The feasibility of the Emfit movement sensor as an automated screening tool for sleep apnea in the ischemic stroke patients

Licentiate's thesis
University of Turku
Physics
2022
M.Sc. Toni Niiniviita
Examiners:
Adj. Prof. Antti Kulkas
Adj. Prof. Mikko Björkqvist

The originality of this thesis has been checked in accordance with the University of Turku quality assurance system using Turnitin Originality Check service.

UNIVERSITY OF TURKU
Department of Physics and Astronomy

Niiniviita, Toni The feasibility of the Emfit movement sensor as an automated screening tool for sleep apnea in the ischemic stroke patients

Licentiate's thesis, 59 pp.
Physics
January 2022

Stroke is a common cause of death and a major reason for disability. Stroke survivors can have very difficult symptoms and require very intensive and expensive rehabilitation. Sleep disordered breathing, sleep apnea, is common among stroke patients, it's a high risk factor for recurrent stroke and untreated sleep apnea has a negative influence on the stroke recovery.

All stroke patients are recommended to be measured for sleep apnea, but the lack of resources don't allow it. Therefore there is a need for a screening tool to find the stroke patients who need the measurement most and who benefit the most of the treatment of the sleep apnea.

We studied the possibility to use the Emfit movement sensor combined with a pulse oximeter as a screening tool. The Emfit movement sensor doesn't have connections to the patient, therefore it wouldn't require lots of resources to set up the measurement and there are no contacts that can cause interference during the measurement. The automatic scoring of the measurement would remove the need for an expert to manually score every measurement.

The test subjects were measured at the same night using both the Emfit movement sensor and a conventional respiratory polygraphy device. The Emfit movement sensor and the standard respiratory polygraphy measurements were scored using Noxturnal's automatic analysis tool and the results were compared. The results were also compared to the manual scoring of the standard respiratory polygraphy.

The Emfit movement sensor measurement slightly overestimates the apnea hypopnea index, as does the automatically scored standard respiratory polygraphy too. The automatic analysis ability to detect correctly the duration and timing of a respiratory event in the Emfit movement sensor measurement seems to depend on the amount of noise in the measurement. Our study indicates that the Emfit movement sensor has potential to be used as a screening tool for sleep apnea in the ischemic stroke patients, but the automatic analysis still needs improvements to provide more accurate results.

Keywords: ischemic stroke, sleep apnea, screening, Emfit movement sensor, automatic scoring

TURUN YLIOPISTO
Fysiikan ja tähtitieteen laitos

Niiniviita, Toni Emfit-liikesensorin soveltuvuus automatisoiduksi uniapnean seulontatyökaluksi aivoverenkiertohäiriöpotilailla

Lisensiaatin tutkielma, 59 s.
Fysiikka
Tammikuu 2022

Aivoverenkiertohäiriö on yleinen kuolinsyy ja merkittävä syy alentuneeseen toimintakykyyn. Aivoverenkiertohäiriöstä selvinneillä henkilöillä voi olla hyvin vaikeita oireita ja he saattavat tarvita erittäin intensiivistä ja kallista kuntoutusta. Unenaikaiset hengityshäiriöt, uniapnea, ovat yleisiä aivoverenkiertohäiriöpotilailla. Uniapnea on myös merkittävä riskitekijä aivoverenkiertohäiriön uusiutumiselle ja hoitamattomalla uniapnealla on heikentävä vaikutus aivoverenkiertohäiriöstä toipumiseen.

Suositusten mukaan kaiki aivoverenkiertohäiriöpotilaat tulisi mitata mahdollisen uniapnean löytämiseksi, rajallisista resursseista johtuen tämä ei kuitenkaan ole mahdollista. Tämän vuoksi tarvittaisiin uniapnean seulontatyökalu, jolla voitaisiin tunnistaa ne aivoverenkeirtohäiriöpotilaat, jotka todennäköisimmin pitäisi mitata uniapnean löytämiseksi ja jotka hyötyisivät eniten uniapnean hoidosta.

Tutkimme mahdollisuutta käyttää Emfit-liikesensoria yhdessä pulssioksimetrin kanssa seulontatyökaluna. Emfit-liikesensorissa ei ole potilaaseen kytkettäviä osia, joten mittauksen käynnistäminen ei vaadi huomattavaa työntekijäresurssia, lisäksi laitteistossa ei ole häiriöherkkiä kontakteja potilaaseen. Mittauksen analysointi automaattisesti vähentäisi tarvittavan asiantuntijatyön määrää, kun asiantuntijan ei tarvitse visuaalisesti analysoida jokaista mittausta.

Testihenkilöillä oli tutkimusyönä samanaikaisesti molemmat mittauslaitteistot, eli Emfit-liikesensori ja tavanomainen yöpolygrafia-laitteisto. Molemmat mittaukset analysoitiin Noxturnalin automaattianalyysityökalulla ja tuloksia verrattiin keskenään sekä manuaalisesti analysoidun tavanomaisen yöpolygrafiamittauksen tulokseen.

Emfit-liikesensorimittauksen automaattianalyysin tulos yliarvioi vähäisesti apnea-hypopneaindeksiä, samoin kuin tavanomaisen yöpolygrafiamittauksen automaattianalyysin tulos. Emfit-liikesensorimittauksen automaattianalyysin kyky arvioida hengitystapahtuman kesto ja ajoitus oikein näyttää riippuvan mittauksessa olevien häiriöiden määrästä. Tutkimuksemme mukaan Emfit-liikesensori voisi soveltua uniapnean seulontaan aivoverenkiertohäiriöpotilailla, mutta automaattianalyysiä pitäisi edelleen kehittää, jotta se tarjoaisi tarkempia tuloksia.

Asiasanat: aivoverenkiertohäiriö, uniapnea, seulonta, Emfit-liikesensori, automaattianalyysi

Abbreviations

AASM	American Association of Sleep Medicine
A/D	Analog to digital converter
AHI	Apnea-hypopnea index
AI	Artificial intelligence
AUC	Area under curve
BBI	Beat-to-beat interval
BCG	Ballistocardiographic
BI	Barthel index
BMI	Body mass index
BPM	Beats per minute
BSG	Ballistography
CPAP	Continuous positive airway pressure
CT	Computer tomography
DC	Direct current
ECG	Electrocardiography
EEG	Electro encephalography
EMFi	ElectroMechanical film
Emfit	Electromechanical film transducer
EMG	Electromyography
EOG	Electrooculography
HHb	Deoxyhemoglobin
HRV	Heart-rate-variability
HSAT	Home sleep apnea testing
ICH	Intracerebral hemorrhage
IMR	Isolation mode rejection
IR	Infrared

IV rtPA	intravenous recombinant tissue plasminogen activator
LED	light emitting diode
MRI	Magnetic resonance imaging
NIHSS	National institute of health stroke scale
NREM	Non rapid eye movement
op amp	Operational amplifier
OSA	Obstructive sleep apnea
O_2Hb	Oxyhemoglobin
PG	Respiratory polygraphy
PLM	Periodic limb movement
PSG	Polysomnography
PTSD	Post traumatic stress disorder
RE	Respiratory event
REM	Rapid eye movement
RMS	Root mean square
ROC	Receiver operating characteristics
RR	Respiratory rate
SAH	Subarachnoid hemorrhage
SDB	Sleep disordered breathing
TIA	Transient ischemic attack

Contents

Preface

Sleep is a natural and reversible state of reduced responsiveness to external stimuli and relative inactivity accompanied by a loss of consciousness that's recurring regularly. Sleep has also positive influence to the restoration of energy resources, the repairing of the cell tissue and the adaptive immune functions [69]. Sleep and specially the rapid eye movement (REM) stage of sleep is believed to be very important factor in the consolidation of memories [82]. The quality and quantity of sleep is very important to an individual's well being.

Breathing disturbances during sleep are usually caused by the obstruction of the airways because the muscles in the throat relax during sleep, another reason is that the signal to breath send by the brain doesn't transmit to the breathing muscles and hence there is no breathing movement in the rip cage [66], [17], [78]. Usually there is a brief arousal at the end of the breathing disturbance, therefore the sleep is not as refreshing as it should be [44]. When the breathing disturbances occur more often than in healthy persons the condition is called sleep apnea [66]. Breathing disturbances during sleep increase the risk to develop several diseases for example stroke, hypertension and heart disease [17].

Stroke is a medical condition where the blood flow of the brain is disturbed, which leads to a damage to the brain tissue. Stroke can be caused by a blockage, called ischemic stroke, or by bleeding, called hemorrhagic stroke [77]. Stroke is the second most common cause of death in the world [74]. Stroke is also a very common reason for a disability [88].

The short amount and the low quality of sleep has a negative effect on the person's capability to perform in memory test in daytime, this can be seen for example in stroke patients [30]. Breathing disturbances during the sleep increase the risk to develop several diseases [45]. Sleep apnea is very common in several neurological diseases [83]. Untreated sleeping disorders have a negative effect on

the quality of the life and the recovery process of the stroke patients [31]. Sleeping disorder prolongs the duration of hospitalization and has a negative impact on the recovery of the stroke patient. This diminishes the quality of life of the stroke patients and increases the medical costs to the society [30].

Around 50 to 70 percentage of the stroke patients in acute treatment have breathing disturbances during sleep and around 10 to 50 percentage of the stroke patients have sleep-wake rhythm disturbances. It's recommended that stroke patients with severe breathing disturbance are treated with the continuous positive airway pressure (CPAP) treatment [30]. If the stroke patient doesn't have a sleep apnea diagnosis prior to the stroke, the patient should be measured to detect the possible breathing disturbance [23]. However breathing disturbances in the stroke patients are not tested and treated on a regular basis in the Finnish health care system.

It is estimated that every year 15 000 to 20 000 people have a stroke in Finland [84]. In Satasairaala there are approximately 600 stroke patients every year. Considering the current resources of standard respiratory polygraphy (RP) devices and medical staff, it isn't possible to test all those 600 stroke patients to find the patients which would benefit most of the CPAP treatment. Also there isn't available an easy to use method to screen the stroke patients for sleep apnea.

Measurement device used for the sleep apnea screening in the stroke patients should be easy to use and enable necessary treatment procedures during the measurement. Data assessment should be automatic so that it doesn't require manual labour. We wanted to test if we could use an ferroelectretfilm Emfit mattress and a Nonin WristOx$_2$ Model 3150 pulse oximeter as such a screening method.

We had a study group of 41 ischemic stroke patients from the Satasairaala stroke unit. All patients underwent simultaneous standard respiratory polygraphy measurement using Nox T3 and Emfit movement sensor measurement. The measurement data from both measurement equipments were scored automatically using the

Noxturnal automatic scoring. Data from the standard respiratory polygraphy measurement was also scored manually according to the American academy of sleep medicine (AASM) rules and that manual scoring was used as the gold standard. Then we compared the automatic analysis results to each other and to the manual scoring of the standard respiratory polygraphy measurement.

1 Sleep apnea

Sleep disordered breathing (SDB) means a regularly repeating pause or an attenuation in breathing during sleep. A pause in breathing is called apnea and reduction in airflow is called hypopnea. The apnea and hypopnea periods usually end to an activation of the sympathetic nervous system and an arousal, thus interrupting the sleep. Sleep disordered breathing is mainly caused by the sleep apnea. [66]

Sleep apnea has three major forms, which are obstructive sleep apnea, central sleep apnea and complex sleep apnea where both obstructive and central apneas occur [43]. In obstructive sleep apnea the pharyngeal collapses repetitively during the sleep. The collapse of the pharyngeal has many reasons, both anatomical and physiological. Anatomical changes include the reduction of the dimensions of the upper airways, this can be caused by anatomical and functional alterations. Physiological reasons include the reduced neuromuscular compensation and the lack of the pharyngeal protective reflex [44]. Central sleep apnea results from a temporary failure in the pontomedullary pacemaker generating the breathing rhythm. Because there is no neural output from the brainstem, the thoracic pump muscles don't produce any respiratory effort [36].

Sleep apnea has a wide variety of symptoms, that can be divided into night time and daytime symptoms. Night time symptoms include breaks in breathing, loud snoring, gasping for air, restless sleep, insomnia, profuse night time sweating and nocturia. Daytime symptoms include fatigue, irritability, poor concentration, forgetfulness, falling asleep inappropriately and mood disturbances [54]. Sleep apnea is a risk factor for many severe diseases [83]. It is associated with arterial hypertension and contributes to the development of the cerebro- and cardiovascular comorbidities [6].

The best way to diagnose sleep apnea is an overnight polysomnography (PSG) in a laboratory [38]. An overnight polysomnography is a complex and resource de-

manding study, therefore there is a need for simpler study. Respiratory polygraphy is widely accepted as a diagnostic method for sleep apnea and it can be conducted at home [5]. Unlike the polysomnography the respiratory polygraphy doen't include electroencephalogram (EEG) and therefore the respiratory polygraphy can't be used to determine sleep stages [59]. The severity of the sleep apnea is determined by the apnea-hypopnea index (AHI), which is the hourly rate of apneas and hypopneas during sleep [83]. Continuous positive airway pressure (CPAP) treatment is considered to be the most recommendable treatment for sleep apnea [73].

According to a review study the prevalence of sleep apnea in the general adult population ranges from 9 percentage to 38 percentage and the prevalence of the moderate sleep apnea ranges from 6 percentage to 17 percentage. Prevalence of sleep apnea is higher in men compared to women. The prevalence of sleep apnea increases with increasing age and the prevalence of sleep apnea is higher in obese men and women compared to overweight men and women [81]. The overall prevalence of sleep apnea in the stroke and transient ischemic attack (TIA) patients is 71 percentage and the prevalence of sleep apnea whit AHI $>$ 30 is 30 percentage [80]. Prevalence of sleep apnea is higher in men than women also in stroke and TIA patients and sleep apnea is more common for patients with recurrent stroke than for patients with initial stroke [37].

