# Benign paroxysmal positional vertigo and treatment in biaxial rotational chair

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Thesis for the degree of Philosophiae Doctor (PhD)
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## Scientific Environment

The studies that are included in this thesis emerged from National Advisory Unit on Vestibular Disorders at the Department of Otolaryngology, Head and Neck Surgery in collaboration with The Department of Clinical Medicine, University of Bergen and Dr. Karl Fredrik Nordfalk at the Department of Otorhinolaryngology and Head Neck Surgery, Oslo University Hospital.
The principal supervisor was Professor Stein Helge Glad Nordahl and the co-supervisor was Dr. Frederik Kragerud Goplen. The Norwegian National Advisory Unit on Vestibular Disorders, have funded this PhD and made the present study possible

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Strong people don't put others down, they lift them up.

– *Michael P Watson*

# Abbreviations

**Alexander's law:** Nystagmus of peripheral vestibular origin that is enhanced with gaze toward the fast phase.

**Ampullofugal flow:** Flow of endolymph away from the ampulla.

**Ampullopetal flow:** Flow of endolymph toward the ampulla.

**Apogeotropic nystagmus:** Nystagmus with movement directed away from the earth.

**Canalithiasis:** Subtype of BPPV where otoconia are free floating within the semicircular canal.

**Cupulolithiasis:** Subtype of BPPV where otoconia are attached to cupula.

**Ewald's Laws**

1st Law: The axis of nystagmus shall match the anatomic axis of the semicircular canal that generated it.

2nd Law: In the horizontal canal an ampullopetal flow of endolymph produces a stronger response; whereas in the anterior and posterior canal, an ampullofugal flow produces a stronger response.

**Geotropic nystagmus:** Nystagmus movement directed toward the earth.

**HSB:** High-speed barbecue manoeuvre.

**ML:** Modified Lempert manoeuvre.

**Oscillopsia:** Blurring or jumping disturbance of the visual field—the objects oscillate.

**PN:** Positional nystagmus.

**PPPD:** Persistant Postural Perceptual Dizziness

**Semicircular canals:** Three circular ducts filled with fluid located in the inner ear responsible for the detection of angular accelerations.

**AC-BPPV:** Anterior semicircular canal BPPV.

**HC-BPPV:** Horizontal semicircular canal BPPV.

**PC-BPPV:** Posterior canal BPPV.

**SPV:** Slow-phase Velocity.

**SM:** Sham maneouvre.

**TRV:** Mechanical chair for treatment of BPPV named after the inventor Thomas Richard-Vitton.

**VNG:** Videonystagmography.

# Papers included in the present thesis

## Paper I

Martens C, Goplen FK, Nordfalk KF, Aasen T, Nordahl SHG.
Prevalence and Characteristics of Positional Nystagmus in Normal Subjects
*Otolaryngol Head Neck Surg. 2016 May;154(5):861-7. doi: 10.1177/0194599816629640. Epub 2016 Feb 23.*

## Paper II

Martens C, Goplen FK, Aasen T, Nordfalk KF, Nordahl SHG.
Dizziness handicap and clinical characteristics of posterior and lateral canal BPPV
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## Paper III

Martens C, Goplen FK, Aasen T, Nordfalk KF, Gjestad R, Nordahl SHG.
Treatment of horizontal canal BPPV-a randomized sham-controlled trial comparing two therapeutic maneuvers of different speeds
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# 1 ABSTRACT

The overall aim of this thesis was to examine a new standardised intervention-tool to provide the best possible treatment for patients with benign paroxysmal positional vertigo (BPPV). BPPV is defined as short attacks of vertigo and nystagmus, which is elicited by certain provocative head positions. In particular, this work consists primarily of three multicentre studies.

The most significant factor in diagnosing BPPV is the examination and evaluation of the characteristics of the nystagmus that is triggered by the diagnostic positional manoeuvres. The character and direction of the nystagmus are specific to the semicircular canal that is affected and the subtype of BPPV. It is important to consider the clinical relevance of nystagmus. For this evaluation, it is crucial to acquire knowledge about the prevalence and quality of positional nystagmus in the normal population. However, there is ass yet no consensus on the interpretation and standardisation of positional nystagmus. **Paper I** aimed to investigate clinical characteristics and prevalence of nystagmus in normal subjects. To our knowledge, this is the first published study to explore positional nystagmus in healthy subjects in standardised test positions in a particle repositioning chair.

We included 75 adult subjects without a history of vertigo or balance disorder. The healthy subjects underwent six standardised positional tests, which are identical to those used to diagnose BPPV patients in repositioning chair. We used videonystagmography to record the eye movements in every test position. We included and analysed 1329 files of the 1350 videos recorded. Our results showed positional nystagmus in 88% of the healthy subjects in one or more of the test positions, and in 55% of the subjects in Dix-Hallpike position. The 95th percentile of the maximum slow-phase velocity was 5.1 degrees pr. second in the horizontal plane and 6.5 degrees pr. second in the vertical plane. Our study has shown that positional nystagmus, especially in the Dix-Hallpike position, which is a part of the test for BPPV, is a common finding in healthy subjects. However, the nystagmus charac-

teristics were not similar to the positional nystagmus that is seen in BPPV patients because it was non-paroxysmal and of slow velocity.

BPPV is diagnosed and divided into the following subtypes: anterior, posterior and horizontal canal BPPV. In **Paper II**, we investigated whether the degree of patient reported symptoms were related to posterior or horizontal canal affection and canal specific nystagmus intensity because this could have clinical and therapeutic consequences.
We analysed 132 consecutive BPPV patients with confirmed BPPV by standardised procedures under diagnostic manoeuvres in a biaxial rotational chair with videonystagmography control. We found that higher DHI scores were associated with horizontal canal BPPV and female gender. Horizontal canal BPPV was associated with longer symptom duration and lower 25-hydroxyvitamin D levels. We investigated the association with D-vitamin levels because imbalance in the metabolism of calcium carbonate crystals is associated with BPPV and a shortcoming of D-vtiamin levels. Furthermore, we found no correlation between DHI scores and nystagmus intensity. This study suggests that patients with horizontal and posterior canal BPPV are clinically distinct. Patients with horizontal canal BPPV differ with respect to symptom severity, vitamin D levels and duration. Patient disability was not related to positional nystagmus slow-phase velocity.

Recently, there has been an extended use of particle repositioning chairs in the treatment of BPPV. However, randomised studies on the treatment of lateral canal BPPV in particle repositioning chairs are lacking and the important question of whether or not to add kinetic energy to the treatment of HC-BPPV has remained unanswered. In **Paper III**, we performed a randomised single blinded placebo-controlled trial that included 57 patients with horizontal canal BPPV. In this study, we wanted to analyse whether adding kinetic energy through acceleration and deceleration in the treatment of horizontal canal BPPV in a biaxial chair had an ef-

fect. We evaluated the therapeutic efficacy of treatment for horizontal canal benign positional vertigo with acceleration and deceleration (high-speed barbecue) HSB, without acceleration (modified Lempert manoeuvre) ML and sham (sham manoeuvre) SM. Patients were analysed after two weeks and after three months. HSB gave a faster initial recovery. However, the cumulative response rate after three months did not show any significant differences between the treatment groups.

In summary, our results highlights the risk of misdiagnosing BPPV patients, especially in patients with low frequency non-paroxysmal positional nystagmus. We also found that the affected canal seems to predict symptom severity, while nystagmus intensity during positional testing does not. The RCT showed a better initial recovery in patients treated with high-speed manoeuvre in horizontal canal BPPV in a TRV chair.

# 2 INTRODUCTION

The last few decades have witnessed advances within the field of vestibular research, and a scientific basis now exists to understand the physiology and pathophysiology of the vestibular system. The most common peripheral vestibular disorder is Benign Paroxysmal Positional Vertigo (BPPV). [2] If not treated properly, this disease can develop into a more severe debilitating condition, such as PPPD. This thesis aimed to investigate the treatment of BPPV with a new mechanical device —the TRV chair. The TRV chair is developed to bypass limitations in conventional repositioning treatment and it offers new analytical possibilities. However, the lack of research on the TRV chair together with more sensitive techniques for detecting nystagmus can lead to misinterpretation, which needs further clinical surveillance and research.

Balance is important, and the capacity to maintain posture and orientation is a fundamental skill. Our balance is regulated by the vestibule, somatic sensation and vision. If there is a malfunction in any of these systems, then it will cause an imbalance that will affect everyday life. Being “dizzy” or “out of balance” refers to the old English word -dysig which meant “foolish, stupid”. From c. 1400 it was referred to as having a “whirling sensation” and in c .1500 it was described as “giddy, thoughtless, headless”. Nystagmus comes from the Greek word nystagmos, which means “nodding, drowsiness” and refers to the brisk movement the head makes when falling asleep sitting up, nodding, followed by a corrective movement. All of these words and their associated meanings describe some of the feelings and disabilities that patients may experience when they acquire BPPV with positional dizziness and positional nystagmus. An overwhelming whirling sensation that arrives in attacks, which often leaves the patient drained of energy, giddy and with a low level of concentration. BPPV is characterised by short episodes of a sensation of spinning that is combined with nystagmus, which are provoked by head movements relative to gravity. However, patients often feel off-balance, even when avoiding brisk head movements. Vertigo is a medical expression for imbalance and dizziness, which is

defined as an erroneous sense of unsteadiness and motion. [3]

The quality of life scores in patients with BPPV have been found to be on a level with patients with macular degeneration, hepatitis B and HIV/AIDS [4]. The disease adversely affects functional capacity, balance and quality of life. [5–8]. BPPV is the only vestibular disease that in most cases can be treated efficaciously by simple intervention. However, there is often a delay in diagnosis and treatment. This can have a tremendous cost and quality of life implications for the patients, which leads to a great direct and indirect cost to the health care system. [5, 9] The benefit of giving these patients an early and correct diagnosis by simple intervention by performing particle repositioning is enormous. [10] Nevertheless, this has have proven to be challenging because patients with BPPV who seek medical care are more likely to undergo brain imaging than to be cured with repositioning. [11]

## 2.1 History

One of the earliest references to BPPV may by found in Shakespeare's "Romeo and Juliet" In Act I, Scene II [enter Romeo and Benvolio] Benvolio says:
*"Tut man, one fire burns out another's burning. One pain is lessened by another's anguish; turn giddy, and be holp by backwards turning. . . ."* [12]

The first description of positional vertigo in the medical literature was by Adler [13] and Barany [14]. Róbert Bárány received the Nobel Prize in 1914 in physiology/medicine for his work on the pathology and physiology of the vestibular apparatus. He was the first to describe BPPV in detail in 1921. In 1952 Margaret Dix and Charles Hallpike [15] presented the currently used provocative positioning technique. They also defined the clinical manifestations of posterior BPPV, as elicited by the Dix-Hallpike test.

The pathophysiology of BPPV was not understood until some time later. Pro-

fessor of Physiology, Julius Ewald (1855–1921) stated three important laws with respect to the vestibular system after his studies in pigeons. In his first law, he declared that the direction of nystagmus should match the anatomic axis of the semicircular canal that is stimulated. In his second law, he stated that an ampullopetal (towards the vestibule) movement of fluid in the horizontal canal causes the strongest response, and in the posterior and anterior canals an ampullofugal (away from the vestibule) fluid movement causes the strongest response. These statements led to further understanding of the disease.

Harlod Schuknecht (1917-1996), who had a passionate interest of the temporal bone, proposed that utricular otoconia acting upon the cupula could cause BPPV. He stated that " to study the temporal bone on a Sunday morning is closer to religion than visiting at church services" [16]. Thanks to his insight, the pathophysiology of BPPV was elucidated. In 1969, Schuknecht presented a theory of "cupulolihiasis" which was explained by otolitic debris attached to the cupula. Hall et al. proposed the concept of canalolithiasis with free-floating particles within the semicircular canals in 1979 and emphasised the importance of the fatigability of nystagmus. [17] Nevertheless, it was not until the early-1990s that the technique of canalith reposition procedures became well-established and physicians to a wider extent became aware of the treatment potential of the disease.

In 1992, Epley published his first report on the Epley manoeuvre, thereby introducing a new form of treatment for BPPV. This may be considered a major breakthrough because the disease could now be treated effectively with simple repositioning manoeuvres. Parnes and McClure made a modification to the concept of BPPV by proposing that BPPV was not a result of cupulolithiasis but was caused by a hydrodynamic gravitational pull exerted by debris on the endolymph. [18] In a recent article, Kao et al. [19] used scanning electron microscope to confirm the presence of otolitic membrane with embedded free-floating particles in patients with BPPV.

