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**Benign Paroxysmal Positional Vertigo:  
Management and Future Directions**

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# 1. History

Benign paroxysmal positional vertigo (BPPV) is the most common vertiginous disorder in the community; it is characterized by brief recurrent episodes of vertigo triggered by changes in head position. BPPV is the most common etiology of recurrent vertigo and is caused by abnormal stimulation of the cupula by free-floating otoliths (**canalolithiasis**) or otoliths that have adhered to the cupula (**cupulolithiasis**) within any of the three semicircular canals. The cardinal symptom is sudden vertigo induced by a change in head position: turning over in bed, lying down in bed, looking up, stooping, or any sudden change in head position. There is a wide spectrum of severity. Mild symptoms are inconsistent positional vertigo. Moderate symptoms are frequent positional attacks with disequilibrium between. When severe, vertigo is provoked by most head movements, giving an impression of continuous vertigo. The symptoms can last for days, weeks, months, or years, or be recurrent over many years.

In the medical literature the first descriptions of positionally induced vertigo are attributed to Adler [2] and later Barany [3], who believed it was a disorder of the otolith organs.

Barany elicited vertigo in a 27-year-old woman by turning her head from side to side in a supine position and noted “...*the attacks only appeared when she lay on her right side. When she did this, there appeared a strong rotatory nystagmus to the right. The attack lasted about thirty seconds and was accompanied by violent vertigo and nausea. If, immediately after the cessation of these symptoms, the head was again turned to the right, no attack occurred, and in order to evoke a new attack in this way, the patient had to lie for some time on her back or on her left side...*”

In 1952 Margaret Dix (1911–1981) and Charles Hallpike (1900–1979) [4] at Queen Square Hospital, based on 100 patients, presented a symptomatological definition and a provocative positional test for what they called “*positional nystagmus of the benign positional type.*” For symptoms they note: “*The story given by the patient is characteristically that the giddiness comes on when he lies down in bed or when he turns over in bed, or when such a position is taken up during the day; for instance lying down beneath a car or in throwing the head backward to paint a ceiling.*” Their diagnostic test: “...*the patient is first seated upon the couch with the head turned to one side and the gaze fixed firmly on the examiner’s forehead. The examiner then grasps the patient’s forehead firmly between his hands and briskly pushes the patient back into the critical position [30 degrees below the level of the couch and turned some 30 to 45 degrees to one side]. The reaction which results calls for some detailed*

*description.*” As did Barany they noted a torsional nystagmus with the upper pole of the eye beating (fast phase) toward the ground and that it “fatigued” on retesting. Additionally, they observed a response latency of approximately 5 seconds, a crescendo and decline of nystagmus, and a reversal of the nystagmus as the patient sits up. To eliminate the possibility that the response could be induced by vascular occlusion from rotation of the neck they tested patients on an apparatus which avoided it. The same response occurred.

In Britain Hallpike was a pioneer of temporal bone histology. The right temporal bone of 40-year-old woman with “*positional nystagmus of the benign positional type. . .to the right with the right ear undermost*” was examined. In the macula of the utricle, the otolithic membrane was absent. They concluded: “*The general picture is one of chronic tissue changes resulting either from infection or trauma. . .*” and “*We are thus directed to the conclusion that the lesion is a peripheral one and in the labyrinth towards which, when undermost, the nystagmus is directed*”. Hallpike provided further evidence for a peripheral cause by abolishing symptoms in two patients with a chemical labyrinthectomy of an acoustically dead ear [5] and in one patient by an eighth nerve section [6]. Both Barany and Dix and Hallpike concluded that “positional nystagmus of the benign positional type” was caused by disorder of the utricular macula.

By the early 19th century the bony and some membranous structure of the inner ear were anatomically well described but their functions unproven. Common notions were the following. The cochlea was responsible for mediating the nature and pitch of sound; the saccule and utricle were for perception of loudness, and the semicircular canals for transmission of bone-conducted sound and perception of sound direction [7]. Marie-Jean Flourens (1794–1867) was a professor of comparative anatomy in Paris, and in 1824 he published his experimental results on pigeon semicircular canals [8]: “*If the membranous ducts are injured, a painful sensitivity to tones is observed, accompanied by abrupt and violent movements of the head. . . . If the horizontal canals are severed, the animal turns on its vertical axis; if the posterior vertical canal is severed the animal rolls over backward, and if the anterior vertical canal is severed the animal falls forward. . .*” Flourens concluded that the semicircular canals inhibited motion (“forces moderatrices”) and influenced direction of motion, rather than having a role in balance. Flourens’ work had been largely ignored but was known to Prosper Meniere and acknowledged in his final paper in 1861 [9]. According to Adam Politzer (1835–1920) in his “History of Otology” [10] “*the realization that the vestibular and semicircular canal structures are not organs of sound perception, that sound*

*perception is transmitted solely through the cochlea, is the single most important result of Flourens' experiments”.*

However it was another sixty years until a more sophisticated understanding of semicircular canal functions and their generated nystagmus was achieved by Julius Ewald (1855–1921) who was later Professor of Physiology at the University of Strassburg (now Strasbourg). In pigeons, he cannulated each semicircular canal and applied negative and positive pressures and observed the directions and intensity of the induced nystagmus [11]. The two major findings have become known as **Ewalds' Laws**: (1) the direction of the induced nystagmus is in the plane of the canal being stimulated, and (2) in the horizontal canal an ampullopetal (towards the vestibule) movement of endolymph causes the greatest response where as in the posterior and superior canals an ampullofugal (away from the vestibule) endolymph movement causes the greatest response. At the time the differences were perplexing, as expressed by a writer in 1920 [12]: “It is, however, difficult to imagine how the same endolymph current can be stimulating for the one endorgan and hindering for the other”. Thirty years later the advent of the electron microscope allowed a more detailed view of inner ear ultrastructure.

In 1954 Wersall [13] showed that each vestibular sensory cell has one kinocilium and many stereocilia. The finding of morphological polarization of kinocilia on vestibular sensor cells [14, 15] explained Ewald's paradox. In horizontal canal cristae the kinocilium is on the vestibule side of the stereocilia; in the posterior and superior canals the kinocilium is on the canal side of the stereocilia.

In the 1960s, experiments in cats [16] clarified the relationship between canal receptors and extraocular muscles. Each receptor is connected to one ipsilateral and one contralateral muscle. The second order neurones are either excitatory (to the agonist muscles) or inhibitory (to the antagonist muscles).

In 1962 Harold Schuknecht (1917–1996) at Harvard University in Boston [17] proposed that BPPV *“might be caused by detached utricular otoconia, acting upon the cupula of the posterior semicircular canal. Although at that time there were no confirming human pathological studies, the concept seemed plausible from a purely theoretical point of view.”*

In 1969 Schuknecht [18, 19] confirmed finding basophilic staining masses attached to the posterior canal cupula in patients who had had BPPV symptoms. He called this cupulolithiasis (heavy cupula) and assumed the masses were detached utricular otoliths which were removed by decalcification in preparation. This was supported by Gacek's report of five patients where the selective resection of the posterior ampullary nerve abolished BPPV symptoms [20].

Cupulolithiasis became the dominant theory for nearly thirty years, although it did not explain the variable and often long latency and fatiguability of the nystagmus. It was the impetus for two early specific treatments. Previously “treatment” had been by Cawthorne’s exercises in which the patient was instructed to repeat continually any movement which caused the vertigo until it ceased, on the assumption that central adaptation was occurring [21].

Based on the cupulolithiasis theory Brandt and Daroff [22] devised an inpatient treatment where subjects lay down to the provocative side, sat up for thirty seconds, and then lay to the other side every three hours. After seven to ten days, 61 of 67 subjects were free of symptoms. The assumed aim was detachment of the particle from the posterior canal cupula.

In France Semont (a physiotherapist) and Sterkers [23, 24] modified this to a logical physician-controlled treatment they called the **Liberatory maneuver**, now known as the **Semont maneuver**. The patient is lain down to the side of the symptomatic ear, facing down. When the nystagmus ceases, the patient is moved rapidly through 90 degrees to the opposite side (where the symptomatic ear becomes uppermost). Either immediately or up to 15 seconds later the patient experiences vertigo and has nystagmus identical to the symptomatic side. The technique was little known outside France.

In attempting to explain the latency and fatiguability of BPPV nystagmus, Hall et al. [25] (at the University of London, Ontario) and later Epley [26] (a solo private practice otologist in Portland, Oregon) made models of the semicircular canals and proposed that they were better explained by free-floating particles in the posterior canal, which Epley called canalithiasis. Also at the University of London, Ontario, Parnes and McClure, in attempting a surgical posterior canal occlusion, observed and photographed free otoconia in the endolymphatic compartment [27]. Based on his models Epley proposed a controlled set of head movements he called the **canalith repositioning procedure (CRP)** [28]. Epley had presented this as an instruction course at the American Academy of Otolaryngology, Head and Neck Surgery meetings since 1980 and endured considerable derision because he used a heavy massage vibrator over the mastoid process [29].

After seeing canaliths at operation, Parnes [30] described an almost identical particle repositioning maneuver (PRM) (often known as the Modified Epley maneuver) whose main difference is its slower pace.

BPPV (85% posterior canal) is now recognized as the most common cause of vertigo in adults. It is estimated that 2.4% of people experience at least episode in their life [31]. 9% of residents in a home for the elderly were found to have BBPV [32]. The onset is most commonly between the fifth and seventh decades. It is the most common cause of vertigo

after a head injury [33, 34]. An episode of vestibular neuritis [35] and a period of bed rest [36] are common antecedents. Omission of a simple clinical test can result in patients undergoing unnecessary, expensive investigations [37]. Previously “nontypical” forms of positionally induced nystagmus were assumed to always have a central cause. While performing CRPS, Epley observed a sudden change of “typical” torsional posterior canal nystagmus to horizontal direction-changing nystagmus and deduced the nystagmus even the superior canal [38]. Without clinical proof Epley predicted the logical treatment for horizontal canal BPPV would be a 360 degree horizontal plane rotation away from the symptomatic ear.

In 1985 McClure [39] had published the electronystagmographic (ENG) traces of seven subjects who had intense positional vertigo and direction-changing horizontal nystagmus when supine. The fast phase was towards the undermost ear (geotropic). McClure suspected a “viscous plug” in the horizontal canal which was causing a piston effect on the horizontal canal receptor. As discovered by Ewald, an ampullopetal (towards the vestibule) cupula deflection is known to cause the most intense nystagmus and vertigo. Horizontal canal BPPV was then reported by others [40–43] and its particularly intense vertigo confirmed. Early repositioning attempts failed [41]. A 270 degree “barbecue” rotation was trialled [44].

These simple horizontal repositioning techniques remain the usual way of treating the horizontal variant of BPPV. Occasionally the most intense nystagmus is away (apogeotropic) from the undermost ear, implying a particle or particles attached to the cupula, or close to it, on its canal or utricular side [43, 45–47]. The cupula becomes “heavy” and is ampullofugal when the symptomatic ear is undermost and ampullopetal when it is uppermost. It can be difficult to ascertain which is the symptomatic ear, but it is likely to be the *undermost ear* which initiates the *least nystagmus*. Horizontal canal BPPV comprises approximately 15% in most series. As for posterior canal it can occur *de novo*, after mild head injury or by “canal conversion” during posterior canal repositioning [45, 46]. It is likely that patients with horizontal canal BPPV inadvertently treat themselves by rolling over in their sleep, if it is in the desirable direction. If they turn in the “wrong” direction they trigger and awake with vertigo.

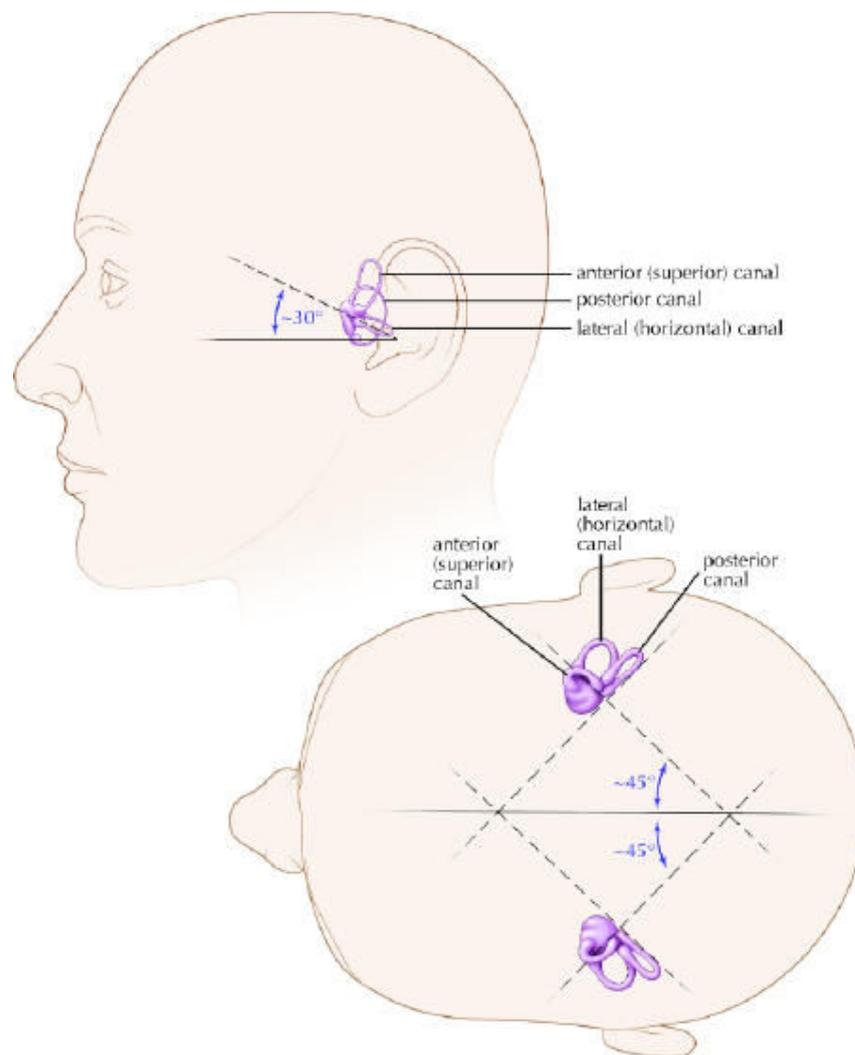
Although Brandt et al. [48] in 1994 had alluded to “the rare anterior [superior] canal BPPV, the spontaneous symptoms occur when the affected ear is uppermost”, the first detailed description of superior canal BPPV is usually attributed to Herdman and Tusa [49] who documented two patients whose positionally induced nystagmus was accompanied by downbeat and torsional nystagmus likely to be caused by a superior canal receptor and which ceased after repositioning treatment, implying it was rare form of BPPV. Subsequently

superior canal BPPV was recognized and reported by others [50–56] in whose series it accounts for approximately 1% of all BPPV diagnoses. In a review [52] of 50 consecutive patients with positionally induced nystagmus, 75% had a central cause: multiple system atrophy, cerebellar degeneration, and other miscellaneous causes with immediate onset of downbeat nystagmus on a Dix Hallpike test. In 25% (“idiopathic”) a Dix Hallpike test or a head-hanging test elicited downbeat nystagmus with a short latency. In half the subjects a torsional nystagmus could be seen through Frenzel glasses, but in one it was only discernible by video imaging. Aw et al. [54] studied forty-four patients whose BPPV had not responded to conventional repositioning, using 3-dimensional research coils and a 2-axis wholebody rotator. Seven had downbeat nystagmus with a small torsional component, and all responded to a “head-overheels” forward rotation in the plane of the superior canal. Differences in the ampullary segments of the posterior and superior canals most likely explain why superior canal BPPV downbeat nystagmus can be triggered by a Dix Hallpike test to either side and for its small (or absent) torsional component. In most cases the symptomatic ear is the *uppermost ear* .

