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Original Paper

Vestibular Implants: 8 Years of Experience with Electrical Stimulation of the Vestibular Nerve in 11 Patients with Bilateral Vestibular Loss

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Key Words
Bilateral vestibular loss · Vestibular implant · Perception · Vestibulo-ocular reflex · Electrical stimulation

Abstract
Background: The concept of the vestibular implant is primarily to artificially restore the vestibular function in patients with a bilateral vestibular loss (BVL) by providing the central nervous system with motion information using electrical stimulation of the vestibular nerve. Our group initiated human trials about 10 years ago. ***Methods:*** Between 2007 and 2013, 11 patients with a BVL received a vestibular implant prototype providing electrodes to stimulate the ampullary branches of the vestibular nerve. Eye movements were recorded and analyzed to assess the effects of the electrical stimulation. Perception induced by electrical stimulation was documented. ***Results:*** Smooth, controlled eye movements were obtained in all patients showing that electrical stimulation successfully activated the vestibulo-ocular pathway. However, both the electrical dynamic range and the amplitude of the eye movements were variable from patient to patient. The axis of the response was consistent with the stimulated nerve branch in 17 out of the 24 tested electrodes. Furthermore, in at least 1 case, the elicited eye movements showed characteristics similar to those of compensatory eye movements observed during natural activities such as walking. Finally, diverse percepts were reported upon electrical stimulation (i.e., rotatory sensations, sound, tickling or pressure) with intensity increasing as the stimulation current increased. ***Conclusions:*** These results demonstrate that

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electrical stimulation is a safe and effective means to activate the vestibular system, even in a heterogeneous patient population with very different etiologies and disease durations. Successful tuning of this information could turn this vestibular implant prototype into a successful artificial balance organ.

Introduction

Bilateral loss of the vestibular function (BVL) has a dramatic impact on the quality of life. The affected patients complain predominantly of chronic imbalance and blurred vision in dynamic conditions [1, 2]. They fear to fall and frequently report having difficulties reading signs or recognizing faces when they are walking. Some even report feeling ashamed to be seen in public as others often think they are drunk. Moreover, due to multifocal cortical and thalamic projections of vestibular afferents, emotions, memory, cognitive abilities and personality can also be affected [3–5]. In most cases, a BVL cannot be compensated and sensory substitution is insufficient so that there is no or little spontaneous improvement to be expected in the long term [6]. As a consequence, BVL imposes a significant social and economic burden on patients and society [7]. Unfortunately, there currently is no evidence for an efficient treatment.

The concept of a vestibular implant to artificially restore the vestibular function is similar to that of cochlear implants, which have a proven track record for hearing rehabilitation in cases of profound deafness. Briefly, in a vestibular implant, head motion is captured with motion sensors (i.e., gyroscopes) and transformed to a pattern of electrical currents by an external processor. This information is then wirelessly transmitted to an implanted stimulator that incorporates vestibular electrodes. Electrical stimulation delivered through these vestibular electrodes would trigger action potentials in the vestibular nerve that, in theory, would be interpreted by the central nervous system as head motion, ultimately allowing the 'artificial' restoration of the vestibular function.

Intensive efforts towards the development of a vestibular implant for clinical applications have been undertaken during the past decade [8]. Devices with single- or multichannel independent vestibular arrays have been designed and/or manufactured [9–13]. Different motion sensor fixation and signal processing strategies have been proposed, leading to the recent filing of several patents [14–18]. Finally, several animal and human studies have established the feasibility of this concept. Electrical stimulation was identified as an effective means for activating the vestibular system in animals already in the 1960s [19, 20]. Most recent animal research efforts have concentrated on meticulously investigating the effects of electrical stimulation parameters on vestibular responses [21], focusing mainly on vestibulo-ocular responses [22–34], but also on orientation percepts and postural responses [35–37]. In humans, extralabyrinthine and intralabyrinthine surgical routes to the lateral (LAN), posterior (PAN) and superior (SAN) ampullary branches of the vestibular nerve have been described and validated in peroperative stimulation trials [38–43]. Our group has reported on the results of the first chronic implantations of a vestibular implant prototype in human subjects [44], followed by a group at the University of Washington [45]. Our most recent results demonstrated that it is possible to elicit an artificial, motion-controlled vestibulo-ocular reflex in implanted patients [46]. Postural responses to electrical stimulation have also been reported in human subjects [47].

Our research group has participated in vestibular implant development for over 10 years. Today, we have a unique pool of 11 BVL patients implanted with a vestibular implant prototype. In this paper, we report on our main results, gathered over a period of 8 years.