## 2.2 Epidemiology

A recent epidemiological survey of 70 million individuals found that BPPV with a prevalence of 0.5 percent was the most common vestibular disease. [2] The cumulative incidence of BPPV is around 10 percent by the age of 80. [20] The prevalence of unrecognised BPPV has been found to be 9% in both a prospective study of 198 young adults aged from 18–34 years and in a geriatric clinic. [6,21] BPPV can occur throughout the lifespan but the incidence increases with age, and is most common between the fifth and seventh decades of life. It is also more prevalent among females. [5]. A familial tendency has been suggested because patients with BPPV have been found to be five times more likely to have relatives with BPPV affection compared to other patients with dizziness. [22]

## 2.3 Etiology

The accepted cause of BPPV are ectopic gravity-sensitive calcium carbonate particles (otoconia) that migrate from the utricle and inadvertently drift into the lumen of the semicircular canal (canalolithiasis). The otoconia can also attach to the cupula (cupulolithiasis) [18,23]. This generates attacks of positional nystagmus and vertigo. It is not the debris or otoliths but the hydrodynamic effect that disturbs the normal endolymphatic flow and bending of the cupula that provokes vertigo and creates the vestibular disturbance. The ampulla has become a gravitational sensor rather than a rotation sensor in cupulolithiasis. In cupulolithiasis vertigo is provoked by rotation. A degenerating otolith apparatus is presumed to be an overall component for increased risk of BPPV. [24] Over half of all BPPV episodes are primary BPPV (idiopathic origin). [25, 26]

Secondary BPPV has been reported to be linked with a with several underlying conditions, including migraine, [27] dental treatment, [28] ear surgery, [29] head trauma, [30] or other inner ear problems. [31] Interestingly, patients with Ménière's disease who develop secondary BPPV are more likely to develop lateral canal involvement, [32] and patients with traumatic BPPV are more prone to get a bilateral

involvement [33] and more positioning manoeuvres are often necessary to obtain relief. [34]

Recent studies that have focused on the risk factors for BPPV have found that low 25-hydroxy vitamin D levels and osteoporosis can be risk factors for both the development and recurrence of BPPV. [35–37] A study from Parnes et al. also found levels of bone turnover to correlate with BPPV. [38] Changes in female sex hormone levels have been shown to associated with BPPV, and a recent study showed that low estradiol levels may lead to increased risk of BPPV in postmenopausal female patients. [39] Another study found that age related increases in BPPV were reversed in women taking oestrogen replacement therapy. [40] Uric acid levels and lipid profiles have been found to be higher in patients with BPPV when compared to controls. Interestingly, uric acid levels have been shown to decrease one month after a BPPV attack. [41] Several recent studies have indicated that the calcium metabolism's relationship with oxidative stress might play a role in the development of BPPV. [42, 43] Sleep disorders, prolonged bedrest and diabetes may also be potential risk factors for BPPV. [44, 45] Ototoxic medications like Gentamycin can increase the risk of BPPV. [46]A study that analysed the comorbidities in 1000 BPPV patients found that patients with a high number of comorbidities had a higher risk of recurrences in BPPV. [47]

## 2.4 Pathogenesis and pathophysiology

The inner ear contributes to both balance and hearing. The vestibular system rises from an elegant network that is designed to perceive the movement and orientation of the head with unique precision, thus guiding our movement and stabilising our visual environment relative to gravity.

The peripheral vestibular system works together with our proprioception, vision and brain to help us maintain our balance.The vestibular complex is an important end organ for balance and it contains receptors for our sense of equilibrium. It consist of five end organs: the sacculus, the utriculus and the three semicircular canals. The

three semicircular canals are organised orthogonally to each other, which enables us to detect the direction and amplitude of the head's movement in three spatial planes. The two vertical semicircular canals are oriented at 45 degrees in the saggital plane and the horizontal canals are tilted upward by approximately 30 degrees. Movement of the semicircular canals will activate the vestibular system and will generate the vestibulo-ocular reflex (VOR) with adjusted eye movements to preserve gaze stability, because the head's movements are followed by compensatory eye movements. This helps us to stabilise vision and muscle tone during movement. The vestibular complex receives a constant flow of information, including when standing and sitting. A change in nerve firing conducts information on how the head is turned with regard to rotation and acceleration.

## 2.5 Otoconia

A certain mass of otoconia is needed to trigger symptoms. [48] House et al's mathematical model [49] estimated that 62 otoconia of approximately 10 micrometers must be involved to produce symptoms. Movement of the otoconia causes an endolymphatic fluid motion which stimulates the ampullary receptors and thereby elicits vertigo, which again explains the symptoms and nystagmus findings. As the crystals move, the brain gets false messages that the individual is spinning. The characteristics of nystagmus (i.e. latency time, fatiguability, direction and transiency) differ between canalo- and cupulolithiasis, and depends on which vestibular canal is affected.

Otoconia weigh 2.95 grams pr. cubic cm, which is three times the density of water and is the reason they sink in the endolymph. Otoconia are most often hexagonal in form. They are normally between 3-30 micrometers long. Because of their mass they sink in the endolymph. A recent study has examined particulate matter intraoperatively from two patients undergoing posterior canal occlusion surgery, and

has shown otoconia measuring roughly 2-8 micrometers. [19] Otoconia are composed of organic (mainly otoconin 90) and inorganic components, which facilitate mineralisation of calcium carbonate around the inorganic matrix to form calcite crystals. Otoconia are anchored together by otolinbased-fibrils. The otolinbased-fibrils are affected by ageing and various disease processes (e.g endolymph change in pH). This includes conditions were otoconia can fragment and separate from the otoconial membrane. Calcium concentration in the endolymph appears to have a considarable influence on the rate of resorption of otoconia and may affect the duration in a BPPV episode. [50] The involvement of particulate matter has been found intraoperatively in patients with BPPV. [18, 19] However, this particulate matter was not found in patients without BPPV. [51] Studies in animals [52–56] and mathematical models [57] support the pathological findings in BPPV. Squires et al. [48] found in their model that an average-sized otoconia requires around 5 seconds to exit the ampulla, which can explain the latency in positional nystagmus in BPPV patients. The latency was predicted to vary depending on the localisation of the otoconia.

## 2.6 Clinical presentation

Patients typically present with vertigo of short duration elicited by certain head movements such as when lying down or turning over in bed. The onset is often after waking up in the morning. The history can sometimes predict which side is affected because the position that initially caused the vertigo is reluctant to be the involved side. [58] Circular acceleration triggers symptoms in canalolithiasis, whereas position change triggers symptoms in cupulolithiasis. Common symptoms with clinical presentation are rotational vertigo (86%), imbalance (49%), nausea (33%), oscillopsia (31%), vomiting (14%), fear of falling (36%) and falls (1%). [5] Interestingly, older patients (i.e. patients older than 70) in 31% of the cases report symptoms that are described by unsteadiness and imbalance rather than vertigo. [59, 60]

## 2.7 Subtypes and examination

### 2.7.1 Canalolithiasis of the posterior canal

**Dix-Hallpike:**

The most common form of BPPV is canalolithiasis of the posterior canal which accounts for 85 % of the cases. [61,62] The essential clinical manifestations of posterior canal BPPV are elicited by the Dix-Hallpike test, which is performed by rotating the patient's head 45 degrees to the side that is examined. This is done to make the posterior semicircular canal parallel to the saggital plane of the body in the seated position. The patient is thereafter moved from the seated to the supine position with the test-ear down and the neck extended approximately 20 degrees. Patients are observed for 30 seconds. In a positive test, after a short latency there will be a vertical up-beating nystagmus in combination with the upper pole of the eye beating toward the affected ear. Commonly a crescendo-decrescendo pattern is detected.

Figure 1: A Dix-Hallpike test in a TRV chair

Geotropic torsional-up beating nystagmus observed during the Dix-Hallpike test indicates that the otoconial debris is descending from the posterior canal ampulla

of the lowermost ear. The vertigo typically lasts less than 30 seconds in PC-BPPV.

### 2.7.2 Canalolithiasis and cupulolithiasis of the horizontal canal

Horizontal canal BPPV (HC-BPPV) is triggered in the the supine position where the head is turned 90 degrees towards each side and it is diagnosed by the presence of direction-changing horizontal paroxysmal positional nystagmus. The horizontal canal BPPV is the second-most frequently affected semicircular canal, with an incidence of around 10-15%. [63–65] The geotropic type (nystagmus beating toward the lower ear) of horizontal nystagmus indicates canalolithiasis of the lateral canal on the side with the more intense nystagmus, whereas the apogeotropic apogeotropic (beating toward the upper ear) variety is indicative of cupulolithiasis (or canalolithiasis of the short arm of the lateral canal) with affection on the side with the less intense nystagmus. The nystagmus is more intense towards the affected side according to Ewalds 2nd law, which tells us that ampullopetal endolymphatic flow (displacement of otoconia toward the ampullated end) produces a stronger response than ampullofugal flow (displacement of otoconia away from the ampullated end) in the horizontal canal. In HC-BPPV vertigo usually lasts longer (about 90 seconds), is more intense and has a shorter latency. HC-BPPV can be difficult to treat, and persistence of symptoms from HC-BPPV varies. [66–72] A recent study found that in a group of intractable BPPV patients, 61% of the patients had horizontal canal affection. [73] Additionally, studies show a lower recovery rate for apogeotropic HC-BPPV. [67, 74] It can, however, sometimes be difficult to determine the affected side based on nystagmus type and subjective symptoms. In the literature different signs for locating the affected side in complicated cases have been investigated and described. These phenomena have been referred to as "secondary signs of lateralisation" by Califano et al. [75] Help in defining the involved side may be found in "pseudo-spontaneous nystagmus" (PS), [76]" neutral position test," (NP), [77] "bowing and leaning nystagmus" [78]and look for the direction of nystagmus in the sitting to supine position test (STS). [67] The bow and lean nystagmus are based

on Ewald's second law. The patient sits on the exam table facing the clinician. The patient is than asked to bow their head 90 degrees forward and the direction, amplitude, and duration of any nystagmus is recorded. The patient thereafter tilts their head backward 45 degrees and again the characteristics of the nystagmus are documented. The affected ear in geotropic nystagmus is the ear where the nystagmus is beating towards in the bowing position. The affected ear in apogeotropic nystagmus is the ear where the nystagmus is beating towards in the leaning position.

*Canalolithiasis of the horizontal canal)* Lateral canal canalolithiasis produces a paroxysmal geotropic positional nystagmus after short or no latency. The nystagmus has a shorter onset latency then with posterior canal BPPV and crescendo-decresendo pattern is normally of longer duration than posterior canal BPPV, but under one minute. [79]

*Cupulolithiasis of the horizontal canal)* Lateral canal cupulolithiasis produces a paroxysmal geotropic positional nystagmus after short or no latency, and is characterised by persistent apogeotropic positional nystagmus normally lasting longer than one minute and typically builds up slowly over 30 seconds and then gradually declines. [79]

### 2.7.3 Anterior canal BPPV

**Dix-Hallpike:**

The prevalence of anterior canal BPPV (AC-BPPV) is probably very low because of its anatomical location. There is still some discussion around the diagnosis and treatment of AC-BPPV, and one should always keep central pathology in mind. A review article by Anagnostou et al. found that anterior canal BPPV only comprises about 3% of all BPPV cases. [80] This type of BPPV is characterised by nystagmus that is predominantly down beating in Dix-Hallpike position, as shown in Figure 1

Atypical presentations:

Apogeotropic posterior canal BPPV (Posterior cupulolithiasis)

Some patients may present with a torsional down beating in the Dix-Hallpike position. This may represent otoconia in the distal arm of the posterior canal. When the patients are positioned in Dix-Hallpike for testing, the otoconia move from the area of the common crus towards the ampulla and produces an inhibitory nystagmus that is torsional down beating. There is normally no latency, but has time course with crescendo –decrescendo pattern and nystagmus is not completely exhaustible. When the patient is raised to the upright position this does not reverse the nystagmus direction, and the nystagmus does normally not fatigue on repeated positional testing. [81]

**Table 1.** BPPV diagnostic criteria according to the Consensus document of the Committee for the Classification of Vestibular Disorders of the Bárány Society (von Brevern et al 2015)

| | Posterior canalithiasis | Lateral canalithiasis | Lateral cupulolithiasis | Anterior canalithiasis | Lithiasis of multiple canals |
|---|---|---|---|---|---|
| Recurrent attacks of positional vertigo or positional dizziness provoked by lying down or turning over in the supine position | Required | Required | Required | Required | Required |
| Duration of vertigo attacks | < 1 min | < 1 min | not specified | < 1 min | < 1 min |
| Diagnostic maneuver | Dix-Hallpike or Semont diagnostic maneuver | supine roll test | supine roll test | Dix-Hallpike or supine straight head-hanging position | Dix-Hallpike or supine roll test |
| Latency of positional nystagmus | one or few seconds | brief or none | brief or none | one or few seconds | not specified |
| Direction of positional nystagmus | torsional upbeat | geotropic direction changing | apogeotropic direction changing | predominantly downbeat | compatible with canalithiasis of more than one canal |
| Duration of positional nystagmus | typically < 1 min | < 1 min | > 1 min | > 1 min | not specified |
| Not attributable to another disorder | Required | Required | Required | Required | Required |

## 2.8 Therapy

Due to the geometry of the semicircular canals and the placement of the cupula, there is only one exit path for the particles. Treatment is done by seeking to move the particles out of the semicircular canals and back to utricle. Otoconial debris seems to be dissolved by the dark cells in the labyrinth. [82] These dark cells are found adjacent to the utricle and the crista ampullaris.

