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Abstract

Recent research has shown promising results for the development of a clinically feasible vestibular implant in the near future. However, correct electrode placement remains a challenge. It was shown that fluoroscopy was able to visualize the semicircular canal ampullae and electrodes, and guide electrode insertion in real time. Ninety-four percent of the 18 electrodes were implanted correctly.

Reference

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Vestibular Implantation and the Feasibility of Fluoroscopy-Guided Electrode Insertion

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INTRODUCTION

Bilateral vestibulopathy, a severe bilateral function loss of the vestibular organs, nerves, or a combination of both, is often disabling.\textsuperscript{1,2} It is a heterogeneous disorder with different etiologies, varying from ototoxicity (eg, gentamicin) to meningitis,
genetic, autoimmune, neurodegenerative (eg, ataxia), and other diseases. However, in up to half of the cases, the cause remains idiopathic. Bilateral vestibulopathy can lead to many symptoms, including imbalance and oscillopsia (the illusory movement of the environment). It has a socioeconomic impact, reduces quality of life, and increases risk of falling up to 31 times. It is estimated that more than 3 million people are affected, but this is likely to be underestimated because of many diagnostic challenges. Unfortunately, current treatment options, such as physiotherapy, often have a low yield and bilateral vestibulopathy cannot yet be sufficiently treated in most of the cases.

Therefore, research groups around the world have investigated the feasibility of an artificial balance organ: the vestibular implant (VI). The VI is in concept analogous to the cochlear implant. Instead of sound, it captures motion using gyroscopes. This motion information is then transferred to a processor that converts it into electrical signals. Subsequently, electrodes implanted in the vicinity of the ampullar branches of the vestibular nerve are used to convey these electrical signals and stimulate the vestibular nerves. By this, motion information is transferred to the brain. Until now, only stimulation of the semicircular canals has been reported in humans (Box 1), although otolith stimulation is also being investigated. The Geneva-Maastricht group was the first group to implant humans with a fully functional VI. This group was able to show the feasibility of a VI in humans and various findings were reported. First, it was possible to elicit an electrically evoked vestibulo-ocular reflex in the plane of the stimulated canal, and (partially) restore vestibular function in the low and high frequencies of movement. However, the vestibulo-ocular reflex was not always aligned with the stimulated canal, because of current spread to the other canals and/or otolith organs. Second, the brain was able to adapt to the baseline stimulation, while still reacting on motion-induced modulation of the implant. Third, the characteristics of the electrically evoked vestibulo-ocular reflex mimicked those of the natural vestibulo-ocular reflex. Fourth, it was possible to also elicit vestibulocollic and vestibulospinal reflexes, recorded by vestibular evoked myogenic potentials and

| Box 1 | Overview VI research in humans |
|-------|-------------------------------|
| Potential indications (current and future) |
| - Bilateral vestibular loss |
| - Incomplete centrally compensated unilateral labyrinthine hypofunction |
| - Fluctuating vestibular hypofunction (ie, “pacemaker” to treat vertigo attacks) |
| Design |
| - Gyroscopes, external processor, and implanted stimulator connected to electrode leads close to the vestibular nerve |
| Surgical approaches |
| - Intralabyrinthine: one electrode lead in each semicircular canal |
| - Extralabyrinthine: electrode leads directly on the nerves, outside semicircular canals |
| Main findings of the VI in humans |
| - The vestibulo-ocular reflex can (partially) be restored |
| - The brain adapts to baseline stimulation, while still responding to motion-modulated stimulation |
| - The electrically evoked vestibulo-ocular reflex (partially) mimics the natural reflex |
| - The vestibulocollic reflex is elicited, and controlled postural responses are generated |
| - Vestibular sensations are elicited, but these perceptions are highly variable |
| - The vestibular implant can overrule natural vestibular function |
| - Dynamic visual abilities are restored during walking and during fast head movements |
change of posture, respectively. Fifth, perception of input from the VI varied: not always vertigo or rotatory sensations were reported, but also other percepts, such as sounds or pressure. Sixth, VI information was able to overrule the residual natural vestibular information, where the brain behaved nonlinearly. This might pave the way for using the VI as a “vestibular pacemaker” in case of fluctuating vestibular function, such as vertigo attacks. Finally, a functional benefit was demonstrated by reducing oscillopsia and improving vision during walking on a treadmill and during fast head movements.