1.1 AASM rules

The American association of sleep medicine (AASM) has gathered a guide that contains comprehensive standardized specifications and scoring rules for characterizing natural sleep. The AASM scoring manual is based on extensive literature review and reflects the current knowledge of sleep and associated events. [34, p. 11]

The AASM rules for scoring divide sleep into four stages, which are N1 (non rapid eye movement (NREM) 1), N2 (NREM 2), N3 (NREM 3) and R (REM).

The scoring into different stages is done visually using the electroencephalography (EEG), electrooculography (EOG) and electromyography (EMG). [34, p. 25-27]

The AASM rules state that a respiratory event is to be scored as apnea when all the following criteria are fulfilled: the airflow is reduced at least 90 percentage from the baseline, the duration of the event is at least 10 seconds and at least 90 percentage of the event duration meets the amplitude reduction criteria for apnea. According to the scoring rules the apnea is obstructive if the apnea event is associated with continued or increased inspiratory effort throughout the entire period of absent airflow. It's central apnea if the event is associated with absent inspiratory effort throughout the entire period of absent airflow. The event is mixed apnea if the event is associated with absent inspiratory effort in the initial portion of the event, followed by resumption of inspiratory effort in the second portion of the event. [34, p. 45]

The rules define that an event is a hypopnea if it meets all the following criteria: the airflow is reduced at least 30 percentage from the baseline, the duration of the event is at least 10 seconds, there is at least 4 percentage desaturation from the pre-event baseline and at least 90 percentage of the event duration meets the amplitude reduction criteria of hypopnea. [34, p. 46]

Respiratory effort-related arousal is defined as following: if there is a sequence of breaths lasting at least ten seconds characterized by increasing respiratory effort or flattening of the nasal pressure waveform leading to an arousal from sleep when the sequence of breaths does not meet criteria for an apnea or hypopnea. [34, p. 46]

2 Stroke

Ischemic stroke is defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction. Stroke can also be caused by intracerebral hemorrhage (ICH) or subarachnoid hemorrhage (SAH) [77]. Transient ischemic attack (TIA) is a similar condition, but it's transient in nature. TIA has a tissue-based definition: a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction [23].

Common stroke symptoms and signs include weakness on one-half of the body, speech disturbance, facial weakness or paresis, paresthesia of a limb, headache, nonorthostatic dizziness and visual field defects. The acute onset of the symptoms is very common in stroke. There are several other conditions that can mimic stroke, those include seizure, conversion disorder, migraine headache, and hypoglycemia. It's very important to correctly diagnose the stroke to be able to start the treatment on time to prevent additional damage to the brain tissue and to diminish the probability of recurrence. [92]

The goal in the treatment of the ischemic stroke is to relieve the arterial occlusion and restore the cerebral blood flow as soon as possible to reduce tissue injury and improve outcome. Ischemic stroke can be treated with intravenous recombinant tissue plasminogen activator (IV rtPA) if the drug can be administrated within 4.5 hours of symptom onset [63]. If the occlusion is located at a large artery, it can be treated with mechanical thrombectomy, this procedure should be done within six hours of symptom onset [28].

Stroke survivors suffer from physical and mental impairments. The physical sequelae of stroke include for example hemiplegia and spasticity, which both cause significant motor performance deficits [4]. The psychiatric complications are also common after stroke, these include depression, anxiety, post traumatic stress disorder (PTSD), aggressive personality change and apathy [20]. Both physical and

mental impairments make it difficult for the stroke survivors to manage the basic activities in the daily life [4].

The aim of the stroke rehabilitation is to promote recovery during the first months after stroke and to reduce disability during the following years [89]. Despite advances in the stroke treatment the need for stroke rehabilitation among stroke patients is at high level [90]. The stroke patients receive physiotherapy to improve balance and functional ability in daily living [65]. They receive occupational therapy to improve patient's independence and to enable training of work skills [62]. The stroke patients can receive speech and language therapy if they suffer of chronic aphasia after stroke [9]. Assistive technology such as canes and walkers can be used to assist the stroke survivors [64].

There are things that can be done to reduce the risk for the recurrent stroke. Hypertension is a major risk factor for the ischemic stroke. The guidelines recommend a lifestyle interventions and if necessary a blood pressure therapy. Treatment of the hypertension can drastically reduce the risk of recurrent ischemic stroke [57]. Diabetes is an another risk factor for the stroke [8]. The guidelines recommend screening all patients with a TIA or ischemic stroke for diabetes [57]. Increased total cholesterol increases the risk of the ischemic stroke [8]. Guidelines advice that patients with recurrent stroke or TIA presumed to be of atherosclerotic origin should receive high-intensity statin therapy. Stroke patients having any symptoms of sleep apnea are recommended to take a polysomnography. Stroke patients should pay close attention to their life style. They are strongly recommended to quit smoking and avoid second hand smoking. Heavy alcohol use may increase the risk for recurrent stroke therefore eliminating or at least reducing alcohol consumption is advisable. Regular physical activity is strongly recommendable for the stroke patients as it improves stroke risk factors [57].

2.1 Risks related to sleep apnea

Sleep-disordered breathing (SDB) is frequent among ischemic stroke and TIA patients, multiple studies indicate that the prevalence of SDB is around 50 to 70 percentage [85]. SDB and especially sleep apnea is a preceding condition and a known risk factor for the ischemic stroke. Recurrent hypoxemia, variable blood pressure, increased cardiac arrhythmias, and cerebral hypoperfusion caused by SBD may contribute to higher disability from stroke. Sleep disorders have a negative effect on the daytime wakefulness, cognitive functions and mood. All this has a negative effect on the stroke rehabilitation worsening the outcome, reducing the quality of life and prolonging the hospitalization. Patients with SDB have been observed to have higher rate of recurrent cardiovascular events and mortality [26]. Treatment of SDB with continuous positive airway pressure treatment may reduce mortality after stroke. An increasing number of studies indicate the need for systematic SDB screenings among the stroke patients [85].

2.1.1 Sleep-disordered breathing detection in the stroke patients

Several studies indicate a need for systematic SDB screening after the stroke as recognizing and treating the SDB after stroke is important part of preventing recurrent stroke and early treatment of the SDB could enhance rehabilitation. The polysomnography is a standard method to assess the severity of SDB. PSG is used to measure the apnea-hypopnea index which indicates the average number of apnea or hypopnea events per hour during sleep. Unfortunately limited resources don't allow systematic PSG testing of all stroke patients. Therefore there is a great need for a SDB screening method that could identify the stroke patients that need to be tested more closely for SDB with PSG. An ideal pre-screening method should be simple, it should be easy to install by the staff and it shouldn't require a specialist to interpret the result. The screening method should be sensitive in finding the stroke patients

at risk so that they could be tested more thoroughly with PSG measurements. [85]

There isn't an existing plausible pre-screening measuring instrument for suggesting SDB in acute or subacute stroke patients [26]. There is a need for a reliable screening method to find those stroke patients which have a high risk of SDB and an elevated need for actual PSG measurement. The aim of our study was to test if the combination of the WristOx$_2$ pulse oximeter and the Emfit motion sensor could be used as a screening tool. They are both easy to administrate, so it's quick to set up the measurement. They both are undisruptive so they don't have a considerable effect on the patient's sleep. We also wanted to study the use of Noxturnal's automatic scoring tool to evaluate if this measurement could be interpreted without a specialist.

3 Measurement devices

Sleep studies can be divided into four types, they are referred to as Level I, II, III and IV. Level I is a monitored polysomnography test performed at the hospital or the sleep laboratory, it's the most comprehensive and considered as the gold standard to which the other studies are compared to [14]. Level I study includes electroencephalogram, left and right electro-oculogram, submental electromyogram, nasal or oral air flow, respiratory movement or effort, oximetry, electrocardiogram, anterior tibialis electromyogram and sleeping position. Level II is non-attended polysomnography performed at the patient's home. The parameters measured are the same as in the level I study [52].

Level III study is a respiratory polygraphy test, which usually includes some type of cardiorespiratory measure for air flow and respiratory effort, oximetry, pulse rate and sleep positioning. Level III studies are usually conducted at the patients home. Because there are no EEG channels in level III studies, there is no information about the sleep stages and therefore there is only an estimation of the amount of sleep time. [14]

Level IV studies measure only one or two parameters such as pulse rate and oximetry. Level IV studies are very limited studies usually performed at the patient's home or used as a screening tool. [14]

In this section we will focus on equipments representing level III and IV devices as they are the ones used in our study. First we will go over techniques used to conduct the respiratory polygraphy measurements.

3.1 Respiratory polygraphy

The respiratory polygraphy or home sleep apnea testing (HSAT) is usually performed using a level III portable device that monitors the respiration during the measurement [47]. The air flow is usually measured with a thermistor or a nasal

pressure monitor, but it's also possible to use inductance plethysmography or pneumotacography [35]. Thermistors are semiconductors made of ceramic materials that are thermal resistors. Thermal resistors have a high negative temperature coefficient, so the resistance of the thermistor decreases as the temperature increases [13, p. 66]. Thermistor can be used to detect air flow by detecting the temperature changes of the air flow from the nostrils as the cooler air is inhaled and the warmer air is exhaled [19]. Nasal pressure monitor measures the air pressure inside the nostrils to detect the air flow [53]. In pneumotacography there is a flow-resistance element inside the instrument, the pressure difference over the flow-resistance element is measured and used to calculate the air flow [13, p. 393]. In respiratory inductance plethysmography (RIP) there are belts placed around the subject's chest and abdomen. Inside those belts there is a wire and there is an electrical current running through the wire. The electrical current creates a magnetic field. According to the Lenz's law the magnetic field is modified by the deformation of the rip cage due to respiratory movement. The modification of the magnetic field can be measured and used to calculate the respiratory effort [40].

The blood oxygen saturation SpO_2 can be measured with the pulse oximeter. The pulse oximeter has two small light emitting diodes (LED) one emitting red light at the 660 nm wavelength and the other emitting near-infrared (IR) light at the 940 nm wavelength. There are two reasons why these two wavelengths are used in the pulse oximetry. First reason is that they penetrate the tissue well. The second reason is that oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) have a significantly different way of absorbing red and near-IR light. The LEDs emit the light from one side of the finger and a photodiode at the opposite side of the finger detects the light transmitted through the finger. The pulse oximeter can calculate the proportion of hemoglobin bound to oxygen by comparing the relative amounts of red and IR light absorbed by the tissue and thus give the blood oxygen saturation.

[12]

In the eye there is a steady potential between cornea and retina, which creates a steady dipole. This dipole can be used to measure the movement of the eye by placing one surface electrode on the left side of the eye and another surface electrode on the right side of the eye. When the gaze is straight ahead, the dipole is symmetrically between the two surface electrodes and the electrooculography (EOG) is zero. When the gaze is turned to the left or the right, the positive cornea will come closer to the electrode in the direction where the gaze is turned to and the electrode will become more positive. The relationship between EOG output and the angle of the gaze is almost linear up to approximately $\pm 30^\circ$ sift of the gaze. [13, p. 162]

A single motor nerve fiber and the bundle of muscle fibers it is attached to creates a motor unit and skeletal muscles are constructed of motor units. A motor unit is the smallest unit that can be activated by volitional effort, then all the muscle fibers in the motor unit activate synchronously. The activation pulse travelling along the nerve fiber creates a triphasic field potential of 20 to 2000 μV with a duration of 3 to 15 ms. The field potential can be detected with a surface electrode. The nerve fibers from different motor units run near each other in the muscle. The surface electrodes can measure activity only form superficial muscles, but they can detect activity from quite large area so they can't be used to monitor specific motor units. [13, p. 144 - 145]

The electrocardiography (ECG) can be used to measure the electrical signal created by the beating heart. The heart pumps blood through the blood circulation. The contraction of the heart muscle causes the pumping function and it's initiated by a well-coordinated series of electrical events that take place within the heart. The electrical potentials generated by the beating heart spread through the body and it's surface. The potential differences can be detected by placing electrodes on

the surface of the body and measuring the voltage between them. [13, p. 147, 243 - 244]

There has to be some kind of interface between the body and the electronic measurement device in order to measure and record the potentials and the consequent currents. Biopotential electrodes act as such interface so they have to be able to conduct the current between the body and the electronic measurement circuit. In the body the current is carried by the ions and in the electronic circuit it's carried by the electrons, therefore the electrode must act as a transducer and convert the ionic current into an electronic current. The conversion is performed by chemical reactions at the interface between the electrode and the electrolyte in the body. There are metallic atoms at the interface, when they oxidise they release one or more electrons. The electrons remain in the electrode and the cation is discharged into the electrolyte. Another possibility is that an anion from the electrolyte arrives at the interface and it's oxidized to a neutral atom, in the process it releases on or more electrons into the electrode [13, p. 189 - 190]. The electrodes dictate to a large extent the composition of the measured signal [10, p. 52-3].

A miniature electret microphone or a condenser microphone can be used to detect the snoring sounds. When conducting the study at a location specially build for the sleep studies, the microphone can be hung in front of the patient's mouth at a distance of approximately 20 cm. The microphone can also be placed directly on the patient's neck or chest. The signal is recorded for later analysis and scoring. [16]

Sleeping position can be detected by using a tri-axis accelerometer [39]. The accelerometer can be constructed using piezoelectric sensors [13, p. 58]. When the body is at rest the Earth's gravity is still affecting all three accelerometers [39]. Under mechanical strain, like the pull of gravitation, the piezoelectric materials generate an electric potential. This potential can be measured by placing electrodes

on the opposite sides of the piezoelectric crystal [13, p. 58]. There are four sleeping positions, supine, prone, left lateral and right lateral, that can be distinguished and the upright position that represents wakefulness. Using a posture estimation algorithm the body position can be evaluated by comparing the gravitational force acting on each axis of the accelerometer [39].

Nox T3 monitor is one of the most widely used HSAT portable monitors. Nox T3 records nasal pressure, rib cage and abdominal movement, pulse oximetry, activity and body position, there are also bipolar channels available. [91]

Our device Nox T3 consists of the central unit that collects the data from the internal microphone to recognize snoring and a sensor to detect the body position. It also collects data from the two respiratory inductance plethysmography belts that measure the rip cage movement when the patient breaths. It has a pressure channel to measure the air flow through the nose using the nasal cannula. It connects via bluetooth to the Nonin wrist oximeter to measure the pulse and blood oxygen levels during the night. Nox T3 has also two EMG channels to measure the masseter muscle to detect nocturnal bruxism or legs to detect leg movements during the night.