Successful treatment of BPPV requires the involved canal to be placed such that gravity can move the particles thorough the exit path. As the mechanisms of BPPV have become more widely accepted, treatment with repositioning has become a better alternative than conservative management with restraint from provocative head movements. The symptoms are resolved using either the Epley or Semont manoeuvre in posterior canalolithiasis and cupulolithiasis. There is level 1 evidence for the efficacy of the Epley, Semont and Gufoni manoeuvre. [83, 84]

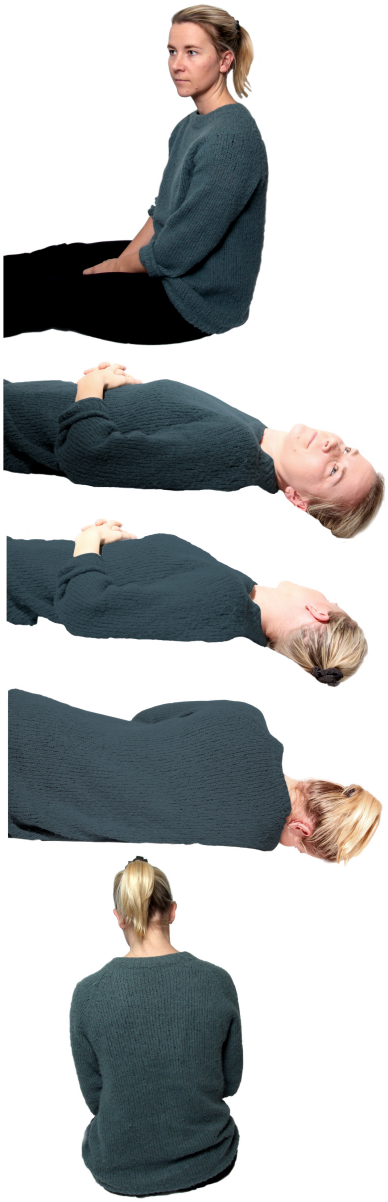


Figure 2: Stepwise Epley for the left posterior canal

Figure 3: Stepwise barbecue for the left horizontal canal

### 2.8.1 Side effects of treatment

Repositioning maneuvers: Nausea and vertigo during the procedure are common, as is light headedness and instability around 48 hours after the procedure. In a retrospective study of 1900 BPPV patients who all underwent repeated repositioning, complications included canal conversion (3.1%), nausea (46.4%), vomiting (4.9%), head heaviness 50.8%), imbalance (31.9%) and hypotension or palpitations (8.3%) during or after the procedure. [85].

Surgery: Patients undergoing canal plugging often experience postoperative imbalance, but spares hearing.

### 2.8.2 Relapses

BPPV typically tends to recur. The estimated 5 year recurrence risk is 30-50% . [86] However, the risk of recurrence between the different semicircular canals is debated. In some studies no differences has been found between the three semicircular canals . [26, 87] In other long-term studies, there is found to be a higher recurrence rate of horizontal canal BPPV. [88] Physical activity is considered protective for BPPV, theoretically due to prevention of otoconial cluster-creation. [89] The presence of abnormal caloric test in patients with horizontal canal BPPV predicts higher risk of recurrence. [90]

## 2.9 Treatment chairs

Since 2005 there has been an extended use of particle repositioning chairs in the treatment of BPPV. Mechanical assistance chairs have been designed to facilitate and optimise the diagnostic and therapeutic manoeuvres and to increase the achievability of treatment in patients with movement restrictions. [91] Examples of cases where adequate positioning of the patients can become a challenge by reason of comorbidities such as mobility restrictions could include: reduced cervical mobility, bodily injures, obesity or lower back pain. All forms of BPPV can be diagnosed and attempted to be treated with mechanical chairs. [92] However, a total of 10-20%

of BPPV patients cannot be diagnosed or treated accurately with ordinary manual manoeuvres. [93] Some authors have argued that a chair also seems to be more effective than conventional reposition. [94, 95]

The TRV chair (Interacoustics, model TRV, France), which is named after its inventor (Thomas Richard-Vitton) is currently the most commonly used biaxial chair for diagnosis and treatment of BPPV. It became commercially available in 2005. [96] As of January 2020, the TRV chair was used by 87 centres in 26 countries. Our centre was the first place in North–Europe to acquire this chair and it has been in use since December 2009. The TRV chair is hand-operated and can swing around two axes, which may be locked in preset positions so that one axis is at the same time earth-horizontal and in line with the approximate axis of any one of the six semicircular canals. The velocity of rotation is also controlled manually. During diagnostics and treatment, the patient is fixed in the chair with a 4-point harness, and is further secured with a headband and straps for the legs. The patient also wears infrared video goggles for visualisation and quantification of positional nystagmus. The setup in the TRV chair provides positioning manoeuvres that are exact and reproducible for diagnosis of each semicircular canal, and further eliminates movement of the spinal column that may interfere proprioceptive signals.

The use of rotational chairs for management of BPPV was pioneered by Dr. John M. Epley (1930-2019), who developed the Omniax System. This chair is a computerised positioning device with similar diagnostic precision. [97] However, this chair is no longer being manufactured.

Furthermore, the Rotundum positioning chair (Prolim engineering GmbH) from Switzerland, has been developed for research and treatment of BPPV.

### 2.9.1 Potential risk factors

The chair should not be used in patients above 150kg. Dumas et al. [98] gave a list of patients who should be cautious using vibration in treatment, and the same could be considered to be applied to treatment in the TRV chair. Recent ear surgery, retinal detachment, history of recent cerebral hematoma and poorly controlled anticoagulant therapy should all be taken into consideration before applying the chair in treatment.

## 2.10 Differential diagnosis

Although BPPV is often easy to diagnose and treat, there are some considerations and differential diagnosis that one needs to bear in mind and the differentiation between peripheral and central positional nystagmus may be challenging. Menières disease and paroxysmal vertigo may also present as recurrent episodes of vertigo with positional nystagmus. It is also well-known that central disorders may present as BPPV-like symptoms with positional nystagmus and positional vertigo(e.g. cerebellar strokes, small cerebellar haemorrhage, especially around the vermis, intracranial tumours etc.) [99].

Vestibular migraine is a prevalent diagnosis that also is also important to consider. It is essential to analyse positional nystagmus and to follow diagnostic criteria for BPPV [100]. Von Brevern et al. wrote a thorough consensus document for the Committee for the Classification of Vestibular Disorders of the Bárány Society [79]. Deviations from diagnostic criteria should always warrant special attention and differential diagnosis should be considered. A recent study compared 27 patients with apogeotropic type of central positional nystagmus with 20 patients with apogeotropic lateral canal BPPV. The authors found that spontaneous horizontal nystagmus differentiated little between the sitting and supine position in CPN, whereas the augmentation of spontaneous nystagmus while supine favours the diagnosis of apogeotropic horizontal canal BPPV. [101]

## 2.11 Present challenges

With a demographic trend towards an ageing population we can expect an increase in patients with BPPV and also an increase in patients with concomitant immobility that for health reasons are unfit for traditional manual treatment. Therefore, an effort should be made to identify factors to improve treatment for these challenged patients. Chronic dizziness is common in elderly patients and persistent or recurrent BPPV may be an important cause of these symptoms. [102]

The high prevalence of BPPV stresses the need to educate clinicians both for early detection and treatment in primary care and for treatment of the rarer, more complicated cases in specialised care. Finally, we need to spread knowledge about treatment of BPPV as one of most effective and straightforward interventions in all of clinical medicine. Particle repositioning for BPPV is largely under-utilised. [103] The severity and nature of presenting complaints vary considerably, and this may lead to a low recognition rate of BPPV in health care settings. In typical cases, diagnostic imaging and vestibular laboratory testing is unnecessary. [100]

Diagnostic measurements and ineffective therapy are common. [9]
BPPV has a considerable negative impact from a humanistic viewpoint, but it is also important to mention the noteworthy impact on work capacity and healthcare resource use.

A study from a registry that included 13 countries with data collected from 4294 patients showed that one-third of the vertigo patients consulting health services were diagnosed with BPPV. Another study from the same material found that BPPV had a considerable impact on work load and healthcare resource use. Among the persons still employed, 70% had reduced their workload, 63% had lost working days and 6% had quit their jobs. In the three months preceding a visit, the use of emergency services, primary care consultations and specialist consultations were extensive [104] The failure in diagnosing BPPV may be due to poor referral patterns

and the low fraction of patients who receive appropriate treatment and symptom relief from the available treatment. Older patients with imbalance and dizziness also wait longer to seek help, and quite often do not present with the classical complains of spinning sensation with positional changes. [59] Patients with BPPV are known to limit their activity level, have a greater incidence of falls, impairments of their daily activities and increased risk of depression. This is of particular concern in the elderly population because of the increased morbidity and mortality from falls. Unrecognised BPPV and associated morbidity is common among the elderly. A study by Oghalai et al. uncovered unrecognised BPPV in 9% of the older population. [6] BPPV has adverse psychosocial consequences, including severe subjective impairment and avoidance behaviour in 70%. [105] BPPV sufferers also report reduced health related quality of life, [7] and are more likely to have depression and reduced daily activities. [6]

# 3 AIMS OF THIS THESIS

The main objective behind these studies was to gain knowledge about BPPV and to explore a new standardised biaxial chair using consistent positioning manoeuvres. Mechanical chairs are currently widely used internationally in the treatment of BPPV. A mechanical device gives us good conditions for research because it gives us an improved analytical feasibility and repeatable test conditions. However, controlled data from the normal population in the chair are missing and RCTs are limited. Consequently, we wanted to conduct these studies where the overall aim was to achieve better treatment for BPPV patients.

There has been a limited amount of research on the findings of positional SPV of nystagmus in normal subjects and cut-point levels of underlying pathology in conjugation with VNG in specific head positions. The widespread use of VNG to detect positional nystagmus in BPPV patients is helpful but can also be challenging because it is very sensitive to detection of nystagmus and may lead to over-diagnosis of the condition. To analyse when to consider nystagmus to be of clinical relevance, it is important to know the prevalence and characteristics of positional nystagmus in the normal population, which was analysed in Paper I. Another interesting concept that we wished to explore was whether the most frequent subtypes of BPPV (posterior and horizontal canal BPPV) entail any divergence in patient perceived handicap because this could have clinical and therapeutic consequences which was analysed this in Paper II. There has been an increase in the number of studies using mechanical devices in the treatment of BPPV. These studies state that there is an increased effect in treatment efficacy compared to conventional manual treatment, [97,106–112]. However, to the best of our knowledge, no randomised placebo-controlled trials have examined the difference in speed during treatment. [113, 114] The important question of whether adding kinetic energy to the treatment of HC- BPPV, which is the type of BPPV that is most persistent to treatment, [73] by using acceleration and deceleration has until now remained unanswered. Consequently, a randomised

placebo-controlled trial on a biaxial chair with three months follow-up was done in Paper III.

