ABSTRACT

PURPOSE: To report short-term results of pulsed ciliary muscle electrostimulation to improve near vision, likely through restoring accommodation in patients with emmetropic presbyopia.

METHODS: In a prospective non-randomized trial, 27 patients from 40 to 51 years old were treated and 13 age- and refraction-matched individuals served as untreated controls. All patients had emmetropia and needed near sphere add between +0.75 and +1.50 diopters. The protocol included four sessions (one every 2 weeks within a 2-month period) of bilateral pulsed (2 sec on; 6 sec off) micro-electrostimulation with 26 mA for 8 minutes, using a commercially available medical device. The uncorrected distance visual acuity (UDVA) (logMAR) for each eye, uncorrected near (40 cm) visual acuity in each eye (UNVA) and with both eyes (UNVA OU) (logMAR), and reading speed (number of words read per minute at 40 cm) were measured preoperatively and 2 weeks after each session. Overall satisfaction (0 to 4 scale) was assessed 2 weeks after the last session.

RESULTS: UDVA did not change and no adverse events were noted in either group. Bilateral and monocular UNVA and reading speed were stable in the control group, whereas they continuously improved in the treated group (Friedman, \( P < 0.0001 \)). Post-hoc significant differences were found for monocular and binocular UNVA after the second treatment and after the first treatment considering words read per minute (\( P < 0.001 \)). One patient (3.7%) was not satisfied and 18 patients (66.7%) were very satisfied (score of 4). Average satisfaction score was 3 (satisfied).

CONCLUSIONS: Ciliary muscle contraction to restore accommodation was safe and improved the short-term accommodative ability of patients with early emmetropic presbyopia.

RESBYOPE, from the Greek words presby meaning “old man” and ops meaning to “see like,” is the inability to comfortably focus on close objects due to aging. This is the most common physiologic alteration of eyesight, affecting more than 1.2 billion individuals worldwide, and leads to a major impact on productivity among healthy adults. Presbyopia also significantly affects quality of life in both developed and developing countries. Unlike ametropic defects or refractive errors (myopia, hyperopia, and astigmatism), caused by genetic and environmental conditions that affect the shape of the eye, presbyopia does affect virtually every individual older than 50 or 60 years due to the progressive loss of the accommodation ability of the eye.

Current treatments for presbyopia are based on optical corrections, but surgical refractive modifications are also possible. Although near vision can be easily recovered by the use of reading glasses, there is nonetheless a great demand for more permanent solutions to avoid the use of corrective lenses. However, available invasive surgical procedures have several limitations and are not devoid of side effects. Pharmaceutical treatments stimulating the

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contraction of ciliary muscles in the presence of different miotics and nonsteroidal anti-inflammatory drugs have been recently described, suggesting the relevance of the stimulation of the ciliary muscle to recover some of its function. An alternative approach could address the revitalization of the accommodation system by stimulating the ciliary muscle to increase its potency so that it can overcome the higher resistance of the system (ciliary muscle and lens) that has become stiffer due to aging. Pulsed electrostimulation is known to work for atrophic muscles and therefore might also be effective on the ciliary muscle.

We describe a non-invasive and innovative method to improve near vision, likely through restoring the accommodation mechanism through pulsed micro-electrostimulation of the anterior segment of the eye to stimulate ciliary muscle contraction to restore accommodation.

**PATIENTS AND METHODS**

The study was conducted in accordance with the tenets of the 1964 Declaration of Helsinki, revised in 2000. All patients signed an informed consent according to the policies of the Associazione Italiana Medici Oculisti. In a prospective non-randomized trial, 27 patients from 40 to 51 years old were treated and 13 individuals matched for age and refraction served as untreated controls. All patients had emmetropia with an uncorrected distance visual acuity (UDVA) of 20/20 (0.0 logMAR) or better and needed near sphere add between +0.75 and +1.50 diopters (D). Manifest refraction in both groups did not change UDVA with any spherical or cylindrical addition; all patients had visual acuity of 20/20 or better and a spherical equivalent of ±0.25 D or less (as measured by the autorefractometer). Based on these data, cycloplegic refraction was performed only on 5 patients at random (to avoid the discomfort caused by this procedure to the rest of the patients), and the resulting spherical equivalent was found to be not more than +0.375 D.

