers are not even aware that they have the disease. Also, as we will see in this section, there are a number of important risk factors influencing the prevalence in a given population.

**Snoring**

For primary snoring, one of the most extensive and most cited articles was written by Lugaresi et al., who did a population-based investigation in 1980 with 5713 people and found 19 % to be primary snorers: 24.1 % of the male and 13.8 % of the female population [65].

**UARS**

Bettencourt et al. recently conducted the first population-bases study in order to determine the prevalence of UARS. In their study they compared the prevalence of OSA and UARS in a population sample of 1042 volunteers in the city of São Paulo, Brazil. The prevalence of UARS in the population sample was 18.75 %. The prevalence was surprisingly higher in women than men, with 21.8 % and 15.2 % respectively. In comparison they reported the prevalence of OSA to be 40.6 % in men and 26.0 % in women [66, 67].

**Obstructive sleep apnea**

Young et al. studied a random sample of 602 employed men and women in 1993 to find the prevalence of OSA, and found that as much as 24 % of men and 9 % of women had a AHI > 5 (apnea-hypopnea index of more than five apneas/hypopneas per hour). From this they estimated that a minimum of 4 % of men and 2 % of women meet the minimum criteria for an obstructive sleep apnea/hypopnea syndrome (OSAHS). OSAHS is the official term for those with AHI > 5 and daytime sleepiness. Those without daytime sleepiness but with AHI > 5 are said to have obstructive sleep apnea/hypopnea (OSAH) and according to Young et al., it is found in 20 % of men and 7 % of women [68]. The quality of the research by Young et al.
has actually made it the most cited research article in the field of OSA [34], and the numbers have been confirmed by further studies [13].

Young et al. also found male sex and obesity to be strongly associated with sleep-disordered breathing, and also that primary snorers tended to have a higher prevalence of AHI > 15 [68]. These and other risk factors commonly mentioned in research articles are summarized in Table 2.4.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Magnitude</th>
<th>Possible mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>+++</td>
<td>Anatomy, vent control stability</td>
</tr>
<tr>
<td>Male sex</td>
<td>++</td>
<td>Anatomy, vent control</td>
</tr>
<tr>
<td>Aging</td>
<td>++</td>
<td>Anatomy, neural reflex impairment</td>
</tr>
<tr>
<td>Alcohol/Medications</td>
<td>++</td>
<td>Impaired dilator muscle activity</td>
</tr>
<tr>
<td>Menopausal status</td>
<td>+</td>
<td>Unknown, possibly anatomy</td>
</tr>
<tr>
<td>Smoking</td>
<td>+</td>
<td>Airway inflammation, edema or both</td>
</tr>
</tbody>
</table>

Table 2.4: Risk factors with possible mechanisms and effect on OSA. Adapted from Malhotra et al. [60]

2.4.1 Aging

In Figure 2.13 are the results from the population-based investigation by Lugaresi et al., where the percentage of primary (also known as habitual) snorers according to age is shown. It can be seen that about 10% of men and less than 5% of women up to the age of 30 years old are primary snorers. On the other hand, in the age group 60 – 65 years old the numbers are roughly 60% for men and 40% for women [65].

Figure 2.13: Primary snoring increases dramatically with age. Adapted from Lugaresi et al. [65]

For OSAHS there is a similar pattern. The prevalence increases with age up to 60 years old where it reaches a plateau, as reported by Bixler et al. [69]. It has been proposed that this age-related increase is caused by advanced deposition of fat in the pharyngeal area, lengthening of the soft palate changes in the structures supporting the pharynx [70]. This results in an age-related increase in pharyngeal resistance and collapsibility which is independent of gender [70] and body mass index [69, 70], and which promotes both snoring and obstructive sleep apnea.
In a retrospective chart review analysis by Shepertycky et al. of 130 men (48 ± 1.1 years old) and 130 women (47.6 ± 1.0 years old) diagnosed with OSA, they found that in men, primary snoring began on average at the age of 34, witnessed apneas without sleepiness (OSAH) at age 39 and apneas with daytime sleepiness (OSAHS) at age 41. In women, snoring began at age 36, witnessed apneas at age 42 and daytime sleepiness at the age 43 [71].

For UARS, there is a different pattern. From the study in Sao Paulo, Brazil, they found the general prevalence to be 18.75% [66], but it showed a decrease in prevalence according to age [67]. In women, UARS also decreased with an increase in weight [66], which would implicate that UARS has developed into a form of OSA in these individuals. Bao et al. has also implicated that unrecognized UARS and the associated anatomical abnormalities will lead to complications and potentially develop into OSAHS with time [55].

### 2.4.2 Male sex

From the studies by Lugasresi et al. and Young et al. it can be estimated that the male to female ratio for both primary snoring and sleep apnea is at least 2 to 1. Young et al. also found women with sleep apnea to have lower AHI index than men in general [68], so there is no doubt that there is a male predisposition for sleep-related breathing disorders. The reason is a gender-specific difference in anatomical and functional properties of the upper airway, as well as differences in craniofacial morphology and fat disposition around the upper airway [72]. An exception is UARS, which has a male to female ratio of about 1:1 [51, 55].

#### 2.4.2.1 Upper airway differences

The effect of retrusive mandibular movement on mean pharyngeal (Pharynx) and oropharyngeal junction (OPJ) cross-sectional areas has been investigated by Mohsenin et al.
and supports the gender-specific difference in anatomical and functional properties of the upper airway; retrusive (i.e. backward) mandibular movement resulted in a significant narrowing of upper airway in men but not women as seen in Figure 2.16 [73].

![Figure 2.16: Retrusive mandibular movement as caused by gravity effects when sleeping in the supine position changes the upper airway cross-sectional area, causing a narrowing in men but not in women according to Mohsenin et al. [73]](image)

This could also explain the results from Itasaka et al., who measured snoring intensity in the supine position at 50 cm in front of the mouth on 73 patients with snoring or OSA. They found that the mean intensity was 61.7 dB in the supine position, but most of the women had a lower snoring intensity. Another finding was that the amplitude of the intra-esophageal pressure which increases with a narrower airway increased linear with snoring intensity [74].

### 2.4.2.2 Differences in symptoms

In general, more women than men remain undiagnosed with OSA. As mentioned, women tend to have less apnea events than men. Still, according to a study by Jordan et al., symptoms of snoring and breathing pauses have higher specificity for OSA in women than men [72].

Unfortunately, women with the same severity of OSA as male subjects reported witnessed apneas less frequently with an odds ratio 0.66. Only 55 % of the female subjects knew about witnessed apneas, whereas 70 % of the male subjects were aware of it. An explanation could be that women with male bed partners are more sensitive and observant to disruptive behavior and breathing problems than men are to their female bed partner [71]. Also, the snoring intensity is lower in female subjects than male subjects [74].

Instead, women with OSA report insomnia as the main symptom (odds ratio 4.20) and are more likely to have a history of depression (odds ratio 4.60) and hypothyroid disease (odds ratio 5.60) [71]. They also complain more frequently about difficulty initiating sleep, fatigue, and headache [72]. Altogether this leads to a higher likeliness for women to be treated for other conditions such as depression or insomnia and to be excluded from OSA treatment [71, 72].
2.4.3 Post-menopause and pregnancy in women

Even though women are less likely to develop sleep-related breathing disorders, there are two exceptions which have a significant impact.

2.4.3.1 Pregnancy

Pregnancy, especially during the third trimester, is associated with a higher prevalence of OSA and snoring. In a study by Iczi et al., they found 41% of pregnant women in the third trimester snore compared to 17% in a comparable non-pregnant group of women. After delivery, snoring returned to nonpregnant levels [75]. This can be explained by weight gain, decrease in pharyngeal size and alterations in pulmonary physiology during pregnancy [72, 76]. This should be taken seriously, since OSA during pregnancy could lead to intrauterine growth retardation, preeclampsia and lower birth weight [77].

2.4.3.2 Post-menopause

Several studies have proven that sleep disordered breathing is more common in post-menopausal women than in pre-menopausal women [78], and hence the onset of menopause is now considered to be a turning point in the prevalence of OSA in women [79].

Bixler et al. determined in a study that post-menopausal women with hormone replacement therapy (HRT) did not have a higher risk of OSA than pre-menopausal women, whereas those without HRT had an almost four-fold risk of OSA [80]. Young et al. came to the same conclusion, with a 3.5-fold risk to have AHI > 15. The results were not subject to influence from age difference or BMI distribution [81]. This indicates that menopause is an independent risk factor for the development of SBD.

The most likely hypothesis to explain this risk factor is that male and female hormones affect the distribution of body fat, which is important for the development of SBD. In men, there is a higher fat deposition around the neck which promotes development. In pre-menopausal women, fat deposition tends to be gynoid (lower body) whereas in post-menopausal women fat deposition tends to be android (upper body and trunk). In addition, the number of years since menopause is a significant predictor for the increase in android fat deposition and BMI as opposed to age [82]. This means that women tend to acquire a male body fat distribution after menopause, which is a risk factor for the development of SBD and especially OSA.

The change in menopausal status is also a turning point for women with UARS; Stoohs et al. reported in their retrospect study that post-menopausal women were presented significantly less frequently with UARS than pre-menopausal women. The odds ratio for a diagnosis of OSAH versus UARS was 5.5 compared to pre-menopausal women. In other words, UARS is more common in pre-menopausal women and decreases with age, whereas OSAH increases and is more common in post-menopausal women, without the influence from BMI [83]. This also supports the hypothesis of hormone and fat distribution influence on the severity and development of SBD.
2.4.4 Supine sleeping position

More than half of snorers and OSA patients predominantly experience snoring and obstructions in the supine position (i.e. they have at least twice as many occurrence of snoring or obstructions when sleeping on their back) and are therefore called *positional patients* [15, 84].

Nakano et al. found the positional dependency of apnea-hypopnea index (AHI) in 76% of the subjects in a snorer group and 49% in an apneic group. They defined the snorer group to be those with AHI < 15 and the apneic group to those with AHI > 15. So in other words, snorers and those with mild OSA (AHI < 15) are more likely to have apneic events in the supine position [15].

For snoring, they found a significant difference between supine and lateral sleeping positions for both snoring duration and intensity in the snorer group, but less in the apneic (Figure 2.18) [15].

Oksenberg et al. conducted a retrospective study on 574 OSA patients with RDI > 10 and BMI > 20 and found 55.9% to be positional patients. Apnea index, RDI and BMI were significantly higher in the non-positional patients. On average, the non-positional patients were 6.5 kg heavier than the positional patients. Hence, a typical positional OSA patient is young and thin with mild to moderate OSA severity whereas an obese, older OSA patient with severe OSA is much less likely to be a positional patient [85].

---

**Figure 2.17**: Example of a positional OSA patient – frequent blood oxygen ($\text{SaO}_2$) desaturations only when sleeping in the supine position (i.e. sleeping on the back). Adapted from Oksenberg et al. [84]

**Figure 2.18**: Snoring time in percent for each sleep stage in lateral compared to supine sleeping position (left). Change in snoring time between lateral and supine sleeping position in snorer group and apneic group (right). Adapted from Nakano et al. [15].
The effect of sleeping position has also significant gender differences. This has been proven in the case of OSA by Mohsenin et al.; men had a decrease in RDI (Respiratory Disturbance Index; number of apneas, hypopneas and RERAs per hour) of 63% in a non-supine sleeping position compared to the supine position, but women only had a 30% decrease [73].

2.4.5 Obesity

The average BMI according to age in Germany is shown in Figure 2.19, which interestingly correlates well with snoring according to age in Figure 2.13, for both men and women. BMI increases steadily with age for men up to 55 years old and for women up to 66 years old, and then starts to fall. The fall can be explained by the negative effect by BMI on general health and life expectancy [17].

Berger et al. investigated the role of increasing weight and age on snoring and OSA. The main finding in their study was that the outcome of untreated primary snorers and OSA patients in the adult male study population is dependent mainly on weight increase and, to a lesser degree, on age. A significant increase in AHl and BMI over time was shown in the participating males with primary snoring and mild to moderate OSA. Interestingly, patients with severe OSA had a non-significant decrease in AHl, suggesting a ceiling effect for OSA severity [86].

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A close link between obesity and SBD has been known for long time – as mentioned with “Fat Joe” from the Charles Dickens’ novel “The Pickwick Papers” (1836) in the introduction. In a Swedish study with 3034 participants with BMI over 35, more than half of the men and one third of the women reported having snoring and apnea, but only 15.5 % of men in the same age group were self-reported primary snorers [88]. Tufik et al. also identified a very high correlation between obesity and OSAHS [87] seen in Figure 2.20. Coughlin et al. even correlated the whole spectrum of SBD according to severity with increasing weight [40]. Hence a weight gain contributes to a worsening of the SDB [40] due to a higher fat deposition around the neck. It is therefore expected that sleep-related breathing disorders will increase in the following years, considering the demographic change in the world and the obesity epidemic not just in western countries, also seen in Figure 2.20 [16].

2.5 Associated diseases and medical conditions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Primary snoring</th>
<th>UARS</th>
<th>OSAH</th>
<th>OSAHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48.7 ± 11.8</td>
<td>45.3 ± 12.3</td>
<td>53.0 ± 12.3</td>
<td>51.5 ± 11.7</td>
</tr>
<tr>
<td>BMI</td>
<td>26.1 ± 3.3</td>
<td>26.2 ± 4.3</td>
<td>28.7 ± 4.6</td>
<td>29.2 ± 5.2</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>5.6 ± 3.4</td>
<td>8.7 ± 4.9</td>
<td>5.9 ± 3.3</td>
<td>9.9 ± 4.9</td>
</tr>
<tr>
<td>Female/male ratio</td>
<td>15.9 %</td>
<td>28.8 %</td>
<td>8.9 %</td>
<td>11.2 %</td>
</tr>
<tr>
<td>History of snoring</td>
<td>11.0 ± 9.0</td>
<td>10.4 ± 8.7</td>
<td>13.5 ± 10.0</td>
<td>13.2 ± 8.8</td>
</tr>
<tr>
<td>Sleep-maintenance insomnia</td>
<td>17 %</td>
<td>44 %</td>
<td>17 %</td>
<td>43 %</td>
</tr>
<tr>
<td>Non-refreshing sleep</td>
<td>25 %</td>
<td>74 %</td>
<td>34 %</td>
<td>76 %</td>
</tr>
<tr>
<td>Headaches</td>
<td>15 %</td>
<td>34 %</td>
<td>12 %</td>
<td>29 %</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>26 %</td>
<td>21 %</td>
<td>40 %</td>
<td>39 %</td>
</tr>
<tr>
<td>BPsys (mmHg)</td>
<td>121 ± 19</td>
<td>122 ± 19</td>
<td>130 ± 19</td>
<td>129 ± 21</td>
</tr>
<tr>
<td>BPdia (mmHg)</td>
<td>75 ± 11</td>
<td>74 ± 11</td>
<td>77 ± 11</td>
<td>76 ± 12</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>6 %</td>
<td>3 %</td>
<td>7 %</td>
<td>9 %</td>
</tr>
</tbody>
</table>

Table 2.5: Differences in clinical features of primary snoring, UARS (obstructive snoring), OSA without sleepiness (OSAH) and OSA with sleepiness (OSAHS). Adapted from Stoohs et al. [89]
Obstructive sleep-related breathing disorders are associated with a number of diseases and comorbidities, which degree depends on the level of sleep-related breathing disorders. Stooohs et al. conducted a retrospective study of 2753 patients who had been diagnosed with SBD by polysomnography [89]; their findings confirmed that there are clinical differences according to the degree of SBD, which have been listed in Table 2.5. Here it can be seen that non-apneic subjects (RDI ≤ 5) have a shorter history of snoring, a lower BMI and blood pressure than those with apneic sleep-related breathing disorders (RDI ≥ 5).

As mentioned earlier, patients with OSA are divided into two groups; those without daytime sleepiness (OSAH) and those with daytime sleepiness (OSAHS). UARS, which also causes daytime sleepiness, has clinical features strongly related to OSAHS (Table 2.5); sleep-maintenance insomnia, non-refreshing sleep and headaches are all caused by fragmented and disturbed sleep by obstructive arousals.

As for prevalence and risk factors, there are also gender differences in medical conditions in patients with obstructive SBD (Figure 2.21) [71]: Women have a higher risk of depression and metabolic diseases such as hypothyroidism and diabetes associated with OSA than men, while men have a higher risk of cardiac diseases and hypertension.

In general, there are two main classes of problems which intensify with increasing levels of obstructive SBD (Table 2.6). One is the previously mentioned daytime sleepiness which is caused by the obstructive arousals and airway resistance primarily found in UARS and OSAHS patients and the other is cardiovascular risks caused or amplified by recurrent blood oxygen desaturations in the night.

<table>
<thead>
<tr>
<th>Cardiovascular risks</th>
<th>Primary snoring</th>
<th>UARS</th>
<th>Mild OSAHS</th>
<th>Moderate OSAHS</th>
<th>Severe OSAHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual narrowing of the upper airway</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In general, there are two main classes of problems which intensify with increasing levels of obstructive SBD (Table 2.6). One is the previously mentioned daytime sleepiness which is caused by the obstructive arousals and airway resistance primarily found in UARS and OSAHS patients and the other is cardiovascular risks caused or amplified by recurrent blood oxygen desaturations in the night.
2.5.1 Daytime sleepiness

A major concern related to obstructive SBD is the “aftermath” of a night of arousals, apneas and hence non-refreshing sleep: daytime sleepiness. In the study by Strohs et al. (Table 2.5), about 75% of UARS and OSAHS patients, 25% of primary snorers, and 34% of OSAH patients complained about non-refreshing sleep. These are all likely to have excessive daytime sleepiness (EDS), which is defined to be the urge to sleep (sleepiness) in a situation where an individual is expected to be awake and alert [91] – not to be confused with tiredness (exhaustion). EDS should be taken very seriously, since it results in a high rate of traffic and work-related accidents as well as personal and psychological problems.

2.5.1.1 Occupational accidents

A study by Cohen-Zion found a correlation between higher RDI and cognitive decline in OSAHS patients, indicating a link between EDS, SDB and cognitive decline [92]. Another study of men between the ages of 30 and 64 showed that risk ratios for reporting EDS at work were 4-fold for snorers in the general population, 20-fold for snoring patients, and 40-fold for patients with OSA as compared with non-snoring men in the general population. Hence, patients with OSA and snorers both showed increased ratios on measures of difficulties with concentration, learning new tasks, and performing monotonous tasks when compared with non-snorers [93]. A third study revealed that industrial workers with EDS were in most cases also SBD patients and had higher rates of work accidents and less job satisfaction [94].

2.5.1.2 Motor vehicle accidents

A major and serious concern is the higher risk of motor vehicle accidents caused by SBD patients with EDS, since most cases result in injury and death, costing billions in damage each year. Young et al. found that, compared to men without SBD, men with SBD have a significantly higher risk of having at least one car crash in 5 years; the odds ratio is 3.4 for primary snorers, 4.2 for AHI 5 to 15, and 3.4 for AHI higher than 15. For men and women with AHI higher than 15, the odds ratio is 7.3 compared to men and women without SBD [8].

In the USA alone, more than 800 000 drivers were involved in accidents related to OSA in the year 2000, resulting in 1 400 deaths and 15.9 billion dollars in damage. The authors calculated that treating all drivers with OSA would cost 3.18 billion dollars and potentially save 11.1 billion dollars and 980 lives per year [95].

2.5.1.3 Personal and psychological problems (quality of life)

A lower quality of life is common in SBD patients. They often experience moodiness, anxiety, lack of motivation and reduced performance in social function, and this seems to be related to the excessive daytime sleepiness in these patients [96-98]. This means that those with EDS and SBD are especially likely to have a lower quality of life.

A large study of overweight patients also revealed that those with OSAHS symptoms reported poorer perceived health, lower economic income, increased odds of having had psychiatric care, multiple divorces, and lower work performance than the overweight patients without OSAHS symptoms [99].
2.5.1.4 **Influence on bed partner**
The saying “people who snore always fall asleep first” gives a hint of the frustration when sharing a bedroom with a snorer. Considering that a snorer can produce a sound which exceeds 80 dB (equaling road traffic or an aircraft) [100], it is safe to say that the quality of life of the bed partner can be affected as well. In most cases it is the women who suffer, since men snore more often and more loudly than women. Beninati et al. examined ten married couples and found that female bed partners lose an hour of sleep per night due to their heavily snoring spouse [101].

A larger study by Ulfberg et al. included 500 women with spouses who had been referred to a sleep clinic because of loud snoring. It revealed that females living with heavy snorers have substantially greater problems with insomnia, daytime sleepiness and headache than females living with non-snorers. More than 10% of the women scored higher than 10 on the Epworth Sleepiness Scale (ESS), which indicates disturbing sleepiness. A common complaint among these women was excessive daytime sleepiness (EDS) and fatigue leading to substantial difficulties in their daily activities. Hence, most of them experienced great relief from their suffering when their spouses started treatment for snoring. This supports the fact that snoring not only affects the snorer but is also an important issue for couples [102].

This was also confirmed in another study by Smith et al. They compared a group of OSAH wives (husband AHI ≥ 15) to a group of women with a husband without OSAH. Independent of age and menopausal status, the wives of OSAH patients had a significant increase in pain threshold, tiredness and poor sleep quality in comparison to the control group. The OSAH wives were also questioned about their coping strategies – the most prevalent strategy was to simply leave the bedroom (23.5%) [103].

### 2.5.2 Cardiovascular problems and mortality

![Figure 2.22: Mechanisms involved in the etiology (i.e. cause of disease) of hypertension and cardiovascular risk in patients with OSA. Adapted from Duran-Cantolla et al. [104]](image-url)
A serious aspect of obstructive SBD is the high risk of cardiovascular problems associated with the respiratory disturbances. Mechanisms causing hypertension and cardiovascular problems have been summarized by Duran-Cantolla et al. and are shown in Figure 2.22.

From this, it is clear that when combined with risk factors like obesity and genetic susceptibility the interaction of obstructive breathing – which also activates intermediate mechanisms like oxidative stress and sleep fragmentation – leads to a higher risk of arterial hypertension and hence cardiovascular problems.

Lately there have been indications that heavy snoring could also be related to cardiovascular problems; Lee et al. published an article in 2008 where they associated heavy snoring with a higher risk of stroke. Their theory was that vibrations from chronic snoring originating in the upper airway during sleep may be transmitted through surrounding tissues to the carotid artery wall. Here it can cause endothelial (i.e. thin layer of cells that lines the interior surface of blood vessels) damage. They referred to studies confirming that vibrations from snoring in rabbits were detected at the carotid artery wall and that vibratory stimuli cause pathologic damage to the endothelial cells of the arterial wall. This could lead to an inflammatory cascade promoting atherosclerosis, i.e. build-up of fatty materials in the artery which ultimately could lead to stroke. They examined 110 volunteers and found a significant increase in prevalence of carotid atherosclerosis – but not femoral (thigh) atherosclerosis – in those with heavy snoring, as can be seen in Figure 2.23.