# 4 MATERIALS AND METHODS

## 4.1 Ethics

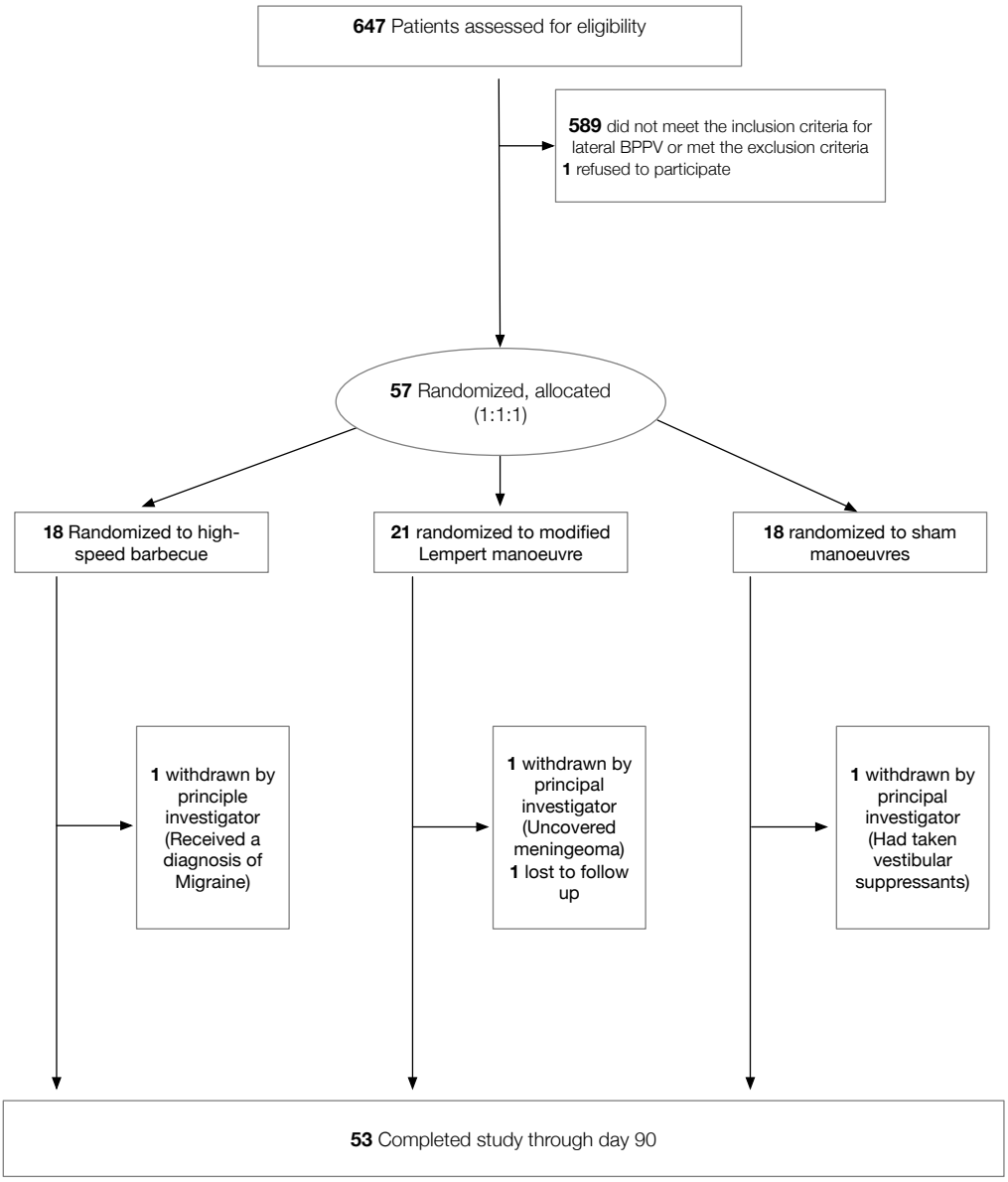
The regional committees for medical and health research ethics of western Norway approved the protocol and consent forms in advance. All of the subjects were fully informed about the aim of the study and the test procedures. In addition, all of the studies were conducted in accordance with the principles of the Declaration of Helsinki. [115] Participation was based on written informed consent. The studies were registered at Clinicaltrials.gov. Identifier: NCT01905800

## 4.2 Design

Studies I and II (Papers I and II, respectively) were prospective observational multi-centre studies. Study III (Paper III) was a multi-centre randomised controlled, single blinded clinical trial with three months follow-up.

## 4.3 Subjects

The first study (Paper I) included 75 healthy subjects aged 21–87 (mean 57, SD 13) years without any previous history of vertigo or balance disorder, and was conducted from 2013–2015. In total 39% of the participants were male and 61% were female. The subjects were collected among hospital staff and voluntaries who met after having seen the advertisement for the research. The second study (Paper II) included 132 consecutive patients aged 27–90 (mean 57, SD 13) years referred with a BPPV and confirmed with active BPPV according to international diagnostic criteria, this study was conducted from June 2013 to June 2016. In the third study (Paper III). 647 patients with positional vertigo referred with BPPV were screened. In total, 57 patients with confirmed active lateral canal BPPV according to international diagnostic criteria from from August 2013 to August 2017 were randomised.


**647** Patients assessed for eligibility
**589** did not meet the inclusion criteria for lateral BPPV or met the exclusion criteria
**1** refused to participate
**57** Randomized, allocated (1:1:1)
**18** Randomized to high-speed barbecue
**21** randomized to modified Lempert manoeuvre
**18** randomized to sham manoeuvres
**1** withdrawn by principle investigator (Received a diagnosis of Migraine)
**1** withdrawn by principal investigator (Uncovered meningeoma)
**1** lost to follow up
**1** withdrawn by principal investigator (Had taken vestibular suppressants)
**53** Completed study through day 90

## 4.4 Clinical examination

All three studies were performed at two university hospitals in Norway (i.e. Bergen and Oslo). Two of the authors performed the examinations, and the same setup and equipment were used. All of the participants underwent a clinical examination, including an ear, nose and throat examination, head impulse testing, static posturography (Synapsys, Marseille, France) and and their serum 25-hydroxy vitamin D levels were measured. Patients in the second and third study (Papers II and III, respectively) also underwent complete otoneurological examination with videonystagmography (VNG) (oculomotor testing, spontaneous eye movements, dynamic positioning and caloric testing (Interacoustics, Denmark). Pure tone audiometry was performed by trained audiologists and positional tests were conducted in a biaxial chair by two trained medical doctors. The same setup and equipment were used at both participating departments. [116] Mental alerting was used throughout the tests.

## 4.5 Biaxial rotational chair

The subjects underwent a standardised examination for positional nystagmus performed with video recording in a biaxial chair. Recording was performed sitting up, in Supine test, in Dix- Hallpike and in Supine roll test /See Figure 2). In Study I, the test pattern was random, in Studies II and III the testing started towards the most symptomatic side, because it is suggested to be the affected side. [117]

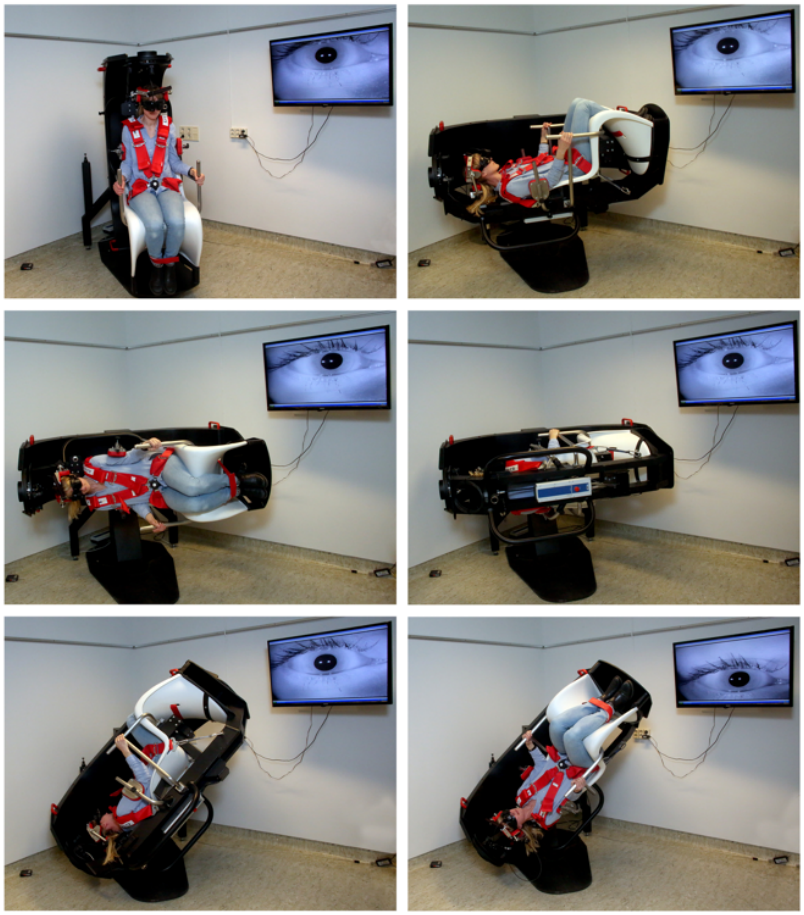


Figure 4: Positional tests in a biaxial chair

The Dix-Hallpike test was performed in the TRV chair by turning the chair 45 degrees towards the right in the earth-horizontal axis, the chair was locked in a preset lockable position and the patient was tilted back until the head was placed 45

degrees below the horizontal plane. The inverse procedure was performed for Dix-Hallpike left. When examining the horizontal canal, the patient was positioned in the supine position and slowly rotated 90 degrees towards the left and the right side aiming to perform the movement with the same acceleration. The head and trunk were stabilised with padded plates on each side to ensure that no active movement in the cervical spine on the part of the patient would occur during testing.

Throughout positional testing, patients were fitted with a standard VNG mask prohibiting visual fixation. The VNG mask holds an infrared camera that records the movements of the eyes in three planes using a dark pupil tracking system with a sampling rate of 25 Hz (Synapsys, Marseille, France). Eye shifts were also analysed in real time visually on a wall-mounted monitor. The recordings were continued for 30 seconds after each diagnostic manoeuvre. The changeover time of movement from one position to another was approximately three to five seconds. All of the subjects were primed with information to keep their eyes open and to blink as little as possible while looking straight ahead during the examination. All nystagmography recordings were reviewed to unmask discrepancies due to flutter, unsatisfactory pupil detection or other types of artefacts. To keep the subjects mentally alert, they were asked various questions during the test.

## 4.6 Electronystagmography and nystagmus

Nystagmus intensity was defined as the maximum slow-phase velocity (SPVmax), which was measured in degrees per second after each diagnostic manoeuvre. Nystagmus seen during the transition time of movement from one position to another was ignored. Nystagmus was considered to be present when at least five or more consecutive nystagmus beats with slow and fast components were identified in each 30-second VNG sequence. Geotropic and apogeotropic nystagmus was defined as nystagmus beating towards the lower and uppermost ear in one or both side-lying position, respectively. Six nystagmus time series —one in each head and body posi-

tion, were recorded for each subject in Studies I to III. The VNG-files were analysed in a LabVIEW program that was developed for this study, and two of the authors did a blind evaluation of the VNG-signals, selecting and measuring the area with highest slow-phase velocity. In case of discrepancies, two of the authors independently reviewed the recordings. The reviewers also checked for cross-talk, to see if any of the horizontal eye movements generated software responses in the vertical channel or opposite, caused by a tilt of goggles or the camera. When analysing SPV as a factor we used horizontal slow-phase velocity in patients with horizontal canal BPPV and vertical slow-phase velocity for patients with posterior canal BPPV. Due to limitations in the VNG technology, the slow phase of torsional nystagmus could not be measured but was quantified visually by the authors as the mean of three independent observations on a visual analogue scale (VAS), anchored at both ends with words descriptive of the maximum and minimum extremes of nystagmus.

## 4.7 Questionnaires

DHI The Dizziness Handicap Inventory (DHI) is a self-assessment inventory that is used to assess the degree of self-perceived disability. The questionnaire was developed by Jacobson and Newman [118] and converted to Norwegian by Tamber et al. [119] Reliability has been found to be high and sustained when translated into Norwegian. The questionnaire contains 25 questions, where an increased disability obtains an increased score. A value of 4, 2, or 0 points is attributed to each answer (Yes- 4 points, Sometimes- 2 points, No- 0 points). The score gives values between 0–100 and indicates mild handicap for scores up to 30, moderate handicap for scores between 31– 60 points, and severe handicap for scores above 60 points. The maximum total score is 100 points. Whitney et al. [120] found that self-perceived disability is related to functional achievement in persons with vestibular dysfunction.

A copy of the DHI questionnaire is available in the Appendix.

## 4.8 Statistical methods

In Study I, we used descriptive statistics to provide summaries about the observations.

In Study II, we used multivariable linear regression and binomial regression models to calculate OR and 95%CI to identify factors associated with dizziness-related quality of life. Backward stepwise elimination of the least significant factor was performed until only significant factors remained. We performed a binomial logistic regression analysis to identify the predictors of lateral vs. posterior canal BPPV.

In Study III, we used Chi-square tests with 3x2 tables and Fishers exact test to compare groups for primary and secondary outcome. We used non-parametric tests because of non-normal distribution of data and also due to the small sample size. Multiple exposure levels were used to study odds ratios. We used a linear regression model to analyse factors associated with change in dizziness-related quality of life using DHI score as dependent variable (continuous, ranging from 0–100) and treatment group and baseline DHI as factors. The significance level $p = 0.05$ was corrected for multiple comparisons by the Bonferroni correction, (0.05/2), giving a value of p=0.03 for significant results. Random multiple imputation(MAR) was used to correct missing data.

Power analysis were performed in Studies II and III. SPSS 22.0 (IBM, Chicago, Illinois), Mplus (version 8.0) and/or STATA SE 15.1 (Texas, USA) were used for statistical evaluation in all three studies.

# 5 SUMMARY OF THE MAIN RESULTS

## 5.1 Summary of the results of Paper I

A total of 75 healthy subjects without a history of vertigo or balance disorders were included in Study I.

