

New insights in diagnostic and therapeutic maneuvers for **BPPV**

Citation for published version (APA):

Bhandari, A. (2024). New insights in diagnostic and therapeutic maneuvers for BPPV. [Doctoral Thesis, Maastricht University]. Maastricht University. https://doi.org/10.26481/dis.20240208ab

Document status and date: Published: 01/01/2024

DOI: 10.26481/dis.20240208ab

Document Version: Publisher's PDF, also known as Version of record

Please check the document version of this publication:

 A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.

• The final author version and the galley proof are versions of the publication after peer review.

 The final published version features the final layout of the paper including the volume, issue and page numbers.

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New Insights in Diagnostic and Therapeutic Maneuvers for BPPV

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New Insights in Diagnostic and Therapeutic Maneuvers for BPPV

Thesis

To obtain the degree of Doctor at Maastricht University, on the authority of the Rector Magnificus, Prof. Dr. Pamela Habibovic, according to the decision of the Board of Deans, to defend in public on February 8, 2024

through

Anita Bhandari born on July 5,1968 in USA. Promotor I Prof. Dr. Dr. Raymond van de Berg

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Confirmation

I would like to thank my promoters and supervisors Dr. Raymond van de Berg and Prof. Herman Kingma for encouragement, outstanding support, and supervision to make this PhD thesis complete. Your suggestions and thoughts have made our research richer and clinically more impactful.

I would like to thank Prof. Dr. Michael Strupp for his contribution, guidance, and support in my publications. A special thanks to Rajneesh Bhandari, my husband, my best friend, and significant co-author for always encouraging me and being able to think unconventionally to come up with novel ideas.

My colleagues from NeuroEquilibrium have helped tremendously in developing technology, working with patients, and managing data, with a special mention to Ajit Chaudhary, Rishi Mathur, Alpana Jain and Sujata Arya. Dr. Arpana Goswami has helped in data analysis, biostatistics and putting the thesis documents in order.

My family has always been my grandest cheerleaders, my support system, and my biggest happiness.

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Abbreviations

All abbreviations are mentioned separately in their chapters.

Most used abbreviations are (in alphabetical order)

AC - anterior canal

BPPV - Benign Paroxysmal Positional Vertigo

HC - horizontal canal

PC - posterior canal

scc - semicircular canal

VOR - vestibulo-ocular reflex

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01

General Introduction

Introduction

Defining the problem and aim of this thesis

Benign Paroxysmal Positional Vertigo (BPPV) is one of the most common causes of vertigo and imbalance with an incidence of 10.7 to 64 per 100,000 population and a lifetime prevalence of 2.4 percent (1). It is characterized by paroxysmal episodes of vertigo brought about by positional changes of the head with respect to gravity. Patients usually complain of a sudden onset of spinning that typically lasts for less than a minute on changing head positions. Although the vertigo typically lasts for less than a minute and BPPV is usually a self-limiting condition, patients often experience debilitating symptoms. The impact on qualityof-life of undiagnosed and untreated BPPV may be far from "benign," as patients with BPPV are at increased risk for falls and impairment in the performance of daily activities (2).

In many patients, positional vertigo and nystagmus can be explained as arising from a mechanical disorder caused by the displacement of otolith debris into the semi-circular canals (3). In this thesis we will focus on this type of positional vertigo and will refer to it as equivalent to BPPV. Normally, the semicircular canals detect angular accelerations only. The presence of otoconial debris makes the canal sensitive to gravity. A change of head position relative to the gravity vector will now stimulate the canal, suggesting an angular acceleration. A patient with BPPV will, therefore, experience rotatory vertigo on head movement. The otolith debris may be present as free-floating particles in the canal (4) or attached to the cupula (5). Movement of the otoliths cause stimulation of the canal to generate a specific eye movement called nystagmus. The direction of the nystagmus is aligned with the orientation of the affected canal. The diagnosis of BPPV is based on the character of nystagmus induced by the various diagnostic positional tests (3,6). These positional tests are based on orienting and moving the head in the plane of the canal. This facilitates movement of the debris within the canal under the force of gravity. Thus, there are different positional tests for the three canals. The Dix-Hallpike test (7) and the side-lying diagnostic Sémont maneuver (8) is used to diagnose posterior canal BPPV. The supine roll test is used to diagnose horizontal canal BPPV (9). Anterior canal BPPV is diagnosed by the supine head-hanging test (10). Different otolith positions in the canals generate different characteristic nystagmus patterns (11). The nystagmus allows identification of the affected canal and where the debris is located in the canal.

The treatment of BPPV is based on liberatory maneuvers to reposition the otolith debris in the semicircular canal back into the utricle. Repositioning procedures for BPPV depend primarily on gravity and inertia. Debris movements in the canals have been studied using various models based on the fluid dynamics of BPPV (6,12,13,14,15,16,17).

This thesis presents a simulation model of BPPV to describe the movement of the head, labyrinth, and otoconial debris in 3-dimensional space for practical clinical use. The simulations have been developed using reconstructed temporal bone CT and MRI images from DICOM files with applied principles of fluid dynamics. Simulations have been used to visualize the nystagmus patterns during the diagnostic positional tests and various repositioning maneuvers to demonstrate movement of debris in the canal during head movement in three-dimensions. These studies aim to improve the understanding of BPPV diagnosis and treatment by clinicians along with how the existing protocols can be optimized. The thesis includes the study of various types of BPPV including the nystagmus patterns in VNG videos and SPV graphs. A

BPPV guidance system using head tracking sensors has been described. This guidance system guides the clinician during each step of the repositioning maneuver to ensure correct angulation and plane of head position. This is a useful tool to reduce the variability during performance of repositioning maneuvers and improve treatment outcomes.

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Applied Anatomy and Physiology of the Vestibular System in BPPV

This chapter has been adapted from the e-book BPPV by Anita Bhandari available on www.neuroequilibrium.in

The inner ear vestibular organs are phylogenetically ancient mechanosensory transducers that provide amniotes with the ability to sense movement and orientation of the head relative to gravity (1).

It consists of two specialized types of sensory systems—the semicircular canals and the otolith organs. The semicircular canals are responsive to angular acceleration of the head (2). The three semicircular canals are arranged in three perpendicular planes to each other to detect head movements in all the three planes — yaw, pitch and roll and thus drive the rotational VOR. The two horizontal canals are angulated upwards by 30° from the horizontal plane. Each pair of the vertical canals lie orthogonally to each other (Figure 1).

Each semicircular canal has a dilated ampullary end and a narrow nonampullary end. The anterior and posterior semicircular canals join at the non-ampullary end to form the crus commune. The ampulla houses the crista ampullaris, which acts as a sensory receptor with its hair cells in the form of stereocilia and kinocilia. These bundle of mechanosensitive hair cells extend out of the crista into the cupula (Figure 2). The stereocilia are arranged in rows and contain "tip-links" that connect them like a rubber band so that they all move together. The cupula is a gelatinous fibrillar matrix which forms an impermeable barrier extending across



Figure 1: Spatial orientation of the three semicircular canals

the width of the ampulla (3). This barrier does not allow endolymph to pass through (4). The cupula is equal in density to the surrounding endolymph and does not exert a force on the hair cells when the head is stationary. However, its position is changed by movements of the endolymphatic fluid (5). The cupula is connected to the nerve cells at its base. Conversion of endolymph displacement into neural signals takes place in the ampulla where fluid displacement generated by angular head acceleration deflects the cupula and activates sensory hair cells (1).

Deflection of the cupula, due to the head movement, is converted to electrical impulses which transmit the signals of angular motion to the central nervous system via the vestibular nerve (3).

Each semicircular canal has two arms:

- Long arm connects the cupula on the canal side to the utricle.
- Short arm connects the cupula on the utricular side to the utricle.

Figure 3 shows the long and short arms of the three semicircular canals.







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Figure 3: Long and short arms of each semicircular canal

The orientation of the kinocilium can be of 2 types:

- The kinocilium is placed towards the utricle seen in the horizontal canals (Figure 4)
- The kinocilium is placed away from the utricle seen in the vertical canals (posterior and anterior).

(Figure 5)



Figure 4: Kinocilium and stereocilia placement in horizontal canal



Figure 5: Kinocilium and stereocilia placement in vertical canals

Head movement can induce two kinds of responses (Figure 6):

• Movement of the stereocilia towards the kinocilium - results in depolarisation which generates an excitatory response

• Movement of the stereocilia away from the kinocilium - results in hyperpolarisation, which generates an inhibitory response



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Figure 6 – Hair cell stimulation is determined by the direction of movement of stereocilia with respect to the kinocilia

Endolymph displacement within each canal in response to angular head acceleration is dependent on key morphological features including the radius, length and the cross-sectional area of the canal duct, the cross-sectional area and thickness of the cupula, and the orientation of the canal plane relative to the direction of head rotation (1).

The semi-circular canals work as pairs. Thus, we have three sets of canal pairs which work in concert:

- Right and left horizontal canals
- Right anterior canal and left posterior canal
- Left anterior and right posterior canal

Movement in the plane of the canal pair will deform the cupula. Thus, if one canal is excited, the other will be inhibited due to different hair cell polarity (7). This can be understood with the example of the horizontal canal. The horizontal canal is sensitive to rotation made in the plane of the canal. When the head is turned to the right, the right labyrinth also moves in the right. However, due to the inertia of endolymph mass, the head moves faster than the endolymph within the canal resulting in a comparative lagging behind of the endolymph. Consequently, when there is movement of the head to the right, the endolymph exhibits a relative movement to the left. This causes the cupula to be deflected towards the utricle, in other words, in the ampullopetal direction. The inertia of the endolymph exerts a force on the cupula, causing the stereocilia to bend towards the kinocilium in the right canal. The resultant depolarization is an excitatory response. On the other hand, the stereocilia move away from the kinocilium on the left generating an inhibitory response due to hyperpolarisation (8). This push-pull arrangement operates for all three pairs of canals (Animation 1).



Figure: Head movement with relative movement of fluid within the canal



Animation 1: Hair cells showing the movement and their associated stimulation and inhibition

Each canal is most sensitive to rotation occurring in its own plane. Deflections orthogonal to the excitatory-inhibitory direction of the canal produces little or no response. Nerve activity is increased on the side towards which the head is turning. The net result is a system that provides information about the rotation of the head in any direction. Ampullopetal movement is excitatory for horizontal canals while ampullofugal movement is excitatory for the vertical canals. It appears that the horizontal canal is especially important for movement in 3D space (9) and that this canal primarily controls navigation, whereas the vertical canals are concerned with reflex adjustments in response to movement.

Extraocular muscle coupling with the semi-circular canals

The extraocular muscles are responsible for movement of the eye in different directions (Figure 7)

Applied Anatomy and Physiology of the Vestibular System in BPPV



Figure 7 – Extraocular muscles and their action

Each semi-circular canal is coupled with extraocular muscles through the vestibular afferent nerves that activates one ipsilateral and one contralateral extraocular muscle. Table 1 lists the connections existing between the semi-circular canals and the eye muscles (10).

Canalv	Excited Muscles		Inhibited Muscles	
	Ipsilateral	Contralateral	Ipsilateral	Contralateral
Posterior Canal	Superior Oblique	Inferior Rectus	Inferior Oblique	Superior Rectus
Horizontal Canal	Medial Rectus	Lateral Rectus	Lateral Rectus	Medial Rectus
Anterior Canal	Superior Rectus	Inferior Oblique	Inferior Rectus	Superior Oblique

Table 1 – Connections of semicircular canals with extraocular muscles

Ewald's laws

Patients with BPPV exhibit different patterns of nystagmus depending on the canal affected and the position of the otoconial debris in the canal. The generated nystagmus follows the three Ewald's laws (11). BPPV follows the principles of physics and the fluid dynamics. Ewald's laws help to understand the excitation or inhibition of the canals. This depends on the direction of the endolymph flow occurring due to the head movement. The hair cells are directionally polarized, and the endolymph flow causes deflection of the stereocilia. Deflection of the stereocilia towards or away from the kinocilium determines whether the canal will exhibit excitatory or inhibitory response. In the horizontal canal, the kinocilium is present on the utricular side of the stereocilia whereas in the vertical canals (posterior and anterior canals), the kinocilium is on the canal side of the stereocilia (12). Thus, ampullopetal movement is excitatory for the horizontal canals and ampullofugal movement is excitatory for the vertical canals.

1. Ewald's first law states that eye movements occur in the plane of the canal being stimulated.

2. Ewald's second law states that excitation of any canal creates a greater response than inhibition.

3. Ewald's third law describes the direction of polarization of the hair cells and states that ampullopetal flow creates a stronger response in the horizontal canal, and ampullofugal flow creates a stronger response in the anterior and posterior canals.

Maximum endolymphatic flow of the canal is seen to occur in its plane. This can explain Ewald's first law as each semicircular canal is coupled with the extraocular muscles explained above that help to detect the affected canal.

Ewald's second law states that the excitatory response is always stronger than the inhibitory response. This is due to the discharge properties of

the vestibular nerve. The resting level of the nerve discharge is between 70 to 100 Hz. This value can be increased up to 500 Hz but cannot be decreased below zero (13). Thus, excitation can result in much higher change in discharge compared to base line activity.

Ewald's third law is related to the orientation of the vestibular hair cells. In 1954, with the help of electron microscope, Wersall (14) described the morphological polarization of kinocilia on the vestibular sensors with the help of an electron microscope. Different arrangement of the hair cells with respect to the utricle is responsible for different patterns of excitation and inhibition of the horizontal and vertical canals (15).

Figure 8 shows the Vestibulo-ocular reflex pathway. This reflex allows the object of interest to remain focussed on the fovea during head movement. Action potentials transmitted to the CNS from the canals encode both the direction and the time course of angular head movements. Directional coding arises from the nearly orthogonal orientation of the canals, which maximizes sensitivity of each canal to a specific direction of head rotation, thereby decomposing three-dimensional (3D) head rotations into three vector components, one transmitted by each individual nerve branch innervating each crista. This vector decomposition is largely preserved in central vestibulo-ocular reflex (VOR) pathways to directly couple specific canals to specific ocular-motor outputs (Figure 8).

Sherrington's law of reciprocal innervation states that for every neural activation of a muscle, there is a corresponding inhibition of the opposing muscle (16). Thus, movements of the" "eyes due to vestibular stimulation are predictable, and the eye movement refers to the particular canal, which is excited or inhibited.

Both the co-planar semicircular canals give a symmetrical output to the vestibular nucleus (9,17). A pathology causing reduction in the signal output from one of the coplanar canals results in asymmetrical vestibular output which is perceived by the CNS as rotation. The eyes move in an

attempt to compensate for this perception of rotation. The movement of the eyes is limited by the elastic forces of the orbit and extraocular muscles. The slow vestibular-driven movement of the eyes is followed by a fast central-driven corrective movement by the cerebellum. This leads to a jerky rhythmic eye movement called nystagmus. The slow phase of the nystagmus is caused by a functional deficit of the labyrinth on the same side. However, as the fast movement is more dramatic and noticeable, by convention, nystagmus has been labelled according to the fast phase.

The velocity of the vestibular induced eye movements is called slow phase velocity (SPV). SPV (measured in degrees per second) is the most useful measurement for quantifying the intensity of nystagmus (18).