Table 1. Demographics and implant details for each patient

Patient	Sex	Hearing loss	Etiology	Onset	Age at implant, years	Implant year	Implanted side	Vestibular electrodes	Surgical approach
S1	M	B	idiopathic	progressive	68	2007	left	PAN	EL
S2	M	B	congenital/idiopathic	progressive	34	2008	right	PAN	EL
S3	M	B	congenital/idiopathic	progressive	46	2008	left	PAN	EL
S4	M	B	Menière's disease	progressive	71	2011	left	PAN	EL
S5	M	U	traumatic	acute (<1 year ago)	63	2012	right	PAN LAN	EL
S6	F	B	mastoidectomy (L) traumatic (R)	acute (<1 year ago)	67	2013	left	PAN LAN SAN	IL
S7	F	U	meningitis	acute (47 years ago)	48	2012	right	PAN LAN SAN	IL
S8	M	B	DFNA9	progressive	67	2012	left	PAN LAN SAN	IL
S9	F	B	DFNA9	progressive	68	2013	left	PAN LAN SAN	IL
S10	M	B	DFNA9	progressive	66	2013	left	PAN LAN SAN	IL
S11	M	B	DFNA9	progressive	64	2013	left	PAN LAN SAN	IL

B = Bilateral; U = unilateral; EL = extralabyrinthine; IL = intralabyrinthine.

Materials and Methods

Patients and Surgery

Eleven patients with bilateral or unilateral deafness (3 females and 8 males, mean age at implantation 60.2 years, range 34–71 years) and concomitant BVL were recruited between 2007 and 2013 at the Service of Otorhinolaryngology, Head and Neck Surgery, Department of Clinical Neurosciences, Geneva University Hospital in Switzerland and at the Division of Balance Disorders of the Maastricht University Medical Centre in the Netherlands. The demographics of the patient population are presented in table 1. They all fulfilled 3 inclusion criteria: (1) mean peak slow-phase velocity of ≤5°/s in bilateral bithermal caloric irrigations, (2) pathological Head Impulse Test for all 6 horizontal and vertical canals, and (3) low (<0.2) or no gain in rotatory chair tests. Standard videonystagmography and electronystagmography were used for vestibular testing. Bilateral bithermal (30 and 44°C) caloric irrigations were performed by highly experienced technicians in standard conditions. Rotatory chair tests consisted of standard clinical horizontal torsion swing tests (0.05–0.1 Hz, ω_{max} = 60°/s). The Head Impulse Test was performed with the Video Head Impulse Test of Ulmer (Synapsis©, Marseille, France), the EyeSeeCam Video Head Impulse Test (EyeSeeCam VOG©, Munich, Germany) and/or the ICS Impulse (Otometrics, Denmark).

The patients received a custom-modified cochlear implant (MED-EL, Innsbruck, Austria) with 1, 2 or 3 vestibular electrodes derived from the main cochlear array (fig. 1). A minimum of 9 electrodes was thus left for the cochlear stimulation, which should not jeopardize the auditory outcome [48].

In 5 patients (S1–S5), an extralabyrinthine transmeatal surgical approach was performed [38, 41]. The PAN (S1–S5) and the LAN (only S5) were exposed. In these patients (except S1), this part of the surgery was

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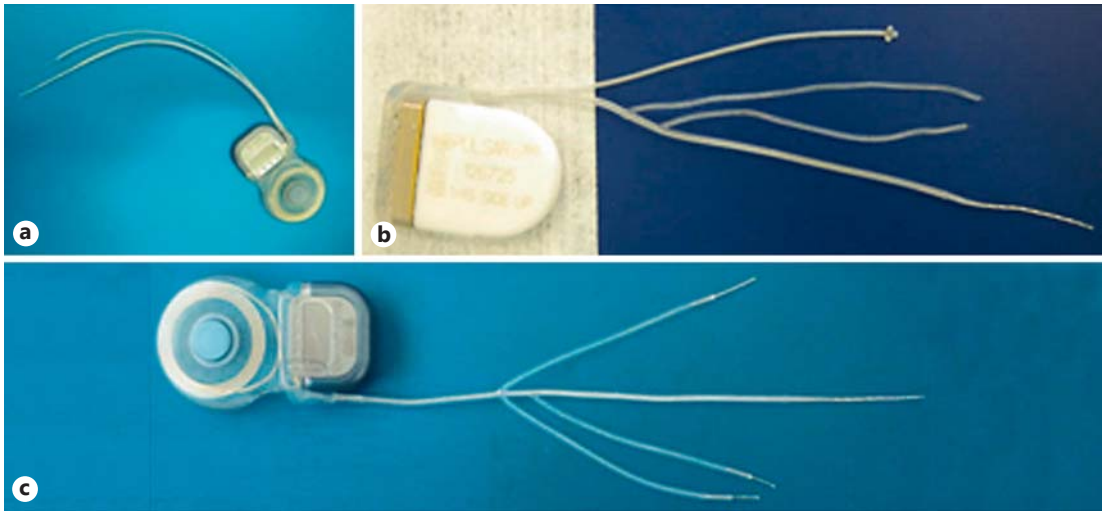

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Fig. 1. The three generations of vestibular implant prototypes developed in collaboration with MED-EL (Innsbruck, Austria) based on existing cochlear implant technology. A standard cochlear implant was customized by removing 1–3 electrodes from the cochlear array. Each of these 'vestibular' electrodes was located on the distal tip of separate leads to allow implantation in the posterior ampullary nerve (extralabyrinthine approach, **a**), in the posterior and lateral ampullary nerves (extralabyrinthine approach, **b**), or in the ampullae of the posterior, lateral, and superior semicircular canals (intralabyrinthine approach, **c**).