Nystagmus prevalence: Positional nystagmus was detected in 88% of the subjects in a healthy population. The most common finding was nystagmus in the Dix-Hallpike position, which occurred in 55% of the subjects.

Nystagmus characteristics: The 95th percentile of the maximum slow-phase velocity for each subject was found to be 5.1 degrees per second (n =54) in the horizontal plane and 6.5 degrees per second (n = 48) in the vertical plane. The positional nystagmus was found to be of low velocity, persistent and not paroxystic. This is important to bear in mind when diagnosing patients with BPPV. Nystagmus that is of low velocity, without latency and that is not paroxystic may be a normal finding.

## 5.2 Summary of the results of Paper II

A total of 132 patients aged 27–90 years (mean 57 years, SD 13 years) were included in Study II. The main part of the patients (n = 103) were female. Higher DHI scores were associated with HC- BPPV 95%CI (1.59–13.95), p=0.01 and female gender 95%CI (0.74–15.52), p=0.03. HC-BPPV was associated with longer symptom duration OR 1.10, 95% CI (1.03-1.17) p=0.01, lower 25-hydroxyvitamin D levels OR 0.80, 95%CI (0.67,0.95), p=0.03 and higher DHI scores OR 2.08, 95%(1.08,4.02),p=0.03.

The most common BPPV subtype was PC-BPPV (n=87) followed by HC-BPPV (n=45). Episodes of previous BPPV that had resolved spontaneously or after therapy were reported by 34 (26%) of the patients. Earlier head trauma within three months prior to BPPV onset was reported by 31 (23%) of the patients. The right-

hand side was affected more often (61%) than the left-hand side (39%). Stress was a provoking factor for dizziness spells in 49 (37%) of the patients. BPPV was most common in the fifth (n=32, 24%) and sixth decades of life (n=41, 31%).

## 5.3 Summary of the results of Paper III

The inclusion criteria were met in 57 patients with horizontal canal BPPV who were randomised (HSB=18; ML=21; SM=18) aged 27–78. The mean age of the patients were 57 (SD 12 years), and 68% (38) of the patients were female. The mean duration of symptoms was 56 weeks (SD129). The duration of the disease ranged from one day to 15 years. A total of 60% (34) of the patients had apogeotropic nystagmus. The right-hand side was involved in 53% (30) cases. Primary outcome was analysed in 54 patients (17 in the HSB group, 20 in the ML group and 17 in the SM group) after two weeks because three of the patients were withdrawn by the principle investigator due to late findings uncovering exclusion criteria. A total of 14 of 17 in the HSB group (82%), 11 of 20 in the ML group (55%), and 4 of 17 (24%) in the SM group, with significantly better recovery in HSB OR 15.17, 95%CI (1.85,124.63), p=0.001using sham as base level. The cumulative therapeutic effect after three months and further treatments (max 3) showed that 40 of 54 cases (75%) had recovered. The cumulative effect was 15 of 17 (88%) in the HSB group and 15 of 19 (80%) in the ML group. There was no significant difference in cure rate after three months between the two treatment groups 95%CI (0.30,13.14), p=0.46.

In the group of no recovery, 10 out of 14 (77%) had cupulolithiasis. Eight patients had short recurrences of BPPV during the study: two patients in the HSB group and six patients in the ML group.

The mean DHI score before treatment was 46.1 ( SD 22.1, range: 0–96). After 3 months, the DHI score in the HSB group was 22.6 (SD 23.3, range: 0–62), in the ML group was 22.5 (SD 23.3, range: 0–62.5) and in the SM group 33.1 (SD 28.2,

range: 0–90). There were no significant correlations between change in DHI and treatment group 95% CI ( -16.56,15,02), p=0.92.

At two-weeks port treatment evaluation, complete recovery was seen in 29 of the patients (54%) secondary outcome, recovery rate after three months were 15/17 (82%) in the HSB group and 15/19 (55%) in the ML group. Cumulative recovery rate showed no significant differences between the two treatment groups 95% CI (0.30,13.14), p=0.46 in cure rate or DHI 95% CI (–16.56,15.02), p=0.92. The period for recruitment started August 2013 and ended August 2017.

## 5.4 Adverse events

We noticed that the patients in the HSB group showed a higher amount of vomiting and complaints of imbalance and nausea straight after treatment than in the ML group. Among our patients, one withdrew in the ML group because of anxiety related to treatment in the biaxial chair. Besides vomiting and dizziness, one patient noticed tinnitus after the Epley manoeuvre. No other side effects were reported.

# 6 DISCUSSION

Our research explored the treatment of BPPV patients in a biaxial rotatory chair, which includes a study on positional nystagmus in the normal population **Paper I**, a descriptive study of the observations of clinical characteristics of lateral and posterior BPPV **Paper II**, and an RCT- exploring treatments for lateral canal BPPV with and without adding kinetic energy to the treatment **Paper III**.

## 6.1 Discussion of the main results

### 6.1.1 Prevalence and clinical characteristics of positional nystagmus in normal subjects

Paper I studied nystagmus in the healthy population. Nystagmus evaluation is considered to be an essential element in diagnosing patients with both central and peripheral vestibular disease. In BPPV, the quality of positional nystagmus is the backbone of diagnosing and differentiating the affected semicircular canal. Nevertheless, positional nystagmus is common, and interpretations must be done with care and as a part of the clinical picture. VNG is in widespread use and represents a considerable diagnostic advancement. However, the evaluation of eye movements in general, and nystagmus in particular, is a highly specialised clinical skill. It is also an ongoing field of research. It is not always trivial to differentiate nystagmus in BPPV patients from nystagmus in the normal population or from central positional nystagmus. In a recent review, atypical nystagmus in Dix-Hallpike position was reported in 97.5% of the patients with central positional nystagmus. [121] Several studies on positional nystagmus in healthy populations have been performed. The prevalence of positional nystagmus in asymptomatic human subjects has ranged from 50-88% [122–127]

No earlier studies have been performed on healthy subjects in a biaxial chair. To achieve normative data for our further studies we examined positional nystagmus

in healthy subjects in the same positions as standardised for patients investigated for BPPV in a TRV chair. In our first study we found that 55% of the population had nystagmus in Dix-Hallpike position, however the nystagmus was persistent and of low amplitude. [116] Downbeat positional nystagmus has earlier been listed as a nystagmus that is central in origin by Brandt, [128] in our study and in a study by Levo et al. [123], downbeat was also found in healthy subjects. There is a consensus that there should be a threshold for the SPV of nystagmus in healthy subjects, although the thresholds found in the different normative studies vary slightly. We found a 95th percentile to be 5 degrees per second horizontal plane, which is in line with the recommendations from Barin et al. [127, 129, 130] ; and 6.5 degrees per second in the vertical plane, which is similar to a recent study by Jeffery et al. [124]

### 6.1.2 Dizziness handicap and clinical characteristics of posterior and lateral canal BPPV

The physical imbalance caused by BPPV is known to disable the patient's daily life, due to anxiety, fear and depression. [131, 132] BPPV most commonly affects the posterior or horizontal canal. The differences in clinical characteristics were studied in Paper II. This exploration is important due to treatment strategies and possible priorities within this group. We conducted a study examining the patients under standardised conditions combined with the use of international diagnostic criteria.

The two groups can be distinguished by the DHI. Horizontal canal BPPV had a trend to give patients a higher score, indicating increased disability. Although there have been expert opinions that lateral canal has an increased symptom score in patients with horizontal canal BPPV, [133–135] but there has been limited research. For example, Kim et al. [136] found a link between horizontal canal BPPV and increased symptoms in terms of functional, emotional and physical limitations. However, their study was based on a very limited number of patients with horizontal canal BPPV(n=18), and the number of patients in the respective groups with

canalo- and cupulolithiasis of the lateral canal varied from section to section in their paper. Furthermore, the criteria for inclusion were not set to following accordance with international guidelines.

A recent study found that the DHI does not correspond very well with vestibular function tests and is influenced by (for example coping) mechanisms and socio-cultural background. [137] Even though DHI might not be a structural indicator for vestibular deficit, it rates the patients subjective disability. Furthermore, BPPV patients with lateral canal affection seem to have an increased perceived handicap compared to patients experiencing posterior canal affection. This could be caused by the fact that they suffer from more symptoms during the day time because their symptoms can be triggered in situations such as sitting, walking, lying and standing due to the anatomical orientation of the canals. The female patients also experienced higher DHI scores, indicating that women experienced a higher handicap than men. The same associations between sex and DHI have been found in other studies on vestibular diseases by Kim et al. [136] There have been speculations that the gender differences, where higher scores in female patients found in Menières and vestibular neuritis, may be caused by higher daily inconvenience and emotional concerns. [136] The same might apply to BPPV because important behavioural and biological differences are connected to gender. Gender differences in the quality of life have been found in earlier reports, with lower scores in females after adjusting for sociodemographic and chronic disease conditions. [138] Gender differences may be important for clinical decision making. Disease management and clinical decision making should also be considered to be adjusted to gender. [139]

### 6.1.3 Serum 25-hydroxy vitamin D and its relevance in BPPV

Low levels of serum 25- hydroxyvitamin D have been found in some studies to increase the risk and recurrence rate in BPPV [140–142] through its role in calcium metabolism. In a study by Talaat et al. [143], the authors found a significantly

decrease in both vitamin D concentrations and bone mineral density in BPPV patients compared to the control group. Studies in mice and rats have found that the size and density of otoconia are increased in mice with osteoporosis. [144–146] In our study, we found that serum 25- hydroxyvitamin D levels were lower in patients with lateral canal affection when compared to posterior canal BPPV. We have found a handful of studies examining the difference in vitamin D levels of cupulo and canalolithiasis, [147] but none have examined the difference in Vitamin D between the subgroups. Consequently, further studies are required to support these findings.

### 6.1.4 Variations of duration in posterior and lateral canal BPPV

The longer symptom duration in patients with BPPV of the horizontal canal (75 weeks) than that of the posterior canal (23 weeks) is in contrast to previous findings. [148, 149] However, the latter studies evaluated only the most recent episode in patients with acute BPPV, while in our research, we asked the patients to report the first onset of dizziness symptoms. In our study, we did not select only those patients with acute vertigo. The natural course of BPPV includes improvements, which may be spontaneous or due to treatment and also relapses. Our findings imply that the total time course of vertigo symptoms is longer in patients with lateral canal BPPV. The reason for longer symptom duration in lateral canal BPPV could be anatomical. In many cases, horizontal canalolithiasis would be expected to resolve spontaneously simply by lying on the healthy side in bed. However, it might recur more easily when turning to the diseased side. Thus, a large accumulation of debris in the utricle could easily cause prolonged symptoms by entering and exiting the lateral canal over a long period of time before dissolving in the endolymph. A study by Sakaida et al. showed a higher risk of recurrence of horizontal canal BPPV (50%) compared to posterior canal BPPV (26%) [88] and the authors also developed a theory about a different consistency of debris in the horizontal canal that increased the risk of recurrence or made it more difficult to treat. In contrast, recurrence of posterior canalolithiasis might be less likely because the ostium of the

common crus is located superiorly in the utricle. In addition, clinicians may be more familiar with diagnosing and treating posterior canal BPPV than lateral canal BPPV. Furthermore, patients who do not recover spontaneously go untreated over longer periods; for example BPPV, persist in 30-33% of untreated patients. [73, 150]

### 6.1.5 Effect of adding kinetic energy

Theoretically, accelerations in the direction of the affected semicircular canal could induce an intracanalicular force, which aids the process of forcing otoconia-debris back into the utricle. Accelerations in a chair may alter the effect of treatment for BPPV because it can move the otoliths in a specific speed with rotation in the right plane. Treatment with acceleration accumulates energy in the otoliths, which might help to move them back to the utricle and theoretically increase the effect of treatment compared to conventional treatment. To our knowledge, this is the first randomised placebo-controlled study on lateral canal BPPV in a particle repositioning chair. The effects of acceleration-deceleration during treatment for HC-BPPV were analysed and the initial treatment result showed superior recovery in patients treated with acceleration and deceleration. However, the cumulative treatment effect did not differ significantly. The efficacy of treatment in a repositioning chair versus manual treatment seems to be in favour of repositioning chairs. [94, 151]

## 6.2 Internal validity

We analysed positional nystagmus in the healthy population (Paper I) aiming to match the BPPV population. The mean age (mean 57, SD 13) was identical in the normal population and in the BPPV population in Study II, which analysed BPPV subtypes and clinical characteristics. With regards to selection bias the healthy population had a higher percentage of health workers than in the general population in Study I, although we cannot rule out some dissimilarities due to differential participation. In Studies II and III, patients who were referred to tertiary care with BPPV were included, in addition to patients who referred directly from general practition-

ers with BPPV symptoms. Even though they were all included due to international diagnostic criteria, the fraction of patients included after having been referred to tertiary care may not necessarily represent patients seen in general practice or in emergency departments.