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03

Development of a 3D Simulation of the Vestibular Labyrinth

Introduction

BPPV is caused by displacement of otolith crystals from the utricle into one or more of the semicircular canals. The displaced crystals cause the affected semicircular canal to become sensitive to gravity when changing head position. Treatment of BPPV is aimed at repositioning the displaced crystals back into the utricle. The inner ear has been described extensively in literature as two-dimensional depictions (1,2,3). However, a practical shortcoming of two-dimensional figures is that it may be difficult for the clinician to understand the orientation of the labyrinth in different head positions in the three-dimensional space. Some three dimensional figures of the inner ear are available (4,5). Many of these 3-D figures do not allow visualization of the orientation of the labyrinth in different head positions. It has been noted that Illustrations offered by the authors of new maneuvers often bear little relation to true anatomy of the membranous labyrinth (6). Clarity in scientific communication around BPPV has been compromised because of the absence of a reference model for labyrinthine anatomy (7). There are a few simulation models described for BPPV, which allow the crystals to be placed in different positions in the ear and show the movement of the crystals linked to head movement (6,7,8).

To improve these simulation models, this chapter describes linking a virtual humanoid with a 3-D labyrinth to create a comprehensive simulation model of BPPV. This allows demonstration of the head and body position at each step of the maneuver, and also allows visualization of the three dimensional labyrinth with movement of the otolith crystals under the influence of gravity.

Methods

Creation of the simulation model included the following steps:

- 1. Anatomical reconstruction of the labyrinth, based on DICOM Data
- 2. Aligning the labyrinth within a virtual head
- 3. Creating a humanoid that can be placed into various positions
- 4. Visualizing relevant components of the labyrinth

5. Simulating crystal movements inside the semi-circular canals (under the effect of gravity)

6. Simulating BPPV maneuvers

Step 1: Anatomical reconstruction of the labyrinth, based on DICOM Data

a. The first step involved acquiring DICOM files of CT scans of the temporal bone of a healthy subject. The DICOM files contained anatomical details, including orientation, dimensions, and angulation of the semi-circular canals. Literature on labyrinthine anatomy shows that the orientation of the bony canals closely match orientation of the membranous canals: the two differed by only $3.48 \pm 1.89^{\circ}(9)$.

b. The next step involved using the software "3D Slicer (Slicer Community, Cambridge, USA)" to extract a 3D model of the inner ear from the DICOM files.

c. DICOM files were extracted from the 3D Slicer software and exported to Blender Software (Blender Foundation, Amsterdam, Netherlands) for further processing.

d. The Imported 3D files were smoothened in Blender. While preserving the external canal geometry, shape, and dimensions, the inner ear canals were created to allow the movement of crystals within the canals.

Development of a 3D Simulation of the Vestibular Labyrinth



Figure 1: Extraction of anatomical details of the semi-circular canals from DICOM files of the CT scan of the temporal bone

Step 2: Aligning the labyrinth within a virtual head

a. The placement of the inner ear within a virtual human head was determined after comparing DICOM orientation with that in literature [Figure 2a and 2b] (9,10,11,12).

b. The 3D Inner Ear was scaled, positioned, and oriented within a virtual human head by juxtaposing it against the DICOM views. Figures 2c and 2d show the orientation of the labyrinth in DICOM data.



a. Side View of Inner ear inside the human head [7]



b. Top View of Inner ear inside the human head [7]



c. Orientation of the labyrinth In DICOM Data (Top View)

d. Orientation of the labyrinth in DICOM Data (Front View)

Figure 2: Placement of the labyrinth in the virtual humanoid head and establishment of orientation in three dimensions

Step 3: Creating a humanoid that can be placed into various positions

a. A humanoid was created using Autodesk Maya (Autodesk, California, US). The humanoid is able to move into the desired positions of the maneuvers (Figure 3).

b. A spherical crystal was animated in the labyrinth to reflect the otoconial debris. Its movement was based on the laws of gravity in the virtual environment (see step 5).



a. Sitting position





Figure 3: Two examples of positions of the humanoid, used in simulations of BPPV maneuvers

Step 4: Visualizing relevant components of the labyrinth

a. In the detailed depiction of the labyrinth, specific elements were marked, using a distinct colour palette to highlight and distinguish between different components.

b. The cupula was marked in green (Figure 4), the affected semicircular canal in transparent grey, non-affected semi-circular canals in translucent grey and the crystal was depicted in yellow (Figure 4).

Legend: Grey = semicircular canal; green = cupula; yellow = BPPV crystal



Figure 4: The labyrinth, as depicted in the simulation model

Step 5: Simulating crystal movements inside the semi-circular canals (under the effect of gravity)

a. A crystal was positioned inside the affected semi-circular canal (Figure 4). The movements of the crystal simulated the movements of the otolith debris.

b. The crystal was programmed to be affected by gravity within the Unity 3D Engine.



a. Character rotational angles causing crystal movement Figure 5: Unity 3D Game Engine Interface For Simulation Of Crystal Movement

Step 6: Simulating BPPV maneuvers

a. The Humanoid was animated in Autodesk Maya. The following maneuvers were animated with the humanoid:

- Epley Maneuver (Figure.5)
- Semont's Plus Maneuver
- Zuma Maneuver
- Appiani Maneuver

- Semont Maneuver
- Roll Maneuver (270° and 360°)
- Gufoni Maneuver
- Yacovino Maneuver
- Modified Yacovino Maneuver

b. Simulations of the humanoid included combined rotational values for each parent axis of the head, neck, and hips, as an actual human would experience while performing any maneuver. For example, Figure 5b shows a 90-degree head turn while maintaining a 30-degree downward tilt of the neck, as shown in Figure 5a.

c. Real time orthographic views were made from different angles, to understand the movement of the crystal within the canal upon each step of the animation.

d. After each step, additional time was included to allow the crystal to reach a resting position, before proceeding with the next step.

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Chapter-3









b. Head 90 degrees towards right

c. Head facing down

d. Crystal has moved out of canal



Software and Services

The Unity 3D Game Engine (Unity Technologies, San Francisco, US) was used to create a detailed and interactive virtual environment. This software was chosen because of its advanced physics engine and scripting capabilities, allowing for a realistic and dynamic simulation, closely resembling real-world conditions.

Limitations of the Simulations

While the simulations could provide valuable insights, it is essential to recognize their limitations. One such limitation is the potential variability in the actual orientation of the canals among individual patients. Although the simulations were based on scientific literature (9,10,11,12,13,14) and DICOM files of a healthy subject, it is crucial to acknowledge that individual variations may exist. These differences could impact the positioning and orientation of the canals, resulting in deviations from the simulation's representation.

Another limitation of the simulations is their focus on canalithiasis, a condition where crystals in the inner ear are free-floating withing into the canal. This is similar to the limitations of other previously described simulation models (6,7,8). Cupulolithiasis, a condition in which the otolith crystals adhere to the cupula, has distinct differences in the underlying mechanics. Thus, while informative and valuable for understanding canalithiasis, the simulations do not provide insights into the mechanisms and otolith/cupula movement associated with cupulolithiasis.

Lastly, the simulations do not fully account for the fluid dynamics within the inner ear canals, nor do they consider the impact of factors such as particle size, the number of particles, and the interactions between particles and the canal walls. Fluid dynamics can influence the movement and behavior of particles within the canals, and a comprehensive understanding of these interactions would require a more in-depth analysis of fluid mechanics. Additionally, the size and number of particles, as well as their interactions with each other and the canal walls, can have an impact on their movement and behavior. The current simulations do not fully incorporate these variables, which may limit their applicability to certain scenarios and conditions.

Future

The simulations enable visualization of the spatial relationships between various components in BPPV: head position, structure of the labyrinth, and the location of otoconial debris. Therefore, this tool can be used to optimize existing diagnostic and treatment modalities. It could be a valuable adjunct to formulate and test new treatment options. The 3D simulation can be used for training, allowing clinicians to practice
procedures in a risk-free environment before performing them on actual patients. In the future, these simulations could be integrated into diagnostic tools or therapeutic applications, such as virtual reality-based rehabilitation programs for patients with vestibular disorders. This could provide a customised approach to therapy, potentially improving outcomes for individuals with these conditions (15).

In conclusion, these simulations can provide a valuable and accurate representation of many aspects of the inner ear, but it remains essential to acknowledge their limitations to better understand their scope and applicability.

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BPPV Simulation: a powerful tool to understand and optimize the diagnostics and treatment of all possible variants of BPPV

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Frontiers in Neurology. 2021;12 https://doi.org/10.3389/fneur.2021.632286

1. Introduction

Benign Paroxysmal Positional Vertigo (BPPV) is amongst the most common causes of vertigo. It is a mechanical disorder of the inner ear caused by the displacement of calcium carbonate particles from the utricle into the semicircular canals (1).

Normally, semicircular canals detect angular accelerations only. The introduction of otoconial debris in the canals makes the canals sensitive to gravity. A change of head position relative to the gravity vector will now stimulate the canal, suggesting an angular acceleration. A patient with BPPV will, therefore, experience rotatory vertigo by head tilts.

Stimulation of the canals by the movement of the otoliths in it, freefloating in the canals or attached to the cupula, generates a specific eye movement called nystagmus. The direction of the nystagmus is aligned with the orientation of the canals affected. Because the canals are oriented in different mutual orthogonal planes, this nystagmus direction allows us to identify which canal is affected and where the debris is located in the canal. The different otolith positions in the canals generate different characteristic nystagmus patterns.

The treatment of BPPV is based on the detection of these characteristic nystagmus patterns to decide the appropriate maneuver required to reposition the otolith debris back into the utricle. The precise debris movements in the canals have been studied and clarified by physics using various models based on the fluid dynamics of BPPV (2,3,4,5,6,7,8). These studies form the basis for our current understanding of the latency, direction, reversal, and fatiguability of the nystagmus as a function of time, the size and number of otoconial particles.

Repositioning procedures for BPPV depend primarily on gravity and inertia. For a successful repositioning maneuver, correct orientation, and angulation of the semicircular canals during the maneuver play a crucial role. Our endeavour in this article is to present a simulation model of BPPV to describe the movement of the head, labyrinth, and otoconial debris in 3-dimensional space for practical clinical use. The simulation software designed by NeuroEquilibrium Diagnostic Systems



Figure 1: Orientation of the three semicircular canals

gives a three-dimensional visualization of the semicircular canals. It simulates the movement of the otoconial particles in the canals due to the head movements executed for diagnostics and treatment. In our opinion, these simulations make it possible not only to understand but also to optimize the various liberation maneuvers.

2. Methodology

In the simulation, the inner ear's 3D morphology was based on reconstructed MRI images of the temporal bone. DICOM files of MRI images were used to extract the 3D inner ear. The three semicircular canals and their orientation planes were determined. Angles were taken to quantify the spatial orientation of labyrinthine structures in relation to each other and in relation to aspects of the cranium (9). A thin tube was inserted at the center of each canal. A crystal resembling otoconial debris was put inside these canals while considering the particle drag (friction caused by the fluid on the object immersed in it) and the gravity acting on the crystal. These parameters helped to study the otoconial movement during the maneuver. The simulation was created on Unity 3D Game engine software. The software allowed us to place the particle in more than one canal at the same time. A humanoid was animated within Autodesk Maya with precise angles for each step of different maneuvers. The head was linked to the semicircular canals such that when the head moves, the associated canals are stimulated. As the humanoid animates into various positions, the crystal within its inner ear moves because of gravity.

Our goal was to study the effect of gravity on these particles, causing them to move towards the lowest dependent position when the head is moved at different angles while performing the maneuver. Different simulations were developed to understand these alterations in detail. This paper has described the simulator for different variations of the Semont and Yacovino maneuver.

Type of BPPV		Therapeutic Maneuver
PC - BPPV	Long arm Canalithiasis	Epley / Semont
	Short arm Canalithiasis	Brisk Epley / Brisk Semont / Side lying position with vibrator
	Non-ampullary end Canalithiasis	Yacovino / QLR
	Canal side Cupulolithiasis	Semont
	Utricular side Cupulolithiasis	QLR from opposite side
HC - BPPV	Canalithiasis	Barbecue / Gufoni
	Cupulolithiasis	Barbecue / Modified Gufoni/Zuma
AC - BPPV	Canalithiasis / Cupulolithiasis	Yacovino

Table 1: Types of BPPV and therapeutic maneuvers (PC - BPPV – Posterior canal BPPV, HC - BPPV – Horizontal canal BPPV, AC - BPPV – Anterior canal BPPV, QLR – Quick liberatory rotation)

3. Maneuvers

3.1. Variations of Semont's Maneuver

Semont's maneuver is used to treat posterior canal Canalolithiasis and Cupulolithiasis (Refer to table 1). Here, we have considered four variants to understand which one of them can deliver the best results. The first simulation is of the classic Semont's liberatory maneuver for a right posterior BPPV. The steps followed are described below –

- 1. The patient is made to sit on the bed with legs hanging down.
- 2. The patient's head is turned to the healthy left side by 45°.

3. The patient is then moved to the right side-lying position with the head pointing upwards.

4. The patient is now rapidly taken to the opposite side-lying position by swinging the body 180 degrees.

5. Finally, the patient is brought upright, and after that, the head is turned to the neutral position.

At step 3, the debris can be seen moving away from the ampulla towards the lowest point of the canal due to gravity acting on it. In step 4, the otolithic debris moves towards the common crus and is replaced into the utricle.

So, the simulator proves that the technique is useful for treating this type of BPPV, but it is important to swing the patient rapidly from the right to the left side (Simulation 1).



Simulation 1 - Semont's Maneuver (scan to view)

If this acceleration is too low, the particle fails to move away from the ampulla. Simulation 2 shows that when step 2 is not done with sufficient high acceleration, the clot falls back into the ampullary arm.



Simulation 2 - Semont's Maneuver with slow acceleration (scan to view)

Obrist et al. (10) described Semont's Plus maneuver. In this modification, when the patient is brought to the side-lying position in Step 2, the head angulation is increased from 90 to 120 degrees. This brings the posterior canal to a position where gravity can act more effectively on the particle (Simulation 3). This makes the modified maneuver more efficient than the classic Semont's liberatory maneuver. It was also seen that the maneuver works well even if the speed of the maneuver is decreased, unlike the previous variant.



Simulation 3 – Semont's Plus maneuver (scan to view)

The fourth variant shows what happens when the angulation is reduced on bringing the patient to the side-lying position. This is done by placing a pillow under the head (Simulation 4). This decreases the head angulation causing the otoconial particle to fall back into the canal. This emphasizes that correct head angulation is very important for the maneuver to reposition the particle back into the utricle.



Simulation 4 – Semont's maneuver with reduced head angulation (scan to view)

1.1. Variations of Yacovino Maneuver

Yacovino maneuver is used to treat BPPV involving anterior semicircular canal, or when the debris is present in the common crus of the posterior semicircular canal. The maneuver consists of 4 steps –

1. The patient is asked to sit with the head facing forward.

2. The patient's head is brought to the head hanging position, 30° below the horizontal.

3. The patient's head is brought quickly forward to the "chin to chest" position while still in the supine position.

4. The patient is brought back to the sitting position.

Simulation 5 explains how the maneuver works for anterior canal BPPV at each step.

In Step 2, when the patient is brought to the head hanging position, the otoconial debris begins to move in the direction away from the ampulla.

Step 3 - Gravity facilitates the particle to move towards the common crus.

Step 4 - Particle falls back into the utricle.

This maneuver is widely accepted, but when we tried the maneuver in the simulator, we found that it has a high chance of canal switch with the particle entering into the posterior canal while treating the anterior canal BPPV.