Respiratory inductance plethysmography has a driver module that generates an oscillating electrical current that travels trough the wire inside the belt. The electrical current creates a magnetic field that is modified by the movement of the chest while the person breathes. The signal returns to the driver module that changes it to an analog signal. [40]

3.2 Emfit movement sensor

The electromechanical film transducer (Emfit) movement sensor has been manufactured from the electromechanical film (EMFi) which is an electret film with cellular internal structure. The internal cellular structure is created by biaxially orienting

a specially fabricated polymer preform. After the foil has been stretched it will be charged by using a point or plane electrode corona discharge system in high electric field. After charging the film is metallized on both sides to create electrodes. Thank to the voided internal structure the EMFi film is very flexible, that combined with the strong permanent charge makes EMFi very sensitive to dynamic forces exerted normal to its surface. The external force causing variation to the thickness of the film can be detected by measuring the change in the capacitance. [58]

The internal structure of the EMFi consists of several polypropylene layers separated by the air voids. An external force applied to the surface of the film's surface will change the thickness of the air voids. The distortion of the air voids will cause the permanent charges residing on the interfaces between polypropylene and the void interfaces to move in respect with each other. This will lead to a generation of mirror charges on the electrodes. The generation of the charge signal is due to the voided internal structure of the EMFi not the piezoelectricity of the polypropylene material. The generated charge is proportional to the change of the film thickness. Due to the elasticity of the EMFi material the charge is also proportional to the force or pressure exerted on the film.

$$\Delta q = k\Delta F \text{ or } \Delta\sigma = k\Delta p, \tag{1}$$

where Δq is the charge (C), k is the sensitivity factor, ΔF is the acting dynamic force (N), $\Delta\sigma$ is the generated charge per unit area ($\frac{\mathrm{C}}{\mathrm{m}^2}$) and Δp is the acting dynamic force per unit area ($\frac{\mathrm{N}}{\mathrm{m}^2}$). The EMFi material is very sensitive to the thickness variation and the sensitivity factor can be up to 600 $\frac{\mathrm{pC}}{\mathrm{N}}$, but it's quite insensitive to the stretching and the sensitivity factor for stretching is only a few $\frac{\mathrm{pC}}{\mathrm{N}}$. A charge amplifier or a voltage amplifier with high input impedance can be used to measure the charge. Due to capacitive principle of the electret sensor the EMFi is at its best when measuring dynamic forces. [58]

3.2.1 Possible clinical applications

There are multiple articles studying possible clinical applications where the Emfit movement sensor could be used, next we will go over some of them. Emfit movement sensor can be used as an additional tool in monitoring convulsive seizures in epilepsy patients [3]. Emfit movement sensor can also be used to monitor limb movements in bed [70].

The low frequency $0.3 - 10$ Hz part of the Emfit movement sensor signal can be used to detect breathing movements. It's possible to visually recognise normal breathing pattern, periodic breathing patterns that include periodic type and obstructive periodic types, and sustained spiking pattern from the Emfit movement sensor data [86]. In one study the Emfit movement sensor was used to monitor hospitalized patients after surgical intervention by measuring the beat-to-beat intervals (BBIs) and the ultra-short-term heart-rate-variability (HRV) with a help of an iterative algorithm [32]. The Emfit movement sensor has also been used to detect sleep stages by measuring the heart beat interval and movement activity from the ballistocardiographic (BCG) measurements with the Emfit movement sensor [41]. In another study it was used for continuous sleep monitoring in patients with incomplete spinal cord injury or stroke. The heart rate (HR) and respiratory rate (RR) were monitored with the Emfit movement sensor [29]. It has even been used to monitor infant sleep cycling in the intensive care unit by measuring the respiratory and gross-body movements [68].

The Emfit movement sensor has also been used for screening of sleep apnea. The objective was to find an unobtrusive measurement method that wouldn't affect the test subjects sleep and could be automatically interpreted to preserve health care resources and help to prioritize the polysomnography measurements for those patients with highest need. The respiratory and ballistocardiography (BCG) signals were monitored using the Emfit movement sensor. [33]

3.3 Amplifier

Biosignals can be recorded as potentials, currents and electrical field strengths generated by the muscles and nerves. The voltages measured have very low level, typically measured values are between 1μV and 100mV. The biosignals measured from the body contain high level superimposed interference signals and noise. The body also has a high source impedance. The biosignals have to be amplified for them to be compatible with devices like displays, recorders or analog to digital converters (A/D). Amplifier has to amplify the selected physiological signal while rejecting superimposed noise and interference signals. Amplifier must also protect both the patient and the electronic equipment from voltage and current surges. The amplifier can't have any influence on the physiological process it's meant to monitor and it isn't supposed to distort the measured signal. The amplifiers input signal contains five components that are the desired biopotential, undesired biopotentials, a power line interference signal of 50 or 60 Hz depending on the country's electrical system and its harmonics, interference signals generated by the interface between the electrode and the tissue, and noise. [10, p. 52-1 - 52-2]

The differential amplifier measures the voltage between two input terminals, it's good at rejecting the line frequency interference that is coupled to the subject either electrostatically or magnetically. The desired biosignal appears as a voltage between the two electrodes where as in the line interference signal there are only very small differences in the amplitude and the phase between the two electrodes so both electrodes experience almost same potential from the interference. For this reason the interference can only be detected between the inputs and the ground and therefore it's called the common mode signal and a strong capability to reject the common mode signal is one of the most important features of a biopotential amplifier. In reality the amplifiers output will always contain small portion of the common mode signal due to imperfect rejection of the common mode interference

and differences in impedance at the different interfaces that will allow a small portion of the common mode signal to appear as differential signal to the amplifier. [10, p. 52-2]

The amplifier gain has to be between 100 and 50000 to provide optimum signal quality and adequate signal level for necessary signal processing and the amplifier has to maintain high signal-to-noise ratio. Avoiding interference signals has to be taken in consideration even in the amplifier design. For example the electrode half-cell potentials originating from the conversion of ion current into electron current at the electrode electrolyte interface can have a magnitude of several times that of the physiological signal, therefore the amplifier has to be designed so that the interference is eliminated before the physiological signal can be amplified into required level in order to avoid the saturation of the amplifier. Thus preamplifier is a critical part of the amplifier as it sets the limits for the quality of the biosignal. A well designed preamplifier can minimize or possibly even eliminate most of the signals interfering with the desired biosignal. [10, p. 52-3]

Noise is an element that has to be taken into account in the amplifier's design. The resistance of the biological source combined with all the transition resistance between the signal source and the amplifier input is called the source resistance R_{S}. The source resistance R_{S} causes thermal voltage noise, it's root mean square (rms) value can be expressed as

$$E_{\mathrm{rms}} = \sqrt{4kTR_{\mathrm{S}}B}, \tag{2}$$

where k is Boltzmann constant, T is absolute temperature, R_{S} is resistance in ohms and B is bandwidth in hertz. There is also noise generated inside the amplifier, it consists of two frequency-dependent components. First one is the internal voltage noise source e_{n} and the second one is the voltage drop across the source resistance R_{S} caused by an internal current noise generator i_{n}. The total input noise for the amplifier with a bandwidth of $B = f_2 - f_1$ can be calculated as a sum of those three

components

$$E_{\mathrm{rms}}^2 = \int_{f_1}^{f_2} e_{\mathrm{n}}^2 \, df + R_{\mathrm{S}}^2 \int_{f_1}^{f_2} i_{\mathrm{n}}^2 \, df + 4kTR_{\mathrm{S}}B. \tag{3}$$

In order to achieve high signal-to-noise ratios one has to use very low noise amplifiers and limit the bandwidth by using low pass and high pass frequency filters. [10, p. 52-3 - 52-4]

An important part of the amplifier is the isolation stage that provides the galvanic decoupling of the patient from the measuring equipment, it also provides safety from electrical hazards. The isolation stage also prevents the galvanic currents from deteriorating the signal-to-noise ratio, this is achieved especially by preventing the ground loops. There are different ways to implement the isolation stage. Analog isolation amplifiers can use transformer, optical or capacitive couplers to transmit the signal through the isolation barrier. Digital isolation amplifiers use voltage/frequency converter to digitalize the signal, then it can be easily transmitted by optical or inductive coupler to the output frequency/voltage converter. Important characteristics for an isolation amplifier are low leakage current, isolation impedance, isolation voltage rejection also called isolation mode rejection (IMR), and maximum safe isolation voltage. [10, p. 52-4]

3.4 Measurement artifacts

Usually measurements are carried out in spaces where there are also other electrical equipment capable of producing strong electric and magnetic fields. In addition to the power line frequency of 50 or 60 Hz and their harmonics there are also high frequency electromagnetic fields. At the power line frequency the electric and magnetic components of the interference field can be considered separately. All connectors connected to the power - even without any flow of current - cause electrical fields. This allows the current to be capacitively connected to the body where it flows to the ground electrode. To minimize the interferences the distance between

the patient and the power lines must be increased, isolation amplifiers and shielded electrode cables are to be used and the body should be grounded using a separate ground contact as far from the measurement electrodes as possible. Magnetic fields cause eddy currents in the patient. The patient, the electrode cables and the amplifier create an induction loop that can receive interference signals. Minimizing the interferences can be achieved by increasing the distance between the patient and the interference source and aligning the patient so that the interferences are at the lowest level. Other counter measures are twisting the connection cables and shielding against magnetic fields. It's also possible to use an additional narrow band rejection filter called the notch filter for the suppression of the line frequency interferences. [10, p. 52-4]

If the tissue and the electrode move relative to each other, there will be changes in the electrode offset potential and the electrode/tissue impedance. So the movement of the electrode will create two interference signals that are called motion artifacts. These motion artifacts can be reduced by using high input impedance for the preamplifier, non-polarized electrodes with low half-cell potentials and electrode gel to reduce the source impedance. The wires connecting the electrodes to the amplifier can also be the source for interferences in the measurement signal. Motion artifacts, interference from external electromagnetic fields and noise can originate from the wires. These interferences can be reduces by using twisted pair cable, shielded wires and input guarding. [10, p. 52-4]

Motion artifacts are possible also in respiratory inductive plethysmography. The RIP signal can be distorted by miscellaneous thoracic or abdominal wall motions or gross-body movements complicating the detection of respiration movement. There are filters that are designed to reduce the motion artifacts in the RIP signal. Most of the filters operate in the frequency domain. Because the occurrence and the frequency content of the motion artefacts are unpredictable, it's possible that the

filters themselves distort the RIP signal by removing both the artifact and important parts of the RIP signals. [71]

In pulse oximetry there are two sources of measurement artifacts. The first one is ambient lightning, second one is motion artifact from voluntary or involuntary movement of the test subject. Measurement artifacts are special concern in ambulatory measurements as the ambient conditions and test subject movements can't be controlled. It's difficult to remove measurement artifacts from the pulse oximetry signal because the signal and the artifacts can be very similar temporally and spectrally. [27]

If the test subject is breathing partially through the mouth the air flow from the nasal pressure measurement doesn't represent the full air flow. Nasal pressure measurement can also contain movement artifacts [72]. The thermistor doesn't measure the air flow directly, it's only estimated from the temperature differences between the inhaled and exhaled air. The displacement of the thermistor will lead to an erroneous estimation of the air flow [1].

The Emfit movement sensor measurements contain also movement artifacts that can distort the breathing signal. The placement of the Emfit movement sensor can affect the amount and severity of the movement artifacts. Filtering the Emfit movement sensor signal to remove the movement artifacts can lead to distortion of the signal as the filter can remove both the artifact and a meaningful part of the Emfit movement sensor signal. [33]

4 Analysis methods

The measurement data was first scored manually by an experienced specialist and this scoring was used as the gold standard. Then the measurement data was scored using the automatic analysis tool created by the Nox Medical for the Noxturnal software. The automatic analysis scorings were then compared to the manual scorings.

Comparing two measurement methods is a common task in medicine [25]. There is always some error in the measurement so the new measurement method has to be compared to the established one rather than comparing it to the true value. There are statistical methods to compare the methods like correlation coefficients [7]. We used various tests to compare the two measurement methods, the standard respiratory polygraphy and the Emfit movement sensor combined with the wrist oximeter.

4.1 Automatic analysis of respiratory polygraphy

It has been shown that respiratory events can be scored using nasal pressure, square root transformation of the nasal presusre or flow derived from the respiratory inductive plethysmography as a measure of airflow [46]. Respiratory events are usually scored manually using the visual rules from the AASM scoring manual [47]. Most device manufacturers have included an option of performing automatic scoring into their software. The automatic scoring tools can be used to speed up the manual review process and to reduce the need for the specialist work input [51]. If a measurement device is to be used as a scoring tool to detect patients with high risk of sleep apnea, there is a need for reliable automatic scoring tool. The automatic scoring must be accurate enough so it can detect the patients with high risk to be tested more accurately and rule out patients with low risk to avoid excess testing.

One can create computer algorithms for signal analysis that are used to detect sleep disordered breathing events from certain signals. These computer algorithms

can also be used to analyse other signal types if they are validated for these other signal types [55]. The quality of the automatic analysis of respiration signal is highly dependent on the measuring equipment [60]. The automatic scoring usually consists of two phases. In the first phase the raw signal is preprocessed [79]. The preprocessing in done to reduce the vast amount of raw data so that it can be managed by statistical tools. As a result of preprocessing a set of features such as the amplitude of the regular EEG waves are obtained. Another important task for the preprocessing is the artifact rejection. Artifact rejection can be achieved by filtering the signal or by correlation analysis. In the second phase the extracted features and waveforms are combined to the correct event that can be a certain sleep stage or a respiratory event. The correct classification of the feature is usually determined using logic rules. The logic rules can be determined at the development of the analysis program or they can be continuously improved by adapting them to the new recorded data [61].

