35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Development of a Very Large Array for Retinal Stimulation*

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Abstract— **Retina degeneration is one of the leading causes of blindness nowadays and cannot be cured in most cases. It has been shown that electrical stimulation of retinal ganglion cells can generate visual perceptions and therefore implantable electrode arrays can be possible treatment for these patients. Most implants developed for that purpose use electrode arrays with a size of a few millimeters squared and therefore could restore only a very small field of vision and hardly improve orientation in an unknown environment. In this paper we present results of the development of an implantable electrode array covering about 100 mm² of retinal tissue.**

I. Introduction

One of the most common causes of legal blindness in industrialized civilizations is the degeneration of retinal tissue. This can be induced, for example by *Retinitis Pigmentosa (RP),* a congenital disease that leads to a slow degeneration of the rods and cones, which starts in the peripheral areas of the retina until after several years the patient is completely blind [1]. Until now RP is not curable despite all progress that has been made in ophthalmic diagnostics and therapies. However it has been shown that electrical stimulation of the retina of patients suffering from RP gives them visual perceptions. That is possible because about 30 % of the neuronal ganglion cells are still active even after a couple of years of total blindness [2][3]. Based on this finding several approaches for retinal prosthesis have been developed and successfully tested in RP-patients. These implants usually consist of a microelectrode array (MEA) embedded in a flexible polymer foil, which is placed on top of the retina (epiretinal [4][5]) or between the retina and the sclera (subretinal [6]), and the necessary electronics providing power and signals for the electrodes.

It has been shown in calculations of the optical properties of the human eye that near the optical axis there is a linear dependency between the retinal arc length of an image and the perceived visual angle [7]. That could conversely mean that every increment of stimulation area also increases the field in which visual perceptions can be generated.

Most implants use MEAs that cover just a few square millimeters of retinal tissue and carry a very limited number of electrodes (see Table I.). These devices are very small which makes the surgery minimal invasive and therefore less stressful for the patient. Due to the small electrode area the peripheral areas of the retina are not affected by stimulation which means the visual perceptions are concentrated on a very small area at the centre of the field of vision, corresponding to an angle of sight of about 10°. This is only sufficient to recognize letters and identify objects.

For mobility and orientation in an unknown environment it is necessary to capture a large scene as fast as possible. That means a large stimulation area with a decent number of electrodes is needed to replicate the visual sensation of a healthy retina [8].

TABLE I. Overview on retina implant projects

Implant project	# of electrodes	Dimensions of the MEA (w/h/t in mm)
Retina Implant AG [6]	1500	3/3/0.1
Argus II [9]	60	5/5/?
EPI-Ret III [5]	25	2/3/0.02

In 2009 Ameri et al. published first studies on a wide-field retinal prosthesis where they presented various shapes of polyimide substrates for wide field arrays which were studied in a mechanical eye model and in porcine cadaver eyes [8]. The objective of our research is also the development of an epiretinal stimulator using a very large microelectrode array (VLARS) that covers an area of ~100 mm² of the retina, corresponding to an angle of sight of 40° while being implantable through a 3 to 5 mm scleral incision. For our studies we used polyimide substrates with a high number of integrated dummy electrodes and feed lines to evaluate possible positionings.

II. Design

There are two fundamental aspects that preset the design of the base structure of the implant. On one hand the implantation procedure and on the other hand the curvature of the retina.

As the epiretinal approach is to be used for the implant it has to be inserted into the eye and placed onto the fundus of the eye. To keep the surgical trauma for the patient as low as possible the necessary incision to bring the device inside the eyeball should not exceed 3-5 mm. That means an implant of our target size needs to be folded during implantation and unfolded inside the eye.

A human eye has a radius of about 12 mm, thus a radius that is in the order of the diameter of the stimulation array. The stimulation array has to adapt to the curvature of the retina therefore the carrier foil has to be smooth and flexible. The device is manufactured with planar processes on silicon wafers. Once released from the wafer it has a flat two dimensional shape. To bring it into a three dimensional

*Research supported by the Jackstaedt Stiftung.

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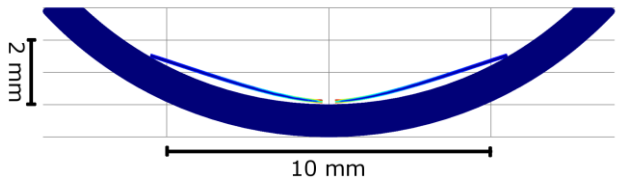

Figure 1. Results of finite element simulation of the mechanical behavior of a PI-foil fixed at the center to an incompressible spherical shell, showing the cross section of the arrangement.

spherical shape the foil needs stress relieving patterns to prevent wrinkling.