In Paper III, we had three treatment arms, where one group received a sham treatment. Due to ethical reasons, the portion of patients without treatment effect in this group were allocated to an active treatment group. Bias due to treatment in the chair cannot be excluded. We aimed to omit confounding bias by making a thoroughly designed randomised study in Paper III. This was a small study group and imbalances in prognostic factors may occur despite randomisation.

## 6.3 External validity

The three studies were all multi-centre studies and were performed at two university hospitals in Norway, which made it possible to include a wider range of population groups and increase the generalisability of the study. Both hospitals have specialised units for investigation of vestibular disorders and they receive referrals from all over the country, which facilitates a geographically dispersed study, even though the main part of the participants came from areas near the research hospitals.The equipment and examination protocols were identical at the two locations.VNGs were standardised and signals interpreted through the same LabView program in all studies. Therefore, we consider the reproducibility and generalisability of the results to be high even though one should consider the following limitations:

The data from Paper I were collected from hospital staff and persons interested in participating after having seen the announcement for the clinical trial, which could represent a potential limitation. However, the aim of the study was to assess the prevalence of positional nystagmus and not describe the population. All of the participants represent healthy subjects without any known risk for a different nys-

tagmus profile. Nevertheless, a homogenous population sample may present better control for confounders because they permit more exact theoretical predictions than may be possible with a heterogeneous group. [152] We believe that estimates from this study have implications in the general population.

The population investigated in Papers II and III were highly selected subjects who fit the international diagnostic criteria for BPPV. Therefore one can expect that they are representative of patients with BPPV. However in Paper III the mean duration of symptoms was 56 weeks and the duration of the disease ranged from 1 day to 15 years. This symptom duration is somewhat higher than BPPV patients seen in general practice or in emergency departments.

# 7 CONCLUSION AND FUTURE PROSPECTS

BPPV is a common condition, with diversity within its semicircular presentations. It is a disease with clinical characteristics that at times might not easily be differentiated from other types of positional nystagmus.

## 7.1 Nystagmus

Clinicians should be aware that positional nystagmus without related vertigo is common in the normal population. [153] Knowledge about the frequency and quality of positional nystagmus in the normal population is necessary to avoid over-diagnosis.

## 7.2 Symptoms

Depending on the involved canal: we found that patients with lateral canal BPPV had increased symptom score and longer durations of symptoms compared to posterior canal BPPV. Further studies are needed to determine whether there are substantial differences between the BPPV groups that would affect the care and vestibular rehabilitation plan for these patients.

## 7.3 25 hydroxy vitamin D

A lower value of 25-hydroxy Vitamin D was found in patients with horizontal canal affection. A recent article by Han investigating serum 25-hydroxy vitamin D in subtypes of BPPV also found a lower level of 25-hydroxy vitamin D in patients with cupulolithiasis of the horizontal canal, but no significant differences were found. [154]. Because low Vitamin D levels have been found to be associated with increased risk and recurrence rate of BPPV, our study indicates the clinicians should have this in mind when treating patients with this subtype of BPPV.

## 7.4 Manoeuvres of different speed

Our study shows that adding velocity to treatment of the horizontal canal gives a higher success rate. Adding kinetic energy to the otoliths may make it easier to reposition the debris.

## 7.5 Future prospects

In Paper III we looked at the effect of horizontal canal BPPV randomly assigned to high-speed barbecue (HSB), modified Lempert manoeuvre (ML) or sham manoeuvre (SM). We have also done a randomised controlled trial of 87 patients with posterior canal BPPV randomised to treatment with and without simultaneously treatment of the horizontal canal, based on the theory that the horizontal canal is often affected on the same side. However, the results have not yet been finalised.
We have also investigated long-term outcome after high-speed barbecue manoeuvre compared to the modified Lempert manoeuvre and sham in patients with benign paroxysmal vertigo of the horizontal canal. We have started a retrospective analysis of follow-up data for these patients.
We have also performed a static posturography test consisting of five different components measured before and after treatment for BPPV, the results have yet to be analysed. An objective evaluation of balance before and after treatment of BPPV would be of clinical interest, but the results are yet not finalised.

Vestibular rehabilitation may often be necessary after long-lasting BPPV. [155] It has previously been shown that residual dizziness after successful repositioning was observed in two-thirds of patients with BPPV but that it often disappeared after three months. [156] A recent study found that experiencing a feeling of being thrown to the ground when assuming the sitting position after the Epley manoeuvre might be linked to treatment success. [157] We have also observed this in some cases. Further studies are needed to confirm these results.
In our this study we found that acceleration during treatment for horisontal canal

BPPV can be helpful in treatment. It would be interesting to investigate if "small shocks" given to enhance the clearance of displaced otoconia from the semicircular canals increases the effect of treatment. It is likely that we will have an increase in BPPV cases in the coming years given that BPPV is more prevalent with age and the aged population is increasing globally. Mobility restrictions increases with age and devices such as the TRV chair appear to be helpful in this population. It is our hope that all patients with BPPV will be effectively diagnosed and treated in the future.

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# A Appendices: Questionnaires

# B Appendices: Article I-III

HELSE BERGEN
Haukeland universitetssjukehus

| | | | |
|---|---|---|---|
| **Fornavn** | | **Etternavn** | |
| **Fødselsdato** | | **Dato for utfylling** | |

Vi ber deg fylle ut dette skjemaet som inneholder spørsmål som har betydning for å vurdere symptomene dine og i hvilke grad de påvirker din livskvalitet.

I noen tilfeller kan du bli bedt om å fylle ut skjemaet flere ganger for å vurdere om symptomene dine endrer seg over tid, for eksempel etter behandling.

Opplysningene i dette skjemaet vil hjelpe legen til å gi deg rett diagnose og behandling og inngår i din pasientjournal.

Dersom du samtykker til det, vil opplysningen også kunne inngå i et medisinsk kvalitetsregister som er et verktøy for å forbedre kvaliteten og behandlingen ved Balanselaboratoriet.

Opplysningene blir registrert og oppbevart konfidensielt i tråd med regelverk fra Datatilsynet og Personvernombudet ved Haukeland Universitetssykehus.

Ansvarlige:

Frederik Kragerud Goplen, overlege

Stein Helge Glad Nordahl, Prof.dr med

Skjemaet skal leveres eller sendes til:
Balanselaboratoriet
Øre-nese-hals avdelingen
Jonas Liesvei 65
5021 Bergen
www.balanselaboratoriet.no

Fylles ut av personalet:

# Generelle opplysninger

**1 Sivilstatus**

☐ Gift ☐ Ugift ☐ Registrert partner ☐ Enke/enkemann

☐ Separert ☐ Samboer ☐ Annen sivilstatus

**2 Yrkesstatus**

Yrke_____

☐ Ikke sysselsatt ☐ Lønnstaker ☐ Selvstendig næringsdrivende ☐ Student

**3 Sykefravær/uførhet de siste 30 dagene**

☐ Ikke hatt sykefravær ☐ Noe sykefravær (mindre enn 50 % av arbeidstiden)

☐ En del sykemeldt/ufør (50 % eller mer av arbeidstiden)

☐ Fullt sykemeldt/ufør siste 30 dager

*Årsaken til eventuelt sykefravær* ☐ Svimmelhet ☐ Andre årsaker

_____

**4 Tidligere sykdommer** *(diagnostisert av lege)*

☐ Krystallsyke (BPPV) ☐ Spenningshodepine ☐ MS ☐ Diabetes

☐ Virus på balansenerven ☐ Migrene ☐ Hjernesvulst ☐ Høyt blodtrykk

☐ Menières sykdom ☐ Hodeskade ☐ Hjertesykdom ☐ Lavt stoffskifte

☐ Svulst på balansenerven ☐ Hjerneslag ☐ Blodpropp ☐ Benskjørhet

☐ Borrelia ☐ Nerveskade i bena ☐ Hjernehinnebetennelse ☐ Ryggoperert

☐ Lavt blodtrykk

**5 Medisiner du bruker fast**

_____

_____

# Svimmelhet og hørsel

**1** **Svimmelhet**

Jeg føler meg ikke svimmel eller ustø ☐, gå til spørsmål 2

**a** **Hvordan begynte svimmelhetsplagene?** ☐ Plutselig / akutt ☐ Gradvis / snikende

**b** **Når begynte svimmelhetsplagene?** *(angi så nøyaktig som mulig: dd.mm.år)*_____

**c** **Utløsende årsak?**

☐ Hodeskade ☐ Infeksjonssykdom ☐ Stress / psykisk påkjenning
☐ Hodebevegelse ☐ Annen sykdom ☐ Ingen åpenbar årsak
☐ Annet: _____

**d** **Forløp**

☐ Kun ett anfall (eller en periode) ☐ Flere perioder
☐ Flere korte anfall (sekunder) ☐ Konstant svimmelhet
☐ Flere lengre anfall (> 20 minutter)

**e** **Type svimmelhet**

☐ Karusell (alt går rundt) ☐ Båtdekk (alt gynger) ☐ Nærbesvimelse ☐ Ustø, dårlig balanse
☐ Annet (forklar) _____

**f** **Symptomer som ledsager svimmelheten**

☐ Kvalme ☐ Hodepine ☐ Lysømfintlighet ☐ Lydømfintlighet
☐ Brekninger ☐ Besvimelse ☐ Synsforstyrrelse ☐ Fall
☐ Hørselstap ☐ Øresus ☐ Trykk/dott i øret ☐ Svartner for øynene

**g** **Hendelser / aktiviteter som utløser eller forverrer svimmelheten?**

☐ Når du legger deg ned eller snur deg i sengen
☐ Utløst av fysisk anstrengelse ☐ Ved trykk (nesepussing, toalettbesøk)
☐ Utløst av migrene ☐ Ved høye lyder
☐ Når du reiser deg opp

**2** **Hørselstap og øresus**

**a** Opplever du redusert hørsel ☐ Ja ☐ Nei
Hvis ja, hvilket øre? ☐ Venstre ☐ Høyre ☐ Begge

**b** Er du plaget med øresus? ☐ Ja ☐ Nei
Hvis ja, hvilket øre? ☐ Venstre ☐ Høyre ☐ Begge

**Vanskeligheter på grunn av svimmelhet (DHI)**

**Vi ber deg om å lese instruksjonene nøye:** Hensikten med dette skjemaet er å identifisere vanskeligheter du kan oppleve **på grunn av din svimmelhet eller ustøhet de siste 4 ukene**. Vennligst besvar hvert av spørsmålene med «ja», «nei», «noen ganger». Besvar hvert spørsmål sett ut fra at det bare er forbundet med ditt svimmelhets – eller ustøhetsproblem.

Jeg føler meg ikke svimmel eller ustø ☐ , gå til side 7

| Nr | Spørsmål | Ja | Nei | Noen ganger |
|---|---|---|---|---|
| 1 | Øker problemet ditt når du ser opp? | | | |
| 2 | Føler du deg frustrert på grunn av problemet ditt? | | | |
| 3 | Begrenser du reising i jobb eller fritid på grunn av problemet ditt? | | | |
| 4 | Øker problemet ditt når du går mellom reolene i et supermarked? | | | |
| 5 | Har du vansker med å komme inn eller ut av sengen på grunn av problemet ditt? | | | |
| 6 | Hemmer ditt problem deg i betydelig grad fra å delta i sosiale aktiviteter som å gå ut på middag, kino, dans eller selskap? | | | |
| 7 | Har du vansker med å lese på grunn av problemet ditt? | | | |
| 8 | Øker problemet ditt når du utfører mer ambisiøse aktiviteter som sport, dans og husarbeid som å feie gulv eller sette oppvasken på plass? | | | |
| 9 | Er du redd for å gå hjemmefra uten å ha noen til å følge deg på grunn av problemet ditt? | | | |
| 10 | Har du vært forlegen/flau foran andre på grunn av problemet ditt? | | | |
| 11 | Øker problemet ditt når du snur fort på hodet? | | | |
| 12 | Unngår du høyder på grunn av problemet ditt? | | | |
| 13 | Øker problemet ditt når du snur deg i sengen? | | | |
| 14 | Er det vanskelig for deg å utføre anstrengende husarbeid eller hagearbeid på grunn av problemet ditt? | | | |
| 15 | På grunn av problemet ditt, er du redd for at folk kan tro du er (be)ruset? | | | |
| 16 | Er det vanskelig for deg å gå på en tur alene på grunn av problemet ditt? | | | |
| 17 | Øker problemet ditt når du går langs et fortau? | | | |
| 18 | Er det vanskelig for deg å konsentrere deg på grunn av problemet ditt? | | | |
| 19 | Er det vanskelig for deg å gå rundt i huset ditt i mørket på grunn av problemet ditt? | | | |
| 20 | Er du redd for å være alene hjemme på grunn av problemet ditt? | | | |
| 21 | Føler du deg handikappet på grunn av problemet ditt? | | | |
| 22 | Har problemet ditt vært belastende på ditt forhold til familiemedlemmer eller venner? | | | |
| 23 | Er du deprimert på grunn av problemet ditt? | | | |
| 24 | Forstyrrer problemet ditt deg i å ivareta dine forpliktelser i jobb eller hjemme? | | | |
| 25 | Øker problemet ditt når du bøyer deg forover? | | | |

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ORIGINAL RESEARCH

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# Treatment of horizontal canal BPPV—a randomized sham-controlled trial comparing two therapeutic maneuvers of different speeds

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## Abstract

**Objectives:** To compare the effect of a high-speed barbecue maneuver with the modified Lempert maneuver and sham in patients with benign paroxysmal positional vertigo (BPPV) of the horizontal canal.