done under local anesthesia, and a probe electrode (125 μm diameter, 90% platinium-10% iridium Teflon-coated wire; MicroProbes for Life Science, Gaithersburg, Md., USA) was used to perform acute peroperative electrical stimulation. The depth and direction of drilling was adjusted following the observation of nystagmic responses obtained upon electrical stimulation. Once the optimum electrode position was found, general anesthesia was induced and the custom-modified device was implanted using a conventional retroauricular approach with a regular mastoidectomy, a posterior tympanotomy and a cochleostomy. The cochlear array was inserted into the cochlea and the vestibular electrodes were put in contact with the PAN (and LAN in S5) and secured with fascia from the temporal muscle and/or glass ionomer (Ketac, 3M, Saint Louis, Minn., USA).

In 6 patients (S6–S11), an intralabyrinthine approach was used to put 1 electrode in each ampulla [43]. The entire procedure is performed under general anesthesia. Briefly, this approach consists of a regular mastoidectomy, a posterior tympanotomy and a cochleostomy. The 3 semicircular canals are blue-lined and an inframillimetric 'canalotomy' is performed close to each ampulla. Electrodes are then inserted into each ampulla. At this stage, the patient is kept under intravenous remifentanil only, allowing to maintain general anesthesia while preserving the slow phase of the vestibulo-ocular reflex (e.g., tonic eye deviation). Peroperative electrical stimulation delivered via the vestibular electrodes is performed and the direction of the resulting tonic eye deviation is used to adjust the electrode position. Finally, electrodes are secured with hydroxylapatite bone cement (Otomimix, Walter Lorenz Surgical, Jacksonville, Fla., USA) and fibrin sealant (Tissucol, Baxter International Inc., Deerfield, Ill., USA), or with fascia from the temporal muscle.

Device activation took place no earlier than 4 weeks postoperatively, when healing of the surgery site was assumed to be complete. For simplicity purposes, from now on, we will refer to PAN, LAN and SAN for electrical stimulation delivered with each of the vestibular electrodes.

Electrical Stimulation

The setup for the electrical stimulation of the PAN, LAN and SAN is composed of a desktop computer that allows customization of the stimulation parameters (current intensity, pulse rate, phase width, modulation depth and modulation frequency). The computer communicates this information to the implanted stimulator via the manufacturer's research interface Board (RIB II, MED-EL) and the system's antenna.

Cochlear electrodes were always switched off during the experimental procedure. Stimulation was delivered to each electrode separately, and consisted of trains of charge-balanced, cathodic-first, biphasic pulses (400 μs/phase) presented at 200 pulses/s. During the device activation, the current amplitude was incremented by steps of a maximum of 50 μA (lowered to 25–10 μA if necessary) to minimize patient discomfort. Vestibular threshold was determined as the first (lowest) level of electrical current where the first vestibular symptom was observed (e.g., a change in nystagmus slow-phase velocity >2°/s) or reported (e.g., 'I feel like turning'). Particular attention was given to the first reported perception. Then stimulation was again increased by 10- to 25-μA steps until the upper comfortable level (e.g., occurrence of pain or facial nerve stimulation) was reached. The dynamic range was determined as the current range from the vestibular threshold up to the upper comfortable level [44].

The next step consisted of characterizing the eye movements that could be elicited by electrical stimulation delivered through each electrode (single-electrode stimulation). A 'baseline' stimulation (constant-amplitude electrical stimulation) was given at an amplitude arbitrarily chosen in the middle of the dynamic range. Once patients were adapted to this 'baseline' stimulation [44], the amplitude of the stimulus was modulated using a sinusoidal signal with a frequency of 3 Hz and a modulation depth corresponding to 75% of each patient's dynamic range. At the end of the experiments, 'baseline' stimulation was gradually decreased to zero.

Eye Movement Recording and Analysis

Two-dimensional eye-in-head angular position was recorded using a fast monocular 2D video oculography system (EyeSeeCam VOG). Ideally, 3D binocular movements should be reported [49]. However, we decided to use 2D video oculography for several reasons. First, although the search coil technique is considered as the gold standard for 3D ocular recording [50], it is invasive and is generally not well tolerated for use longer than 20–30 min; therefore, we did not consider it acceptable to add this burden to our test patients who had to undergo long, repeated testing sessions. Second, search coil measurements require a relative complex infrastructure consisting of a cubic structure (about 1 m^3) incorporating the 3D coils by which the magnetic field is generated. For accurate measurements, the patient's head must stay in the linear area (center) of this magnetic field. This is a major drawback as our future goal is to test patients at least partly moving freely in their environment. Moreover, previous studies have demonstrated that 2D analysis of eye movements is sufficient to assess the vestibulo-ocular reflex during natural activities [51]. Third, several portable, light-weight, high-speed, infrared monocular video oculography systems, incorporating motion sensors have recently been developed, providing accurate measurements of 2D eye movements and 6D head movement [52, 53], but the detection of the eye torsion (3rd dimension) by video eye trackers is still more troublesome, less reliable and less accurate. Therefore, being aware of its limitations, we considered it acceptable to use monocular 2D video oculography as a first approach. All eye movement recordings were done in darkness with patients sitting in an upright position.