## 2. Anatomy and physiology

### 2.1 Peripheral Vestibular Anatomy

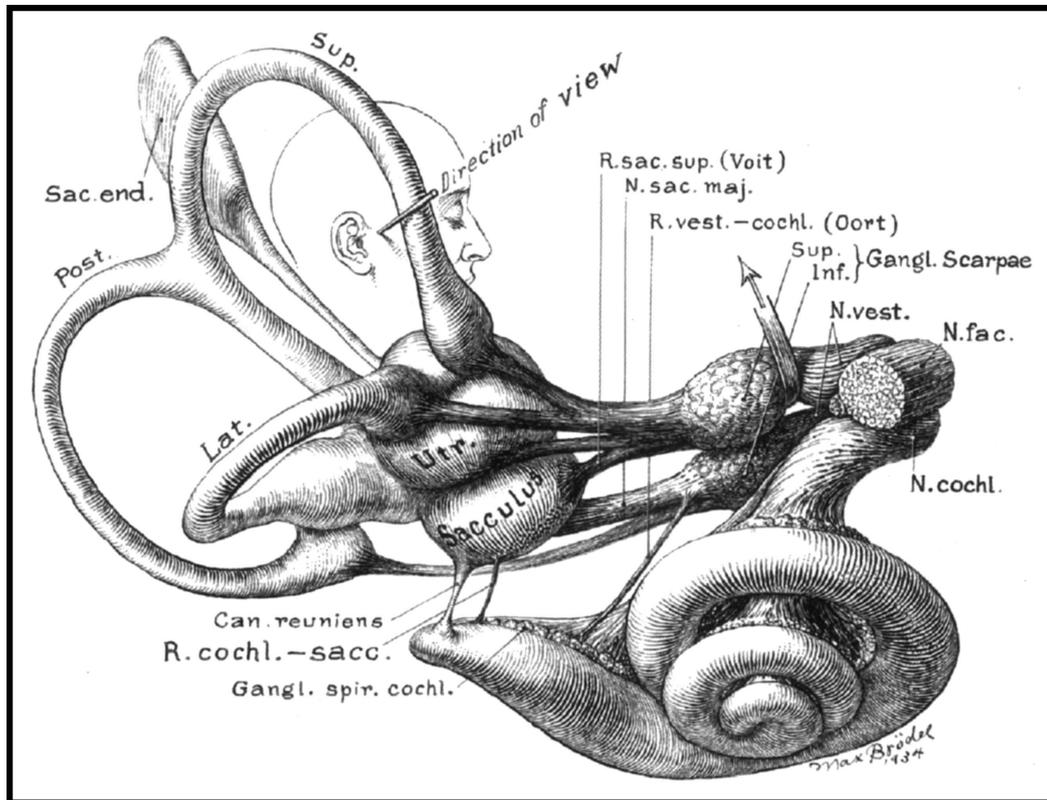
Within the petrous portion of each temporal bone lies the membranous vestibular labyrinth (Figure 1). Each labyrinth contains 5 neural structures that detect head acceleration: 3 **semicircular canals** and 2 **otolith organs** (Figure 2).



**Fig. 1: Spatial orientation of the semicircular canals.** Note how the posterior canal on 1 side is in the same plane as the contralateral superior canal. Both lateral canals are in the same plane, 30° above the horizontal.

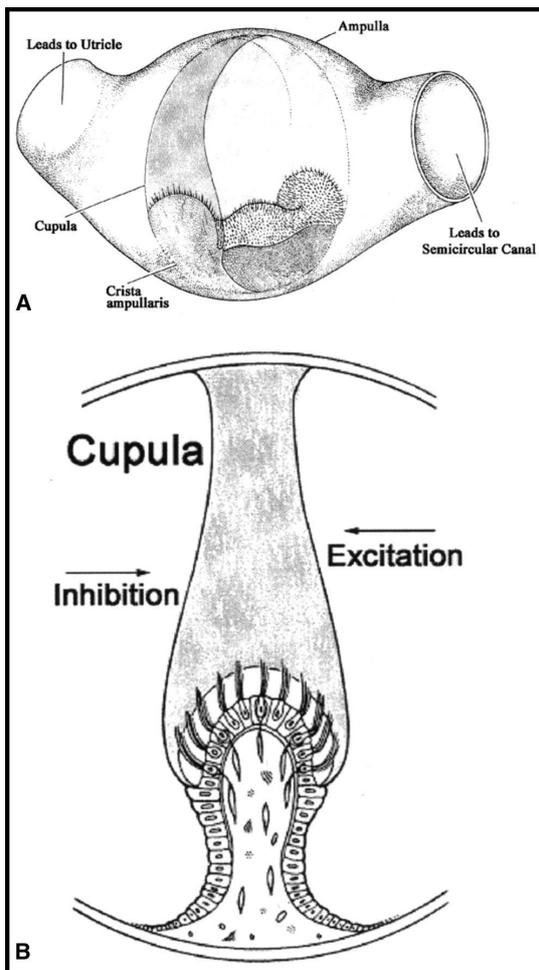
The 3 semicircular canals (SCC) (lateral, posterior, and anterior) respond to angular acceleration and are orthogonal with respect to each other. Alignment of the SCCs in the temporal bone is such that each canal has a contralateral coplanar mate. The lateral canals form a coplanar pair, whereas the posterior and contralateral anterior SCC form coplanar pairs. The anterior aspect of the lateral SCC is inclined 30 degrees upward from a plane

connecting the external auditory canal to the lateral canthus. The posterior and anterior SCCs are inclined about 92 and 90 degrees from the plane of the lateral SCC. Because the SCCs are not precisely orthogonal with earth vertical or earth horizontal, angular rotation of the head stimulates each canal to varying degrees.



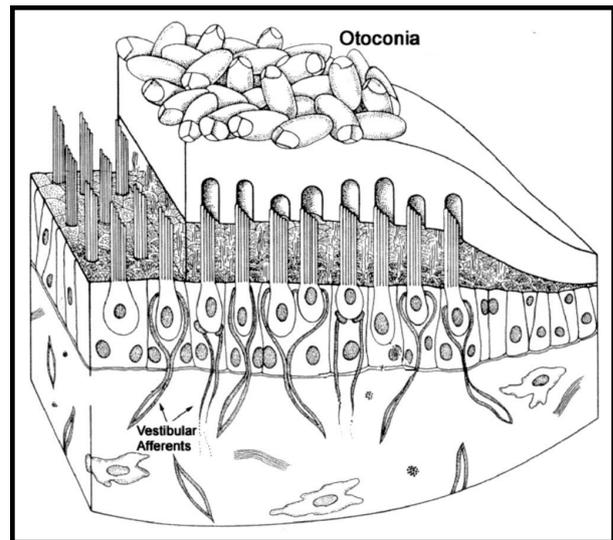
**Fig. 2: Anatomy of the vestibular labyrinth.** Structures include the utricle (Utr.), saccule, anterior (or superior) semicircular canal (Sup.), posterior semicircular canal (Post.), and the lateral semicircular canal (Lat.). Note the superior vestibular nerve innervating the anterior and lateral semicircular canals as well as the utricle. The inferior vestibular nerve innervates the posterior semicircular canal and the saccule. The cell bodies of the vestibular nerves are located in Scarpa's ganglion (Gangl. Scarpae).

The SCCs are filled with **endolymph** that has a density slightly greater than that of water. Endolymph contains a high concentration of potassium, with a lower concentration of sodium, and moves freely within each canal in response to the direction of the angular head rotation. The SCCs enlarge at one end to form the **ampulla**. Within the ampulla lies the **cupula**, a gelatinous barrier that houses the sensory hair cells (Figure 3A). The kinocilia and stereocilia of the hair cells are seated in the crista ampullaris (Figure 3B). Deflection of the stereocilia caused by motion of the endolymph results in an opening (or closing) of the transduction channels of hair cells, which changes the membrane potential of the hair cells. Deflection of the stereocilia toward the single kinocilia in each hair cell leads to excitation (depolarization), and deflection of the stereocilia away from the kinocilia leads to inhibition (hyperpolarization).



**Fig. 3 A:** The semicircular canals enlarge at one end to form the ampulla. The cupula of the ampulla is a flexible barrier that partitions the canal. The crista ampullaris contains the sensory hair cells. The hair cells generate action potentials in response to cupular deflection.

**Fig. 3 B:** Cross-section of crista ampullaris showing kinocilia and stereocilia of hair cells projecting into the cupula. Deflection of the stereocilia towards the kinocilia causes excitation; deflection in the opposite direction causes inhibition.



**Fig. 4:** Otoconia are embedded in a gelatinous matrix and provide an inertial mass. Linear acceleration shifts the gelatinous matrix and excites or inhibits the vestibular afferents depending on the direction in which the stereocilia are deflected.

Hair cells are oriented in the lateral SCC so that endolymph motion toward the ampulla causes excitation. In contrast, hair cells of the vertical SCCs (posterior and anterior) are oriented so that depolarization occurs when endolymph moves away from the ampulla. Each of the SCCs responds best to motion in its own plane, with coplanar pairs exhibiting a push-pull dynamic. For example, as the head is turned to the right, the hair cells in the right lateral SCC are excited, whereas the hair cells in the left lateral SCC are inhibited.

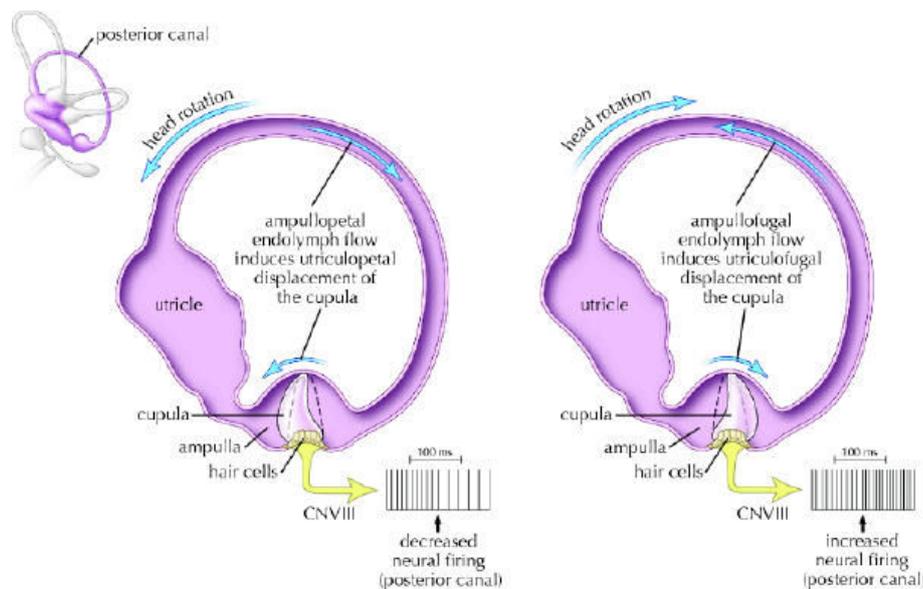
The brain detects the direction of head movement by comparing input from the coplanar labyrinthine mates.

The **saccul**e and **utricle** make up the otolith organs of the membranous labyrinth. Sensory hair cells project into a gelatinous material that has calcium carbonate crystals (**otoconia**) embedded in it, which provide the otolith organs with an inertial mass (Figure 4). The utricle and the sacculle have central regions known as the striola, dividing the otolith organs into 2 parts. The kinocilia of the utricular hair cells are oriented toward their striola, whereas the

kinocilia of the saccular haircells are oriented away from their striola. Motion toward the kinocilia causes excitation. Utricular excitation occurs during horizontal linear acceleration or static head tilt, and saccular excitation occurs during vertical linear acceleration.

## 2.2 Vestibular Afferent Physiology

In primates, primary vestibular afferents of the healthy vestibular system have a resting firing rate that is typically 70 to 100 spikes per second. The discharge regularity (determined by the spacing of the interspike intervals between action potentials of vestibular nerve afferents) provides a useful marker for the information carried by these afferents. The coefficient of variation (standard deviation/mean discharge) of the interspike interval provides a useful measurement for classifying afferents into irregularly and regularly discharging groups. The information carried by irregular and regular afferents varies over the spectral range of frequency and acceleration that encompasses natural head movements. Generally, irregular afferents are more sensitive to rotations during large head accelerations than regular afferents are. The increased sensitivity of the irregular afferents may be more critical for the rapid detection of head movements as well as initiation of the VOR. The regular afferents, in contrast, provide a signal that is proportional to head velocity over a wide spectral range. In addition, the regular afferents may be the primary source of input to the VOR for steady-state responses to sinusoidal rotations because temporarily silencing the irregular afferents has no effect on the VOR during low-frequency and small head accelerations.



**Fig. 5: Schematic drawing of the physiology of the left posterior semicircular canal.**

In the image on the right, note the excitatory response (increased neural firing) with utriculofugal cupular displacement. The same excitatory response would occur in the superior (anterior) canal with utriculofugal cupular displacement, whereas the opposite (inhibitory) response would occur with utriculofugal cupular displacement in the lateral canal. The same rules would apply to the image on the left. CNVIII = vestibular nerve, ms = millisecond.

The cell bodies of vestibular nerve afferents are located in the superior or inferior divisions of Scarpa's ganglia, which lie within the internal auditory canal near the emergence of the vestibular nerve into the cerebellopontine angle. From the vestibular labyrinth, the afferent information travels ipsilateral in 1 of 2 branches of the vestibular nerve. The superior vestibular nerve innervates the lateral and anterior SCC as well as the utricle. The inferior vestibular nerve innervates the posterior SCC and the saccule. It is estimated that between 15,000 to around 25,000 vestibular nerve fibers exist in humans. Variation of nerve fiber counts among studies appears to be a function of age, although rate of decline of the number of afferent fibers also appears to be variable. The branches of the vestibular nerve travel together into the pontomedullary junction where they bifurcate. Primary vestibular afferents in the superior division of the vestibular nerve include axons that synapse in the superior and medial vestibular nuclei or the uvula, nodulus, flocculus, or fastigial nucleus of the cerebellum. Primary vestibular afferents from the inferior branch synapse with neurons in either the medial, lateral, or inferior vestibular nuclei, which, along with the superior vestibular nuclei and other subnuclei, comprise the vestibular nuclear complex.

### **2.3 Central Vestibular Anatomy**

Secondary vestibular afferents have been identified as relaying signals from the vestibular nuclei to the extraocular motor nuclei, the spinal cord, or the flocculus of the cerebellum. Central vestibular neurons differ in terms of the inputs they receive from regular and irregular afferents. Those central vestibular neurons that project to the extraocular motor nuclei receive a majority of their monosynaptic inputs from regular afferents, whereas those that project to the spinal cord receive a majority of their inputs from irregular afferents. Those central vestibular neurons projecting to the flocculus of the cerebellum receive relatively equal contributions from regular and irregular afferents.

Many vestibular reflexes are controlled by processes that exist primarily within the brain stem. Tracing techniques, however, have identified extensive connections between the vestibular nuclei and the reticular formation, thalamus, and cerebellum. Vestibular pathways appear to terminate in a unique cortical area. In studies of primates, fibers terminating in the junction of the parietal and insular lobes have been identified and considered the location for a vestibular cortex.

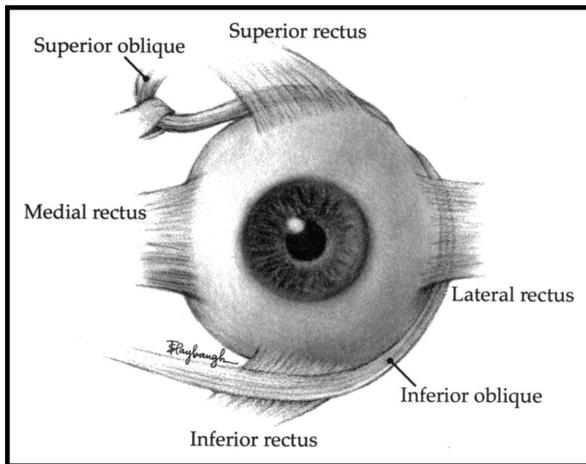
Recent evidence in studies of humans using functional magnetic resonance imaging appears to confirm the parietal and insular regions as the cortical location for processing vestibular information [57]. Connections with the vestibular cortex, thalamus, and reticular formation enable the vestibular system to contribute to the integration of arousal and conscious awareness of the body and to discriminate between movement of self and the environment. The cerebellar connections help maintain calibration of the VOR, contribute to posture during static and dynamic activities, and influence the coordination of limb movements.

## 2.4 Vestibulo-ocular Physiology

The ability of the VOR to elicit rapid compensatory eye movements that maintain stability of images on the fovea depends on relatively simple patterns of connectivity in the central vestibular pathways. In its most basic form, the pathways controlling the VOR can be described as a 3-neuron arc. In the case of the lateral SCC, primary vestibular afferents from the lateral SCC synapse in the ipsilateral medial and ventrolateral vestibular nuclei. Some of the secondary vestibular neurons receiving innervation from the ipsilateral labyrinth have axons that decussate and synapse in the contralateral abducens nucleus, whereas others ascend ipsilaterally to the oculomotor nucleus. Motoneurons from the abducens nucleus and the medial rectus subdivision of the oculomotor nucleus then synapse at the neuromuscular junction of the lateral rectus and medial rectus muscles, respectively. Similar patterns of connectivity exist for the anterior and posterior SCC and the eye muscles that receive innervations from them (Table 1).

**Tab. 1: Innervation Pattern of Excitatory Input From the Semicircular Canals**

Primary Afferent	Secondary Neuron	Extraocular Motoneuron	Muscle
Lateral (right)	Medial vestibular nucleus	Right oculomotor nucleus Left abducens nucleus	Right medial rectus Left lateral rectus
Anterior (right)	Lateral vestibular nucleus	Left oculomotor nucleus	Left inferior oblique Right superior rectus
Posterior (right)	Medial vestibular nucleus	Left trochlear nucleus Left oculomotor nucleus	Right superior oblique Left inferior rectus



**Fig. 6:Muscle insertions of the left eye.**

The 6 extraocular muscles insert into the sclera and can be considered as complementary pairs. The medial and lateral rectus muscles rotate the eyes horizontally, the superior and inferior rectus muscles principally rotate the eyes vertically, and the superior and inferior oblique muscles rotate the eyes torsionally with some vertical component. By convention, the torsional rotation is noted as it relates to the superior poles of the eyes. The superior oblique muscle rotates the eye downward and toward the nose [intorsion], whereas the inferior oblique muscle rotates the eye upward and away from the nose [extorsion]. The superior oblique muscle travels through the fibrous trochlea, which attaches to the anteromedial superior wall of the orbit.