Simulation 5 - Yacovino maneuver (scan to view)

In a variant of the described Yacovino maneuver, the patient is brought from the head hanging position to the sitting and kept there for 20 seconds. Finally, the neck is flexed forward after 20 seconds (Simulation 6). This demonstrates a better way of repositioning the particle back into the utricle than the classic Yacovino maneuver with a lesser chance of particle entering into the posterior canal.



Simulation 6 - Yacovino maneuver with head brought straight up (scan to view)

In the third simulation, when the patient is brought to the sitting position from the deep head hanging one, the neck is bent immediately (Simulation 7). We can see that due to this, the particle fails to move towards the common crus and instead falls back towards the ampulla.



Simulation 7 - Failed Yacovino Maneuver (scan to view)

2. Results

The model allowed a visual simulation of the semicircular canals. The dependent portion of the canal during the maneuvers causing head movement can be visualized clearly. This helps to see the otoconial particle moving in the canal during the maneuvers. The whole simulation was created with an aim to understand the dynamics of the otoconial debris with respect to the position of the head.

3. Discussion

The simulator is able to change the camera angulation that makes the

three-dimensional spatial movement of the head, semicircular canals, and the otoconial debris easier to understand. The user can define the angulation at each step of the maneuver and have a three-dimensional visualization of the canal and the otoconial movement. The simulation developed allows alteration of various parameters like the angulation of the head, the initial position of the otoconial debris in the canal, size and the number of these particles, fluid dynamics of endolymph, and the time of each step of the maneuver. The simulator helps to understand the otoconial movement with respect to the movement of the head. This helps us to understand the optimum plane and angulation required to get the best results. It also helps to understand why the maneuver is ineffective when these planes and angles are not achieved. The mechanism of action of different maneuvers for each type of BPPV could be evaluated. Multi-canal BPPV occurs when there are clots in more than one canal. This can be studied well using this simulator. Canal switch may be seen during or after BPPV repositioning. Using this simulator, one can understand the different mechanics of the fluid and the canal and thereby can avoid canal switch. In addition, this can also be used as a tool to devise and test the efficacy of new maneuvers.

4. Conclusion

A simulator based on the reconstructed human MRI images works as a guidance system during the maneuvers of BPPV. It helps to understand and observe what actually happens when the head moves. It provides a better understanding of what happens on incorrect angulations while performing the maneuver, which can complicate the treatment (e.g., Canal switch). It can be used as a learning and a teaching tool for medical students and practitioners to understand the behaviour of the particle present in the canal in relation to head movement. The highquality 3D visualization of the canal linked to head movement helps to understand the importance of each step of the therapeutic maneuver. It also highlights the important head movements that bring the canals at an angle at which the gravity can act on the particle and remove it from the canal. Correct head angulation is the key to a successful maneuver. Thus, it can provide a thorough explanation for the maneuvers done incorrectly and eliminate the incorrect and unnecessary steps of the maneuver. Multi-canal BPPV is a complicated variant of BPPV as it affects more than one canal of the same or different ears. It is difficult to understand which canal needs to be treated first and what direction the particle moves when one of the affected canals is being treated. For example, if the otoconial debris is present in both the posterior and horizontal canal of the same side, Epley's maneuver will obviously remove the particle from the posterior canal. However, the simulator

will also show what happens to the particle present in the horizontal canal due to the maneuver being performed. It can also provide a visual explanation for the need of specific maneuvers for each type of BPPV and why Gufoni maneuver can treat BPPV of the horizontal canal but not the posterior canal BPPV. Due to the increased prevalence of the disorder, many new therapeutic maneuvers have been tried to treat its variants. The simulator can test and compare the efficacy of these maneuvers.

Currently, the major limitation of this simulator is that it does not entirely represent the population as the orientation of the semicircular canals vary from patient to patient. Our study is based on the orientation obtained from the reconstructed MRI images. We are fully aware that the natural variations in the orientation and morphology have a substantial impact on the validity of the extrapolation to the individual patient.

However, we experienced that simulators are an effective way to understand all the types of BPPV and their therapeutic maneuvers. This tool provides insights that can lead to a more accurate diagnosis and treatment of BPPV.

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05

Three-dimensional Simulations of Six Treatment Maneuvers of Horizontal Canal BPPV Canalithiasis: Evaluating theoretical efficacy of BPPV maneuvers

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Eur J Neurol. 2021;28(12) doi: 10.1111/ene.15044

Abbreviations:

BPPV: Benign Paroxysmal Positional Vertigo hc- horizontal canal ca: canalithiasis scc: semicircular canal

Introduction

BPPV is one of the most common causes of vertigo. This mechanical inner ear disorder affects posterior canal most commonly followed by horizontal canal. Several different maneuvers have been elaborated over two decades for the treatment of horizontal canal BPPV canalithiasis (hc-BPPV-ca) (1). The most commonly used liberatory maneuvers include the roll maneuver (2), the Gufoni maneuver (3), forced prolonged position (4), and the Zuma maneuvers (5). In canalithiasis, the free-floating otoconial debris move due to gravitational and, in some of the maneuvers, also inertial forces causing cupular deflection during head movement. Based on the orientation of the canal during these maneuvers and the underlying biomechanics, each maneuver theoretically has its advantages and disadvantages, and their efficacy has been compared in studies (6,7,8). Even the combination of two maneuvers has been recommended, e.g., performing the roll maneuver in the clinic and subsequently the forced prolonged positioning as a home exercise (9,10). However, as several maneuvers have been described and recommended, one might infer that not all of them work perfectly or that one might be superior to another (10,11).

To clarify the precise mechanism of the different treatment maneuvers for hc-BPPV-ca, the debris movement of these maneuvers in 3D was simulated, based on a software we recently developed (12,13); in the roll maneuver the effect of orientation of the horizontal canal relative to gravity was also evaluated. Further, the impact of several possible otolith locations within the horizontal canal (Fig 1) was also examined. The ampullary and non-ampullary arms of the horizontal canal are illustrated in Fig 2.



Figure 1. Different otolith debris positions in horizontal canal BPPV. A) Canalithiasis non-ampullary arm, B) Canalithiasis in the ampullary arm, C) Cupulolithiasis on the canal side, D) Cupulolithiasis on the utricle side, E) Canalithiasis in the short arm (6)



Figure 2. Anatomy of horizontal canal showing ampullary arm and non-ampullary arm

Many two-dimensional illustrations are already available to help the clinician in understanding the initial and final location of the debris at each step of a liberatory maneuver (6,14,15). However, 2D images are limited because they demonstrate the findings only from one angle. This means that there is a need for a simulation that can give a clearer picture of the movement of the debris during each step of the maneuver and facilitate visualization from different angles (12,13). It is important to note that we did not perform simple animations, but rather true simulation of the debris movement based on the biophysics of BPPV. The resultant simulation depends, among other things, on basic assumptions regarding the debris size and distribution, the endolymph viscosity, and the canal geometry.

Methodology

A 3D model of the inner ear based on reconstructed MRI images of the temporal bone was used for the orientation of the semicircular canals. The 3D image of the inner ear was extracted from DICOM files of MRI images. The orientation of the canals in the head and the angles between the canals were in accordance with the various studies reported (16,17,18). The simulation was created on Unity 3D software. A humanoid was animated within Autodesk Maya with precise angulations for the maneuvers. The head of the humanoid was linked to the semicircular canal in such a way that any head movement causes reciprocal movement of the canals. A thin tube was inserted into the center of each canal. Otoconial debris in the form of a crystal was put inside the canal. The diameter of the tube was 1.5 mm and the crystal size used was 0.7 mm. 35N linear drag and 0.05 angular drag were applied to the fluid. The time taken for the particle to move at each step of the maneuver was accelerated in all simulations presented here to make it more user-friendly.

We are aware that our simulations and underlying physics model cannot precisely represent the in vivo movement of the otoconia in the SCC of an individual patient because there are many variables among patients. For example, the pressure difference on both sides of the cupula of the crista ampularis due to the debris movement is related to the exact volume, number, and location of the otolith particles in the membranous labyrinth (11).

Results

The following maneuvers were studied with the simulator: the two roll maneuvers (2), the Gufoni maneuver (3), and the two Zuma maneuvers (4).

Roll Maneuver: two types - non-ampullary versus ampullary arm

The initial roll maneuver for hc-BPPV-ca (2,19) was described as a 2700 roll of the head and body in 90° steps starting with the patient in supine position. In the simulation, the head is raised by 30° to make the horizontal canal vertical with respect to gravity (20). The maneuver uses gravity to move the debris through the canal and brings it in the direction of the utricle. In the next step, the subject is turned 90° to the healthy side, followed by moving into the prone position and then turning another 90° to turn to the affected side. This maneuver works

when debris is present in the non-ampullary arm of the horizontal canal. Simulation 1 demonstrates the movement of the debris present in the non-ampullary arm of horizontal canal by the roll maneuver (speed accelerated for clarity). The debris present in this position would cause geotropic nystagmus on the supine roll test. The video of the simulation is available in the supplementary file.



Simulation 1: Roll Maneuver for Debris in the Non-Ampullary Arm (scan to view)

The simulations show that the 270° roll maneuver is effective in repositioning debris in the horizontal canal only if it is near enough to the utricular opening. If the debris is closer to the ampulla, the debris will move from the ampullary to the non-ampullary arm, but not to the utricle leading to treatment failure. This is illustrated in Simulation 2. The video of the simulation is available in the supplementary file.



Simulation 2: 270° Roll Maneuver – Failed Repositioning (scan to view)

A modified roll maneuver (21,22) was recommended for the treatment of hc-BPPV-ca of both ampullary and non-ampullary arms along with hc-cupulolithiasis by adding a step to the above-described procedure by first turning the head 90° relative to gravity to the affected side first. This is followed by a return to the central supine position and then following up with the steps previously described in the roll maneuver enables debris present in any position in the horizontal canal to move towards the utricle.

Simulation 3 shows the debris movement in each step of hc-BPPV when the debris is present in the ampullary arm close to the cupula in which apogeotropic nystagmus occurs. The video of the simulation is available in the supplementary file.



Simulation 3: Modified Roll Maneuver for Debris in the Ampullary Arm (scan to view)

The practical clinical implications of these three simulations show which maneuver would theoretically be the most effective. It can be seen that by turning the head to the affected side relative to gravity and performing the roll maneuver as a 360° rotation, this maneuver would be effective in treating BPPV with debris in any position in the horizontal canal. Therefore, the modified roll maneuver (21) is recommended for the treatment.

Gufoni Maneuver

This maneuver is used to treat the geotropic form of hc-BPPV. The otoconial debris in the non-ampullary arm is repositioned using centrifugal force due to a rapid deceleration and by the gravitational force (23). When the patient is moved into the side-lying position on the healthy side, the debris moves from the non-ampullary arm of the horizontal canal towards the utricle. By turning the head so that the nose points downwards, the repositioned debris cannot re-enter into the canal. Then the patient is brought back to the sitting position. This is demonstrated in Simulation 4. The video of the simulation is available in the supplementary file.



Simulation 4: Gufoni Maneuver (scan to view)

When the otolith debris is found floating near the ampulla, the resultant canalithiasis will produce apogeotropic nystagmus on the supine roll test. When the Gufoni maneuver is to be performed for particles present in the ampullary arm of the horizontal canal, it has to be started from the affected side. The patient is moved into the side-lying position on the affected side to allow the debris to move from the ampullary arm of the horizontal canal to the most dependent position. In the next step when the nose is turned up, the debris moves to the non-ampullary arm of the horizontal canal. The patient is finally brought back to the upright sitting

position. However, the simulator shows that there is a chance that the debris does not reach the utricle and may fall back into the canal. This will result in failure of the maneuver, which is demonstrated in Simulation 5. The video of the simulation is available in the supplementary file.



Simulation 5: Gufoni Maneuver for Apogeotropic Nystagmus (scan to view)

Zuma Maneuvers

This maneuver was proposed to treat apogeotropic hc-BPPV which can

occur when the debris is in the ampullary arm of the horizontal canal (as canalithiasis) or attached to the cupula (cupulolithiasis) on the canal or utricular side (23, 24). The maneuver uses the endolymph inertia and gravitational force acting on the particle to bring the debris back into the utricle.

The simulation shows that by moving the subject into the sidelying position on the affected side in the first step, brisk deceleration and inertia can detach the otoconia from the cupula (if attached to the canal side). Upward turning of the head in the second step aims to facilitate the movement of the detached otoconia through the canal. By moving the subject to the dorsal decubitus followed by turning the head by 90° toward the unaffected side, the otoconia are brought closer to the utricle. The patient's head is bent forward, followed by a slow return of the patient to the sitting position. The aim of this is to prevent the particles from moving back into the horizontal canal (25). This is demonstrated in Simulation 6. The video of the simulation is available in the supplementary file.



Simulation 6: Zuma Maneuver (scan to view)

Modified Zuma Maneuver

The modified Zuma maneuver is recommended for treatment of geotropic hc-BPPV. It is a modification of the original Zuma maneuver (6). The simulation shows that by turning the head 45° towards the unaffected side in the first step and then moving the subject into the side-lying position on the affected side in the next step, the horizontal canal is brought to the vertical plane. The otolith debris moves away from the ampulla into the non-ampullary arm of the canal due to gravity. Turning the head 90° towards the unaffected side takes the debris further away, towards the utricle. Tilting the head forward in the final step prevents the debris from reentering the canal. This is demonstrated in Simulation 7. The video of the simulation is available in the supplementary file.

Three-dimensional Simulations of Six Treatment Maneuvers of Horizontal Canal BPPV Canalithiasis: Evaluating theoretical efficacy of BPPV maneuvers



Simulation 7: Modified Zuma Maneuver (scan to view)

Simulation 8 shows that the Zuma maneuver is an effective treatment option for debris present in the non-ampullary arm. Thus, we found further evidence that the Zuma maneuver can be used for hc-BPPV-ca affecting both ampullary and non-ampullary arms. The video of the simulation is available in the supplementary file.



Simulation 8: Zuma Maneuver for debris in the Non-Ampullary Arm (scan to view)

Discussion

Different liberatory maneuvers use different mechanisms of action, head positions and head movements. The simulations provide the viewer with a three-dimensional visualization of the head movement and how this movement influences semicircular canal orientation and finally the movement of the otolith debris. Chapter-5

Roll maneuver - The debris movement in the canals depends on the orientation of canal relative to the gravitational force; by that the debris moves in the canal through different positions of the canal at each step of the maneuver. The simulator shows that if the otoconial debris is present in the ampullary arm of horizontal canal, the 270° roll maneuver will not be able to liberate the debris; it will work only for removal of the debris from the non-ampullary arm. In contrast, the 360° roll maneuver will be able to accomplish the repositioning of debris present in all positions of the canal, in both the ampullary and non-ampullary arms. This brings us to the conclusion that the modified roll maneuver with 360° rotation is a better maneuver for hc-BPPV-ca irrespective of the precise location of the debris (25).