**Methods:** Randomized sham-controlled, single blinded multicenter clinical trial in two university hospitals investigating consecutive patients with horizontal canal BPPV. Patients were randomly assigned to high-speed barbecue (HSB), modified Lempert maneuver (ML), or sham maneuver (SM). All treatments were performed in a biaxial rotational chair with weekly follow-up to a maximum of three treatment sessions. The final follow-up was 3 months after the last treatment.

**Results:** Primary outcome: 2-week recovery rate per protocol. Secondary outcome: Cumulative recovery rate and Dizziness Handicap Inventory (DHI) scores after 3 months per protocol (HSB and ML) and intention to treat (all groups).

Fifty-four patients were analyzed after 2 weeks (HSB = 17; ML = 20; SM = 17). Two-week recovery rate was 14/17 after HSB, 11/20 after ML, and 4/17 after SM, with significantly better recovery in HSB [OR 15.17, 95% CI (1.85, 124.63), $P = .001$] using sham as base level. Recovery rate after 3 months was 15/17 after HSB and 15/19 after ML. Cumulative recovery rate showed no significant differences between the two treatment groups [95% CI (0.30, 13.14), $P = .46$] in cure rate DHI [95% CI (−16.56, 15.02), $P = .92$]. No unexpected adverse events were observed.

**Conclusion:** Velocity change in horizontal canal BPPV treatment gives a faster initial recovery. Rapid recovery could reduce the disease burden.

**Trial Registration:** Clinicaltrials.gov. Identifier: NCT01905800.

**Level of Evidence:** 1b

KEYWORDS

barbecue, benign positional vertigo, horizontal semicircular canal

## 1 | INTRODUCTION

The effect of acceleration and deceleration during barbecue maneuvers for horizontal canal benign paroxysmal positional vertigo (HC-BPPV) has been debated.[1-4] is the most common cause of vertigo, and HC-BPPV is the second most common subtype,[5,6] with a prevalence ranging from 5% to 30% in patients with BPPV.[7-9]

The commonly accepted cause of BPPV is ectopic otoconia located within the lumen of the semicircular canals (canalolithiasis) or attached to the cupula (cupulolithiasis),[10,11] generating attacks of positional nystagmus and vertigo after certain head movements. BPPV is often a self-limiting condition,[12,13] but can be persistent or recurrent.[14-17] BPPV may cause considerable handicap for patients, restricting work as well as other activities of daily living. A rapid recovery is therefore important for both the patient and society in general. Treatment is based on effectively removing the displaced otoconia. HC-BPPV is typically treated with barbecue roll or Gufoni maneuvers.[14,18] HC-BPPV can be difficult to treat, and persistence of symptoms ranges from 5% to 61%,[19-26] with a lower recovery rate for apogeotropic HC-BPPV.[21,27] Recently, the use of particle repositioning chairs has become more common in the treatment of difficult BPPV cases.[28] Manual chairs give the possibility to perform the maneuvers with acceleration and brisk deceleration that may promote the removal of otolithic debris from the semicircular canal.[29] A mathematical model developed by Hain et al suggests that strong and prolonged accelerations could move otoconia a significant distance through a semicircular canal.[30] However, the important question of whether acceleration and deceleration adds an effect to treatment of HC-BPPV, has remained unanswered.

The aim of this study was to compare the effect of a high-speed barbecue maneuver with a modified Lempert maneuver in a sham-controlled randomized trial.

## 2 | MATERIALS AND METHODS

### 2.1 | Ethics

This study was approved in advance by the regional Committee for Medical and Health Research Ethics of Western Norway. Participation was based on written informed consent. The study was registered at clinicaltrials.gov (identifier: NCT01905800).

### 2.2 | Design and setting

This was a prospective randomized, single blinded multicenter trial, conducted at two university hospitals in Norway, including patients from August 2013 to August 2017. Data were reported according to the CONSORT statement.[31] Participants were equally allocated (1:1:1) to the three interventions being compared.

### 2.3 | Participants

Consecutive patients referred with a history suggestive of BPPV were considered for inclusion, which was based on confirmed active HC-BPPV according to international diagnostic criteria.[32] In total, 647 patients with positional vertigo were screened (CONSORT flowchart Figure 1). The inclusion criteria were having HC-BPPV, symptomatic at the time of examination, with canal-specific positioning nystagmus under positional testing in a biaxial chair. The exclusion criteria were BPPV of the vertical canals identified during the diagnostic procedure, history of neurological disease including migraine or inner ear disease other than BPPV.

Magnetic resonance imaging (MRI) was ordered in case of severe imbalance or treatment failure. In some of the patients, MRI had been taken prior to referral. A total of 32 patients (56%) underwent head MRI.

A total of 57 patients were enrolled, 18 were assigned to receive the high-speed barbecue (HSB) maneuver, also called the dynamic barbecue by the manufacturer of the biaxial chair, 21 were assigned to the modified Lempert maneuver (ML), and 18 were assigned to receive the sham maneuver (SM). Three patients were excluded and one lost to follow-up. Reasons for exclusion was a diagnosis of migraine (n = 1), meningioma (n = 1), and use of vestibular suppressants (n = 1). All audiograms for the included patients were within normal limits for age and gender[33] or showed symmetrical presbycusis. None of the included subjects had spontaneous nystagmus when fixating with the unrecorded eye or nystagmus during lateral gaze or after a 10-second headshake.

### 2.4 | Procedure and interventions

On the day of examination, the history was verified by interview, and symptom questionnaires were completed. The subjects underwent a physical examination as well as a standardized examination for positional nystagmus (roll test and Dix-Hallpike maneuver). Further assessment included a physical ear, nose and throat-examination, otoneurologic examination, videonystagmography, head impulse testing, and pure tone audiometry.

The diagnostic procedure started with mounting the patient in a biaxial chair (TRV, Synapsys, Marseille, France). The patient was secured to the chair with a four-point harness, with headrest, headband, and leg straps. The chair is operated manually and can be rotated so that each of the six semicircular canals is oriented in the earth-vertical position and rotated 360° in the plane of the canal.

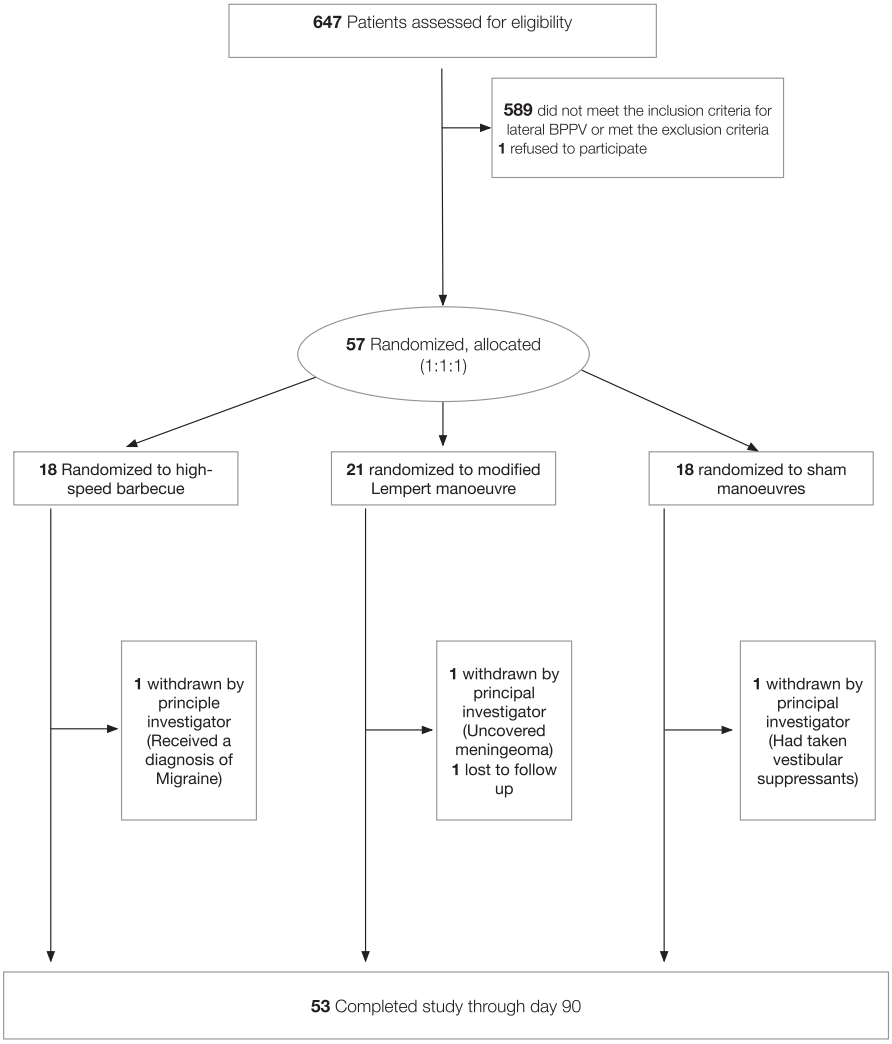


**FIGURE 1** CONSORT flow diagram showing participant flow through the stages of the randomized sham-controlled trial

The Dix-Hallpike maneuver was performed toward both sides, starting on the symptomatic side as determined by the interview. Then, the roll test was performed to both sides and repeated as necessary to determine the side with strongest nystagmus.

HC-BPPV was diagnosed by the presence of positional vertigo in combination with horizontal geotropic paroxysmal or apogeotropic prolonged nystagmus provoked by the supine position test. Geotropic and apogeotropic nystagmus were defined respectively as nystagmus beating toward the lower and uppermost ear in both side-lying positions. The causative site of HC-BPPV was determined by using Ewald's second law. In geotropic HC-BPPV, nystagmus is most intense toward the affected ear, in apogeotropic HC-BPPV, nystagmus is strongest on the side opposite to the affected ear. Dix-Hallpike right and left, supine position test, and bilateral roll test were performed. In cases where it was difficult to determine the affected ear using Ewald's second law, we used the "bow and lean test."[34]

The treatment procedure in each group followed standardized management depending on group allocation: HSB, ML, or SM.

The HSB maneuver with rapid acceleration and rapid deceleration started with the patient in the side-lying (lateral) position with the affected ear down.

Step 1: The patient was rotated $8 \times 360^{\circ}$ in the axial plane toward the unaffected side. The rotations were performed manually with a speed of approximately 180-240° per second (velocity

measured by calculating average time per maneuver of 360°). Step 2: After the rotations, the patient was abruptly stopped and kept in a position with the unaffected ear down and the face directed 45° downwards toward the ground for 30 seconds. Step 1 was repeated, this time ending with the face directed downwards toward the ground. The patient was kept in this position for 60 seconds and returned to the upright position.

The ML started with the patient in the side-lying (lateral) position with the affected ear down. The patient was then rotated slowly 360° toward the unaffected ear. A 30 second stop was applied every 45°. After a pause of 1 minute, the procedure was repeated, and the patient was returned to the upright position.

The SM treatment consisted solely of the diagnostic maneuvers as described above, conducted in random order.

Patients were considered to have recovered when no positional vertigo or pathological positional nystagmus could be elicited by the diagnostic maneuvers as described above.

Video recordings of nystagmus were evaluated after the study by two of the authors blinded to the patients' symptoms and treatment allocation.

Treatment was given weekly until no symptoms or a maximum three times. Thereafter, the patients were given a new appointment for the last follow-up after 3 months. Patients in the SM group were transferred to active treatment (HSB) if still symptomatic after two SM. No home exercises were administered during the follow-up.