The VOR has been tested across multiple frequencies and velocities and shows velocity-dependent nonlinearities, which may correlate with unique afferent physiology. The gain of the VOR remains constant (linear) across multiple frequencies of sinusoidal rotations, with peak velocities of  $<20^{\circ}/s$  [58]. For rotations at higher frequencies and velocities, the VOR gain rises with increases in stimulus velocity (nonlinear). Similar effects of stimulus frequency and velocity are seen in responses to steps of acceleration. Therefore, it may be that the output of the VOR is the combined result of linear and nonlinear components. Adaptation experiments in which spectacles were used to modify the gain of the VOR support the notion that a linear component and a nonlinear component may be responsible for mediating the VOR. Using different frequency and velocity profiles for the adaptation stimulus, the nonlinear component has been shown to be adaptable only with highfrequency and high-velocity stimuli.

## 3. Clinical features

### 3.1 Epidemiology

BPPV is the most common disorder of the peripheral vestibular system. Mizukoshi and colleagues estimated the incidence to be 10.7 to 17.3 per 100 000 per year in Japan, although this is likely to be an underestimate because most cases of BPPV resolve spontaneously within months [60].

Several studies have suggested a higher incidence in women, but in younger patients and those with posttraumatic BPPV the incidence may be equal between men and women. The age of onset is most commonly between the fifth and seventh decades of life.

BPPV is more likely to involve the right ear, a factor that may be related to the habit of sleeping on the right side in the general population [61].

BPPV most often involves a single semicircular canal, usually posterior (60-90%), but may involve both posterior and lateral canals in the same inner ear. Posterior canal BPPV may convert to lateral canal BPPV following repositioning manoeuvres. Head trauma is the most common cause of simultaneous bilateral posterior canal BPPV.

Tab. 2

<b>Incidence</b>	95,8/100000/year	
<b>Prevalence</b>	131,6/100000/year	
<b>Man</b>	37,2	W/M 1,7/1
<b>Women</b>	62,8	
<b>Age</b>	Range 6-89 years	Average 57 years
<b>Posterior canal BPPV</b>	79,4%	Unilateral 72%
		Bilateral 7,4%
<b>Lateral canal BPPV</b>	16,9%	Geotropic 80%
		Apogeotropic 20%
<b>Atypic form</b>	3,7%	

Caruso et al 1995

### **3.2 Symptoms of BPPV**

Patients describe sudden, severe attacks of either horizontal or vertical vertigo, or a combination of both, precipitated by certain head positions and movements. Patients typically develop vertigo when getting out of bed, rolling over in bed, tilting their head back, for example to look up shelves, or bending forward, for example when fastening their shoes. Patients can often identify the affected ear by stating the direction of movement that precipitates the majority of the attacks (e.g., when rolling over in bed to the right, but not the left, precipitates dizziness, this indicates right ear involvement).

The attacks of vertigo typically last fewer than 30 seconds, however, some patients overestimate the duration by several minutes. Reasons for this discrepancy may include the fear associated with the intense vertigo along with the nausea and disequilibrium that may follow the attack. The vertigo attacks occur in spells; patients have several attacks a week (23%) or during the course of 1 day (52%). In addition to vertigo, many patients complain of lightheadedness, nausea, imbalance and, in severe cases, sensitivity to all directions of head movement.

Many patients also become extremely anxious for 2 main reasons. Some fear that the symptoms may represent some kind of sinister underlying disorder such as a brain tumour. For others, the symptoms can be so unsettling that they go to great lengths to avoid the particular movements that bring on the vertigo. For this reason, some may not even realize that the condition has resolved, as it so often does over time without any treatment at all. BPPV can be described as selflimited, recurrent or chronic. As the name implies, BPPV is most often a benign condition, however, in certain situations it may become dangerous. For example, a painter looking up from the top of a ladder may suddenly become vertiginous and lose his or her balance, risking a bad fall. The same would hold true for underwater divers who might get very disoriented from acute vertigo. Heavy machinery operators should use great caution especially if their job involves significant head movement. Most people can safely drive their car as long as they are careful not to tip their head back when checking their blind spot.

### **3.3 Causes**

The cause of BPPV is mostly unknown (idiopathic). In view of the high prevalence of BPPV in middle-aged women, hormonal factors may play a role in the development of BPPV. In a recent study, bone mineral density score was decreased in both women and men with

idiopathic BPPV compared with that in normal controls without a history of dizziness [59]. The prevalence rates of osteopenia and osteoporosis were also found to be higher in both women and men with BPPV than in normal controls. Furthermore, in women aged  $\geq 45$  years, the lowest T-scores were also decreased in the recurrent group, compared with those in the de novo group. These findings suggest the involvement of deranged calcium metabolism in idiopathic BPPV and a significant association between osteopenia/osteoporosis and idiopathic BPPV. Otoconia are deposits of calcium carbonate in the form of composite calcite crystals, and bone contains 99% of the calcium found in the body. Decreased estrogen levels may disturb the internal structure of the otoconia or their interconnections and attachments to the gelatinous matrix. Alternatively, an increase in the concentration of free calcium in the endolymph due to increased calcium resorption may reduce the capacity to dissolve the dislodged otoconia.

BPPV may develop secondary to various disorders that damage the inner ear and detach the otolith from the utricular macule. Head trauma causing mechanical damage to the ear is the most common cause of BPPV. Patients rarely develop BPPV after mastoid surgery or if they engage in a persistent head-tilt position, such as among barbers or dentists. Compared with the idiopathic form, traumatic BPPV exhibits several distinctive characteristics, including a higher incidence of bilaterality, involvement of multiple canals on the same side, equal occurrence among women and men, a younger and more even age distribution, more difficult to treat, and frequent recurrences.

In addition, BPPV may develop secondary to any of the inner ear diseases (e.g., vestibular neuritis, Meniere's disease) that give rise to degeneration and detachment of the otoconia, but do not totally impair semicircular canal function [63]. BPPV appears to be more frequent (9.8%) in vestibular neuritis patients than in the general population, consistently affecting the posterior canal of the same ear. BPPV occurrence after vestibular neuritis predominantly affects patients who did not fully recover from the disease. BPPV after vestibular neuritis appears to be more difficult to treat than idiopathic BPPV.

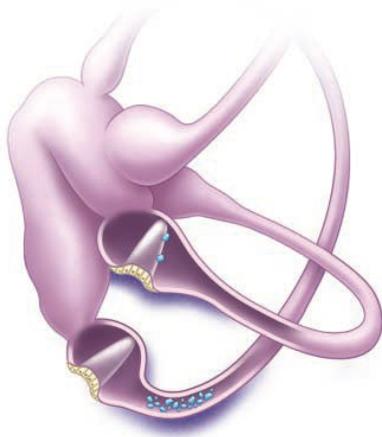
The incidence of BPPV is also known to be higher in patients who suffer from migraine, even though the exact mechanism remains to be elucidated [63, 64] BPPV has been reported to occur in association with giant-cell arteritis, diabetes, and hyperuricemia [ 65-68].

### 3.4 Pathomechanism

BPPV can theoretically affect each of the 3 semicircular canals, although superior canal involvement is exceedingly rare.

The detached otolith debris could be either attached to the cupula (**cupulolithiasis**) or may be free-floating in the semicircular canals (**canalolithiasis**) (Figure 7). Pathological studies have shown that both of these conditions exist (Figure 8).

The otolithic debris deflects the cupula and gives rise to a spinning sensation via a direct gravitational effect on the cupula or by inducing endolymph flow during head motion in the direction of gravity. According to the cupulolithiasis theory, a cupular deposit (heavy cupula) would induce a gravitational effect on the crista. However, the action of free-floating debris is the currently accepted pathophysiologic mechanism of typical BPPV. According to the canalolithiasis theory, the free-floating particles move under the influence of gravity when changing the position of the canal in the earth-vertical plane. The hydrodynamic drag of the particles induces endolymphatic flow, resulting in cupular displacement and leading to the observed typical responses.



**Fig. 7: Left inner ear.**  
Depiction of canalolithiasis of the posterior canal and cupulolithiasis of the lateral canal.



**Fig. 8:** Sequential computer-regenerated photographs taken from an intra-operative video of a fenestrated posterior semicircular canal. Note the single white conglomerate mass within the membranous duct (arrow) (left). Note how the mass has fragmented into tiny particles 2–3 minutes later, after the membranous duct has been probed (right).

## 4. Diagnosis and Treatments

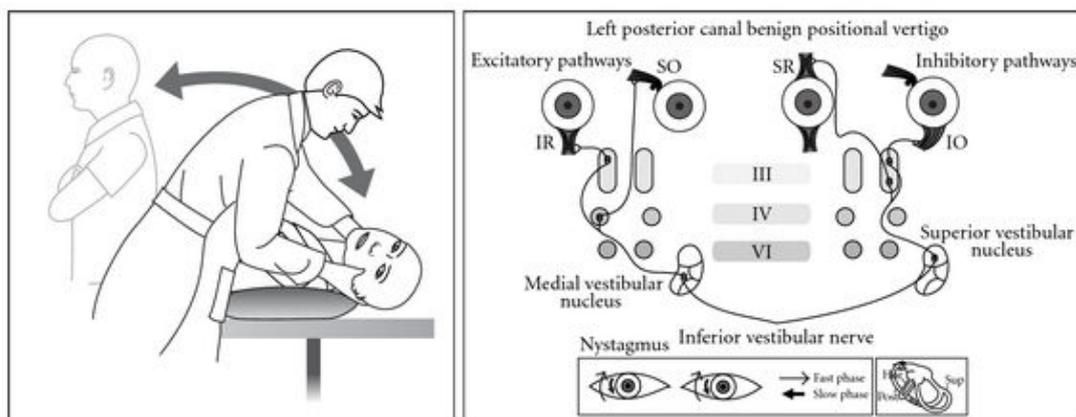
Each type of BPPV is diagnosed by observing the patterns of nystagmus induced during positioning maneuvers that have been designed to move only the involved canal in the direction of maximal gravity. However, accurate observations of the nystagmus require the fixation to be removed during the maneuvers.

BPPV is usually a self-remitting disorder and may resolve as time goes on without specific treatment. According to a report on the natural course of untreated BPPV, most HC-BPPVs resolve within  $16\pm 19$  days and PC-BPPVs within  $39\pm 47$  days of their onset.<sup>26</sup> However, a correct diagnosis and proper repositioning maneuvers may allow a rapid and simple cure for the BPPV [69].

### 4.1 Posterior Canal BPPV (PC-BPPV)

#### 4.1.1 Diagnosis

In PC-BPPV, the positioning nystagmus is typically induced by **Dix-Hallpike maneuvers** in the direction of the involved canal (Figure 9). During the Dix-Hallpike maneuver, it is thought that the free-floating otolithic debris (canalolithiasis) in the posterior canal moves away from the cupula and stimulates the posterior canal by inducing ampullofugal flow of the endolymph (Ewald's first law). Excitation of the posterior canal in turn activates the ipsilateral superior oblique and contralateral inferior rectus muscles, which results in tonic downward deviation of the eyes with a torsion in the direction of the uppermost ear. Accordingly, the resultant nystagmus would be upbeat and torsional, with the upper pole of the eyes beating toward the lowermost ear.



**Figure 9: Posterior canal BPPV in a left ear showing Dix Hallpike test, inner ear, and receptor connections to the extraocular muscles.**

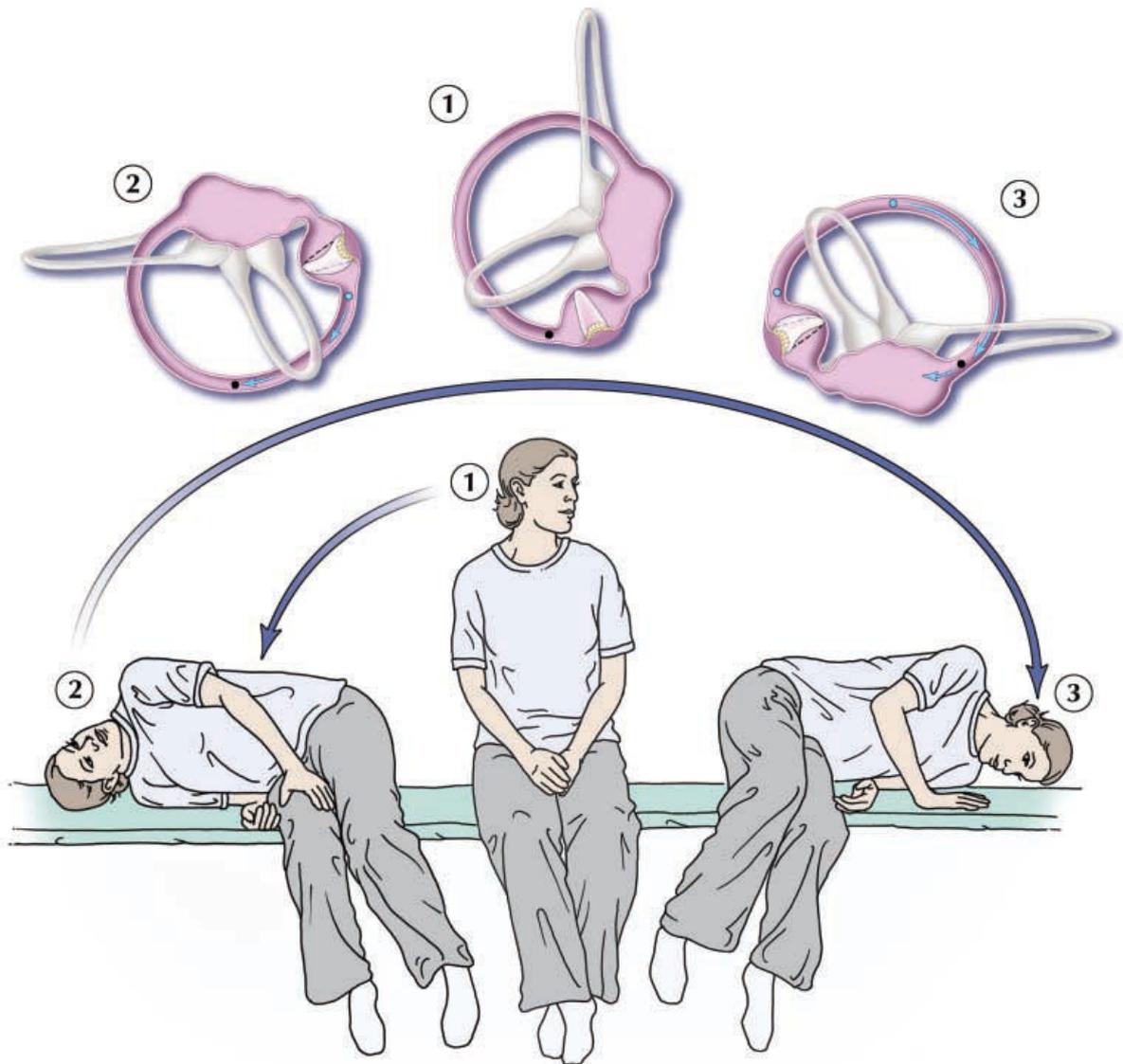
The nystagmus usually develops with a brief latency of several seconds, resolves within 1 minute (usually within 30 seconds), and its direction is reversed on sitting. The nystagmus diminishes (i.e., it fatigues) with repeated examinations. The Dix-Hallpike maneuver has been considered the gold standard for diagnosing PC-BPPV. However, this maneuver should be performed with caution in patients with a history of neck surgery, cervical radiculopathy, and vascular dissection syndrome, since it requires rotation and extension of the neck during the positioning.

#### **4.1.2 Treatments**

The most popular methods for treating PC-BPPV are **Semont's liberatory** and **Epley's maneuvers**. These maneuvers employ stepwise changes in head position (Fig. 6) to flush freefloating otolithic debris out of the semicircular canals and back into the utricle.

##### **Liberatory manoeuvre**

In 1988, Semont and colleagues<sup>37</sup> described the “liberatory manoeuvre” (Fig. 10) based on the cupulolithiasis theory. It was believed that this series of rapid changes of head position freed deposits that were attached to the cupula. The manoeuvre begins with the patient in the sitting position and the head turned away from the affected side. The patient is then quickly put into a position lying on his or her side, toward the affected side, with his or her head turned upward. After about 5 minutes, the patient is quickly moved back through the sitting position to the opposite position lying on his or her side with his or her head now facing downward. The patient remains in this second position for 5–10 minutes before slowly being brought back to the sitting position. In their series of 711 patients, Semont and colleagues<sup>37</sup> found an 84% response rate after 1 procedure and a 93% response rate after a second procedure 1 week later [70]. Several other case series have had response rates of 52%–90% [71-73] with recurrence rates of up to 29%. There has been no difference in efficacy shown between the liberatory manoeuvre and particle repositioning manoeuvre, which is described in the following section, in randomized studies by Herdman and colleagues[72] and Cohen and Jerabek [74]. The liberatory manoeuvre is effective, but is cumbersome with elderly and obese patients, and shows no increased efficacy compared with the simple particle repositioning manoeuvre.

