A Fully Implantable Epiretinal Vision Prosthesis for Retinitis Pigmentosa Patients

Thomas Schanze, Uwe Thomas
EpiRet GmbH
Winchester Straße 8
D-35394 Gießen

Abstract Retinal implants are an important approach to restore vision in patients that are blind due to photoreceptor loss from retinitis pigmentosa. There are two main approaches. One is the subretinal implant, which is implanted at the level of the degenerated photoreceptors. The second approach is the epiretinal implant, which is favourably placed on the inner retinal layer of an eye. In this, visual information is captured with an external camera, processed and transmitted to a retinal stimulator that is secured at the level of ganglion cells. As with most electrical prostheses advances are often related to advances in technology. Of equal importance are pre-clinic studies and surgical aspects of being able to implant such devices. Recently, the EpiRet group implanted and tested their epiretinal vision prothesis in blind subjects with retinitis pigmentosa. We present implant's design and results of a clinical study to demonstrate the applicability of the EpiRet vision prosthesis.

Introduction

Retinitis pigmentosa is a blinding disease in which retinal cells of the eye slowly and progressively degenerate. Postmortem analyses of retinitis pigmentosa patients have shown that a lot of retinal neurons, e.g. bipolar cells or ganglion cells, are retained compared to the light sensitive photoreceptor cells of the outer nuclear layer (Stone et al. 1992; Santos 1997). These remaining cells are functionally still intact and might be stimulated with electrical currents to restore vision (Eckmiller et al. 1994; Humayun 1996).

Retinal implants are an important approach to restore vision in patients that are blind due to photo-receptor degeneration. Two main approaches are under development (Rizzo and Wyatt 1997; Hesse et al. 2000; Zrenner 2002; Schanze et al. 2002, 2007; Humayun et al. 2003; Laube et al. 2005; Dowling 2005; Walter et al. 2005; Javaheri et al. 2006; Yanai et al. 2007; Mokwa 2007; Roessler et al. 2009). Subretinal implants are implanted between the pigment epithelial layer and the outer layer of the retina and try to stimulate the remaining intact retinal neurons – bipolar or horizontal cells, the initial neuronal processing stage of the retina – with electrical currents. Epiretinal implants have been designed to stimulate retinal ganglion cells – the final retinal processing stage – with an electrode array implanted onto the inner retinal membrane. In short, retinal implants stimulate retinal neurons electrically to restore a simplified visual image in the subject's brain.

The challenge of restoring vision is immense and progress is often related to advances in technology, which cross many scientific disciplines, from neurophysics to electrical engineering. Of equal importance are pre-clinic studies and surgical aspects of being able to implant such devices. Here, we report on a fully implantable epiretinal vision prosthesis. We describe its design, implantation and testing in blind volunteers with retinitis pigmentosa.

Implant Design

The notion of the EpiRet epiretinal implant approach is to affix an electrode array onto the retinal surface and to stimulate ganglion cells by adequate electric currents generated by an electronic device (Figure 1). This electronic device consists of a coil, a receiver and a stimulation chip. The implant can be wireless activated by an external transceiver which is also intended to assure an adequate data processing of visual scenes captured by a camera.

