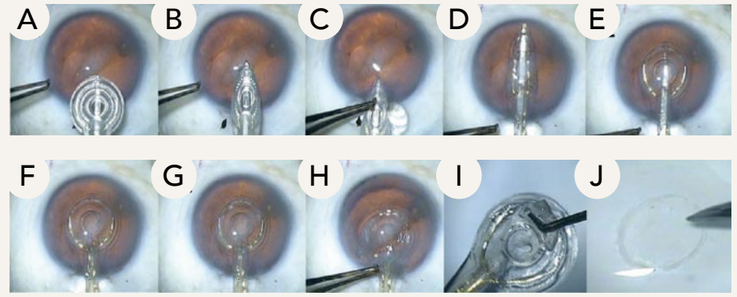
# The revolution in cataract surgery

From its inception just a decade ago, the Zepto capsulotomy device has come a long way. **CEO John Hendrick** tells us the Mynosys story, which shows how a small start-up can shake up the medical field by tackling one of the most challenging and crucial steps in cataract surgery.






The Zepto capsulotomy tip can collapse to enter the primary corneal incision (A–D), then re-expand to a circle within the anterior chamber (E). Once aligned over the visual axis (F), suction is used to appose the nitinol ring against the capsule. Using a multipulse algorithm, precision-pulse technology is used to cause rapid phase transition of the water molecules underneath the ring, cleaving the capsule membrane and simultaneously creating all 360° of the capsulotomy (G). The tip can then be collapsed and removed (H) along with the excised tissue (I–J).

Cataracts develop when the lens of the eye gradually becomes less transparent, preventing light from entering the eye, and thereby affecting sight. They are often associated with age, and eventually require surgery to treat. According to the NHS, cataracts are the number one cause of impaired vision globally, and most people aged over 65 in the UK have some kind of visual impairment as a result of cataracts. Fittingly, therefore, cataract surgery is the most commonly performed surgery in the USA and EU. Thus, the potential impact of improved technology for cataract surgery is huge, says CEO John Hendrick at Mynosys, who have developed a new 'Zepto' device for the job.

## THE CRUCIAL STEP: CAPSULOTOMY

The most important and difficult part of cataract surgery is the capsulotomy. Cataract surgery starts with a small incision in the cornea, the transparent covering over the eye. The surgeon then has to create an opening in the lens capsule, a delicate thin membrane that surrounds the cataractous lens itself. It is through this capsulotomy opening that the surgeon performs the rest of the procedure, including the removal of the clouded lens and the implantation of an intraocular lens (IOL) implant for the best vision after surgery. The capsulotomy is the one step in the operation that is crucial to determining patient outcomes, guaranteeing procedural success, and minimising potential negative side effects.

At present, about 85% of capsulotomies are conducted manually, using a procedure called Continuous Curvilinear Capsulorhexis (CCC). However, this is a challenging step, and surgeons vary greatly in their skill – indeed, it is often one of the final lessons of an eye surgeon's training.

## IMPROVING EXISTING TECHNOLOGY

The need for a technology that can automate and improve the precision of the capsulotomy has been apparent for some time. This has led to the development of femtosecond lasers, which were first demonstrated on human eyes in 2008. Around 15% of capsulotomies now use this method, which is more precise and accurate when making the incision in the lens capsule. This means the surgery is safer and more predictable, so this method can be used in more complex surgeries.

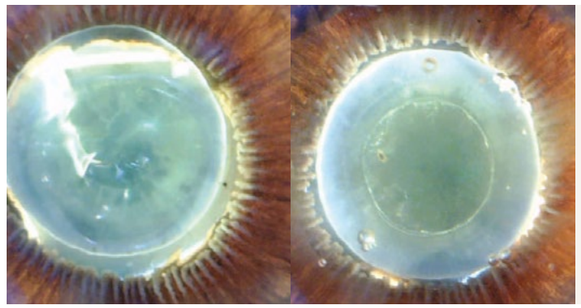
However, 'femto' has its downsides, and the most obvious one is the price tag. The upfront cost is around $500,000 and there are also ongoing associated maintenance costs. Besides, there is little discernible difference in visual benefits to patients compared with the CCC method, and there have been studies reporting higher rates of certain complications associated with femto. These include 'postage stamp' perforations on the edges of capsulotomies, which can cause the capsule to tear. On top of that, it is difficult to operate on patients with corneal opacities or small pupils, who together with those with other comorbidities can make up around a quarter of the patients that a surgeon sees. Lastly, the high cost translates into additional out of pocket expenses of around $1500 to $2000 per eye, making this technology out of reach for the vast majority of cataract surgery patients.