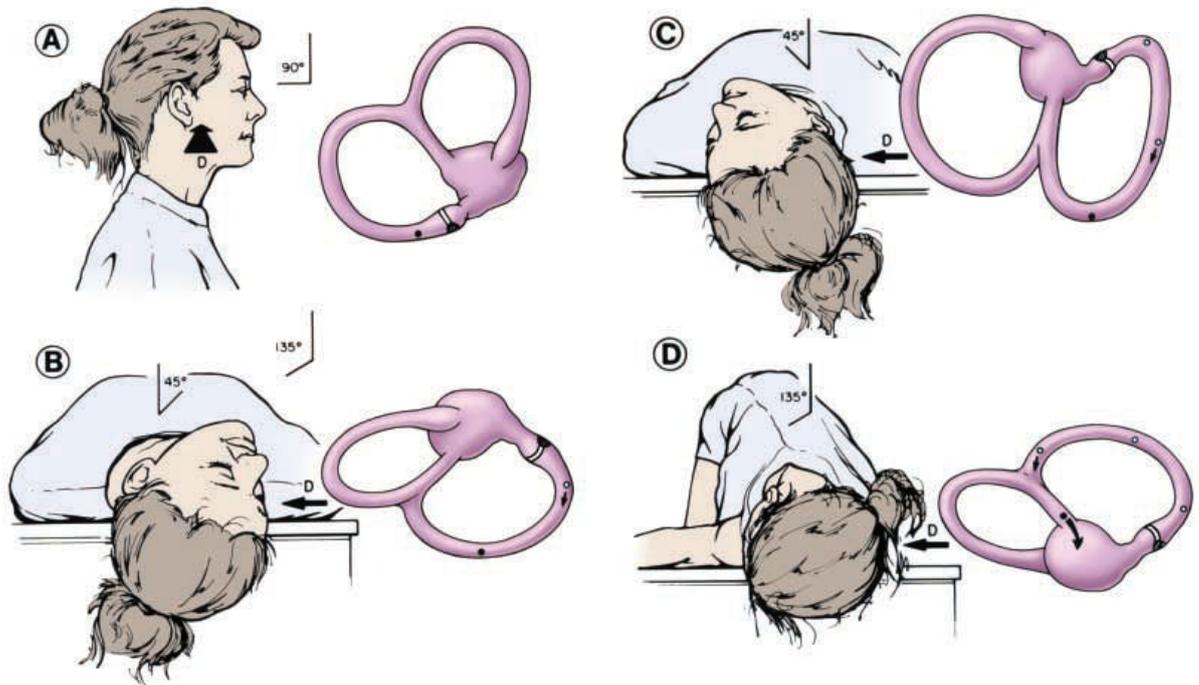


**Fig. 10: Liberatory manoeuvre of Semont (right ear).** The top panel shows the effect of the manoeuvre on the labyrinth as viewed from the front and the induced movement of the canaliths (from blue to black). This manoeuvre relies on inertia, so that the transition from position 2 to 3 must be made very quickly.

### Particle repositioning manoeuvre

Although he had been teaching his technique for many years, it was not until 1992 that Epley published his first report on the “**canalith repositioning procedure**” (CRP) [75]. This highly successful “Epley manoeuvre” is performed with the patient sedated. Mechanical skull vibration is routinely used and the patient’s head is moved sequentially through 5 separate positions. Epley postulated that the procedure enabled the otolithic debris to move under the influence of gravity from the posterior semicircular canal into the utricle.

Most clinicians today are thought to use a modified version of the CRP. One modified CRP is the particle repositioning manoeuvre (PRM) which is a 3-position manoeuvre that eliminates the need for sedation and mastoid vibration [76-77] (Fig. 11).



**Fig. 11: Particle repositioning manoeuvre (right ear).**

Schema of patient and concurrent movement of posterior/superior semicircular canals and utricle. The patient is seated on a table as viewed from the right side (A). The remaining parts show the sequential head and body positions of a patient lying down as viewed from the top. Before moving the patient into position B, turn the head 45° to the side being treated (in this case it would be the right side). Patient in normal Dix–Hallpike head-hanging position (B). Particles gravitate in an ampullofugal direction and induce utriculofugal cupular displacement and subsequent counter-clockwise rotatory nystagmus. This position is maintained for 1–2 minutes. The patient’s head is then rotated toward the opposite side with the neck in full extension through position C and into position D in a steady motion by rolling the patient onto the opposite lateral side. The change from position B to D should take no longer than 3–5 seconds. Particles continue gravitating in an ampullofugal direction through the common crus into the utricle. The patient’s eyes are immediately observed for nystagmus. Position D is maintained for another 1–2 minutes, and then the patient sits back up to position A. Overall, the PRM should take less than 5 minutes to complete. Patients are then typically asked to remain upright for the next 24–48 hours in order to allow the otoliths to settle, so as to prevent a recurrence of the BPPV.

With proper understanding of inner ear anatomy and the pathophysiology of BPPV, various appropriately trained health professionals, including family doctors and physiotherapists, should be able to successfully carry out the PRM in most straightforward cases. Atypical cases or cases that do not respond to this manoeuvre should be referred to a tertiary care dizziness clinic.

The results of Epley’s maneuver can be predicted even during the maneuver. When the head is turned 90° toward the unaffected side after the Dix–Hallpike maneuver, the positioning

nystagmus develops in the same direction as the maneuver (orthotropic nystagmus) if a clump of particulate matter moves in the correct direction into the common crus, resulting in a successful repositioning. However, the direction of the nystagmus would reverse if a heavy cupula with attached otolithic debris deflects ampullopetaally or if the particles move back toward the cupula, which implies that the repositioning will be unsuccessful [78].

It is difficult to compare studies that use the repositioning manoeuvres, because they vary considerably in the length of follow-up, number of treatment sessions, number of manoeuvres per session, the use of sedation and the use of mastoid vibration. The overall response rates range from 30% to 100%. Most of these studies are case series, but Lynn and colleagues [79] and Steenerson and Cronin [80] provide good evidence from randomized studies.

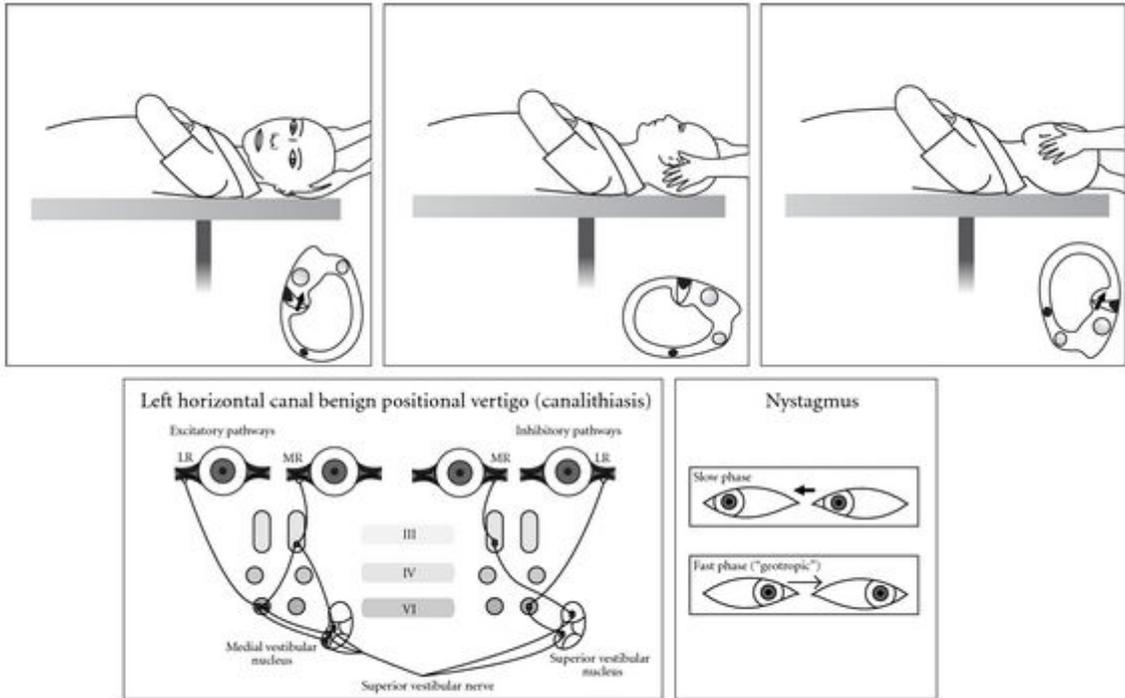
Epley's maneuver is the only recommended method of treating PC-BPPV, with confirmed evidence level A according to the American Academy of Neurology [81].

## **4.2 Horizontal (Lateral) Canal BPPV (HC-BPPV)**

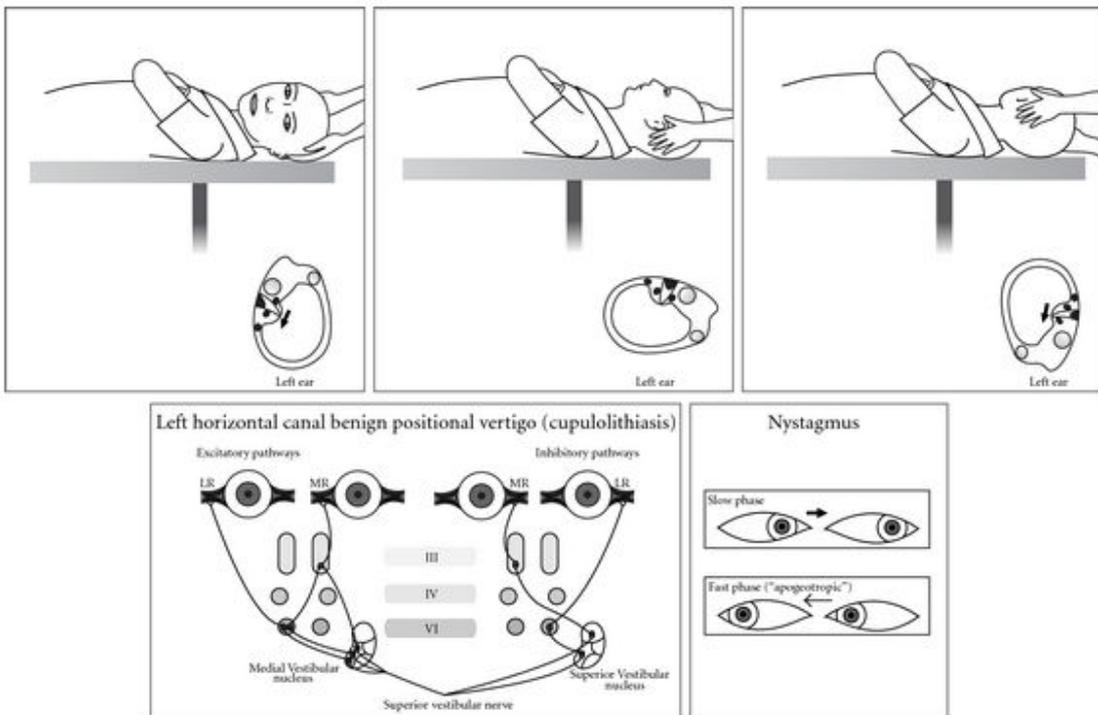
### **4.2.1 Diagnosis**

HC-BPPV is diagnosed by the supine roll test (the **Pagnini-McClure manoeuvre**), in which the head is turned by about 90° to each side while supine. During this maneuver, horizontal nystagmus may beat toward the ground (geotropic nystagmus) (Figure 12) or toward the ceiling (apogeotropic nystagmus) (Figure 13). The evoked during positioning in HC-BPPV usually tends to be more persistent, less fatigability and a shorter latency than in PC-BPPV.

Determination of the involved side (lateralization) is very important for the proper treatment of HC-BPPV (Table 3). Since ampullopetal flow of the endolymph evokes a greater response than ampullofugal flow in the horizontal canal (Ewald's second law), the induced nystagmus is stronger when the head is turned toward the affected ear in the geotropic type of HC-BPPV. In contrast, head turning to the healthy ear generates a stronger nystagmus in apogeotropic HC-BPPV. Determination of the involved ear is sometimes difficult due to rather symmetrical responses, especially if the induced nystagmus is not recorded. In these instances, other findings may provide clues toward determining the affected ear. Subjective sensation can be helpful: the patient is sometimes able to detect the more uncomfortable side. Caloric test can show hypoexcitability in the affected ear.



**Figure 12: Horizontal canal BPPV (canalithiasis)** in a left ear showing Head Roll test, inner ear, and receptor connections to the extraocular muscles.



**Figure 13: Horizontal canal BPPV (cupulolithiasis)** in a left ear showing Head Roll test, inner ear, and receptor connections to the extraocular muscles.

**Tab. 3.** Lateralization of HC-BPPV, based upon the direction and intensity of nystagmus (Ny)

	<b>Geotropic nystagmus</b>	<b>Apogeotropic nystagmus</b>
<b>Intensity of Ny</b>	Stronger side	Weaker side
<b>Subjective sensation</b>	Affected side	Affected side
<b>Pseudospontaneous Ny</b>	Healthy side	Affected side
<b>Stead Supine Positioning Test</b>	Healthy side	Affected side
<b>Lying-down Ny</b>	Healthy side	Affected side
<b>Head-bending Ny</b>	Affected side	Healthy side
<b>Reversal of initial Ny</b>	Possibly occurs Affected side	Uncommon
<b>Null point</b>	Uncommon, laterality is uncertain	Usually present on Affected side
<b>Caloric Hypoexcitability</b>	Affected side	Affected side

Another sign to diagnose the affected side is the direction of the nystagmus when the patient is briskly brought from the seated position to supine position (**Stead Supine Positioning Test**). When the patient lies supine, having the head flexed  $30^{\circ}$ , the lateral canal is on a vertical plane; therefore, due to both gravity and the brisk deceleration caused by this manoeuvre, the otoliths are pushed downwards: when they are in the posterior arm they float towards the utricle, and when they are near the cupola they float towards the ampulla. The Stead Supine Positioning Test evokes a nystagmus beating towards the healthy side in the geotropic forms and towards the affected side in the apogeotropic forms.

In HC-BPPV, nystagmus may be induced by **Bow and Lean test**: when the patient bows the head over  $90^{\circ}$  (bowing nystagmus) and leans the head backward over  $45^{\circ}$  (leaning nystagmus) in the sitting position. In up to 80% of HC-BPPV cases, bowing and leaning nystagmus are in the opposite direction. In geotropic HC-BPPV, bowing nystagmus beats mostly toward the affected ear (ampullopetal migration of the otoliths), while leaning is directed mostly toward the healthy ear (ampullofugal displacement of the otoliths). In contrast, bowing nystagmus is mostly contralesional and leaning nystagmus is usually ipsilesional when observed in apogeotropic HC-BPPV. Bowing and leaning nystagmus in apogeotropic HC-BPPV are explained by deflection of the heavy cupula in response to the positional change [82-85].

In apogeotropic HC-BPPV, the induced horizontal nystagmus may disappear when the head is turned to the affected ear by  $10-20^{\circ}$ , while supine (**null point**)[86]. The null point is explained by alignment of the heavy cupula in the direction of the gravitational vector.

Spontaneous nystagmus, also known as **pseudospontaneous nystagmus**, is not uncommon in HC-BPPV. In previous reports, 66-76% of HC-BPPV patients exhibited spontaneous nystagmus [87]. The spontaneous nystagmus in HC-BPPV may be related to the anatomical

position of the horizontal semicircular canal, which is inclined 30° backwards from the horizontal plane. Accordingly, the gravitational force may affect the otolithic debris inside the canal or the heavy cupula, even when in the upright sitting position. For the same reason, pseudospontaneous nystagmus disappears when the patient's head is bent forwards by about 30°. In this position, since the horizontal canal is aligned with respect to the earth horizontal plane, the effect of gravity is negated. However, pseudospontaneous nystagmus should be differentiated from continuous nystagmus with sustained vertigo resulting from so-called canalith jam and negative endolymph pressure between the plug and the cupula [88].

In BPPV, **secondary (spontaneous reversal)** of the initial positioning nystagmus rarely occurs without further position changes. In geotropic HC-BPPV, the initial geotropic nystagmus occasionally reverses spontaneously its direction when the head is turned toward the lesion side, and the induced nystagmus is intense [89]. Short-term adaptation of the vestibulo-ocular reflex seems to be the main mechanism underlying this spontaneous reversal of the initial positioning nystagmus.