Given these results, it can be hypothesized that indications for the VI might not only remain restricted to bilateral vestibulopathy in the future. Other indications include: uncompensated unilateral vestibular hypofunction, presbyvestibulopathy, and therapy resistant vertigo attacks. However, still many challenges are met in VI research. One major challenge is refining vestibular implantation surgery, to lower risks of hearing loss and to get optimal electrode placement. Two types of surgery were developed: the extralabyrinthine approach and the intralabyrinthine approach. With the extralabyrinthine approach, the electrodes are placed outside the labyrinth. Under local anesthesia, the nerves are directly approached and electrodes are placed onto the ampullar branches of the vestibular nerves. Because the labyrinth is not opened, the risk of sensorineural hearing loss is minimized. However, it is a challenging surgery (eg, higher risk of damaging the facial nerve) that requires extensive training. Furthermore, electrode fixation is difficult. Therefore, the intralabyrinthine approach is nowadays preferred by most groups. With the intralabyrinthine approach, the semicircular canals are fenestrated close to the ampulla, because previous research showed optimal stimulation near the ampullary nerves. Therefore, electrodes are inserted as close as possible to these nerves. However, by opening the inner ear, the risk of sensorineural hearing loss increases. Previously, implantation of the vestibular system by another group resulted in postoperative sensorineural loss in their population. Because many patients with bilateral vestibulopathy still have sufficient hearing, it is important that research focuses on hearing preservation during vestibular implantation surgery. Fortunately, it was shown that electrode insertion of the semicircular canals is possible without acutely changing the auditory function as measured with auditory brainstem response. Nevertheless because of ethical reasons, the Geneva-Maastricht group currently only implants patients with bilateral vestibulopathy who are already deaf in the ear to be implanted.

Next to hearing preservation, it is challenging to get the electrode as close as possible to the ampullary nerve (in the ampullae of the semicircular canals) using the intralabyrinthine approach. After all, when the semicircular canal is fenestrated, the sensory epithelium is often not directly visible. It is not preferred to widely open the fenestration until the sensory epithelium is reached, because this might induce hearing loss. This implies that the electrode is inserted “blindly,” without the surgeon knowing exactly how far the electrode needs to be inserted, to make close contact with the sensory epithelium of the ampullary nerve. As a result, electrode position was previously not always optimal. Therefore, there is a need to optimize electrode placement during surgery. Several options have been explored to facilitate proper electrode positioning, but none of them have proven to be infallible: (1) vestibular evoked compound action potentials might be of benefit, but similarly to cochlear implantation, they are not always obtained during vestibular implantation surgery; (2) surgical landmarks show too many interindividual differences to get a precise position in a large group of individuals; (3) vestibulo-ocular reflex testing to verify the position of the electrodes is compromised by general anesthesia; and (4) additional electrodes on the electrode lead might increase the chance of hitting the target.
but do not guarantee proper positioning. One of the possibilities to improve electrode positioning is real-time visual guidance of electrode insertion. Multiple imaging techniques can potentially aid electrode insertion but each have their own pros and cons. Preliminary studies by the Geneva-Maastricht group demonstrated that high-frequency ultrasound and optical coherence tomography have a superior image quality, but often lack the ability to penetrate the bony labyrinth deep enough to visualize the ampullae of the semicircular canals. Therefore, imaging techniques containing better penetration properties were considered.

Fluoroscopy is an imaging technique that captures moving images in real-time using x-rays. The x-ray technique was developed in 1895 and within a few months fluoroscopes became commercially available. Soon after its availability, it already proved useful in otolaryngologic practice. Although nowadays many advanced imaging techniques are used in otolaryngology, fluoroscopy is still an important technique in daily practice of many medical specialties requiring real-time guidance. Its utility in cochlear implantation is still being investigated, but studies suggest that it may be useful in challenging cases, such as abnormal cochlear anatomy. This technique can clearly display the structures of the inner ear and cochlear implant electrodes during surgery. Considering the similarities with VI surgery, fluoroscopy could possibly overcome the blind insertion in this procedure.