These results were remarkable because the increase was independent of other risk factors such as age, sex, nocturnal hypoxia and OSA severity [105]. However, the article has been criticized by Drager and Lorenzi-Filho [107] because Lee et al. did not clearly discriminate OSA patients from their study and hence, in their opinion, overinterpreted the data.

They referred to a large cohort study by Marin et al., who found no significant increase in the risk of fatal and non-fatal cardiovascular events in the subset of 377 patients with primary snoring. Hence, further studies are required to confirm the direct association of heavy
snoring and stroke. The results from the study by Marin et al. show that the cardiovascular risk increases with increasing level of OSAH and is especially high in sever OSAH patients [108].

<table>
<thead>
<tr>
<th></th>
<th>Healthy men</th>
<th>Simple snorers</th>
<th>Untreated mild-mod. OSAH</th>
<th>Untreated severe OSAH</th>
<th>OSAH treated with CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fatal cardiovascular events</td>
<td>0.45</td>
<td>0.58</td>
<td>0.89</td>
<td>2.13</td>
<td>0.64</td>
</tr>
<tr>
<td>Cardiovascular deaths</td>
<td>0.3</td>
<td>0.34</td>
<td>0.55</td>
<td>1.06</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Table 2.7: Incidence of cardiovascular events (per 100 person years) during a 10-year follow-up in healthy men, primary snorers and OSAH patients. Updated from Marin et al. [108]

Their numbers have been confirmed by Young et al., who found a 5.2 times higher risk of cardiovascular mortality in patients with untreated severe OSAH (AHI ≥ 30) compared to those with no OSAH (AHI < 5), even after adjusting for age, sex, BMI, and daytime sleepiness. For all-cause mortality, the risk was 3.8 times higher [30].

2.5.3 Association with sleep bruxism

Considering the high prevalence of both sleep-related breathing disorders and sleep bruxism (8.2 % [109]), there have been investigations to find a correlation and link between the two. Sato et al. reported as early as 1971 that sleep bruxism is an arousal response [110]. Another study by Macaluso et al. compared a group of healthy volunteers to a group of sleep bruxism patients: They found a much higher number of transient arousals in the bruxism group. Also, 88 % of bruxism episodes were associated with cyclic alternating pattern and occurred always during transient arousals [111].

Hence, since obstructive sleep apnea is known to cause repetitive short arousals throughout the night, it is suggestive that these arousals could trigger bruxism episodes. Phillips et al. investigated 24 patients and found a higher degree of sleep bruxism in those with sleep apnea (12.2 vs. 7.6 per hour) [112]. Sjöholm et al., on the other hand, could not find a direct association with the obstructive apneas. In their study with 21 patients they concluded that it is more likely to be related to the disturbed sleep of OSA patients [113]. It seems that larger studies must be carried out in order to determine the exact association between sleep bruxism and OSA.

A large epidemiical study including more than thirteen thousand patients could at least confirm that OSA was the highest risk factor from associated sleep symptoms and disorders for sleep bruxism (odds ratio 1.8), followed by loud snoring (odds ratio 1.4) [109]. Oksenberg et al. therefore investigated the effect of OSA treatment on a patient with both OSA and sleep bruxism. Without treatment, 67 events of tooth grinding were identified and most of them appeared as an arousal response at the end of an obstruction. With treatment, most of the obstructions were eliminated and no tooth grinding events were observed. This suggests that a treatment to eliminate breathing abnormalities may also eliminate sleep bruxism in patients with both sleep-related breathing and sleep bruxism, [114].
2.6 Summary

By analyzing sleep-related breathing disorders it has become clear that they are related across a complex spectrum of medical conditions. Some of the main aspects have been summarized in Figure 2.24. Corresponding diagnosis and treatment options will be investigated in the next chapter in order to compile a complete overview of all aspects related to the sleep-related breathing disorders.

Figure 2.24: Summary of the development, causes and consequences of sleep-related breathing disorders
3 Existing diagnosis and treatment options

“Jim begun to snore – soft and blubbery at first, then a long rasp, then a stronger one, then a half a dozen horrible ones like the last water sucking down the plug-hole of a bath-tub, then the same with more power to it, and some big coughs and snorts flung in, the way a cow does that is choking to death; and when the person has got to that point he is at his level best, and can wake up a man that is in the next block with a dipperful of loddanum in him, but can't wake himself up although all that awful noise of his'n ain't but three inches from his own ears.”

- Mark Twain’s Tom Sawyer Abroad (1894); thoughts on why a snorer cannot hear himself snore

Mark Twain also wrote in Tom Sawyer Abroad: “There ain't no way to find out why a snorer can’t hear himself snore”. 87.5 dB is one of the highest measured sound levels from snoring, from a recording of a chronic snorer in England in 1984. His wife had already gone deaf in one ear, whereas the snorer did not appear to take any harm from this himself [57]. A plausible theory to how this is possible: body sounds are filtered out when we sleep, but we are still alert to external sounds. Hence, this automatic body defense reaction allows the snorer himself to remain undisturbed.

Sleep-related breathing disorders are very common but have often not been diagnosed. One of the reasons is probably that the snorer or OSA patient is not aware of the extent of the problem themselves. There are therefore a variety of appliances on the market which offer a diagnosis. Research was done to determine which appliances for diagnosis and therapy are on the market and how they are evaluated by patients and professionals. Since approximately 80 % of sleep laboratory visits are in relation to obstructive sleep apnea [14], the main focus in literature and hence in this section will be centered around screening, diagnosis, and therapy for OSA.

3.1 Clinical evaluation

When a doctor suspects a sleep disorder, the patient is sent to a sleep physician who asks questions about sleep habits like time going bed, time out of bed, nighttime habits (smoking, eating, snoring, pain etc.), profession and other important influences on sleep quality. According to the German guidelines, this should be done by the patient in form of a diary or questionnaire filled out ahead of the doctor’s appointment [115]. This conversation alone can in many cases confirm the doctor’s suspicion. The patient will then be told if a sleep laboratory check or other examinations are necessary.
3 Existing diagnosis and treatment options

3.1.1 Snoring

A clinical evaluation is recommended when the patient or the bed partner complains about snoring during the night according to the guidelines for diagnosis and treatment of snoring adults by the German Society of Otorhinolaryngology, Head and Neck surgery from 2010 [64].

The degree of annoyance reported by the bed partner is particularly essential for the evaluation. And since snoring has such a high prevalence it could easily occur simultaneously but independently of other sleep disorders such as insomnia, which should be evaluated as well. Snoring and associated symptoms should be the focus of a medical history check in addition to situations that worsen the condition such as alcohol and nicotine consumption and sleeping position. This could be done using standardized questionnaires including Epworth Sleepiness Scale and Pittsburg Sleep Quality Index. A timeline including weight gain is necessary to analyze how the snoring developed. In addition, the presence of nasal obstruction and allergic rhinitis are also important as they could be the cause [64].

A clinical examination should include:

- Measurement of body mass index (BMI)
- Inspection of naso-, oro-, and hypopharynx and larynx with a pharyngoscope and laryngoscope
- Inspection and endoscopic examination of the nose to measure nasal airflow and allergy testing to investigate allergic rhinitis
- Clinical evaluation of dentation and skeletal morphology

Further diagnostic measurements are not necessary if

- Snoring is an isolated symptom
- Subjects do not ask for treatment for their snoring
- Medical history and clinical evaluation produce normal findings

If the medical history and/or clinical evaluation cannot rule out sleep-related breathing disorders, further assessment and sleep testing should be performed to check for obstructive sleep apnea [64].

3.1.2 Obstructive sleep apnea

Hence, further assessment is necessary if the patient in addition has symptoms of sleep-related breathing disorder such as morning headache, fatigue and daytime sleepiness. The patient will be examined for metabolic diseases caused for example by the thyroid gland, since they can also be related to sleep disorders and daytime sleepiness. If doubt remains, it is most likely to be obstructive sleep apnea and diagnosis and severity of the disease can only be established with a sleep study. Different options for this are described in the following pages.
3 Existing diagnosis and treatment options

![Flowchart](image.png)

Figure 3.1: Indications for sleep-related breathing disorders to perform a sleep study. Adapted from Chesson et al. [116].

### 3.2 Diagnosis

Polysomnography (PSG) is considered the gold standard for diagnosing sleep-related disorders, but because of the expensive costs and inconvenience for the patients a number of other options have been developed. These are classified in four groups: Level I (full attended polysomnography) to level III (portable polygraphy) are classified as diagnostic devices, whereas level IV includes screening devices. The differences are shown in Table 3.1 and are essentially differentiated by the number of signal channels included in the recording.

<table>
<thead>
<tr>
<th>Signal</th>
<th>Level I</th>
<th>Level II</th>
<th>Level III</th>
<th>Level IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO2</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Airflow</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Respiratory effort</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Electrocardiogram (ECG) / Heart rate</td>
<td>+ / +</td>
<td>+ / +</td>
<td>- / +</td>
<td>-</td>
</tr>
<tr>
<td>Electroencephalogram (EEG)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Electrooculogram (EOG)</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Electromyogram (EMG), chin</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Electromyogram (EMG), leg</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Body position</td>
<td>+</td>
<td>Optional</td>
<td>Optional</td>
<td>-</td>
</tr>
<tr>
<td>Attended setting</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 3.1: Differentiation of diagnostic and screening devices. Adapted from Banno et al. [117]

### 3.2.1 Level I – Full attended polysomnography

Polysomnography is considered the gold standard for sleep-related disorders with good reason: more than 7 different sensors are used, as seen in Figure 3.2. But it also has disadvantages: it is expensive, complex, and patients have to sleep with a tangle of cables attached to the body, in a clinical setting.
A sleep laboratory in Munich was visited to observe how a full-night check for sleep disorders with polysomnography (PSG) is conducted. A visit to a sleep laboratory costs several hundred Euros per patient, so there are certain steps the patient has to go through before they qualify for a sleep laboratory check [118].

The examination and screening

After the clinical evaluation, the patient is given a portable monitoring device (level III) to use at home (or unattended in the clinic). Only when doubts remain will the patient be given an attended polysomnography in the sleep laboratory. This is the officially recommended procedure according to both German guidelines [115] and the American Academy of Sleep Medicine (AASM) as seen in Figure 3.3 [119]. The reason for this procedure is to reserve the sleep laboratory for those who really need it, since a visit to a sleep laboratory is expensive and requires trained personnel to attend the patients and then to analyze the eight hours of complex physiological data from the night.

Figure 3.2: Sensors applied to the patient for polysomnography (level I-II, left) and for polygraph (level III, right)

Figure 3.3: Flow chart by AASM in order to identify suitable candidates for portable monitoring ahead of in-lab polysomnography [119]
The sleep laboratory PSG investigation
The patient must arrive at the sleep laboratory at around 20:30. The patients are greeted by trained personnel who bring each patient to a private room where they start the procedure of attaching the polysomnograph with all its electrodes. At the sleep clinic they use the SOMNOscreen™ EEG 10-20 PSG [120] to examine the patients. This PSG has the advantage that it is portable. That is, all the cables are attached to the main unit on the abdomen and the data is transferred wirelessly to a computer which records the measurement. Each member of the staff is responsible for up to four patients, and they need about 30 to 45 minutes to attach and adjust all electrodes and sensors to each patient.

Experiences at the sleep laboratory
Three patients were to be examined on the night of the visit to the sleep laboratory
- Patient Nr. 1: First night of investigation in the sleep laboratory. The patient has already been pre-screened with a level III device, and has heavy snoring and obstructive sleep apnea. The investigation in the sleep laboratory is required to determine how severe these conditions are and to prepare a suitable therapy. A follow-up night with the adjustment of CPAP treatment is likely to be conducted.
- Patient Nr. 2: Fourth night in the sleep laboratory. The patient was diagnosed with obstructive sleep apnea during a previous visit, and is having the CPAP titration adjusted. The titration will start at 5 mBar and be set at a level where all OSA events disappear.
- Patient Nr. 3: Eight week follow-up of CPAP therapy. Has also been diagnosed with OSA and has started a CPAP treatment. The follow-up will ensure that the CPAP therapy is working properly.

The attaching and adjustment of the polysomnography equipment on patient Nr. 2 was observed. It took a long time to attach everything. Following this, the staff member returned to the control room to initialize the computer used to observe the patient using a camera in the room and wireless transmitting polysomnograph. He then called the telephone in patient Nr. 2’s room and began the long list of biological calibration procedures required of the patient. The patient was told to:
  - Move their eyes left to right, roll their eyes, and open and close their eyelids
  - Press their lips together
  - Breath in and out heavily
  - Breath in heavily and hold their breath
  - Snore loudly and quietly
  - Wiggle their right toe, then their left

The member of the staff had to return to the room a number of times to reattach some of the electrodes worn by the patient. The patient had a total of 10 electrodes attached in pairs on his head. The staff member is able to control the quality of the signals via the computer. If the impedance between the two electrodes in a pair is higher than 5 kΩ, they need to be reattached.
At around midnight the three patients were all asleep. The staff member observed all three via the computer, and if anything seemed strange, he could turn on the camera to see if the patient was out of bed or similar. Patient Nr. 1 had an OSA event every 15 seconds. Patient Nr. 2 was not sleeping well and remained in a light sleep phase, in addition to severe snoring. Patient Nr. 3 did not seem to have any OSA events, indicating that the CPAP treatment is working properly.

3.2.2 Level II – Full unattended polysomnography

There is little data available on level II devices; they are basically a wireless PSG, but instead of conducting the measurement in the sleep laboratory, the sensors are applied by professionals and the measurement is conducted unattended at home. This increases the probability for signal-loss, so the normal procedure involves either full attended polysomnography, or portable devices with limited channels that are used according to the decision tree in Figure 3.3.

3.2.3 Level III – Portable limited channel devices

Since PSG examination is complex and expensive, it is more and more common that the patient has initially to conduct a home polygraphy, also known as portable monitoring. A second test with PSG is conducted only if the results are ambiguous. Some of the current polygraphs are presented in this section, but as can be seen, there are only minor differences between the different models. What they all have in common is the possibility to record, at the least, the four signals required by a polygraph examination (Table 3.1).

3.2.3.1 Embletta (ResMed)

Embletta is one of the most popular level III devices in Germany. Embletta PDS (portable diagnosis system) measures – like the other level III devices – airflow, through a nasal cannula connected to a pressure transducer; oxygen saturation and heart rate, using a pulse oximeter; and respiratory and abdominal movement, via built-in effort and body position sensors. A study by Ng et al. showed a high correlation of apnea detection with polysomnography; at AHI ≥ 5 it demonstrated a sensitivity of 0.924 and specificity of 0.857, for AHI ≥ 20 0.853 and 0.957 [121].

![Figure 3.4: Embletta portable diagnose system (PDS), a typical polygraphy system worn by a patient [121] Embletta Gold, the current polygraph from Embla [122]](image)
Embletta Gold, the new version of Embletta also seen in Figure 3.4, is one of the newest level III polygraphs on the market, providing new features such as up to three nights of recording. The recordings are read into the analysis program automatically when connected to the computer via USB [122].

3.2.3.2 SOMNOcheck2 (Weinmann)
SOMNOcheck2 is another level III device which is almost identically to the Embletta device. It includes the option of measuring electrophysiological signals using electrodes attached to the level III device, so that sleep parameters and muscle activity also can be recorded in the same way as polysomnography [123].

3.2.3.3 MediByte (Braebon)
Medibyte, one of the world’s smallest level III devices, is just 71 x 76 x 19mm and weighs less than 100 g. It also provides a FFT frequency analysis of audio sounds (i.e. snoring) for precise frequency identification [124].

Figure 3.5: Miniaturized level 3 recorder from Braebon. Snoring signal is shown, and the possibility of frequency analysis. From Braebon Medical Corp. [124]

3.2.4 Level IV – Screening devices
Because of the high prevalence of snoring and obstructive sleep apnea in the general population, a broad variety of screening devices has been developed in order to identify and conduct initial screening of candidates for sleep-related breathing disorders. The motivation for this is to reserve the more time-consuming, costly, and limited use of a sleep laboratory for those with moderate to severe sleep apnea so that they can become improved access and better patient care.

For this reason, a screening device should preferably screen patients in – i.e. have a high level of sensitivity (correct-positives) and acceptable specificity (correct-negatives) – rather than screen patients out (i.e. through a high number of false negatives). In other words, it is not acceptable for a screening test to misidentify patients with sleep apnea as normal since they will not receive a PSG evaluation and the appropriate therapy needed [125]. The following pages describe different screening methods and devices. A summary of comparisons with PSG that identifies sensitivity and specificity is found in Table 3.2.
3.2.4.1 **ApneaLink (ResMed)**
ApneaLink is a single-channel screening device to identify patients at risk for obstructive sleep apnea from nasal pressure measurement. The nasal cannula is attached to a pressure transducer in the device, which is worn around the user’s chest as demonstrated in Figure 3.6 on page 40. Information about both snoring and flow limitation can be provided from the flow data.

![ApneaLink device and user](image)

Obstructive sleep apnea cannot be distinguished from central sleep apnea since there is no recording of respiratory effort. Also, like all the other screening devices, ApneaLink cannot register if the patient is asleep or awake; consequently, the apnea-hypopnea-index is divided on the total study time (from start to stop), whereas a polysomnography AHI is based on the total sleep time. ApneaLink defines an apnea as a decrease in airflow by 80 % of baseline for at least 10 seconds, maximum 80 seconds. An hypopnea is defined as a decrease in airflow between 50 and 80 % of baseline for at least 10 seconds, maximum 100 seconds [125].

3.2.4.2 **Oximetry**
Oximetry is a widely used screening tool for sleep apnea, although previous studies have shown a wide range of sensitivity from 40 to 100 % [127]. Sleeping position, sleep state, and breathing rate have an influence on arterial blood oxygen saturation (SaO₂) and could explain these results [128]. This tool can only indicate apneic events and can hence not be used to detect snoring.

![SaO₂ recordings](image)

**Figure 3.7:** SaO₂ recording from a subject a) without apneic events, b) with apparent OSA events and c) with weak desaturations, difficult to analyze. From Alvarez et al. [129].
3 Existing diagnosis and treatment options

Figure 3.7 shows three common pulse oximetric recordings and demonstrates the difficulties in diagnosing apneic events using oximetry alone; a) displays a $\text{SaO}_2$ recording for a normal subject without OSA, b) for a patient with apparent OSA because of the clearly marked oxygen desaturations, and c) for an uncertain OSA patient. In the last case, the desaturations are not extreme and diagnosis by visual inspection is difficult [129].

Another observation by Nakano et al. indicated that the diagnostic ability of oximetry for OSA is BMI dependent: the degree of desaturation from an apnea event is known to be affected by the degree of obesity. Hence, oxygen saturations are more distinct with higher BMI, meaning that the desaturation cutoff level (e.g. 4 %) must be selected appropriately according to patient BMI for a better result [130].

3.2.4.3 **NovaSom QSG**

NovaSom QSG utilized an airflow sensor worn on the upper lip to measure airflow from nose and mouth. It has also two microphones to be placed on the upper lip: one microphone captures the snoring sound and ambient noise, whereas the other captures sound from respiration. These signals are separated from each other by adaptive noise canceling filters within the integrated audio digital-signal processing (DSP) unit. In this way, a pure respirational signal can be subtracted from the microphone signal and compared to the airflow signal, which should be correlated linearly.

![NovaSom QSG breath sensor](image)

**Figure 3.8:** NovaSom QSG has a breath sensor recording both flow and sound signal. From Hunsaker et al. [131]

In addition, it has both an effort sensor in the form of a Tygon tube placed around the chest and connected to a pressure transducer in the recording module, and a pulse oximeter finger sensor. NovaSom QSG uses algorithms to perform automatic scoring and to generate an automatic report [132].

3.2.4.4 **RUSleeping RTS (Philips)**

RUSleeping from Philips Respironics uses just a nasal cannula to screen for OSA. The window area of the device, seen in Figure 3.9, displays both the total number of apneic events and the average hourly number of apneic events. There is no software or possibility of downloading the data, so it can only be used as an initial screening device to complement existing, subjective screening methods. Another possibility is to use it to complement oral appliances in treating snoring and mild to moderate OSA; it can be used by a dentist to evaluate the effectiveness of jaw advancement in oral appliances therapy and adjust the titration prior to sending the patient back to the sleep lab for an expensive validation of treatment [133].
3 Existing diagnosis and treatment options

Figure 3.9: RUSleeping nasal cannula from Philip Respironics. From Herrle et al. [133]

However, there has been no impartial clinical study of the accuracy of the device; there has only been an internal study with 25 patients showing 92% sensitivity and 77% specificity at AHI>15, which is rather high for a one-parameter screening device [134]. Hence, the accuracy of RUSleeping cannot be confirmed until an impartial clinical study has been conducted.

3.2.4.5 SOMNOcheck micro (Weinmann)

SOMNOcheck micro from Weinmann also uses a nasal cannula with a pulse oximeter in addition, but the recording device is worn as an armband. The results are automatically calculated and displayed in the morning [135].

Figure 3.10: SOMNOcheck micro is worn as an armband with a nasal cannula and pulse oximeter connected [135]

Again, there has been no impartial clinical study confirming the accuracy of the device, but a study by Sommermeyer et al. found that the correlation coefficient between manually scored AHI and automatically calculated RDI to be 0.967, based on a Matching Pursuit algorithm using pulse oximeter data only. The algorithm first calculates the parameter’s pulse wave amplitude (PWA) and pulse rate (PR), which are taken from the unfiltered pulse wave signal as demonstrated in Figure 3.11. PR and PWA, in addition to the SaO2 signal, are analyzed using the algorithm, which creates an automatic arousal index based on the morphological changes of the pulse wave signal. The flow signal delivers further information but was not used in the study [136].

Figure 3.11: Calculation of pulse wave parameters pulse wave amplitude (PWA) and pulse rate (PR). From Sommermeyer et al. [136].
3.2.4.6 **ARES**
Apnea Risk Evaluation System (ARES) is an advanced sleep-wearable, wireless physiological recorder worn on the forehead. It can acquire and store up to four nights of nocturnal data, measuring blood oxygen saturation (SpO2), pulse rate (reflectance pulse oximetry), airflow (nasal cannula connected to a pressure transducer), respiratory effort (a combined signal using pressure transducer sensing forehead venous pressure [137], venous volume by photoplethysmography and actigraphy), snoring levels (microphone), head movement, and head position (accelerometers).