### 2.5 | Outcomes

The primary outcome was the 2-week recovery rate, and the secondary outcome was recovery rate and Dizziness Handicap Inventory (DHI) scores after 3 months. Patient-reported symptoms were collected by DHI questionnaires in conjunction with the screening visit and at the end of study. DHI scores range from 0 to 100 with higher scores indicating a greater disability. To correct for missing values, the mean score for the answered items was multiplied by the total number of questions (25) to obtain a corrected total score. In general, missing items were few. We used the DHI questionnaire adapted to Norwegian with verified internal reliability and validity.[35,36]

Changes with respect to grading of cure rate were done after trial commencement based on findings from our previous study on nystagmus in a normal population.[37] Complete recovery was defined as absence of positional vertigo and absence of pathological apogeotropic or geotropic nystagmus at positional tests. Pathological nystagmus was defined as 95% CI of 4°/s for horizontal nystagmus.[37,38] Treatment failure was defined as residual positional vertigo and pathologic positional nystagmus on positional tests. Recurrence of symptoms and positional nystagmus following complete recovery were considered to indicate BPPV recurrence.

Videonystagmography (VNG) was performed with light occluding goggles to avoid fixation during the positional maneuvers, and both nystagmus traces and videos were recorded for later analysis. Nystagmus intensity was defined as the maximum nystagmus slow-phase velocity ($SPV_{max}$), measured in degrees per second after each diagnostic maneuver. The VNG-files were imported into a LabVIEW program developed for this study. One of the authors conducted a blinded evaluation of the VNG-signals, selecting and measuring the area of the horizontal nystagmus with highest slow-phase velocity. If there were any doubts interpreting the nystagmus, the series were reviewed independently by three of the other authors.

The objective measurements of $SPV_{max}$ of the horizontal component of the nystagmus elicited by supine roll left and right were quantified. Registrations were done the day of inclusion, at every post-treatment control, and at the end of the study, 3 months after last treatment.

### 2.6 | Cases with recurrence

If patients developed a new episode of BPPV after having been evaluated as recovered, the case was registered as a recurrence.

### 2.7 | Statistical analysis

The null hypothesis was that the two maneuvers would be equally effective with respect to primary and secondary outcomes. Power analysis showed that for chi-square tests with two degrees of freedom, power of 80%, and significance level of 0.05, the minimum detectable effect size would be $w = 0.53$ with 17 participants in each group. Chi-square tests with 3 × 2 tables and Fisher's exact tests were used to compare groups for primary and secondary outcomes. Non-parametric tests were used due to distribution of data. Multiple exposure levels were used to estimate odds ratios.

A multiple linear regression model was used to identify factors associated with change in dizziness-related quality of life using changes in DHI score as the dependent variable (continuous, ranging from 0 to 100) and treatment group and baseline DHI as factors. The significance level, $P < .05$, was corrected for multiple comparisons by the Bonferroni correction, (0.05/2), giving a value of $P < .03$ for significant results. STATA version SE 15.1 was used for statistical evaluation.

## 3 | RESULTS

### 3.1 | Patients

The inclusion criteria were initially met in 57 patients. The mean age of the patients was 57 ± 12 years (mean ± SD, range: 27-78), and 68% (38) were female. Sixty percent (34) of the patients had apogeotropic nystagmus. The right side was involved in 53% (30). Table 1 shows the characteristics for each group of patients at baseline. Of the 57 patients, three discontinued the study and did not provide outcome data because of later findings uncovering exclusion criteria (Figure 1). The primary outcome was analyzed in 54 patients (17 in the HSB group, 20 in the ML group, and 17 in the SM group).

Of the 53 that completed the study, 17 completed in the HSB group, 19 in the ML group, and 17 in the SM group. One patient in the ML group was lost to follow-up. Recruitment and follow-up were from August 2013 to August 2017.

Two-weeks post-treatment, 29 patients had recovered (54%), 14 of 17 in the HSB group (82%), 11 of 20 in the ML group (55%), and four of 17 (24%) in the SM group. The recovery rate in the HSB group was significantly higher compared to the SM group [OR 15.17, 95% CI (1.85, 124.63), $P = .001$] (Table 2).

The total recovery rate after 3 months was 75% (40 of 54 cases) (75%). At this time, there was no significant difference between the HSB group (88%) and the ML group (80%) (Fisher's exact, $P = .66$) (Table 3). The SM group was not analyzed at this point, since patients in this group that did not recover received active treatment.

In the group that did not recover, 10 out of 14 (77%) had cupulolithiasis. Eight patients had short recurrences of BPPV during the study, two patients in the HSB group and six patients in the ML group.

The mean DHI score before treatment was 46.1 ± 22.1 (mean ± SD, range: 0-96). After 3 months, the DHI score in the HSB group was 22.6 ± 23.3 (mean ± SD, range: 0-62) and in the ML group was 22.5 ± 23.3 (mean ± SD, range: 0-62.5). There were no significant

**TABLE 1** Baseline characteristics of patients with lateral canal BPPV (N = 57)

| Characteristics | High-speed barbecue N = 18 | Modified Lempert N = 21 | Sham N = 18 |
|---|---|---|---|
| Gender | | | |
| Female | 14 | 13 | 12 |
| Male | 4 | 8 | 6 |
| Age years (range) | 36-78 | 34-71 | 27-74 |
| Mean ± SD | 55.8 ± 12.13 | 57.6 ± 11.6 | 58.3 ± 11.6 |
| Involved side | | | |
| Right | 11 | 13 | 7 |
| Left | 7 | 8 | 11 |
| Type | | | |
| Canalolithiasis | 7 | 11 | 5 |
| Cupulolithiasis | 11 | 10 | 13 |
| DHI score (range) | 0–96 | 6-76 | 2-96 |
| Mean ± SD | 47.6 ± 23.6 | 48.1 ± 20.6 | 46.5 ± 25.5 |
| MRI | | | |
| Yes | 10 | 10 | 12 |
| No | 8 | 11 | 6 |
| Rec. BPPV | | | |
| Yes | 10 | 12 | 10 |
| No | 8 | 9 | 8 |

*Note:* There were no significant differences between the groups in baseline characteristics. Chi-square, Fisher's exact for categorical variables, and ANOVAor continuous variables.
Abbreviations: BPPV, benign paroxysmal positional vertigo; DHI, Dizziness Handicap Inventory; Rec. BPPV, patients with earlier episodes of BPPV prior to inclusion in study.

**TABLE 2** Primary outcome (2-week recovery rate) according to treatment group

| | Recovery after 2 weeks | | | | |
|---|---|---|---|---|---|
| | Yes | | No | | Total |
| Intervention | N | % within study group | N | % within study group | N |
| High-speed barbecue | 14 | 82.4 | 3 | 17.6 | 17 |
| Modified Lempert maneuver | 11 | 55 | 9 | 45 | 20 |
| Sham maneuver | 4 | 23.5 | 13 | 76.5 | 17 |
| Total | 29 | | 25 | | 54 |

*Note:* Chi-square = 11.85. Two degrees of freedom, $P = .003$. Fisher's exact $P = .003$.

**TABLE 3** Secondary outcome: Three-month recovery rate according to treatment group (sham excluded)

| | Recovery after 3 months | | | | |
|---|---|---|---|---|---|
| | Yes | | No | | Total |
| Intervention | N | % within study group | N | % within study group | N |
| High-speed barbecue | 15 | 88.2 | 2 | 12.8 | 17 |
| Modified Lempert maneuver | 15 | 79.0 | 4 | 21.0 | 19 |
| Total | 30 | | 6 | | 36 |

*Note*: Chi-square = 0.56. One degree of freedom, $P = .46$. Fisher's exact, $P = .66$.

correlations between change in DHI and treatment group [95% CI (−16.56, 15.02), $P = .92$].

### 3.2 | Adverse events

No serious adverse events were noted. Although discomfort during and immediately after maneuvers was not recorded as a part of the study protocol, it was the impression of the authors that the HSB maneuver was associated with a higher degree of immediate discomfort (dizziness, nausea, and vomiting) than the other maneuvers. One patient withdrew from the study due to anxiety related to treatment; this was from the ML group.

## 4 | DISCUSSION

This study found a higher 2-week recovery rate in patients with HC-BPPV treated with HSB compared to ML and sham. The difference between the two active treatments was not retained after 3 months. There was no significant difference in DHI between the treatment groups. The findings are of importance, since rapid clinical recovery is desirable.

Most studies recommend rapid position changing[20,24,39] to allow facilitation of otoconia, but the effect of acceleration or deceleration has not been established to date. Tian et at[40] showed, from their comparative study on the implication of the number of accelerations in the treatment of posterior canal BPPV, that more accelerations and smaller rotation angle improved effectiveness. Hwang et al[1] conducted a prospective randomized study to evaluate the effect of an accelerated Gufoni maneuver in 50 patients with apogeotropic HC-BPPV, and found that faster maneuvering added little benefit, but that the gravitational force may be a more important contributor to the treatment effect. However, no previous study has documented the effect of the HSB in a biaxial chair. Biaxial chairs facilitate the consistency of speed, angle, and amplitude of the diagnostic maneuvers.[41,42] Another study by Shan et al[4] found that treatment for geotropic HC-BPPV with rotation at 120°/s succeeded by two slower rotations had a higher success rate compared to conventional barbecue. The study did not have a control group and bias of being treated in a biaxial chair compared to conventional treatment was not corrected for. The latter was also the case in a recent study by Wang et al[43] finding biaxial chair treatment superior to manual treatment in HC-BPPV. The use of acceleration was not accounted for in this study.

Fourteen patients recovered after 2 weeks of treatment. The reason for this could be the need for repeated maneuvers in some cases or possibly due to spontaneous recovery.

Of the patients that did recover, 16/40 (40%) still had weak horizontal nystagmus. This finding is in agreement with our earlier study on positional nystagmus in healthy subjects, and may be explained by asymptomatic canalo-or cupulolithiasis or even asymptomatic central vestibule-ocular reflex asymmetry.[37] It is doubtful whether total elimination of positional nystagmus is a relevant measure of therapeutic success in BPPV,[44] since infrared video-frenzel systems used today are highly sensitive, making it possible to detect positional nystagmus of low velocity in 88% of the normal population.[37,38,45-47]

Our DHI results are in line with Lee et al who found that patients with BPPV on average score 45.9 ± 8.8 (mean ± SD), a substantial improvement in DHI after successful maneuvers to 19.8 ± 7.2 (mean ± SD), but never reaching the level of healthy controls 11.8 ± 5.2 (mean ± SD).[48] In our study we found a pretreatment score of 46.1 ± 22.1 (mean ± SD) and a post-treatment score of 25.6 ± 24.7 (mean ± SD), indicating that subjective imbalance was improved but not completely resolved.[48] There was no significant difference in DHI between the treatment groups.

According to earlier reports, most cases of HC-BPPV resolve within 3.7 ± 3.9 (mean ± SD) days in patients with cupulolithiasis and 6.7 ± 4.1 (mean ± SD) days in patients with canalolithiasis.[12] However, BPPV persists in 30% of patients if left untreated,[5] and a recent study found that 61% of patients with persistent BPPV suffered from horizontal canal involvement.[26]

### 4.1 | Limitations and strengths of this study

The strengths of this study were its prospective design, use of a standardized mechanical chair, which ensured reproducible diagnostic maneuvers in preset positions, rigorous use of international diagnostic criteria for the BPPV subtypes, as well as the use of video documentation and computerized videonystagmography that facilitates the analysis of positional nystagmus. Biaxial chairs facilitate consistency of speed, angle, and amplitude of diagnostic maneuvers, which is critical when evaluating the latency and intensity of nystagmus,[41,42] and can be of valuable assistance in the sometimes challenging determination

of involved side in HC-BPPV.[49] Objective measurement of nystagmus, and diagnostic maneuvers with a biaxial chair make the diagnosis of BPPV more objective and gives the examination and treatment increased consistency.[50]

A possible limitation of the study was related to generalizability as we are a tertiary clinic and the patients may differentiate from patients seen in general practice or in emergency departments.

## 5 | CONCLUSION

To our knowledge, this is the first randomized sham-controlled study on treatment of HC-BPPV in a biaxial chair. The effects of the HSB maneuver were analyzed in comparison with the ML maneuver and SM, and the former treatment showed a higher 2-week recovery rate. After 3 months, there were no differences in recovery rate or dizziness handicap between treatment groups.

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### CONFLICT OF INTEREST

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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**Errata for**
**Benign paroxysmal positional vertigo and treatment in biaxial rotational chair**

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Avhandling for graden philosophiae doctor (ph.d.)
ved Universitetet i Bergen

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(dato sign. kandidat) (dato sign. fakultet)

# Errata

Side vi Mangler Abbreviation PPPD- rettes til PPPD: Persistant Postural Perceptual Dizziness

Side vi Mangler Abbreviation TRV – rettes til TRV: Mechanical chair for treatment of BPPV named after the inventor Thomas Richard-Vitton.

Side 50 Stavefeil: “idiopathoc” – rettes til “idiopathic”

Side 50 Stavefeil: “taiwan” – rettes til “Taiwan”

Side 55 Stavefeil: “paroxysml” – rettes til “paroxysmal”

Side 61 Stavefeil: “ncidence” – rettes til “incidence”

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