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The Argus® II Retinal Prosthesis System

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ABSTRACT

The Argus® II Retinal Prosthesis System (Second Sight Medical Products) is the first prosthetic vision device to obtain regulatory approval in both Europe and the USA. As such it has entered the commercial market as a treatment for patients with profound vision loss from end-stage outer retinal disease, predominantly retinitis pigmentosa. To date, over 100 devices have been implanted worldwide, representing the largest group of patients currently treated with visual prostheses.

The system works by direct stimulation of the relatively preserved inner retina via epiretinal microelectrodes, thereby replacing the function of the degenerated photoreceptors. Visual information from a glasses-mounted video camera is converted to a pixelated image by an external processor, before being transmitted to the microelectrode array at the macula. Elicited retinal responses are then relayed via the normal optic nerve to the cortex for interpretation.

We reviewed the animal and human studies that led to the development of the Argus® II device. A sufficiently robust safety profile was demonstrated in the phase I/II clinical trial of 30 patients. Improvement of function in terms of orientation and mobility, target localisation, shape and object recognition, and reading of letters and short unrehearsed words have also been shown. There remains a wide variability in the functional outcomes amongst the patients and the factors contributing to these performance differences are still unclear. Future developments in terms of both software and hardware aimed at improving visual function have been proposed. Further experience in clinical outcomes is being acquired due to increasing implantation.

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1. Introduction

The Argus® II Retinal Prosthesis System (Second Sight Medical Products Inc., Sylmar, California, USA) is a commercially available device that aims to restore a basic level of vision to patients with profound vision loss from outer retinal dystrophies. The device elicits visual perceptions by means of electrical stimulation of the residual diseased retina. It was the first device to go into widespread clinical use with regulatory permission in multiple countries.

The discovery by Foerster (1929) that it is possible to elicit transient and reproducible visual percepts (known as phosphenes) upon direct electrical stimulation of the visual pathway took place almost a century ago. Since then extensive research efforts have been focused on understanding and controlling such phosphene responses. The ability to reliably elicit and modify phosphenes in a controllable way by manipulating the stimulating parameters, such that they reflect the surrounding visual scenes, has been the common goal of all electrical stimulation-based visual prostheses.

The Argus® II has become the most widely used and most successful retinal prosthesis currently available in terms of regulatory approval. Since obtaining the CE mark in 2011 and FDA approval as a humanitarian device in 2013, commercial implantation has begun in many countries worldwide. Use of the device has been predominantly for patients with profound vision loss from retinitis pigmentosa and to a lesser extent, choroideremia as well as for a planned cohort with extensive geographic atrophy from age-related macular degeneration (AMD) (ClinicalTrials.gov Identifier: NCT02227498). To date, over 100 devices have been implanted and the number is likely to increase. With its integration into clinical practice, it seems timely to review the pioneering work leading up to the regulatory approval of this product, as well as the subsequent clinical outcomes with the use of this device. In particular, we will evaluate the practical implications of using this device for the patients in real-life settings based on published literature.

The issues of electrical stimulation safety, choice of stimulating wave forms, biocompatibility and hermeticity in the development of the device will not be discussed in this review as these topics have already been covered comprehensively elsewhere (Humayun, 2001; Margalit et al., 2002). Stronks and Dagnelie (2014) gave a didactic account of how different stimulating parameters such as amplitude and frequency affects the phosphene brightness and size, while Ahuja et al. (2013) discussed the factors affecting electrode thresholds in detail. These topics will therefore also not be discussed in any detail.

1.1. Retina: the site of choice for electrical stimulation

In 1952, Hodgkin and Huxley first described the electrical nature of signal propagation in all nervous systems by the means of action potentials (Hodgkin and Huxley, 1952). During electrical stimulation of any neural tissue with an external electrode, the injection of electrical charges creates a localised depolarisation and subsequent initiation of action potentials. As such, electrical stimulation at any point along the visual pathway could elicit visual phosphenes. Commencing with cortical stimulation by Brindley et al., in 1968 (Brindley and Lewin, 1968a) and later by others (Dobelle, 2000; Normann et al., 2009), electrical stimulation has also been described at the levels of lateral geniculate nucleus (Panetsos et al., 2009, 2011), the optic nerve (Sakaguchi et al., 2009, 2012; Wang et al., 2011) and the retina.

Of all of the anatomical sites listed above, retinal stimulation (e.g. the epiretinal implant Argus® II and the subretinal implant alpha-IMS) has been the most successful. There are many reasons for this and they can be best summarised as: a) greater accessibility at lower surgical risk than the intracranial visual pathways; b) straightforward monitoring of the device by direct visualisation; and c) potentially predictable and reproducible retinotopy by applying stimulation at a pre-processing site.

With the advent of modern vitreoretinal surgical techniques, access to the retina and the subsequent implantation of stimulating electrodes are comparatively easier than other sites of implantation. This is exemplified by the widespread implantation of the Argus® II System in many countries by many different surgeons over a relatively short period, at a level of surgical morbidity acceptable to regulators (Humayun et al., 2012; Rizzo et al., 2014). Despite the relative accessibility and safety discussed here, implantation still requires advanced vitreoretinal surgical skills. Complications and problems were also easily identified during the phase I/II clinical trials due to the ability to directly visualise the device (Humayun et al., 2012).

The other advantage of a retinal prosthesis is the theoretically predictable retinotopy by stimulating the visual system at a site before significant processing of the signal has occurred. Brindley and Lewin (1968b) have demonstrated that although stimulation of cortical electrodes gave rise to phosphenes in locations in agreement with the classic Holmes' retinotopic map of the visual cortex (Holmes, 1945), many of the phosphenes were complex and non-discrete in nature. This was predominantly thought to be due to the fact that the retina, as well as the rest of the pre-cortical visual pathway, carried out significant processing of the signal.