![Figure 3.12: Patient wearing the ARES unicorder. From Westbrook et al. [138]](image)

Audio and visual indicators notify the user when the unicorder requires adjustment, thus increasing the reliability when used at home. The goal is to provide an affordable screening process and follow up for OSA patients [138].

3.2.4.7 **WatchPAT**
The WatchPAT is a wrist-worn screening device based on the so-called peripheral arterial tonometry (PAT). The technology uses a finger-mounted optic/pneumatic sensor to utilize the finger pulsatile arterial volume changes through sympathetic activation and peripheral vasoconstriction (i.e. narrowing of the blood vessels) during arousal events.

![Figure 3.13: WatchPAT worn by a patient. Schematic of PAT’s structure, from Chouraqui et al. [139]](image)

A pulse oximeter is also mounted on another finger and connected to the main body of the device. Apneic events will result in an attenuation of both the PAT signal and blood oxygen saturation. The device also has a built-in accelerometer for the detection of limb activity (actigraph) used in combination with the PAT signal to differentiate between sleep and waking. From these signals, the WatchPAT automatically calculates the frequency of respiratory events per hour of sleep [140].
3 Existing diagnosis and treatment options

3.2.4.8  **SleepStrip**
The SleepStrip is a screening device for determining AHI events in OSA patients. The device is self-adhesive and placed on the upper lip at bedtime. It must be adjusted so that respiration is detected, signaled by a flashing light. The flow signals are derived from 3 thermistors; two nasal and one oral. The internal CPU tracks the signal continuously, calculating the average amplitude of normal respiration cycles, peak-to-peak amplitude for each consecutive breath cycle, and the other parameters of the respiration pattern. The data are processed in the CPU and the result is displayed on the SleepStrip single digit display area.

![Figure 3.14: The SleepStrip OSA screening device is placed on the upper lip](image)

However, in a study by Pang et al. it demonstrated a very low sensitivity (54.6 and 43.8 %) and specificity (70 and 81.3 %) for diagnosing mild (AHI ≤ 15) and moderate (AHI ≤ 25) OSA. The SleepStrip only demonstrated usefulness in excluding severe OSA (AHI > 40) [142]. Hence, as of 2010, the product page does not exist and the product is no longer on the market.

### 3.2.5 Summary of screening options

<table>
<thead>
<tr>
<th>Main author</th>
<th>Year</th>
<th>Equipment</th>
<th>Patients</th>
<th>Device AHI in comparison to polysomnography</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>AHI (AHI &gt; 15)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-laboratory (in %)</td>
<td>At home (in %)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>#</td>
<td>Age</td>
</tr>
<tr>
<td>Oeverland [143]</td>
<td>2002</td>
<td>Oximetry</td>
<td>93</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Reichart [132]</td>
<td>2003</td>
<td>NovaSom QSG</td>
<td>51 52 30</td>
<td>95 91 91</td>
<td>83</td>
</tr>
<tr>
<td>Westbrook [138]</td>
<td>2005</td>
<td>ARES (AHI &gt; 10)</td>
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<td>97.4</td>
<td>85.6</td>
</tr>
<tr>
<td>Pang [142]</td>
<td>2006</td>
<td>SleepStrip</td>
<td>37 52 36</td>
<td>54.6</td>
<td>70</td>
</tr>
<tr>
<td>Pang [140]</td>
<td>2007</td>
<td>WatchPAT</td>
<td>37 50 35</td>
<td>96</td>
<td>79</td>
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<tr>
<td>Erman [125]</td>
<td>2007</td>
<td>ApneaLink</td>
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<td>32.6</td>
<td>90.9</td>
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<tr>
<td>Grover [134]</td>
<td>2008</td>
<td>RUSleeping</td>
<td>25 42.4 31</td>
<td>92</td>
<td>77</td>
</tr>
<tr>
<td>Sommerm. [136]</td>
<td>2009</td>
<td>SOMNOcheck micro (oximetry)</td>
<td>62 52.4 28</td>
<td>96.2</td>
<td>91.7</td>
</tr>
<tr>
<td>Ng [121]</td>
<td>2010</td>
<td>Embletta PDS (level 3 device)</td>
<td>80 51.4 27.1</td>
<td>87.8</td>
<td>94.9</td>
</tr>
</tbody>
</table>

Table 3.2: Studies showing correlation between polysomnography and home sleep testing
Different technologies and approaches for OSA diagnosis and screening have been presented in this section. Table 3.2 summarizes the results from the studies on the screening devices described and the Embletta PDS (polygraph level III), giving an important indicator of the requirements needed for the planned long-term monitoring system.

What they all have in common is the high sensitivity of above 85 % (correct-positives) acceptable to very high specificity (correct-negatives) which is important in order to screen in patients rather than out. An exception is the SleepStrip, but this is probably the main reason it was pulled from the market.

### 3.3 Therapy

Snoring has annoyed humans for centuries. According to one legend, one of the first snoring remedies was small cannonballs sewn into the backs of soldiers to keep the snorers from alerting the enemy during the American Civil War in the 1860s. Hence, it had already been observed that most people snore more loudly and longer when they are sleeping on their back. The principle was optimized and patented by Liebhardt in 1908 [144]; it was probably the first of many anti-snoring devices that involved strapping a ball to the snorer’s back.

![Figure 3.15: Anti-snoring device to prevent supine sleeping position. Patented by Liebhardt in 1908 [144]](image)

With the discovery of OSA and snoring as one of the main symptoms in 1965, the therapy of sleep-related breathing disorders has been taken more seriously and resulted in a wide spectrum of treatment options.

As with PSG for diagnosis, there is also a gold standard of therapy for OSA: CPAP (Continuous Positive Airway Pressure). It was introduced by Sullivan et al. in 1981 [28] as treatment for OSA patients – up until then the only two options had been weight loss [145] and tracheotomy (i.e. an incision in the trachea to open a direct airway) [146].

However, CPAP has only a high compliance with those who have severe OSA, so alternatives have emerged for those who have snoring and mild to moderate OSA. Still, the general rule for OSA treatment (with some exceptions to be mentioned) is to first offer the patient CPAP. If he refuses or is cannot tolerate the treatment then other options should be discussed. These options are divided in four main categories in addition to CPAP, and are presented on the following pages of this section.
3 Existing diagnosis and treatment options

3.3.1 Continuous Positive Airway Pressure (CPAP)

The principle of CPAP treatment is shown in Figure 3.16; when the patient is awake, the muscle tone prevents collapse of the airway. During sleep however, the tongue and the soft palate can be sucked against the posterior oropharyngeal wall and create an obstruction. CPAP provides a so-called pneumatic splint and keeps the airway open [28].

![Figure 3.16: Principle of CPAP treatment as discovered and explained by Sullivan et al. in 1981](image)

**Variations of CPAP treatment**

CPAP is conventionally delivered through a nasal mask with a fixed pressure that remains constant throughout the respiratory cycle. However, some patients have problems exhaling against pressure and thus do not tolerate constant pressure. Other variations of CPAP are therefore available nowadays.

*AutoPAP*, short APAP, is an auto-titrating PAP machine that has the ability to automatically adjust pressure settings throughout the night to ensure that the correct pressure is being used to splint open the airway at all times. Although they are more efficient and can be used for PAP treatment, they are also much more expensive than CPAP and for this reason mainly used for initial titration and trial; in this way, the patient does not have to spend a night in the sleep laboratory to find the right PAP titration level, but rather take home an autoPAP and use it for 3-7 days. The prescribing physician can then read out the data and prescribe an adequate CPAP level for the patient [39].

*Bi-level PAP*, short BIPAP, differs from CPAP by delivering one pressure during inspiration and a lower pressure during expiration. BIPAP is commonly given to patients who require higher CPAP pressures above 12-14 cmH₂O since they often have difficulty exhaling against the high pressure from the machine. The correct levels must be set in the sleep laboratory, however newer models known as autoBIPAP can adjust the levels automatically [39].

3.3.1.2 Initiation of treatment with CPAP

When OSA is diagnosed, CPAP is normally the first choice of treatment. Treatment options are discussed with the patient according to clinical guidelines. The clinical guidelines of the American Academy of Sleep Medicine (AASM) for CPAP treatment are shown in Figure 3.17.
3 Existing diagnosis and treatment options

3.3.1.3 CPAP as treatment in OHS patients

Although CPAP is considered the gold standard of OSA treatment, the optimal management of patients with OHS remains uncertain. But given that most OHS patients also have severe OSA, treatment with CPAP seems reasonable. There have also been several studies that report improvement in chronic daytime hypercapnia and hypoxia with CPAP (or bilevel PAP) treatment. About half of the patients with OHS need oxygen therapy in addition to CPAP at the initiation of treatment, which should be investigated during polysomnography and CPAP treatment. It should be noted that autoadjusting PAP (autoPAP), which are used to bypass in-lab titration in patients with OSA, cannot be used in patients with OHS because autoPAP is not able to register hypoventilation and hypoxemia. Hence, OHS patients require in-lab CPAP and oxygen titration [62]. A study by Banerjee et al. showed that more than half of OHS patients could resolve sleep-disordered breathing and nocturnal hypoxemia using CPAP alone as therapy [147].

3.3.1.4 Problems

There are many limitations to CPAP, which reduce the overall compliance. As mentioned, some patients have trouble sleeping with constant airway pressure. Also, others complain about sleeping with a nasal mask, which must fit perfectly. A known and common side effect to CPAP is that the dry air can cause a sore throat and a runny or blocked nose [148]. To prevent this, a humidifier can be used to add (heated) humidification. But humidification makes the equipment and tubing prone to mold growth and therefore requires a more aggressive daily cleaning program, which has to be adopted by the patient [39].

Optimizing the comfort and fit of the nasal mask dramatically reduces the reports of side effects, emphasizing the importance of adequate expertise in the personnel responsible for
initiation the therapy. Furthermore, side effects usually occur early on after initiating therapy, and close patient follow-up in the initial weeks of therapy is very important [149].

Another problem, despite careful CPAP titration, is that a relatively high proportion of patients with moderate to severe OSA still have an AHI > 10. This phenomenon is called residual sleep apnea, and a new study by Mulgrew et al. revealed that the proportion could be as high as 25 %. This is of course associated with worse compliance and outcomes, and must be taken very seriously. Given the increasing demand and limited access to in-lab PSG, it is unusual to repeat an in-lab PSG, for the purpose of determining CPAP therapy efficiency, after initial CPAP titration. For this reason, many patients on CPAP can continue with an undiscovered sub-optimal CPAP treatment, which increases the risk of cardiovascular complications and motor vehicle crashes [150].

### 3.3.1.5 Long-term follow-up and compliance

Yamamoto et al. investigated the long-term effects of CPAP treatment on the rate of traffic accidents, excessive daytime sleepiness (EDS), and moodiness in patients with OSA by questioning the patients before CPAP treatment and after two years of treatment. No car accidents were caused during treatment, while one third of the patients had been in car accidents before treatment. Further, near-miss accidents had been reported by 82 % of the patients ahead of treatment, but only by less than 10 % after two years of treatment. Also, the mean score of the Epworth Sleepiness Scale (ESS) was significantly reduced and the Self-related Depression Scale (SDS) decreased, implying an improvement of ESS and mood in patients with OSAS [151].

Sin et al. also tried to determine long-term compliance rates of CPAP therapy by equipping the CPAP devices of 296 patients with a monitoring chip. The mean duration of CPAP use was between 5.8 hours per night after six months, and the percentage of patients still using CPAP more than 3.5 hours per night were 89 % at two weeks, 86.6 % at four weeks, 88.6 % at three months, and 88.5 % at 6 months. Also, there was a decrease in the Epworth Sleepiness Scale (ESS) of 44 % after two weeks of therapy, which continued to improve with the lowest score observed after six months. Three variables were found to be significantly correlated with increased CPAP use, female gender, increasing age, and reduction in ESS score [18].

As of 2010, some social insurance programs require a CPAP data report on compliance in order to pay for the therapy. An example is Medicare (USA), which requires a report showing that the patient has used the CPAP for at least four hours on more than 70 % of nights during the first month of therapy. As a result, the newest series of CPAP devices such as ResMed S9 are now offering this feature [152].

### 3.3.2 Behavioral therapy

Behavioral treatment options include weight loss for those who are overweight (BMI > 25), exercise, avoidance of alcohol and sedatives, and positional therapy [19]. These options could provide sufficient therapy for primary snorers or patients with mild to moderate OSA,
especially those who are positional patients. This approach, according to the AASM guidelines, is shown in Figure 3.18.

3.3.2.1 Weight loss
Increased body weight is associated with snoring, and weight reduction is often accompanied by snoring reduction. Therefore, according to the guidelines for diagnosis and treatment of snoring adults by the German Society of Otorhinolaryngology, Head and Neck surgery, weight reduction should be recommended for every overweight subject who snores [64].

Weight loss should also be recommended for all overweight OSA patients according to the AASM guidelines [19]. However, it should be combined with a primary treatment such as CPAP, because of low the low cure rate by dietary approach alone [153]. After a substantial weight loss of more than 10 % of body weight, a follow-up PSG should be conducted to ascertain whether CPAP therapy is still needed or can be adjusted [19]; more than 60 % of OSA patients are overweight, and a 10-15 % weight loss reduces in general 50 % of AHI events in these patients [154-156].

Figure 3.18: Approach to initiation, management and follow-up of behavioral treatment. Adapted from the AASM guidelines [19].

3.3.2.2 Positional therapy
Sleep position affects the airway size and patency with a decrease in the area of the upper airway, especially in the lateral dimension when sleeping in the supine position. Positional therapy is a method that keeps the patient in a non-supine sleeping position. As mentioned, more than half of snorers and OSA patients have snoring and apnea events predominantly in the supine position. Hence, positional therapy is an effective therapy for snoring and a secondary therapy or supplement to primary therapies for OSA patients. Since not all patients normalize snoring or AHI when sleeping in the non-supine position, the positional...
benefit should be documented with diagnosis before initiating this treatment form as the primary therapy according to the AASM guidelines. Also, the positioning device (for example alarm, pillow, back pack or tennis ball) should be provided with an objective position monitor. The treatment specific outcome indicators to monitor with positional therapy include self-reported compliance, objective position monitoring, side effects and symptom resolution [19].

Lee et al. investigated how effective a lateral position during sleep is in reducing sleep disorder symptoms in mild or moderate sleep apnea patients. They pointed out, that the effect of head and shoulder posture in lateral position on reducing sleep disorders had not previously been reported. In their study, effective sleep positions and a combination of sleep position determinants were evaluated. The positions included the following: cervical vertebrae support with head tilting (CVS-HT), scapula (shoulder blade) support (SS) and lateral position (LP). The results showed that the optimal sleep position for reducing mild snoring (baseline snoring rate 20 % in supine position) was LP 30° and SS 20 mm when CVS-HT was 60 mm, which reduced the snoring by more than 80 %. When the baseline snoring rate was more than 30 %, more than 40° rotation was needed to achieve an 80 % reduction of the snoring rate. More than 40 % could not be reduced by more than 5 % with any of the combinations. Similarly, for sleep apnea with 10 AHI and CVS-HT 60 mm, an 80 % reduction of AHI was achieved with LP 30° and SS 20 mm. For 20 and 30 AHI, a > 40° rotation with higher levels of CVS-HT (> 70 mm) and SS (30 mm) was recommended for an AHI reduction of > 80 % [157].

Figure 3.19: Thoracic anti-supine sleeping band (also known as tennis ball technique, TBT). Comparison of scores for AHI of total sleep time for patients at baseline (blue), with CPAP therapy (green) and TBT (yellow). Adapted from Skinner et al. [158].

One of the original, simple methods of positional therapy is the tennis ball technique (TBT), i.e. a tennis ball or similar object attached to the back in order to avoid sleeping in the supine position. Skinner et al. conducted a study where they compared TBT with CPAP as treatment in twenty patients with mild to moderate severe positional-dependent OSA; the results can be seen in Figure 3.19 and show that most of these and other positional-dependent OSA patients benefit from positional therapy. With TBT, treatment success
(AHI < 10) was achieved in 13 from 18 subjects, whereas success was achieved in 16 of 18 patients with CPAP. Mean percentage supine sleeping time was 6.3 ± 5.9 % with TBT and 35.4 ± 34.1 % with CPAP [158].

However, the long-term compliance of the tennis ball technique appears to be very poor; Bignold et al. contacted 108 patients approximately 30 months after being prescribed with TBT. Only 6 % reported that they still used the TBT (group A), 13.4 % claimed to have learned to avoid the supine position and were no longer using TBT (group B), and 80.6 % where neither using TBT nor avoiding the supine position (group C). In group C, the main reason given for no longer using TBT was that it was too uncomfortable (34/54 patients). They therefore concluded that alternative forms of positional therapy appear to be needed [159].

An experiment with an acoustic alarm to treat position-related obstructive sleep apnea was explained as early as in 1985 by Cartwright et al. [160], one of the pioneers in positional treatment of OSA [161]. They selected ten moderately obese male patients with OSA associated with the supine sleep position and trained them for one night with a gravity-activated position monitor/alarm on the chest. If the patient remained for more than 15 seconds in the supine position, an auditory alarm was emitted by the device. This dramatically reduced the average supine sleep time from 51.4 % to 2.1 %, and thus also the number of apneic events (AHI from 54.7 to 21.4) and episodes of significant O₂ desaturation. For seven of the patients, the apnea index remained within or near normal limits (AHI < 5) while wearing the alarm. Without the device, being only instructed to avoid the supine position for a 3-month period, the test afterwards showed that the initial 51.4 % sleep time in the supine position was reduced to 24.1 %. For five of the ten patients, the supine sleeping time was less than 10 % [160].

Cartwright et al. also used the alarm system continuously for eight weeks in 20 patients with position-related OSA. When the alarm system was used, they all had less than 5 minutes sleeping time in the supine position, but on a following night without the device, only 11 (55 %) of the patients had less than 5 minutes of supine sleeping time. For the other patients, supine sleeping time ranged from 11.2 to 172 minutes, where five of them (25 % of the whole group) slept more than one hour in the supine position [84].

In yet another study by Cartwright et al., also ranging 8 weeks, four groups of 15 positional OSA patients each were examined in a comparison of behavioral treatment. Here, in the groups where the alarm system and the alarm system in combination with a tongue retaining system were used, the results were the similar to the previous study mentioned. In the group where only general health advice including the avoidance of supine position was given, 66.7 % of the patients had less than 16.5 minutes of supine sleep time, while 33.3 % had supine sleep ranging from 40 to 148.5 minutes. From these studies, the conclusion could be drawn that some patients can successfully learn to avoid the supine position with or without such a device, while other require the continuous use of such a device [162].
3 Existing diagnosis and treatment options

3.3.2.3 **Avoidance of alcohol and sedatives before bedtime**

Often, changes in habits should be recommended to OSA patients and subjects who snore: including avoiding sleeping pills or alcohol intake in the evening, abstaining from nicotine, and maintaining a regular sleep-wake cycle [64]. The reasons were mentioned in chapter 2.4; namely, medication and alcohol can cause impaired dilator muscle activity and smoking can cause airway inflammation that contributes to a worsening of snoring and OSA events.

3.3.3 **Oral appliances**

Oral appliances (OA) are being increasingly used as treatment for snoring and OSA [42]. Custom-made OAs could decrease upper airway collapsibility during sleep by enlarging the upper airway. Most OAs cover the upper and lower teeth and hold the mandible in an advanced forward position with respect to the resting position [19]. These are called mandibular retaining devices (MRA) and treatment principle can be seen in Figure 3.20.

![Figure 3.20: Schematic diagram of upper airway (black) anatomy during (a) obstructive sleep apnea without mandibular retaining appliance (MRA) and (b) with MRA. From Cistulli et al. [42]](image)

The other group of OAs is called tongue retaining devices (TRD), which only hold the tongue in an advanced forward position by suction without mandibular repositioning, preventing the tongue from retrolapsing with inspiration, and subsequently blocking the airway. Although not as popular as MRAs, TRDs could be useful when the patient lacks the prerequisites for treatment with MRAs (e.g. healthy teeth or adequate jaw range) [19].

![Figure 3.21: Example of a tongue retaining device (TRD, left) holds the tongue in a forward position with a suction bulb. A mandibular retaining appliance (MRA, right) maintains the mandible in a forward position. From Friedman et al. [39].](image)

3.3.3.1 **Initiation, management and follow-up of OA treatment**

The approach to initiation, management and follow-up of patients using custom-made OA therapy according to the AASM is shown in Figure 3.22.

Oral appliance is an appropriate treatment for patients with primary snoring who do not respond to behavioral treatment such as weight loss or positional therapy. MRAs have been demonstrated to be particularly useful in relieving snoring, at least subjectively by
questioning the patients [163]. Also, there is emerging evidence of the benefit with MRA as treatment of UARS, although there has been no randomized controlled trial to confirm it [164]. Hence, non-apneic snorers represent the largest subgroup for which such treatment should be considered [42].

For OSA, OAs can be used to treat patients with mild to moderate OSA who do not prefer or tolerate CPAP treatment, or who fail CPAP or behavioral treatment. Since OA is not as efficient as CPAP, patients with severe OSA should first have an initial trial of CPAP. Also, the presence and severity of OSA must be determined ahead of OA therapy to provide the baseline needed to prove the effectiveness of subsequent OA treatment [19].

Further, to assess candidacy for an OA treatment, patients should undergo a thorough dental examination, including soft tissue, periodontal and temporomandibular joint (TMJ) assessment, characteristics from nocturnal bruxism and evaluation of occlusion. Optionally, a cephalometric evaluation (i.e. study of the dental and skeletal relationships in the head) could also be conducted [165]. Candidates for a MRA in particular need to have adequate set of healthy teeth and jaw range, no TMJ disorder, and adequate manual dexterity and motivation to insert and remove the MRA as determined by a qualified dental professional. OAs should also be fitted by qualified dental personnel, with training and experience with TMJ, dental occlusion, and associated oral structures. The dental management of patients using OAs should also be overseen by personnel with training in sleep medicine with a focus on proper protocol for diagnosis, treatment, and follow-up of OSA while using an OA [19, 166].

3.3.3.2 Long-term follow-up of OA treatment
To ensure therapeutic benefit with OA treatment, patients with OSA should undergo a sleep study (level I or III) with the oral appliance in place after final adjustments of fit – for patients
with primary snoring this is optional, according to the AASM practice parameters. Patients should, after the final adjustment, also return to a follow-up visit with the dental specialist. Follow-ups should occur every six months in the first year, with regular follow-ups at least once a year after that to ensure and monitor patient adherence, and to evaluate the health of the oral structures and device maladjustments. Close communication between patient and dental specialist is important to guarantee good patient care and therapy adherence. Also, signs and symptoms of (a worsening) OSA must be assessed. If so, a reevaluation of apneic events with a sleep study is necessary [166].