Exclusion criteria included any ocular pathology, including demyelinating and vascular diseases that may reduce blood perfusion of the ciliary body, and epilepsy. Patients who had a pacemaker were also excluded because of possible electrical interactions. In addition, patients receiving specific treatments that could possibly influence accommodation, such as antidepressant, antispasmodic, antihistaminic, and diuretic drugs, were also excluded. To exclude patients with obvious psychological problems, all of those enrolled had to complete the psychological Minnesota Test questionnaire (MMPI-2), consisting of 567 questions to which a true or false answer has to be given. The results were elaborated by the Psychology Department of the University “La Sapienza” in Rome, Italy. Enrolled patients were advised about the possible advantages and limitations of the procedure.

The protocol, established after previous experience, included four sessions of bilateral pulsed (2 sec on; 6 sec off) micro-electrostimulation with 26 mA for 8 minutes, with 2-week intervals, using the Ocufit medical device (Soof; Montegiorgio, Italy) consisting of special lenses and a calibrated power supply to which the lenses have to be connected (see below). Micro-electrostimulation treatments were performed by the first author (LG) at the Diagnostica Oftalmologica e Microchirurgia Oculare clinic in Rome, Italy. Two drops of 0.4% oxybuprocaaine were instilled before treatment with the patient in the supine position.

A 20-mm polycarbonate scleral contact lens equipped with four microelectrodes at the four cardinal points positioned 3.5 mm outside the limbal area corresponding to the ciliary body region (Figure A and Video 1, available in the online version of this article) was used. The micro-electrodes were connected through four electric pins and cables to the electrical generator (Figures AA-AC). The lens was carefully applied onto the eye (Figure AD) to avoid trauma to the ocular surface. The electrostimulator (Soof) generates biphasic compensated square waves for a low voltage micro-electrostimulation of the ciliary muscle. The amount of electrical current flowing from the positive to the negative pole remained stable, and any risk of thermal damage was prevented. During the 8 minutes of treatment, 60 cycles of electrostimulation were given, with each cycle consisting of 2 seconds of electrical impulse and 6 seconds of rest (Figure AE).

After each treatment, two drops of an antibiotic-steroid were instilled in each treated eye to prevent postoperative inflammation or infection. No other medications were needed. Although both eyes could be treated simultaneously, treatments were generally performed in one eye with immediate sequential treatment of the fellow eye. The ciliary muscle contraction to restore accommodation didactic demonstration of the procedure is available online (https://youtu.be/724pb1Kyp80).

Clinical examinations were performed 1 hour prior to the ciliary muscle contraction to restore accommodation treatment and 2 weeks after each treatment (just before starting the next one). Because the protocol included four sessions, the last examination was approximately 2 weeks after the fourth treatment (or 2 months after enrollment). LogMAR UDVA for each eye, logMAR uncorrected near (40 cm) visual acuity in each eye (UNVA) and in both eyes (UNVA OU), and reading speed (number of words read per minute at 40 cm) were taken preoperatively and 2 weeks after each session. UNVA was measured on standard MNREAD charts at a fixed distance of 40 cm, under standard (500 lux) illumination and no extra lighting. Reading speed was measured by two orthoptists, one holding a chronometer and the other counting the words, under standard room illumination on MNREAD charts at 40 cm distance.
Objective variations of the accommodation system were measured (only in one eye randomly chosen from 7 patients) by ultrasound biomicroscopy (Optikon, Rome, Italy), which was recorded under standard illumination with the patient in the supine position after the instillation of two drops of anesthetic (oxybuprocaine) 2 minutes before the examination. Three good quality images were recorded for far vision (with the eye focused on infinity, with the lens in the relaxed position) and three for near vision (with the eye focused on a near point at 30 cm, with the lens at the maximum accommodation and thickness).

Overall satisfaction (0 to 4 scale, where 0 is no satisfaction and 4 is high satisfaction) was assessed 2 weeks after the last session, at the time of the last clinical examination.

**Statistical Analysis**

Statistical analyses were performed by different software packages: MedCalc Statistical Software (version 16.8.4; MedCalc, Ostend, Belgium: https://www.medcalc.org) and the R Core Team (version 3.3.1.2016; R Foundation for Statistical Computing, Vienna, Austria: https://www.R-project.org). The non-parametric Friedman test was used for testing the differences between the several time points for the same patients for each outcome variable analyzed. If the null-hypothesis was rejected with a P value of less than .001, pairwise post-hoc analysis was conducted based on Conover’s method.12 Because the Friedman test is for related samples, all cases had no missing observations for the analyzed variables.

**RESULTS**

Among the 27 treated patients, 17 (63%) were women. The average patient age was 45.74 ± 3.35 years (range: 40 to 51 years). The control group of 13 individuals had 7 women (53.84%) and the average age was 45.8 ± 3.1 years (range: 40 to 49 years).