Soon the automatic scoring methods that are based on the deep learning algorithms and the artificial intelligence (AI) algorithms will be available and in everyday use. One of the advantages of these algorithms is that they can be applied directly to the raw data with minimal artifact removal. The training of the algorithm can be done without preliminary information or precise mathematical formulation. But the quality of the training dataset is crucial, the training of the machine learning algorithm requires a heterogeneous training dataset to take into account the vast heterogeneity in human sleep and human scoring. [22]

According to a study the Noxturnal automatic scoring of the AHI has a strong agreement with scoring performed by an experienced manual scorer. There is a strong agreement between automatic scoring and manual scoring even when alternative airflow signals such as transformed nasal pressure or respiratory inductance plethysmography flow signal are used as a airflow signal for the automatic scoring

[47]. Because there are no EEG signals in the HSAT the arousals can't be detected by the HSAT, this may lead to underestimation of OSA severity compared to the PSG. The automatic analysis scores an artifact when the signal is absent or deemed to be invalid. Signal quality reported by the automatic analysis is defined as the ratio of total duration of scoreable signal within the analysis period to the total duration of signal within the analysis period. Noxturnal calculates the AHI as average number of apneas per hour of analysis time in the standard respiratory polygraphy measurements [91].

4.2 ROC curves

A receiver operating characteristics (ROC) curve is a technique for visualising, organising and selecting classifiers based on their performance. ROC analysis was originally used for signal detection in radar technology, but it's usage has spread to a wide field of applications including medicine [18]. ROC analysis is a valuable tool for evaluating the performance of diagnostic test which classifies subjects into one of two categories, diseased or nondiseased [93].

Using a cutoff level or threshold an ordinal scale can be dichotomized. When applying the ROC analysis one has to have a reference method to determine the subjects true condition without error, this method is called the gold standard. The sensitivity, also known as the true positive rate, and the specificity, also known as the true negative rate, are the fundamental measures of the diagnostic accuracy [93]. The sensitivity is defined as

$$\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}} \tag{4}$$

and the specificity is defined as

$$\text{Specificity} = 1 - \text{false positive rate} = 1 - \frac{\text{false positive}}{\text{false positive} + \text{true negative}}. \tag{5}$$

ROC curve is drawn by plotting the sensitivity on the y axis and the specificity on the x axis [18].

By calculating the area under the curve (AUC) one can effectively summarize the overall diagnostic accuracy of the test method. AUC of 0.5, when the ROC curve is a straight line from point (0,0) to point (1,1), represents a situation where the accuracy of the test method is 50 percentage. AUC of 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent and above 0.9 is considered outstanding. ROC curves can be used to compare the diagnostic ability of two or more screening tests. The screening method with higher AUC can be considered better. [50]

4.3 Bland-Altman analysis

Bland-Altman analysis can be used to compare two measurement methods. The measurement of variables always includes some degree of error [25]. Because none of the measurement methods doesn't give the absolute true value, therefore the new measurement method has to be evaluated against the established technique instead of the true quantity. The new method can be accepted if it agrees sufficiently with the established one [7]. Bland-Altman analysis is frequently used in method comparison studies with quantitative outcomes [24].

To perform the Bland-Altman analysis there has to be paired measurement data from the same subject with both measurement methods [7]. Bland-Altman plot is a scatter plot, where the y axis represents the difference between the two paired measurements and x axis represents the average of these two measures [25]. The mean difference $\bar{d}$ represents the relative bias and the standard deviation of the differences s is the estimate of the error [2]. The limits of agreement are calculated as $\bar{d} \pm 2s$. If the differences are normally distributed (Gaussian), 95 percentage of the differences will be between these limits [7].

4.4 Spearman's rank correlation coefficient

Spearman's rank correlation coefficient r_S also known as Spearman's ρ is a non-parametric statistic [75]. It can be used for both continuous and discrete ordinal variables [67, p. 438]. Spearman's rank correlation coefficient describes the strength of an association between two variables X and Y [75]. If the correlation is complete the smallest values of variables X and Y are measured from the same sample, also the second smallest values will be measured from the same sample and so forth to the largest values that will be measured from the same sample. This is called the positive correlation. The complete correlation can also be inverted, then the smallest value of X corresponds to the largest value of Y and vice versa. This is called the negative correlation. If the correlation isn't complete but there is still a strong correlation then in positive correlation large values of X are connected to the large values of Y [67, p. 438 - 439].

The values of variable X need to be organized from the smallest value to the largest. The smallest value will be replaced by the rank $R(X_1) = 1$, the second smallest by the rank $R(X_2) = 2$ until the largest value will be replaced by the rank $R(X_n) = n$. Similarly the values of the variable Y will be organized by value and replaced by the rank $R(Y_i)$. If there are ties, $X_i = X_{i+1}$, among the values, they both will be given the average of the ranks they would have received if there were no ties $R(X_i) = R(X_{i+1}) = \frac{1}{2}(n + (n + 1)) = n + \frac{1}{2}$. [15, p. 245]

If there are no ties, the measure of correlation is defined as

$$r_S = 1 - \frac{6\sum_{i=1}^{n}[R(X_i) - R(Y_i)]^2}{n(n^2 - 1)} \ [15, p.246]. \tag{6}$$

If there are many ties among the values, the correlation coefficient should be calculated using the following equation

$$r_S = \frac{\frac{(n^3-n)}{6} - \sum_{i=1}^{n}[R(X_i) - R(Y_i)]^2 - T_X - T_Y}{\sqrt{[\frac{n^3-n}{6} - 2T_X] \cdot [\frac{n^3-n}{6} - 2T_Y]}}. \tag{7}$$

To take into account the ties for the variable X a correction factors T_X and T_Y has to be calculated using the following equation

$$T_X = \frac{\sum_{i=1}^{n}(t_i^3 - t_i)}{12}, \tag{8}$$

where t_i is the number of tie values associated with the ordinal number i [67, p. 440]. If there are only a moderate number of ties in the data, then it's recommended to use the equation (6) for the computational simplicity [15, p. 246].

The Spearman's rank correlation coefficient is often used as test statistic to test for the independence between two random variables [15, p. 247]. The hypotheses will be presented as

$$H_0 : \text{The } X_i \text{ and } Y_i \text{ are mutually independent.}$$

H_1 : There is either positive or negative correlation between variables X_i and Y_i. [67, p441].

5 Materials and methods

In this section the outline of the study is described.

5.1 Study population

This study is a part of a larger study about sleep-disordered breathing in Finnish stroke patients at Satakunta Hospital District. Test subjects were recruited from Satakunta's Central Hospitals stroke unit between March 2013 and November 2016. Total of 102 patients were recruited for this study. Inclusion criteria included that the test subjects had no previous stroke or TIA, they were able to give informed consent and the study could be conducted within 72 hours from the hospital admission. Most patients had less than 72 hours from the appearance of the ischemic stroke or TIA symptoms. Few of the patients reported later that they had experienced fluctuating symptoms or prior symptoms within the preceding week. Patients with previous strokes, diagnosis or treatment of sleep apnea were excluded from the study. The requirement was that the patient was conscious and not suffering of disabling aphasia to be able to give written informed consent to participate into this study.

The diagnosis of a ischemic stroke or TIA was confirmed by the Neurologist based on the sudden onset of neurological deficit, clinical examination and brain imaging. A detailed medical history and neurological examination was conducted by the Neurologist according the hospital protocol. Following demographic data was collected from all the test subjects by the Scientist: sex, age, smoking, previous diseases, marital status, education and occupation. Body mass index (BMI) was calculated for all except for five patients. The severity of the ischemic stroke was evaluated using the National Institute of Health Stroke Scale and disability was evaluated using the Barthel index scale (BI) on the registration day [11], [48]. All participants were scanned using the computer tomography (CT) and selected pa-

tients were also scanned using the magnetic resonance imaging (MRI). All routine laboratory tests, ECG, chest x-ray and blood pressure were conducted according to the hospitals normal protocol of stroke and TIA patients.

This research project was approved by the ethical board of Hospital District of South west Finland. Participation to the study was voluntary and every participant had to give a written informed consent. By the rules of the ethical committee a caregiver or a relative could not give the informed consent on the behalf of the patient.

5.2 Patient measurements

All test subjects underwent a standard respiratory polygraphy registration on the first or second night at the stroke unit. The registrations were conducted by the Scientist during weekdays from Monday to Thursday. The Scientist applied the standard respiratory polygraphy measurement device on the patient in the afternoon except for the nasal cannula which was applied by the the stroke units nurses right before the patient went to sleep. In the morning the Scientist returned to the stroke unit to help the patient to remove the recording device.

The respiratory polygraphy measurement was conducted using the Nox T3 recorder manufactured by the Nox Medical, Katrìnartùn 2, 105 Reykjavik, Iceland. The Nox T3 measuring device consisted of an EMG channel monitoring the leg movements, an ECG channel monitoring the heart rate, an abdomen and a thorax RIP belt monitoring the breathing movements of the chest, a nasal cannula measuring the air pressure from the nostrils, internal microphone monitoring snoring sounds, internal accelerometer monitoring the body position and an external wrist oximeter monitoring the blood oxygen saturation from the tip of the patients finger. The oximeter used was the Nonin WristOx$_2$ Model 3150 wrist oximeter manufactured by the Nonin Medical Inc, 13700 1st Ave N, Pymouth, Minnesota. The oximeter

was connected to the Nox T3 recorder via bluetooth and the saturation data was recorded on the Nox T3 device.

Simultaneously with the standard respiratory polygraphy measurement conducted with the Nox T3 device every test subject underwent also an sleep mattress recording using the Emfit movement sensor manufactured by Emfit Ltd, Konttisentie 8 B, Vaajakoski, Finland. The Emfit movement sensor was placed around the thoracic area under the bed mattress in the test subjects bed and it was used to measure ballistography (BSG) including the respiratory movements and the movements caused by the beating heart during the recording night. The Emfit movement sensor signal was complemented with the oximeter signal. The Emfit signal was recorded using the Nox T3 device which ensured that all measurements signals were perfectly synchronized.

41 out of the recruited 102 patients were included in this analysis, the rest were rejected because of technical issues relating to the registration. One reason to reject a registration was a technical malfunction of one or both measuring devices, at the start there were problems with the quality of the batteries and some registrations were incomplete because the battery had run out during the night. Another reason for incomplete registration was that the nursing staff at the stroke unit had to take off the measuring equipment at night in order to perform medical procedures for the patient. Due to the smaller staff resource at night time they didn't have resources or experience to place the equipment back on the patient.

5.2.1 Scoring the registrations

The standard respiratory polygraphy registered with the Nox T3 was scored visually by the Scientist according to the scoring rules of American Academy of Sleep Medicine [34]. The visual scoring made by the Scientist was considered as the gold standard to which the automatic scoring results were compared to. Both studies

were scored automatically using the automatic analysis tool in the Noxturnal software version 4.3.0 by Nox Medical.

Automatic analysis of the standard respiratory polygraphy recording used saturation and flow signals to detect apneas and hypopneas, in addition the respiratory inductive belt signals from the abdomen and thorax belts were used to classify apneas into obstructive, central or mixed apnea and flow signal was used also for artifact detection. The saturation signal was obtained from the wrist oximeter, flow signal from the nasal pressure channel and respiratory inductance plethysmography signals from abdomen and thorax RIP belts. The automatic analysis settings for apnea and hypopnea duration was from 10 seconds to 120 seconds, apnea was defined as 90 percentage drop and hypopnea as 30 percentage drop in the flow signal. Automatic analysis settings defined that the hypopneas would be linked to concurrent desaturation drops if detected.

The pulse oximeter signal was used to detect desaturation events. The lower limit for desaturation event was defined as three percentage and duration was set to be atleast three seconds with 45 seconds as the longest duration for the plateau. The phase signal was used to detect paradoxical breathing. Threshold was set to be 40°, minimum duration 30 seconds and join interval 10 seconds.

The flow limitation events were detected from the cannula flow signal. Threshold value for flow limitation was set at 0.15.

Similarly automatic analysis of the Emfit movement sensor recording used saturation and flow signals to detect apneas and hypopneas. The saturation signal was obtained from the wrist oximeter but in the absence of actual flow signal from the nasal pressure channel it was substituted with the respiratory movement signal from the Emfit movement sensor. For the algorithm of automatic classification of apneas the respiratory movement signal from the Emfit movement sensor was used instead of the missing respiratory inductive belt signals from the abdomen and thorax belts.

The automatic analysis settings for apnea and hypopnea scoring were identical with the settings used for the analysis of the standard respiratory polygraphy recordings. Because there is no actual flow data the algorithm can't correctly classify the detected events and therefore all the detected events in the Emfit movement sensor recording are called respiratory events.

The signals and settings for detecting desaturation events were identical with the ones used for automatic analysis of the standard respiratory polygraphy recording. The same wrist oximeter data was used for both recordings.

The algorithms used in the automatic analysis tool compares the signal to the thresholds and time periods defined in the settings to detect the events it's searching for. The apnea hypopnea algorithm scans the flow and RIP signals to detect moments of abnormal breathing. The apnea hypopnea algorithm also compares the detected hypopnea events to detected drops in blood oxygen level in order to link corresponding hypopneas and desaturations. The desaturation algorithm observes the pulse oximeter signal to detect if the blood oxygen level drops below the threshold defined in the settings. The desaturation algorithm marks the detected events as desaturations. The apnea classification algorithm compares the flow signal to the RIP signals to determine if there is breathing effort during the detected apnea event. The automatic analysis tool follows the AASM rules and it's results are validated against manually scored clinical data [56, p. 78 - 81], [47], [91].