3.3.3.3 Long-term efficiency and side-effects of OA treatment
Cistulli et al. reviewed a series of clinical long-term studies of MRA as a treatment for snoring and OSA with follow-up periods of 2-5 years [167-170], which suggested a high success rate of up to 80%. However, the studies were biased since they only included 30 to 77% of all originally treated patients, excluding those who initially discontinued treatment because of poor efficiency or failure to attend follow-up. Cistulli et al. therefore predicted a much lower success rate, perhaps below 50% depending on the patients included. To increase the long-term success rate, the most efficient way is to only select patients who are notably interested and likely to respond to treatment with oral appliances. Long-term follow-up of patients, including reassessment to adjust for the effect of treatment due to weight gain or (re-)development of symptoms of sleep apnea in order to adjust the oral appliance or recommend other treatment, is also important [42].

![Figure 3.23: Long-term effect of MRA on apnea-hypopnea-index (AHI, left), short-term versus long-term effect on AHI with the device (center) and without the device (right). From Marklund et al. [168]](image)

Intolerance because of side effects, lack of motivation, and improper use of oral appliance therapy are potential problems when using an oral appliance. OAs may enhance TMJ disease or cause dental misalignment and discomfort that are, because of individual fit, unique to each device. Also, the oral appliance can be rendered ineffective because of patient alteration [166].

Discomforit is the major cause of discontinuation or poor compliance for about 20 to 50% of initially treated patients with MRA. This could worsen when using a single position appliance or through too rapid titration with the appliance [42]. According to experts, this should be
done step-wise over a timespan of up to three months. Pain in the teeth or jaws will be in relation to the magnitude of the forces generated. Since the teeth experience a permanent force during the night, they may change their inclinations and the whole jaw may also be displaced during long-term treatment. However, jaw and teeth discomfort, increased salivation, and experiences of an abnormal bite become less prominent with time. Long-term dental changes with MRA appear to be common, but are generally minor and should be managed with appropriate dental follow-ups [42].

The interpretation of compliance rates of OA treatment is subject to limitation because of a lack of objective data for verification. Notably, this does not occur with CPAP. This lack of self-perceived efficacy is also one the main reasons for patient refusal to start or continue OA treatment; hence, high initial usage declines over time. After one year of treatment the compliance rate varies between 55 and 82% in different studies [169, 171-173], after three years of treatment Clark et al. reported 51% [174]. Lowe et al. used a compliance monitor (i.e. thermistor which triggered a timer when the temperature limit of 31°C was reached) embedded in an MRA and revealed an average nightly usage of 6.8 hours which was comparable to diary data in a 4-week trial [175].

3.3.4 Surgery

Surgery was the first method to treat OSA, and meanwhile there is a broad variety of upper airway reconstructive or bypass procedures, which are mostly site-directed. Hence, in addition to the diagnosis of OSA, there must be an evaluation of eligibility for surgery ahead of any procedure including an anatomical evaluation to identify possible surgical sites, an assessment of comorbidities that could affect surgical outcome, and a desire from the patient for surgery. The patient must of course be informed on surgical options, the likelihood of success, goals of treatment, risks and benefits as well as possible side effects, complications, and alternative treatments [19].

<table>
<thead>
<tr>
<th>URT surgery</th>
<th>CPAP therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>&gt; 40 years</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>Mallampati</td>
<td></td>
</tr>
<tr>
<td>1 or 2</td>
<td>3 or 4</td>
</tr>
<tr>
<td>Tonsil grade</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Waist</td>
<td></td>
</tr>
<tr>
<td>&lt; 102 cm</td>
<td>&gt; 102 cm</td>
</tr>
<tr>
<td>EDS</td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>Nose</td>
<td></td>
</tr>
<tr>
<td>Polyps</td>
<td></td>
</tr>
<tr>
<td>Tongue base</td>
<td></td>
</tr>
<tr>
<td>Wide open at endoscope</td>
<td>Narrow at endoscope</td>
</tr>
</tbody>
</table>

Figure 3.24: Factors favoring a upper respiratory tract (URT) surgery instead of CPAP treatment. Adapted from Davidson et al. [176]
Because of the irreversible effect of surgery and side effects, the patient should first be tested with CPAP or OA treatment. Surgery should be seen as a secondary treatment when the outcome of CPAP or OA treatment is inadequate or not tolerated by the patient. Surgery could also be used in combination with CPAP or OA when obstructive anatomy or functional deficiencies are obvious. In general, those who have mild OSA with severe obstructing anatomy (e.g. enlarged tonsils) are most likely to benefit from surgical correction. Factors favoring surgery over CPAP treatment are shown in Figure 3.24. Further, the success rate of surgery is much lower in obese patients, and weight loss is therefore often seen as a requirement for surgical intervention [177]. The initiation and management of surgical treatment in OSA patients according to AASM are shown in Figure 3.25 [19].

For snoring, invasive treatments need to be considered with great care. It is recommended that surgical interventions should take individual anatomy into account and favor the least invasive procedure. Since snoring is not a medical disease associated with a direct medical hazard, only minimally invasive procedures with low morbidity and complication rates should be recommended upon the request of surgical intervention from the snorer. Like for OSA patients, the success rate for surgery to treat snoring also decreases with increasing BMI [64].

3.3.4.1 **Long-term follow-up, efficiency and side-effects of surgical treatment**
Post-surgical follow-up must be conducted by the surgical team to evaluate wound healing, anatomical results, side effects and complications. After healing is completed, an evaluation
of change in OSA symptoms is recommended, and a long-term follow-up with a sleep specialist should be scheduled according to the procedure determined by the AASM [19].

In a retrospective study by Hicklin et al., they found that 76% of the 200 patients who underwent uvulopalatopharyngoplasty (UPPP) surgery had a reduction of 50% or more in snoring level after the operation. But, after two years only 45% maintained such a reduction in snoring level. Also, the postoperative pain was 7.5 and the satisfaction 5.0 on a scale from 1-10, with 61% of the patients stating they would not have it done again [178]. Bearing this fact and that other surgical methods have similar or even worse success rates in mind [177], surgery should only be recommended for those with considerable anatomic limitations of the airway and if other treatments are not working; this is similar to the recommendations for OSA in Figure 3.24.

An interesting study by Walker-Engstrom et al. compared a group of OSA patients with dental therapy to a group of OSA patients who underwent UPPP surgery. They found a significant higher success rate in the dental therapy group (81% versus 53% having more than 50% reduction in apnea events on 4-year follow-up) as demonstrated in Figure 3.26. Unfortunately, the compliance was only 62% in the dental group. Subsequently, they recommended the use of dental appliance with regular follow-up over surgery for long-term treatment of OSA [169].

![Figure 3.26: Comparison of dental appliance (left) and UPPP surgery on apnea index before intervention, at 1-year and 4-year follow-up after treatment. Adapted from Walker-Engstrom et al. [169]](image)

### 3.3.5 Adjunctive therapy

For the extreme obese with BMI > 40, physical activity and dietary changes are not enough to achieve the major weight loss needed for a reduction in sleep-related disorders. Therefore, bariatric surgery (also known as weight loss surgery) may be used as adjunctive therapy in addition to other therapies such as CPAP if the other therapy approaches are not sufficient. The remission rate of OSA patients after bariatric surgery is 40% which indicate a strong need for continuous clinical follow-up [19].
3.4 Innovative appliances for diagnosis or therapy of sleep disorders

This section presents appliances offering screening, diagnoses and therapies that are currently being developed.

3.4.1 Obstruction site localization

ApneaGraph is an innovative device designed to locate the upper airway obstructive site. The probe, which is introduced in the nose of the patient and leads in the airway, has two thermistors (T0, T1) and two pressure sensors (P0, P2). In addition, an oximeter is used to support the detection of obstructions. Tschopp et al. tried the system on 119 patients with snoring and OSA. 41% were identified with predominantly upper obstruction, 29% with predominantly lower obstruction and 30% with about the same amount of upper and lower obstruction [179].

Figure 3.27: Example of a lower airway obstruction because of higher pressure at P0. The pressure at P2 is significantly lower and has no obstructive pattern [179].

Morales Divo et al. conducted a study with PSG as comparison. They concluded that the distribution of sites of obstruction could be identified by the ApneaGraph in all 14 patients. There was also a good correlation of ApneaGraph and PSG for AHI, pulse, SaO2, body position, and central apnea, but less correlation in obstructive apnea, apnea index, hypopnea index, and mixed apnea. Hence, ApneaGraph cannot substitute PSG, but could be used in conjunction with PSG to increase the quality of diagnosis. Further, it could be used to better localize the area of interest for the surgeon if surgery is being considered. The lack of a reliable method for characterizing functionally relevant upper airway narrowing may be the cause of disappointing results in many sleep-related surgeries in OSA patients [180]. But, one of the drawbacks of the ApneaGraph is the invasive placement of the probe which is not well tolerated by many patients. There is also a need for further evaluation to ensure a reliable classification in upper and lower obstruction in order to provide an improvement in patient selection for surgery [181].
3.4.2 Implantable neurostimulators

For a long time, implantable neurostimulators that activate upper airway muscles in OSA patients have been investigated with promising results [182], but without any significant breakthrough. The neurostimulator Apnex HGNS Device from Apnex Medical is a new approach to implants, as seen in Figure 3.28, with both a stimulation lead implanted on a branch of the hypoglossal nerve and respiration sensing leads tunneled under the skin on the chest attached to the neurostimulator. In 2009, Apnex Medical reported that they are currently conducting a clinical trial [183].

![Figure 3.28: Description of the hypoglossal nerve stimulation (HGNS) device from Apnex Medical™[183]](image)

Also in 2009, Inspire Medical Systems reported that they too are developing an almost identical implantable neurostimulator. In a paper by Kezirian et al., they presented results from human trials on eight patients with the Inspire device. Previous studies have indicated that the genioglossus in particular (one of the major tongue muscles), plays an important role in keeping the upper airway open during sleep [184]. Therefore, stimulation of the hypoglossal nerve was started four weeks after implantation and adjusted for each patient. The effect of stimulation on breathing and sleep architecture is demonstrated in Figure 3.29; before stimulation is turned on, there is a clear pattern of hypopneas. After stimulation, a normalization of respiration and oxygen saturation occurs. A stimulus artifact is visible on the EMG signal during stimulation, confirming that the muscles are stimulated. At the same time, there is an absence of arousals on the EEG signal which indicates no disturbance of the patient’s sleep [185].

![Figure 3.29: The effect of hypoglossal nerve stimulation on sleep and respiratory parameters. From Kezirian et al. [185]](image)
3.4.3 Air mattress sensor systems and ballistocardiography

The principle of ballistocardiography (BCG) has been known for more than 50 years, and is a simple, noninvasive method to record the body movement due to left ventricular pump activity [186]. In other words, it can be used to measure heart rate from the mechanical force that the heart exerts on the body.

![Figure 3.30: The principle of ballistocardiography based on a suspension table (left) [186]. Comparison of BCG and ECG signal (right). From Eichmeier et al. [187]](image)

The heart ejects the blood mainly upwards along the ascending aorta, and when it pulls the blood back in, the motion is also mainly along the axis parallel to the spine. Hence, the major motion is longitudinal. According to Newton’s 3rd law, the force exerted on the blood by the heart is the same as the force on the body by the blood, but in the opposite direction.

The principle of BCG is shown in Figure 3.30 (a); a patient is placed on a table with very low friction, so that the force on the body by the blood causes the body and table to move back and forth. There is no need for electrodes to be connected to the subject; the body impulse transmitted to the table can simply be recorded by adequate transducers, i.e. displacement, force, or acceleration measurement. Because the mass of the accelerating blood is small in comparison with the table and patient, measurement errors have been large. But modern signal processing techniques have reduced these errors, so that BCG is nowadays often used in medical contexts, primarily in teaching cardiac cycle physiology [186].

![Figure 3.31: Air mattress sensor system [188]](image)
3 Existing diagnosis and treatment options

Shin et al. has used the principle of ballistocardiography in an air mattress sensor system (air-mattress with balancing tube, AMBT) seen in Figure 3.31; the bed type sensor is implemented by a pneumatic pressure transducer, air mattress, and balancing tube (a, b). The raw signal from the air mattress (c) is separated into heart rate (d, lower signal; upper signal ECG), respiration signal (e, lower signal; upper signal flow measurement), and snoring (f, blue signal from air mattress; red signal from microphone). They tested two patients for three months and found a high correlation with the reference measurements; ballistic heart rate and ECG heart rate 98.1 %, respiration signal and flow measurement 98.6 %, and snoring signal and microphone 96.3 % [188].

The newest version of the AMBT system (2010) has multiple cylindrical air cells, two sensor cells, and 18 support cells. The physiological signals are measured by the changes in pressure difference between the sensor cells. With this sensor arrangement detection algorithms, they reported a sensitivity and positive predictive value (PPV) of 93% and 96% for snoring events, 93% and 88% for sleep apnea events, and 86% and 100% for movement events [189].

3.4.4 Microphone-based screening devices

There are a great number of simple microphone-based devices that were developed in order to register snoring events. In general, they use a sound level threshold to detect snoring.

Snoring U is an iPhone application which uses the internal microphone in order to record snoring (Figure 3.32). When the noise level is above a certain threshold (indicated with a red line), it is registered as a snore. When it detects a snoring pattern (i.e. four consecutive snores), it can play a message or give a nudge with the vibration motor (red dots). Snoring U is not a medical or clinical application, but a simple application for those who are troubled by snoring or interested in knowing how much they snore [190].

![Figure 3.32: Snoring U iPhone application from Pointer Software Systems](image)

A similar device, which uses the same principle, is the HIVOX snore watch. When three consecutive sounds above 65 dB are detected, an electrical pulse is released, which shall inform the patient to change position [191].

![Figure 3.33: HIVOX snore stopper with microphone and neurostimulator worn on the wrist](image)
3 Existing diagnosis and treatment options

Figure 3.34 demonstrates a more sophisticated microphone-based device developed by Cheng et al., which is intended for long-term telemonitoring of snoring and OSA symptoms. In a validation test with five regular snorers and five OSA patients, it showed an average sensitivity of 94% and positive predictive value (PPV) of 94% in detecting snoring. For OSA events, the average sensitivity was 81.1% and PPV 73.3%. If OSA symptoms are detected, the sound recorder records a one minute episode, so that the patient can consult a doctor for further diagnosis and treatment.

In order to differentiate between snoring and OSA, Cheng et al. used the principle of weighted intermittent snoring ratio (W-ISR). As seen in Figure 3.34, the patient stopped breathing after a series of snoring and started snoring (and breathing) again after 34 seconds. Intermittent snoring intervals which last between 10 and 60 seconds can be registered as intermittent snoring and are assumed to be OSA related. When the interval is longer than 60 seconds it is assumed to be a sign that the patient has stopped snoring and is breathing normally. This principle was used in MESAM IV, a 4-channel screening device, which calculated the intermittent snoring index (ISI) defined as number of intermittent snoring intervals per hour in order to automatically score OSA events [193]. Cheng et al. modified ISI to a weighted intermittent snoring ratio (W-ISR) which can identify OSA symptoms in real time (every minute). Figure 3.35 shows the W-ISR of a normal snorer, which is relatively low throughout the night, whereas the W-ISR of the OSAS patient is high. The extract from the OSA patient between 04:00 and 05:00 demonstrates a good correlation between W-ISR and PSG detection of OSA episodes.
3.4.5 Sleep-Wake-Applications – Zeo Sleepwave

The Zeo Sleepwave is a low cost, wireless headband system monitoring sleep with dry fabric sensors that acquires EEG, EOG, and EMG information on a single channel. The goal is to monitor and report trends on sleep data such as total sleep time (TST) and sleep efficiency (SE) to the user. They tested the system on three healthy subjects who were co-monitored in the sleep lab with the headband system and PSG. Their preliminary results versus PSG were TST \(326 \pm 22.5\) minutes versus \(307.9 \pm 30.1\) minutes and SE \(81 \pm 3\%\) versus \(76 \pm 5\%\), suggesting that further data collection and analyses are needed to evaluate the system [194]. The inclusion of further sensors is not foreseen.

Figure 3.36: Zeo Personal Sleep Coach wireless headband with computer software. Adapted from Zeo, Inc. [195]

3.5 Summary

The available diagnosis and therapy options are allocated according to degree of diagnosis and therapy. The traditional partitioning of diagnosis and therapy is of interest: After an initial diagnosis and start of treatment, there is a very limited possibility of follow-up measurement to see how the treatment efficiency and symptoms develop.

The right therapy option depends on numerous factors. A simplified overview of therapy alternatives according to level of disease is summarized in the figure below.

Figure 3.37: Therapy alternatives according to level of disease and efficiency
4 Development and evaluation

4.1 Starting point of proposed system

The project was first initiated with a bachelor thesis by the author at the Heinz Nixdorf-Chair for Medical Electronics at TU München [196]. The purpose was to see if an intra-splint sensor platform that was developed to detect bruxism events [197] could also be used to detect snoring events. Different sensors were tried out in the intra-splint prototype (Figure 4.1).

Figure 4.1: Intra-splint prototype with external components in order to find a suitable sensor for snoring detection [196]

An accelerometer was found suitable for the purpose of snore detection. Up to now, most devices use a microphone to detect the sound of snoring. This requires a sound level through the air, and the microphone must therefore be attached to the patient externally. An accelerometer, on the other hand, detects the vibrations from snoring as changes in acceleration and can therefore be potentially built into a closed implant system like a tooth splint. In the thesis, it also became obvious that the DC component of the accelerometer signal was defined by the head position because of the influence of gravity on the axes.

Figure 4.2: First headband prototype used to analyze the possibilities with different analog accelerometer; measurement possibilities with an analog 3D-accelerometer as determined in the previous work [198]
In the following master thesis, the possibilities with the accelerometer were therefore investigated [198]. The thesis indicated that sleeping position, movement, and heart frequency could be detected by a 3D-accelerometer, as shown in Figure 4.2. The heart rate signal was detected by the accelerometer as the slight body movement imposed by the pulse of blood. With the use of active filters, the different frequency ranges of the different parameters could be split up from the accelerometer signal.

![Figure 4.3: SPICE simulation model showing the complexity of analog signal filtering and amplification in order to detect sleeping position, snoring, heart rate and breathing movement [198]](image-url)

A questionnaire was distributed to receive opinions on such a device. The main reason for wanting a device is suspicion of sleep apnea, and the device should be a calibrated product delivered by a dentist/doctor indicating both the severance of the snoring problem and appropriate treatment options. The preferred diagnostic device would be in the form of a headband, followed by an adhesive patch, tooth splint, and eye mask. For the sleeping partner, a tooth splint is preferred.

In the course of the master thesis, the complexity of the assignment became clear; as seen in Figure 4.2 and Figure 4.3, the analog signal from the accelerometer had to the split up into snoring, heart rate, and breathing movement with active filters, which ended up having a high complexity in order to filter and amplify efficiently, hence requiring a lot of space on the PCB and high current usage. This would make it difficult to develop a comfortable, miniaturized sensor system and impossible to include in for example a tooth splint [198].
Hence, further research would be needed in order to demonstrate the full potential of an accelerometer-based sleep monitoring, which is part of the purpose of this thesis. First, the measurement principle will be explicated.

### 4.2 Measurement principle

As indicated in the previous work, it is possible to use an accelerometer in order detect the heartbeat, breathing movement, and vibrations from snoring generated by the body. It benefits from the fact that the body is at rest with little or no other movement. Also, the heartbeat, breathing movement, and snoring are periodic signals which occur in distinct patterns. This was only possible because of the emergence of new, miniaturized accelerometers with high resolution and low noise, known as MEMS accelerometers.

#### 4.2.1 MEMS accelerometers

MEMS (microelectromechanical systems) started to evolve from the integrated circuit industry in the mid-1960s, but it was not until the 1990s that it received its name (MEMS) and entered a period of rapid and dynamic growth worldwide that was supported by government and private funding agencies. Several companies also conducted research, that lead to successful products which integrate both mechanical elements and electronics in one chip. The most famous example is perhaps the integrated inertia sensors by Analog Devices which were developed for automotive air-bag deployment, and which today has led to a broad spectrum of possible applications with accelerometer measurement including the measurement system in this thesis [199].

##### 4.2.1.1 First developments

The first Analog Devices accelerometer was developed with a MEMS process, the ADXL series, had a suspended mechanical element and signal-processing electronics integrated on the same substrate. The initial purpose was to monitor the immense negative acceleration in the event of a collision, so that air-bag deployment can be automatically initiated. The sensing principle is shown in Figure 4.4; the mechanical sensing element is a free-moving proof mass, suspended by four support rings. Interdigital finger electrodes are connected to the proof mass, with fixed finger electrodes in between. In this way, the fixed and moving electrodes form a bank of parallel-connected capacitors. The total capacitance depends on the distance between the moving and fixed fingers and hence on the inertial force on the proof mass \(F = m \times a\).

The capacitance change is detected using on-chip signal-processing electronics. The integration of both mechanical elements and electronics in one chip is critical for reducing noise and avoiding parasitic capacitance from long conductor leads. The MEMS technology therefore offers some significant advantages in terms of high sensitivity and low noise in a small package, when comparing to macroscopic electromechanical sensors. It also eliminates manual assembly steps with batch fabrication, decreasing the cost per sensor [199].
Prior to the silicon MEMS invention, accelerometers were mechanical, hand-assembled from metal parts and typically had a suspended mass and a detection mechanism, and cost more than $500 per unit. The migration to silicon in the mid-80s lowered the price to under $100 [200]. From that point on, the automotive applications were to motivate the inertial sensor development with its applications. The use in airbag control systems soon made accelerometers one of the largest volume micromachined products and drove the price to less than $10 per unit by the early 1990s. The design requirement for airbag systems is typically 20 to 100 g full-scale for front impact airbags and 100 to 250 g full-scale for side impact airbags, but low-g accelerometers in the range of 0.5 to 10 g are also needed in vehicle dynamics for active suspension systems. Future safety systems will even require further development and more sensors to adjust the rate of airbag deployment according to impact location, occupant position and weight and crash severity, and accelerometers will be increasingly integrated in cars and used in other safety systems such as traction control and rollover safety systems [201].