Three of the 27 treated patients (11.11%) reported a dry eye sensation soon after treatment, which was completely resolved in 48 hours by using artificial tears containing hyaluronic acid. No other side effects were observed.

**DISCUSSION**

This is the first clinical report of the results of pulsed ciliary muscle contraction to restore accommodation. Although we have reported short-term results (up to 2 months), our findings support ciliary muscle
contraction to restore accommodation as a promising treatment for presbyopia.

The complete pathophysiology of presbyopia remains poorly understood. Donders (1864) proposed that presbyopia is caused by a decrease in the force of contraction of the ciliary muscle with age and Helmholtz (1855) suggested that the lens becomes more difficult to deform with age due to lenticular sclerosis. According to the latter theory, accommodation occurs as a result of the elastic properties of the lens and possibly the vitreous, which allow the lens to expand and increase its power when zonular tension is relieved during ciliary muscle contraction. As the lens changes with age, the ability to expand and increase its refractive power is progressively lost. Possibly, a combination of these two mechanisms determines the evolution and natural course of presbyopia. Interestingly, Helmholtz’s theory of sclerosis of the crystalline lens as the cause of presbyopia was challenged by Schachar, who suggested that when the longitudinal muscle fibers of the ciliary muscle contract during accommodation, they place more tension on the equatorial zonules while relaxing the anterior and posterior zonules. This force distribution causes an increase in the equatorial diameter of the lens, decreasing the peripheral volume while increasing the central volume. As the central volume increases, so does the power of the lens. According to Schachar’s theory, presbyopia occurs because of the increasing equatorial diameter of the aging lens. Once the lens diameter reaches a critical size, usually during the fifth decade of life, the ability of the ciliary muscle to provide resting tension on the zonules is significantly reduced.

Although there are several approaches to manage the visual disability associated with presbyopia, most of the currently available treatments are compensatory optical tools rather than corrective, involving more pseudo-accommodation rather than true accommodation. Methods used so far for the correction of presbyopia include contact lenses and spectacles, whereas the surgical correction of presbyopia remains a challenge for refractive surgeons. Pharmacological attempts to counteract presbyopia also exist. They are focused on relieving lens rigidity (eg, eye drops containing lipoic acid) or enhancing iris and ciliary muscle contractility (with a combination of one parasympathetic agent, one NSAID, two alpha-agonists agents, and one anticholinesterase agent).

Accommodation occurs by the contraction (forward and inward movement) of the ciliary muscle and relaxation of the zonular fibers, resulting in lens thickening and steepening with consequent increase in the convergence refractive power of the eye. Therefore, age-related changes in each component of the accommodative apparatus (either separately or combined) have been implicated in the pathophysiology of presbyopia, including lens hardening and posterior restriction of the ciliary
muscle. Crystalline lens weight progressively increases with aging due to the gradual loss of water content and the increase of glycoproteins such as albumin and electrolytes such as calcium and potassium. Moreover, there is an increment of disulfide bonding, oxidation of methionine, and deamination and degradation of glutamine and asparagine leading to protein backbone cleavage. The consequence is lens stiffening with a progressive decrease of the refractive power during accommodation. Therefore, considering the ciliary muscle as the engine of the accommodative process, and because its magnitude of forward centrally and inward movement is reduced with increasing age, an alternative approach for presbyopia might be to address its revitalization.

Our hypothesis is that ciliary muscle contraction to restore accommodation addresses such an active part of the accommodation system by working out the ciliary muscle to increase its potency, so that it can overcome the higher resistance of the system that has become stiffer due to aging. This approach is already known to work for atrophic muscles and might also work on the ciliary muscle. If this hypothesis is correct, then the contraction of the ciliary muscle is expected to stretch the tendinous formation in direct contact with the sclerocorneal trabeculate, thus increasing the distance between the lamellae of the sclerocorneal angle. In this way, it could also restore the natural function of the trabeculate in aged patients, thus reducing their intraocular pressure. Accordingly, electrostimulation was found to be effective in decreasing intraocular pressure in patients affected by ocular hypertension and glaucoma.

However, based on recent evidence, the question remains as to how ciliary muscle contraction to restore accommodation partially restores “true physiological accommodation” differently from other more invasive procedures, which create some form of “pseudoaccommodation” or other corneal or lenticular aberrations. This may be the subject of further research, likely also based on different evaluation methods.