5.3 Data analysis

Apnea-hypopnea indexes (AHI) obtained from the automatic scorings were compared to the AHI obtained from the visual scoring. The automatic scoring of the standard respiratory polygraphy measurement and the Emfit movement sensor measurement were conducted using the same algorithms and settings so the differences between results should originate from the differences in the signals not from different

interpretation of signal as it could be if a person would have scored both. The aim of the comparisons was to evaluate if the Emfit movement sensor could be used to screen ischemic stroke patients with sleep apnea and if the automatic analysis could be used for scoring the recording instead of labour consuming visual scoring by a person. The performed analyses are described in detail at next section along the results obtained.

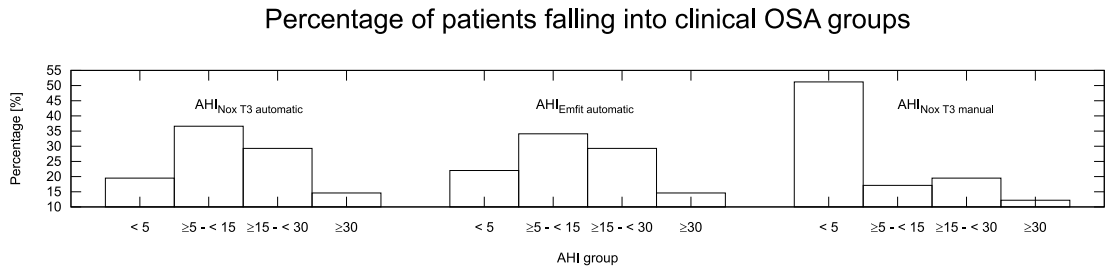

Figure 1. Patients divided into different groups depending on the clinical severity of their obstructive sleep apnea according to different scoring methods.

6 Results

We used several tests to compare the automatic analyses to each other and to the manual analysis. In this section we go over the results acquired from each test and the comparisons.

6.1 Patients falling into clinical obstructive sleep apnea groupings

We wanted to study how the different scoring methods categorize patients into different classes of clinical severity of obstructive sleep apnea. Therefore we plotted a bar graph of patients falling into different clinical obstructive sleep apnea (OSA) classes in each of the scoring methods. Results are presented in the figure 1.

Compared to the manual scoring the automatic scoring methods categorize the patients with more severe sleep apnea as we can see from the figure 1. The manual scoring sets 50 percentage of the patients in to the no obstructive sleep apnea class as the automatic scoring methods sets less than 25 percentage of the patients in to the same class. We can also see from the figure 1 that the distribution of patients are very similar between the both automatic scoring methods.

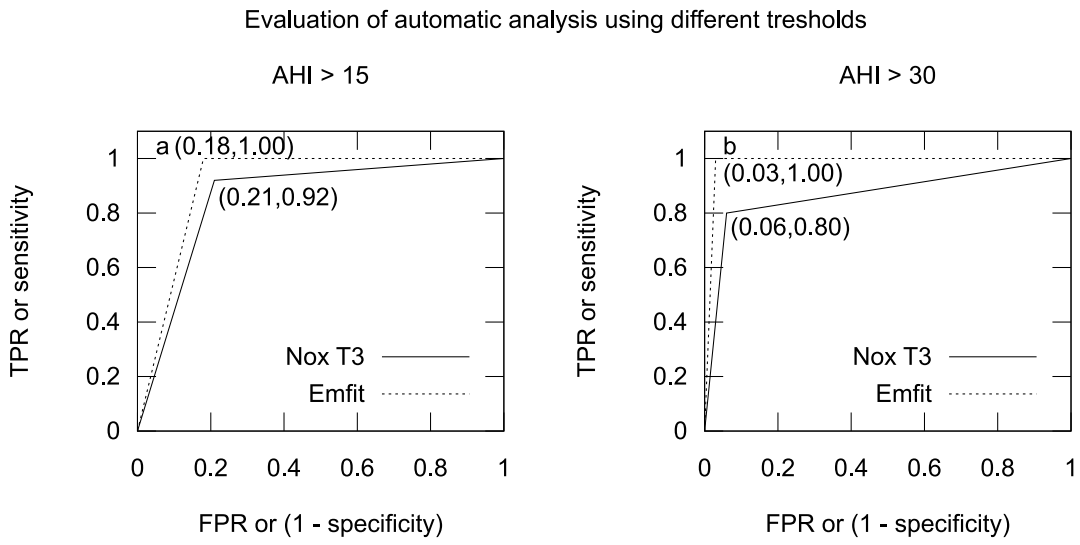

Figure 2. a) ROC curve using AHI > 15 as threshold comparing the automatic scoring of the Nox T3 measurement and the automatic scoring of the Emfit movement sensor measurement to the manual scoring of the Nox T3 measurement, b) same comparison using AHI > 30 as threshold.

6.2 Receiver Operating Characteristic analysis

We created receiver operating characteristic (ROC) curves to determine how well the two automatic scoring methods can detect patients with atleast moderate sleep apnea (AHI > 15) or severe sleep apnea (AHI > 30). Resulted ROC curves are seen in the figure 2.

ROC analysis for the automatic analysis of the standard respiratory polygraphy data revealed that the sensitivity was 92 percentage and the specificity was 79 percentage. For the automatic analysis of the Emfit movement sensor the sensitivity was 100 percentage and the specificity was 82 percentage. We also made the ROC analysis using the AHI value of 30 events per hour, the limit for the severe sleep apnea, as a threshold. Then the results for the automatic analysis of the standard respiratory polygraphy data were sensitivity 80 percentage and specificity 94 percentage and for the automatic analysis of the Emfit movement sensor results were sensitivity 100 percentage and specificity 97 percentage.

The automatic analysis of the Emfit movement sensor data has better results compared to the automatic analysis of the standard respiratory polygraphy data with both thresholds. The results suggest that the Emfit movement sensor might be used to screen for sleep apnea in the ischemic stroke patients.

6.3 Bland-Altman analysis

Then we wanted to analyse the agreement between the manual scoring of the standard respiratory polygraphy measurement and the automatic scoring of the standard respiratory polygraphy measurement and the automatic scoring of the Emfit movement sensor measurement. We decided to use Bland-Altman plot as a method to do this analysis. Bland-Altman plots are presented in figure 3.

In figure 3 a) we can see that the automatic scoring of the standard respiratory polygraphy measurement overestimates the sleep apnea compared to the manual scoring of the standard respiratory polygraphy measurement as the mean 5.1 is positive. In figure 3 b) we can see that also the automatic scoring of the Emfit movement sensor measurement overestimates the sleep apnea compared to the manual scoring of the standard respiratory polygraphy as the mean 4.5 is also positive. In figure 3 c) we can see that the automatic scoring of the standard respiratory polygraphy and Emfit movement sensor have quite good agreement, all tough the automatic scoring of the standard respiratory polygraphy measurement yields little bigger values as the mean -0.5 is negative.

6.4 Spearman's rank correlation coefficient

We used Spearman's rank correlation coefficient to assess the relationship between the different scoring methods. First we ranked our data, we gave each value a number from 1 to the number of our samples, so that the biggest value gets number 1 and the smallest one gets the biggest rank. Then we used equation (9) to calculate

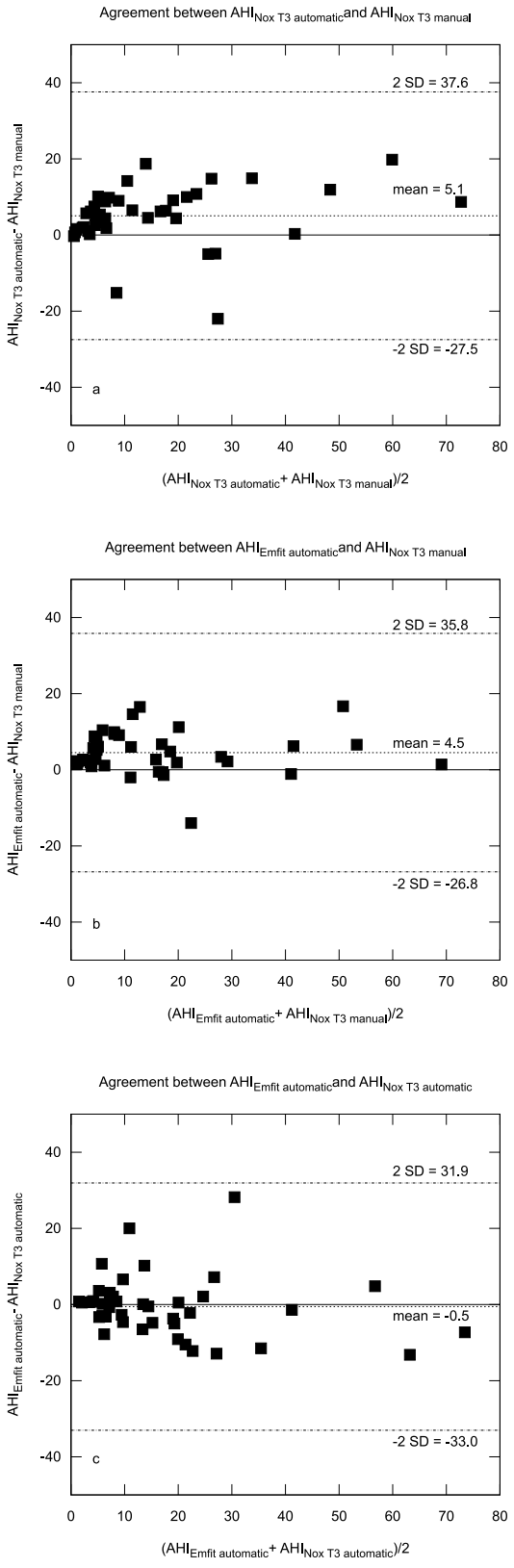

Figure 3. Bland-Altman plots between a) Nox $T3_{manual}$ and Nox $T3_{automatic}$ b) Nox $T3_{manual}$ and $Emfit_{automatic}$ c) Nox $T3_{automatic}$ and $Emfit_{automatic}$.

the Spearman's rank-ordered correlation.

$$\rho = \frac{\Sigma_i(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\Sigma_i(x_i - \bar{x})^2 \Sigma_i(y_i - \bar{y})^2}} \tag{9}$$

The Spearman's rank-ordered correlations are presented in the figure 4.

From figure 4 a) we notice that there is a positive correlation between the manual and the automatic scoring of the standard respiratory polygraphy measurement and that the automatic scoring gives higher values than the manual scoring. From figure 4 b) we see similarly that there is a positive correlation between the manual scoring of the standard respiratory polygraphy measurement and the automatic scoring of the Emfit movement sensor measurement and the automatic scoring yields higher values than the manual scoring. From figure 4 c) we notice that there is also a positive correlation between the automatic scoring of the standard respiratory polygraphy measurement and the automatic scoring of the Emfit movement sensor measurement and that the automatic scoring of the standard respiratory polygraphy measurement gives a little higher values than the automatic scoring of the Emfit movement sensor measurement.

6.5 Signal graphs

We also took screen captures from the analysis software Noxturnal to visually analyse how the shape of the signal affects the automatic analysis and why both the automatic scoring methods give higher values than the manual scoring. We chose those signals that are used for scoring. For the standard repsiratory polygraphy scoring it includes the SpO_2, the airflow from the nasal cannula and the abdominal and the thoracic respiratory inductance belt, for Emfit movement sensor it includes the SpO_2 and the Emfit movement sensor signal. In the Emfit movement sensor automatic scoring the Emfit movement sensor signal was used as airflow signal and as respiratory inductance belt signal. In every figure at the top there are the signals and events from the manual scoring of the standard respiratory polygraphy ,

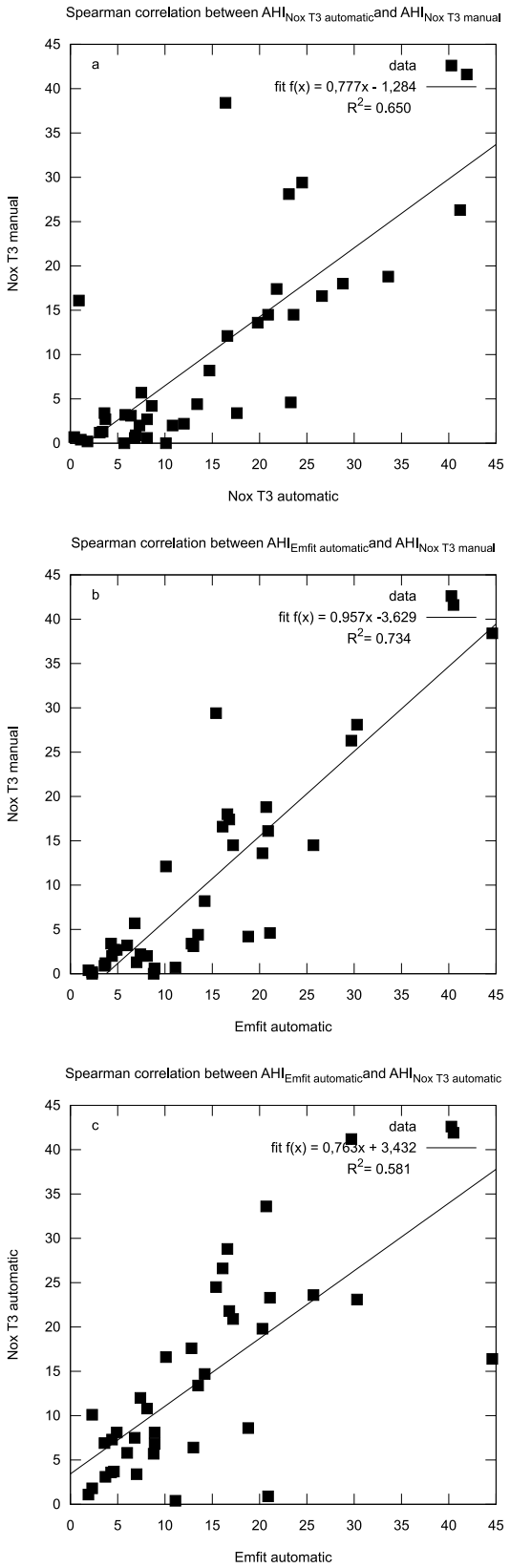

Figure 4. Spearman correlations between a) Nox $T3_{manual}$ and Nox $T3_{automatic}$ b) Nox $T3_{manual}$ and $Emfit_{automatic}$ c) Nox $T3_{automatic}$ and $Emfit_{automatic}$.

in the middle are the signals and events from the automatic scoring of the standard respiratory polygraphy and at the bottom are the signals and the events from the automatic scoring of the Emfit movement sensor.