4.2.1.2 State of the art
Further development driven by the automotive requirements mentioned has also made advanced features like three-axis sensing and ultra-high sensitivity in nano-g range available, even in low-cost accelerometers for consumer products, leading to broad spectrum of new applications such as:
4 Development and evaluation

- Smart writing instruments (detect and transmit handwriting strokes to computer)
- Virtual-reality headgears and electronic game controllers (Nintendo Wii)
- Sport utilities such as actigraphy, step counters [202] and shoes that measures running distance
- Hard disk drive protection (stop the spinning of the hard disk immediately if it is accidentally dropped) [203]
- Camera and video camera motion correction
- Automatic display rotation on handheld devices

Figure 4.5 demonstrates the broad variety of applications possible with a MEMS accelerometer integrated in a mobile phone, as listed by Freescale Semiconductor, Inc. [204]. The production technology can also be easily modified to produce rotational sensors or gyroscopes, enabling even more applications such as gyro computer mouse [199].

4.2.1.3 Future roadmap

Today, the strongest growth markets for inertial sensing are in smart phones, gaming and toys [204]. There is also a wide variety of MEMS accelerometers based on different sensing principles available: capacitive sensing, thermal transfer, optical interferometry, piezoresistivity, and piezoelectricity. Current and further development will see an expansion of the capacitive sensors when it comes to performance and price, as seen in the future roadmap from Analog Devices in Figure 4.6 [205].

Figure 4.5: Multiple solutions with only one MEMS accelerometer integrated in a mobile phone. Adapted from Freescale Semiconductor, Inc. [204].

Figure 4.6: Accelerometer technologies in 1998 (left), current and future roadmap of development (right). Adapted from Analog Devices, Inc. [205]
This shift will mainly go in the direction of low-cost accelerometers (< 1 €) with low current usage (< 200 µA), which will also mean moderate to high noise values (~ 200 µg/√Hz) and low to average resolution (8-12 bit). These accelerometers will meet the requirements of most applications in the growth markets, as confirmed by application specialists from Analog Devices and STMicroelectronics.

4.2.2 Ideal placement of the accelerometer

In the previous works, the accelerometer has been tested in a tooth splint and in a headband with promising results. The vibrations from snoring originate in the soft tissues in the mouth, which are connected to the skull. Hence the vibrations propagate from the soft tissue to the skull, where the accelerometer can be attached in order to register the vibrations as change in acceleration. But, to obtain a maximum transduction of the biosignals emerging from snoring and movement to the accelerometer the human skull anatomy has to be analyzed.

4.2.2.1 Skull anatomy

The human skull is a bony structure divided in two parts, the cranium and the mandible as seen in Figure 4.7. Whereas the mandible is movable, the cranium is fixed. This means that an accelerometer placed in an upper-jaw tooth splint will be expected to deliver the same results as an accelerometer placed in a head band on the forehead.

![Figure 4.7: Facial bones and muscles. From Patel et al. [206]](image)

Further, when considering the facial muscles, also seen in Figure 4.7, the center of the forehead seems to be an ideal placement to pick up the vibrations from snoring, since the forehead is only covered by the *frontalis* muscle (2, Figure 4.7) on both lateral sides. In the center is the *galea aponeurotica* (1, Figure 4.7): a layer of dense fibrous tissue covering the upper part of the cranium [206]. Other facial placements would mean a signal transduction through an additional layer of muscle tissue, creating an uneven basis for sensor placement. This would make it difficult to ensure repeatability of the measurement considering signal amplitude and recording of head position. A placement of the accelerometer on the lateral or anterior side of the cranium is difficult since these parts are covered with hair. It is also painful to sleep directly on the accelerometer. A possibility would be to place it in an
earplug; however this would require an extreme miniaturization in order to provide comfortable sleep in the lateral sleeping position.

The previous works have also indicated that the heart beat can be detected with the accelerometer. The assumption is that the powerful beat of the heart creates a tiny movement throughout the body which is detected as change in acceleration. This is known as \textit{ballistocardiography} and was thoroughly described in chapter 3.4.3 on page 56. But, considering the artery supply of the forehead demonstrated in Figure 4.8, it must be investigated if this holds to be true or if the pulsation through the arteries also has an influence.

![Figure 4.8: Artery supply to the forehead. From Seline et al. [207]](image)

### 4.2.3 Similar usage of the same measurement principle

The principle of using accelerometers to measure parameters relevant for sleep-related breathing disorders has also been investigated by other researchers.

#### 4.2.3.1 Patient respiration measurement

In an application note, Analog Devices, Inc. describes how an accelerometer can be used to measure patient respiration measurement. By placing it on the chest, the accelerometer detects the rise and fall of the chest due to respiration movement. It can also be used together with thoracic body impedance respiration measurement for a more reliable measurement, to compensate for patient movement and poor electrode connections [208].

#### 4.2.3.2 University of Cadiz

During the course of this thesis, a project from the University of Cadiz in Spain with a similar usage of the same measurement principle was discovered. According to the US patent application, they are claiming \"a method of monitoring and processing cardio-respiratory and snoring signals, the method comprising: securing an acceleration sensor to skin of a patient at the suprasternal notch; collecting from the sensor a continuous acceleration signal that includes acceleration components indicative of cardiac, respiratory and snoring parameters; and filtering the signal\" [209].
Although similar, the project uses an analog accelerometer with high current consumption (mA) and is only to be used for OSA screening. This is limited to the supine position because of limitations in signal transduction. Also, therapy monitoring or therapy is not foreseen [210].

4.2.3.3 Actigraphy – Sleep-Wake detection
At the sleep laboratory, an accelerometer is used for body position measurement and further accelerometers can be attached to the feet in order to detect restless leg syndrome (RLS). But outside the sleep laboratory it has also been used for automatic sleep-wake detection based on actigraphy; using smart algorithms, the amount of activity can be correlated with the probability of being awake.

In Figure 4.10, an example of registered activity with two actigraph watches compared to sleep stage scoring at the sleep laboratory can be seen. The amount of activity correlates well with being awake, so that current algorithms can detect sleep-wake patterns with 80 % agreement [211].
4.3 Evaluation prototype

4.3.1 Overview

Based on the knowledge from the previous work and scientific research presented in the previous chapters, a new evaluation prototype was developed with the components shown in Figure 4.11. The prototype was developed in multiple steps and mainly attached as a headband for evaluation. The components of the final evaluation prototype are described in this section. The evaluation prototype was first used to record and evaluate data from the accelerometer sensor.

Figure 4.11: Schematic overview of the evaluation prototype
4.3.2 Microcontroller input

4.3.2.1 Digital accelerometer

In the previous works, an analog accelerometer had been used – its disadvantages are described in chapter 4.1. At the same time a new type of accelerometer had been developed enough to be of interest: digital accelerometers, which have a built-in analog/digital converter (ADC), delivering a digital signal direct to the microcontroller over a (shared) data bus. This eliminates the need of analog filters and high-resolution, external ADCs. The advantages and disadvantages of analog versus digital accelerometers are listed in Table 4.1.

<table>
<thead>
<tr>
<th>Analog accelerometer</th>
<th>Digital accelerometer</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Filtering can be done by analog filters which reduces digital processing required</td>
<td>+ Digital communication allows for a more flexible setup of sensor output</td>
</tr>
<tr>
<td>- Active analog filters required, which demands extra components (operational amplifiers, resistors, capacitors, etc.)</td>
<td>+ Digital accelerometer has built-in digital filters and sleep modus</td>
</tr>
<tr>
<td>- Amplification of low frequencies difficult to control (large capacitors required → slow decay)</td>
<td>+ A/D-conversion done by sensor itself, no external ADC needed and thus noise from analog components is avoided</td>
</tr>
<tr>
<td>- Optimization of analog filters difficult</td>
<td>- Digital signal processing requires more usage of microcontroller</td>
</tr>
<tr>
<td>- No sleep mode</td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1: Differences between analog and digital accelerometers

Because of the many advantages and the need for a miniaturized sensor system, it was decided to evaluate different digital accelerometers. It is of course important that noise levels are extremely since snoring has relative high frequency components and the noise is related to bandwidth (typ. µg/√Hz). But extremely low current usage is also of importance, which means higher noise levels, and a trade-off had to be found. Since the signal amplitude levels are expected to be low, a high resolution is also needed.

At the start of the project, Bosch offered one of the lowest current-consumption accelerometers on the market, SMB380 [215]. In preliminary tests it was already clear that the noise level was too high, that is higher than the signal levels when simulating snoring and breathing movement. Hence, the current/noise trade-off together with the poor resolution (8-bit) was too low to detect the desired parameters related to sleep-disordered breathing.

<table>
<thead>
<tr>
<th>Accelerometer</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMB380 [212]</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td>ca. 10 / ca. 30</td>
</tr>
<tr>
<td>Current / Standby</td>
<td>200 / 1 / &lt; 1000 / 1 µA (typ.)</td>
</tr>
<tr>
<td>Noise density</td>
<td>500 / &lt; 100 µg/√Hz</td>
</tr>
<tr>
<td>Measuring range</td>
<td>± 2 / ± 2 g</td>
</tr>
<tr>
<td>Max. resolution</td>
<td>8 / 16 bit</td>
</tr>
<tr>
<td>Max. sensitivity</td>
<td>256 / 16384 LSB/g</td>
</tr>
</tbody>
</table>

Table 4.2: The digital accelerometer to be evaluated compared to SMB380
On the other side of the spectrum, there are conventional MEMS accelerometers with 16-bit resolution, higher current usage (< 1 mA), and larger size, but with very low noise levels (< 100 µg/√Hz). Such an accelerometer was therefore integrated in the evaluation prototype for thoroughly testing.

The digital accelerometer communicates with the microcontroller via SPI (serial peripheral interface) as demonstrated in Figure 4.12. The SPI interface (MOSI, MISO, SPI serial clock SCLK) was connected to the microcontroller according to the SPI standard. The CS (chip select) is connected to the microcontroller using a pull-up resistor since CS is active low. Hence, if the accelerometer CS is set low by the microcontroller, the accelerometer is activated and can start communicating with the microcontroller. In this way, multiple slave devices can communicate with the microcontroller (master) using the same SPI bus. Instructions and data read out commands are sent from the SPI master on the MOSI (master out slave in) pin, whereas sampled data and status conditions are communicated by the slave via the MISO (master in slave out) pin. The interrupt pin can indicate when a set of new acceleration data is available and shall be used to find an optimum sampling rate. To ensure minimum noise, power supply decoupling capacitors were placed as near the accelerometer voltage supply as possible.

![Figure 4.12: Electrical connections between the accelerometer and microcontroller](image)

4.3.2.2 Microphone for reference measurement
A microphone was used as the reference for the accelerometer snoring recording. The microphone has a constant sensitivity of -46 ± 3 dB from 20 to 2000 Hz, and was therefore suitable for recording snoring. An amplification and filter circuit was also implemented in order to reduce noise and amplify snoring frequencies.

4.3.2.3 Buttons
The evaluation prototype was fitted with buttons which were connected to I/O pins on the microcontroller with interrupt enabled. In this way, different functionalities such as the biofeedback signal could be (de)activated without reprogramming the microcontroller.

4.3.3 Microcontroller
In the previous works, an 8-bit PIC microcontroller with 20 pins from Microchip was used. But, with a 16-bit output digital accelerometer, memory card, and the demands of low current usage, a new microcontroller had to be found. The choice fell on a microcontroller from the MSP430 2xx 16 MHz 16-bit series by Texas Instruments which has:

- 16-bit architecture, meaning that it can easily operate and store 16-bit integers,
- 1024 Byte RAM – the memory card alone requires 512 Byte for data buffering and
- less than 1 µA supply current in low-power mode (LPM3) [213].
With the MSP430, a better power management with extremely low supply current in low-power mode is possible. The only disadvantage is the maximum current 2 mA on an I/O-port, meaning that for example LEDs must be switched on by transistors or be limited to a maximum current of 2 mA.

### 4.3.4 Microcontroller output

#### 4.3.4.1 Vibration motor (Biofeedback signal)

A vibration motor shall be tested as positional therapy. That is, with a vibration signal, the patient shall learn to avoid certain practices such as sleeping on their back. A vibration motor is an electrical motor with an unbalanced mass on its shaft. When the motor is turned on, the unbalanced mass rotates and causes vibrations.

There are different vibration motors available on the market. The problem is that they all require up to 100 mA start-up current at 1.5 V (because of the unbalanced mass), which is impossible to deliver over an I/O port from the microcontroller. The solution is to switch on the motor by the microcontroller using a transistor, and with the current supply stemming directly from the battery. Also, the strength of the vibrations has to be adjustable so that the biofeedback signal can be set individually and with minimum sleep disturbance. Since the microcontroller lacks an analog output and to avoid the use of an external motor driver, the PWM (pulse width modulation) output was used to create a variable output signal.

#### 4.3.4.2 Status LEDs

Four LEDs (light emitting diodes) were included and can be turned on by the microcontroller to provide status messages, i.e. successful initiation of accelerometer, microSD card or biofeedback therapy activated. Because of the MSP430 I/O diode current of ± 2 mA, special low-current LEDs were selected.

#### 4.3.4.3 Quartz crystal 32768 Hz

An external quartz crystal 32768 Hz was included for low-power management and real-time clock implementation on the microcontroller. The MSP430 has different operational modes with different power usage. At 8 MHz, it uses approximately 3.3 mA in active mode (AM), in low-power mode 2 (LPM2) 25 µA, LPM3 less than 1 µA and LPM4 0.1 µA. In LPM4, only an external interrupt on an I/O port can wake up the microcontroller. In LPM3, all internal clocks are also turned off, but the external quartz crystal can be used to trigger an interrupt in order to return to active mode. In addition to low-power management, the quartz crystal allows the software implementation of a real-time clock in the microcontroller C code.

### 4.3.5 Power management

A solution with a charge and system power path chip from the Texas Instruments BQ-series was included. The power management chip manages the difficult process of charging and monitoring a Li-Ion battery in order to prevent battery malfunction.
A lithium-ion polymer battery pack from Varta was chosen because it has the maximum size that fits under the PCB in the prototype, with a capacity of 150 mAh. The nominal voltage is on average 3.7 V, but varies from 4.2 V fully charged to a minimum of 2.75 V.

Since the circuit consists of both analog and digital components, a dual low-dropout regulator (LDO) was chosen to ensure an analog signal without digital disturbances, for example digital SPI bus transmission or read/write operations to the memory card. Such disturbances are attenuated by decoupling capacitors but could still influence analog signals. Also, the digital accelerometer has a dedicated analog voltage supply for the sensor element in addition to digital voltage supply for the digital interface. Hence, the dual-channel LDO divides the voltage for the circuit in digital and analog voltage supply. In order to ensure a stable data recording to the microSD card (> 2.7 V) and a higher signal resolution from the accelerometer, the digital and analog voltage supply were set to 3.3 V.

### 4.3.6 Computer communication

#### 4.3.6.1 SD card

In the previous works (Figure 4.3 on page 61), an RS-232 interface was used to transfer the data to a computer. This requires a cable connection and would also require the presence of a laptop in the bedroom of the test persons.

![Figure 4.13: Connection between a microcontroller (MSP430) and a MMC/SD card [214]](image)

Therefore, a better solution for data recording had to be found. Since the digital accelerometer has a 16-bit output and raw data has to be collected in order to investigate the possibilities of signal processing, the initial use of wireless transmission would be difficult given the large data amount generated. Thus, a possible and by way in comparison simple solution was to integrate a microSD card in the prototype. Figure 4.13 shows which connections with a microcontroller are needed. The microcontroller communicates with the memory card via SPI (serial peripheral interface). Since memory cards use the FAT file system, the data has to be buffered and written in blocks of 512 Byte. This means that the microcontroller needs > 512 Byte RAM in order to buffer the data. Also, the power supply
must be at least 2.7 V to ensure proper data transmission \[215\] - both of which have already been accounted for in the choice of microcontroller and power supply (3.3 V).

4.3.6.2 Programming interface

The MSP430 standard programming and debugging interface, JTAG (Joint Test Action Group), uses four wires for programming. The selected MSP430 supports another standard as well, Spy-Bi-Wire, which is a serialized JTAG protocol found on selected MSP430 devices. Spy-Bi-Wire requires only 2 wires for programming and debugging (bidirectional data output) and was therefore utilized \[216\].

4.3.7 Wireless communication

A wireless transceiver from Texas Instruments has been used successfully in various projects at the chair for medical electronics. Wireless communication was included to investigate the possibility of wireless transmission of measurement parameters, which is necessary if the sensor system should be further miniaturized or even built into a closed, miniaturized system such as a tooth splint.

![Diagram](http://example.com/diagram.png)

Figure 4.14: Wireless transceiver to be used for wireless transmission of certain measurement parameters

4.4 Data evaluation and signal processing in Matlab

The evaluation prototype was first used to gather data with the headband which needs to be evaluated and digitally processed in order to understand the limitations and possibilities of the sensor system. Matlab from The MathWorks, Inc. was selected for this purpose, because of the numerous possibilities in data visualization, processing and analysis \[217\].

4.4.1 Overview

A summary of the first prototype data evaluation and digital processing in Matlab to be presented in this chapter is visualized in Figure 4.15. The process is divided in three steps:

- **Data recording**: This was done in an easy way so that multiple recordings can be recorded to a microSD card and then easily be read in Matlab.
- **Raw data import and filtering in Matlab**: When a data recording is chosen in Matlab, the text file is read out and divided into the different signals recorded. The raw data from the accelerometer is divided by filters in order to split it into snoring, heartbeat, activity, breathing and sleeping position signals. The microphone raw data is also filtered.
- **Parameter detection**: Algorithms were developed in order to detect parameters related to snoring and the other signals, which then are visualized with a Matlab GUI to the user.
4 Development and evaluation

4.4.2 Data recording

A microSD card was prepared with pre-stored text-files (.txt), each of 38.1 MB (40 000 000 Bytes) size. In this way, a FAT system which is complicated to implement on a microcontroller is not needed; the microcontroller knows the sector addresses of the nine text-files and can simply write the data from each measurement in the sector part of a different text-file, and the text files can simply be read into Matlab afterwards. Each text-file can thus store 8 hours of sleep monitoring from the parameters Y-axis raw signal (16-bit) and microphone (8-bit). According to the FAT system standard, data is stored in blocks of 512 Bytes (sector). For the headband system, the data is buffered in a 512 Byte 8-bit character array and stored to the memory card as seen in Figure 4.15.

*Sync byte* is increased before a new recording starts; the first sector of the text file is read and the previous synchronizing byte is increased by one. This value is written to the first value of each sector, to be used when the values from the txt-file are read out on the computer afterwards. Since the last recording simply overwrites the values from the previous recording, this is the simplest way to know when the last recording stopped.

*Position X* is an 8-bit value calculated by the microcontroller: the accelerometer X axis is read simultaneously with the Y axis, but filtered (averaged) so that the recorded sleeping position from the X axis equals the DC signal component.

*Y-signal MSB + Y-signal LSB* is a 16-bit signed integer value from the digital accelerometer. An internal accelerometer low-pass filter of < 200 Hz was used to limit the bandwidth. When a new value is available from the accelerometer, a status register is set. By monitoring this status register, it was found that a new value was available every 2.222 ms, meaning that the sampling frequency can be set to 450 Hz. Thus, in order to keep the recorded data at a minimum and save power, the sampling rate was set to 450 Hz.
Microphone byte is an 8-bit ADC value from the microcontroller, recorded from the analogue microphone circuit on the prototype. This is used for comparison with the snore signal from the accelerometer. The sample frequency is 450 Hz.

The data recording flow-chart for the MSP430 microcontroller is shown in Figure 4.16. When a new recording is started, the yellow LED on the prototype indicates which text file is used for recording, i.e. blinks two times for output02.txt, three times for output03.txt so that the user knows which recording to view in Matlab afterwards.

### 4.4.3 Raw data import and filtering in Matlab

With the microSD card inserted into the computer, a program in MATLAB is run and the user is prompted with the input boxes seen in Figure 4.17. The sync byte makes it possible to count the number of sectors recorded so that the length of the recording in hours is known.

![Figure 4.17: In MATLAB, the recording of choice must be selected from the microSD card](image-url)
After the right recording has been selected, MATLAB needs about one minute to read out the raw signal from the digital accelerometer, the microphone and position data. The signal data are then filtered by MATLAB with 10\textsuperscript{th} order Butterworth filters (Figure 4.18); the relatively low filter order of 10 was used because of the large size of raw data which has to be processed.

Butterworth was chosen over other filter types like Chebyshev because of the smooth and constant frequency response in the passband. Experiments with higher filter orders increased the processing time tremendously because of large data arrays. For snoring and breathing it was possible to achieve a good magnitude response.

Figure 4.18: Filter on raw signal for snoring and microphone (upper left), breathing movement (upper right) and heart rate (lower left: initial band-pass, lower right: low-pass filter with better attenuation)

Figure 4.19: Frequency analysis of a raw signal with heart rate to identify the frequency bandwidth of the heart rate signal (i.e. < 15 Hz)
However, it was more difficult to achieve a satisfying magnitude response on the band-pass for the heart rate. Because of influence of snoring, which can drop to 20 Hz, a better attenuation was needed. Therefore, the band-pass was changed to a low-pass 15 Hz, 10th order, with the magnitude response also depicted in Figure 4.18. A frequency analysis of raw signal segments with heart rate signal, seen in Figure 4.19, was used to determine the upper limit of the heart rate filtering at 15 Hz. Instead of a subsequent high-pass filter, the difference between two samples was used as heart rate signal. In this way, the DC component and breathing movement were excluded from the heart rate signal.

4.4.3.1 Head position
Position recording was divided in two signals, the X axis and Y axis. As demonstrated in Figure 4.20, the X axis is used to detect lateral or supine sleeping position. Figure 4.21 explains why the X axis and not the Z axis is used for this purpose: The X axis gives a clear, almost linear distinction of the level of left/right lateral or supine sleep position, whereas the values from the Z axis are the same in both left and right direction from the supine position. Therefore, the Z axis cannot distinguish between left and right lateral position.

The Y axis is used to detect if the head is in a sleeping position, or if the patient is standing/sitting upright. The Y angle can hence be used to determine if the patient snores less if he sleeps with his head in a more upright position, or to see if the patient is sleep walking or getting up in the night.

![Figure 4.20: X axis measuring lateral and supine sleeping positions (left figure), Y axis measures head inclination (i.e. sitting, lying down)]
4.4.3.2 Noise levels
The noise levels were visually inspected with no signal input; the prototype was on a soft underlay with no disturbance and no electronic device in the room. On the raw signal and filtered snore signal, the noise peaks reached +/- 25 LSB (least significant bits). On the filtered heart rate signal, the noise peaks reached +/- 10 LSB, and +/- 0.5 LSB on the breathing signal.