## THE MYNOSYS STORY

The founders of Mynosys, Christopher Keller and David Sretavan, were inspired by the development of femto, but knew that the new technology could still be improved upon. They had been working on developing micro knives for use in glaucoma operations, but had run up against some brick walls when it came to funding their start-up in a post-recession world. They tried a similar approach with capsulotomies, but soon found that the use of micro knives or any kind of physical cutting on a thin membrane was problematic.

That's where they came up with the idea for Zepto. Chris Keller developed a method called precision pulse capsulotomy (PPC) that uses fast, low-energy pulses of direct current delivered in a hand-held device that replaces capsulotomy forceps directly, meaning it is easily integrated into the surgical procedure.

The Zepto device consists of a console, a disposable handpiece and a capsulotomy tip, equipped with a Nitinol ring. Nitinol is an alloy that has shape memory, meaning it can be bent to fit though a tiny (2.2 mm) incision in the cornea, but still springs back to its original size and shape once in place. The ring creates the capsulotomy opening all at once, and does not use tissue cauterisation or burning, therefore minimising the likelihood ▶



Miyake-Apple view footage shows that, compared with CCC, Zepto capsulotomy results in very little zonular movement.

of rips and tears. The tip also includes a suction device, inspired by how squid suckers work to help catch prey, that exerts force to gently pull the membrane against the electrical cutting element without placing strain on other areas. This makes it even more precise and less likely to cause complications.

Other benefits of the device include the ability to achieve intraoperative centration – essentially this means centering the capsulotomy opening and placing the IOL over the visual axis (an imaginary line from the fovea, where cones in the eye are most concentrated and visual acuity is highest, through the pupil) during the procedure. If this cannot be achieved then the patient experiences visual problems because the lens is off kilter. Neither femto nor CCC can currently do this. If you add into this mix the fact that Zepto can shave 12-15 minutes off the cataract procedure in comparison to femto, then you start to see why people are excited about it, and begin to understand where the technology gets its name. Femto is the metric unit meaning $10^{-15}$, while Zepto means $10^{-21}$: so you can think of it as a nerdy way of saying PPC is a million times quicker, smaller and better.

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**A MILLION TIMES BETTER**

The origin of Zepto sounds like a classic tale of the underdog – two guys working alone, competing with giant companies who were developing femto. They didn't have the same kind of upfront cash to throw at the project, so they knew they'd have to keep it cheap, simple and effective to succeed. Luckily, they did - and the low costs in design have translated into low costs in application. Mynosys CEO John Hendrick says that he's had a very positive response from surgeons who are keen to get their hands on an easy replacement for forceps that costs around $100 a pop.

Hendrick got on board after being convinced by the data on Zepto – he's certain that it can mount a very serious challenge to both other methods on the market, and the peer-reviewed literature suggests the same. In a 2015 paper testing Zepto's performance, they showed that there were no differences in safety between PPC and CCC, and that the capsulotomy edge was much smoother using Zepto compared with femtosecond technology. When considering the financial angle, time savings and the ease with which Zepto can be adopted, it emerges as a clear front runner.

So where next? Zepto has received a CE mark and a 100 patient trial is expected to commence by September. The trial is a single-arm trial that has a four-week follow up. Soon after the trial completion the company plans on filing the 510(k) submission for approval from the FDA. They plan to expand into the market by highlighting the benefits in difficult cases which make up approximately 25% of the market. There has been excitement not only from physicians and surgeons, but also distributors worldwide, who are keen to see Zepto take off. With this in mind the company will be launching Zepto outside the US in January of 2017. With the recent approval of the small trial in the US it is very possible that the US market could also see a launch about the same time.

Zepto's evolution from early prototypes to the product being demonstrated today.

## Q&A

***Capsulotomy is one of the most difficult parts of cataract surgery, what makes Zepto so much better than existing technology?***

Compared to the manual method of continuous curvilinear capsulorhexis (CCC), it provides fast and consistently excellent capsulotomy results across the entire range of surgical skill. It is very gentle on the zonules so is particularly good for patients with weak zonules, pseudoexfoliation and other complex cataract cases. Zepto also allows for the centration of the capsulotomy anywhere the surgeon desires, including on the patient's own visual axis to ensure best visual outcome, especially for premium multifocal lenses.