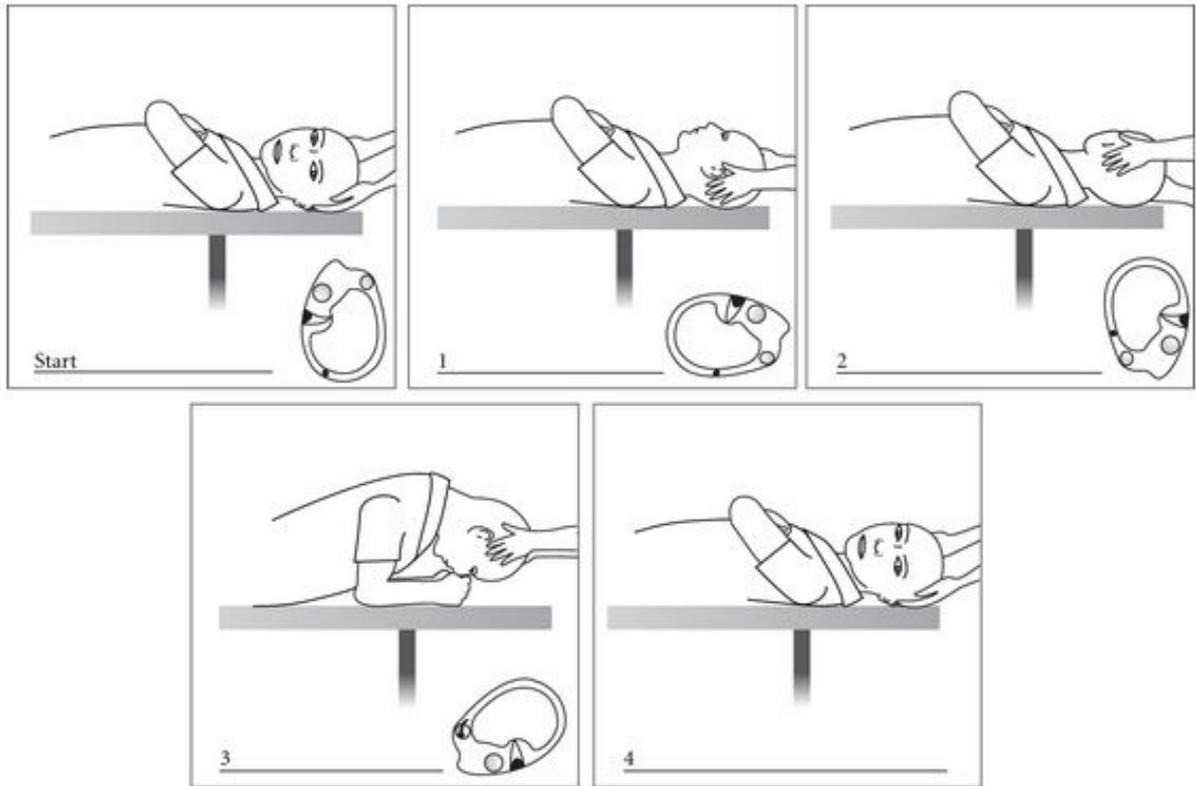
#### 4.2.2 Treatments

##### **Geotropic HC-BPPV**

Rotations of 270° or 360° around the yaw axis (the so-called **barbecue maneuver**) toward the unaffected ear are popular methods for the treatment of geotropic HC-BPPV [90]. These maneuvers consist of sequential head turning of 90° toward the healthy side while supine (Figure 14). With these maneuvers, the free-floating otoconial debris migrates in the ampullofugal direction, finally entering the utricle through the nonampullated end of the horizontal canal.

Lying with the healthy ear downward for approximately 12 hours (**forced prolonged position**) can be employed, especially in patients suffering from severe symptoms who cannot perform sequential position changes [92, 96].

The **Gufoni maneuver** is another alternative [93, 94]. After being seated on an examination couch, the patient lies down on the healthy lateral side with a quick lateral movement and is maintained in this position for 1-2 minutes until resolution of the evoked nystagmus. A quick 45° rotation of the head toward the floor is then performed, with the patient maintaining this position for another 2 minutes, followed by a slow return back to the starting position. A major advantage of the Gufoni maneuver is its simplicity.



**Figure 14:** “Barbecue” repositioning for horizontal canal BPPV in a left ear.

### **Apogeotropic HC-BPV**

Apogeotropic HC-BPPV is attributed to either cupulolithiasis or canalolithiasis within the anterior arm of the horizontal semicircular canal. In apogeotropic HC-BPPV, the therapeutic goal should be to detach the otolithic debris from the cupula or shift the debris from the anterior into the posterior arm of the horizontal canal [95].

If the otolithic debris is attached at the utricular side of cupula, its detachment should result in immediate resolution of the positional vertigo and nystagmus. In the case of adhesion from the canal side of the cupula or free-floating particles in the anterior arm, detachment and shifting of the otolithic debris into the posterior arm would give rise to a transition into geotropic HC-BPPV [96]. Therapeutic head-shaking in the horizontal plane, a modified Semont maneuver, and the Gufoni method have been proposed as treatment regimens for apogeotropic HC-BPPV [95].

The aim of head-shaking is to detach the otolithic debris from the cupula, irrespective of the side to which it is attached, using alternate accelerating and decelerating power.

The modified Semont maneuver comprises the following three steps: 1) the patient is brought briskly into a side-lying position with the affected ear downward; 2) the patient’s head is

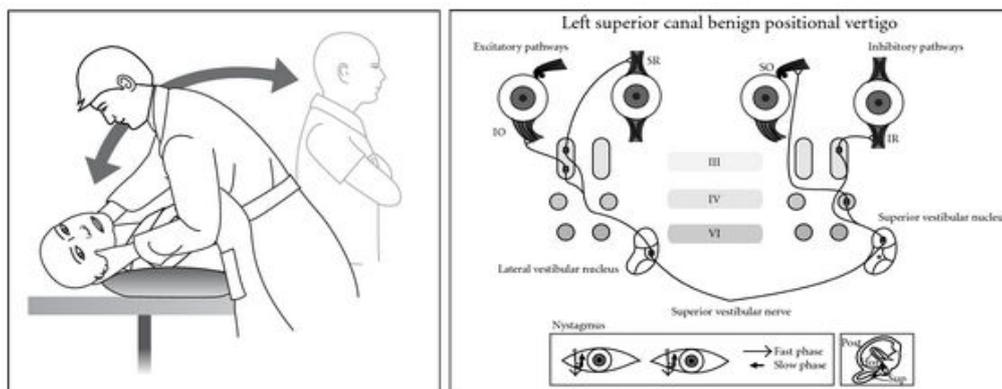
turned 45° downward, with this position being maintained for 2-3 min; and 3) the patient resumes the original sitting position. This maneuver was initially designed to dislodge the debris attached to the utricular side of the cupula.

In the Gufoni maneuver for apogeotropic HC-BPPV, the patient sits with the head directed straight ahead and then quickly moves into a side-lying position on the affected side, remaining in this position for 1 or 2 more minutes after the end of apogeotropic nystagmus. The head is then turned 45° upward very quickly and is kept in this position for 2 minutes, followed by a slow return to the sitting position. The Gufoni maneuver was designed to remove the otolithic debris from the anterior arm of the horizontal semicircular canal near the cupula.

### 4.3 Anterior Canal BPPV (AC-BPPV)

#### 4.3.1 Diagnosis

BPPV rarely involves the anterior semicircular canal, and AC-BPPV exhibits several characteristics that contrast with those of PC-BPPV. In AC-BPPV the Dix-Hallpike maneuver on either side may evoke downbeat nystagmus with an ipsitorsional (upper poles of the eyes beating toward the involved ear) component (Figure 15). Furthermore, the torsional nystagmus in AC-BPPV may not be evident, as it is in PC-BPPV.

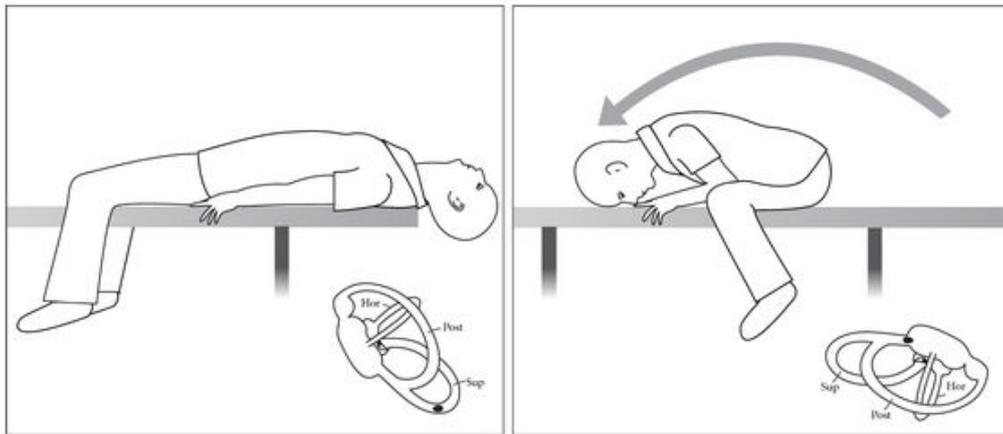


**Figure 15: Superior canal BPPV** in a left ear showing Dix Hallpike test, inner ear, and receptor connections to the extraocular muscles.

#### 4.3.2 Treatments

Various repositioning maneuvers have also been advanced to treat AC-BPPV. In the reverse Epley maneuver, the patient submits to the same sequence of positional changes after the Dix-Hallpike maneuver on the side of the healthy ear. Modified repositioning maneuvers and forced prolonged position have also been adopted in treating this particular BPPV [99, 100].

Li maneuver [101] where the patient is moved rapidly from a supine (midline) head-hanging position to a face-down position at the opposite end of the couch (Figure 16).

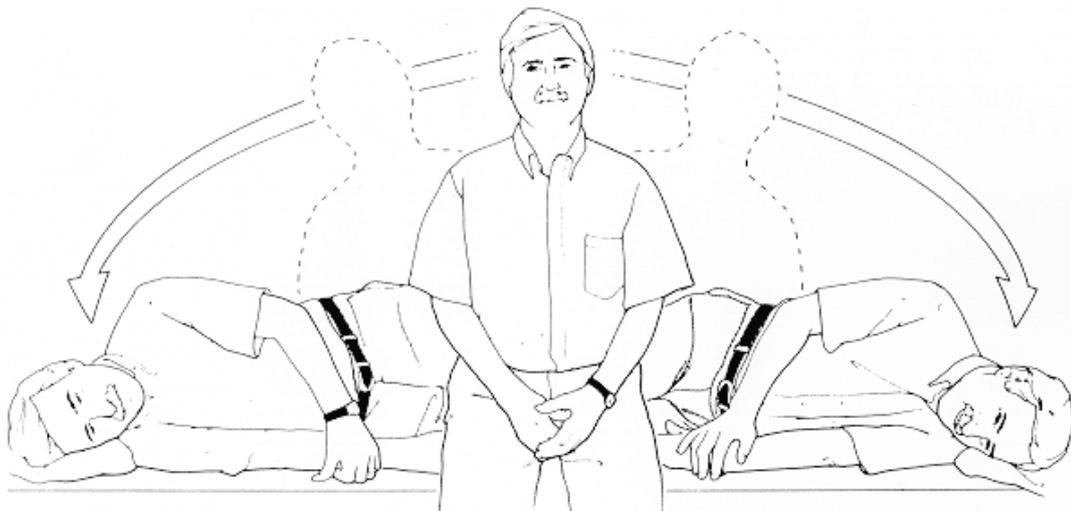


**Figure 16:** The Li manoeuvre for superior canal BPPV in either ear (left ear).

#### 4.4 Rehabilitation

Irrespective of the involved canals, the **Brandt-Daroff** exercise may be attempted when the repositioning maneuvers fail or if patients cannot tolerate the repositioning maneuvers (Figure 17). The exercise may be repeated at liberty until resolution of the symptoms.

With respect to PC-BPPV, vestibular rehabilitation demonstrates superior treatment outcomes compared with placebo [102]. However, vestibular rehabilitation is less effective than canalith repositioning procedure in producing complete symptom resolution. There are as yet insufficient data concerning the response of HCBPPV to vestibular rehabilitation.



**Figure 17:** Brandt-Daroff exercise. Patients are instructed to rapidly lie on their side, sit up, lie on the opposite side, and then again sit up. Each position should be maintained for at least 30 seconds. These exercises are repeated serially 5-10 times a day until resolution of the symptoms.

## 4.5 Surgical treatment

BPPV is a benign disease and, therefore, surgery should only be reserved for the most intractable or multiply recurrent cases. Furthermore, before considering surgery, the posterior fossa should be imaged to rule out central lesions that might mimic BPPV.

Transection of the posterior ampullary nerve innervating the posterior canal (singular neurectomy) or posterior semicircular canal occlusion (canal plugging) have been performed for intractable PC-BPPV.

**Singular neurectomy** (section of the posterior ampullary nerve, which sends impulses exclusively from the posterior semicircular canal) as described by Gacek in 1974, is an efficient procedure that was designed to control the symptoms of intractable BPPV, with an acceptable risk of postoperative hearing loss [103]. Although initial reports by Gacek demonstrated high efficacy, there was a significant risk of sensorineural hearing loss, and the procedure has been found to be technically demanding [104, 105]. It has largely been replaced by the simpler posterior semicircular canal occlusion.

Parnes and McClure [106-108] introduced the concept of **posterior semicircular canal occlusion** for BPPV. Obstruction of the semicircular canal lumen is thought to prevent endolymph flow. This effectively fixes the cupula and renders it unresponsive to normal angular acceleration forces and, more importantly, to stimulation from either free-floating particles within the endolymph or a fixed cupular deposit. Because the occlusion also impairs the normal inner ear physiology, all patients are expected to have postoperative imbalance and disequilibrium. For most people, the brain adapts to this after a few days to a few weeks, with vestibular physiotherapy hastening this process.

## 5. Results

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**Double-blind randomized trial on short-term efficacy of Semont maneuver for treatment of posterior canal benign paroxysmal positional vertigo**  
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**Double-blind randomized trial on short-term efficacy of Gufoni maneuver for treatment of lateral canal benign paroxysmal positional vertigo**  
UNDER REVUE

**GIOVANNI PAOLO SANTORO**  
**Lateral canal BPPV with uncertain side: a new therapeutic procedure**  
Poster per il 98<sup>o</sup> CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Bari, 23-26 Maggio 2012.

## **Vestibular neuritis: recurrence and incidence of secondary benign paroxysmal positional vertigo**

MARCO MANDALÀ<sup>1</sup>, GIOVANNI PAOLO SANTORO<sup>1</sup>, JULIANNE AWERY<sup>2</sup> & DANIELE NUTI<sup>1</sup>

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### **Abstract**

*Conclusions:* Recurrence of vestibular neuritis (VN) is a rare event in long-term follow-up. The incidence of benign paroxysmal positional vertigo (BPPV) in VN patients represents a quite common outcome. To our knowledge, this study represents the only long-term longitudinal study on recurrence of VN and incidence of secondary BPPV in VN.

*Objectives:* To study a large number of VN patients longitudinally to identify the recurrence rate of VN and incidence of BPPV, other peripheral vestibular disorders, sudden hearing loss or Bell's palsy.

*Methods:* This prospective cohort study assessed a VN patient-based clinic population. All patients received a complete bedside clinical examination and caloric irrigation.

*Results:* Long-term (range 4– 6 years, mean 4.9 years) longitudinal follow-up examination of 51 VN patients demonstrated a low recurrence rate (1/51 patients, 2.0%). With recurrence, VN affected the same ear after 6 months and caused less severe symptoms. BPPV appears to be more frequent (5/51 patients, 9.8%) in VN patients than in the general population, consistently affecting the posterior canal of the same ear. BPPV occurrence after VN predominantly affects VN patients who did not fully recover from the disease. Moreover, BPPV after VN appears to be more difficult to treat than idiopathic BPPV.

*Keywords:* Long-term follow-up, bedside examination

### **Introduction**

Acute vestibular neuritis (VN) is a common and debilitating disease. It is associated with severe vertigo, disequilibrium, nausea, and vomiting, but is not associated with hearing changes. In most patients, symptoms largely resolve over a period of weeks, but more protracted courses are not uncommon. Moreover, VN patients can develop a recurrence in the same [1] or contralateral ear [2], and can also go on to develop benign paroxysmal positional vertigo (BPPV) [3]. The etiology of VN is thought to be viral, although labyrinthine ischemia may be the cause in rare instances [4]. Very few studies have investigated the recurrence rate of peripheral vestibular disorders in VN patients. We studied a large number of VN patients

longitudinally to identify the recurrence rate of VN and the incidence of BPPV, other peripheral vestibular disorders, sudden hearing loss or Bell's palsy.

### **Material and methods**

This prospective cohort study assessed a patient-based clinic population from January 2002 to January 2008. The study was conducted at an ambulatory clinic of the tertiary referral center (Neuro-Otology Department of Siena Medical School). Patients were examined in the acute stage of the disease (1–3 days from onset of symptoms) and all were eligible for inclusion in the study. The criteria for inclusion in the study were (1) acute vertigo lasting for at least 24 h, (2) horizontal unidirectional spontaneous nystagmus lasting for at least 24 h, (3) no hearing loss, (4) no additional neurological signs or symptoms, and when obtained, normal brain imaging, and (5) a caloric test abnormality (canal paresis or paralysis).

A total of 68 patients met these criteria. All patients underwent a complete bedside clinical examination by the same investigator (M.M.). Vestibular function was determined using caloric irrigation with hot, cold, and ice water. Technical details of the tests performed are reported elsewhere [5]. Patients were considered recovered when both caloric testing and bedside examination had normal results. Patients were asked to return for follow-up evaluation at least twice per year (every 6 months, with detailed interviews). In addition, patients were instructed to contact the investigator (M.M.) by phone if experiencing vertigo, dizziness, sudden hearing loss or Bell's palsy at any time. If so, all patients were seen in the acute phase of recurrence by the same investigator (M.M.). Positive bedside examination and caloric testing were considered diagnostic criteria for recurrence of VN or other peripheral vestibular disease. Written informed consent was obtained from all patients, and the study was approved by the medical ethics committee of Siena University Hospital. The study was conducted in accordance with the Helsinki Declaration.