Consequently the implant needs to be very flexible and elastic, to ensure that the device regains its shape after implantation and does not experience a permanent plastic deformation. The most common materials used for implants like ours are parylene and polyimide as well as silicones like PDMS. They are biocompatible and easy to handle with classic photolithographic processes. For the VLARS implant we use the polyimide PI2611 produced by HD-MicroSystems™. It has all necessary mechanical properties and can be structured with common photolithography.

Simulations were carried out with finite element methods to visualize the position of an implant having a substrate made from PI2611. The modeled implant consists of a continuous flat circular shaped polyimide foil with a diameter of 12 mm and a thickness of 100 µm that is placed onto a spherical shell with the typical radius of 12 mm of a human fundus. For the polyimide we used material properties given by the material data sheet and Patel et al. [10] (Young's modulus: 8.5 GPa, Poisson ratio: 0.23), the spherical shell is handled as a non compressible geometry. The behavior of the foil was evaluated by displacing the upper edge of the fixation hole in the middle of the implant model in steps of 150 µm from a starting point where it just does not touch the shell downwards until the bottom of the foil touches the ground. The results of the simulation (see Figure 1) clearly show that the polymer foil is not in contact with the shell over the whole area. Half way between the fixation hole in the middle of the structure and the outer edge the gap is about 300 µm wide. Stimulation electrodes having a height of 20 µm would mostly have no contact to the retina. For a successful stimulation a very good contact of the stimulation electrodes to the retinal nerve cells is crucial. Having these aspects in mind dummy implants having different shapes were designed, fabricated and used for implantation experiments in simple silicone models and cadaver eyes of pigs. The four principle implant designs are listed below:

Design 1: A continuous circular shape without stress-relieving patterns as a reference (Figure 2a).

Design 2: A spiral shape that can be unwound during surgery and pushed through the incision bit by bit (Figure 2b).

Design 3: A star shape with wings that can bend back during surgery and regain their original position when placed on the retina (Figure 2c).

Design 4: A "globe" shape which can be folded for the implantation and unfurled inside the eye. (Figure 2d)

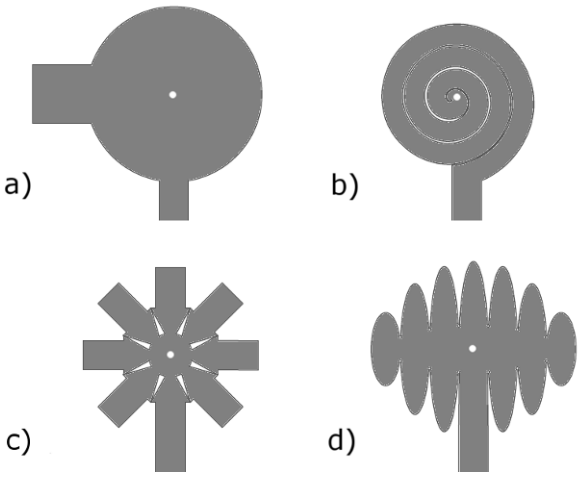

Figure 2. First generation of VLARS designs.

III. Fabrication

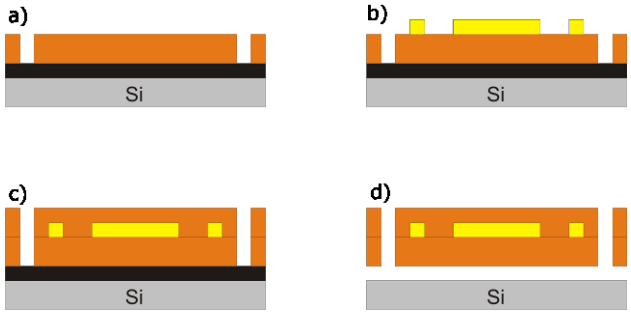

Figure 3. Scheme of the manufacturing process of VLARS prototypes.

Figure 3 shows the manufacturing steps of the VLARS prototypes. We use standard lithographic processes on 4" silicon wafers, which are coated with an aluminum sacrificial layer of 1µm thickness and titanium adhesion layers underneath (50 µm thickness) and on top (150 µm thickness).