Gufoni maneuvers - Their mechanism of action is based on centrifugal and gravitational forces. The simulator shows that the Gufoni maneuver is effective for geotropic hc-BPPV with debris in the non-ampullary arm of the horizontal canal. The modified Gufoni for apogeotropic hc-BPPV with the debris in the ampullary arm may possibly lead to a failure because theoretically it is not able to move the otolith debris completely out of the canal (23). It can convert an apogeotropic nystagmus into a geotropic nystagmus by bringing the debris from the ampullary arm to the non-ampullary arm. The simulations bring us to the conclusion that the Gufoni maneuver is effective for hc-BPPV-ca in the non-ampullary arm while the modified Gufoni may fail in treatment of hc-BPPV-ca in the ampullary arm. Therefore, it is recommended that after the modified Gufoni maneuver, an additional maneuver in the form of a Gufoni maneuver for geotropic nystagmus or a roll maneuver is required to complete the repositioning. The simulation also shows that the Zuma maneuver, which adds an additional 900 rotation to the modified Gufoni maneuver, makes it an effective treatment option.

Zuma maneuvers - Zuma maneuvers utilize gravity along with inertia for debris mobilization. The modified Zuma maneuver is effective for repositioning of the otoliths present in the non-ampullary arm. With

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the simulator, it is evident that the original Zuma maneuver is useful in repositioning otoliths in all positions in the horizontal canal, in both the ampullary and non-ampullary arm. We can thus conclude that the original Zuma maneuver works effectively in hc-BPPV-ca and no modifications are required.

Timing

For an effective repositioning, it is important for the particle to reach the lowest position of the canal at the end of each step of the maneuver, as was also shown in studies on posterior canal BPPV (26,27). If the next step is performed before the particle reaches the desired position, the maneuver may fail. The simulation emphasizes the importance of waiting between the steps to allow gravity to take the debris to the most dependent position. To our knowledge, there is no hard evidence currently available that indicates what the minimum time interval between the different positions must be. We currently wait at least 45 seconds between two successive movements and wait until the induced nystagmus has disappeared completely (by exception, the nystagmus decreases in amplitude and velocity but might be persistent).

Finally, it is important to note that in our simulations, the time taken for the particle to move at each step of the maneuver has been accelerated to make the simulation more user-friendly.

Limitations

Our study is based on the orientation obtained from reconstructed MRI images. Currently, the major limitation of this simulator is that the orientation of the semicircular canals varies from patient to patient and hence it does not entirely represent the situation in every individual patient. We are also aware that the natural variations in the orientation and morphology have a substantial impact on the validity of the extrapolation to the individual patient and may explain why the maneuvers need more time or fail in some patients. This indicates that one should switch maneuvers if a patient does not respond. The Chapter-5

simulations present ideal planes and angulations. Restrictions in patient mobility may not allow these ideal parameters and affect the final outcome of the maneuver. Despite the inherent limitations, we feel that simulators are an effective way of understanding BPPV and therapeutic maneuvers for BPPV treatment.

Conclusion

The simulator provides a useful tool for the clinician to understand the orientation of the head, semicircular canals and debris in different positions in the canals in a three-dimensional space. The simulator helps us to understand the movement of the otoconia with respect to the movement of the head, which improves our understanding of the optimum plane and angulation required to get the best results.

Our study shows that the modified roll maneuver and Zuma maneuver are effective treatment options for canalithiasis of the horizontal canal in all positions in the canal. The Gufoni maneuver works well when the otolith debris is in the non-ampullary arm of the horizontal canal. The simulator showed that the Gufoni maneuver for apogeotropic nystagmus may be inadequate for repositioning and there are higher chances of treatment failure.

This simulator can also be used for teaching and research purposes to help to modify existing maneuvers to make them more effective and to develop new maneuvers.

Finally, we encourage clinical validation of our theoretical results, i.e., randomized controlled clinical trials directly comparing the efficacy of the various maneuvers discussed here.

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Diagnostic and Therapeutic Maneuvers for Anterior Canal BPPV Canalithiasis: Threedimensional Simulations

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Front Neurol. 2021;12

Introduction

Anterior canal BPPV (ac-BPPV) was first described in 1987 (1). It is

considered the rarest form of semicircular canalolithiasis (2). Two factors may explain its low incidence: The anterior canal is situated in the superior position of the labyrinth with the non-ampullary arm of the canal descending directly into the common crus and onward into the vestibule (Figure 1). The anterior canal is higher than both the posterior and horizontal canals. This anatomical position makes it less likely for the otoconial debris to enter the canal against gravity (3). Further, this anatomical orientation should also facilitate self-clearance of the otoconial debris due to gravity (4). The low incidence might be one of the major reasons for the paucity of studies and literature describing this clinical entity, which the Barany Society Consensus document still calls an emerging and controversial entity (5).



Figure 1: Anatomical orientation of the semicircular canals in supine head position

Diagnostic maneuvers. In addition to its low incidence, there are many ambiguous issues in terms of the diagnosis and the treatment (see below) of ac-BPPV. The positional tests described for diagnosis are the Dix-Hallpike and supine head-hanging tests. ac-BPPV is characterized by a vertical downbeat nystagmus with a torsional component towards the affected side (5) evoked by the Dix-Hallpike and supine head-hanging tests. However, the torsional component is not always clear and is less intense than the vertical one and hence needs to be differentiated from posterior canal down beating BPPV (6,7). Therefore, determining the affected side based on the Dix-Hallpike examination can often be difficult, thus further complicating proper diagnosis and treatment (8,9,10). The supine head-hanging test is considered to be a more sensitive test for ac-BPPV as it acts in the sagittal plane and thus stimulates both anterior canals at the same time (5,10,11). However, there is so far no generally accepted diagnostic maneuver for ac-BPPV. Down-beat nystagmus on positional tests can be associated with central disorders and should be excluded from peripheral down beating nystagmus (12).

Therapeutic maneuvers. Various therapeutic maneuvers have been described for the treatment of ac-BPPV. Considering the posterior and anterior canals as co-planar, reversal of maneuvers used for posterior canal-BPPV treatment, such as the Epley and Sémont maneuvers, were recommended to treat ac-BPPV (13,14,15). The reversed maneuver is started from the healthy side. The Yacovino maneuver was proposed as a treatment option with the distinct advantage that the side of involvement does not need to be identified for treatment (16). The short canal repositioning maneuver (short CRP maneuver) works on the basis of a modified form of the Epley maneuver which can be used in the treatment of ac-BPPV after determining the side of involvement (6). Various other maneuvers described in literature which require identification of the side of involvement have been described (17,18,19,20). Based on the orientation of the canal during these maneuvers and the underlying biomechanics, each maneuver theoretically has its advantages and disadvantages similar to treatment maneuvers for posterior and horizontal canal BPPV (4,16,21,22).

Simulation of the maneuvers. Many two-dimensional illustrations for BPPV have been described, but they have the limitation of providing the view from only one angle and showing only the initial and final position of the debris. In this article, we present the simulation of ac-BPPV in the 3-dimensional space to optimally visualize the movement of the head, labyrinth, and otoconial debris for practical clinical use. We used a software-based simulator (4,21,23) to study different positional tests and liberatory maneuvers in ac-BPPV by demonstrating the continuous dynamic movement of the otoconial debris in the anterior canal as a function of time and angulation. The simulation depicts the movement of the debris in the canal at each step. It is important to note that these are true simulations of the debris movement based on the biophysics of BPPV and not simple animations. Basic assumptions regarding the debris size and distribution, endolymph viscosity and canal geometry have been taken into consideration (4,23).

In this study, we specifically used simulations of a) the supine headhanging test for the diagnosis of ac-BPPV, b) the Yacovino maneuver (16) and its modifications for the treatment of ac-BPPV, c) the Epley maneuver done from the opposite side (reverse maneuver), and d) the short CRP maneuver (6). The aim of the simulations was to find out which maneuver might theoretically work and which not and which one might even be superior. These findings can also be the basis of controlled trials for the diagnosis and treatment of ac-BPPV.

Methods

Based on reconstructed MRI images and fluid dynamics, a 3D dynamic simulation model (as a function of time) was developed and applied (for more details refer to ref 23) The simulation allowed placement of the debris at variable positions within the canal and also in more than one canal simultaneously. The time between the two steps of the maneuver required for the debris to reach the desired position is accelerated for better understanding and ease of demonstration.

Results

The results of the simulations of the following maneuvers will be presented: For the diagnosis of ac-BPPV, the supine head-hanging test; for its treatment, the Yacovino maneuver and its modifications, the Epley maneuver done from the opposite side (reverse maneuver), and the "short CRP' maneuver".

Diagnostic maneuvers

Supine head hanging test for the diagnosis of ac-BPPV

Clinically ac-BPPV is characterized by a vertical downbeat nystagmus with a torsional component towards the affected side when the individual is looking straight ahead as evoked by the supine head-hanging test. There is usually no inversion (see below) of the downbeat nystagmus on returning to the sitting position.

The simulation shows that in the deep head-hanging position, there is

ampullofugal movement of the debris which leads to an excitation of the anterior canal (Simulation 1). This causes a downbeat nystagmus with torsion toward the side of involvement when the individual looks straight ahead. This implies that the supine head-hanging test is useful for the diagnosis of both anterior canals. In the second step when the subject comes back to the sitting position, the debris moves further towards the utricle (continuing the ampullofugal movement) and not back towards the ampulla. This explains why there is no inversion of nystagmus when the subject returns to sitting position and the natural remission. Simulation 1 is available in the Supplementary material.



Simulation 1 – Supine head-hanging test (scan to view)

Treatment maneuvers

Yacovino maneuver, new modified Yacovino maneuver and failed Anterior canal maneuver

We studied two types of this maneuver using the simulator: the original Yacovino maneuver (16) and a new modified Yacovino maneuver, which – as will be shown below – has a lower risk of a transition from anterior canal to posterior canal BPPV, based on our simulation.

The original Yacovino maneuver consists of 4 steps each performed at an interval of 30 seconds as the otoconia moves down about 1% of the diameter of the canal per second under the influence of the gravity acting on it (24,25). The four steps are as follows: step 1: sit straight; step
2: bring to the head to the head-hanging position, 30 degrees below the horizontal plane; step 3: head is elevated so that the chin touches the chest; and step 4: back to the sitting position.

As the anterior canal lies in the vertical plane, the head should remain straight on starting the maneuver. In the next step, the subject's head is taken down to 30° below the horizontal plane. This inverts the anterior canal such that the ampullary arm lies at the most superior position, whereas the non-ampullary arm is placed inferiorly. The otolith debris moves ampullofugally to reach the most dependent position in the canal. Next, the subject is taken to the chin-to-chest position. This takes the debris further ahead in the canal. However, the simulation shows that at this point, there is a risk that the debris enters the posterior canal, leading to a canal switch. In the final step, the subject sits up and bends the head forward, leading to the debris being repositioned to the utricle. Simulation 2 is available in the Supplementary material.



Simulation 2 – Yacovino maneuver (scan to view)

If the subject is kept for a longer duration in the chin-to-chest position, there is an even higher risk of the debris entering into the posterior canal. This can be seen in Simulation 3 which is available in the Supplementary material.



Simulation 3 – Canal Switch in Yacovino maneuver (scan to view)

To avoid the risk of canal switch, we propose a modification of the Yacovino maneuver. In this variation, the subject is brought directly from the head-hanging position to the sitting position. After an interval of 30 seconds, the subject's neck is flexed forward at an angle of 45°. Simulation 4 shows that this modification brings a better repositioning of the otoconial debris into the utricle. The chin-to-chest position has been omitted to avoid the risk of moving the debris from crus commune to posterior canal. Simulation 4 is available in the Supplementary material.



Simulation 4 – Modified Yacovino maneuver (scan to view)

Correct angulation of the head and waiting in between each step of the maneuver is important to allow the debris to move further in the canal. Simulation 5 demonstrates how incorrect head angulation and inadequate time between steps can lead to failure of treatment by the maneuver. In this case, the subject is moving from the head-hanging position to the sitting position and then immediately bending the neck on sitting. The simulation demonstrates that the debris falls back towards the ampulla instead of moving towards the utricle, thus leading to a failed repositioning. Simulation 5 is available in the Supplementary material.



Simulation 5: Failed Anterior Canal Maneuver (scan to view)

Reverse Epley maneuver (13,14)

As the ipsilateral anterior and contralateral posterior canals are coplanar, repositioning maneuvers used for pc-BPPV treatment have been advocated for ac-BPPV treatment as well. In this way, an Epley maneuver is performed from the right side for repositioning of left ac-BPPV and vice versa, i.e., a reverse maneuver. Simulation 6 demonstrates that the reverse Epley maneuver is theoretically not very effective as there is a high risk that the debris moves backwards and falls back towards the ampulla instead of moving towards the utricle. Simulation 6 is available in the Supplementary material.



Simulation 6 - Reverse Epley Maneuver (scan to view)

"Short canal repositioning maneuver"

The short CRP maneuver (6) or short Epley was proposed to improve the results of the classic repositioning maneuvers in ac-BPPV treatment. The steps for this maneuver are step 1: seated upright with head turned to the affected side by 45°; step 2: head-hanging position with the head 40° below the horizontal; step 3: while still in the head-hanging position, the head is turned to the healthy side; and step 4: back to sitting position.

This maneuver is similar to the classic Epley maneuver with the variation of omitting the step of turning to the nose-down position to the healthy side. This modification facilitates progressive movement of the debris out of the canal. Simulation 7 shows that short canal repositioning is an effective treatment option for ac-BPPV. However, it requires determination of the side of involvement, as in the reverse Epley maneuver. Simulation 7 is available in the Supplementary material.



Simulation 7- Short CRP maneuver (scan to view)

In this simulation, it was seen that the 30° head hanging position is as effective as the 40° angulation described by the authors. This shows that increasing the angle of the head beyond 30° does not influence treatment outcome.

Discussion

BPPV involving the anterior canal has a low incidence. However, its low incidence contrasts with the clinical importance of its most prominent characteristic, positional downwardly beating nystagmus, which also occurs as central positional nystagmus associated with various brainstem and cerebellar lesions and may indicate a sinister pathology (26). In contrast to BPPV affecting the other canals, data on the diagnostic techniques and therapeutic maneuvers for ac-BPPV are sparse,

The major findings of this study using software simulations are as follows:

1. Diagnostic tests for ac-BPPV – the supine head-hanging test is an effective diagnostic test for ac-BPPV in which both canals can be tested together.

2. Therapeutic maneuvers: a) The treatment outcome of the Yacovino maneuver can be improved with a modification in steps as demonstrated in the new "simplified Yacovino maneuver"; b) the reverse Epley

maneuver is not an effective treatment option; and c) the short CRP maneuver is a useful treatment option; however, it requires the determination of the side of involvement.

Diagnostic tests for ac-BPPV

The Dix Hallpike maneuver and the supine head-hanging test have been described as the positional tests to diagnose ac-BPPV. There are, however, conflicting reports regarding which side the Dix Hallpike test generates stronger nystagmus – ipsilateral, contralateral or both (1,6,8,26). These reports indicate that the results from the D-H examination may vary in different patients. The Bárány Society has classified ac-BPPV canalithiasis (5) as positional nystagmus elicited by the Dix-Hallpike maneuver (on one or both sides) or in the supine straight head-hanging position. The nystagmus beats predominantly vertically downward in the Dix Hallpike position and nystagmus may be stronger or exclusively present with the affected ear up or down.

Based on our simulations, the supine head-hanging test seems to be a more suitable positional test for the anterior canals as it aligns the parasagittally placed canals closest to the mid-sagittal plane (22). Keeping the head in a non-rotated position is more beneficial for movement of debris within the anterior canal compared to the rotated position of the Dix Hallpike maneuver. Further, as the head reaches a lower position in the supine head-hanging test compared to the Dix Hallpike maneuver, the effect of gravity on the debris in the canal will be enhanced. The angle of the ASC relative to the earth-horizontal is approximately 20° larger during the straight head hanging position than during the D-H test (8,27). The simulation model demonstrated that the otoconial debris in ac-BPPV affecting either side would move ampullofugally in the canal during the supine head-hanging test.