### **Results**

In all, 51 patients completed the study. The mean follow-up period was 4.9 years (range 4–6 years). The mean age of the population was  $54.7 \pm 16.9$  years (74% male prevalence). Only one patient (male, 56 years), who recovered after 1 month, presented a recurrence of VN in the same ear at 6 months from the onset. At the 6 month follow-up this patient again presented positive bedside examination (spontaneous nystagmus, positive head shaking, head impulse, and vibration test) and caloric paresis of the same side. We did not identify any recurrence in the contralateral ear in respect to the first manifestation. The overall recurrence rate of VN was 2.0%. BPPV occurred in five patients (9.8%; two women, three

men; mean age  $50.2 \pm 12.9$  years). BPPV developed within 3 months ( $n = 3$ ), between 4 and 12 months ( $n = 1$ ), or between 2 and 6 years ( $n = 1$ ). All BPPV episodes were in the same ear as the VN and affected the posterior canal. Three of the five patients had recurrent (more than three) episodes of BPPV. Three patients presented with BPPV that was difficult to treat (more than three Semont particle repositioning manoeuvres). Of the five patients who developed BPPV, only one had recovered from VN at the time of the episode. No patients showed spontaneous nystagmus. On bedside examination, all the other four patients showed positive head shaking and mastoid vibration tests with some degree of caloric deficit. Two patients presented a positive head impulse test and one a positive head heave sign (Table I). No patient reported sudden hearing loss or Bell's palsy during follow-up.

Long-term clinical and caloric testing results of the whole population are beyond the scope of this short paper and will be reported in another long-term longitudinal follow-up study.

**Table I.** Results of the bedside examination and caloric testing of the five patients who developed secondary BPPV after VN.

<b>Patients</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Spontaneous nystagmus</b>	-	-	-	-	-
<b>Head shaking test</b>	-	+	+	+	+
<b>Head impulse test</b>	-	+	-	-	+
<b>Head heave test</b>	-	-	-	-	+
<b>Vibration test</b>	-	+	+	+	+
<b>Positional nystagmus</b>	+	+	+	+	+
<b>Caloric testing</b>	0	Paralysis	Paresis	Paresis	Paralysis

## **Discussion**

Acute vestibular neuritis is a common cause of peripheral vestibular vertigo and accounts for approximately 8% of patients who present to the neurologic dizziness unit [2]. In our study, the mean age of VN patients with recurrence of the disease or subsequent diagnosis of BPPV was slightly lower than the mean age of the whole examined population (51.2 vs 54.7 years). A limited number of studies are available on the recurrence rate of VN. In one small retrospective study, 3 of 18 patients had recurrent VN in the same ear [1]. This high relapse rate (17%) conflicts with our study's recurrence rate of 2%. Huppert et al. [2], suggested that this may be due to less strict diagnostic criteria for VN. In our long-term followup, we could

identify only one recurrence of VN in the originally affected ear. This result is in part supported by the finding of another long-term follow-up study in which the recurrence rate was estimated at 1.9%, although the recurrence was consistently contralateral [2]. Our low recurrence rate could be due to the fact that we considered only clear-cut recurrences of VN where patients had to meet the original inclusion criteria again.

Molecular biologic studies have presented strong evidence that VN is caused by a reactivation of latent herpes simplex virus type 1 (HSV-1) in the vestibular ganglia [6,7]. Compared with the annual frequency of VN in the normal population of 3.5 per 100 000 [8], the frequency of recurrence is considerably higher (odds ratio OR 118, 95% confidence intervals 20– 710, Fisher exact test,  $p = 0.009$ ). The percentage of ipsilateral relapses for Bell's palsy, which probably also has an HSV-1 etiology, has been reported to be more frequent: 7.1% [9]. These recurrence rates appear to be even higher compared with our findings in VN patients. Recurrence of sudden hearing loss is reported to be rare (0.8%) [10], and is even lower than our results for VN.

In a large study based on a neurotologic survey of the general population, the annual incidence of BPPV in the normal population was 0.6% [11]. In our follow-up, five patients developed a BPPV of the posterior semicircular canal. This rate was higher than expected if the two events had been independent (odds ratio OR 3.5, 95% confidence intervals 1.4–9.2, Fisher exact test,  $p = 0.023$ ).

In the literature, posterior canal BPPV in VN patients (also known as Lindsay-Hemenway syndrome [12]) is thought to be of vascular origin. It has been reported to have higher rates (16.3%) than reported in our study [13]. With a longer follow-up of 9 years, BPPV rate after VN appears to be even higher [1].

All BPPV occurrences arose from the posterior semicircular canal in the same ear as had been affected by VN. This finding supports the conclusions of large retrospective studies where VN represented the inner ear disease that most frequently caused BPPV [14]. It seems that VN could, in some way via direct damage of the macula or nerve deafferentation, cause detachment of otoconia, but leave posterior semicircular canal function intact. This is in agreement with the data that VN generally spares the inferior branch of the vestibular nerve, which provides fibers for the posterior semicircular canal [15].

All but one patient who developed BPPV demonstrated some degree of vestibular dysfunction as determined by bedside examination or caloric abnormalities. The most sensitive tests to elicit unilateral peripheral deficit in BPPV patients were the head shaking test, the mastoid vibration test, and caloric irrigation. All of these tests explore the function of the superior

branch of the vestibular nerve. It is also speculated that the patient who recovered from VN before developing BPPV could have had some degree of subclinical vestibular damage leading to otoconial detachment.

In conclusion, recurrence of VN is a rare event in long-term follow-up. Finally, incidence of BPPV in VN patients represents a quite common outcome. To our knowledge, this study represents the only long-term longitudinal study on recurrence of VN and incidence of secondary BPPV in VN. Larger follow-up studies with strict inclusion criteria are necessary to confirm our results.

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## **Comorbidities of BPPV**

### **BACKGROUND**

VPPB is the most common vestibular disorder with the one-year incidence of 0,6% and lifetime prevalences of about 6,4%. the mean age is 45-65 years, with a marked female preponderance among individuals with vertigo 2:1.

VPPB is caused by dislodged otoconia making its way from the utricle mainly into the posterior semicircular canal (72%), or into the horizontal one (17%) (Caruso e Nuti 2005), where could cause an alteration into the movements of endolymph during head's replacements. More rare are the involvement of the anterior semicircular canal, the multicanalar forms or bilateral. The latest two are easily found in BPPV caused by head trauma. All the other not post traumatic forms of BPPV must be considered like idiopathic forms. There are many factors which could make easier the otoconial move from vestibule to semicircular canal, many hypothesis have been formulated trying to find etiologic factors of BPPV. Have been detected some inner disease like: vestibular Neuritis, Menière's disease, Otosclerosis; or systemic disease like: hypertension, Diabetes, blood (haematic) hyperviscosity, migraine or osteoporosis.

The largest incidence of some of these disease that we have mentioned in female, like migraine and osteoporosis, could explain why female are affected by BPPV more than male.

### **OBJECTIVES**

The aim of our study was to detect co-morbidities between BPPV and recurrences of BPPV (BPPVr), vestibular Neuritis (VN), Menière's disease (MdM), Otosclerosis, Migraine, hypertension and Diabetes (DM).

## **PATIENTS AND METHODS**

We conducted a multicentric study from 1 March to 31 May 2009 organized by ORL department of University of Siena. Have been involved the followed Clinical ORL Departments:

**Tabella 1**

<b>SIENA</b>	
<b>FIRENZE</b>	<b>LIVORNO</b>
<b>PISA</b>	<b>PERUGIA</b>
<b>NAPOLI</b>	<b>MATERA</b>

### **Subjects**

During the related period were diagnosed 285 patients with BPPV; 266 of them were able to be enrolled in our study, the remaining 19 patients were excluded, 16 because of missing data, 13 missing consent to our study. All enrolled patients gave their written informed consent to this multicentric study. All data were anonymised.

Everyone of them received a detailed examination performed by an otolaryngologist specialized in otoneurlogy who has performed an anamnestic valuation following these criteria, with particular attention to: age, sex, period of arising symptoms, other otological disease (OMC, vestibular Neuritis, Menière's disease, Otosclerosis), systemic disease (hypertension, osteoporosis, hyperlipidemia and Diabetes), neurologic disease( Head injury, Migraine).

### **Inclusion Criteria**

Certain diagnosis of BPPV:

- positive response to Dix-Hallpicke maneuvers for the posterior semicircular canal
- positive response to Pagnini-Mc Clure maneuvers for the lateral semicircular canal
- the finding of a paroxysmal positional nystagmus

### **Statistical Methods**

SPSS 15.0 for windows XP has been used for the analyses. T-test, Chi-square di Pearson, Odds ratio has been used to evaluate the data. The value that we obtained have been divided

and compared into BPPV with impairment of CSP and BPPV with impairment of CSL, further more, among sporadic disease (first time) and recurrent disease.

At the end we analysed the associations among BPPV and the diseases that we've pointed up comparing our group with population, to do that we have used ISTAT data about chronic disease 2005 or data from Literature.

## **DISCUSSION**

### **Age**

We observed that the 70,7% of our patients was in a range of age between 45 and 75 years old, with an increased incidences between 55 and 64 (21,1%). The BPPV affected often patients over 75 years old (16,1%) but it was rare in the group down 35 years old (7,1%). No significant data has been found comparing the CSL vs CSP in the different ranges of age.

### **Onset of VPPB (days of arising)**

The mean period between the first symptoms and the diagnosis, done by one of the Clinical ORL Departments involved in our study, was 17 days; 19 days for CSP and 9 days for CSL. There was a significantly higher prevalence ( $p < 0,025$ ). Probably when the semicircular canal affected is the lateral one there is a biggest association with neuro-vegetative symptoms, moreover the CSL is subject to more stimulations daily than the CSP.

### **Head trauma**

We asked in our anamnesis if the patients had head trauma, sometimes (10 days max) before the arising of VPPB. Eight patients had head trauma (3%) with no statistically significant differences among the CSP (6:214) and the CSL (2:52). We didn't find any differences linked with the age or the sex, but in our group the number of patients with head trauma was too small.

### **BPPV Recurrence**

Seventy-eighth (29,3%) patients of our group had a recurrence, but we had no possibility to understand if the recurrence has been involved the same side and/or the same semicircular canal. We didn't find any statistically significant differences between the patients with the first event of BPPV and the BPPVr about (concerning) age, sex, canal impairment, traumatic

etiology, or days of arising symptoms. The last finding is understandable, the patients with BPPVr known that the disease is benign and so they underwent to a specialist after few days. Our data, according with literature, shown that the BPPV has an higher incidence in who already developed an event of BPPV (18-50%) comparing BPPVr vs population. We can say that the possibility to have BPPVr will be higher in the first year after the first diagnosis (event) and will decrease in five years; after this period the risk to have BPPVr is really rare (Brandt et al, 2006).

### **Vestibular Neuritis**

Amongst our patients 6 of them had an anamnesis positive for Vestibular Neuritis (2,3%), everyone had a BPPV with impairment of CSP according with the study of Mandalà et al. (2009). Has not been possible to know the side involved by NV. These patients showed an higher incidence of recurrence ( $p=0,260$ ). The prevalence of NV in the population is about 3,5-4/100.000 (Strupp e Brandt, 2009) but in our group we found value 600 times higher than these ( $OR=577$ ) with a  $p=0,001$ . We can absolutely affirm that NV is a very important risk factor for BPPV, probably for the hypotrophy and denervation.

### **Ménière's disease (Mdm)**

Just 6 of our trial (2,3%) had Mdm; every of them had an impairment of right CSP, but there isn't a statistically significant differences between CSL and CSP ( $p=0,222$ ). Neither the comparing of BPPVr and BPPV were significant( $p=0,827$ ).Has not been easy to compare our trial with the population, because of the differences, in the Literature, about the data regarding prevalences of Mdm. We used the epidemiological study (Radzke et al. 2008) performed by phone interviews with 5000 patients, applying the AAOO criteria of 1995, the prevalence of Mdm in the population is 0,12%. The prevalences in our trial is very significant,  $p<000,1$  and  $OR= 19,208$  almost 20 times higher than the value of Radzke's study. We can say that Mdm is a very important risk factor for the development of BPPV.

### **Otosclerosis**

Two of our patients were affected by otosclerosis (0,8%), one had an involvement of CSL and the other of CSP. Both of them underwent a stapedectomy, the first one bilaterally, the other one from the same side with the VPPB. Both of them have already been affected by a VPPB episode, that could look more frequent in these patients ( $p= 0,28$ ). These data are probably due to the surgery and not to the otosclerosis, because of the trauma on otolithic body during

surgery or because of the prosthesis, if it is too long could stress the vestibular membranes. At the end we can affirm that the stapes surgery can be a risk factor for VPPB.

### **Migraine**

About migraine we didn't find the value that we expected from the comparison with the Literature. On 266 patients just 20 were affected by migraine (7,5%). Our data have been compared with ISTAT data 2005 about population, with no statistical significance ( $p=0,912$ ;  $OR = 0,975$ ). Probably this disagreement was due to the anamnesis. Migraine patients are used to be affected by headache, so they always forgive to refer the physician to the disease. To make Migraine's diagnosis is enough to undergo to few headache attacks in all life (International Headache Society nel 1988).

At the end of our researches we obtained an interesting value. Between the patients affected by migraine the CSP was involved in 12 (5,6%), 8 of them had an impairment of the CSL (15,4%). Comparing our findings is easy to note how in these patients there is a higher involvement of the CSL vs the CSP ( $p= 0,016$ ). Finally we didn't find any association between BPPV and migraine, but we found a significant association between migraine and BPPV of CSL .

### **Hypertension**

67 of our patients had high blood pressure (25,2%). We compared our group with general populations and we noticed a strong association between BPPV and Hypertension ( $p= 0,0001$ ;  $OR= 2,139$ ). In agreement with other AA (von Breven et al., 2008) we assert that high blood pressure can be a risk factor for BPPV, probably for a vascular lesion in the inner ear.

### **Diabetes**

We didn't find any statistically significant association between DM and BPPV ( $OR= 0,829$ ), the same thing we can say about comparing CSL vs CSP and BPPVr and BPPV.

## **CONCLUSIONS**

Many factors have been associated to BPPV like: mature age, female sex, some systemic diseases (hypertension, diabetes, osteoporosis), neurological diseases (migraine, head trauma) and otological diseases (Ménière's disease, Vestibular Neuritis, otosclerosis, chronic otitis media), head surgery and intubation.

In most cases that have been studied by Literature the association between these factors and BPPV is just speculative (Neuhauser e Lempert, 2009; Warninghoff et al., 2009; von Brevern et al. 2006; Cohen et al., 2004).

For that reason we have started our researches, with the aim to investigate which comorbidities and/or risk factors could be associated with BPPV.

We found a link with the mature age, with an increased incidence between 55-64 years and female sex like usually observed in Literature.

The 3% of our patients had BPPV probably caused by head trauma, without significant differences between CSP and CSL.

We observed a 30% of BPPV recurrence in our group, higher than the population. We would like to know if the recurrences involved the same side and the same semicircular canal but has been impossible to do because of the lack of data.

Six of our patients had a medical history of vestibular neuritis and all of them have been affected by a BPPV of CSP. We can't study if BPPV and neuritis involved the same side. The prevalences of neuritis in population is 3,5-4/100.000; in our group we found value 600 times higher, with an association between the two diseases than can make of this one a risk factor of BPPV.

About the MDM 6 patients showed a BPPV, in everyone there were an impairment of the right CSP. Has not been simple to compare our group with the common population because of the disagreement of Literature about the prevalences of this disease. At the end we used, to compare our data, the last and more numerous study that we found (2008 da Radzke et al.). The prevalences of MDM in our group was quite 20 time higher, a very signifiant associations between the two disease.

Two patients were affected by otosclerosis both of them underwent to stapedotomy, one bilaterally, the other one by the side affected by BPPV. Both of them referred a recurrence of BPPV the could look to be very frequent in these patients. We use to think that this data has been caused by the surgery and not by the disease.

About migraine our data dissent from the Literature, but comparing migraine patients with impairment of CSL with the other with impairment of CSP we found a signifiant difference between the two groups, with a higher prevalences of the first one. We can't get a reason for this data.

We found a very strong association with Hypertension but we didn't find any associations with DM, like other study in Literature.

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**Double-blind randomized trial on short-term efficacy of Semont maneuver for treatment of posterior canal benign paroxysmal positional vertigo**

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**KEY WORDS:** Benign paroxysmal positional vertigo, Semont’s liberatory maneuver, evidence-based medicine, double blind randomized trial, vestibular, neuro-otology, semicircular canals.

## **Abstract**

The need for Class I and II studies on the efficacy of Semont's liberatory maneuver (SLM) in the treatment of posterior canal benign paroxysmal positional vertigo (PC-BPPV) motivated the present double-blind randomized trial on the short-term efficacy of SLM. A total of 342 patients with unilateral PC-BPPV were recruited for a multicenter study. Patients were randomly assigned to treatment by SLM (n = 174) or sham treatment (n = 168). Subjects were followed up twice (1 and 24 h) with the Dix–Hallpike maneuver by blinded examiners. At the 1 and 24 h follow-up, 79.3 and 86.8%, respectively, of patients undergoing SLM had recovered from vertigo, compared to none of the patients undergoing the sham maneuver ( $p < 0.0001$ ). Patients who manifested liberatory nystagmus at the end of SLM showed a significantly higher percentage of recovery (87.1 vs. 55.7%;  $p < 0.0001$ ). To the best of our knowledge, this is the first Class I study on the efficacy of SLM. SLM proved highly effective with respect to the sham maneuver ( $p < 0.0001$ ). Liberatory nystagmus was demonstrated to be a useful prognostic factor for the efficacy of treatment. The present Class I study of efficacy of SLM changes the level of recommendation of the maneuver for treating PC-BPPV from level C to level B.