A segment of 10 cycles was analyzed for each experimental trial. Eye position data were first filtered at 30 Hz with a low-pass moving average filter (zero-phase shift). Eye velocity and acceleration were then obtained via the first and second derivatives of the eye position. Blinks and quick eye movements (e.g., saccades and nystagmus quick phases) were detected as segments where eye acceleration was >1,000°/s. These segments were removed from the data and were not replaced by interpolated values (fig. 2a).

Peak horizontal and vertical velocity (respectively, $PV_{horizontal}$ and $PV_{vertical}$) were estimated using best-fit frequency-fixed sinusoids (fig. 2b). Total peak velocity was then computed as the vector norm of these 2D components:

$$\left(\sqrt{PV_{horizontal}{}^2 + PV_{vertical}{}^2}\right).$$

The axis of eye movements (angle with respect to the horizontal) was computed as:

$$tan^{-1}\left(\frac{PV_{vertical}}{PV_{horizontal}}\right).$$

Eye movements with an angle >45° were considered as predominantly vertical and those with an angle <45° as predominantly horizontal. Finally, asymmetry is presented using the index

$$\frac{PV_E - PV_I}{PV_E + PV_I},$$

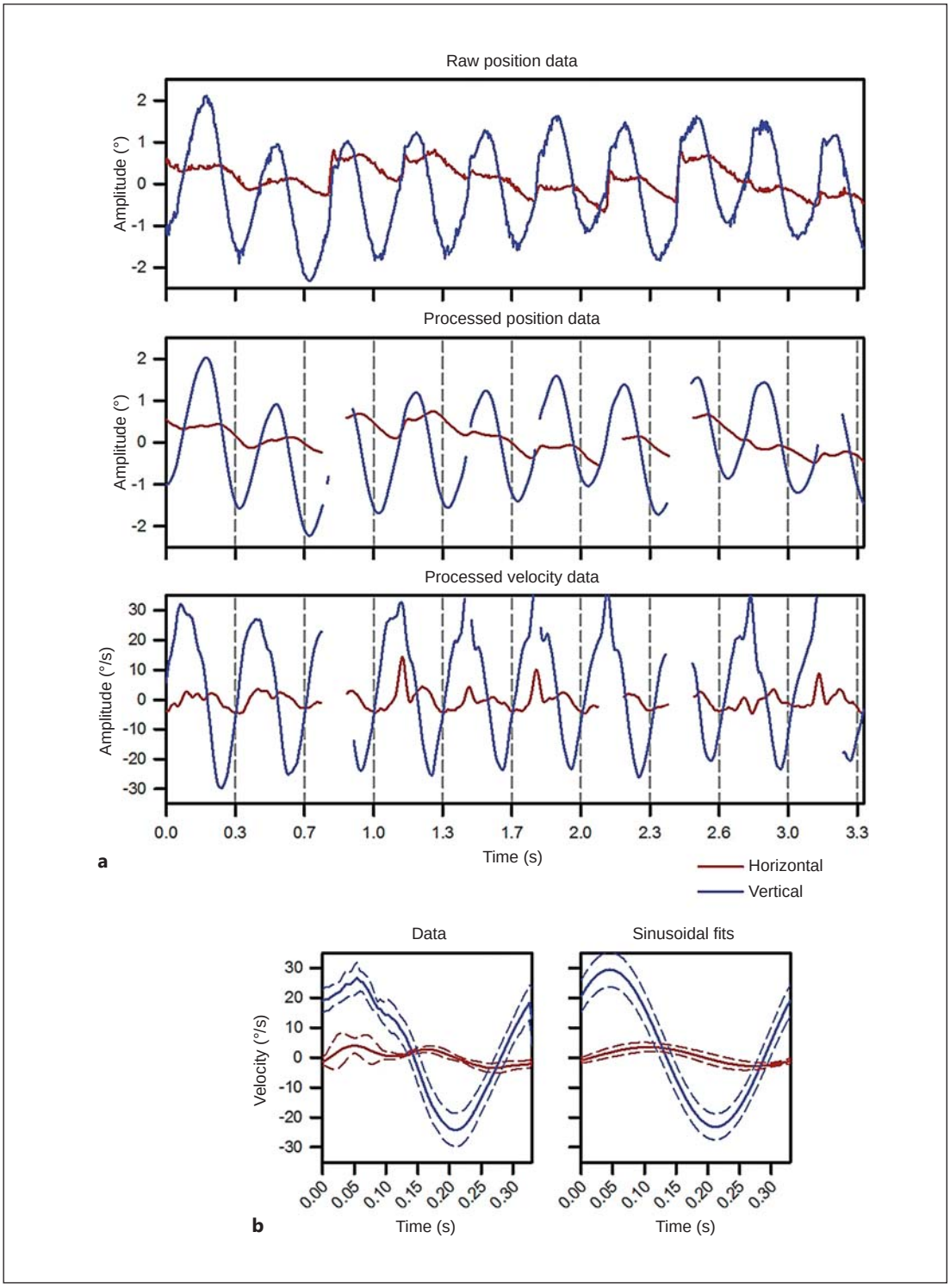

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Fig. 2. Illustration of eye movement data processing. The panels present eye movement data tracings for patient S7, gathered during the amplitude modulation experiments (frequency 3 Hz, modulation strength corresponding to 75% of the patient's dynamic range). **a** Three steps are illustrated: raw eye position (e.g., before any processing was performed), processed eye position data (e.g., eye position data after low-pass filtering and after blinks and quick eye movements >1,000°/s had been removed), and processed eye velocity data (e.g., obtained from the derivative of the processed eye position data). **b** Average cycle data ± standard deviation (left) and their corresponding sinusoidal fits (right).

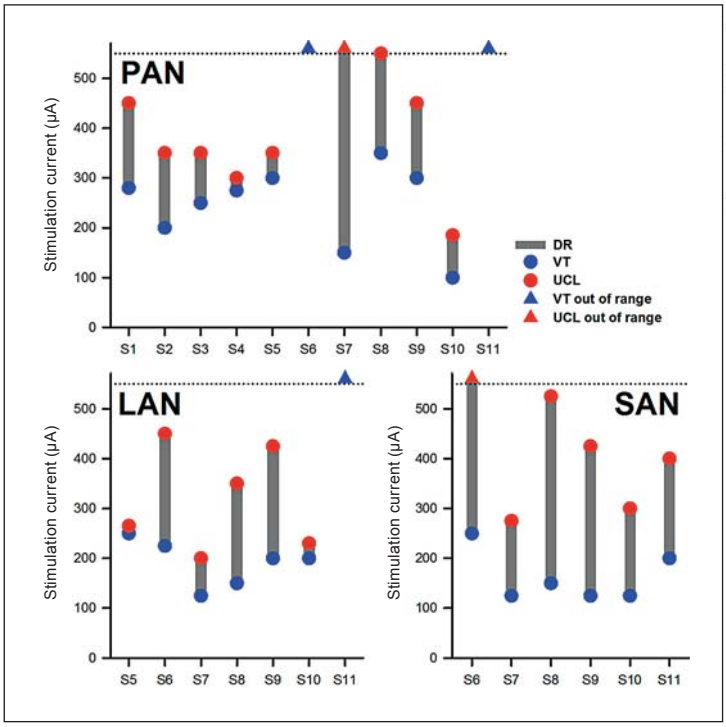