With this background provided on the VI, the aim of this work is to demonstrate the potential of fluoroscopy-guidance in the intralabyrinthine surgical approach, to correctly place the three VI electrodes in the semicircular canals. It was hypothesized that the semicircular canal ampullae and electrode leads could be identified and that the insertion could be improved using real-time visual guidance by fluoroscopy.

**MATERIALS AND METHODS: INVESTIGATIONS OF FLUOROSCOPY-ASSISTED VESTIBULAR IMPLANTATION**

**Subjects and Preparation**

Formalin-fixed cadaveric human heads with intact skull from donor subjects were included. A canal-wall up mastoidectomy was performed bilaterally and the semicircular canals were skeletonized. Subsequently, a single fenestration of approximately 0.7 to 1 mm was made in each bony semicircular canal: the lateral semicircular canal was fenestrated near the tip of the short process of the incus, the posterior semicircular canal was fenestrated at the intersection with Donaldson line, and the superior semicircular canal was fenestrated at an estimated similar distance from its ampulla as the lateral semicircular canal fenestration.

**Surgical Set-Up**

The cadaveric head was placed on a computed tomography (CT) scan table, rotated away from the surgeon (30°). A Ziehm Vision RFD three-dimensional (3D) mobile fluoroscopy unit (Ziehm Imaging GmbH, Nürenberg, Germany) was used to visualize the semicircular canal ampullae. This C-arm encompasses a 3D functionality, but for this experiment only the two-dimensional functionality was used. Based on preliminary findings to optimize semicircular canal visualization, the C-arm was arranged in a modified Stenvers position: from orbitomeatal plane 10° craniocaudal and 30° left anterior oblique (right ear) or 30° right anterior oblique (left ear). If necessary, the C-arm was slightly adjusted until all ampullae (superior, lateral, posterior) were visualized in the same image.

**Implanting the Semicircular Canals**

The aim was to position the electrode tips as close as possible to the center of the semicircular canal ampullae. First, the electrodes were blindly inserted using silicone...
electrodes (ø0.6 mm) with an enclosed platinium-irididium wire of ø0.5 μm (MED-EL, Innsbruck, Austria), until the estimated position of each electrode tip was in the ampulla of the inserted canal. This way, radiation exposure could be minimized to only the visualization and repositioning procedure. Then, fluoroscopy was used to visualize the electrode and adjust its position. The optimum location of the electrode tip (ie, the center of the ampulla of the inserted semicircular canal) in the fluoroscopy images was determined by a radiologist (AP) and an ear, nose, throat surgeon (RvdB) in consensus. Both persons cooperated together with the surgeon performing the implantations (JS) in placing the electrode tips in their final positions. Directly after implanting the three semicircular canals, a CT scan of the head was performed with a slice thickness of 0.4 mm using Somatom Force CT (Siemens, Forchheim, Germany) to determine the final position of the insertion. The whole procedure was repeated for the contralateral ear.

Analysis

The CT scan images were used for image analysis. Because each head was implanted on both sides subsequently, each head was scanned twice (after implanting each side) and thus two scans were available of each inner ear: one with and one without electrodes implanted. The two CT scans of each head were manually aligned using the open source software 3D Slicer version 4.8. Then, automated fusing using the BRAINSFit registration algorithm was applied, as previously described. The unplanted ear of each scan was manually segmented and a 3D model was created (Fig. 1A). Based on the CT images and the 3D model, a fiducial was placed at the center of the ampulla of each semicircular canal (Fig. 1B). This was explicitly not performed in the scan with electrodes, to avoid confounding caused by the electrode tip position (eg, placing the fiducial closer to the electrode tip). Separately, in the implanted ear of each scan, fiducials were placed at the electrode tips (Fig. 1C).