Because the Emfit movement sensor automatic scoring doesn't have the information about the airflow, it can't classify the events. Therefore all the events the Emfit movement sensor automatic scoring has detected are classified as respiratory events (RE). We were studying the possibility to use the Emfit movement sensor as a screening method, therefore we are not interested about the classification of the events only about the capability to detect the breathing disturbances.

In figure 5 we see a situation where the automatic scoring of the Emfit movement sensor has detected the breathing disturbances quite well even though some event durations are off. In figure 6 the automatic scoring of the Emfit movement sensor has misplaced some events and detected incorrectly the duration of almost all of the events. This was quite common error for the automatic scoring of the Emfit movement sensor signal and it's probably because of the different measurement method the Emfit movement sensor signal contains some noise during the breathing disturbance and the automatic analysis interprets it as a movement from breathing.

6.6 Overlapping events

We wanted to study if the automatic scoring of the Emfit movement sensor can find the actual breathing disturbances. We did this by comparing the timing of the Emfit movement sensor automatic scoring events to the timing of the standard respiratory polygraphy automatic scoring events to see how well they overlap. There is an example of event timing and duration from different scoring methods in the figure 8. When comparing the events we looked both the actual duration that the Emfit movement sensor events overlapped with the standard respiratory polygraphy manual and automatic scoring events in figure 8 and the percentage of Emfit

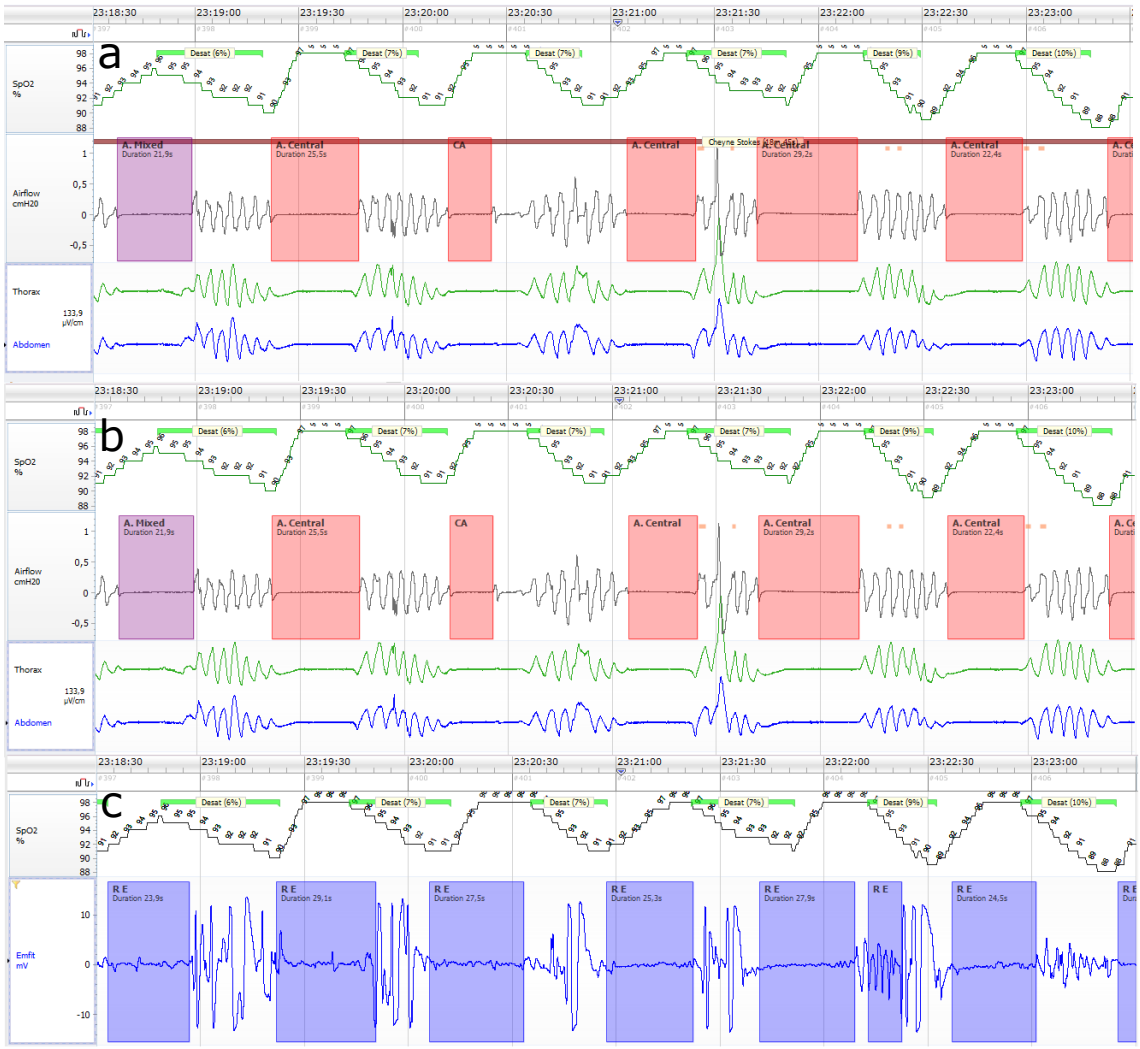

Figure 5. Comparision of signals and events between a) the Nox T3 $_{\text{manual}}$, b) Nox T3$_{\text{automatic}}$ and c) Emfit$_{\text{automatic}}$. The Emfit$_{\text{automatic}}$ scoring has detected the breathing disturbances quite well, possibly because the Emfit movement sensor signal is almost flat during the breathing disturbances.

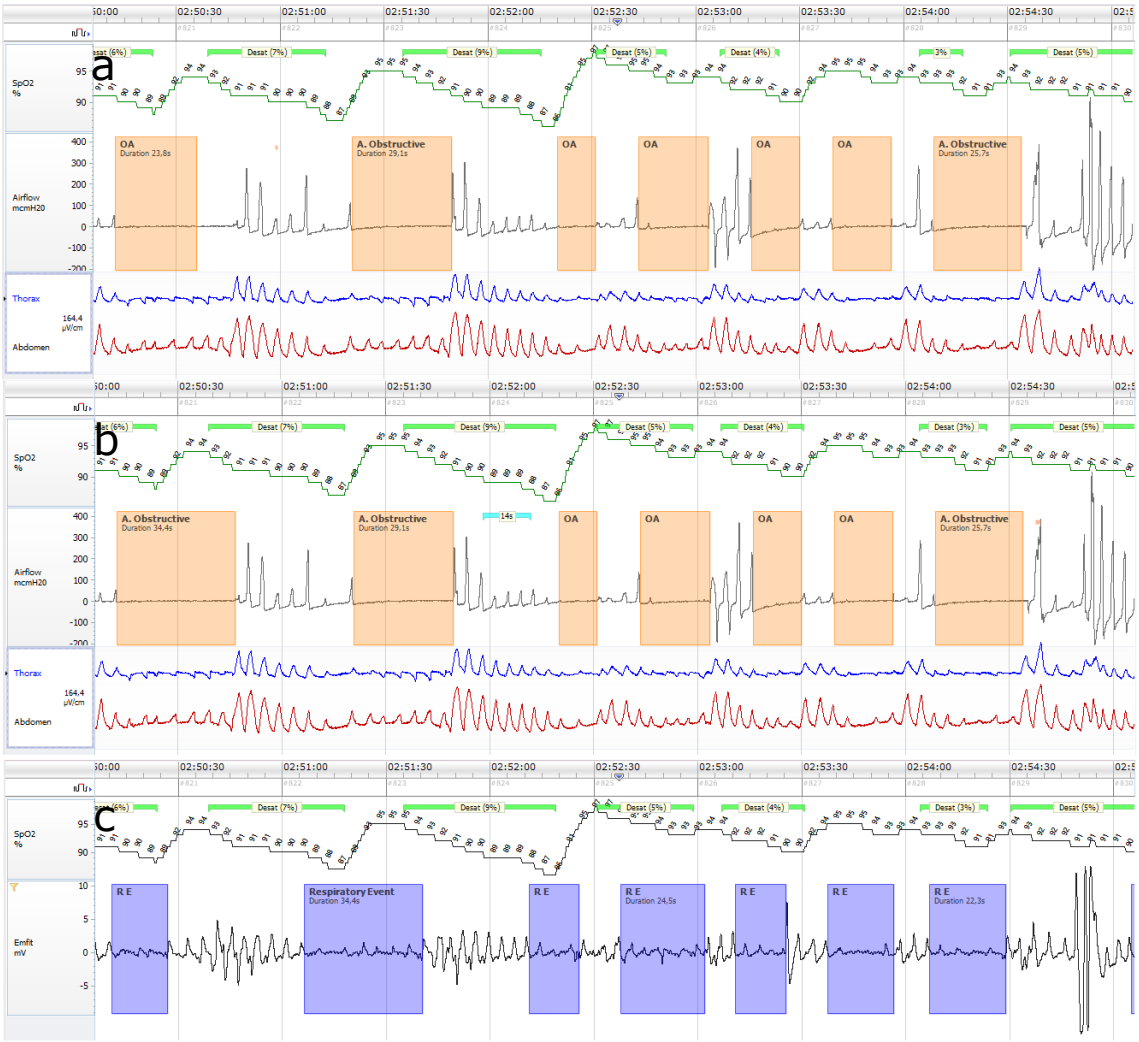

Figure 6. Comparision of signals and events between a) the Nox T3 $_{\text{manual}}$, b) Nox T3$_{\text{automatic}}$ and c) Emfit$_{\text{automatic}}$. The Emfit$_{\text{automatic}}$ scoring hasn't assessed the duration of the events correctly, probably because there is some noise in the Emfit movement sensor signal due to a different measurement technique.

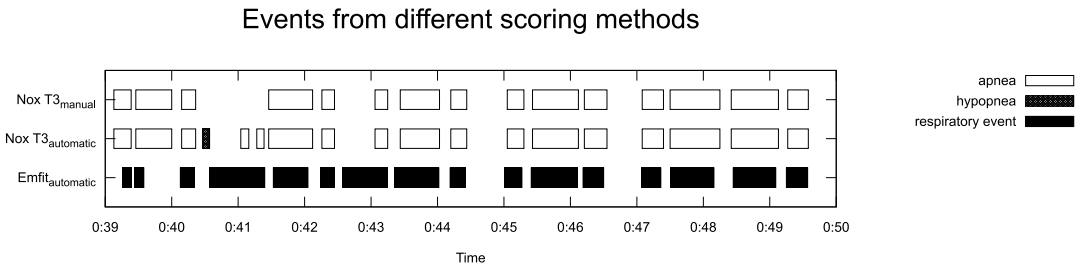

Figure 7. An example showing the timing and duration of breathing disturbances from different scoring methods from 0:39 to 0:50. This patient had AHI index of 68.4 manually scored, the standard respiratory polygraphy automatic scoring yielded an AHI of 77.1 and Emfit movement sensor automatic scoring AHI 69.8.

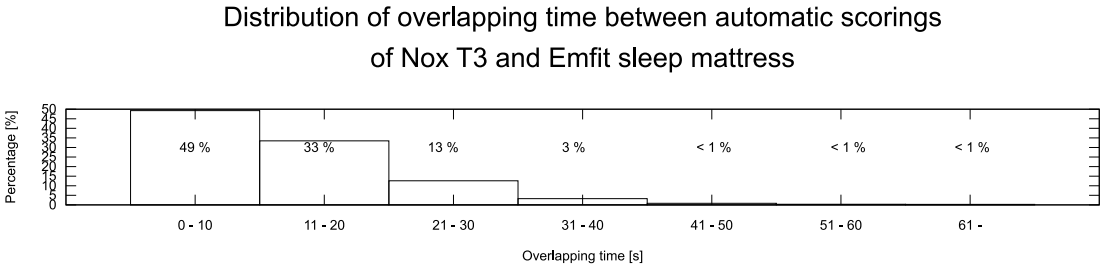

Figure 8. How long time of Emfit movement sensor automatic scoring events duration is overlapping with the standard respiratory polygraphy automatic scoring event.

movement sensor event duration that is overlapping with the standard respiratory polygraphy automatic scoring event in the figure 9.

From figure 8 we can see that almost half of the Emfit movement sensor automatic scoring events have less than or equal of 10 seconds of overlapping time and 95 percentage of event have less than or equal of 30 seconds of overlapping time. From figure 9 we notice that 34 percentage of Emfit movement sensor automatic scoring events have less than or equal of 10 percentage of overlapping time of event total duration with the standard respiratory polygraphy automatic scoring events, we also notice that 18 percentage of Emfit movement sensor events have less than or equal of 90 to 100 percentage of overlapping time of total event duration with the standard respiratory polygraphy automatic scoring event.

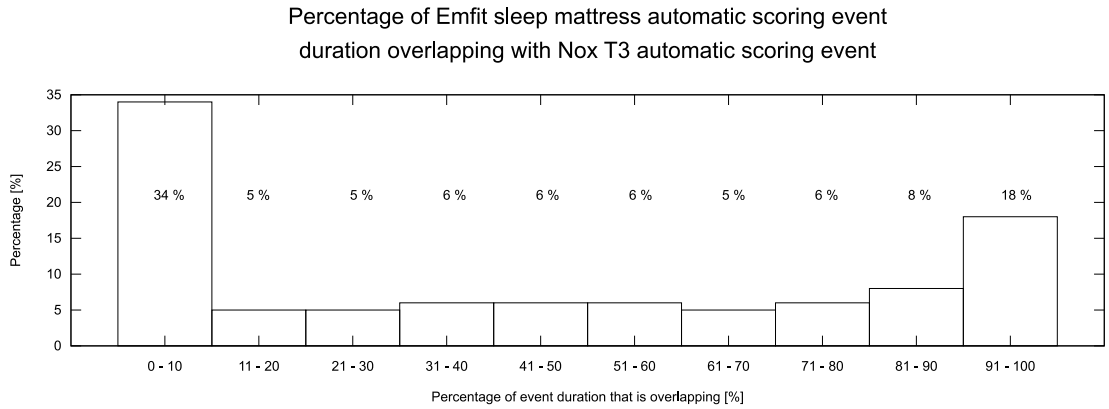

Figure 9. Which percentage of Emfit movement sensor automatic scoring events duration is overlapping with the standard respiratory polygraphy automatic scoring event.