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Fig. 3. Vestibular thresholds (VT – blue circles), upper comfortable level (UCL – red circles) and corresponding dynamic range (DR – gray columns) are shown. Twenty-one out of the 24 available electrodes were responsive, and a dynamic range could be established. No response was obtained with 3 electrodes (blue triangles), even at the highest current tested (550 μA, dotted lines in each panel). In 2 electrodes, no UCL could be determined, even at 550 μA (red triangles). Note that in the case of the LAN electrode of subject S5, both the VT and the UCL were at the same current level (250 μA) so the blue and red circles had to be slightly offset for visibility. For colors see online version.

where PV_E and PV_I stand for the excitatory and inhibitory peak of the sinusoidal eye movement, respectively (i.e., away from and towards the implanted ear). These excitatory/inhibitory peak velocities were calculated using best fits to stimulus half-cycles (e.g., only positive or only negative), similar to previous studies [31, 46].

Individual patient results did not always follow a normal distribution; therefore, results are reported as median values (25th–75th percentiles). Mean results across patients followed a normal distribution (Shapiro-Wilk $p > 0.05$) and are therefore presented as mean values (± standard deviation).

Ethics Considerations

Experiments were designed and conducted in accordance with the 1964 Declaration of Helsinki. Local Ethics Committees of the Geneva University Hospitals (NAC 11-080) and of the Maastricht University Medical Centre (NL36777.068.11/METC 11-2-031) approved this experimental protocol. All participants gave their informed consent prior their inclusion in the study.

Results

A total of 24 vestibular electrodes were available for electrical stimulation in 11 patients. At the time of writing this paper, the longest follow-up period was 8 years (patient S1, implantation in July 2007), and the shortest was 2 years (S10 and S11, implantation in July 2013). No complications related to the surgery or to the experimental procedure were reported.