Reversal of the nystagmus. Most positioning tests show a reversal of nystagmus on returning to the initial position. ac-BPPV is characterised by vertical downwardly beating paroxysmal nystagmus evoked by the

supine head-hanging test without inversion of the down-beating vertical nystagmus on returning to the sitting position. This can be explained by the fact that the SHH test inverts the ac to allow debris to reach the peak of the ac, and then, upon returning the patient to the sitting position, allows it to migrate further into the common crus (1). Towards the end of the SHH, if the otoconia debris traverses the common crus, the pressure field of the moving otoconia is exerted across both the anterior and posterior canals and the direction of the nystagmus is affected accordingly (8). Simulation 1 shows the debris moving from the ampullary arm at the beginning of the test to the lowest position of the canal in the head-hanging position. The lowest position is actually the most superior part of the ac. When the subject is brought back to the sitting position, the debris moves further ampullofugally in the same direction. Hence the nystagmus trajectory will remain the same. This finding is in agreement with the statement that both ac and apogeotropic posterior canal BPPV are characterised by paroxysmal nystagmus evoked in different positions and rarely inverting when returning to the sitting position (1).

However, this is in contrast to what was reported in some studies where the authors report that on returning to the sitting position, there should be a less intense nystagmus in the opposite direction, that is, up beating with the torsional component beating away from the affected ear (1,2,11). Thus, we see that when returning to the sitting position some authors have described a lack inversion of the down-beating vertical nystagmus (1,17) while others described an inversion (2,11,17,22). Therefore, this has to be re-evaluated in clinical studies.

Treatment maneuvers for ac-BPPV

As a general rule in BPPV, there is only one optimal geometry to maneuver debris in a particular canal (11) and all maneuvers attempt to bring the debris around a circle of the affected canal. For treatment of ac-BPPV, the anterior canal is positioned upside-down to allow debris to fall to the "top" of the canal, and then further steps prompt the debris

to further migrate into the common crus and then into the vestibule. Various attempts to modify maneuvers often lead to another unique way to accomplish the same goal of particle repositioning (6). Several maneuvers have been described and recommended for ac-BPPV, but there is so far no consensus on its best treatment. Our simulation has evaluated the pros and cons of these maneuvers which will have clinical implications.

Yacovino maneuver (16) and the new modified Yacovino maneuver based on our simulation.

Both utilize the principle of gravity to move the debris through the canal back into the utricle. This maneuver has the distinct advantage over other maneuvers in that determination of the side of involvement is not a pre-requisite. The Yacovino maneuver involves taking the patient to the supine head-hanging position, followed by flexing the neck to the chinto-chest position and then bringing the patient up to the sitting position, finally bending the neck. Simulation 2 shows how the original Yacovino maneuver is effective in treating ac-BPPV. In this simulation, it was also demonstrated that in the chin-to-chest position, there is a chance of the debris entering into the posterior canal, resulting in canal switch instead of repositioning to the utricle. In fact, if the patient is kept in this chin-tochest position for a longer time, Simulation 3 shows that the chances of canal switch increases. Canal switch is a complication of CRP where the debris moves from one canal to another. It is most commonly described for posterior canal BPPV converting to the superior or horizontal canal (28,29). The classification of ac-BPPV (1) includes canal conversion to the posterior canal during or immediately after the therapeutic maneuver as "certain" evidence of ac-BPPV. Studies have shown canal conversion from anterior canal into typical posterior canal BPPV after Yacovino maneuver which required additional maneuvers (two-step therapy) (1). The Yacovino maneuver can result in uncontrolled conversions into a PC-BPPV after performing the maneuver (1,22). All semicircular canals could be affected by free- moving otoconia, and an iatrogenic canal switching during CRM is possible (30).

To solve this problem in the classic Yacovino maneuver, we propose a modification to make the maneuver simpler and theoretically more efficient. Simulation 1 showed that in the supine head-hanging position, the debris reach the apex of the canal and in the sitting position, the debris move further ahead in the canal rather than falling back to the ampulla. As we mentioned before, this is why inversion of nystagmus does not occur in the supine head-hanging test. Taking this fact into consideration, we have proposed a modification of the Yacovino maneuver. In this modified maneuver shown in Simulation 4, after the supine head-hanging position, the subject is taken immediately from supine head deep hanging 30° below the horizontal to the sitting position. After waiting for 30 seconds in the sitting position, the subject's neck is flexed. The simulation shows that the debris reaches the highest point of the ac under the influence of gravity in the supine head-hanging position. When the subject goes to the sitting position next, the debris travels further ahead through the crus commune and onward to the utricle. The final step of bending the neck prevents the repositioned debris from re-entering into the ac.

Timing. One of the most critical factors to achieve successful repositioning is to allow adequate time between the two steps of the maneuver so that the particle reaches the lower most position of the canal due to gravity before moving to the next step (5,6). An insufficient waiting period between the steps does not allow gravity to take the particle to the required position. In Simulation 5, when the neck is bent immediately without waiting for the particle to come to the lowermost position, the otolith debris fails to move towards the common crus and instead falls backwards towards the ampulla. This underlines the importance of waiting between each step of the maneuver for the debris to reach the most dependent position. Although the minimum time interval between two steps is not fixed, we propose 30 seconds between each step or till the induced nystagmus subsides. Yacovino maneuver was subsequently re-described with subtle differences: a 3-min pause in each position rather than 30 s, and rapid transitions

(31). However, we recommend a 30-second interval between steps as longer waiting time may encourage canal switch and rapid transition may result in inadequate debris progression.

"Reverse Epley maneuver"

This was one of the first repositioning maneuver proposed for the treatment of ac-BPPV (14,32,33). Various studies have shown the efficacy of this maneuver to treat ac-BPPV (1,16,24,26) however detailed data on the number and the history of the patients, as well as the outcome of this treatment are lacking (8). In the reverse Epley maneuver, the head is dropped into the Dix-Hallpike position with the affected ear up and the patient is then moved in 90° steps toward the unaffected side as in the CRP (10). Thus the same positioning sequence as for the contralateral posterior canalithiasis is performed. The geometry of the ac is such that one would expect this maneuver could even make it worse, because it involves nose-down positioning (11). Simulation 6 demonstrates the Epley maneuver performed for a contralateral ac-BPPV. It is seen that turning the head by 45° to the healthy side and going down by 30° brings the debris ampullofugally to the lowest position. Turning the head to the affected side by 90° takes the debris to the apex of the canal. When the subject is further turned by 90° to the nose pointing down position, this leads to retrograde movement of the debris towards the ampulla. This brings us to the conclusion that the 'reverse Epley' is evidently not effective for the treatment of ac-BPPV.

"Short canal repositioning maneuver"

To overcome the drawback of the 'reverse Epley', a modified maneuver called the "short canal repositioning maneuver" was proposed (6). It also requires determination of the side of involvement. After determination of the side, the subject's head is turned 45° to the affected side and taken to the head hanging position. An enhancement of hanging the head to lower than 30° in this position was described to promote more definite progression of the otolith mass around the circumference of the canal. In the next step, the subject's head is turned to the healthy

side by 90°. Then the subject is brought back to the sitting position (the nose pointing down position of the classic Epley maneuver has been omitted). Simulation 7 shows the 'short CRP' to be an effective treatment option for ac-BPPV. The simulation also showed that 30° head hanging is sufficient to help the debris progress through the canal and an increase in the angle may not really be required.

The past few decades have increased our knowledge about BPPV; however, some aspects are still not understood or are controversial (34,35,36). Perhaps, answers will come when we can image the material in the semicircular canals and see its motion (2). Until direct imaging of debris becomes possible, the 3D simulations provide a useful tool to understand the changing orientation of the semicircular canals with changes in head positions and angulations. This tool can aid in optimizing treatment modules.

Limitations

Our study is based on the orientation of the semicircular canals obtained from the reconstructed MRI images. However, the orientation of the canals varies from one patient to another. Different morphology and orientation of the canals are an important factor for the success or failure of a repositioning maneuver. The major limitation of our study is that it fails to represent the complete population due to these variables. The simulations we have used do not take into account the impact of different debris sizes and the possibility that debris can be located in different parts of the canal at the same time; issues that may differ from patient to patient. This is not implemented as there are many unknown variables and visualizing the otolith movement for each and every patient is beyond the scope of our study. Despite these limitations, the simulators provide an effective detailed understanding about the mechanism of the maneuvers and conclude which therapeutic maneuver could be most effective.

Conclusion

These simulations show that the new simplified Yacovino maneuver is an effective treatment option for ac-BPPV. It also reduces the risk of canal switch which may occur in the original Yacovino maneuver. In both there is no need to determine the affected side as required in the short CRP and the (theoretically not effective) reverse Epley maneuvers.

Based on our findings, we encourage clinical validation of our theoretical results, i.e., randomized controlled clinical trials directly comparing the efficacy of the various maneuvers discussed here.

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07

Modified interpretations of the supine roll test in horizontal canal BPPV based on simulations: How the initial position of the debris in the canal and the sequence of testing affects the direction of the nystagmus and the diagnosis

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Frontiers in Neurol. 2022;13 https://doi.org/ 10.3389/fneur.2022.881156

Abbreviations:

BPPV: Benign Paroxysmal Positional Vertigo hc- horizontal canal ca: canalithiasis SRT-Supine Roll Test

Introduction

Benign paroxysmal positional vertigo (BPPV) is caused by a displacement of otolith debris from the utricle to the semicircular canals. The diagnosis of BPPV is based on the character of nystagmus induced by

the various positional tests (1, 2). The Dix-Hallpike test (3) and the sidelying diagnostic Sémont maneuver (4, 5) are used to diagnose posterior canal BPPV, which is associated with torsional, upwardly beating nystagmus. The supine roll test (SRT) is considered useful to diagnose horizontal canal BPPV (hc-BPPV) (6) by eliciting horizontal nystagmus. Other tests like the Bow and Lean test (7) and Upright Roll test (8) have also been described as diagnostic tests for hc-BPPV. Anterior canal BPPV is diagnosed by the supine head-hanging test with the generation of characteristic downwardly beating nystagmus, which may have a torsional component (9,10).

BPPV may occur due to free-floating debris (canalithiasis) (11) or debris adherent to the cupula (cupulolithiasis) (12). The variants of BPPV are also classified based on the position of the debris within the canal (13, 14). For instance, in canalithiasis of the horizontal canal, the debris could be present either in the ampullary or the non-ampullary arm of the canal (15). (Fig.1) Debris in the non-ampullary arm generates geotropic nystagmus, while debris in the ampullary arm generates apogeotropic nystagmus which can be misinterpreted as hc-cupulolithiasis. The typical clinical picture of hc-canalithiasis has been described as a bidirectional horizontal geotropic nystagmus which is bi-positional on the right and left sides (16). The present study shows that the latter statement is not always true, as we will show that the direction of the nystagmus depends on whether the affected or the unaffected side is tested first with the diagnostic maneuver.

In this study, we systematically evaluated the different factors which can affect the nystagmus patterns and results of the SRT. Simulations (17) were also used to study how the diagnostic outcome of SRT is affected by the initial position of the debris in the horizontal canal and the side from which the SRT was started. The nystagmus generated in different positions of SRT was visualized with the simulations. This study a) demonstrates the effects of the sequence of SRT maneuvers on the direction of the nystagmus, b) explains direction-changing nystagmus versus direction-fixed nystagmus versus unilateral nystagmus in different types of hc-canalithiasis, and c) shows that the assumption that the otolith debris returns to the initial position on turning the head to the opposite side in SRT may be fallacious.





Methodology

The simulation used a 3D model of the inner ear based on reconstructed images from DICOM files of the temporal bone. The orientation of the canals and the angles between the canals were in accordance with the various reported studies (17, 18). The simulation was created on Unity 3D software. A humanoid was animated within Autodesk Maya with the head linking the semicircular canals to head movement. Otoconial debris in the form of a crystal was put inside the canal using a thin tube (17). By linking the semicircular canals with the respective oculomotor muscles, the nystagmus generated due to canal stimulation was simulated. Ewald's laws have been incorporated in the simulations (19). The time taken for the particle to move at each step of the maneuver

was accelerated in all simulations presented here to make it more userfriendly.

Procedure of Supine Roll Test:

1. The patient is moved to the supine position with the head inclined

forward at an angle of 30° (usually done by placing a pillow under the head).

- The head is turned 90° to the right side and held in this position for 30 seconds or until the nystagmus subsides.
- 3. The head is turned back to the central position.
- 4. The head is then turned 90° to the left side and held for 30 seconds or until the nystagmus subsides.

5. The head is turned back to the center, and the patient is brought to an upright position.

Results

Simulations of hc-canalithiasis were used to study the effect of the SRT on the position of otolith debris within the canal. Exemplarily, canalithiasis of the right ear of the ampullary and non-ampullary arm of the horizontal canal was evaluated. In addition, the study compared the effects of starting the SRT from the affected side and the non-affected side.

Findings of the Simulations of the four test procedures:



Simulation 1 - Supine Roll test for right hc-canalithiasis non-ampullary arm starting by rotation to the right side (scan to view)

This simulation demonstrates right hc-canalithiasis with the debris in the non-ampullary arm. The otolith moves towards the ampulla after the head is rotated to the affected side due to gravity. This ampullopetal movement is excitatory. Therefore, geotropic nystagmus beating to the affected right ear is seen. Bringing the head to the center position moves the debris away from the ampulla. When the head is turned to the unaffected left side, the otolith moves towards the utricle. This ampullofugal movement produces an inhibitory stimulus resulting in geotropic left-beating nystagmus. Thus, direction-changing geotropic nystagmus is seen in hc-canalithiasis when the SRT is started from the affected side.

SRT R – R beating nystagmus

SRT L – L beating nystagmus



Simulation 2 - Supine Roll test for right hc-canalithiasis non-ampullary arm starting by rotation to the left side (scan to view)

This simulation demonstrates the SRT when starting by turning to the left side in hc-canalithiasis of the non-ampullary arm of the right ear. When the head is turned to the left, the debris in the right nonampullary arm moves towards the utricle. This generates left-beating nystagmus. However, the simulation shows that the debris may move out of the canal in this step. Subsequently, no nystagmus is induced when the SRT is performed on the right, as the debris has already been repositioned, and BPPV would be resolved. Thus, unilateral geotropic nystagmus beating to the unaffected side is seen in hc-canalithiasis of the non-ampullary arm when SRT is started from the healthy side. There

Modified interpretations of the supine roll test in horizontal canal BPPV based on simulations : How the initial position of the debris in the canal and the sequence of testing affects the direction of the nystagmus and the diagnosis

may be no nystagmus on turning to the affected side. SRT L – L beating nystagmus SRT R – no nystagmus



Simulation 3 - Supine Roll test for right hc-canalithiasis ampullary arm starting by rotation to the right side (scan to view)

This simulation demonstrates the performance of SRT starting by turning to the right side in hc-canalithiasis of the ampullary arm of the right ear. On turning the head to the right, the debris moves from the ampullary arm to the non-ampullary arm. This results in apogeotropic nystagmus beating to the left. When the head is turned back to the center, the particle remains in the non-ampullary arm. When the head is turned to the left side, the debris moves further through the non-ampullary arm. This generates geotropic left-beating nystagmus. If this position is maintained for longer, it may result in repositioning the debris out of the canal. Thus, starting SRT from the affected side in ampullary arm hc-canalithiasis results in direction-fixed nystagmus with left-beating apogeotropic nystagmus on turning to the affected side and left-beating geotropic nystagmus on turning to the non-affected side. In both positions, the nystagmus is beating to the non-affected side, i.e., direction-fixed nystagmus.