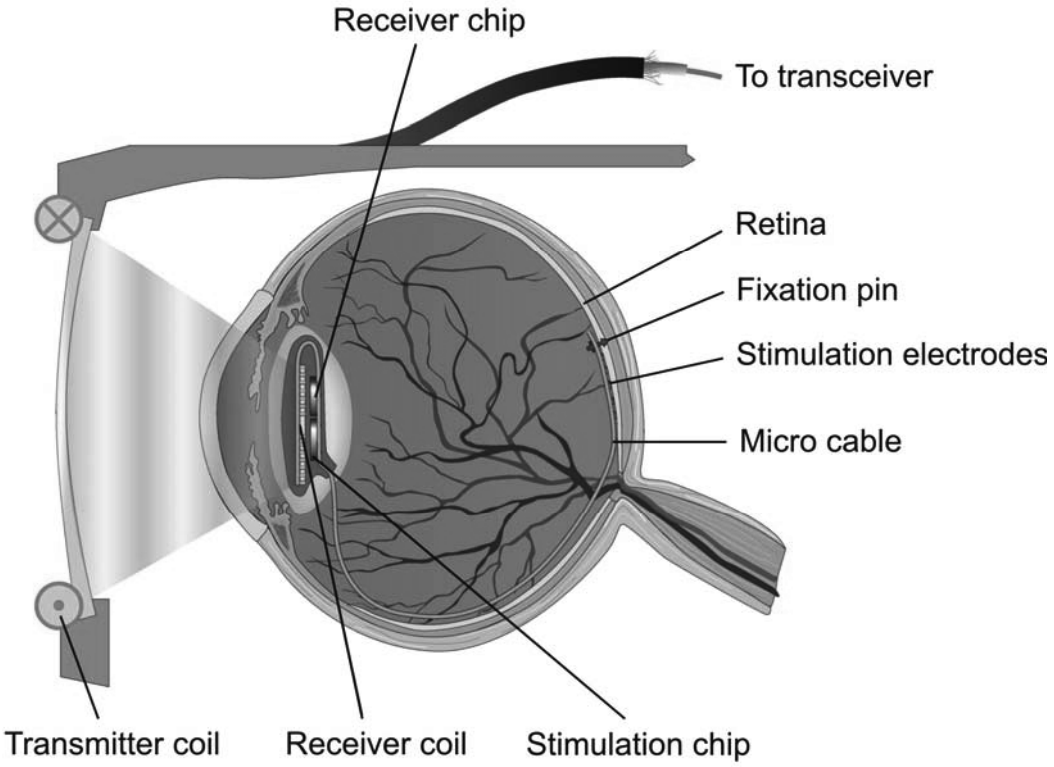

Figure 1. EpiRet retina implant system for vision restoration. Video camera captured visual information is processed by an external device (not shown) and, as energy, inductively transmitted to the intraocularly positioned receiver. After signal decoding the stimulation chip acitivates epiretinally placed electrodes for stimulation of remaining intact retinal neurons.

Figure 2. Fully implantable epiretinal retina implant. The implant can be telemetrically activated and has 25 electrodes (top side). Each iridium-oxide electrode has a three-dimensional shape and was activated to ensure excellent stimulation impulse charge transfer. On the right side of the picture are the receiver coil and the electronics embedded in silicone rubber. Note the picots required for thread-fixation in the eye's lens-capsule. The five-cent coin serves as a ruler.

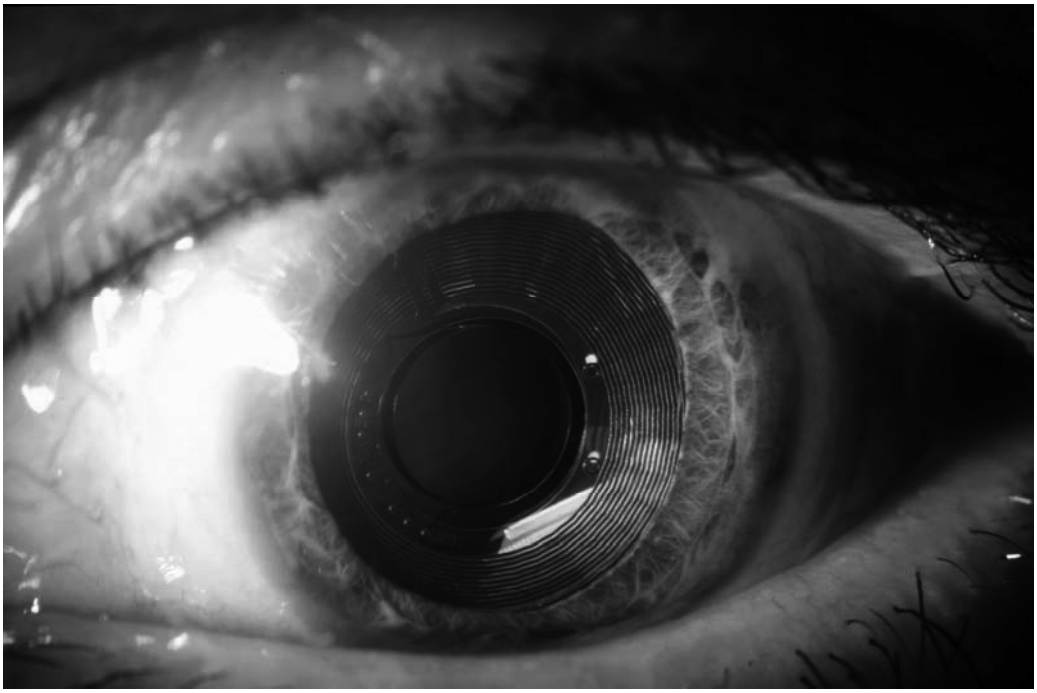

Figure 3. Implanted epiretinal retina implant.