Measured Dynamic Range

A vestibular threshold could be determined in 21 of the 24 available electrodes (blue circles in fig. 3). In 19 of these electrodes, the upper comfortable level corresponded to facial nerve stimulation (red circles in fig. 3). In 2 electrodes, no upper comfortable level could be determined even at the highest current amplitude tested (550 μA; red triangles in fig. 3). The dynamic range was highly variable across patients and across electrodes (gray columns in fig. 3). It was null for 1 electrode. In 3 electrodes, no vestibular reaction was

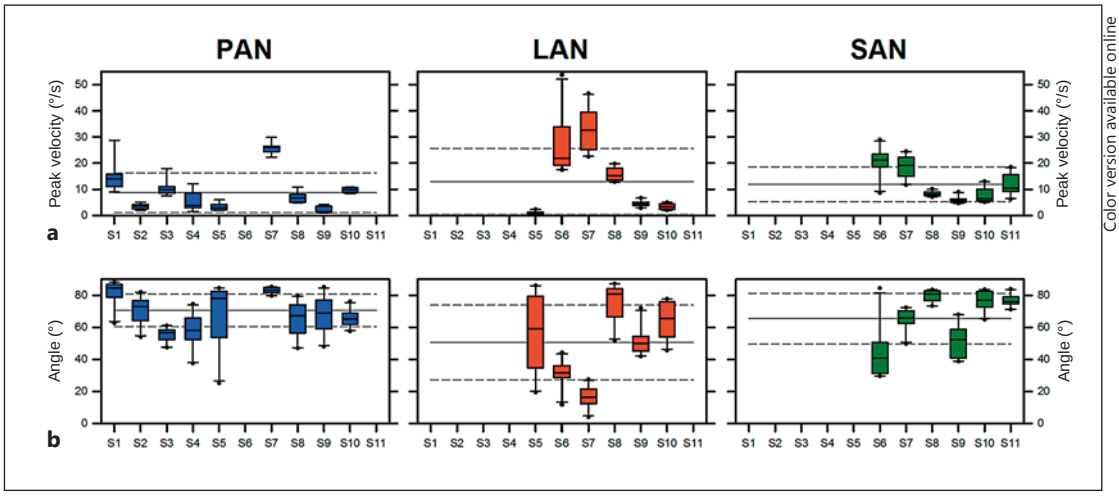

Fig. 4. Main characteristics of electrically evoked eye movement. Each individual panel shows individual data for a given electrode (PAN: first column, blue box plots; LAN: middle column, red box plots; SAN: right column, green box plots). Box plots indicate median values, 25th and 75th percentile values (colored box), 10th and 90th percentile values (error bars), and 5th and 95th percentile values (black circles). Mean values across patients, per electrode, are presented as gray solid lines (± standard deviation, gray dashed lines). **a** Total peak velocity. **b** Axis (angle with respect to the horizontal plane) of the elicited eye movements, calculated over 10 consecutive cycles. For colors see online version.

observed nor reported, even at the highest stimulation currents tested (550 μA; blue triangles in fig. 3).

Electrically Elicited Eye Movements

The main characteristics of the electrically elicited eye movements (total peak velocity and axis) are presented in figure 4. The largest eye movements per electrode were observed in patient S7 for PAN (26°/s; 24.4–26.5°/s) and LAN (32.7°/s; 25.2–39.4°/s) and in patient S6 for SAN (21.3°/s; 18.5–23.4°/s). Consistent with the very variable dynamic ranges measured, the range of eye velocities was also very variable. Mean peak velocities per electrode across patients were 8.7 ± 7.6°/s for PAN (n = 11), 13 ± 12.5°/s for LAN (n = 6), and 11.9 ± 6.6°/s for SAN (n = 5).

As expected from previous experiments [39, 42], stimulation via 15 out of the 16 PAN and SAN electrodes resulted in eye movements with a predominantly vertical component. The mean angle for PAN stimulation was 70.6 ± 10° and of 65.4 ± 15.8° for SAN stimulation. Note, however, that for 1 SAN electrode, the angle was predominantly horizontal (S6: 40.8°; 31.1–50.5°). In contrast, stimulation of LAN electrodes resulted in a larger misalignment from the expected angle. The mean angle for LAN stimulation was 50.6 ± 23.3°; only 2 out of the 6 LAN electrodes elicited eye movements predominantly in the horizontal plane (S6: 31.7°, 28.5–36°; S7: 16.5°, 12.4–21.5°).

The asymmetry index of the responses is presented in figure 5. The most symmetrical responses were observed with PAN stimulation (0.04 ± 0.07). SAN stimulation (0.08 ± 0.15) and LAN stimulation (0.14 ± 0.11) showed a slightly higher asymmetry index. The less symmetrical responses per electrode were observed in patient S3 for PAN stimulation (0.15, 0.01–0.19), in patient S5 for LAN stimulation (0.34, 0.22–0.55), and in patient S10 for SAN stimulation (0.20, –0.08 to 0.24).