SRT R – L beating nystagmus

SRT L – L beating nystagmus

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Modified interpretations of the supine roll test in horizontal canal BPPV based on simulations : How the initial position of the debris in the canal and the sequence of testing affects the direction of the nystagmus and the diagnosis



Simulation 4 - Supine Roll test for right hc-canalithiasis ampullary arm starting by rotation to the left side (scan to view)

This simulation demonstrates SRT starting by turning to the left side in right hc-canalithiasis with the debris in the ampullary arm. Turning the head to the left causes little or negligible movement of the debris in the ampullary arm. However, it may convert the effect from canalithiasis to cupulolithiasis with nystagmus generated due to the force effect on the cupula, as seen in **Simulation 5**. On turning the head to the right, the debris moves away from the ampulla resulting in left beating apogeotropic nystagmus.

SRT L –no nystagmus or right-beating prolonged nystagmus SRT R – L beating nystagmus



A. Debris in right ear non-ampullary arm

	Start rotating to the Right	Start rotating to the Left
SRT right	Right-beating nystagmus	Right-beating nystagmus
SRT left	Left-beating nystagmus	Left-beating nystagmus

B. Debris in right ear ampullary arm

	Start rotating to the Right	Start rotating to the Left
SRT right	Left-beating nystagmus	Left-beating nystagmus
SRT left	Right-beating nystagmus	right-beating nystagmus

Table 1: Present understanding of the effect of Supine Roll test on horizontal canalithiasis affecting (A) the non-ampullary and (B) ampullary arm (6, 20, 21, 22, 23, 24).

C. Debris in right ear non-ampullary arm

	Start rotating to the Right	Start rotating to the Left
SRT right	Right-beating nystagmus	No nystagmus
SRT left	Left-beating nystagmus	Left-beating nystagmus

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D. Debris in right ear ampullary arm

	Start rotating to the Right	Start rotating to the Left
SRT right	Left-beating nystagmus	Left-beating nystagmus
SRT left	Left-beating nystagmus	No nystagmus or right-beating prolonged nystagmus

Table 2: Simulation studies of horizontal canalithiasis right ear: (A) Nystagmus patterns of SRT in non-ampullary canalithiasis on starting to the right and left (B) Nystagmus patterns of SRT in ampullary canalithiasis on starting to the right and left



Figure 2: (A) Horizontal canalithiasis with debris in the non-ampullary arm (B) Starting SRT by turning to right elicits right-beating nystagmus. (C) The head is turned back to the center. (D)The head is turned to the left which elicits left-beating nystagmus. Direction-changing nystagmus is seen

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Figure 3: (A) Horizontal canalithiasis with debris in the non-ampullary arm (B) Starting SRT by turning to the left elicits left-beating nystagmus (C) The head is turned to the center (D)Turning head to the right elicits no nystagmus as the debris has been repositioned out of the canal. Thus, unilateral nystagmus is seen on the unaffected side and no nystagmus on the side involved



Figure 4: (A)Horizontal canalithiasis with debris in the ampullary arm. (B) Starting SRT by turning to right elicits left-beating nystagmus. (C) The head is turned to the center. (D)Turning head to the left elicits left-beating nystagmus. This is direction-fixed nystagmus

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Figure 5: (A) Horizontal canalithiasis of the ampullary arm right ear (B) On turning the head to the left in the first step, there is little movement of the debris with no nystagmus elicited, or the debris may exert force on the cupula, leading to generation of prolonged right-beating nystagmus. (C) The head is turned to the center. (D) On turning the head to the right, there is left-beating nystagmus

Discussion

Supine Roll Diagnostic Test

The SRT is the preferred positional test to diagnose hc-BPPV (2, 25). Precise diagnosis of BPPV, the side affected, and the subtype is critical for successful treatment (26). Determination of the initial location of the debris is based on observation of nystagmus induced by gravity-dependent movements of the otoconia (27). In canalithiasis, the debris may initially be present in the ampullary or non-ampullary arm of the horizontal canal. Debris in the non-ampullary arm generates geotropic nystagmus, which is the more frequent presentation (25) as it is the most dependent region in the upright position. Less commonly, the otoconia may be initially located in the ampullary arm. This position will generate apogeotropic nystagmus on the SRT (6). Clinically, this can lead to the misdiagnosis of cupulolithiasis. The present understanding is that in the non-ampullary arm involvement, there will be geotropic

nystagmus on both sides and in ampullary arm involvement, there is apogeotropic nystagmus on both sides (Table 1).

3D-Simulations of SRT show that the sequence of testing changes debris position and nystagmus patterns.

Simulations provide a valuable tool for understanding the threedimensional spatial movement of the head, semicircular canals, and otoconial debris (18) and the nystagmus induced. The simulations are based on the biophysics of BPPV and depend on basic assumptions regarding the debris size and distribution, the endolymph viscosity, and the canal geometry (15, 28). By linking the semicircular canals with the respective oculomotor muscles, the nystagmus generated on the SRT due to stimulation of canals can also be visualized. An important observation from the simulations is that the otolith debris moves from its original position during the SRT, and the sequence of the diagnostic test affects the clinical findings (Fig.2-5).

Studies have suggested that the particles may not go back to their initial position after the first maneuver such that a second maneuver leads to different particle trajectories causing smaller cupula displacements (29, 30).

Nystagmus patterns: Direction-changing, direction-fixed or unilateral

The concept of changing otolith position in hc-canalithiasis during the SRT has implications on its results. The simulations show that SRT presents the possibility of the observer effect which refers to the possibility that an act of observation may affect the properties of what is observed (31). Thus, we see that depending on the side, which is tested first, there are variations in nystagmus direction. Intensity of nystagmus is determined by 2 factors:

- 1. Direction of debris movement in the canal excitatory/inhibitory
- 2. The time for which the gravitational force was appliable on the debris

which is a function of the distance the debris moves In Figure 2, with the debris in the right non-ampullary arm - on turning to the right, there is an ampullopetal movement which is excitatory. However, we also see that the distance that the debris moves is much smaller than on turning 900 to the left. In other words, on the right, nystagmus is produced by less debris movement, but it is excitatory. On the left side, there is more debris movement but inhibitory. This could be the reason why the difference between nystagmus intensity on both sides is often similar, making determination of the side of involvement difficult.

Due to the changing otolith positions and consequently different trajectories, the nystagmus may be bilateral directional-changing (as seen in Simulation 1), bilateral direction-fixed (seen in Simulation 3), or nystagmus on one side only (seen in Simulation 2 and 4) (Table 2, Figures 2-5). Thus, unilateral nystagmus indicates that the affected side is opposite to the side of nystagmus and the debris may be repositioned by the diagnostic test itself. Simulation 4 shows that in canalithiasis affecting the ampullary arm, turning the head to the non-affected side causes very little movement of the debris towards the ampulla. As seen in the simulation, if the debris remains in the floating form as canalithiasis, no nystagmus will be generated. However, if the debris exerts force on the cupula, as seen in Simulation 5, it will cause a transition into a cupulolithiasis effect, leading to a very long-lasting apogeotropic nystagmus; i.e., the time constant allows discrimination between canalithiasis and cupulolithiasis (Fig.6).

Some studies have described that if otoconial debris is located in the ampullary end of the horizontal canal, rotation of the head to the affected side causes the debris to fall away from the ampulla, causing an inhibitory nystagmus that beats toward the unaffected uppermost ear. Rolling onto the opposite side causes debris to return toward the ampulla, triggering a more intense nystagmus, again apogeotropic, beating toward the affected uppermost ear (32, 33). The transition

from an apogeotropic nystagmus to a geotropic may be due to displacement of otoconia from the ampullary part of the canal to the non-ampullary part. This displacement may be spontaneous or caused by diagnostic maneuvers (6). The conversion of apogeotropic nystagmus to geotropic is called geotropization (34). The transformation into the classical geotropic form suggests the pathophysiological mechanism is canalolithiasis rather than cupulolithiasis, also to be differentiated by the time constant of the nystagmus.

The mechanism of direction-fixed paroxysmal nystagmus in hc-BPPV has been attributed to causes such as canalith jam (13, 27, 33, 34) or multiple otolith masses in different arms of the horizontal canal (35). The transformation of the nystagmus from an apogeotropic to a geotropic form is explained by the migration of the otoconial mass from the ampullary arm of the horizontal canal (20). Simulation 3 shows that ampullary arm hc-canalithiasis, when tested from the affected side, presents with direction-fixed paroxysmal nystagmus, which is directed towards the non-affected side. This is proposed as a logical and straightforward explanation of the mechanism of direction-fixed nystagmus.

Modified interpretations of the supine roll test in horizontal canal BPPV based on simulations : How the initial position of the debris in the canal and the sequence of testing affects the direction of the nystagmus and the diagnosis



Figure.6: Debris moving from the ampullary arm to exert force on the cupula and produce a cupulolithiasis-like effect

Changing debris position during diagnostic maneuvers

Many studies have illustrations of the SRT which show the otolith debris returning to the initial position after turning the head to one side and then back to the center (6, 36, 37) (Table 1). The present study shows that the position of the debris in the horizontal canal is affected by the tests followed (Table 2). Therefore, it may be fallacious to assume that the debris returns to the initial position in the canal on changing head positions. As the particles may be displaced at different steps of the SRT, different testing sequences will alter the nystagmus generated, thus affecting the diagnosis.

Interpretation of SRT with a standardised protocol

By standardising the sequence of testing during the SRT, it is possible to interpret the initial position of the debris in the canal and the side of involvement. We propose that in SRT, after going from sitting to supine position, the head should be turned to the right side first by 90°. The nystagmus is observed. Wait in this position for 30 seconds or until the nystagmus subsides. Now turn the head to the center. Wait another 30 seconds or until the nystagmus. Finally, the head is turned back to the center. Our findings from the simulations are seen in Table.3.

A. Debris in right ear non-ampullary arm

SRT right	Right-beating nystagmus
SRT left	Left-beating nystagmus

B. Debris in right ear ampullary arm

SRT right	Left-beating nystagmus
SRT left	Left-beating nystagmus

C. Debris in left ear non-ampullary arm

SRT right	Right-beating nystagmus
SRT left	No nystagmus

D. Debris in left ear ampullary arm

SRT right	No nystagmus or prolonged left beat
SRT left	Right-beating nystagmus

Table 3: Supine Roll Test Interpretations of hc-canalithiasis on starting theSRT by turning to right first

Based on this table, it becomes easier to interpret the findings of SRT. The clinician can decide the side of involvement and initial position of the otolith debris to be able to choose the correct repositioning maneuver.

Resolution of BPPV during SRT

The simulations also demonstrate why even though horizontal nystagmus was seen on the SRT, no nystagmus may be seen on performing the repositioning maneuver. This can be explained by the fact that the debris has already been repositioned out of the canal, as seen in Simulations 2 and 3.

The success of the treatment of hc-BPPV depends on the correct identification of the pathological side: if the pathological side is not correctly identified, the maneuver may cause the otoconia to move in the wrong direction (6). In addition, the simulations show that different test sequences may generate variable nystagmus patterns. Therefore, it is crucial for the clinician to follow the nystagmus pattern to ascertain the position of the debris within the canal to perform the correct treatment maneuver.

Limitations

Our study is based on the orientation of the semicircular canals obtained

from the reconstructed MRI images. We are aware that our simulations and underlying physics model cannot precisely represent the in vivo movement of the otoconia in the semicircular canals of each patient because there are many variables amongst patients. The simulations we have used do not take into account the impact of different debris sizes and the possibility that the debris can be located in different parts of the canal at the same time. There are several unknown variables, and visualizing the otolith movement for each patient is beyond the scope of our study. In this study, we have demonstrated only simulations of canalithiasis and excluded cupulolithiasis. We encourage clinical validation of our theoretical results, i.e., randomized controlled clinical

trials directly comparing the findings of the various tests discussed here.

Conclusions and clinical implications

The simulations provide a helpful tool to dynamically understand the orientation of the head, horizontal canal, and otolith debris in different positions in three-dimensional space, along with visualization of the nystagmus generated. The paper provides a new interpretation of the findings of SRT. The study shows how the sequence of the diagnostic tests affects the otolith position and impacts test results. The simulation model can explain varying nystagmus patterns seen in hc-canalithiasis such bilateral direction-changing nystagmus, bilateral direction-fixed nystagmus, and nystagmus on only one side. The simulations explain the phenomenon of direction-fixed nystagmus as a logical consequence of starting the SRT with the head turned towards the non-affected side in hc-canalithiasis with debris in the ampullary arm.

Unilateral nystagmus seen on SRT indicates canalithiasis of the non-ampullary arm of the side opposite to the side of nystagmus. Identifying these different nystagmus patterns will help the clinician determine the side of involvement and location of the debris within the canal. It is recommended that a standard sequence for positional testing be followed globally to ensure uniformity in test conditions and interpretation of results.

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Large variability of head angulation during the Epley maneuver: Use of a head-mounted guidance system with visual feedback to improve outcomes

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The Journal of International Advanced Otology 2023;19(3) https://doi.org/ 10.5152/iao.2023.22969

Introduction

Dizziness as a primary complaint, accounts for 5.6 million clinic visits in the United States annually, and 17-42% of patients with vertigo ultimately receive a diagnosis of benign paroxysmal positional vertigo (BPPV) (1,2). BPPV has an incidence of 10.7 to 64 per 100,000 population and a lifetime prevalence of 2.4 percent (1,3). Though BPPV is one of the most common causes of vertigo, only 8% of BPPV patients receive effective treatment (4,5). The time between first symptoms and appropriate treatment can extend to several weeks (6).

BPPV is usually a self-limiting condition, and the vertigo typically lasts for less than a minute, however, patients often experience debilitating symptoms. The impact on the quality of life of undiagnosed and untreated BPPV may be far from "benign," as patients with BPPV are at increased risk for falls and impairment in daily activities. As BPPV is more common in older individuals, the associated risks increase multifold (7).

BPPV is caused by the displacement of otoconial debris from the utricle to the semi-circular canals. The debris makes the canal sensitive to gravity (6) and by that, dizziness occurs during certain head movements that change the orientation of the head relative to the gravity vector. Clinical guideline statements for BPPV state that the positional tests for BPPV like the Dix-Hallpike (8) and Supine Roll tests are simple procedures to diagnose the presence and type of BPPV (9).

Despite its significant prevalence and health impact, considerable practice variations exist in managing BPPV across disciplines (10). Numerous randomized controlled trials demonstrated that canalith repositioning maneuvers (CRM) are highly effective in treating BPPV [10]. For each involved canal, the appropriate repositioning maneuver should be performed. For posterior canal BPPV, maneuvers like Epley (11) are recommended; for horizontal canal BPPV, maneuvers like the Roll (12) or forced prolonged positioning (9) are recommended. For anterior canal BPPV, the Yacovino (13) and modified Yacovino maneuver (14) are recommended.