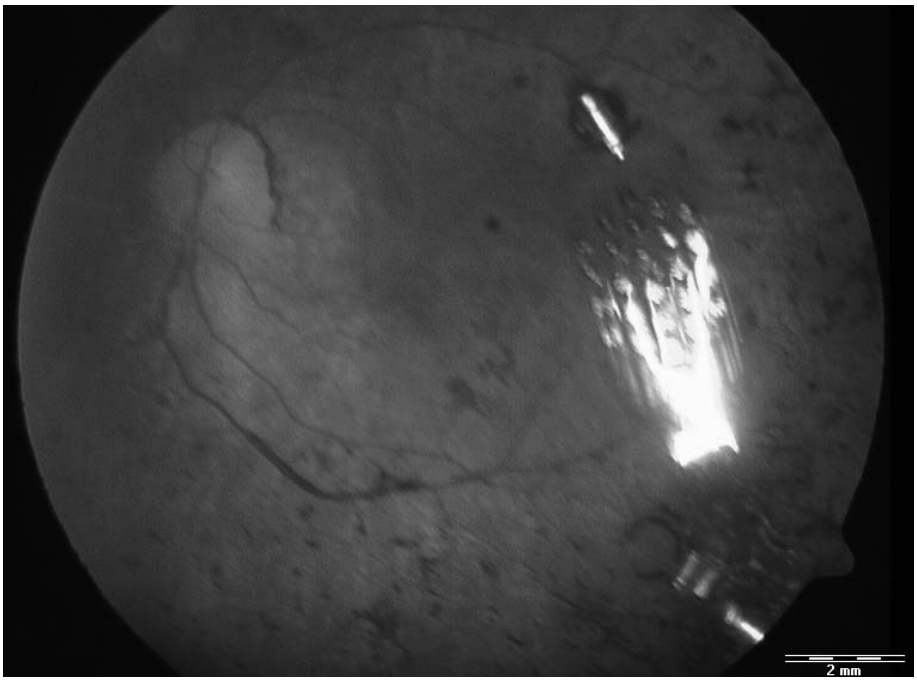

Figure 4. Fundus photography of the epiretinal implant's electrode array. The stimulation electrode array was secured safely with a modified retinal fixation pin on the central area of retinal surface; the optic disk is in the upper left quadrant. This approach establishes an intimate electrical contact between electrode and ganglion cells as required for successful low-threshold stimulation. The dark retinal spots are due to retinitis pigmentosa.

The materials for electrodes and for supporting and housing of the electronic chips have to fulfil a variety of tasks. They have to be highly flexible, smooth, stable, light-weighted, robust, easily implantable and biocompatible. In addition, the printed circuit board has to connect the chips and has to be a base for the electrodes.

We selected polyimide as a basic substrate and housing material for the conductors, the metallic contact pads, the micro cable, the electrode array and the galvanically deposited high-Q receiver coil. Electronic circuits were protected by Parylene C and by silicone rubber. Form and shape of the silicone rubber is like that of an intraocular lens as required for safe implantation. A crucial point for low-threshold and high resolution and information transfer stimulation is the electrode design (Schanze et al. 2002, 2003, 2006, 2007; Eger 2005; Eckhorn et al. 2006; Eckhorn 2007). Raised or three-dimensional electrodes prospect superior stimulation results compared to flat electrodes. Thus we designed three-dimensional electrodes. The contact area of a three-dimensional electrode consists of sputtered and activated iridium-oxide. This ensures a high charge delivery capacity as required for safe and local low threshold stimulation. More details concerning principles of wafer-level production processes, assembly and packaging, and electrode design are given elsewhere (Stieglitz et al. 2000; Mokwa 2004, 2007; Hungar et al. 2005; Mokwa et al. 2008). Implant materials and implants were, of course, tested to be biostable and biocompatible (Schanze et al. 2007; Sellhaus et al. 2008).

Clinical Study

A clinical study was designed and approved by local governments for implantations and implant testing at the Departments for Ophthalmology at RWTH Aachen University and University Essen. Eight blind volunteers suffering from retinitis pigmentosa received the EpiRet implant (Figures 2, 3, and 4). All implantations were successful and after four weeks the implants were explanted. Retinal stimulation and recording of the volunteers' perceptions proofed that vision can be restored with a fully implantable epiretinal vision prosthesis. The volunteers clearly reported visual sensations evoked by electrical stimulation. These phosphenes were related to stimulation parameters like stimulation current's amplitude and the duration of the biphasic charge-balanced current impulses. In correspondence with preceding animal studies (e.g. Schanze et al. 2002; 2003) we demonstrated for the first time ever that low threshold stimulation (< 10 µA, < 10 µC/cm²) is feasible in patients with degenerated retinae. The perception of electrical stimulation was tested over four weeks and showed that important stimulation parameters like threshold, orientation, form, contrast and colour of basic visual objects as well as stimulation resolution and stability can be assessed and optimized.

Discussion and Conclusions

The major result of this paper is that with retinal implants restoring of vision in patients with retinitis pigmentosa is feasible. However, it had taken an interdisciplinary approach and more than 15 years to proof this. Pre-clinical trials were necessary and important for verification of design, implantation procedures and proof of principle. The clinical trials yielded important knowledge about retinal implant evoked visual sensations/perceptions. These results are the basis to solve the upcoming challenge: the intelligent epiretinal implant with adaptive high quality information processing of visual scenes as a medical product to restore vision in blind subjects with retinitis pigmentosa.

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Picture credits (©). Fig. 1: RWTH Aachen, IWE I, 2008; modified. Fig. 2: EpiRet GmbH, 2008. Fig. 3. University Essen, Dept. Ophthalmology, 2008; modified. Fig. 4: RWTH Aachen, Rössler et al., 2009; modified.

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