Because of the previous alignment of the CT scans, the distances between the fiducials in the centers of the ampullae and the corresponding electrode tips could be calculated in 3D Euclidean space (Fig. 1D). Median distances were determined. Additionally, a distance less than 1.5 mm was defined as correct electrode placement. This was based on the fact that stimulation of the ampullae seems to be most effective, and that the average diameter of an ampulla is approximately 1.5 to 2 mm (height-length).

Additionally, these obtained distances were compared with previously reported mean distances from blindly inserted electrodes in humans. The Mann-Whitney U test was used to test for differences between the two insertion techniques (all placements of fluoroscopy-guided vs blind insertion). The proportions of correctly placed electrodes (ie, <1.5 mm) were calculated for both techniques, and the 95% confidence intervals (CI) were calculated using Wilson score interval.

Ethics

This study was performed by virtue of three donors. Handwritten and signed codicils from the donors are kept at the Department of Anatomy and Embryology, according to the Dutch Corpse Disposal Act (“Wet op de lijkbezorging”, 1991). The procedures in this investigation were in accordance with legislation and ethical standards in the Netherlands.

RESULTS

Six ears from three donors were sequentially implanted, guided by fluoroscopy, and underwent CT scanning. Fluoroscopic visualization of the ampulla and real-time visual
guidance of electrode insertion was possible in all 18 semicircular canals. The ampulla was visible as a widening of the inner border of the bony semicircular canal, adjacent to the vestibule (Fig. 2). After the first blind insertion, all electrodes were adjusted using fluoroscopy. The distance between the center of the ampulla and the electrode tip is presented for all semicircular canals in Table 1. The biggest deviation from the target location was 2.0 mm. The median distances for the superior, lateral, and posterior semicircular canal were 0.60 mm, 0.85 mm, and 0.65 mm, respectively (Fig. 3). The proportions of correctly placed electrodes were 100% for superior and lateral semicircular canal and 83% for the posterior semicircular canal. All semicircular canals taken together, the median distance was 0.7 mm (interquartile range, 0.5–1.0 mm), and 94% of the electrodes (95% CI, 74%–99%) was placed correctly (bold in Table 1).

Comparison of the current data with the blind insertion technique (based on the raw data from Nguyen and colleagues29) showed that the electrode tips of the fluoroscopy-guided insertion technique were significantly closer to their target (P = .01). After all, the blind insertion technique resulted in 75% correctly placed electrodes (95% CI, 47%–91%), with an overall median distance of 1.2 mm (minimum 0.4 mm; maximum 5.3 mm).

DISCUSSION

This work reviewed a comprehensive list of indications for vestibular implantation and some of the basic concepts that underlie this new cranial nerve implant. Specifically, the feasibility and utility of fluoroscopy as an imaging technique to provide real-time visual guidance during intralabyrinthine vestibular implantation was investigated. All
Electrode tips were placed close to their intended target location. This was significantly closer than previously described with blind insertion. Overall in this study, 94% of the electrodes were correctly inserted (ie, <1.5-mm distance), compared with 75% with blind insertion. Therefore, these results suggest that fluoroscopy may aid adequate electrode placement during vestibular implantation.

Although promising, still some challenges are met when applying fluoroscopy for vestibular implantation. One of the challenges in fluoroscopy-guided implantation is to sufficiently visualize the ampullae of the semicircular canals. With the applied position of the C-arm in the modified Stenvers plane described previously, the resulting image was deemed optimal for simultaneous visualization of all three semicircular canals. This configuration is almost perpendicular to the lateral and superior semicircular canals, but not perpendicular to the posterior canal. This made it more difficult to determine the ampullar region of the posterior semicircular canal, also because of

![Fluoroscopy image](image)

**Fig. 2.** Fluoroscopy image of a right ear with implanted electrodes (Ear #4) in the superior, lateral, and posterior semicircular canal (top-bottom). Red lines indicate the ampullae.

| Ear | Superior SCC | Lateral SCC | Posterior SCC |
|-----|--------------|-------------|--------------|
| 1   | 0.9          | 0.6         | 0.8          |
| 2   | 0.5          | 0.7         | 0.5          |
| 3   | 0.3          | 1.2         | 2.0*         |
| 4   | 0.2          | 1.0         | 0.5          |
| 5   | 0.7          | 0.6         | 1.4          |
| 6   | 0.9          | 1.1         | 0.0          |

* Except this, all other values indicates correctly placed electrodes in the SCCs according to the predetermined criteria (ie, <1.5-mm distance).