7 Discussion

Our results indicate that the AHI obtained by the automatic scoring of the Emfit movement sensor recording coincides quite well with the gold standard visual scoring of the standard respiratory polygraphy recording. The automatic scoring of the Emfit movement sensor measurement in general slightly overestimates the AHI compared to the manual scoring, but it doesn't overestimate the AHI as much as the automatic scoring of the standard respiratory polygraphy, although the difference are quite small. This can be seen in the Bland-Altman analysis which yields very similar mean values for both comparisons between visual scoring and automatic scorings. There are other studies that yield similar results. Patients with paroxysmal atrial fibrillation were studied, the recordings were scored both manually and automatically. The AHIs obtained in the study showed a good agreement [42]. The automatic scorings of the standard respiratory polygraphy measurements done with the Noxturnal's automatic analysis were compared to the visual scorings done by experienced professionals in these two studies. The agreement between AHIs obtained from the automatic analysis and the visual scoring was strong in both studies [91], [47].

We found out that both automatic scoring methods slightly overestimate the severity of sleep apnea. We also noticed that the distribution of the patients falling into clinical obstructive sleep apnea groups obtained from the automatic scoring of the Emfit movement sensor greatly resembles that given by the automatic scoring of the standard respiratory polygraphy. If the Emfit movement sensor would be used for screening sleep apnea in ischemic stroke patients, it's favourable that the method doesn't underestimate the AHI in order not to miss the sick patients in need of more accurate and reliable measurements and treatment. Although it's also important that there aren't too many false positives among the screened patients so that resources won't be wasted measuring many healthy subjects for vain, but

if all the patients selected for more thorough measurements turn out to be positive then it's most likely that the screening tool has ruled out some true positive cases as negative. Therefore it's important that part of the patients selected for the thorough measurement turn out to be negative cases. If the decision about the treatment would rely solely on the screening tool then the method would need to be more precise in order not to treat patients which don't need the treatment or don't get as much benefit from it. As automatically analysed screening tool the Emfit movement sensor seems to be as promising as the automatically analysed standard respiratory polygraphy measurement as both overestimate the severity of the sleep apnea in a similar manner.

There are also studies about the impact of the device on the accuracy of the automatic scoring and comparisons between manual and automatic scoring on different devices. One study suggests that the accuracy of the automatic analysis depends greatly upon the device used. The study consisted of recordings done on two different devices, recordings from both devices were automatically analysed using the same software and results were compared to the manual scoring of the same recording. The study found out that the recordings made using the first device gave more frequently a false negative result for a patient with mild sleep apnea compared to the second device [87]. In another study a new measurement device was validated against an old one. The automatically scored and manually scored new device was compared to the manually scored old device and it was found out that there is a good relation between manually scored result but not so good relation between the automatically scored new device and manually scored old device, it was found out that the automatic scoring of the new device underestimated the AHI [21]. Third study evaluated the use of a new automated scoring software compared to the computer-assisted manual scoring. AHIs obtained from the automated scoring were similar to the AHIs obtained from the experienced technologists. Results indicate

that automated scoring software manufactured by a third party can give reliable results and reduce the need for manual labour and standardize the results within and across sleep centers [49].

According to the receiver operating characteristic analysis the Emfit movement sensor measurement seems to be the more promising method of these two to be used as a screening tool because the ROC analysis indicates that the Emfit movement sensor measurement has higher sensitivity and specificity compared to the automatically scored standard respiratory polygraphy measurement. The ROC analysis suggests that the automatic analysis of Emfit movement sensor measurement is slightly better to pick up ischemic stroke patients with moderate sleep apnea compared to the automatic analysis of the standard respiratory polygraphy measurement. The ROC analysis results show also that the Emfit movement sensor measurement performs even more effectively when screening for stroke patients with severe sleep apnea. It's desirable to find a screening tool that can effectively recognize the patients who need to be measured more precisely in order to find the patients that profit the most of the treatment.

The Spearman's rank correlation coefficient indicates that there is a positive correlation between the manual scoring of the standard respiratory polygraphy measurement and both automatic scorings. The same positive correlation can be seen between the automatic scoring of the standard respiratory polygraphy measurement and the automatic scoring of the Emfit movement sensor measurement.

We found out that the ability of the Noxturnal automatic analysis to correctly detect the timing and duration of the breathing disturbance events from the Emfit movement sensor measurement varied a lot. It seems that it depends upon the amount of noise in the Emfit signal. When there was only minimal noise the automatic analysis tool could quite well detect the correct timing and duration of the respiratory events. On the other hand when there was more noise in the Emfit sig-

nal the automatic analysis tool didn't perform so well. Our results indicate that 56 percentage of Emfit movement sensor automatically scored events have less than 50 percentage of event duration overlapping with the standard respiratory polygraphy automatically scored events. For 49 percentage of the Emfit movement sensor events the overlapping time is less than or equal to 10 seconds. Hence there is a need to reduce the amount of noise in the Emfit movement sensor signal.

Noxtrunal automatic analysis can't recognize the sleep onset and wake up from the measurement data because the data doesn't contain information about the EEG to detect sleep stages. These time points were manually determined by the person scoring the measurement. If the sleep onset and wake up points aren't determined the automatic analysis will also analyse data obtained when the subject is awake, this will distort the AHI as there are no sleep disordered breathing during the wake and it will result to lower AHI than in reality. This deficiency will disadvantage the use of the Emfit movement sensor as an automatic screening tool. In future studies we have to try to find a way to estimate the sleep onset and wake up points from the measurement data automatically without the information about the EEG in order to create a truly automatic screening tool.

The personal informed consent was a definitive condition for the participation therefore we couldn't recruit severe stroke patients to our study group if they couldn't co-operate and communicate their consent. Therefore our study group consisted mostly of mild and moderate stroke patients and we didn't have so many severe stroke patients. If the Emfit movement sensor would be used as a screening tool for sleep apnea for ischemic stroke patients it would be important to study its performance also on the severe ischemic stroke patients to see if the results are valid also for them. The severe ischemic stroke patients are an important subsection as they would probably benefit the most from the treatment of the sleep apnea.

We didn't find any distinctive differences in the reliability between the Nox T3

and the Emfit movement sensor. At the beginning we had some technical issues due to low quality batteries that caused the Emfit movement sensor system to power down during the night. We overcame these problems by switching to better quality batteries, after that we had no more problems with the Emfit movement sensor powering down during the night. The big advantage of the Emfit movement sensor is that there are no cables attached to the patient. This is a big advantage especially if there is a need to give medical treatment to the patient during the measurement at night, usually the nurses have to remove the standard respiratory polygraphy measurement equipment in order to be able to perform necessary procedures and after the treatment the night sift doesn't have resources to put the equipment on again. Also when there are no cables connected to the patient there is no risk of them getting tangled up during the night and causing the sensors to misplace or fall off during the night.

8 Conclusions

There is a great need for a sleep apnea screening tool for ischemic stroke patients as it would favourably impact their recovery if their possible sleep apnea would be treated properly. It would also be economically important to promote the recovery of the ischemic stroke patients as the treatments and therapy they require is expensive, intensive and they might be dependent on it for very long time, possibly the rest of their lives. A highly automated screening tool would be desirable also because it requires less manual work then the standard respiratory polygraphy especially if we could do the scoring automatically instead of time consuming manual scoring by an expert.

The Emfit movement sensor combined with the Nonin wrist oximeter seems to be a promising option that has certain advantages over the conventional equipment as there are no wires attached to the patient. Still there is lot of development to be done on this method. The automatic scoring algorithm needs to be improved so that it will better recognize the timing and duration of the breathing disturbances and give more realistic AHI instead of overestimating the amount of breathing disturbances. The filtering needs to be adjusted to better filter out the noise that's causing the automatic scoring to misinterpret the apneas as low amplitude breathing. There is also a need to find a solution to estimate the sleep onset and wake up time points automatically from the data so that they don't need to be determined manually and the AHI won't be distorted by including wake into the analysis period. These are topics that need to be reviewed more in the coming studies.

In the future studies it's also important to investigate how the automatic analysis will recognize Cheyne-Stokes respirations as it wasn't reviewed at all in this study.

Acknowledgements

This study was carried out at the Stroke unit of Satasairaala and the Department of medical physics at Turku university hospital.

I wish to express my deepest gratitude to my supervisors adjunct professor Anu Holm and adjunct professor Tom Kuusela for their valuable assistance and guidance throughout the years. I also want to thank Professor Petriina Paturi for reviewing my thesis along with Anu and Tom and helping out with the practical matters.

I wish to thank adjunct professor Antti Kulkas and adjunct professor Mikko Björkqvist for reviewing my thesis and giving valuable feedback.

I wish to thank master of science Mari Takala for carrying out the patient measurements and the manual scoring of the measurement data.

I owe my deepest gratitude to my beloved family, my wife Hannele and our daughter Helena. Your support and love can illuminate even the darkest moments and give support when it's needed most.

References

[1] F. AL-Khalidi, R. Saatchi, D. Burke, H. Elphick, S. Tan, Respiration Rate Monitoring Methods: A Review, Pediatric Pulmonology, **46** (4), 523 (2011)

[2] D. Altman, J. Bland, Measurement in Medicine: The Analysis of Method Comparison Studies, The Statistician, **32** (3), 307 (1983)

[3] J. Anderson, V. Grant, M. Elgammal, A. Campbell, J. Hampshire, S. Hansen, A. Russel, Safety at the William Quarrier Scottish Epilepsy Center, Seizure, **53**, 10 (2017)

[4] G. Babulal, T. Huskey, C. Roe, S. Goette, L. Connor, Cognitive Impairments and Mood Disruptions Negatively Impact Instrumental Activities of Daily Living Performance in the First Three Months after a First Stroke, Topics in Stroke Rehabilitation, **22** (2), 144 (2015)

[5] B. Barriuso et al. Self-setup of Home Respiratory Polygraphy for the Diagnosis of Sleep Apnea Syndrome: Cost-efficiency Study, Sleep Breathing Physiology and Disorders, **24**, 1067 (2019)

[6] F. Baty M. Boesch, S. Widmer, S. Annaheim, P. Fontana, M. Camenzind, R. Rossi, O. Schoch, M. Brutsche, Classification of Sleep Apnea Severity by Electrocardiogram Monitoring Using a Novel Wearable Device, Sensors, **20** (1), 286 (2020)

[7] J. Bland, D. Altman, Statistical Methods for Assessing Agreement between Two Methods of Clinical Measurement, The Lancet, **1** (8476), 307 (1986)

[8] A. Boehme, C. Esenwa, M. Elkind, Stroke Risk Factors, Genetics, and Prevention, Circulation Research, **120** (3), 472 (2017)

[9] C. Breitenstein et al. Intensive Speech and Language Therapy in Patients with Chronic Aphasia after Stroke: A Randomised, Open-label, Blinded-endpoint, Controlled Trial in a Health-care Setting, The Lancet, **389** (10078), 1528 (2017)

[10] J. Bronzino, Medical Devices and Systems, the Biomedical Engineering Handbook 3rd edition, Taylor & Francis Group, United States of America, 2006

[11] T. Brott, et. al, Measurements of Acute Cerebral Infarction: A Clinical Examination Scale, Stroke, **20** (7), 864 (1989)

[12] E. Chan, M. Chan, M. Chan, Pulse Oximetry: Understanding its Basic Principles Facilitates Appreciation of its Limitations, Respiratory Medicine, **107** (6), 789 (2013)

[13] J. Clark Jr. et al. Medical Instrumentation Application and Design, 4th edition, John Wiley & Sons, Inc. United States of America, 2010

[14] J. Coleman, Sleep Studies, Current Techniques and Future Trends, Otolaryngologic Clinics of North America, **32** (2), 195 (1999)

[15] W. Conover, Practical Nonparametric Statsitics, Wiley International Edition, United States of America, 1971

[16] F. Dalmasso, R. Prota, Snoring: Analysis, Measurement, Clinical Implications and Applications, European Respiratory Journal, **9** (1), 146 (1996)

[17] L. Donovan, V. Kapur, Prevalence and Characteristics of Central Compared to Obstructive Sleep Apnea: Analyses from the Sleep Heart Health Study Cohort, Sleep, **39** (7), 1353 (2016)

[18] T. Fawcett, An Introduction to ROC Analysis, Pattern Recognition Letters, **27** (8), 861 (2006)

[19] J. Fei, I. Pavlidis, Thermistor at a Distance: Unobtrusive Measurement of Breathing, IEEE Transactions on Biomedical Engineering, **57** (4), 988 (2010)

[20] J. Ferro, L. Caeiro, M. Figueira, Neuropsychiatric Sequelae of Stroke, Nature Reviews Neurology, **12** (5), 269 (2016)

[21] J. Ficker, G. Wiest, J. Wilpert, F. Fuchs, E. Hahn, Evaluation of a Portable Recording Device (Somnocheck) for Use in Patients with Suspected Obstructive Sleep Apnoea, Respiration, **68** (3), 307 (2001)

[22] L. Fiorillo et al. Automated Sleep Scoring: A Review of the Latest Approaches, Sleep Medicine Reviews, **48**, 101204 (2019)

[23] K. Furie et al. Guidelines for the Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association, Stroke, **42** (1), 227 (2011)

[24] O. Gerke, Reporting Standards for a Bland-Altman Agreement Analysis: a Review of Methodological Reviews, Diagnostics, **10** (5), 334 (2020)