At the first step a polyimide layer of 5 µm thickness is spin coated on the wafer, structured with a wet etching process and baked out under a nitrogen atmosphere at 400 °C for one hour (compare Figure 3a). Afterwards dummy conducting paths, electrodes and bond pads are created by electroplating with a thickness of 2.5 µm (compare Figure 3b). For a better adhesion between gold and polyimide a chromium layer with a thickness of 30 nm is deposited on the polyimide prior to electroplating. In the next step another 5µm thick polyimide layer is created by spin coating for encapsulation of the gold layer (compare Figure 3c). As the polyimide has a very low dielectric constant ($\varepsilon = 2.9$) crosstalk effects should be controllable. To separate the device from the wafer the titanium layer is opened by HF-etching followed

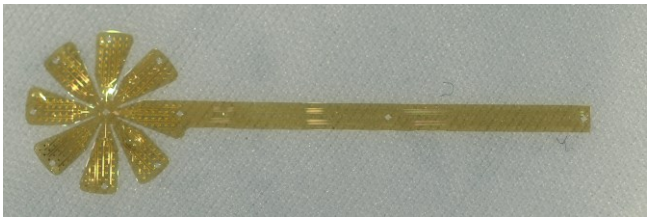

Figure 4. A VLARS dummy structure design 3 of the second generation.

by the removal of the sacrificial aluminum layer (compare Figure 3d).

For the second generation of prototypes we added an additional layer of Parylene C as it will be on the final implant. The Parylene layer is deposited from the gas phase what gives us a uniform coating of the devices and especially the electrodes. The side walls of the electrodes which will have a three dimensional conical form have to be isolated. This will guide the electrical field more towards the retina and reduces the crosstalk between neighboring electrodes. Figure 4 shows a tethered implant of the second generation with modifications of design 3 after fabrication.

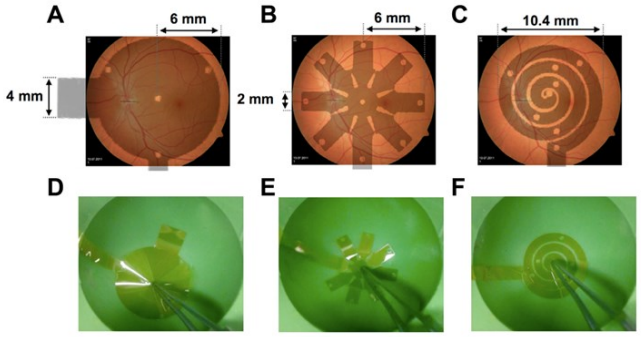

Figure 5. A-C: Fundus images overlaid with drafts of first generation VLARS structures (Designs 1, 2, 3). D-F: Their behavior in the silicone model (Designs 1, 2, 3).

IV. Results

To evaluate the proper dimensions, the positions of the electrodes, the fixation concept and techniques to handle the implant a series of experiments in silicone models and cadaver eyes were carried out. In Figure 5 one can see the first generation designs with their respective behavior in silicone impressions. The silicone models allow a view on the overall performance of the structures regarding the curvature adaption.

As expected, design 1 does not adapt to the curvature of the silicone impression at all, thus is discarded for further development. But one can see in Figure 5d the wrinkling of the foil when pressed down in the hollow hemisphere at the center of the structure. This pretty well illustrates the problem that we have to approach. The other approaches worked well in the silicone model and were developed further for experiments with cadaver eyes.

In Figure 6 we present photographs of the second generation designs, which are further developed from the findings of the experiments with silicone models and in porcine cadaver eyes. The implantation experiments in cadaver eyes give information about the behavior of the structures during surgery. The prototypes have a fixation hole in the middle of the structure. For implantation the implant is put over a retinal tack and pushed through the opening of the sclera.

Design 2 adapts very good to the curvature of the model. But as one can see in Figure 7A-B the implantation is very difficult, because when the spiral is unwound during surgery it tends to intertwine inside the eye and the time needed to place the implant properly on the retina is far too long. During this process the device also experienced an irreversible buckling (see Figure 7C). However when placed on the retina properly it showed again a very good adaption to the retinal surface.

Design 3 and 4 combine a very good curvature adaption with a fairly easy implantation behavior. The structures withstand the implantation and the following explantation and show no signs of damage or buckling. Also the placement of the implant on the retina was fairly easy. However we observed that the outer edges of the implant generated enough pressure to dent the retina.

Nevertheless we decided to pursue the development of the star- and globe shape design. The latest revisions of these

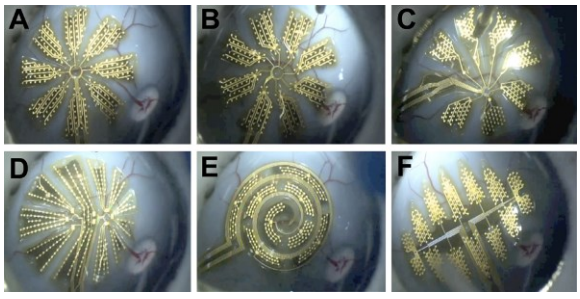

Figure 6. VLARS structures in porcine cadaver eyes. A-D: Four modifications of the star-shape pattern. E-F: spiral and globe shape pattern.