The data presented demonstrate that electrostimulation is effective in improving near vision ability in patients with early presbyopic emmetropia, which is likely related to restoring the accommodation process because the data suggest that ciliary muscle contraction to restore accommodation enhances the ability of the ciliary muscle to contract and thereby perform accommodation. Electrostimulation works like training in physiotherapy, so that the best results are expected for young presbyopic patients (40 to 50 years), when the ciliary muscle starts needing more strength to move a stiffer and bigger lens. Also, there should be an age limit for the efficiency of such treatment. Interestingly, because presbyopia is considered a preliminary stage prior to age-related cataract, in a continuum process described as “dysfunctional lens syndrome,” ciliary muscle contraction to restore accommodation could be associated with other treatments that aim to reverse the lens aging process, which leads to presbyopia and is also associated with ocular hypertension and possibly cataract formation.

Because ciliary muscle contraction to restore accommodation is a passive exercise, the effect of electrostimulation is expected to last for a limited time period and then progressively regress. To maintain the benefit, it is necessary to periodically repeat the treatment, which requires developing customized programs based on the individual response related to the observed effect. Patient
education is fundamental to ensure realistic expectations, but also challenging. Further studies are under way in our clinic (and several others) to optimize the electrostimulation parameters (time, voltage, and device) to improve such results. Moreover, it is possible that novel approaches may play a synergistic role in ciliary muscle contraction to restore accommodation such as pharmacologic treatments with lipoic acid\textsuperscript{17,32} or N-acetylcarnosine eye drops\textsuperscript{33} that appear to work by restoring lens elasticity and preventing age-related changes.

AUTHOR CONTRIBUTIONS

Study concept and design (LG, FG, RA, VC, MG); data collection (LG, DR, TF); analysis and interpretation of data (LG, DR, RA, MQS, BL, TF); writing the manuscript (LG, DR, RA); critical revision of the manuscript (LG, FG, DR, RA, MQS, BL, VC, TF, MG); statistical expertise (RA, BL); administrative, technical, or material support (LG, TF); supervision (LG, FG, VC, MG)

REFERENCES

Figure A. Illustration of the medical device for the electrostimulation of the ciliary muscle. (A) Bottom side of the lens showing the four electrode contacts. (B) Upper side of the lens showing the four cables to be connected to the power generator. (C) Positioning of the lenses on the ocular surface of a patient. (D) Power supply during a bilateral simultaneous treatment in which two scleral contact lenses in polycarbonate are stabilized by two syringes creating a vacuum and connected by cables directly to the Ocufit (Sooft; Montegiorgio, Italy) electrostimulator medical device. (E) Pulse trains are in the form of compensated biphasic square-waves. The graph illustrates treatment cycle sequences consisting in pulsed repetitions of 2 seconds of electrical impulse followed by 6 seconds of rest.
### Table A

**Binocular UNVA (Smallest Character) Data Measured by MNREAD Charts at 40 cm Distance**

<table>
<thead>
<tr>
<th>Time</th>
<th>Minimum</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
<th>Maximum</th>
</tr>
</thead>
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<td>Preop</td>
<td>-0.2</td>
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<td>0.1</td>
<td>0.233</td>
<td>0.33</td>
</tr>
<tr>
<td>T1</td>
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<td>0.01</td>
<td>0.1</td>
<td>0.18</td>
<td>0.3</td>
</tr>
<tr>
<td>T2</td>
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<td>0.05</td>
<td>0.11</td>
<td>0.23</td>
</tr>
<tr>
<td>T3</td>
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<td>0</td>
<td>0.02</td>
<td>0.1</td>
<td>0.31</td>
</tr>
<tr>
<td>T4</td>
<td>-0.2</td>
<td>-0.075</td>
<td>0.02</td>
<td>0.1</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*UNVA = uncorrected near visual acuity; preop = preoperative*

### Table B

**No. of Words Read per Minute at 40 cm Distance**

<table>
<thead>
<tr>
<th>Time</th>
<th>Minimum</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
<th>Maximum</th>
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<tbody>
<tr>
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<td>116</td>
<td>142</td>
<td>161.25</td>
<td>261</td>
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<tr>
<td>T1</td>
<td>103</td>
<td>137.75</td>
<td>162</td>
<td>188.75</td>
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</tr>
<tr>
<td>T2</td>
<td>106</td>
<td>152.75</td>
<td>176</td>
<td>212.75</td>
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<tr>
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<tr>
<td>T4</td>
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<td>178.5</td>
<td>203</td>
<td>217.75</td>
<td>284</td>
</tr>
</tbody>
</table>

*preop = preoperative*