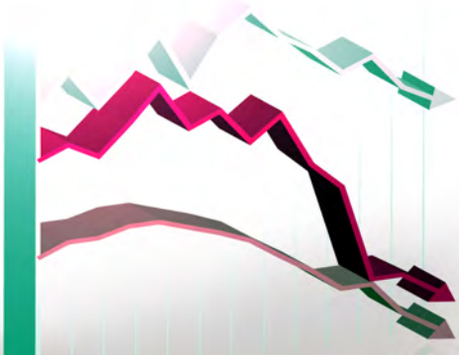
STUDY RESULTS

Elderly women may not be benefiting from new advances in breast cancer treatment

Data collected over three decades indicate aging women have shown less improvement in outcomes than younger women.

A new study published in the *Journal of Clinical Oncology* has claimed that over the last three decades, not all women have benefited from breast cancer treatment. It appears that older women suffering from this form of cancer show a poorer survival rate when compared with younger groups. The authors of the study proposed that this difference may be due to elderly patients not experiencing the new treatments and detection methods that have become available.

The research, performed at The University of Texas MD Anderson Cancer Center (Houston, TX, USA), utilized data collected between 1980 and 2007 from the National Vital Statistics Report published by the Center for Disease Control and Prevention to examine age-related data in groups of women suffering from breast cancer. This was combined with another set of data from The Surveillance, Epidemiology and End Results registry (collected between 1980 and 1997), which was used to assess the risk of breast cancer-related death at different ages.



The results of the analysis indicated that during the 1980s, breast cancer deaths remained stable in women aged 20–64 years. However, an increase in deaths was seen in women aged 65 years and over. Furthermore, a difference between decreases in death rate was observed between young and older sufferers during the 1990s. Women aged 20–49 years showed the largest decrease in death rate (2.4% per year). However, sufferers over the age of 75 years showed the smallest decrease (1.1%). The researchers suggested that these improvements in death rate were most likely due to advances in treatment, such as the use of endocrine therapy and adjuvant chemotherapy. However, it is clear from this analysis that elderly women were not experiencing the same level of improvement as younger women. To reinforce this, analysis also showed that during the 1980s, women over 75 years of age had the lowest risk of 10-year breast cancer-related death (24%), and that by 1995–1997, this had decreased to 17.3%. However, a much greater improvement was seen in women below 75, who had a 30% risk of 10-year breast cancer death in the 1980s, which significantly decreased to 16% by 1995–1997.

The study also found that, like the elderly, black women are not experiencing improvements in outcome either; in

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2008 the absolute death rate for this group was 38% higher than whites.

Benjamin Smith, an author of the study, claims that many factors, such as a limited knowledge of optimal treatment or chemotherapy toxicity, could account for the contrast seen across different groups of women suffering from breast cancer. Smith comments that, "We really need to focus research exclusively on developing optimal treatments for older women with breast cancer, evaluating how we can predict which older women can tolerate treatments, and develop new treatments that work better."

– By Jonathan Wilkinson

Sources: Smith BD, Jiang J, McLaughlin SS *et al*. Improvements in breast cancer outcomes over time: are older women missing out? *J. Clin. Oncol.* doi:10.1200/JCO.2011.35.8408 (2011) (Epub ahead of print); Press Release: www.mdanderson.org/newsroom/news-rwleases/2011/ut-md-anderson-study-finds-advances-in-breast-cancer-don-t-extend-to-older-women.html

Dopaminergic stabilizer pridopidine shows promise for Huntington's disease patients

The results of a recent Phase III randomized, double-blind, placebo-controlled trial investigating the potential of pridopidine to improve movement control and coordination in Huntington's disease patients have recently been published.

The MermaiHD trial, recently reported in the *The Lancet Neurology*, was conducted by a group of researchers led by Justo Garcia de Yebenes from the Hospital Ramón y Cajal (Madrid, Spain). The study looked at 437 individuals with Huntington's disease, recruited from 32 European centers across eight EU countries. Patients were aged 30 years or older and at baseline they all had a modified motor score (mMS) of ten points or higher.

The patients were randomly assigned to one of three groups. The first group received 45 mg of pridopidine once daily, the second received 45 mg twice daily, and the last group received a placebo. All groups were treated for a total of 26 weeks; the primary end point was a change in mMS score during this time period.

The effects of the drug were evaluated using the mMS designed to measure ten items associated with voluntarily movements from the unified Huntington's disease rate scale total motor score. The researchers also assessed behavior, depression and anxiety, as well as cognitive function.