Despite the established efficacy of the repositioning maneuvers, various studies confirmed their underuse (15,16,17), and only 10% of BPPV patients are treated with CRM (1,2). Furthermore, it is estimated that over 65% of patients with BPPV undergo potentially unnecessary diagnostic testing or therapeutic interventions (17). Early and effective treatment could significantly improve the quality of life, save repeated visits to the Primary Care Physician, and reduce medical costs due to unnecessary tests such as head CTs and referrals to specialists in tertiary care (15,16). Although BPPV may resolve spontaneously without treatment, up to 50% of cases may take longer than three months to

resolve. Therefore, the CRM is the preferred treatment option (18,19).

In literature, the reported success rate of the CRM to treat BPPV is high (50-89.9%) (16,17). However, these studies were mainly conducted in well-controlled settings in centres with expertise in BPPV. Therefore, the reported success rate of CRM's in literature might overestimate their success in routine clinical practice. After all, it is not unlikely that the CRM's are less effective in the hands of less experienced professionals. One of the reasons why CRM's might fail is the inability to identify the affected canal correctly, followed by successful repositioning of the debris. Regarding this latter point, accurate head angulation is desired to bring the affected canal aligned with gravity to facilitate the correct repositioning (20,21,22,23).

There is not much literature on studies which assess whether the maneuvers were appropriately used and accurately performed [7,16,17]. The aim of this study was to investigate the variability in head angulation during the canalith repositioning maneuvers (CRMs) to treat BPPV. It was hypothesized that obtained head angulations significantly varied between examiners and that a head mounted BPPV guidance system to measure head orientation, would significantly improve accuracy of head angulations during CRMs.

This study assessed how trained technicians performed the maneuvers. This was done by measuring the head angle at each step and comparing the difference between the angle achieved with the angle advised. This would shed more light on the variability of head positioning during the maneuvers.

Methods

Study design

This study was performed at the Vertigo and Ear Clinic, Jaipur, India. Twenty-five experienced examiners and 25 healthy volunteers (age 21-35 years) were recruited. Each examiner applied the Epley maneuver Chapter-8

twice in one volunteer: without and with the use visual feedback from a guidance system (details in supplementary material). The examiner performed the Epley maneuver during the first maneuver while the guidance system measured head orientation. However, the examiner was blinded to the results. During the second maneuver, the examiner performed the Epley maneuver while the guidance system measured head orientation, but it also provided visual feedback and instructions to the examiner about the head orientation. The head orientations at each step of the Epley maneuver, with and without the tracker, were measured and compared.

The study design included only the Epley maneuver of the right side to eliminate any confounding effects of side variability. The maneuver was always performed first without feedback from the tracking device to ensure that there was no learning effect from the device on the performance of the maneuver the second time (24).

Inclusion and exclusion criteria

The examiners included laboratory technicians with a minimum of 6 months of training in testing vestibular patients. In addition, the study included healthy volunteers with 1) no history of dizziness, vertigo, motion sickness, or migraine; 2) no restriction of head movements.

BPPV Guidance system

A guidance system for BPPV was developed by NeuroEquilibrium Diagnostic Systems Private Limited, Jaipur, India [see Supplementary materials, Figures 1-6, Video 1]. The objective of the guidance system was to measure head orientation and provide visual feedback and instructions to examiners during various maneuvers for BPPV.

Each step of the BPPV maneuver [in this study: the Epley maneuver] is displayed on a screen, using a 3D model of the human body [including the orientation of the inner ear]. The head position is also shown on the screen to provide accurate information to the examiner about the relative orientation of the inner ear. A headband with customChapter-8

made sensors [the "tracker"] measured head orientation. The tracker comprises a 9-axis absolute orientation sensor, integrating a triaxial 14bit accelerometer, a triaxial 16-bit gyroscope, and a triaxial geomagnetic sensor integrated with a microprocessor. The device is placed on the head with the patient in the initial position. "Align" button is pressed in the software which allows the device to know the initial position of patient's head. The device then self-calibrates.

The desired head position for each step of the BPPV maneuver is demonstrated by the 3D model on the screen of the guidance system. The examiner needs to precisely match the orientation of the patient's head with that of the 3D model at every step of the maneuver, with a tolerance of 40 peak to peak head angle. To keep a low two-sided tolerance level, 40 was chosen as the cut-off point. The examiner can only continue the maneuver if the appropriate head orientation is obtained. A green light is displayed once the predetermined 3D head orientation is reached. The software then displays the text instructions for the next step. In other words, the patient's head position needs to be matched with that of the 3D model at each step until the complete maneuver is successfully performed. The system is configured with a waiting period of 30 seconds between each step of the maneuver. This waiting period ensures that the debris reaches the desired position in the canal before proceeding to the next step. This waiting time can be modified by the examiner.

The steps and predetermined [desired] head orientations for the Epley maneuver of the right side included:

Starting position - Subject sitting on the examination table with face forward.

Step 1: Head is turned 45° to right.

Step 2: Subject taken to lying down position with head 30° below horizontal and head turned 45° to the right.

Step 3: Head turned 90° to the left with the head 30° below horizontal. Step 4: Head turned another 90° to the left. Step 5: Subject brought back to sitting position with face forward.

Angles of the head were measured in one dimension at predetermined angles of 45°, 30°, 90° and a further 90° at Steps 1-4. This was to ensure that the study design was simple and user-friendly.

Figure 1 shows the information displayed on the screen while performing an Epley maneuver of the right posterior semicircular canal in the starting position with face forward. On the left side of the screen, each step of the maneuver is displayed, together with the patient details. On the right side of the screen, the top view of the 3D model is seen. This view helps ensure the correct head orientation of the actual executed step. The center of the screen shows the three semicircular canals. The movement of these canals is synchronized with the head movement. This enables visualization of the orientation of the affected canal when the head is moved at the desired angle. Additionally, a timer at the center of the screen shows the time that the head should be held in that position. The examiner can use a button on the screen to restart or quit the maneuver.



Figure 1: Screen display of the steps of the Epley maneuver with the movement of the 3D model and respective labyrinth orientation

Figure 2 shows the instructions to turn the head by 45°. The yellow light shows the present head position, and the blue light indicates the target head position. The light becomes green when the subject reaches the desired head position.

In the next step, the subject is brought to the head hanging position with the head taken 30° below the horizontal (Figure 3). Once the subject's head matches the position of the 3D model, the next step is displayed.



Figure 2: Screen display of the first step of the Epley maneuver to turn head to the right by 45°

The next step is to turn the head by 90° to the left (Figure 4). This step brings the posterior canal into the vertical plane allowing the debris to be repositioned further ahead in the canal under the effect of gravity. In the next step, the subject is turned another 90° (Figure 5) and finally returned to the sitting position. As the recording has been done on healthy volunteers, the time between each step has been reduced to 5 seconds.



Figure 3: Screen display of the second step of the Epley maneuver to hyperextend the neck by 30°



Figure 4: Screen display of the third step of the Epley maneuver



Figure 5: Head is turned by another 90°

Figure 6 shows the guidance system and its placement on the head.



Figure 6: Guidance system placed on subject's head

Video 1 demonstrates how the tracking device guides the clinician during each step.



Video 1: Tracking device that guides the clinician during each step

In the present study, the Epley's maneuver was performed on healthy volunteers and the examiners held the head in that position for about 5 sec and then went to the next step. The videos in the supplementary materials show this short interval between steps to make the video more user-friendly. The final head angle at each step was measured.

Statistical Analysis

The head orientations achieved by the examiner at each step of the maneuver [measured by the tracker] were compared to the predetermined head orientations in two conditions – without and with visual feedback from the guidance system. The difference in angulations of each step and cumulatively of the procedure were calculated and statistically analysed. Descriptive statistics were performed with statistical software SPSS [IBM version 21] to calculate and compare the two means. The data was found to be not normally distributed on the Kolmogorov-Smirnov test. The Friedman and Mann-Whitney U tests were used to detect the differences between dependent and independent variables within and between groups pre- and postinterventions, respectively. The non-parametric Wilcoxon signed-rank test was used to find the differences among the groups before and after the intervention. Post hoc analysis with Wilcoxon signed-rank test was used to see whether significant differences occurred at 95% confidence intervals ($p \le 0.05$).

To find out the actual difference that occurred in each group postintervention, post hoc analysis with Wilcoxon signed-rank test was used. All results were considered significant at p<0.05.

Ethical considerations

All the study participants gave written informed consent for the study. No ethical committee approval was required as the study was conducted on healthy individuals, and the burden and risks of performing two Epley maneuvers were considered very low. (6,9)

Results

The head orientation achieved at each step of the maneuver was

compared to the predetermined head orientation in two conditions – without feedback from the guidance system and with feedback from the system. Figure 7 demonstrates that during each step of the Epley maneuver, the head orientation of the volunteers was significantly closer to the predetermined head orientation when using the guidance system as compared to without using the guidance system. Furthermore, head orientation between both conditions significantly differed for each step of the maneuver (step 1: Z = -2.222, p=0.026; step 2: Z = -2.044, p=0.041; step 3: Z = -2.769, p=0.006; step 4: Z = -2.705, p=0.007).

The width of the box plots also illustrates that by using the guidance system, much lower variabilities of head orientation were found for each step of the maneuver. For example, a 6-fold decrease in variability was demonstrated: with the guidance system +/- 3 to 4 degree of variability was seen at each step. However, without the guidance system, a variability of +/- 17 to 26 degrees was seen at step 1, +/- 19

to 20 degrees at step 2, +/- 10 to 29 degrees at step 3 and +/- 25 to 29 degrees at step 4 was seen.

The class of evidence in this study is Class IV.



Figure 7: Head orientation for each step of the Epley maneuver. Each set represents each step (Step 1, 2, 3 and 4) consecutively, without (blue boxes) and with (red boxes) using visual feedback of the guidance system (n=25 examiners). The dotted line represent the desired angulation at each step. The asterisk at step 2, 3 and 4 shows the different angulations obtained with and without the guidance system. The boxes represent the interquartile ranges, the top of the box denotes the upper quartile, the line passing through the box denotes the median quartile and the lower part of the box denotes the lower quartile. The upper and lower whiskers represent the extreme lines (values that vary outside the upper and the lower quartiles). Outliers are represented by blue dots. The asterisk inside the box represents the mean

Discussion

The aim of this study was to investigate the variability in head angulation during the canalith repositioning maneuvers (CRMs) to treat BPPV. It was hypothesized that obtained head angulations significantly varied between examiners and that a head mounted BPPV guidance system to measure head orientation, would significantly improve accuracy of head angulations during CRMs.

This study showed that trained examiners demonstrate a large variability

in head orientation (39-65°) during

the Epley maneuver. Furthermore, it was found that using a guidance system, which provides visual feedback of head orientation during BPPV maneuvers, significantly improves the accuracy of head orientation during the Epley maneuver. These are significant findings since previous literature suggests that correct head orientation might improve treatment efficacy (20,21,25,26,27). After all, patients with reduced neck mobility (leading to incorrect head orientation) have a higher failure rate of liberatory maneuvers [25,28].

Clinicians who do not perform CRMs in their routine practice have been shown to be reluctant to perform the repositioning maneuver in BPPV patients (18). This could be related to previous unpleasant experiences with performing the maneuvers or not being able to remember the steps of the maneuvers (28,29). The guidance system could help clinicians accurately perform repositioning maneuvers by providing a visual feedback system along with tracking the head position (22,23). In this way, the use of a guidance system might improve care for patients with BPPV. We also hypothesize that this guidance tool can also help physicians in emergency rooms in properly treating BPPV after a correct diagnosis is made (22,23).

Additionally, the guidance system could be used as a teaching tool for medical students and practitioners to learn how to perform the maneuver

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correctly. It could also be used as a tool to guide the paramedical staff at remote locations to carry out the BPPV maneuvers accurately.

Limitations

The BPPV Guidance tracker's position on the head, as presented here, is not calibrated relative to the orientation of the semi-circular canals in an individual patient. This could, in theory, be done for each individual patient using imaging techniques. But such a procedure is costly, timeconsuming, and not very practical in daily practice. Furthermore, the orientation of the semi-circular canals varies up to about 200 in humans (30). Despite this drawback of possible misalignment, the accuracy of maneuvering with the guidance system is well below that natural variance of canal orientation and, therefore, substantially allows a better angulation of the canals in the maneuvers in the general population. The movement of the debris as a function of time is based on a physics model describing the "standardised average" debris movement as a function of the canal orientation relative to gravity (20,22,26,27). The time taken for the debris to move to the most dependent position at each step of the maneuver depends on various factors like endolymph viscosity, friction, and debris size, which are not taken into account here. However, a waiting period of pre-determined time interval at each step of the maneuver would be sufficient to offset these variables.

This study has been performed on healthy volunteers. Further clinical trials should be done to validate the results.

Conclusion

This study demonstrated that the use of a guidance system that provides visual feedback on head orientation during BPPV maneuvers significantly improves the accuracy of head orientation during the Epley maneuver. This guidance system could be used as a clinical to improve the treatment efficacy of BPPV maneuvers.

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Discussion and valorisation

This thesis described new insights in diagnostic and therapeutic maneuvers for BPPV, which resulted from computer simulations of these maneuvers and investigating variability in maneuvers when performed by different examiners. The main findings included:

• Development of a 3D simulation model of the vestibular labyrinth was created for a more comprehensive understanding of BPPV (Chapter 3).

• Computer simulations of BPPV are able to provide a better understanding of otoconial movements within semicircular canals, during diagnostic and therapeutic maneuvers for BPPV (Chapter 4).

• The modified roll maneuver and Zuma maneuver might be effective treatment options for canalithiasis of the horizontal canal in all positions in the canal, while the Gufoni maneuver most likely mainly works well when the otolith debris is in the non-ampullary arm of the horizontal canal (Chapter 5).

• A new and simplified Yacovino maneuver might be an effective treatment option for anterior canal BPPV, while also reducing the risk of canal switch compared to the traditional Yacovino maneuver (Chapter 6).

• The sequence of diagnostic tests for BPPV influences the type of nystagmus obtained in horizontal canal BPPV (Chapter 7).

• The use of a guidance system that provides visual feedback on head orientation during BPPV maneuvers significantly improves the accuracy of head orientation during the Epley maneuver (Chapter 8).

These findings could have significant implications for routine clinical practice, as discussed below.

Emphasizing the importance of correctly performing therapeutic maneuvers

These simulations demonstrated the importance of correctly performing all therapeutic maneuvers. After all, it is imperative to wait at each step of a maneuver, to ensure that the debris reaches the most dependent position in the canal at each step. In addition, the simulations show that at each step of any maneuver, the affected canal should be in the plane of gravity to achieve optimum results.

Regarding the treatment of horizontal canal canalithiasis, the simulations showed that the 3600 roll maneuver should be started by turning the head to the affected side, and sequential 90° turns must be made to reposition debris in both the ampullary and non-ampullary arm of the horizontal canal.

Optimizing current therapeutic maneuvers

The simulations of the Epley and Semont maneuvers illustrated that increasing the head angulation as seen in the Semont's Plus maneuver, takes the debris further through the posterior canal in the second step. By crossing the apical curvature of the posterior canal, there is a much higher chance of the debris being reposited out of the canal leading to a successful maneuver. On the other hand, a reduction in the angle of Semont's maneuver could lead to the debris falling back to the ampullary end of the canal resulting in treatment failure. In the Semont's Plus maneuver, where the head angulation is increased by 30° in the side-lying position and a $180 + 30^\circ$ swing to the opposite side, there is a better chance of otolith debris reposition, allowing this to be a useful modification to the previously described Semont maneuver.