## **INTRODUCTION**

Benign paroxysmal positional vertigo (BPPV) is a labyrinthine disorder caused by dislodged otoconia floating in the semicircular canals (canalolithiasis) or, less frequently, by otoconia attached to the cupula (cupulolithiasis). Because of its anatomical position, the posterior canal (PC) is the canal most frequently involved. The major treatment for BPPV relies on physical maneuvers that enable the otoconia to leave the canal by gravitation and centrifugal inertia. Epley's canalith repositioning procedure (CRP) and Semont's liberatory maneuver (SLM) are the most widely used procedures for treating PC-BPPV. CRP and SLM were first described in 1979 and 1983, respectively, and subsequently simplified; the first became more popular in the United States and the second in Europe [1]. Although both maneuvers are considered highly effective by many experts, the guidelines for treatment of BPPV produced by the American Academy of Neurology [2], the American Academy of Otolaryngology [3] and a recent review [4] concluded that CRP is “an effective and safe treatment that should be offered to patients of all ages” with PC-BPPV (Level A recommendation), while “SLM, based on currently published articles, can only be classified as “possibly effective” (Level C recommendation) since Class I and II studies are missing”.

The need to determine the evidence-based efficacy of SLM, as highlighted by the “BPPV guidelines” produced by the American Academies of Neurology and Otolaryngology [2,3] motivated the present trial. The main aim of the study was to determine the short-term efficacy of SLM by a double-blind randomized trial. The prognostic value of liberatory nystagmus (at the end of SLM) and short-term follow-up (within 1 hour) were also assessed.

## **METHODS**

Three hundred and fortythree patients with unilateral PC-BPPV were recruited for a multicentric study that involved seven otoneurology units in Italy (Firenze, Livorno, Matera, Napoli, Perugia, Pisa, and Siena) from March 2009 to December 2010. PC-BPPV was diagnosed according to the following criteria [3]: a) history of vertigo associated with changes in head position; b) torsional-vertical nystagmus (with the upper pole of the eye beating toward the affected ear) detected with Frenzel glasses or videoculography in the Dix-Hallpike position; c) vertigo associated with the nystagmus elicited; d) latency between completion of the Dix-Hallpike test and the resulting vertigo and nystagmus that increase and resolve within one minute.

Patients with bilateral PC-BPPV, multiple canal atypical positional nystagmus or previously treated with repositioning maneuvers were excluded.

Patients were randomly assigned by a computer generated code to treatment by SLM (n=174) or sham treatment (n=168). Once the pathological side had been identified by the Dix-Hallpike test, SLM was performed with the examiner standing in front of the patient who was seated on one side of the examining table with his/her legs hanging freely. The patient’s head was rotated 45° to the unaffected side, and then in a quick and continuous movement, the patient was moved so as to lie on his pathological side, with the back of the head resting on the table. The patient was kept in this position for two minutes and was then quickly brought up to sitting position and then lowered onto the opposite side, maintaining the head in the same position relative to the shoulders. Care was taken not to exceed 1.5 seconds in executing the 180° swing, in order to elicit sufficient acceleration on the canal to allow the debris to fall into the utricle [5]. At the end of the maneuver, the patient was lying on the shoulder of the unaffected side with the cheekbone and nose in contact with the bed. In this position the investigator checked for liberatory nystagmus (nystagmus with the same direction as that evoked by the Dix-Hallpike test) [6]. The patient was finally brought back to sitting position. The sham manoeuvre consisted of SLM performed for the unaffected side. The

maneuvers were only performed once and patients did not receive any subsequent instructions.

One hour and twenty four hours after SLM or the sham maneuver, outcome was assessed by a second and a third blind investigator who repeated the Dix-Hallpike test without interviewing the patient. Patients responding negatively were considered to have recovered. Patients of both groups, who showed typical PC-BPPV at 24-hour follow-up were treated again by SLM for the affected side.

Patients were instructed to return to the hospital if BPPV symptoms persisted or reoccurred. Follow-ups of patients recruited for the study were recorded up to 2 weeks after treatment. Patients who still manifested PC-BPPV were treated again by SLM.

The study was approved by the local Ethics Committees of all hospitals where the clinical trial was conducted. Informed consent was obtained from all participants. Comparisons between groups were assessed by the Fisher's exact test or t-test, as appropriate, at a significance level of  $p < 0.05$ . Statistical analysis was performed with SPSS software (SPSS, Inc., Chicago, IL, USA).

## **RESULTS**

Clinical and demographic data of the two populations (SLM and sham groups) are shown in Table 1. Groups did not differ in demographic or clinical baseline characteristics, only the affected side showed a prevalence of the right canal in the SLM group despite non statistically significant ( $p = 0.0508$ ). All patients underwent follow-up up to 24 hours after treatment. At the one-hour follow-up, 79.3% of patients who underwent SLM had recovered. Twenty-four hours after treatment, 86.8% of subjects in the SLM group were free of BPPV, whereas none of patients who underwent the sham maneuver recovered ( $p < 0.0001$ ). No statistically significant differences were observed between the one-hour and 24-hour follow-ups in the SLM group ( $p = 0.0859$ ).

In three subjects, positional nystagmus changed into typical lateral canal BPPV after SLM. Patients who manifested liberatory nystagmus after SLM for the affected side showed a significantly higher percentage of recovery at one-hour follow-up (83.8% versus 16.1%;  $p < 0.005$ ), irrespective of whether SLM was performed as first treatment or 24 hours after the sham maneuver (Figure 1). SLM was performed without serious adverse effects in all patients. Side effects of SLM were transient nausea, vomiting and loss of balance, and occurred in 35 subjects.

## **DISCUSSION**

In 1983, Alain Semont presented a new therapeutic technique for PC-BPPV at the NES conference in Leuven; the technique subsequently became very popular in Europe. The physical maneuver “would free the cupola using the addition of the pressure of the endolymph and the inertia of the heavy materials”. The results were quite extraordinary but were not published until some time later [1]. Since then SLM has been simplified and a plausible explanation provided for its peculiar mechanism of action. Despite its widespread adoption by otoneurologists, SLM is only considered “possibly effective”, due to a lack of class I and II studies.

To the best of our knowledge this is the first class I study on the efficacy of SLM in the treatment of PC-BPPV. SLM proved highly effective in the treatment of PC-BPPV compared to the sham maneuver ( $p < 0.0001$ ). As postulated by other authors [7], to minimize the confounding effect of spontaneous remission and highlight the effect of the maneuver, we decided to perform a short-term follow-up. Despite the well-known phenomenon of fatigue that can mimic successful treatment due to dispersion of particles in the canal after repeated positional maneuvers [7], we did not find any statistically significant differences between the 1-hour and the 24-hour follow-up. We confirmed the utility of the so-called “liberatory nystgmus” [6] as a prognostic factor for efficacy of treatment in most cases. Fifteen percent of subjects needed more than one maneuver to treat the PC-BPPV.

A class II study on SLM outcomes showed a significant decrease in vertigo intensity and frequency after treatment [8]. Another class III study obtained cure rate of 94.2% with one maneuver [9], very close to the 86.8% recovery achieved in the present trial. Both these studies confirmed the efficacy of the SLM with respect to the sham group.

Two class I studies on CRP demonstrated a ~ 90% recovery rate of PC-BPPV after a few weeks, which is very close to the present 24 hours recovery rate [7,10]. When comparing the short-term (24 hours) results after one maneuver of either procedure (SLM or CRP), outcomes of SLM (86.8% recovery) were slightly better than those of CRP (80% recovery [7]). Unfortunately, there is currently insufficient data to establish the relative efficacy of SLM and CRP [2].

In conclusion, the present class I study of efficacy of SLM changes the level of recommendation of the method for treating PC-BPPV from level C to level B. As in the case of CRP, another class I or II study will be necessary to establish SLM as an effective and safe treatment recommended for subjects of all ages suffering from PC-BPPV (level A recommendation).

Acknowledgments, Competing interests, Funding: nothing to declare

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## **Double-blind randomized trial on short-term efficacy of Gufoni maneuver for treatment of lateral canal benign paroxysmal positional vertigo**

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**KEY WORDS:** Benign paroxysmal positional vertigo, Gufoni liberatory maneuver, evidence-based medicine, double blind randomized trial, vestibular, neuro-otology, lateral semicircular canals.

## **ABSTRACT**

The need for Class I and II studies on the efficacy of liberatory maneuvers in the treatment of lateral canal benign paroxysmal positional vertigo (LC-BPPV) motivated the present double-blind randomized trial on the short-term efficacy of Gufoni liberatory maneuver (GLM). Seventy two patients with unilateral LC-BPPV were recruited for a multicentric study. Patients were randomly assigned to treatment by GLM (n=37) or sham treatment (n=35). Subjects were followed up twice (1 and 24 h) with Pagnini–McClure maneuver by blinded examiners. At 1 and 24 h follow-up, 75,7% and 83.8%, respectively, of patients undergoing GLM had recovered from vertigo, compared to none of the patients undergoing the sham maneuver ( $p<0.0001$ ).

To the best of our knowledge, this is the first Class I study on the efficacy of GLM. GLM proved highly effective with respect to the sham maneuver ( $p<0.0001$ ). The present Class I study of efficacy of GLM changes the level of recommendation of the maneuver for treating LC-BPPV from level U to level B.

## **INTRODUCTION**

Benign paroxysmal positional vertigo (BPPV) is a labyrinthine disorder caused by dislodged otoconia floating in the semicircular canals (canalolithiasis) or, less frequently, by otoconia attached to the cupula (cupulolithiasis). [1]

Horizontal canal BPPV accounts for 10% to 17% of BPPV, though some reports have been even higher. [2] The Authors describe the typical clinical picture of a BPPV of the LSC, characterised by a bidirectional horizontal geotropic or apogeotropic nystagmus, bipositional in the lateral right and left positions. [3]

The major treatment for BPPV relies on physical maneuvers that enable the otoconia to leave the canal by gravitation and centrifugal inertia.

A large number of maneuvers have been devised for the treatment of LC-VPPB. Variations of the roll maneuver (Lempert maneuver or barbecue roll maneuver) are the most widely published treatments for horizontal canal BPPV. Using this approach, all Class IV study reported remission rates probably of 75% but ranges from approximately 50% to nearly 100%. [2] Another treatment reported as effective is referred to as “forced prolonged positioning”. With this method, the patient lies down laterally to the affected side, and the head is then turned 45 degrees toward the ground and maintained in that position for 12 hours

before the patient is returned to the starting position. Success in treatment, based on only one Class IV studies, ranges from 75% to 90%.

The Gufoni maneuver is another technique that has been reported as effective in treating horizontal canal BPPV. Several studies, all Class IV, have reported success using this maneuver for horizontal canal BPPV for both the geotropic and apogeotropic nystagmus forms.

The need to determine the evidence-based efficacy of Gufoni maneuver as highlighted by the “BPPV guidelines” produced by the American Academies of Neurology and Otolaryngology motivated the present trial [4]. The main aim of the study was to determine the short-term efficacy of GLM by a double-blind randomized trial and short-term follow-up (within 1 hour) were also assessed.

## **METHODS**

52 patients with unilateral LC-BPPV were recruited for a multicentric study that involved seven otoneurology units in Italy (Firenze, Livorno, Matera, Napoli, Perugia, Pisa, and Siena) from march 2009 to December 2010. LC-BPPV was diagnosed according to the following criteria:

- a) history of vertigo associated with changes in head position;
- b) geotropic or apogeotropic nystagmus detected with Frenzel glasses or videoculography by the supine roll test or so-called Pagnini–McClure maneuver;
- c) vertigo associated with the nystagmus elicited;
- d) latency between completion of the supine roll test and the resulting vertigo and nystagmus that increase and resolve within one minute.

Patients with multiple canal atypical positional nystagmus or previously treated with repositioning maneuvers were excluded. Firstly, informed consent was obtained from all participants.

Patients were randomly assigned by a computer generated code to treatment by GLM (n=30) or sham treatment (n=22).

Once the pathological side had been identified by the supine roll-test, GLM was performed with the examiner standing in front of the patient who was seated in centre of examination couch, is briskly brought down to one side (healthy side in geotropic forms, affected side in apogeotropic forms); head is then quickly inclined downwards 45° and waiting 2-3 minutes in this position; finally the patient is returned to the starting position. The sham maneuver consisted of GLM performed for the healthy side. The maneuvers were only performed once

and patients did not receive any post-treatment restrictive instructions. After 1 h and 24 h of GLM or the sham maneuver the patients were examined and the outcome was assessed by a second and a third blinded investigator who repeated the supine roll test without interviewing the patient. Patients responding negatively were considered to have recovered. Patients in both groups who showed typical LC-BPPV at the 1h or 24 h follow-up were treated again by GLM for the affected side. Patients were instructed to return to the hospital if BPPV symptoms persisted or reoccurred. Follow-ups of patients recruited for the study were recorded up to 2 weeks after treatment. Patients who still manifested LC-BPPV were treated again by GLM.

The study was approved by the local Ethics Committees of all hospitals where the clinical trial was conducted. Comparisons between groups were assessed by the Fisher's exact test or t-test, as appropriate, at a significance level of  $p < 0.05$ . Statistical analysis was performed with SPSS software (SPSS, Inc., Chicago, IL, USA).

## RESULTS

**Table 1.** Clinical and demographical characteristics of the GLM and sham groups.

	<b>GUFONI LIBERATORY MANOUVER (n=37)</b>	<b>SHAM MANOUVER (n=35)</b>	<b>P value</b>
Age	60.4±16.3	55.8±15.2	p=0.2244 <sup>+</sup>
Sex (M/F)	13/24	10/25	p=0.6183 <sup>++</sup>
Affected side (R/L)	23/14	21/13	p=0.8105 <sup>++</sup>
Type (Geotropic/Apogeotropic)	27/10	26/9	p=1.000 <sup>++</sup>
Onset of PPV (days)	7.6±8.4	12.1±11.8	p=0.0654 <sup>+</sup>
Previous PPV episode (y/n)	11/26	8/27	p=0.5972 <sup>++</sup>
1 HOUR CONTROL (Absence/presence of positional nystagmus [nystagmus transformation])	28/9[4]	3/32[1]	p<0.0001 <sup>++</sup>
24 HOURS CONTROL (Absence/presence of positional nystagmus [nystagmus transformation])	31/6[1]	4/31[0]	p<0.0001 <sup>++</sup>
1 hour control after GLM in the sham group (Absence/presence of			

positional nystagmus [nystagmus  
transformation]))

/

27/8[0]

/

**Statistical analysis:** <sup>+</sup>T-test; <sup>++</sup>Fisher's exact test.

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**Giovanni Paolo Santoro**

### **Lateral canal BPPV with uncertain side: a new therapeutic procedure**

**Objective:** One of the problems in the management of lateral semicircular canal benign paroxysmal positional vertigo (LC-BPPV) is the difficulty to detect the affected ear using Ewald's second law. In these instances, other findings may provide clues toward determining the affected ear. However in a few cases we can't know the affected side. The purpose of this study is to develop a new therapy for treating all subtypes of LC-BPPV. We called this procedure, that is build on Forced Prolongate Position (FPP), Alternate Forced Position (AFP).

**Study Design:** Prospective study.

**Methods:** Patients with LC-BPPV (n 32) were diagnosed when the supine to the head-lateral test resulted in geotropic (25) or ageotropic (7) bilateral horizontal nystagmus. 5 (15,7%) patients (3 with geotropic nystagmus, 2 with apogeotropic nystagmus) didn't show a prominent affected ear in any test. We treated all patients with a forced position in tree steps changing the side every four hours and starting from a side that we have chosen random.

**Results:** In 29 (90,6%) patients, including the cases with uncertain side, we had complete resolution of symptoms and positional nystagmus after one treatment sessions. In tree cases we had complete resolution after two treatment sessions. Just in two patients had a nystagmus transformation (geotropic lateral canal in posterior canal; apogeotropic lateral canal in geotropic lateral canal).