At 26 weeks the difference in mean mMS was -0.99 points (97.5% CI: -2.08–0.10; p = 0.042) in the 90 mg group (n = 145) versus those who received placebo (n = 144), and was -0.36 points (97% CI: -1.44–0.72; p = 0.456) in the 45 mg per day group (n = 148) versus those who received placebo. No change in nonmotor end points was identified at either dose.

> "Pridopidine has the potential to complement available treatments by improving a different range of motor deficits."

Although after 6 months of treatment there was no significant difference in the average mMS scores between the three groups, at the tertiary examination the team found that the drug treatment resulted in improvement in total motor function in individuals that received the higher dose of the drug when compared with patients who had taken the placebo. Hand movements, eye movements, dystonia, gait and balance scored particularly well, as measured by unified Huntington's disease rate scale total motor score.

In the study the authors explained, "Pridopidine has the potential to complement available treatments by improving a different range of motor deficits. Its lack of severe side effects … suggests that pridopidine might be useful even for those patients who are treated at sites that are not centers of excellence for Huntington's disease."

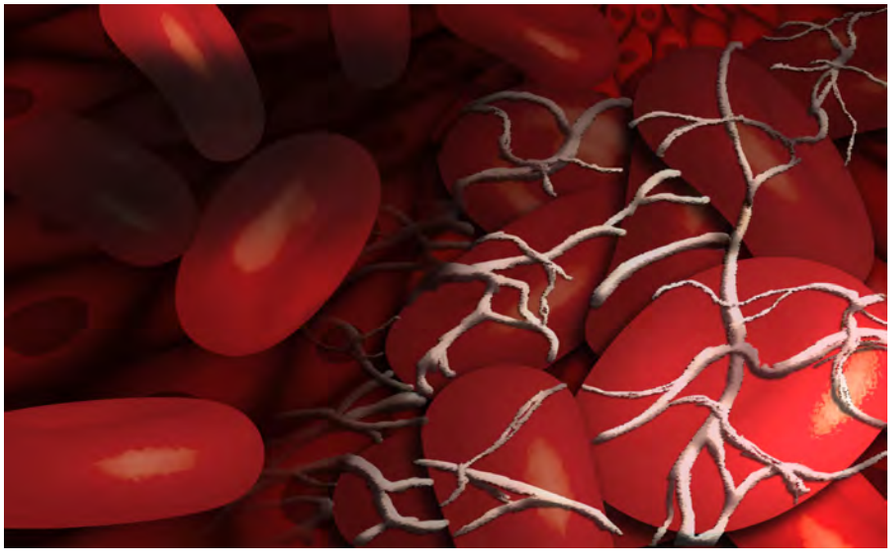
Pridopidine belongs to a novel class of medications known as dopidines. These medications are dopaminergic stabilizers, which act to return dopamine levels in the brain to normal.

Huntington's disease is a condition associated with an imbalance in the signaling chemical dopamine. At present, the only medication approved for Huntington's disease is tetrabenazine, which treats chorea, an involuntary movement disorder. To date, no medication has demonstrated the ability to improve the loss of the ability to move muscles voluntarily.

In the associated editorial, Andrew Feigin from The Feinstein Institute for Medical Research, (NY, USA), commented that "a well-tolerated drug that produces even small benefits for patients with Huntington's disease would be a very welcome addition to the currently available treatments for this debilitating disorder".

– By Laura McGuinness

Source: de Yebenes JG, Landwehrmeyer B, Squitieri F *et al*. Pridopidine for the treatment of motor function in patients with Huntington's disease (MermaiHD): a Phase III, randomized, double-blind, placebo-controlled trial. *Lancet Neurology* 10(12), 1049–1057 (2011).



Early results are encouraging for Angiomax® as compared with heparin in transcatheter aortic valve interventions

STUDY RESULTS

Initial results of a pilot study comparing patients treated with the anticoagulant Angiomax® (bivalirudin; The Medicines Company, NJ, USA) to those treated with heparin showed reduced rates of both in-hospital major bleeding and in-hospital net adverse clinical events for the Angiomax patients.

The results of the study carried out by George Dangas of Mount Sinai Medical Center (NY, USA) and teams at the University of Miami Health System (FL, USA) were announced at the Cardiovascular Research Foundation annual Transcatheter Cardiovascular Therapeutics conference held in San Francisco in early November 2011. A 60% reduction in major bleeding events was reported for those patients treated with Angiomax compared with patients treated with heparin.