4.4.4 Evaluation GUI and parameter detection in Matlab
In order to investigate signal processing and parameter detection algorithms efficiently, a graphical user interface (GUI) was developed, as demonstrated in Figure 4.23.

The user can choose to open a file from the microSD card or from a saved location (1). The window below (2) then lists the text files available on the microSD card or *.mat (Matlab file) at the saved location. Recordings read from the microSD card can be saved as a *.mat file to the saved location (3). In this way, all the filtered parameters and automatic calculations are saved to the file and the opening and visualization of the *.mat file in the GUI is done in
seconds, compared to the up to two minutes required when reading the text file from the microSD card with filtering and automatic calculations.

Figure 4.23: MATLAB GUI for visualization of filtered parameter and automatic detection

In the small window (4), automatic calculations of detected snoring, sleep/wake calculation based on movement, heart rate and breathing frequency, and sleeping position summarized across the whole recording are shown. By clicking on a location on the sleeping position plot, the user can navigate to this position in the recording.

The plots in the main window then show the raw signal (7), followed by the filtered snoring, heart rate, and breathing signal. The red dots indicate detected snoring, heart beats, and
breathing cycles. The snoring can be compared to the microphone signal (8) which is filtered with the same filter as the one for snoring signal from the accelerometer. The bottom graph (9) shows the sleeping position; the red graph is from the Y axis and indicates if the patient is lying down or sitting upright (or standing upside down), i.e. the head inclination. The blue graph indicates the degree of lateral or supine sleeping position, in this case a sleeping position far to the left lateral.

The user can use the scroll bar (10) to display the next/previous 1, 10, 30, or 60 minutes of the recording, according to the setting “select interval” (6). In addition it is possible to arbitrarily zoom in on one axis, with the zoom interval then changing on the other axes automatically.

When the user presses the “Trend” button (5), a new GUI figure appears, also shown in Figure 4.23. Here, an automatic calculation of the parameters of the night appears. A moving average filter on snoring (11) visualizes the snoring activity of the night, followed by an automatic scoring of the snoring (12). The heart rate frequency (13), breathing frequency (14), breathing amplitude (15), and sleeping position (16) throughout the night are also depicted. Finally, the percentage of supine sleep, average heart rate and breathing rate are pictured (17). The algorithms for the detection of these parameters and automatic calculation will now be explained.

4.4.4.1 Heart signal and breathing effort

The heart rate signal is band-pass filtered, as already described, and then peak detection algorithms were used to find the peaks. By taking the quadratic signal of the filtered heart rate signal, the peaks from the heart pulse were amplified and peak detection could be used to find the peaks over a certain amplitude (red horizontal line). Then, the time interval had to correspond to heart rate, with a minimum of 30 beats per minute (BPM) and a maximum of 220 BPM. Subsequently, the time interval had to be between 0.272 and 2.0 seconds for the peaks to be considered as valid heart rate, or else they would be discarded as noise.

In a similar, but simpler way, breathing effort could be found. The breathing effort with its periodic nature was calculated by finding the positive peaks on the breathing signal; the amplitude before the peaks indicates breathing amplitude and the time interval between two peaks, breathing frequency.
Figure 4.25 illustrates an example where both heart rate and breathing amplitude were detected. The breathing movement signal seems to be very reliable since it is correlated with snoring upon breathing. It should be noted that the heart rate signal could be filtered despite snoring overlapping on the raw signal.

4.4.4.2 **Snoring and respiratory disturbances**

In Figure 4.25, the verification of snoring detection from the raw signal versus microphone recordings of snoring can also be seen. Snoring, with its periodic pattern, can therefore be put through a moving average filter with peak detection in order to register snoring; if the time interval between two peaks is valid, it is registered as snoring. A moving average filter was found suitable as verified in Figure 4.26, showing one hour recording from a snoring test person in the night (GUI window “Trend”). The moving average of snoring signal in the upper graph indicates that the snoring starts after about 20 minutes and was successfully detected by validating the time interval between peaks. It should also be noted that breathing amplitude increases before snoring starts, which could be used as an indicator for the level of airway resistance. The lower part of the figure is a zoom on a small segment of the recording, which shows the individual detected snoring peaks.

Figure 4.27 shows another 30 minute example from a recording with a snoring test person which shows a similar pattern to the recording from the other test person (Figure 4.26); the breathing amplitude increases and then, as detected by the moving average snoring signal, the snoring starts. However, it can be seen that short periods of two-three snores correlated with an increase in breathing amplitude at the end of the recording (zoom segment), indicating obstructive sleep apnea according to ICSD-2 [37] and observations from the sleep laboratory.
Figure 4.26: Snoring detection from a snoring test person; one hour zoom in the GUI window “Trend” (top) and a one minute zoom segment (bottom)
Figure 4.27: Detection of respiratory disturbances; increased breathing amplitude correlated with snoring followed by decreased breathing amplitude and no snoring, indicating obstructive sleep apnea.
In comparison, Figure 4.28 shows a one hour recording of a test person without snoring or respiratory disturbances. It should be noted that during this calm normal sleep with no position changes, the heart rate, breathing frequency, and breathing amplitude are all stable. The breathing amplitude without any obstruction is also very low, making it hard to provide a reliable breathing frequency and amplitude recording in those without SBD.

4.4.4.3 Sleep-wake scoring based on movement detection (actigraphy)

Actigraphy can be used for sleep-wake detection based on the principle that a lack of movement indicates sleep, whereas the presence of movement indicates wakefulness. Actigraph watches have been used for the purpose of sleep quality and sleep efficiency, as mentioned in chapter 4.2.3, demonstrating a correlation of more than 80% with polysomnographic classification of sleep-wake. In this project, such an indication of movement and sleep-wake detection using the accelerometer would support the quality of a long-term monitoring of sleep-related breathing disorders, and was therefore implemented.

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity</th>
<th>Complexity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sadeh [218]</td>
<td>94.35 %</td>
<td>Low</td>
<td>78.9 %</td>
</tr>
<tr>
<td>Sazonov</td>
<td>93.2 %</td>
<td>Low</td>
<td>75.4 %</td>
</tr>
<tr>
<td>Webster</td>
<td>-</td>
<td>High</td>
<td>83.86 %</td>
</tr>
<tr>
<td>MLP</td>
<td>94.4 %</td>
<td>High</td>
<td>80.3 %</td>
</tr>
<tr>
<td>Decision tree</td>
<td>94.6 %</td>
<td>High</td>
<td>82.1 %</td>
</tr>
</tbody>
</table>

Table 4.3: Comparison of different algorithms for sleep-wake scoring based on actigraphy [219]
First, a simple and reliable algorithm had to be found. Since the development of a new algorithm would be extremely difficult and time consuming, existing algorithms found in the research were investigated and are summarized in Table 4.3.

From these algorithms, the Sadeh algorithm was the most promising, with low complexity, high sensitivity, and fairly high accuracy of almost 80%:

$$PS \text{ (minute)} = 7.601 - 0.065\mu - 0.056\sigma - 0.0703LogAct - 1.08NAT$$

Equation 4.1: Sadeh algorithm, as developed by Sadeh et al. [219]

The Sadeh algorithm from Equation 4.1 was developed by Sadeh et al. in 1994 by identifying the five most efficient variables derived from actigraphy. Based on the analysis of these variables, the algorithm identifies the current epoch (one minute) as sleep if the sleep indicator is higher than zero (i.e. $PS \text{ (current epoch)} > 0$) [219]:

- $\mu$ is the average activity in a 11 minute window centered on the current epoch (current minute $\pm$ 5 minutes)
- $\sigma$ is the standard deviation of the activity in the last six minutes including current epoch
- LogAct is the natural logarithm of the activity in the current epoch increased by one
- NAT is the number of epochs that has an epoch activity between 50 and 100 in an 11 minute epoch centered on the current epoch

The algorithm was modified and implemented in the Matlab GUI as shown in Figure 4.29 below. For the activity signal, a low pass filter at 1 Hz was used to filter find activity, since the body movement is concentrated below 1 Hz [220].

![Figure 4.29: Implementation of the Sadeh algorithm in Matlab](image)

Figure 4.30 illustrates how the algorithm works; the activity is strongly correlated with position change. The amplitudes up to 25 on the activity signal are from breathing and heart rate, therefore the calculated mean of the activity was not calculated as in the original Sadeh algorithm, but as in a number of samples, above the amplitude 25. NAT was therefore also modified to fit the head mounted accelerometer measurement and defined as 1 if the mean for that minute was above 100 (i.e. more than hundred samples above amplitude 25), or otherwise 0. In this way the PS and sleep-wake detection correlated with the amount of movement on the activity signal.
4.4.4.4 Sleeping position and biofeedback therapy
The recording of the sleeping position is important in order to identify positional patients, i.e. patients who primarily snore or have respiratory disturbances when sleeping on their back (supine sleeping position). Further, the evaluation prototype has a vibration motor included which shall be used for the purpose of biofeedback therapy in order to avoid the supine position in positional patients. The limits for supine sleep were originally defined as 30° rotation from the supine position in either the left (L-Sup) or right (R-Sup) direction (Figure 4.20).

Figure 4.31 demonstrates the impact of biofeedback therapy on a sleeping subject; the test person turned over from the left position to the supine sleeping position and after a few seconds the vibration motor automatically started to vibrate softly with increasing magnitude. After a few seconds, the test person responded to the vibration alarm by turning over to the right lateral position.
4.5 Evaluation of placement options and improved data recording

After the initial evaluation of the accelerometer in a headband, a new data recording management system was developed. This was done to both allow multiple placements of the accelerometer to be recorded simultaneously for comparison, such as headband and tooth splint, and to prepare for more advanced data analysis and sleep laboratory verification.

4.5.1 Improvement of data recording management

The data management system was changed in order to simultaneously record raw data from two accelerometers and prepare for comprehensive studies of signal processing possibilities.

Since only 8-bit values can be stored on the microSD card, the 16-bit accelerometer values are divided into 8-bit MSB (most significant bits) and 8-bit LSB (least significant bits). In addition, two more slots for 16-bit variables (var#1, var#2) were needed to investigate other parameters and signals such as the raw data from the X axes of the accelerometers. A real-time clock was also implemented in the software on the microcontroller so that a time stamp is recorded for each data point.
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stamp is available in every block of data (512 Byte), on the microSD card. Because of the large amount of data signals to be recorded, a single text file of 40 MB will not be sufficient for a one night recording; therefore number of text files on the 2 GB card was expanded from 9 to 25, and the microcontroller was programmed to continue the recording in the next text file on the microSD card when a text file is full. With the synchronizing byte and time stamps, the Matlab data import is able to identify how many text files must be read in order to read the complete recording.

4.5.2 Comparison of placement options

An important aspect of developing a long-term monitoring and therapy system for sleep-related breathing disorders is off course the placement of the device to ensure minimal disturbance to the patient and ensure firm attachment so that patient compliance and signal quality are guaranteed on a long-term basis. Based on the comprehensive study of literature, existing systems, and consulting sleep experts, three placements with different advantages and disadvantages were investigated as seen in Table 4.4.

<table>
<thead>
<tr>
<th>Headband</th>
<th>Tooth splint</th>
<th>Patch</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>- Headband can move or fall off in the night</td>
<td>- Must be individually assembled by a dental technician</td>
<td>- Patch must be changed on a daily basis and would lead to skin irritation if used for long-term monitoring (\rightarrow) only reasonable if used for screening assessment</td>
</tr>
<tr>
<td>- Depending on head sleeping position, the firmness of the sensor attachment varies, leading to signal variance</td>
<td>- Batteries must be recharged in the tooth splint (i.e. inductive charging), vibration alarm and data recording in external unit</td>
<td></td>
</tr>
<tr>
<td>- Easy to use on multiple patients, individual adjustments with straps</td>
<td>- Sensor firmly attached to the teeth, not visible</td>
<td>- Strap or cable for attachment not needed</td>
</tr>
<tr>
<td>- Vibration alarm, data recording, all in one unit</td>
<td>- Mandibular retaining devices used as treatment</td>
<td>- Vibration alarm, data recording, all in one unit</td>
</tr>
</tbody>
</table>

Table 4.4: Advantages and disadvantages of different placement options

4.5.2.1 Headband prototype assembly

The headband option has already been thoroughly investigated in the first evaluation prototype and the improved second evaluation prototype is also based on this solution. It has the advantages that that it is easy to test on multiple patients and has the complete hardware in one unit. But, it is not firmly attached to the head and could fall off in the night or lead to signal variance according to strap adjustments and sleeping position.
4.5.2.2 Tooth splint prototype assembly and tests

The *tooth splint* option is highly interesting because a miniaturization of the hardware, wireless transmission and extreme utilization of low-power management could lead to the direct integration of the sensor system into a tooth splint, such as a mandibular retaining device. The sensor is firmly attached to the teeth and not visible to the sleep partner, which could be an argument for better patient compliance.

However, it is a challenge to integrate the accelerometer measurement into the tooth splint because of the current usage; in order to be used as a long-term management system the batteries would require recharging from an external unit, for example with inductive charging. In the previous work, it was confirmed that snoring detection is possible when the accelerometer is attached to the teeth. Therefore, just the digital accelerometer was integrated in a PMMA\(^1\) tooth splint, as demonstrated in Figure 4.34, to verify if the results are comparable to the measurement in a headband.

\[1\] Poly(methyl methacrylate); standard material for dentures and tooth splints
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electric wires with protective coating. The electric wires were then channeled to a biocompatible Tygon flexible tube and the accelerometer was dipped in protective, biocompatible lacquer up to be point of the Tygon flexible tube. In this way, the accelerometer was hermetically sealed in a water-proof coating and could be molded in PMMA on a tooth profile cast (Figure 4.34).

Figure 4.35: Assembly of the accelerometer tooth splint integration

With the electric wiring connected to the microcontroller in the headband via SPI and to the analog and digital power supplies of 3.3 V, the recording from the tooth splint accelerometer can be done simultaneously with the headband accelerometer for direct comparison.

Figure 4.36: Testing with the tooth splint accelerometer; simulated snoring on and visible heart rate on raw signal; one hour of sleep with testing person without snoring

Figure 4.36 demonstrates initial testing with the tooth splint accelerometer. The ability to detect snoring was done by simulating snoring (top). The heart beat can also be seen on the
raw signal. The one hour recording on a test person without snoring demonstrates that heart rate and breathing parameters can be detected as well, and is comparable to the one hour recording with the headband demonstrated in Figure 4.28 on page 84.

A direct comparison between headband and tooth splint measurement was also made; according to the new data management shown in Figure 4.32, raw data from two accelerometers can be recorded simultaneously. The X axes from both accelerometers were also recorded in this context to investigate if the recording of an additional axis would be beneficial.

![Figure 4.37: Raw data from Y, X and Y+X (combined) axes from headband in comparison with Y and X axes recorded simultaneously.](image)

![Figure 4.38: Raw data with simulated snoring from headband and tooth splint](image)
Figure 4.37, taken from a recording on a sleeping test person, exhibits how the Y axis of both headband and tooth splint is sufficient to detect both breathing and heart beats. The X axes have a lower sensitivity and the combination of the X and Y axes does not improve signal quality in most cases. Moreover, the combination of two axes makes it even more difficult to determine the heart rate since the pulse components of the Y and X axes’ raw signals have slight offsets.

Simulated snoring was also tested with Y and X axes from both headband and tooth splint (Figure 4.38), demonstrating a comparable detection of snoring. Again, the additional inclusion of X axis recording is not needed to enhance the signal quality of snoring recording.

4.5.2.3 Patch prototype assembly and tests

The patch option has the advantage that no strap or cable is needed to attach the sensor to the body firmly. Testing was conducted with the patch attached to the forehead, with similar results as with the headband and tooth splint option. But, the patch must be removed from the skin on a daily basis, which is not a realistic option for long-term monitoring system (skin irritation, costs). The only meaningful application would be a screening system for a single night. However, since the University of Cadiz has filed a patent application for such a device (screening of OSA, device attached at the suprasternal notch), as described on page 67, the patch option was not considered further for our long-term management system.

Figure 4.39: Testing with the accelerometer on an ECG electrode patch (upper left); simulated snoring on and visible heart rate on raw signal; one hour of sleep with testing person without snoring
4.6 Automatic data interpretation software in Matlab

The presented results from the data evaluation have shown that an automatic interpretation of the results is potentially possible in Matlab, but since all parameters are mechanically recorded with only one sensor, the extracted parameters become sensitive to movement, signal artifacts and noise once they have been filtered. Also, the signals have different amplitudes, and the pulse signal has different shapes according to sleeping position, which makes an automatic detection utilizing signal amplitudes difficult. Therefore a more powerful processing was implemented, which could be especially useful for a more reliable initial screening with the device.

4.6.1 Methods for signal analysis

In order to improve reliability in automatic interpretation, a new and improved signal processing in Matlab had to be tested. Prospective methods based on signal transformation are exemplified in Figure 4.40.

Figure 4.40: Comparison of methods for signal analysis based on signal transformation. Adapted from Misiti et al. [221]

*Fourier Transform* divides the time signal in sinusoids of different frequencies and is useful for determining the frequency composition of periodic signals. As mentioned, Fiz et al. has used fast Fourier transformation (FFT) to decide between snorers and apneic patients since snoring normally has a fundamental frequency and apneic events have a broader frequency spectrum [50]. But off course, single events, and thus the severity of snoring and apneic events, cannot be decided from FFT because the time information is lost; the signals from sleep-disturbed breathing and their events are not spaced regularly throughout the recording and hence a reconstruction of the time signal is not possible [221].

The *Short-Time Fourier Transform (STFT)* is a technique to compensate for this deficit by only analyzing a small part of the signal at the time by windowing the signal. But, this is only a
compromise between time- and frequency-based observations of the signal; the window is the same for all frequencies and limits the accuracy in time and frequency [221].

Wavelet Transform is a rather new technique offering the next step towards a solution of the problem; in short, it is a windowing technique with a variable size so that low frequency information can be found with longer time intervals, and in order to obtain more accurate information, higher frequency information with shorter time intervals [221]. Wavelet-based analysis of snoring has already been used by others to obtain a denoised signal in order to register snoring from acoustic recordings [222, 223]. Because of the interesting prospects offered by wavelet transformation in terms of signal quality and the problems mentioned, it was decided to implement it in the Matlab signal processing.

4.6.2 Wavelet analysis

The wavelet analysis was investigated and implemented as a part of a master thesis [224].

An integral part was to find the right wavelet settings. Compared to Fourier analysis where periodical sinusoids with unlimited duration are used, the wavelet analysis has a defined duration with an average value of zero and normally an irregular and asymmetric shape (Figure 4.40). Instead of breaking up the signal in various sinusoidal frequencies, the wavelet analysis uses shifted and scaled versions of an original (i.e. mother) wavelet.

An efficient way to implement a wavelet analysis was described by Mallat in 1988, which is called the Discrete Wavelet Transform (DWT) [225]. With DWT, the scales and positions are chosen based on the powers of two (dyadic scales and positions) which have the same accuracy but are much more efficient.

The method can be seen as a type of filtering, although it is time-scale and not time-frequency based; the signal S is decomposed in approximations A (high-scale, low-frequency components) and details D (low-scale, high-frequency components), as demonstrated in Figure 4.41. Afterwards, the approximation and detail signals are downsampled and both decomposed in A and D again. The process can be continued indefinitely in theory, but in practice a suitable number of levels has to be selected based on the nature of the signal [221].

Figure 4.41: Example of a one-stage discrete wavelet transform (DWT) decomposition of a signal and the iterative DWT process to obtain the desired signal [221]
Afterwards, the discrete wavelet transformation the components can be reconstructed the original signal $S$ by the inverse discrete wavelet transformation (IDWT) without loss of information. Hence the reconstruction consists of upsampling and filtering as demonstrated in Figure 4.42 (left) [221].

![Figure 4.42: Decomposition (DWT) and reconstruction (IDWT) of the original signal (left). Reconstruction without details $D$ and only approximation $A$ can be used to suppress noise (right) [221]](image)

After the wavelet decomposition with DWT in approximations and details, the different levels can be analyzed and if a level (detail part mostly) has a lot of signal disturbances it can be removed from the wavelet reconstruction as exemplified in Figure 4.42 (right); in the IDWT, the coefficients from this level are simply set to zero [221].

In order to suppress undesirable signal components in the parameters detected by the accelerometer, different variations of wavelet families, numbers of levels, and methods to adjust filtering for the different signals were tested [224].

### 4.6.2.1 Snoring

Snoring, with its high frequency components, broad spectrum, and consequently high noise level from the accelerometer, is a challenge for normal filters. With wavelet analysis, different wavelet families were tested and the Daubechies (db) family provided the best results; the shape is very similar to the shape of a snoring signal and therefore a good choice for wavelet analysis. A multilevel decomposition with reconstruction using the db12 wavelet in Matlab was therefore conducted. Since snoring consists of high-frequency components, the detail components are the most interesting, shown in Figure 4.43.

![Figure 4.43: Wavelet decomposition (cD1-5, cA5) of 30 seconds raw signal with snoring [224]](image)
From these, the optimal components for the snoring signal were chosen and used for reconstruction. Even though it consists mostly of the desired snoring signal, there is still some noise remaining between snoring episodes. To remove as much noise as possible, a soft threshold based on the Stein’s unbiased risk estimate (SURE) and “minimax” function was used as a filter [226]. This removal of noise is useful for detecting snoring with low amplitude, where signal to noise ratio is critical. The final wavelet processing of the snoring signal in comparison to normal filtering is demonstrated in Figure 4.44.

![Figure 4.44: Raw signal compared with normal bandpass filtering (turquoise) and wavelet processing (red)](image)

4.6.2.2 Heart rate

Using a similar approach, a suitable wavelet was found for the heart rate signal. The Symlet wavelet family was chosen for this purpose because of its resemblance to the heart rate signal [224].

![Figure 4.45: Wavelet processing (red) compared to low-pass filtering of the heart rate signal](image)
4.6.2.3 Breathing
The breathing signal could also be successfully extracted from the raw signal using wavelet processing. In contrast to snoring, the approximation components were analyzed, and not the detail components, until a satisfying result was achieved [224].

![Wavelet processing of breathing movement](image)

Figure 4.46: Wavelet processing of breathing movement [224]

4.6.3 Automatic detection of snoring and obstructions

4.6.3.1 Removal of movement artifacts
Before an automatic detection of snoring and obstructions can be implemented, it is necessary to remove signal artifacts caused by movement. Therefore, the first and last five minutes of a recording is automatically excluded from automatic detection.