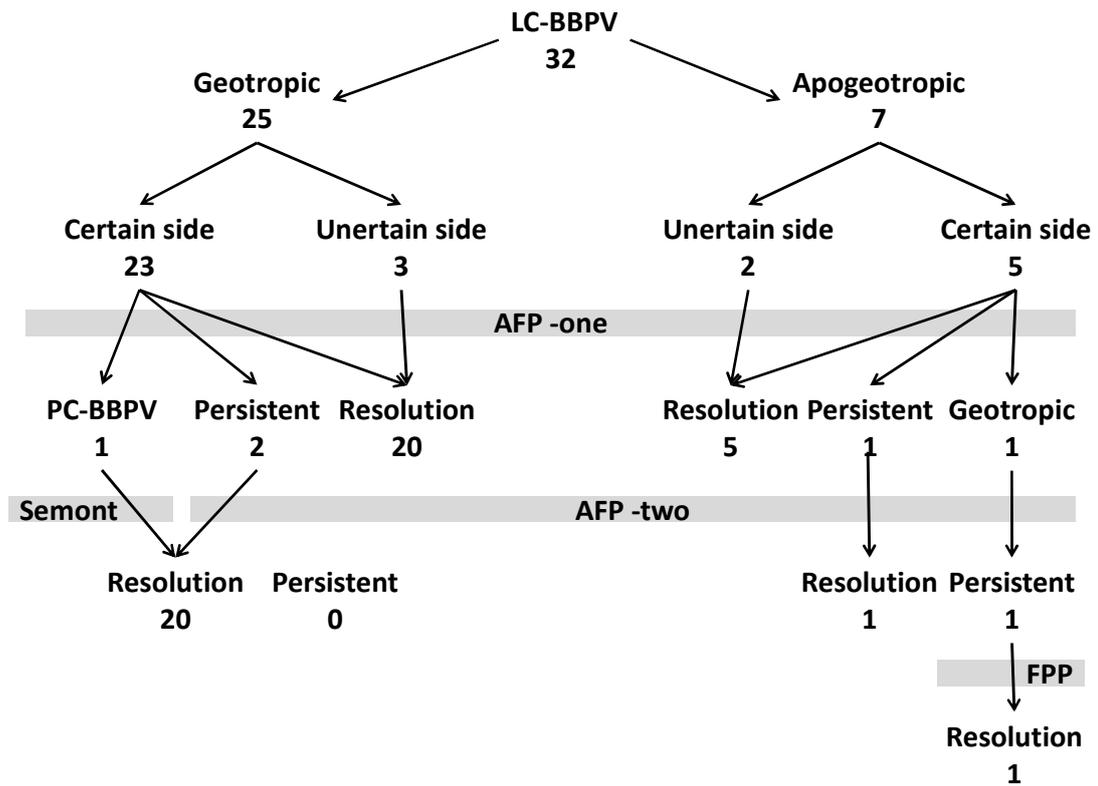
**Conclusions:** The excellent results of our study substantiate our hypothesis that AFP is effective treatment for all subtypes of LC-BPPV, most of all in cases in which there is uncertain side. Furthermore our research prove that to obtain an otoliths migration into the utricle using a forced position, there isn't need more than four ours of forced position. This procedure is easy to do and can be performed by general physicians too, just with medical history.

**Key Words:** Lateral canal, benign paroxysmal positional vertigo, alternated forced position.

**Table 1:** Lateralization of HC-BPPV, based upon the direction and intensity of nystagmus (Ny)

	<b>Geotropic nystagmus</b>	<b>Apogeotropic nystagmus</b>
<b>Intensity of Ny</b>	Stronger side	Weaker side
<b>Subjective sensation</b>	Affected side	Affected side
<b>Pseudospontaneous Ny</b>	Healthy side	Affected side
<b>Stead Supine Positioning Test</b>	Healthy side	Affected side
<b>Lying-down Ny</b>	Healthy side	Affected side
<b>Head-bending Ny</b>	Affected side	Healthy side
<b>Reversal of initial Ny</b>	Possibly occurs Affected side	Uncommon
<b>Null point</b>	Uncommon, laterality is uncertain	Usually present on Affected side
<b>Caloric Hypoexcitability</b>	Affected side	Affected side

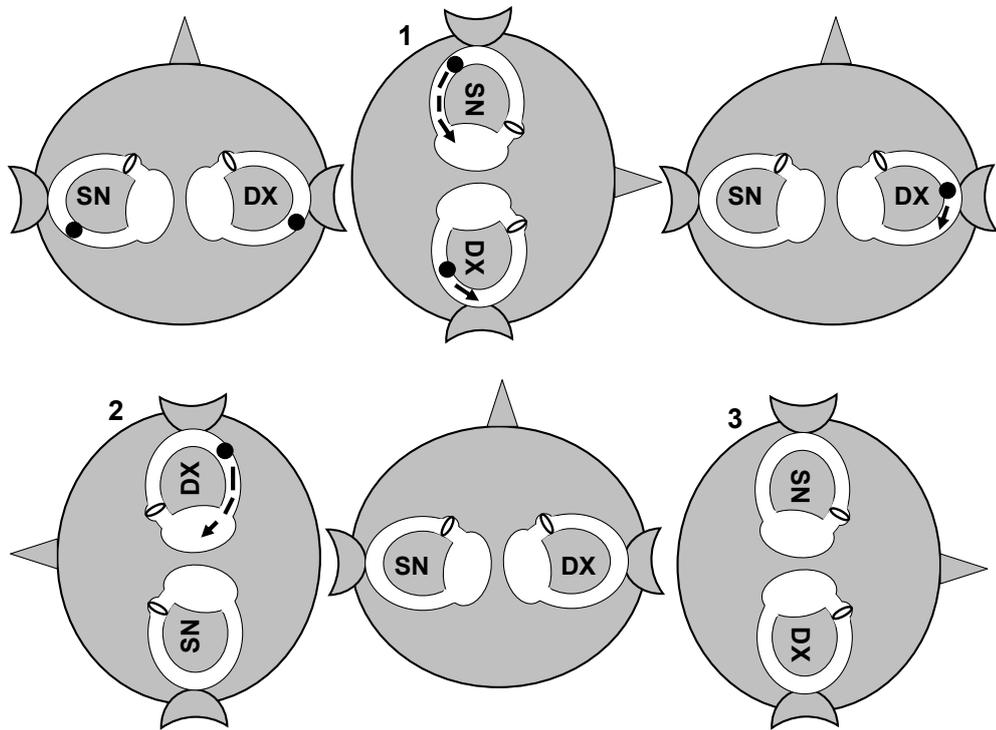
**Figure 1:**



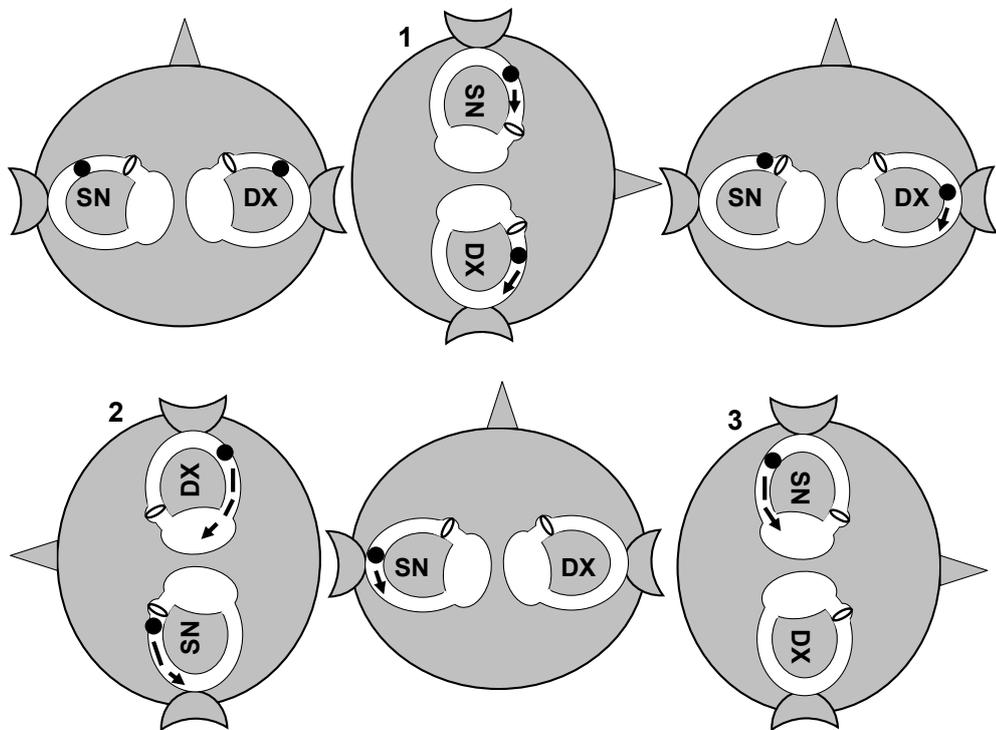
Case	Age	Sex	Type	PPN	SSPT	BLT	Side > Ny	Side > vert.	Rever Ny	SIDE	Side AFP	Result	Side AFP	Result
1	45	M	GEO	/	DX	/	SN	SN	SN	SN	SN	Resolution	SN	Resolution
2	68	F	APO	/	DX	DX	/	/	/	DX	SN	Persistent	SN	Resolution
3	80	F	GEO	DX	/	SN	SN	/	/	SN	DX	Resolution	DX	Resolution
4	73	M	GEO	/	/	DX	DX	SN	/	DX	DX	Resolution	DX	Resolution
5	55	F	GEO	/	SN	/	DX	/	DX	DX	SN	Resolution	DX	Resolution
6	53	M	GEO	DX	/	SN	SN	DX	/	SN	DX	Resolution	DX	Resolution
7	42	F	GEO	/	DX	SN	/	/	/	SN	SN	Resolution	SN	Resolution
8	68	M	APO	SN	SN	SN	DX	/	/	SN	DX	Resolution	DX	Resolution
9	70	M	APO	/	/	/	/	/	/	/	SN	Resolution	SN	Resolution
10	56	F	GEO	/	SN	DX	/	DX	/	DX	DX	Resolution	DX	Resolution
11	59	F	GEO	/	/	/	DX	/	/	DX	DX	Transfor.*	DX	Resolution
12	65	F	GEO	/	/	/	DX	/	DX	DX	SN	Resolution	SN	Resolution
13	36	M	GEO	DX	DX	SN	SN	/	/	SN	SN	Resolution	SN	Resolution
13	67	F	GEO	SN	/	DX	DX	DX	/	DX	DX	Resolution	DX	Resolution
15	29	M	GEO	/	/	/	/	/	/	/	SN	Resolution	SN	Resolution
16	75	M	APO	/	/	/	DX	DX	/	SN	DX	Resolution	DX	Resolution
17	41	F	GEO	DX	DX	SN	SN	/	/	SN	DX	Resolution	DX	Resolution
18	44	M	APO	/	/	/	/	/	/	/	SN	Resolution	SN	Resolution
19	60	M	GEO	/	/	/	DX	/	DX	DX	SN	Resolution	SN	Resolution
20	54	F	GEO	SN	SN	DX	DX	SN	/	DX	DX	Persistent	DX	Resolution
21	32	F	GEO	/	DX	SN	/	/	SN	SN	SN	Resolution	SN	Resolution
22	47	M	GEO	/	/	/	/	/	/	/	DX	Resolution	DX	Resolution
23	75	F	GEO	/	SN	DX	DX	DX	/	DX	DX	Resolution	DX	Resolution
24	38	M	APO	/	SN	SN	/	/	/	SN	SN	Resolution	SN	Resolution
25	41	F	GEO	/	/	DX	DX	DX	DX	DX	SN	Persistent	SN	Resolution
26	56	F	GEO	/	/	/	/	/	/	/	DX	Resolution	DX	Resolution
27	58	F	GEO	SN	SN	DX	DX	DX	/	DX	SN	Resolution	SN	Resolution
28	36	F	GEO	/	SN	DX	DX	DX	/	DX	DX	Resolution	DX	Resolution
29	45	M	APO	/	/	SN	/	/	SN	SN	SN	Transfor.**	SN	Persistent§
30	57	F	GEO	SN	/	/	DX	/	/	DX	DX	Resolution	DX	Resolution
31	83	M	GEO	/	DX	SN	SN	SN	/	SN	SN	Resolution	SN	Resolution
32	52	F	GEO	SN	SN	/	DX	/	/	DX	DX	Resolution	DX	Resolution

Figure 2: AFP as single therapy for LC-BPPV

**Geotropic**



**Apogotropic**



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## **Abstracts of Conference during the PhD program 2009-2012**

**GIOVANNI PAOLO SANTORO, MARIANNA MAFFEI, ROSA MARIA LAGANÀ, ANNALISA PANARESE, WALTER LIVI**

***“A new prosthesis self-crimping for stapes surgery”***

Comunicazione al 96<sup>o</sup> CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Rimini, 13-16 Maggio 2009.

**GIOVANNI PAOLO SANTORO, MARIA CELESTE CHIAPPETTA, ROSA MARIA LAGANÀ, ANNALISA PANARESE, WALTER LIVI**

***“Risultati audiologici a lungo termine della stapidotomia con inversione dei tempi chirurgici”***

Poster per il 96<sup>o</sup> CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Rimini, 13-16 Maggio 2009.

**ROSA MARIA LAGANÀ, GIOVANNI PAOLO SANTORO, MARCO MANDALÀ, DANILE NUTI**

***“Coomorbidità della VPPB”***

Poster per il 97<sup>o</sup> CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Riccione, 19-22 Maggio 2010.

**MATTEO CHIARLONE, MARCO CASTELLI, PAOLO PRINA, GIOVANNI PAOLO SANTORO, SILVIA PONZO, MICHELA LIDIA CARRU, TONI PAZZAIA, CARLA ZAVATERO, MARCO PAGANO.**

***“Tumore a cellule dendritiche interdigitate: segnalazione di due casi di pertinenza ORL”***

Poster per il 97<sup>o</sup> CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Riccione, 19-22 Maggio 2010.

**GIOVANNI PAOLO SANTORO**

***“La chirurgia dell’impianto cocleare”***

Comunicazione al corso: IL TRATTAMENTO CHIRURGICO DELLA SORDITÀ: ATTUALITÀ E PROSPETTIVE.

Siena, 18 Dicembre 2010

MATTEO CHIARLONE, **GIOVANNI PAOLO SANTORO**, MARCO CASTELLI, PAOLO PRINA, SILVIA PONZO, MICHELA LIDIA CARRU, TONI PAZZAIA, CARLA ZAVATERO, MARCO PAGANO.

***“Sarcoma di cellule interdigitate dendritiche: nella diagnosi differenziale delle masse latero-cervicali”***

Poster per il I° CONGRESSO NAZIONALE AIOVV ASSOCIAZIONE ITALIANA DI ONCOLOGIA CERVICO-CEFALICA.

Alba (CN) 7-9 Aprile 2011.

**GIOVANNI PAOLO SANTORO**, FRANCO TRABALZINI, GIAMPAOLO RESTIVO

***“Cochlear implant surgery in CHARGE syndrome”***

Comunicazione al: 10TH EUROPEAN SYMPOSIUM ON PAEDIATRIC COCHLEAR IMPLANTATION.

Atene (Greece), 12-15 Maggio 2011

FRANCO TRABALZINI, GIAMPAOLO RESTIVO, **GIOVANNI PAOLO SANTORO**

***“Cochlear implant in cochlear ossification”***

Comunicazione al: 10TH EUROPEAN SYMPOSIUM ON PAEDIATRIC COCHLEAR IMPLANTATION.

Atene (Greece), 12-15 Maggio 2011

**GIOVANNI PAOLO SANTORO**, LOGLISCI MICHELE, WALTER LIVI

***“Chirurgia endoscopica delle perforazioni epitimpaniche per la prevenzione del colesteatoma”***

Comunicazione per il 98° CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Udine, 25-28 Maggio 2011.

**GIOVANNI PAOLO SANTORO**, ROSA MARIA LAGANÀ

***“Concha bullosa e cefalea rinogena”***

Poster per il 98° CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Udine, 25-28 Maggio 2011.

**GIOVANNI PAOLO SANTORO**

***“VPPB del CSL: nuova strategia terapeutica nei casi di incertezza di lato”***

Poster per il 98° CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Bari, 23-26 Maggio 2012.

GIANDOMENICO MAGGIORE, **GIOVANNI PAOLO SANTORO**, ALESSIO DE MASSIMI, MASSIMO SQUADRELLI SARACENO

***“Un raro caso di granuloma faringeo da dislocazione di spaziatore intersomatico vertebrale”***

Poster per il 98° CONGRESSO NAZIONALE SIO SOCIETÀ ITALIANA DI OTORINOLARINGOLOGIA E CHIRURGIA CERVICO-FACCIALE. Bari, 23-26 Maggio 2012.

## **Publications during the PhD program 2009-2012**

**GIOVANNI PAOLO SANTORO**

***“Risultati audiologici a lungo termine della stapedotomia con inversione dei tempi chirurgici”***

***“Attualità in ORL 2009”***: Supplemento di Argomenti di ACTA Otorhinolaryngologica Italica.

**GIOVANNI PAOLO SANTORO, MARCO MANDALÀ**

***“La VPPB ricorrente”***

Atti del congresso La Vertigine Parossistica Posizionale (Benigna): Stato dell'arte  
GRUPPO ALTA ITALIA DI OTORINOLARINGOIATRIAE CHIRURGIA CERVICO-  
FACCIALE

Siena, 5 Dicembre 2009

**MARCO MANDALÀ, GIOVANNI PAOLO SANTORO, JULIANNE AWERY, DANILE NUTI**

***“Vestibular neuritis: recurrence and incidence of secondary benign paroxysmal positional vertigo”***

Acta Otolaryngologica; Maggio 2010; 130(5):565-7.

**MARCO MANDALÀ, GIOVANNI PAOLO SANTORO, ASPRELLA LIBONATI G, CASANI AP, FARALLI  
M, GIANNONI B, GUFONI M, MARCELLI V, MARCHETTI P, PEPPONI E, VANNUCCHI P, NUTI D**

***“Double-blind randomized trial on short-term efficacy of Semont maneuver for treatment of posterior canal benign paroxysmal positional vertigo”***

JOURNAL OF NEUROLOGY, OCTOBER 2011