Regarding horizontal canal BPPV, it is important to raise the head by 30° during the maneuvers for the horizontal canal (practically done by placing a pillow under the patient's head) to align the horizontal canal

into the vertical plane.

Optimizing current diagnostic procedures

It might be considered to change the order of positional testing in BPPV. Previously, many studies described that the Dix-Hallpike test is the first positional test to be performed followed by the Supine roll test (1,2). However, these simulations illustrated that the order in which positional tests are performed can affect the results of the test as there is an "Observer effect". This means that performing the test itself can influence the results of the test. In the case of BPPV, the Dix-Hallpike test can cause displacement of the debris present in the horizontal canal, while the supine roll test does not displace the debris present in the posterior canal. Additionally, the supine head hanging test would displace debris present in the posterior, horizontal, and anterior canals. Therefore, these findings indicate that the supine roll test should be performed as the first positional test, followed by the Dix-Hallpike test for the posterior canal, and supine head hanging test for the anterior canal.

Regarding horizontal canal BPPV specifically, simulations of the supine roll test demonstrated that in the case of canalithiasis, the results also vary if the test is started from the right or left side. This could result in confusing and, often, misleading results. For the sake of uniformity in performing the positional tests, it was therefore advised that the tests should be started from the right side. Previously, various articles described findings of direction-fixed nystagmus seen on the supine roll test which were attributed to different causes like canalith jam (3,4). However, this thesis presents a simple explanation for the findings of direction-changing nystagmus, direction-fixed nystagmus (nystagmus beating to the same side on turning to the right and left), and unilateral nystagmus (nystagmus seen in only one position). Since these findings might have significant diagnostic implications (e.g. leading to different diagnoses), it would be advised to validate these findings with randomized clinical trials. The thesis also describes why though nystagmus was seen in the diagnostic supine roll test, it may not be seen on performing the treatment maneuver. The simulations show that the supine roll test itself may result in repositioning of the debris and hence, no nystagmus would be seen afterward. Also, we should be aware of the fact that when we move the head to a next position before all debris is settled down by gravity at the lowest point, the outcome of the test is influenced as well. This is especially important as the duration and speed of the head movements, when moving to the subsequent positions is not yet standardized in the clinic and still disputed among experts.

Identifying less and more optimal therapeutic maneuvers

The simulations presented in this thesis were also able to identify the less and more optimal therapeutic maneuvers for different types of BPPV. After all, it was demonstrated that the 2700 roll maneuver which starts by turning the patients from the center to the healthy side, does not reposition debris that is present near the ampulla of the horizontal canal. Furthermore, the Appiani modification for apogeotropic HC-BPPV was found to be an incomplete maneuver to properly reposition the otoconial debris. This could lead to treatment failure.

On the other hand, simulations demonstrated the Zuma maneuver to be effective for all types of horizontal canal BPPV (5), and the Gufoni maneuver for horizontal canal BPPV with debris located in the nonampullary arm (6). These results still need to be validated by clinical trials, to investigate whether these findings of the simulations are comparable to the results in patients of BPPV. If this would be the case, this would imply that more specific advice could be given for the treatment of different types of BPPV.

Findings of Anterior Canal BPPV Simulations

Anterior canal BPPV is a relatively rarer entity in comparison to posterior and horizontal canal BPPV. The supine head-hanging test is considered to be a more sensitive test for ac-BPPV than the Dix-Hallpike test as it acts in the sagittal plane and thus stimulates both anterior canals at the same time (10). Positional tests for posterior canal BPPV show a reversal of the nystagmus on bringing the patient back to the sitting position. The anterior canal is also vertically oriented, however, there is no reversal of the nystagmus in the supine head hanging test when the patient is brought back to the sitting position. Simulations show that the debris moves from the ampullary end through the canal to cross the apical curvature. When the patient is brought back to the sitting position, the debris continues to move further through the canal and hence the same nystagmus pattern continues without reversal of nystagmus.

Several repositioning maneuvers have been described for anterior canal BPPV like the reverse Epley and reverse Semont (11). However, these maneuvers require the recognition of the side of involvement for the anterior canal. The Yacovino maneuver for the anterior canal does not require the determination of the affected side (12). Simulations in Chapter 5 show that the Yacovino maneuver carries the risk of a "canal switch" of the debris, moving from the anterior to the posterior canal when the patient is taken to the chin-to-chest position. To avoid this complication of canal switch and also to simplify the procedure, a modified Yacovino maneuver has been described. In this modified maneuver, by omitting the step in which the head is taken to the chinto-chest position, the maneuver has been simplified and the risk of canal switch has been reduced.

BPPV Guidance System

The steps of various repositioning maneuvers have been described in many studies and their efficacy has been established in numerous randomized clinical trials (13,14,15,16). However, there are no studies on monitoring how the maneuvers are performed by clinicians. Chapter 7 describes the large variability in head angulation observed when Epley's maneuver is performed in healthy volunteers. This could adversely affect the results of treatment. A head-mounted guidance system that provides visual feedback to guide the clinician while performing the maneuvers has been shown to drastically reduce the variability in head angulations by sixfold.

The angular velocity and duration of each step in the various diagnostic and therapeutic maneuvers are also crucial for the displacement of debris in the canals. For example, if the head turns at the supine roll test are made fast after each other, not allowing the debris to descend to the lowest possible position, it can cause a fallback of the debris rather than movement further ahead in the canal. These factors are not standardized at all in the definition of the maneuvers and still subject of discussion worldwide in expert panels. The guidance system has an in-built waiting period at each step to make sure that each position is maintained for ample time.

The guidance system could also be used by clinicians who do not regularly perform the repositioning maneuvers for example in emergency departments and primary care centers. This kind of guidance system could also be used in other fields of medicine where head angulation is important for example for subarachnoid blocks and spinal anaesthesia.

Mechanical BPPV chairs are useful to perform the BPPV maneuvers in the standardized and reproducible exact plane and angle (17,18,19,20) avoiding intra- and inter-examiner variations. Clinical trials comparing the findings and results of the guidance system versus the mechanical chairs would help to understand if the guidance system can provide a simpler and cheaper alternative to the mechanical chairs in the treatment of BPPV. In the future, tracking devices may be miniaturized or linked with smartphones to increase availability and reduce costs.

Recording nystagmus during positional tests provides an opportunity to understand the pathophysiology of debris movement within the canal. Measuring slow phase velocity, peak velocity, decay time and graphically plotting the nystagmus could give further insights about the type of BPPV- canalolithiasis or cupulolithiasis, size of debris, variabilities in the position of debris within the canal, multichannel BPPV, etc. The incidence, presentation, and nystagmus of BPPV affecting the short arm of the semicircular canals are also not well-understood. The orientation of the cupula within the ampulla remains a significant unknown in the anatomy of the labyrinth. Its clinical significance in the understanding of cupulolithiasis – from the appropriate diagnostic test to the best method to dislodge the debris from the cupula and perform a successful repositioning remains a matter of debate. These studies could further our understanding of BPPV. Further studies are required on recurrent BPPV and its management.

Impact of this thesis

Scientific impact

This thesis provides a model of BPPV based on physics. This allows to visualize and quantify in 3D the movement of the debris and associated eye movements during diagnostic and liberatory maneuvers. The scientific impact is that various parameters that are expected to influence the debris movement and eye movements, like debris size and amount, multiple debris locations, precise angulation, angular velocity, timing of the different steps, the individual orientation (anatomy) of labyrints in the head, can now relatively easy be studied and visualized in detail. New maneuvers introduced in the literature can be easily verified and examined. Additionally, some findings of this thesis (based on the model), pave the way for future clinical studies: they should be verified in real-life settings.

Clinical impact

The BPPV model and visualization developed in this thesis, allow to optimize existing diagnostic and therapeutic manoevres, and allow development of more effective maneuvers. For example, based on this thesis, the order of testing (lateral canal first) should be changed to facilitate a higher detection rate of lateral canal BPPV. Furthermore, the existing Yacovino maneuver should be adjusted to facilitate maximum effect. It also explains certain types of eye movements obtained during clinical testing, which were previously not described (e.g. unidirectional nystagmus in lateral canal BPPV).

These findings also imply that, based on this thesis, new guidelines for optimal diagnosis and treatment of BPPV should be developed.

Societal and educational impact

The model clearly visualizes BPPV in a way that can easily be understood by the general lay audience, but also for students and all professionals that are involved in the management of BPPV. This can improve understanding of BPPV for a broad audience.

Commercial impact

It was shown in this thesis that a precise detection and analysis of eye movements is crucial for a correct diagnosis. It therefore supports the use of video eye trackers and especially supports the applied research to develop low-cost video eye trackers. Furthermore, it was shown that precise angulation of the head during a liberatory maneuver is only possible with a guidance system that provides visual feedback. This system should be incorporated in commercially available vestibular testing equipment.

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10

Summary

BPPV is amongst the most common causes of vertigo caused by migration of otoconial debris into the semicircular canals, rendering them sensitive to head motion. As a mechanical inner ear disorder, the movement of the debris stimulate the hair cells in the affected semicircular canal resulting in a feeling of spinning with generation of nystagmus. Chapter 2 describes the anatomy and physiology of the vestibular labyrinth clinically relevant to BPPV.

BPPV is treated by performing repositioning maneuvers to bring the otolith debris out of the involved canal back to the utricle. However, it is often difficult for the clinician to be able to visualize the threedimensional orientation of the head in relation to the semicircular canals to be able to understand how best to treat different kinds of BPPV. In view of this drawback, a 3D simulation model of the vestibular labyrinth was created for a more comprehensive understanding of BPPV. Chapter 3 discusses the steps of the development of this 3D model. The simulations provide a valuable and accurate representation of many aspects of the inner ear and serve as a powerful tool in enhancing our understanding and management of the balance disorders. The simulation model provides a useful tool to visualize the three-dimensional structure of the semicircular canals. It allows the viewer to see the effect of gravity on the debris present in all the canals and at different positions within the canals as well. Chapter 4 shows how the plane and angle at each step of the repositioning maneuver is important to make the treatment

a success or failure. Showing the example of Semont's maneuver in the form of a simulation allows the clinician to understand how the otolith crystals move at each step. The simulation of Semont's Plus maneuver which extends the head and neck by an additional 30°, allows the debris to move further through the posterior canal crossing the apical turn. This additional angulation has two advantages. First, it ensures that the debris does not fall back towards the ampulla. The Semont's maneuver is dependent on gravity and inertia to move the debris and hence requires a brisk swinging of the trunk to the opposite side. The Semont's Plus maneuver requires only the effect of gravity to move the debris and hence does not require a fast swinging. This is a distinct advantage in patients where fast movement is difficult like pregnant women, obesity, spinal problems, etc.

Different debris positions within the canal will generate different nystagmus patterns. Chapters 4 and 5 describe the different debris positions within the posterior and horizontal canal where BPPV will generate different kinds of nystagmus, for example, long arm posterior canal generates torsional upbeat nystagmus while non-ampullary arm posterior canal BPPV generates down beating nystagmus on the Dix-Hallpike test. The clinical implication of recognition of the nystagmus is to choose the maneuver best suited to reposition the crystals out of the canal.

Chapter 5 demonstrates the nystagmus generated in horizontal canal BPPV in the simulations by linking the canals with the oculomotor muscles in the software, following Ewald's Laws and the principles of gravity. Simulations of Roll maneuver and Zuma maneuver demonstrate that both these maneuvers are useful in repositioning of debris in canalithiasis involving the ampullary and non-ampullary arms. The Gufoni maneuver simulation showed successful repositioning of canalithiasis of the non-ampullary arm. However, the simulation of Gufoni maneuver for ampullary arm showed failure of repositioning. Simulation of Appiani

modification of Gufoni maneuver also showed incomplete repositioning of debris from the ampullary arm of the horizontal canal.

Anterior canal BPPV is less common due to the anti-gravity position of the canal. Chapter 6 shows simulations of diagnostic tests and treatment maneuvers for ac-BPPV. It is a common finding to see reversal of nystagmus when performing the Dix-Hallpike test when the patient is brought back to the sitting position. Simulations in Chapter 4 show that this is because of the otolith debris falling back towards the ampulla. In contrast to this finding of Dix-Hallpike test, the Supine Head hanging (SSH) test does not show reversal of nystagmus when the patient is brought back to the sitting position. The simulation of SSH shows that the debris moves in the same direction further through the anterior canal on coming back to the sitting position. This chapter also describes a modification of the Yacovino maneuver used to treat ac-BPPV making the maneuver simpler and also reducing the chance of canal switch. This modification omits the chin-to-chest position in the Yacovino maneuver and brings the patient back to the sitting position.

The Supine Roll test is considered to be the gold standard test for diagnosis of horizontal canal BPPV. Simulations show that this test has an 'Observer Effect' meaning that the actual test can influence the result of the test by causing movement of the debris from their original position. Chapter 7 shows that the order in which the test is performed, whether starting from the right or left, will have an impact on the type of nystagmus seen. Different kinds of nystagmus patterns seen on the supine roll test have been described in Chapter 7 along with simulations to show how the debris is being displaced. This allows the clinician to understand the pathophysiology of direction-changing, directionfixed and unilateral nystagmus. This chapter also extols the need for a standardized testing protocol for BPPV to enable global uniformity and comparability in results.

Maneuvers used for the treatment of BPPV are based on taking the head

into the plane of the involved semicircular canal and then moving the head in the direction to facilitate movement of the otolith debris out of the canal. Incorrectly performed maneuvers may reduce their efficacy. A guidance system to assist in performing repositioning maneuvers has been described in Chapter 8. The guidance system provides visual feedback to the clinician showing the actual head position and desired head position at each step of the maneuver. This would help in reducing variability in performance of the maneuvers and also help clinicians who do not treat BPPV routinely.

Though BPPV is such a common cause of dizziness, there are still many unknowns in our understanding disorder. Simulations have helped us understand BPPV in the three-dimensional space. The simulations can help in improving existing testing and treating maneuvers as well as help in development of new treatment options. 11

List of Publications

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This is a comprehensive e-book on all aspects of BPPV including VNG videos and graphs of various BPPV sub-types, animations of the pathophysiology and simulations of treatment maneuvers for better understanding.

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Curriculum Vitae

Anita Bhandari decided that she wanted to become a doctor at the early age of eight years. Excelling in studies throughout school, she then did her MBBS medical training at RNT Medical College, Udaipur. She pursued M.S(ENT) in Jaipur under the guidance of Prof. A.S.Bapna at SMS Medical College. She worked as Assistant Professor in ENT at her alma mater SMS Medical College and Hospital from 1997-2006, where she provided medical and surgical patient care. She was also actively involved in under- and post-graduate teaching. She worked on a UNICEF-funded project to evaluate and screen 5000 children in slum areas for hearing loss as Principal Investigator. In 2006, she did an observership training in Otology and Neurotology at Singapore General Hospital.

In 2016, she and her husband, Rajneesh, founded the company NeuroEquilibrium, which has now grown to become the largest chain of Vertigo and Dizziness Clinics globally. NeuroEquilibrium has indigenously developed a battery of equipment for vestibular assessment including VNG, DVA,CCG, Posturography, Rotary chair etc. She has seven Indian and three USA patents to her name.