The raw signal is then downsampled and processed with wavelet filtering. If the values are above a certain threshold, it is identified as movement; additionally, the time interval with movement ± five seconds is set as invalid and excluded from the automatic detection [224].

![Removing movement disturbances](image)

Figure 4.47: Removing the first five minutes (yellow) and movement artifacts (orange) from the measurement raw signal [224]

4.6.3.2 Snoring
From the previous measurements, it could be seen that the signal amplitude might be influenced by sleeping position, i.e. depending on head/headband position the signal transduction can vary. Hence, a dynamic threshold would be needed to identify peaks as snoring.

This was solved by calculating the short-time energy with a Gauss window of fitting length, and resulted in a smooth energy signal (Figure 4.48; pink curve) from the wavelet filtered snoring signal (green curve). Based on the root mean square of the energy signal, a moving average threshold is calculated (blue curve) [224].
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Figure 4.48: Snoring signal with wavelet processing (green), short-time energy of snoring signal (pink) and threshold (blue) to identify peaks above the threshold as snoring [224]

Afterwards the peaks from the energy signal above the threshold can be found using peak detection; if the time interval between two peaks corresponds to normal breathing intervals they are verified as snoring. Finally, subsequent snores are grouped together to identify snoring episodes.

Figure 4.49: Procedure to identify snoring

4.6.3.3 Respiratory disturbances based on breathing pattern and snoring

The most difficult challenge is to ensure reliable detection of respiratory disturbances (apneas, hypopneas and RERAs). In the sleep laboratory, several sensors work to provide not just a sufficient basis for such detection, but also a classification of obstructive and central sleep apneas, hypopneas, and respiratory disturbances. Here, all of the measurement parameters are limited and based on accelerometry; therefore a novel method for detection had to be conceived.

In the ICSD-2, obstructive sleep apnea is defined as a complete (apnea) or partial (hypopnea) obstruction that lasts longer than 10 seconds, which is often accompanied by blood oxygen desaturation, and terminated by brief arousals [37]. A RERA is also defined to be a reduction in inspiration airflow following arousal, but without blood oxygen desaturation.

With the accelerometry measurement as previously indicated in Figure 4.27 on 83, these events can be observed as reduced breathing effort, followed by increased breathing effort, and accompanied by snoring. Based on the ICSD-2 information and previous observations of the headband measurements, the following procedure was implemented.
Figure 4.50: Procedure for identifying obstruction based on breathing and snoring

The breathing signal with wavelet processing (Figure 4.51; top blue curve) was therefore used as the originator for the identification of OSA. Like snoring detection, an energy signal was calculated, but then used to create a multiplicative inverse (green curve). In this way, identifiable peaks are produced where breathing effort decreases. Furthermore, a dynamic threshold based on the multiplicative inverse was developed (red curve) so that peaks reaching above the threshold could be identified as obstructions – when the cross section between inverse and threshold corresponds to the length of an obstruction, that is longer than 10 seconds [224]. Also, at least one registered snore had to be within the 10 seconds following such a detected event on the breathing signal. In the middle graph, the pink areas show the detected obstructions, and compare detected obstruction length to PSG detection in the lower graph. Obstructive sleep apnea and hypopnea are distinguished by the level of flow limitation in polysomnographic measurement; apnea requires a flow limitation of more than 80 %, whereas hypopneas are defined by a flow limitation of 50-80 %. From Figure 4.51 it is obvious that such a differentiation cannot be done with the headband measurement, but apneas and hypopneas can still be jointly detected as obstructions with the changes in breathing amplitude.

Figure 4.51: Segment with apneas (pink) and a hypopnea (yellow); breathing signal with wavelet processing (blue curve), multiplicative inverse of short-time energy of breathing signal (green) and threshold (red) to identify peaks above the threshold as obstructions in the upper graph. Middle graph shows three obstructions successfully detected (pink areas) compared to the obstructions detected with PSG [224]
4.6.3.4 **Respiratory disturbances based on intermittent snoring**

An alternative approach to the detection of respiratory disturbances was also implemented, in order to see which one would accomplish a better detection of respiratory disturbances. Intermittent snoring intervals between 10 and 60 seconds has been registered as intermittent snoring and used to calculate an intermittent snoring index (ISI) to indicate obstructive sleep apnea in other screening systems [192, 193], as described in chapter 3.4.4.

A modified version of ISI detection was implemented in Matlab (Figure 4.53); the energy signal of snoring is the same as previously described, and then a moving average creates a smooth curve (bottom curve, blue). If amplitude falls below a certain threshold for more than 10 seconds, but less than 60 seconds, it is potentially intermittent snoring. If, in addition, snoring is registered directly before and after the time interval, it is registered as an episode of intermittent snoring (bottom curve, red bars).

![Diagram of intermittent snoring index (ISI) detection](image)

**Figure 4.52: Procedure to indentify respiratory disturbances based on intermittent snoring index (ISI)**

![Figure 4.53: Intermittent snoring (ISI) found from pauses in snoring when the amplitude of the moving average on energy signal of snoring was below a certain threshold between 10 and 60 seconds](image)

4.6.3.5 **Matlab GUI**

An improved Matlab GUI was designed in a similar way to those used together with polysomnography so that inspection of recordings with the automatic data interpretation could be easily conducted. The main window is demonstrated in Figure 4.54. Here, the recording with all the processed parameters from the whole night is displayed at once. By zooming and dragging the cursor over one of the parameters, different sections from the recording can be easily inspected.

![Diagram of Matlab GUI](image)
4 Development and evaluation

In addition a patient management system was implemented so that patient data can be saved similar to polysomnographic devices. In this way, recordings can be allocated to patients and the data stored systematically.

The most important new feature is the automatic generation of a sleep report that is generated from the automatic data interpretation; here the patient data is listed with a summary of snoring, respiratory disturbances, and sleeping positions. This is a light version of the sleep report generated at the sleep laboratory after polysomnographic measurement and shall be used to compare the automatic data interpretation with the polysomnographic diagnosis. If successful, this could be used as a tool for initial screening of SBD.
4.7 Microcontroller data processing

Important aspects of a long-term monitoring system are miniaturization and the handling of the large amount of data produced over time. In order to reduce the data amount and processing needed, real-time filtering and data processing should be a part of the microcontroller firmware. Based on the data evaluation and initial signal processing in Matlab (chapter 4.4) this was implemented to prove the possibility with the proposed measurement system.

4.7.1 Data filtering and downsampling

With a microcontroller such as the MSP430 from Texas Instruments, the data processing capacities are very limited in comparison to the Matlab possibilities presented in this thesis. 16-bit samples at a sampling rate of 450 Hz have to be handled in an efficient way or else the capacities soon become exhausted. A possible solution would be to filter and then downsample the data to produce an envelope of the different parameters. This was tested on the snoring and breathing movement signals which are the most essential for the detection of snoring and obstructive sleep apnea.

The filter design was done in Matlab with the Filter and Analysis Tool to create filter coefficients. This tool can be used to create infinite (IIR) or finite impulse response filters (FIR). IIR filters have the advantage that they can be designed with a lower filter order than corresponding FIR filters. But since IIR filters have a feedback loop which could potentially lead to an overflow on the microcontroller, it was decided to use design FIR filters which in comparison to IIR are always stable with linear phase and simple to implement [227, 228].

4.7.1.1 Snoring

An optimized filter for the snoring spectrum was designed to band-pass the raw signal. Due to the limited capacity of the microcontroller the filter had to be limited to an order of \( N = 17 \) with a 40 dB attenuation in the cut-off region. As seen in Figure 4.57, the filtered snoring signal is still noisy, yet the peaks from snoring can be clearly identified. Next the absolute values of the filtered signal are calculated to intensify the peaks. Because of the high signal bandwidth, a moving average filter was used to smooth out the snoring peaks and provide a low-frequency signal which could be significantly downsampled (2 Hz) to create the envelope of the signal. From this it is possible to do snoring detection based on peak detection.
4 Development and evaluation

1.03

Figure 4.57: Microcontroller filtering and downsampling process of snoring signal [227]

4.7.1.2 Breathing movement

In a similar way the breathing movement must be filtered and downsampled. Since the breathing movement signal is < 0.5 Hz and the sampling frequency is 450 Hz, a single efficient low-pass filter with cut-off frequency 0.5 Hz is not possible to create with a filter order of less than N = 1000 and hence not feasible with the microcontroller. The solution was to divide the filtering and downsampling in multiple steps (Figure 4.58): first a low-pass filter with cut-off frequency 15 Hz and 20 dB attenuation in the cut-off region was used. In this way the signal could be downsampled to 30 Hz and a very simple low-pass filter (N = 5) could be used to further reduce bandwidth and sampling frequency. After the third step, the breathing movement signal is reduced to the minimum bandwidth of 0.5 Hz and a 1 Hz sampling frequency.

Figure 4.58: Microcontroller filtering and downsampling process of the breathing movement signal
4.7.2 Wireless transmission and data reconstruction

With a sampling rate of $fs = 2$ Hz for the snoring signal and $fs = 1$ Hz for the breathing movement signal it is possible to transmit this small amount of sampled data wirelessly to a receiver unit. This would potentially eliminate the need of a memory card and extensive Matlab signal post-processing which is beneficial for the long-term measurement system.

The feasibility was proven by testing the integrated wireless transceiver which provided a lossless output of both downsampled signals. Further, the signal reconstruction in Matlab was also verified (Figure 4.59): through upsampling ($fs \times 30$) and successive filtering the reconstructed signals are almost identical to the microcontroller filtered snoring and breathing signals, except for a slight aliasing resulting from the extreme downsampling [227].

![Figure 4.59: Microcontroller filtered snoring and breathing movement (top). Downsampled with $fs = 2$ Hz and 1 Hz (middle) for wireless transmission. Reconstructed signals in Matlab by upsampling ($fs = 60$ and 30 Hz) and successive low-pass filtering (bottom) [227]](image)

4.8 Summary

The development and extensive evaluation in this chapter was done to explore the possibilities and limitations of an accelerometer-based measurement and therapy appliance. For this purpose, raw data was recorded to a microSD card then processed and filtered in Matlab. The first simple filtering to obtain snoring, heart rate, breathing, and movement with GUI showed that these signals are recordable with the accelerometer (chapter 4.4).

Similar filtering techniques were implemented directly on the MSP430 microcontroller for snoring and breathing (chapter 4.7). It showed that these signals can be processed and reduced to envelope signals with a very low sampling frequency. With the reduced amount of data it is possible to do real-time microcontroller processing or wireless transmission and simpler post-processing of snoring and obstructive breathing, which is an important feature of a long-term monitoring system.

However, in order to compare an automatic detection of snoring and obstructive breathing with polysomnographic recordings, an improved and complex data processing approach was developed in Matlab (chapter 4.6). Signal noise was reduced to a minimum with Wavelet filtering, and algorithms to remove movement artifacts and automatic detection of all
parameters were implemented. This approach could hence be used for a more reliable initial screening.

Figure 4.60 summarizes these software developments; four minutes of the raw data from a recording of a patient with obstructive sleep apnea is shown, followed by the Matlab Wavelet filtering with the automatic detection of snoring (yellow), obstructions based on breathing movement (pink), obstructions based on ISI (red stems), and heart rate (turquoise stems). The head sleeping position is calculated directly on the microcontroller as the DC component of the X axis (blue). In addition, the microcontroller processed envelope signals of snoring and breathing movement are shown. Although they were downsampled to 2 and 1 Hz by the microcontroller and then upsampled in Matlab, they are comparable to the Matlab processed signals and could be utilized for long-term monitoring of SBD.

![Figure 4.60: Matlab GUI with raw data, Matlab processed data with automatic parameter detection (screening) and MSP430 output of head sleeping position, snoring and breathing (long-term monitoring)](image)

The recording of sleeping position can be used to identify positional patients, i.e. patients who primarily experience snoring or having respiratory disturbances when sleeping on their back. With the integration of a vibration motor it is possible to provide biofeedback therapy in order to avoid the supine position in positional patients.

![Figure 4.61: The vibration motor as biofeedback therapy for positional patients](image)
5 Results from polysomnographic reference measurements

In this chapter, the hardware and software developments from chapter 4 will be compared to polysomnographic data to unveil the potential in detecting sleep-related breathing disorders and provide biofeedback therapy.

5.1 Sleep laboratory signal evaluation tests

The first reference tests with polysomnographic equipment were done to evaluate the signal data quality after filter processing, as well as the sleep-wake detection and biofeedback signal alarm settings investigated in chapter 4.4.

5.1.1 Snoring and OSA measurement verification

A patient with obstructive sleep apnea and heavy snoring (male, age 55, BMI 30.3) was recruited for simultaneous recording with headband and polygraph (Embletta Rekorder, level III). The results from a seven hour recording are illustrated in Figure 5.1.

![Figure 5.1: A seven hour recording comparing headband to polygraph (here called PSG) on a subject with heavy snoring and OSA.](image)

The moving average of the snoring demonstrated in chapter 4.4 had a similar pattern as the Embletta snoring recording. The head position is also well correlated with the sleeping
position from the polygraph recording, indicating that positional snoring can be detected with the headband as well.

Figure 5.2: Obstructive sleep apneas (pink) and hypopneas (yellow); comparison of headband and polygraph (here: PSG) parameters

The zoom in on obstructive sleep apnea events in Figure 5.2 reveals the potential of OSA detection with the headband; the periods of snoring correlated with increased breathing effort could be used as an indicator for respiratory disturbances. Figure 5.3 is a detail zoom on snoring and an obstruction, showing the ideal case of intermittent snoring and modulated breathing amplitude as an indicator for an obstruction using the headband measurement.

Figure 5.3: Detail zoom on snoring and an obstructive sleep apnea (hypopnea)
5.1.2 Heart rate, sleep-wake detection and biofeedback therapy verification

Further, to verify heart rate, sleep-wake detection, and the influence of biofeedback signal alarm on sleep quality, also presented in chapter 4.4, a sleep laboratory test was conducted at a sleep clinic. A fully attended polysomnography (level I) was done parallel to the headband recording. Because of all the measurement equipment, the test person had a night of poor sleep, being awake for more than 2 hours of the total recording, but the recordings from the headband and PSG are still viable.

5.1.2.1 Heart rate

The heart rate is the most difficult parameter to measure reliably using the accelerometer since the signal can easily be influenced by movement or slight disturbances. This was confirmed at the sleep laboratory; most of the error peaks in the heart rate detection from the headband recording could be correlated with activity and almost all were in wake phases as demonstrated in Figure 5.4.

![Figure 5.4: Heart rate from PSG, heart rate from headband, sleep-wake from PSG and activity measured with the headband indicating that errors in heart rate](image)

5.1.2.2 Sleep-Wake detection

The sleep-wake detection with the implemented Sadeh algorithm related to the amount of activity was compared to the PSG hypnogram classification. Supplementary to the headband sleep-wake detection was tested using an additional accelerometer in a tooth splint. Both the sleep-wake detection with the headband (82 %) and tooth splint (81.1 %) had a very high correlation with the sleep-wake classification on the PSG hypnogram.
Figure 5.5: Sleep-wake detection based on actigraphy with the headband and tooth splint measurement compared to PSG hypnogram

5.1.2.3 Biofeedback therapy

The microcontroller was programmed to trigger the vibration alarm 10 seconds after turning over in the supine sleeping position to investigate its potential as biofeedback therapy in avoiding the supine sleeping position. The vibrations would last 10 seconds, and then pause 10 seconds followed by 10 seconds of vibrations and so on until the subject changed sleeping position (to the left or right lateral sleeping position).

Figure 5.6: Vibration alarm triggered 10 seconds after turning over in the supine sleeping position

At the sleep laboratory, it could be seen that the subject was always awake or in a light sleep phase when changing sleeping position. This was also the case in the example in Figure 5.6; the subject turned over into the supine sleeping position in the waking state and had not fallen into deep sleep when the vibration alarm was triggered after 10 seconds. The
vibrations from the biofeedback signal are indicated on the raw signal from the Y axis. The blue line from the X axis shows how the sleeping position goes from right to supine, and then left as a reaction to the biofeedback signal.

In addition, the microcontroller was also programmed to trigger the vibration alarm after 45 minutes of sleep in the same lateral sleeping position in order to investigate the effect on deep sleep. Every time the subject was in a deep sleep phase, there was no reaction to the vibration alarm (three times), as demonstrated in an example in Figure 5.7. Twice, the subject was either awake or in a light sleep phase and reacted immediately to the vibration alarm by changing sleeping position.

![Figure 5.7: Vibration alarm triggered after 45 minutes of sleep in the right lateral position](image)

This indicates that a biofeedback therapy can successfully be used to avoid the supine sleeping position, and if it is accidentally triggered in a deep sleep phase it will not disturb the subject’s sleep. The automatic supine sleep vibration alarm was therefore tested on a subject at home, first one night without biofeedback therapy and then on a following night with biofeedback therapy enabled. The patient slept 11.68 % in the supine position without biofeedback therapy. With biofeedback therapy enabled, the patient was prevented from remaining in the supine position by the vibration alarm five times (indicated by arrows) and had a total of 0.85 % supine sleep.

![Figure 5.8: Test person sleeping one night without biofeedback therapy with 11.68 % supine sleep; on a following night with biofeedback therapy only 0.85 % supine sleep with the vibration alarm preventing supine sleep five times (arrows)](image)
5.2 Sleep study to assess automatic detection algorithms

Up till now the recordings have only been evaluated by investigating sections of the accelerometer-based measurement compared to reference systems. To unveil the true potential, a sleep study was conducted to compare the automatic data interpretation presented in chapter 4.6 with the polysomnographic diagnosis. The study was conducted at the ENT (ear, nose and throat) clinic at Klinikum rechts der Isar, Munich. Here, patients suspected of having obstructive sleep apnea are evaluated with a full-night in-lab polygraphic (level III) recording. Patients approved to participate in the study were fitted with the headband in addition to the polygraphic recorder. The data from the headband was read in Matlab GUI with the automatic detection algorithms presented in chapter 4.6.

In Figure 5.9, the results of the MSP430 microcontroller data processing of the snoring and breathing movement described in chapter 4.7 can also be seen; the 2 Hz snoring signal produced by the microcontroller was upsampled in Matlab to 60 Hz and is similar to the recorded snoring from the polygraph. The 1 Hz breathing movement signal was also upsampled and can be related to the breathing amplitude from the accelerometer in Matlab.
5.2.1 Overview

Table 5.1 is a summary of the automatic polygraphic in-lab results from the seven participating patients which will be used to verify the headband scoring.

<table>
<thead>
<tr>
<th>Sleep lab</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
<th>Patient 7</th>
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<tbody>
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<td>06:00:00</td>
<td>06:07:30</td>
<td>06:34:00</td>
<td>6:22:30</td>
<td>06:36:30</td>
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<td>Snoring duration</td>
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<td>00:10:40</td>
<td>02:49:50</td>
<td>02:03:20</td>
<td>03:18:50</td>
<td>02:01:40</td>
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<td>214</td>
<td>2461</td>
<td>2212</td>
<td>3545</td>
<td>1933</td>
<td>2777</td>
</tr>
<tr>
<td># apneas-hypopneas</td>
<td>17</td>
<td>22</td>
<td>56</td>
<td>244</td>
<td>265</td>
<td>135</td>
<td>5</td>
</tr>
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<td>AHI</td>
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<td>3.4</td>
<td>9.3</td>
<td>39.8</td>
<td>40.4</td>
<td>21.2</td>
<td>1</td>
</tr>
<tr>
<td># limitations</td>
<td>82</td>
<td>54</td>
<td>26</td>
<td>160</td>
<td>141</td>
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<td>40</td>
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<td># RD (AH + lim.)</td>
<td>99</td>
<td>76</td>
<td>82</td>
<td>404</td>
<td>406</td>
<td>225</td>
<td>45</td>
</tr>
<tr>
<td>RDI</td>
<td>18</td>
<td>11.8</td>
<td>13.7</td>
<td>66</td>
<td>61.8</td>
<td>35.3</td>
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<td>29.4</td>
<td>23.4</td>
<td>29.1</td>
<td>22.9</td>
</tr>
</tbody>
</table>

Table 5.1: Results from the polygraphic measurement in the sleep laboratory

5.2.2 Snoring

Snoring could be identified correctly in patient 1, 2, 4 and 6. However, the classification of patient 5 was problematic because forceful obstructive apneas occurred throughout the night. Patient 3 and 7 had lower snoring amplitude, which made detection with the headband recording difficult.

Figure 5.10: Number of snores and snoring duration calculated from headband and polygraph (here: PSG) measurements
5.2.3 Respiratory disturbances based on breathing pattern and snoring

The method based on changes in the breathing pattern with following snoring described in chapter 4.6.3.3 was compared to the number of RDI (respiratory disturbance index, apneas/hypopneas and RERAs) detected by the polysomnographic classification. The results are compared to apneas/hypopneas in Figure 5.11, and were not satisfying. The reason for the poor correlation is caused by the complexity of developing an identifier of respiratory disturbances based on breathing amplitude; the detection was not dynamic enough and hence unable to detect the apneas and hypopneas correctly. In other words, it was not possible to find a combined algorithm sensitivity level valid for all patients.

![Number of apneas/hypopneas](image)

Figure 5.11: Number of apneas/hypopneas identified with the headband compared to polygraph classification

5.2.4 Respiratory disturbances based on intermittent snoring

A much more satisfying result was delivered by the identification of respiratory disturbances based on intermittent snoring (chapter 4.6.3.4) when compared to the RDI from the polygraphic output (Figure 5.12).

![Respiratory disturbances](image)

Figure 5.12: Respiratory disturbances (RDI) from polygraphic measurement compared to identification of respiratory disturbances based on intermittent snoring (ISI) with the headband
5.2.5 Sleeping position

The recording of the sleeping position is important in order to identify positional patients, i.e. patients who primarily experience snoring or having respiratory disturbances when sleeping on their back (supine sleeping position). Since the headband measures the head sleeping position and the polygraph body sleeping position, a comparison had to be made.

The results in Figure 5.13 show that the headband measurement that uses 45° as the limit between lateral and supine sleeping positions indicates less supine sleep than the PSG (patient 1, 2 and 5) which also has the limit set to 45°. This is understandable since the subject is able to rotate their head into the lateral position when lying on their back. This seems to be very individual since patient 3, 4 and 6 had a very good correlation with the PSG and headband, meaning that the head stayed in the same position as the body also when lying on the back.