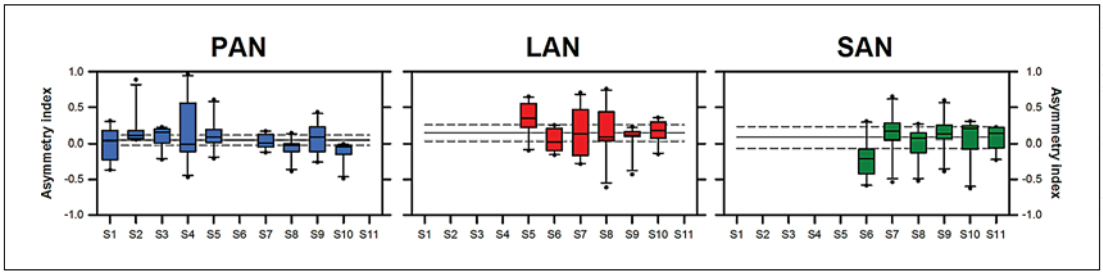

Fig. 5. Asymmetry of the eye movements elicited via electrical stimulation of the PAN (left panel, blue box plots), the LAN (middle panel, red box plots), and the SAN (right panel, green box plots). Box plots indicate median values, 25th and 75th percentile values (colored box), 10th and 90th percentile values (error bars), and 5th and 95th percentile values (black circles). Mean values across patients, per electrode, are presented as gray solid lines (± standard deviation, gray dashed lines). This index was calculated using best fits to excitatory/inhibitory stimulus half cycles (see Materials and Methods). For colors see online version.

Table 2. First-reported sensation upon stimulation of each of the vestibular electrodes

	PAN	SAN	LAN
S1	sound, vertigo	n.a.	n.a.
S2	sound	n.a.	n.a.
S3	sound	n.a.	n.a.
S4	sound	n.a.	n.a.
S5	sound	n.a.	needle in the ear
S6	none	rotatory sensation	rotatory sensation
S7	eyes moving	eyes moving, 'tickling' sensation	ear 'tickling'
S8	'tickling' sensation	'tickling' sensation	'tickling' sensation
S9	vibration, sound	vibration, sound	'current-flow' sensation
S10	rotatory sensation	sound	sound
S11	none	pressure	pressure

n.a. = Not applicable.

Evoked Percepts

The first-reported perceptions for each electrode are summarized in table 2. During PAN stimulation, sound was most frequently the first reported perception (6 out of 9). For LAN and SAN stimulation, diverse perceptions were reported, such as rotatory sensation, sound, tickling or pressure. The intensity of the perception reported for each electrode was also very variable. In general, the intensity of the reported percepts increased as the stimulation current increased. However, it was rarely consistent with evoked ocular responses.

Discussion

The results presented here demonstrate that the concept of a unilateral vestibular implant is feasible in human patients. Motion information provided by the vestibular system is artificially mimicked by delivering a constant 'baseline' stimulation, which can be up- or downmodulated to evoke vestibulo-ocular responses. This allowed eliciting controlled eye movements in the 11 patients suffering from a BVL who received a vestibular implant. A

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particularly promising outcome of this study is that eye movements could be successfully evoked in a heterogeneous group of patients regarding the etiology of the deficit or the duration of the disease. This is particularly relevant since a significant concern was that vestibular dendrites could degenerate with time, precluding electrical stimulation of the vestibular nerve after long periods of sensory deprivation.

Efficacy of Electrical Stimulation

The efficacy of stimulation was very different across patients and across electrodes. Eye movements evoked by electrical stimulation of an ampullary nerve were expected to have an axis orthogonal to the plane of the corresponding semicircular canal. This was optimally achieved for PAN, LAN and SAN stimulation in 1 patient (S7). Moreover, in this case, mean peak eye velocities were 26, 32.7, and 19.1°/s for PAN, LAN, and SAN stimulation, respectively. This is a very promising finding, since in this case, evoked eye movements are within the range of compensatory eye movements previously reported during important dynamic daily activities, such as walking or running (20–30°/s) [51, 54]. Group results, however, showed some misalignment and lower mean peak eye velocities. Animal research reports suggest that adaptive processes could help improve the overall characteristics of the artificial eye movements in the long term [26, 30, 33]. Furthermore, particular stimulation strategies (e.g., incorporation of precompensatory 3D coordinate transformations [29], comodulation of the amplitude and pulse rate of the stimulation [32] have also been suggested as possible alternatives to improve the characteristics of the electrically evoked vestibulo-ocular response.

It was expected that only very small eye movements could be elicited via electrodes with a narrow dynamic range (e.g., LAN responses for S10). However, surprisingly, eye movement responses were minimal in some cases with a relatively large dynamic range (e.g., LAN stimulation for S9). Despite this, patients still reported strong sensations related to vestibular stimulation (e.g., being pulled to the side or rotatory sensations). Such a dissociation between eye movement amplitude and sensation has also been reported by the team of the University of Washington [55]. This suggests that electrical stimulation might be activating vestibular structures other than those involved in the generation of the vestibulo-ocular reflex. This finding deserves further investigation.

Three out of the 24 implanted electrodes were unresponsive. Some hypotheses can be put forward. In subject S6, the PAN electrode was unresponsive. A CT scan revealed an intraotic fracture line crossing the posterior ampulla and fibrosis filling the canal was found during surgery. Traumatic section or severe posttraumatic degeneration of the dendrites as well as fibrosis of the ampulla might drastically reduce the excitability of the vestibular nerve. The other 2 unresponsive electrodes were those implanted in the PAN and LAN of patient S11. This patient was suffering from DFNA9, an autosomal dominant nonsyndromic congenital disease due to COCH gene mutations [56]. This adult-onset disorder is characterized by a progressive bilateral loss of cochlear and vestibular function. Severe loss of cochleovestibular nerve dendrite is a characteristic histological feature of this disease [57]. This might preclude the success of intralabyrinthine electrical stimulation, due to the distance between the ampulla and the Scarpa ganglion. This hypothesis is reinforced by the fact that 7 out of the 9 vestibular electrodes of BVL patients diagnosed with DFNA9 (S9–S11) showed the smallest responses.