The drug was investigated for use as an adjunct to catheter-based procedures in aortic valve patients for whom surgery is not an option. Transcatheter aortic valve interventions require anticoagulants periprocedurally in order to prevent clotting in the treated area and also in other organs, for example, clotting in the brain, could result in a stroke. However, the use of anticoagulants can increase the risk of vascular and bleeding complications.

Lead author of the study, Dangas commented that "advances in procedures, such as percutaneous coronary intervention, valvuloplasty and transcatheter aortic valve implantation may require improvements in anticoagulation to yield improved patient outcomes".

Looking to the future Dangas also noted, "Technologies to enable heart valve replacement or repair without cracking open a patient's chest are emerging rapidly. Last week's US approval of the Sapien valve is the most recent example."

– By Laura McGuinness

Sources: Transcatheter Cardiovascular Therapeutics conference 2011: www.tctconference.com; Medical News Today. First results of Angiomax (bivalirudin) vs. heparin in transcatheter aortic valve interventions: www.medicalnewstoday.com/releases/237386.php

TRIAL OUTCOMES

Transdermal carbidopa: no more levodopa lows?

Levodopa, the dopamine precursor, is the most commonly used treatment for Parkinson's disease. The most significant weakness of levodopa is widely acknowledged to be the drug's low bioavailability, which leaves Parkinson's sufferers enduring frustrating periods of reduced motor control between doses. A new dermal patch could provide a solution.

The patch, developed by NeuroDerm® (Ness Ziona, Israel), administers a continuous dose of carbidopa subcutaneously. Carbidopa acts by inhibiting an enzyme that catalyzes the synthesis of dopamine from levodopa. Unlike levodopa, it cannot cross the blood–brain barrier, so only prevents dopamine synthesis peripherally, ensuring more levodopa reaches its target site, potentially increasing both the plasma half-life and the bioavailability of levodopa in the brain.

Although carbidopa is already widely used as an adjunctive therapy to lepodova, it is generally administered orally. NeuroDerm, a biotechnology company that specializes in improving the bioavailability of drugs by developing transdermal delivery systems, hopes that this unique method of delivery will significantly increase levodopa's efficacy. Whereas oral carbidopa prevents levodopa metabolism in the gastrointestinal system, the transdermally delivered formulation, called ND0611, can prevent metabolism anywhere outside the brain.

Continued on page 14

Excitement surrounding the development of ND0611 has mounted with the imminent release of the Phase II study data. In this placebo-controlled, randomized, double-blind trial, funded by the Michael J Fox Foundation for Parkinson's research (NY, USA), ND0611 significantly improved the bioavailability of three orally administered formulations of levodopa versus placebo, and met all of its primary and secondary end points.

NeuroDerm claims that ND0611 improved the bioavailability of even the most-effective oral levodopa formulation currently available, however, full data have yet to be presented.

While the early trials of this formulation have yielded undeniably positive results, an early Phase II trial involving 24 patients across 4 weeks is not conclusive. It will take considerably larger studies conducted over the coming years to convince many Parkinson's specialists.

Nonetheless, the trial represents a positive start for a novel formulation of an important drug.

– By Lucy Abel

Source: NeuroDerm. NeuroDerm announces positive results of a Phase II study of ND0611 dermal patch in patients with Parkinson's disease: www.neuroderm.com/pdf

Etanercept could be a promising therapy for juvenile idiopathic arthritis sufferers

A third of study participants demonstrated an excellent response to the fusion protein drug.

Research performed at the Erasmus MC Sophia Children's Hospital (Rotterdam, The Netherlands) has highlighted beneficial outcomes for patients with juvenile idiopathic arthritis (JIA) who initiated treatment with the drug etanercept. A third of the participants treated with etanercept achieved an excellent response, as assessed by a number of factors including disability scores and age of onset.

> "A poor response was found to be associated with systemic juvenile idiopathic arthritis and was also linked to female gender."

The work was carried out using The Arthritis and Biologicals in Children Register, an ongoing prospective observational study established in 1999, which included all Dutch JIA patients who have been treated with biologic agents. All biologically naive patients who used etanercept before 2009 were included in the study, with follow-up data to early 2011. The researchers categorized responses into three groups; excellent response (inactive disease or discontinuation due to disease remission), intermediate response (more than 50% improvement from baseline, but active disease) or poor response (less than 50% improvement from baseline or discontinuation due to ineffectiveness or intolerance).