![Supine sleep (% of time in bed)](image)

Figure 5.13: Supine sleep recorded with PSG compared to supine sleep recorded with headband at different angles separating the lateral sleeping position from supine sleeping position

5.3 Comparison of therapy monitoring with headband and PSG

A patient diagnosed with snoring and OSA (male, age 55, BMI 30.3) was recruited for an additional test study of therapy monitoring with the headband. A total of six nights were recorded. The patient wore an Embletta level III polygraph device parallel to the headband recordings on the four last nights of recording for verification (Night #3-6). A mandibular retaining appliance (MRA tooth splint) was used as therapy on the 4th and 5th night. A good approximation of snoring duration was possible with the headband in comparison to the polygraph recording (PSG). The headband snoring duration was calculated using the automatic data interpretation software in Matlab from chapter 4.6.
5 Results from polysomnographic reference measurements

The recording of snoring duration with the polygraph recorder depends on the threshold value for snoring duration in the PSG software settings; different settings were tested to ensure that the right setting was used. In Figure 5.14, the snoring signal from the nasal cannula was set a threshold of 15 µbar. In Figure 5.15, the snoring durations with the threshold set at 10, 20 and 40 µbar are shown. The best setting remains 15 µbar since the headband still provides a slight oversensitivity in three of the four nights.

Figure 5.14: Snoring duration over six nights with headband recording, with two nights of therapy. A polygraph was for used as verification of snoring detection on the four last nights

Figure 5.15: Snoring duration with the threshold value for PSG snoring detection set at different values compared to the headband detection

Figure 5.16 shows the graphic output of the automatic detection of snoring and sleeping position with the headband and PSG. Detected snoring periods are indicated with black dots for the PSG and as blue stems for the headband software. Head position correlated well with the PSG sleeping position in all four nights. The PSG sleeping position can only differentiate between sleeping positions, whereas the headband position indicates the exact angle.
Figure 5.16: Results from the four nights of headband and PSG automatic detection of snoring and sleeping position for comparison
6 Discussion

6.1 Sleep-related breathing disorders – who needs help?

The spectrum of obstructive sleep-related breathing disorders (SBD) was systematically investigated in chapter 2 of this thesis. It is apparent that most of those suffering from these breathing abnormalities are yet to be diagnosed, especially those at the beginning of the spectrum.

SBD typically start with primary snoring in the mid-thirties in both men and women. An important factor is aging, which changes the supporting soft structures in the upper airway and therefore causes an increase in upper airway resistance. Men are predisposed because of anatomical differences such as a higher fat deposition around the neck, hence the male female ratio of 2:1 for both snoring and OSA. This changes when women reach menopause, since the hormonal changes promote a male body fat distribution.

This means that weight gain and obesity are also important factors, especially in OSA patients: More than 60 % are overweight, and in general a 10 % weight loss would reduce up to 50 % of the obstructive apneas. It is interesting that more than half of snorers as well as OSA patients are so-called positional patients as their symptoms predominantly occur when sleeping in the supine position. The typical positional patient is a young male with normal weight and up to a moderate degree of OSA.

For snoring, it is usually the (in most cases, female) bed partner who is affected by health problems, triggered by daytime sleepiness resulting from the annoying and loud sound of snoring. When obstructive snoring (UARS) occurs, daytime sleepiness can affect the snorer as well. Daytime sleepiness reduces concentration and productivity at the work place, and a serious concern is the resulting increase in motor vehicle accidents.

In addition for OSA sufferers, the recurrent blood oxygen desaturations caused by obstructions longer than 10 seconds is a tremendous burden for the cardiovascular and respiratory systems, especially in those who are already overweight and have high blood pressure. In Germany, the number of polysomnographic examinations provided by the Federal Statistical Bureau according to age groups in 2002 demonstrated a noticeable accumulation in the higher age groups compared to the prevalence statistic. A plausible theory is that OSA diagnosis in men is on average delayed by years, caused by patient hesitation to seek help [12].

From this, it is obvious that early diagnosis and correct treatment is important in order to avoid the dangers from an advanced degree of SBD. Still, 70 to 80 % of OSA patients have not been diagnosed and are not aware of the dangers related to their medical condition. Hence the patients at the beginning of the spectrum are those who primarily need to be addressed with adequate diagnosis and treatment options.
6.2 Available diagnosis and therapy options – what is missing?

Diagnosis and therapy options were therefore thoroughly investigated in chapter 3. It is evident that classic approaches are either diagnosis or treatment options: First a diagnosis is made using a screening, polygraph, or PSG device; then a treatment option is offered. None of the treatment options, except for AutoPAP and some upcoming CPAP devices, have the ability to report therapy efficiency or compliance. This can only be done subjectively by the bed partner or by a follow-up night with a diagnostic device. Therefore, as seen with the innovative appliances presented in chapter 3.4, there is a trend towards systems that can measure multiple nights at home. At the same time there is a trend towards measurement systems which allows the users to do in-home monitoring of certain parameters and actively evaluate the results themselves, such as sleep quality with the Zeo Sleepwave shown in chapter 3.4.5.

Still, no one offers a solution for the long-term management of sleep-related breathing disorders – a system that measures and reports symptom changes or lack of therapy efficiency with regular follow-ups at home. This is especially important in those who are at the beginning of the SBD spectrum, since daytime sleepiness and medical conditions have not reached serious levels yet. Also, those who use CPAP alternatives such as oral appliances are not guaranteed a 100% efficient therapy and there is therefore a need for better follow-up in order to ensure therapy efficiency and compliance in the long term. In contrast, those with severe OSA know what happens when they decide to sleep without the CPAP device for one night. Therapy abortion is therefore more likely when there is a lack of psychological strain, and the fact that snorers cannot hear themselves snore serves to further reduce motivation to stick to the treatment.

Behavioral therapy is a simple and convenient therapy approach for these patients, but current methods like the tennis ball technique for positional patients still have very low compliance. Current screening devices and upcoming innovative appliances also lack the ability to record sleeping position – an objective report on positional therapy efficiency is therefore not possible. Thus, a long-term motivational tool is needed in order to objectively report both the development of the disease and efficiency of the therapy.

6.3 Requirements for long-term monitoring

The most important requirement for long-term monitoring is a miniaturized measurement system which is comfortable enough to wear multiple nights without disturbing sleep. With the measurement system proposed in chapter 4, multiple parameters relevant for sleep-related breathing disorders could be detected using only one accelerometer, which is small enough to fit in a miniaturized headband or even in a tooth splint. The measurement principle utilizes that the body is at rest when we sleep and the main part of movements and vibrations are related to breathing, heart beat and snoring. These movements and vibrations
are however very small, so without the recent development of miniaturized MEMS accelerometers with high resolution, this would not be possible.

A second aspect is the reliability of the measurements. Since the accelerometer can record and detect multiple parameters related to sleep-related breathing disorders, it has a great advantage compared to other screening and diagnostic devices with multiple sensors and cables attached to the patient. This is also a potential disadvantage, since the single recorded signal – which is prone to disturbances such as movement – has to be divided in different parameters. This require signal processing which can handle the disturbances.

It is also important to identify which parameters are relevant for a long-term monitoring in order to avoid an overload of unnecessary data which accumulates over time. We have identified snoring, breathing amplitude, and sleeping position as the most relevant parameters. The number of snores is more relevant than the amplitude from a medical point of view; and generally, those who are heavily built will have a higher amplitude but this does not necessary correlate with increased symptoms. The breathing amplitude and not the frequency is significant because the amplitude normally correlates with snoring, indicating that snoring increases the resistance in the airway as shown in the evaluation of snoring recording. Variations in the amplitude could therefore be an indicator of respiratory disturbances. Moreover, the patients would have great interest in knowing their snoring amplitude because this indicates how much the sleeping partner is disturbed. And finally, sleeping position is left out in most screening devices but is important for identifying of candidates for positional therapy.

The importance of including sleep position in the evaluation of SBD can be shown using an example from the surgical treatment of OSA patients. Uvulopalatopharyngoplasty (UPPP)\(^2\) is performed as one of the surgical curative treatment options for OSA. But, it has been considered to only be effective in approximately 40% of patients on the basis of overall AHI criteria, which are judged on the basis of polysomnography outcomes. The proportions of sleeping position changes from day to day and therefore a single-night polysomnography may not be representative, especially in positional patients. Surgeons can therefore be surprised to see that the patient has a higher postoperative AHI than preoperative. Without appropriate correction regarding sleeping position, the fluctuation of sleeping position in each polysomnography might confound treatment outcomes. For sleep-related breathing disorders it is therefore important to consider the positional effect on snoring AHI when treatment results are evaluated [229].

This can be confirmed when speaking to sleep physicians; for them, reliability is a great concern. Even the raw data from a polysomnograph is visually inspected because they cannot completely rely on the computer analysis. An automatic analysis will thus only be regarded until the first false diagnosis appears. Long-term monitoring with limited measurement channels is not to be seen as a diagnostic device, but rather as a means to indicate developments in the medical condition and therapy efficiency over time.

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\(^2\) Surgery in order to remove throat tissue i.e. parts of the uvula, soft palate, tonsils, adenoids and/or pharynx
6.4 Possibilities and limitations of the proposed long-term management system

The possibilities of the proposed long-term management system were thoroughly evaluated using the headband evaluation prototypes. The digital accelerometer has a high signal resolution and showed promising results in the evaluation. Snoring was – compared to a microphone signal – recorded with a good signal to noise ratio, even without amplification. Heart rate was also identifiable on the raw signal in most cases. However, small disturbances influence the signal and the recording of a continuous heart rate throughout the night is currently impossible. This possibility would of course be very interesting for the many patients who develop cardiovascular diseases amplified by recurrent obstructions. A “double heart beat” is often seen on the filtered heart rate signal (Figure 4.37); the heart rate is detected with the principle of ballistocardiography (chapter 3.4.3) but in addition, the artery supply to the forehead (Figure 4.8) seems to cause a delayed extra heart rate signal most of the time. The short delay however does not falsify the heart rate but requires more dynamic detection algorithms. The breathing signal is influenced by certain sleeping positions. In the supine position, for example, it normally has a very weak signal on healthy test persons. This means that a continuous breathing signal cannot be expected from healthy persons. But for those with snoring and obstructive breathing, the recordings show that the patient is breathing heavier than normal and that a good breathing effort signal can be expected. This could also limit the possibility of detecting central sleep apnea, as explained in chapter 2.2.2 since it only modulates the breathing amplitude. But, central sleep apnea is caused by an imbalance in the brain’s respiratory center and cannot be treated by means other than medications or CPAP. It is also relatively uncommon, being found in less than 5 % of patients referred to a sleep clinic [230] – hence the focus on obstructive sleep-disordered breathing in this thesis.

Automatic detection algorithms for snoring, respiratory disturbances and sleeping position were compared to polysomnographic data in chapter 5.

In general, a very good approximation of the number of snoring instances could be confirmed in the study. There are naturally some limitations when recording the snoring indirectly via the vibrations on the skull; in patient #3, only half of the snores could be registered because of a lack of snoring amplitude. The reason was probably that the headband, and hence the accelerometer, was not properly attached, which is important for the relatively high-frequency signal of snoring. Another reason could be a very high frequency at which the patients snore: sleep physicians point out that some snorers tend to have high-frequency snoring when the mucous membranes hit against each other, rather than palatal vibrations. If most of the power spectrum is above the cut-off frequency of 200 Hz, the snores will not be detected. The AASM recommendation for acoustic registration is however 100 Hz [231], meaning that the proposed snoring measurement cut-off frequency is well above the recommendations.

Respiratory disturbances were first registered in an approach when changes in breathing amplitude appeared that were followed by snoring caused by the arousal. The results were
not satisfying because the breathing amplitude is too sensitive to small movements and disturbances. In addition, the breathing amplitude is very low when there is no snoring or airway resistance, which makes automatic detection even more difficult. This means that breathing movements, as the primary indicator of OSA, require complex dynamic detection algorithms which are not reasonable for the proposed measurement system. The second approach, where pauses in snoring were used to register respiratory disturbances, proved to be much more reliable as an indicator for OSA. This approach is known as intermittent snoring and has previously been used by other researchers to indicate OSA by evaluating the snoring sound (chapter 3.4.4). We on the other hand can enhance this approach by including further parameters such as breathing amplitude and sleeping position in order to increase reliability. The detected heart rate could also be included for this purpose: According to sleep physicians, three to four correct heart rate values per minute would be needed to assess in the detection of obstructions: if an OSA event occurs, the heart rate will typically increase by 10 to 15 BPM within 15 seconds. REM (rapid eye movement) sleep also increases the heart rate, but for a longer period of time. Hence, the sudden heart rate changes must be identified with at least four reliable heart rate values per minute, which is feasible.

Another study was conducted to demonstrate the possibility of long-term monitoring on a snoring patient over multiple nights both with and without therapy. A good approximation of snoring duration was possible with the headband in comparison to the polygraph recording (PSG), which confirmed a reduction in snoring when using the therapy.

Sleeping position recorded using the headband was also compared to the polygraph recording in the sleep studies. An advantage of the proposed measurement system is that the angle of the sleeping position is recorded; PSG or polygraph recordings only offer an automatic classification in left, right, supine or prone sleeping position. A possible disadvantage is that the head can be in a lateral position although the thorax is in a supine sleeping position. There has been no study published to confirm which placement is more relevant. For positional patients, the gravity influence on the upper airway and root of the tongue is decisive and probably more influenced by head position. This however can only be verified in a clinical study. Still, in the sleep study in chapter 5 the head position recording set at 45° was, in most cases, similar to the polygraph thorax sleeping position recording. An exception was patient #1 who slept most of the time in a lateral position although the thorax sleeping position indicated supine sleep.

Positional patients can therefore be identified with the measurement system; snoring or obstructions are then registered mostly in the supine sleeping position. Experiments conducted on test persons confirmed that the biofeedback signal applied with the vibration motor can prevent them from sleeping in the supine position, and without disturbing their sleep. This was done by starting the biofeedback signal softly a few seconds after the test persons changed sleeping position to supine position. An approach where the biofeedback signal is turned on every time a series of snores is detected (for example SnoringU presented in chapter 3.4.4) is not useful since it will disturb sleep even more than the medical condition does. Therefore, the only justifiable approach occurs when the patient is identified as a positional patient and the biofeedback used to prevent the supine position, as successfully
demonstrated. Earlier clinical studies by Cartwright et al., described in chapter 3.3.2.2, confirmed that an acoustic alarm was successful for this purpose in OSA patients. Our approach with a vibration motor instead of an acoustic alarm has the advantage of not disturbing the bed partner when the biofeedback signal is turned on. In general, patients will seek less risky and convenient therapy alternatives. Compared to other innovative therapy approaches, such as implanted neurostimulators, the biofeedback approach is a non-invasive, harmless alternative, and can easily be tested on the subgroup of patients responsive to positional therapy. It also follows the AASM guideline for behavioral therapy in Figure 3.18 by first identifying positional patients, verification of treatment efficiency and the possibility of long-term follow up.

The implemented sleep-wake detection related to the nocturnal amount of activity proved an accuracy of more than 80% in comparison to the PSG hypnogram classification, which is similar to other activity-based sleep-wake classification devices (actigraphs). There are evidently individual differences concerning the amount of activity when awake in the night, therefore the algorithm will not provide a correct indication for all patients. But it would still be useful in order to track sleep quality through the relative changes in nocturnal activity over time, in the same way as other actigraphs or the Zeo Sleepwave that are presented in chapter 3.4.5.

The ideal placement of the measurement system was also evaluated. The headband prototype has the advantages that it is easy to use, individually adjustable using the straps provided, and the complete hardware is in one unit. The forehead is also a solid basis for the transfer of vibrations and movements related to snoring and respiratory disturbances. A headband could fall off in the night if not properly attached – in the sleep study, this was never the case. But if the straps are too loose the signal amplitudes are attenuated, most notably on the snoring signal. Another possibility is the integration of the measurement system in a tooth splint. The comparison of the headband and tooth splint measurements confirmed that a tooth splint measurement is also possible. In this case it must be individually assembled by a dental technician and is therefore predominantly meaningful for the many patients on oral appliance treatment.
7 Conclusion

The aim of this thesis was to analyze the current state-of-the-art technology in diagnosis of and therapy for sleep-related breathing disorders and then develop a more comfortable, miniaturized sensor system which can provide long-term management of sleep-related breathing disorders.

It is evident that the current infrastructure of diagnosis and therapy of SBD could be improved, considering the high percent of patients without a proper diagnosis, a lack of alternatives to CPAP therapy and limited follow-up possibilities, especially for those at the beginning of the SBD spectrum (from snoring to obstructive sleep apnea).

The technical possibility of such a system was confirmed in an in-depth evaluation of an accelerometer-based measurement system placed in a headband and also tested in a tooth splint; the most essential measurement parameters for SBD – snoring, breathing movement, and sleeping position – could be automatically detected and reliably recorded. Heart rate (with limited beat-to-beat accuracy) and sleep-wake detection (based on the amount of activity) was also demonstrated. Intermittent snoring was used to indicate the degree of respiratory disturbances (obstructive sleep apnea).

The inclusion of a vibration motor enables intelligent biofeedback therapy as an alternative to other, more inconvenient treatments for positional patients. These patients make up the largest percentage of snorers and those with up to moderate OSA. The biofeedback therapy was tested and proven useful in order to avoid the critical supine sleeping position, without disturbing the sleep of the positional patient as well as the bed partner.

The current status is a miniaturized headband system that can register important parameters related to SBD, including a reliable registration of snoring, positional patients, and an indicator for obstructive sleep apnea which can also be used to provide biofeedback therapy in positional patients. Further developments will primarily be related to long-term data handling, further miniaturization, and an enhancement of OSA detection by utilizing the other recording signals in addition to snoring in order to reach out to the many patients still in need of a long-term management of their sleep-related breathing disorders.
8 Future work and application areas

The proposed measurement system with included biofeedback therapy has the potential to help patients at the beginning of the spectrum who are in need of adequate screening and treatment options in particular, but could also be used across the complete spectrum of obstructive sleep-disordered breathing for long-term follow-up of diagnosis and therapy.

Figure 8.1: Summary of the potential application areas with the proposed long-term management system

8.1 Screening

“The ideal screening device for OSA should be cheap, easily accessible, easily used with the minimal instructions, have no risk or side effects to the patient, and be safe and accurate. It should be capable of being issued by relatively unskilled staff and even sent through the mail to reduce patient travel and staff costs.” Pang et al. [232]

The monitoring system could first be used to screen snorers over multiple nights, since up to a third of the adult population are primary snorers and also potentially have obstructive sleep apnea without being aware of it. This should be done with a more complex signal processing approach and with raw data available, such as the approach demonstrated with Wavelet analysis in chapter 4.6.

If severe obstructive sleep apnea is indicated, a visit to a sleep laboratory would be required. But for primary snoring and mild to moderate obstructive sleep apnea, especially when
8 Future work and application areas

positional, a treatment option based on the screening results like positional therapy could be proposed and long-term monitoring used to evaluate the treatment.

8.2 Positional therapy

“Standardized approaches for the maintenance of a non-supine position during sleep should be developed in clinical trials. These might include positional alarms, sleep shirts, and special pillows. The role of positional therapy, indicators for treatment response, and long-term outcomes should be clarified in large-sample, well-designed studies.”

Recommendations for future research by the Practice Committee of the American Academy of Sleep Medicine (AASM) [153]

For most snorers and many of those with mild to moderate OSA, a positional therapy could be used as an alternative and initial therapy, but currently there is no efficient system on the market to provide this – hence the effort to include a biofeedback therapy in order to avoid the supine position.

The proposed measurement system with biofeedback therapy has the advantage that the patient can observe and understand the purpose of the treatment since snoring, obstructions, and sleeping position are recorded parallel with the treatment. The patient is presented with an objective evaluation of the treatment and therapy efficiency, which could motivate him to use continue to use the positional therapy and increase the learning effect. This still has to be confirmed in long-term studies with positional patients, which in general as seen in the recommendations for future research by the AASM above, have yet to be conducted.

8.3 Long-term monitoring and therapy management

“All patients with OSA should have ongoing, long-term management of their chronic disorder. Those on chronic therapy (PAP, OA, positional therapy) should have regular, ongoing follow-up to monitor adherence to therapy, side effects, development of medical complications related to OSA, and continued resolution of symptoms. Those with elimination of OSA (weight loss, surgery) should be monitored for continued risk factor modification and to look for return of symptoms.”

Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine [19]

“Adherence data for oral appliances (OA) mostly relies on subjective reports. In contrast, CPAP adherence can now be routinely monitored in an objective fashion. Development of similar capabilities for OA therapy should be pursued for both research and clinical purposes.”

Practice Parameters for Oral Appliances—AASM Practice Parameters [166]
When reviewing the current state-of-the-art technology for diagnosis and therapy and talking to sleep experts, it became clear that the possibility of monitoring therapy efficiency and compliance are very limited, especially for those wearing a tooth splint and undergoing behavioral therapy.

Both therapy efficiency measurement and the indication of any worsening in the condition over a longer period of time are potentially possible with the proposed measurement system. In this way, it can alert the patient and advise him to see a doctor if the treatment is insufficient for the current severity of the disease. Unnecessary sleep laboratory visits could hence be avoided, which means cost savings and the ability to diagnosis more patients through more tightly focused sleep laboratory selection. In this way the patients could initially begin with a milder form of treatment, such as behavioral therapy, and cross over to more effectual therapy such as a CPAP mask only when really needed. This too has to be confirmed in a clinical study.

For this purpose, the signal filtering techniques implemented directly on the microcontroller for snoring and breathing in chapter 4.7 has to be further optimized and enhanced with automatic detection, so that a reliable detection and an indication of the severity of respiratory disturbances can be efficiently monitored over a longer period of time.

The headband solution is an excellent platform for an easy to use, individually adjustable, and compact device for long-term monitoring and regular follow-ups. An important future assignment would be to reduce the size of the system to a minimum to enable more discrete placement. The accelerometer can be used in a closed implant system, as was demonstrated in a tooth splint assembly. For those using an oral appliance therapy for long-term monitoring, it would be advantageous to include the electronics directly in the tooth splint. This approach is still limited by the power supply available, so that the additional inclusion of inductive charging would be necessary.
9 Bibliography


[34] P. Lavie, "Who was the first to use the term Pickwickian in connection with sleepy patients? History of sleep apnoea syndrome," *Sleep Med Rev*, vol. 12, pp. 5-17, 2008.


Bibliography


[107] L. F. Drager and G. Lorenzi-Filho, "Heavy snoring and carotid atherosclerosis: is there more than an association?", *Sleep*, vol. 31, p. 1335; discussion 1337, 2008.


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**Hofsøy, D. A.**, Clauss, J., Wolf, B. A new approach to provide and monitor Biofeedback therapy in positional snorers and OSA patients in order to prevent supine sleeping position, 15th Annual Biofeedback Foundation of Europe Meeting 2011, February 22.-26., Munich, Germany, 2011