**Abbreviation:** SCC, semicircular canal.
overprojection of other structures of the temporal bone. This probably also explains why electrode distances in this canal showed the widest variability, although half of the electrode tips were within 0.5 mm of the target. Other configurations of the C-arm were tried in a preliminary study, including a separate configuration for the visualization of the posterior semicircular canal, but they did not yield better visualization than the modified Stenvers plane. Second, taking this into account, applying fluoroscopy for vestibular implantation requires training to correctly position the C-arm and to interpret the fluoroscopy images. The total dose is influenced by the duration of exposure, the number of images per second, the required quality of the images, and the field size. If the team is able to swiftly set up the C-arm to obtain images in the modified Stenvers plane, this also reduces radiation dose because exposure during repositioning is limited and a narrowed beam can be applied. Because this involved a feasibility study, and limited training of the team was performed, administered radiation dose was not yet taken into account. However, studies investigating the use of fluoroscopy in cochlear implantation surgery estimated that with modern fluoroscopy devices, the total doses stay well lower than recommended total exposure limits. Therefore it was assumed that electrodes should be positioned as close as possible to the sensory epithelium of the ampullary nerves, which are not visible with fluoroscopy. These structures are actually not located in the centers of the ampullae, but in the ampullary walls. However, because vestibular electrodes are not yet fully designed to hug the walls of the ampullae, it was not possible to reproducibly position the electrodes against these walls. Therefore for this study, it was chosen to use the centers of the ampullae as the target locations. After electrode design modifications, electrode contact with the sensory epithelium could be tested in the future. The inability to visualize this epithelium with fluoroscopy is not expected to be a drawback, because the ampullary walls (its primary location) are clearly visible with fluoroscopy. Lastly, it seemed that of the 18 inserted electrodes, one electrode was inserted greater than 1.5 mm too far off the center of the ampulla (Ear #3, PSCC, 2.0 mm). This electrode turned out to be inserted too deep into the canal,
almost reaching into the vestibule. However, with multiple electrodes on the lead and the right selection of the stimulating electrode postoperatively, stimulation could still take place in close proximity to the target.

The following approach is advised for further investigations: before fenestration of the semicircular canals, optimize the fluoroscopic visualization (ie, adequate window and angles in craniocaudal and left/right plane); after fenestration, insert the electrodes blindly; then, adjust the position of the electrodes using fluoroscopy. This approach confines the administered radiation dosage while also limiting electrode manipulation. Further research should investigate the value of this technique in the operation room in a larger patient group, before definite conclusions about its benefit in VI surgery can be drawn.

Limitations

The fiducials used for calculating the distances from electrode tip to ampulla were placed manually. This could have introduced a bias, especially for determining the centers of the ampullae. However, observer bias was minimized by determining this target position on the CT scan without inserted electrodes and fusing these images with the postimplantation images. Still, one drawback of the fusion is an inaccuracy of the alignment. Because the misalignment can occur in every direction, this may lead to an underestimation of correctly placed electrodes, although this inaccuracy is on average only 0.05 to 0.16 mm. Furthermore, because of the small sample size, only descriptive statistics were applied. No predictions can be made regarding the robustness of the results (eg, the relationship with patient characteristics).

SUMMARY

Vestibular implantation is an emerging technology that offers direct cranial nerve stimulation for bilateral vestibulopathy and potentially other vestibular disorders. Although there are still challenges to overcome in the development of this device and its implantation technique, research demonstrates feasibility and utility of the VI to improve clinical outcomes for patients with certain vestibular disorders that do not respond to traditional therapies. This article showed that fluoroscopy can provide the VI-surgeon with direct feedback on the location of the VI electrodes and consequently improve correct electrode placement. A future trial should validate this approach in a larger patient group, before its clinical value can be determined.

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