At 15 months after treatment initiation, data indicated that 32% of participants were characterized to be excellent responders, 36% were intermediate responders and 32% were poor responders. Participants considered to be excellent responders were associated with a lower baseline disability score than intermediate responders, fewer disease modifying antirheumatic drugs used for initiating etanercept and a younger age of onset. A poor response was found to be associated with systemic JIA and was also linked to female gender.

Marieke Otten, the study leader, explained to *Clinical Practice*, "From these results we can conclude that the focus should be on early introduction of etanercept (i.e., less previous DMARD use and lower disability scores before introduction of etanercept) to improve outcomes for JIA."

> "...the focus should be on early introduction of etanercept ... to improve outcomes for juvenile idiopathic arthritis."

Otten commented, "This study is important because the insight into patients who are more (and less) likely to respond to etanercept treatment could be an important step towards tailored patient care. Ultimately, directing therapy to patients who will benefit the most could minimize unnecessary exposure. However, more research is still needed, because it is unknown whether patients with a poor treatment response would have responded better to other treatments or whether these factors are related to the prognosis of these patients."

– By Jonathan Wilkinson

Source: Otten MH, Prince FH, Armbrust W *et al.* Factors associated with treatment response to etanercept in juvenile idiopathic arthritis. *JAMA* doi:10.1001/jama2011.1671 (2011) (Epub ahead of print).

CLINICAL TRIAL

Antiepileptic brain stimulation offers new hope to unresponsive sufferers

Currently, the standard treatment for patients who respond poorly to several types of antiepileptic medication is surgery to remove the abnormal part of the brain responsible: the seizure focus. However, while this surgery is associated with a high cure rate, approximately half of the total number of patients who could benefit from it are ineligible.

It is now hoped that a new brain stimulation device, currently awaiting US FDA approval following a clinical trial, could dramatically improve the quality of life for these epilepsy sufferers.

Brain stimulation has been approved for essential tremor since 1997 and for Parkinson's disease since 2002, but this is the first time approval has been sort for epilepsy. The device, known as the responsive neurostimulation system (RNS™), has been developed by NeuroPace®. It consists of electrical leads that are implanted in or near to the seizure foci and connected to a programmable microprocessor. This miniaturized computer detects abnormal brain activity and responds by electrically stimulating the foci, normalizing the electrical impulses before seizure symptoms become apparent.

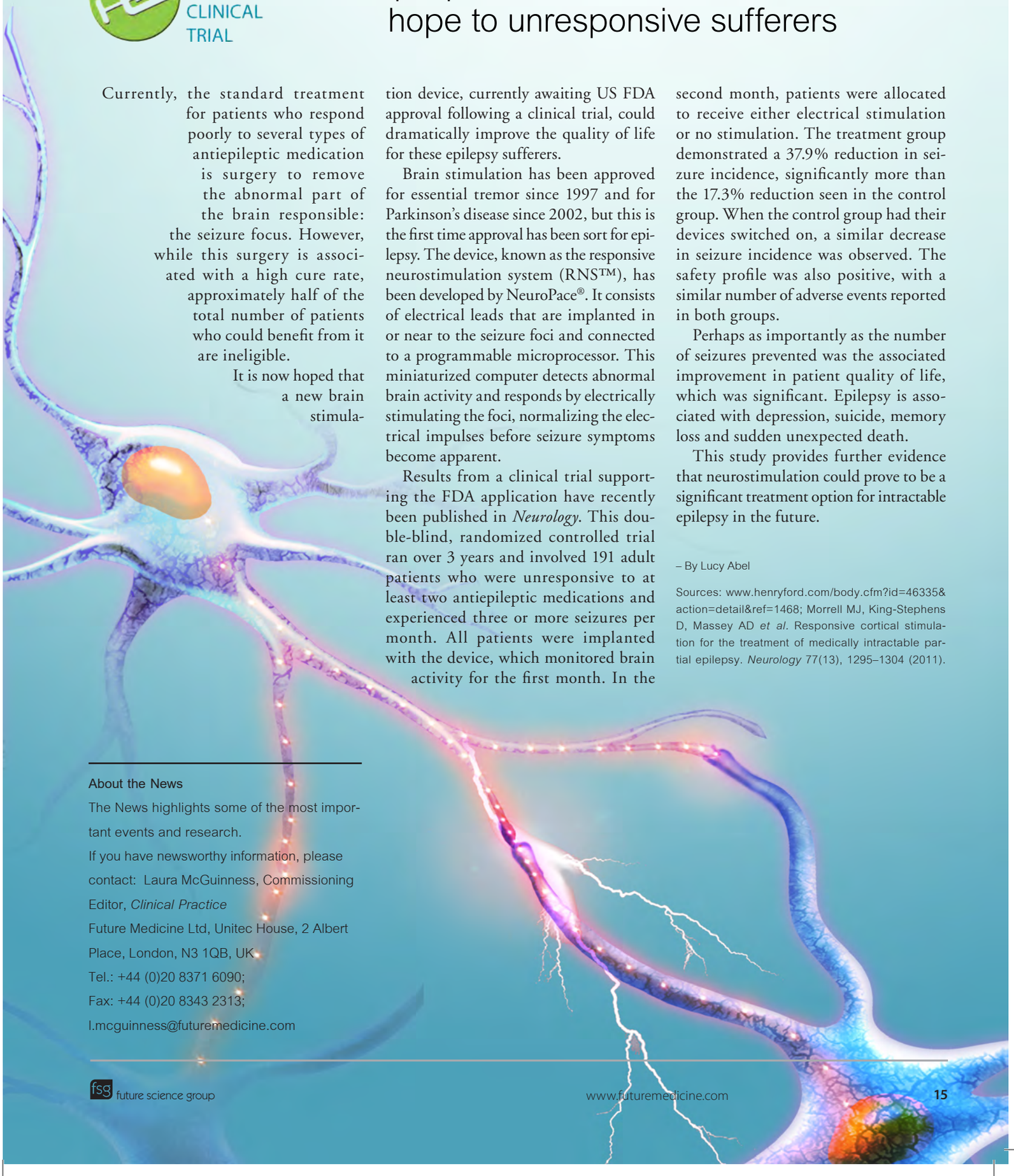
Results from a clinical trial supporting the FDA application have recently been published in *Neurology*. This double-blind, randomized controlled trial ran over 3 years and involved 191 adult patients who were unresponsive to at least two antiepileptic medications and experienced three or more seizures per month. All patients were implanted with the device, which monitored brain activity for the first month. In the second month, patients were allocated to receive either electrical stimulation or no stimulation. The treatment group demonstrated a 37.9% reduction in seizure incidence, significantly more than the 17.3% reduction seen in the control group. When the control group had their devices switched on, a similar decrease in seizure incidence was observed. The safety profile was also positive, with a similar number of adverse events reported in both groups.