Finally, another factor that can significantly influence the effectiveness of electrical stimulation is optimal positioning of stimulating electrodes. Indeed, it has been observed that minimal position changes of the electrodes resulted in drastic changes of nystagmic responses [39]. So far, peroperative stimulation under local and general anesthesia was performed to improve the electrode positioning. Peroperative vestibular electrically evoked action potentials could be an additional tool to improve the electrode positioning in the future [58].

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Perception Evoked via Electrical Stimulation

Patients were actively requested to describe what they felt during the stimulation sessions. After unsuccessfully attempting to categorize the percepts described by the first implanted patients, raw description of any perception was documented. As can be seen in the results, described percepts were quite heterogeneous. This could be at least partially explained by the concomitant, spurious activation of nonvestibular neural structures due to current spread (i.e. the cochlear nerve, the branches of the glossopharyngeal nerve, and, to some extent, possibly also the vagal and the facial nerves).

Extralabyrinthine versus Intralabyrinthine Electrode Placement

In 5 patients, electrodes (n = 6) were implanted close to vestibular nerve branches (extralabyrinthine approach), while in 6 patients, electrodes (n = 18) were implanted in the ampullae (intralabyrinthine approach). The first approach was initially chosen in the perspective of reducing the risk of inducing hearing loss (estimated around 4% as observed by Gacek and Gacek [59] in 252 neurectomies of the PAN for intractable benign paroxysmal positional vertigo). In contrast, the intralabyrinthine approach might allow better selectivity of the stimulation but the risk of inducing hearing loss in this case is still unclear. Results of animal studies are controversial: some demonstrate that intralabyrinthine electrode insertion with or without electrical stimulation impairs hearing in most of the cases [60–62], while others show that it is possible to preserve auditory and vestibular function [63]. The results in human patients are not very encouraging in this respect. The group at the University of Washington has implanted 4 patients diagnosed with an intractable Menière's disease. They all had some preoperative residual vestibular and hearing function. An intralabyrinthine approach was used and postoperative hearing (reported only for 1 out of the 4 implanted patients) was almost totally lost [45, 47]. Nevertheless, there are reports showing that hearing is preserved after plugging of a dehiscent superior semicircular canal, plugging of the posterior superior semicircular canal for intractable benign paroxysmal positional vertigo [64, 65], and plugging of the lateral superior semicircular canal in patients with severe Menière's disease [66]. Since most patients suffering from a BVL have normal or near-normal hearing, it is crucial that the incidence of hearing loss upon vestibular implant surgery is thoroughly investigated and reported in the near future.

Additional Considerations

In the natural vestibular system, motion is coded by modulation of the discharge rate of the spontaneous 'baseline' neural activity (i.e., number of spikes per second) of the vestibular nerve. For the lateral semicircular canal, the discharge rate increases with ampullopetal movements of the endolymph and decreases with movement of opposite direction. For example, for the horizontal semicircular canal, a head rotation in the direction of the canal (i.e., rightwards for the right ear) will result in an increase in the neuronal discharge rate. Conversely, a horizontal head rotation in a direction opposite to the canal (i.e., leftwards for the right ear) will result in a decrease in the discharge rate. The reverse is true for the vertical semicircular canals [67]. In light of this physiological motion modulation scheme, discharge rate modulation has often been chosen as the stimulation method [29, 68]. However, in our experiments, eye movements were produced using amplitude modulation, not discharge rate modulation. This choice was motivated in a previous observation that in humans, discharge rate modulation resulted in smaller eye movements than amplitude modulation [44]. Furthermore, our prototype vestibular implants are modified cochlear implants, which are designed to use amplitude modulation.

Consistent with previous data [26, 31, 46], some asymmetry was observed in the responses obtained upon stimulation with the majority of the electrodes. It is still unclear

whether lack of symmetry will turn out to be a clinically relevant issue that will fundamentally limit the patient's benefit with the system. Furthermore, the vestibular system itself might be able to adapt to the electrical stimulus and improve the characteristics of the response with time [26, 30, 33]. The use of different signal processing strategies (e.g., logarithmic vs. simple linear transfer functions) could also provide a potential solution.

Conclusion

These results confirm the feasibility of the concept of a vestibular implant for human use. We observed no medical complications related to the surgery or the device. Furthermore, the implant was successful at eliciting vestibulo-ocular responses even after long periods of implantation and in a very heterogeneous patient population. This, taken together with previous work [46], suggests that our objective of providing a first clinical tool to patients with a BVL might not be so far away.

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Disclosure Statement

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