[25] D. Giavarina, Understanding Bland Altman Analysis, Biochemia Medica, **25** (2), 141 (2015)

[26] T-M Haula, J. Puustinen, M. Takala, A. Holm, Relationship Between SDB and Short-term Outcome in Finnish Ischemic Stroke Patients, Brain and Behavior, **10** (10), e01762 (2020)

[27] M. Hayes, P. Smith, A New Method for Pulse Oximetry Possessing Inherent Insensitivity to Artifact, IEEE Transactions on Biomedical Engineering, **48** (4), 452 (2001)

[28] S. Henderson, J. Weitz, P. Kim, Fibrinolysis: Strategies to Enhance the Treatment of Acute Ischemic Stroke, Journal of Thrombosis and Haemostasis, **16** (10), 1932 (2018)

[29] M. Hendriks, J. van Lotringen, M. Vos-van der Hulst, N. Keijsers, Bed Sensor Technology for Objective Sleep Monitoring Within the Clinical Rehabilitation Setting: Observational Feasibility Study, JMIR Mhealth Uhealth, **9** (2), e24339 (2021)

[30] D. Hermann, C. Bassetti, Sleep-related Breathing and Sleep-wake Disturbances in Ischemic Stroke, Neurology, **73** (16), 1313 (2009)

[31] D. Hermann, C. Bassetti, Role of Sleep-disordered Breathing and Sleep-wake Disturbances for Stroke and Stroke Recovery, American Academy of Neurology, **87** (13), 1407 (2016)

[32] C. Hoog Antink, Y. Mai, R. Aalto, C. Brüser, S. Leonhardt, N. Oksala, A. Vehkaoja, Ballistocardiography Can Estimate Beat-to-Beat Heart Rate Accurately at Night in Patients After Vascular Intervention, IEEE Journal of Biomedical and Health Informatics, **24** (8), 2230 (2020)

[33] D. Huysmans, P. Borzée, D. Testelmans, B. Buyse, T. Willemen, S. Van Huffel, C. Varon, Evaluation of a Commercial Ballistocardiography Sensor for Sleep Apnea Screening and Sleep Monitoring, **19** (9), 2133 (2019)

[34] C. Iber, S. Ancoli-Israel, A. Chesson, S. Quan, The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, 1st edition, American Academy of Sleep Medicine, Westchester, Illinois, 2007

[35] B. Jafari, V. Mohsenin, Polysomnography, Clinics in Chest Medicine, **31** (2), 287 (2010)

[36] S. Javaheri, J. Dempsey, Central Sleep Apnea, Comprehensive Physiology, **3** (1), 141 (2013)

[37] K. Johnson, D. Johnson, Frequency of Sleep Apnea in Stroke and TIA Patients: A Meta-analysis, Journal of Clinical Sleep Medicine, **6** (2), 131 (2010)

[38] A. Jordan, D. McSharry, A. Malhotra, Adult Obstructive Sleep Apnoea, Lancet, **383** (9918), 736 (2014)

[39] Y. Kishimoto, A. Akahori, K. Oguri, Estimation of Sleep Posture for M-Health by a Wearable Tri-axis Accelerometer, Proceedings of the 3rd IEEE-EMBS International Summer School on Medical Devices and Biosensors, MIT, Boston, 45 (2006)

[40] D. Kogan, A. Jain, S. Kimbro, G. Gutierrez, V. Jain, Respiratory inductance plethysmography improved diagnostics sensitivity and specificity of obstructive sleep apnea, Respiratory care, **61** (8), 1033 (2016)

[41] J. Kortelainen, M. Mendez, A. Bianchi, M. Matteucci, S. Cerutti, Sleep Staging Based on Signals Acquired Through Bed Sensor, IEEE Transactions on Information Technology in Biomedicine, **14** (3), 776 (2010)

[42] S. Kristiansen et. al, Comparing Manual and Automatic Scoring of Sleep Monitoring Data from Portable Polygraphy, Journal of Sleep Research, **3** (2), e13036 (2021)

[43] T. Kuźniar, T. Morgenthaler, Treatment of Complex Sleep Apnea Syndrome, Chest, **142** (4), 1049 (2012)

[44] P. Lévy, M. Kohler, W. McNicholas, F. Barbé, R. McEvoy, V. Somers, L. Lavie, J-L Pépin, Obstructive Sleep Apnoea Syndrome, Nature Reviews Disease Primers, **1** (15015), ? (2015)

[45] J. Lin, M. Suurna, Sleep Apnea and Sleep-Disordered Breathing, Otolaryngologic Clinics of North America, **51** (4), 827 (2018)

[46] U. Magalang et al, Agreement in the Scoring of Respiratory Events Among International Sleep Centers for Home Sleep Testing, Journal of Clinical Sleep Medicine, **12** (1), 71 (2016)

[47] U. Magalang et al, Home Sleep Apnea Testing: Comparison of Manual and Automated Scoring Across International Sleep Centers, Sleep and Breathing, **23** (1), 25 (2019)

[48] F. Mahoney, D. Barthel, Functional Evaluation: The Barthel Index, Maryland State Medical Journal, **14**, 56 (1965)

[49] A. Malhotra, et. al. Performance of an Automated Polysomnography Scoring System Versus Computer-Assisted Manual Scoring, Sleep, **36** (4), 573 (2013)

[50] J. Mandrekar, Receiver Operating Characteristic Curve in Diagnostic Test Assessment,Journal of Thoracic Oncology, **5** (9), 1315 (2010)

[51] J. Masa et al, Effectiveness of Sequential Automatic-manual Home Respiratory Polygraphy Scoring, European Respiratory Journal, **41** (4), 879 (2012)

[52] A. Masood, B Phillips, Sleep Apnea, Current Opinion in Pulmonary Medicine, **6** (6), 479 (2000)

[53] P. Meriläinen, H. Hänninen, L. Tuomaala, A Novel Sensor for Routine Continuous Spirometry of Intubated Patients, Journal of Clinical Monitoring, **9** (5), 374 (1993)

[54] J. Morley, A. Sanford, R. Bourey, Sleep Apnea: A Geriatric Syndrome, Jamda, **18** (11), 899 (2017)

[55] H. Nakano, T. Tanigawa, T. Furukawa, S. Nishima, Automatic Detection of Sleep-Disordered Brathing from a Single-Channel Airflow Record, European Respiratory Journal, **29** (4), 728 (2007)

[56] Nox Medical, Noxturnal Manual, version 4.2, Nox Medical ehf, Reykjavik, Iceland, 2021

[57] R. Oza, K. Rundell, M. Garcellano, Recurrent Ischemic Stroke: Strategies for Prevention, American Family Physician, **96** (7), 436 (2017)

[58] M. Paajanen, J. Lekkala, K. Kirjavainen, ElectroMechanical Film (EMFi) - a New Multipurpose Electret Material, Sensors and Actuators, **84** (1-2), 95 (2000)

[59] S. Patil, What Every Clinician Should Know about Polysomnography, Respiratory Care, **55** (9), 1179 (2010)

[60] T. Penzel, R. Conradt, Computer Based Sleep Recording and Analysis, Sleep Medicine Reviews, **4** (2), 131 (2000)

[61] T. Penzel, K. Kesper, V. Gross, H. Becker, C. Vogelmeier, Problems in Automatic Sleep Scoring Applied to Sleep Apnea, Proceedings of the 25th Annual International Conference of the IEEE EMBS, **1**, 358 (2003)

[62] D. Petruševičienė, A. Kriščiūnas, Evaluation of Activity and Effectiveness of Occupational Therapy in Stroke Patients at the Early Stage of Rehabilitation, Medicina (Kaunas), **44** (3), 216 (2008)

[63] S. Prabhakaran, I. Ruff, R. Bernstein, Acute Stroke Intervention, A Systematic Review, JAMA, **313** (14), 1451 (2015)

[64] S. Pyo, K. Cho, S. Kwon, D. Lee, S. Song, G. Lee, Gait Analysis in Hemiplegic Stroke Survivors Who Used the One-arm Motorized Walker, Technology and Health Care, **28** (2), 135 (2020)

[65] U. Rahayu, S. Wibowo, I. Setyopranoto, M. Hibatullah Romli, Effectiveness of Physiotherapy Interventions in Brain Plasticity, Balance and Functional Ability in Acute Stroke Survivors: A Randomized Controlled Trial, Neuro Rehabilitation, **47** (4), 463 (2020)

[66] F. Ralls, L. Cutchen, A Contemporary Review of Obstructive Sleep Apnea, Current opinion in pulmonary medicine, **25** (6), 578 (2019)

[67] E. Ranta, H. Rita, J. Kouki, Biometria, Tilastotiedettä Ekologeille, 4th edition, Yliopistopaino, Helsinki, Finland, 1992

[68] J. Ranta, M. Airaksinen, T. Kirjavainen, S. Vanhatalo, N. Stevenson, An Open Source Classifier for Bed Mattress Signal in Infant Sleep Monitoring, Frontiers in Neuroscience, **14** (602852), 1 (2021)

[69] B. Rasch, J. Born, About sleep's role in memory, Physiological reviews, **93** (2), 681 (2013)

[70] E. Rauhala, J. Virkkala, S-L Himanen, Periodic Limb Movement Screening as an Additional Feature of Emfit Sensor in Sleep-disordered Breathing Studies, Journal of Neuroscience Methods, **178** (1), 157 (2009)

[71] Y. Retory, P. Niedzialkowski, C. de Picciotto, M. Bonay, M. Petitjean, New Respiratory Inductive Plethysmography (RIP) Method for Evaluating Ventilatory Adaptation during Mild Physical Activities, PLoS ONE, **11** (3), e0151983 (2016)

[72] L. Rofail, K. Wong, G. Unger, G. Marks, R. Grunstein, The Utility of Single-channel Nasal Airflow Pressure Transducer in the Diagnosis of OSA at Home, Sleep, **33** (8), 1097 (2010)

[73] B. Rotenberg, D. Murariu, K. Pang, Trend in CPAP Adherence over Twenty Years of Data Collection: a Flattened Curve, Journal of Otolaryngology - Head & Neck Surgery, **45** (1), 43 (2016)

[74] G. Roth et al, Global Burden of the Cardiovascular Diseases and Risk Factors, 1990-2019, Journal of the American College of Cardiology, **76** (25), 2982 (2020)

[75] J. Ruscio, Constructing Confidence Intervals for Spearman's Rank Correlation with Ordinal Data: A Stimulation Study Comparing Analytic and Bootstrap Methods, Journal of Modern Applied Statistical Methods, **7** (2), 416 (2008)

[76] A. Sabil et al, Automatic Identification of Sleep and Wakefulness Using Single-channel EEG and Respiratory Polygraphy Signals for the Diagnosis of Obstructive Sleep Apnea, Journal of Sleep Research, **28** (2), e12795 (2019)

[77] R. Sacco, et al. An Updated Definition of Stroke for the 21st Century, A Statement for Healthcare Professionals from the American Heart Association/American Stroke Association, Stroke, **44** (7), 2064 (2013)

[78] M. Sateia, International Classification of Sleep Disorders - Third Edition, Chest **146** (5), 1387 (2014)

[79] T. Schlüter, S. Conrad, An Approach for Automatic Sleep Stage Scoring and Apnea-Hypopnea Detection, Frontiers of Computer Science, **6**, 230 (2012)

[80] A. Seiler et al. Prevalence of Sleep-disordered Breathing after Stroke and TIA A Meta-analysis, Neurology, **92** (7), 648 (2019)

[81] C. Senaratna et al. Prevalence of Obstructive Sleep Apnea in the General Population: A Systematic Review, Sleep Medicine Reviews, **34**, 70 (2017)

[82] R. Stickgold, Sleep-dependent memory consolidation, Nature, **437**, 1272 (2005)

[83] E. St Louis, Diagnosing and Treating Co-Morbid Sleep Apnea in Neurological Disorders, Practical Neurology, **9** (4), 26 (2010)

[84] Stroke and TIA. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Neurological Society. Helsinki: The Finnish Medical Society Duodecim, 2014 (referred April 22, 2021). Available online at: www.kaypahoito.fi

[85] M. Takala, J. Puustinen, E. Rauhala, A. Holm, Pre-screening of Sleep-disordered Breathing after Stroke: A Systematic Review, Brain and Behavior, **8** (12), e01146 (2018)

[86] M. Tenhunen, E. Rauhala, J. Virkkala, O. Polo, A. Saastamoinen, S-L Himanen, Increased Respiratory Effort During Sleep Is Non-invasively Detected with Movement Sensor, Sleep and Breathing, **15** (4), 737 (2011)

[87] P. Tiihonen, et. al. Accuracy of Automatic Analysis of Ambulatory Recordings of Nocturnal Breathing Disorders is Significantly Instrumentation Dependent, Journal of Medical Engineering & Technology, **33** (5), 386 (2009)

[88] A. Towfighi, J. Saver, Stroke Declines from Third to Fourth Leading Cause of Death in the United States, Historical Perspective and Challenges Ahead, Stroke, **42** (8), 2351 (2011)

[89] I. van de Port, L. Wevers, E. Lindeman, K. Kwakkel, Effects of Circuit Training as Alternative to Usual Physiotherapy After Stroke: Randomised Controlled Trial, BMJ, 344 (2012)

[90] C. Winstein et al. Guidelines for Stroke Rehabilitation and Recovery, A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association, Stroke, **47** (6), 98 (2016)

[91] L. Xu et al, Validation of the Nox-T3 Portable Monitor for Diagnosis of Obstructive Sleep Apnea in Chinese Adults, Journal of Clinical Sleep Medicine, **13** (5), 675 (2017)

[92] K. Yew, E. Cheng, Diagnosis of Acute Stroke, American Family Physician, **91** (8), 528 (2015)

[93] K. Zou, A. O'Malley, L. Mauri, Receiver-Operating Characteristic Analysis for Evaluating Diagnostic Test and Predictive Models, Circulation, **115** (5), 654 (2007)