Perhaps as importantly as the number of seizures prevented was the associated improvement in patient quality of life, which was significant. Epilepsy is associated with depression, suicide, memory loss and sudden unexpected death.

This study provides further evidence that neurostimulation could prove to be a significant treatment option for intractable epilepsy in the future.

– By Lucy Abel

Sources: www.henryford.com/body.cfm?id=46335&action=detail&ref=1468; Morrell MJ, King-Stephens D, Massey AD *et al.* Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. *Neurology* 77(13), 1295–1304 (2011).



About the News

The News highlights some of the most important events and research.

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First person receives US FDA-approved implantable miniature telescope

IN THE CLINIC

VisionCare™ Ophthalmic Technologies (CA, USA) have announced that the first person has received their US FDA-approved implantable miniature telescope, indicated to improve vision in patients with end-stage age-related macular degeneration (AMD). The procedure was performed on an outpatient basis at Carondelet Health Network's St Joseph's Hospital in Tucson (AZ, USA).

After removing of the lens of the eye, the telescope implant is surgically placed in the capsular bag. Implantation inside the eye allows the patient to see using natural eye movements in both stationary and dynamic environments. By leveraging the healthy areas of the patient's eye, light that enters the telescope is magnified by around 2.5-times and projected onto the portion of the retina unaffected by macular degeneration.

"Our patients who have exhausted all wet AMD treatment options, or who have the untreatable, advanced form of dry AMD, now have a potential for improved vision and quality of life."

"Our patient's procedure is a milestone that brings new hope and a first treatment option for our most visually debilitated AMD patients," said Henry Hudson, a retinal specialist at Retina Centers PC (Tucson, AZ, USA), a principal investigator in the pivotal trial for US FDA approval and lead author of the trial outcomes publications. "Patients with end-stage AMD have been underserved, and they have had limited options until now. Our patients who have exhausted all wet AMD treatment options, or who have the untreatable, advanced form of dry AMD, now have a potential for improved vision and quality of life. We're talking more than just seeing better on the eye chart but about being more independent in their daily activities and reconnecting with their social network of friends, family, and their community."

– By Paolo Reveglia

Source: VisionCare™ Ophthalmic Technologies. Press Release: www.visioncareinc.net/press_releases/pr_1320950344