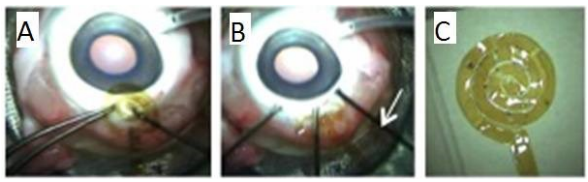

Figure 7. First im- and explantation trials of Design 2 on a porcine cadaver eye. A-B show the pictures taken during the im- and explantation procedure, C shows the implant after surgical trials.

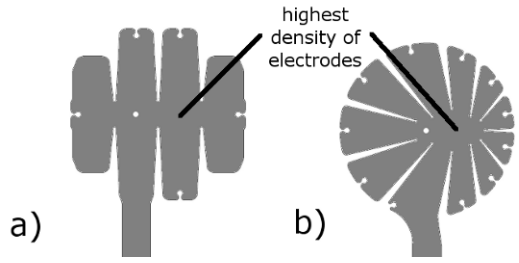

Figure 8. Last revision of VLARS designs that are going to be used for stimulation experiments.

designs are sketched in Figure 8. As one can see we gave up the symmetry of the concept to allow a better distribution of the electrodes. In the macula region there should be the highest density of electrodes. Therefore the retinal tack fixation hole was moved away from the macula region to the opposite of the optical nerve. Retinal tack holes were also placed at the tips of the arms to allow an additional fixation when needed, e.g. one of the arms is not in contact with the tissue.

V. Conclusion

Within this work a suitable polymeric base structure was developed that combines a good adaption to the spherical shape of the retina with a very good operability during the implantation process. It has been demonstrated that it is possible to place a large MEA with an area of 100 mm² into the eye and place it on the retina. To reduce any negative effects like the pressure onto the retina at the edges the designs have to be further improved. This could possibly be achieved by controlling the inherent curvature of the PI-foil. The designs also give much room for an anatomically sensible distribution of the electrodes.

For the acute stimulation experiments on narcotized animals with the first functional, tethered devices, eye-movement won't be an issue. In the far future the whole device including the stimulation electronics is integrated into the eye-ball. Signal and power will be transmitted inside through electromagnetic coupling.

The electrodes will be coated with sputtered iridium oxide, which provides high charge delivery capacity and low electrode impedances. That allows lower currents during stimulation and reduces the risk of cell damage in long-term experiments.

References

[1] D. T. Hartong, et al., "Retinitis pigmentosa," *Lancet*, vol. 368(9549), November 2006, pp. 1795-1809.

[2] A. Santos, et al., "Preservation of the inner retina in retinitis pigmentosa: A morphometric analysis," *Archives of Ophtalmology*, vol. 115(4), April 1997, pp. 511-515.

[3] T. Fujikado, et al., "Evaluation of phosphenes elicited by extraocular stimulation in normals and by suprachoroidal-transretinal stimulation in patients with retinitis pigmentosa," *Graefe's Archive for Clinical and Experimental Ophtalmology*, vol. 245(10), March 2007, pp. 1411-1419.

[4] M. S. Humayun, et al., "Visual perception in a blind subject with a chronic microelectronic retinal prosthesis," *Vision Research*, vol. 43(24), November 2003, pp. 2573-2581.

[5] G. Roessler, et al., "Implantation and Explantation of a Wireless Epiretinal Retina Implant Device: Observations during the EPIRET3 Prospective Clinical Trial," *Investigative Ophthalmology & Visual Science,* vol. 50(6), April 2009, pp. 3003 – 3008.

[6] E. Zrenner, et al., "Visual Sensations Mediated By Subretinal Microelectrode Arrays Implanted into Blind Retinitis Pigmentosa Patients," in *Proc. 13th Annu. Conf. of the IFESS*, Freiburg, 2008.

[7] N. Drasdo, et al., "Non-linear projection of the retinal image in a wide-angle schematic eye." *British Journal of Ophtalmology,* vol. 58, 1974, pp. 709.

[8] H. Ameri, et al., "Toward Wide-Field Retinal Prosthesis," *Journal of Neural Engineering*, vol. 6(3), May 2009, pp. 035002

[9] V. Kandagor, et al., "In situ Characterization of Stimulating Microelectrode Arrays: Study of an Idealized Structure Based on Argus II Retinal implants." in *Implantable Neural Prostheses,* Springer New York; 2010. pp. 139-56.

[10] K. S. Patel, et al., "Dual capacitor technique for measurement of through-plane modulus of thin polymer films," *Journal of Polymer Science Part B: Polymer Physics*, vol. 38(12), May 2000, pp. 1634-1644