Compared to the femtosecond laser, Zepto does not require the hefty $500,000 upfront cost, extra costs per procedure, and it does not require a dedicated space to house a large laser or new personnel to help operate the equipment. The femtolaser adds time to the standard cataract surgery as the patient has to first undergo the laser procedure in a different room, then be transported into the operating room for the cataract procedure itself. That is, the laser introduces inefficiency into a procedure where increasing efficiency is the goal. Zepto integrates seamlessly into the existing cataract procedure without requiring surgeons to alter their routine.

***How will the device benefit patients?***

More precise capsulotomy may be beneficial for optimal intraocular lens stability, effective lens position, and to minimize lens tilt. Centration on the patient's visual axis likely will benefit patients who receive multifocal intraocular lenses that can provide spectacle-free vision post surgery.

It can also help to prevent posterior capsular opacification, which is a common complication of cataract surgery that can cause additional visual disability. The capsulotomy edge produced by Zepto has been demonstrated to be stronger than that produced by CCC or the femtosecond laser. Thus, Zepto may provide a larger margin of safety during surgery against capsular complications.

There is a great deal of interest in future new generations of IOLs that can use the capsulotomy edge to secure their position post-operatively and thus allow the intended effective lens position to be achieved every time. Zepto facilitates the development of this new IOL technology.

Patients with comorbidities, i.e. other concurrent eye diseases, such as pseudoexfoliation, weak zonules, poorly dilating pupils, and glaucoma, may benefit from the use of Zepto as its use is not affected by these conditions and will not worsen these conditions. Patients with these comorbidities comprise on average 25% of cataract surgery patients.

Zepto was developed using a pre-clinical model that is regarded to be an excellent simulation of pediatric cataract surgery. Pediatric cataract surgery has a lifelong impact on the patient. It restores vision in cases of congenital blindness due to lens cataract. The capsulotomy step in pediatric cataract surgery is much more difficult than in adults due to the elastic properties of the capsule. Manual CCC in children has a very high rate of failure and there is no other purpose-designed instrument.

***Has being part of a start-up given you more opportunities for creativity in developing the technology?***

It allowed the Company to listen carefully to surgeons, make it easy for others to work with us and react and implement solutions to problems very quickly.

***What impact do you believe Zepto will have on the capsulotomy technology market?***

Many surgeons believe Zepto can become the standard of care by automating the most difficult part of the surgery. It can greatly influence how the rest of the surgery will progress and the quality of the outcome for the patient.

***What applications do you envisage the technology having in future? Could the principles be applied to other areas of medicine?***

Our precision pulse capsulotomy technology can be potentially applied to any clinical situation where delicate tissue membranes need to be managed surgically.

In fact, Mynosys has obtained preliminary proof of principle that a Zepto-like device can be used to create a capsulotomy in the posterior capsular bag to potentially assist in the prevention of posterior capsular opacification (PCO). PCO is the most common complication of cataract surgery and can lead to a serious deterioration of vision months to years after the original surgery. It is possible that with optimisation for use on the posterior capsular bag, the technology can be used to prevent a complication that currently has a great impact on patient quality of life and is a very large cost burden on the health care system.

## Detail

**RESEARCH OBJECTIVES**

Our research team brings together diverse technological skills from electrosurgery, shape memory alloys, as well as micro electro-mechanical system design to focus on what many companies have tried to do over the last 30 years. That is to place in the hands of cataract surgeons a disposable capsulotomy device for automated consistent capsulotomies that are dimensionally perfect each and every time. A target market is the adult patient population, where cataract surgery is the most commonly performed surgical procedure in the US and the EU. A second market is for the treatment of lens cataract in infants and children, where capsulotomies in a child's eye requiring surgery can help restore lifelong vision.

**CO-FOUNDERS**

- Christopher Keller, PhD
- David Sretavan MD, PhD

**BIO**

John N Hendrick has over three decades of executive experience, building both early stage medical device companies as well as large divisions in medical device corporations. Currently, Mr Hendrick is president and CEO of Mynosys Cellular Devices, an ophthalmic company. Previously, he was CEO of NeoVista Inc. a company in the field of Age Related Macular Degeneration. Prior to his accepting the role of CEO with Neovista, he created the Medical Division of Sanmina-SCI. Mr Hendrick has been through a successful IPO of VidaMed which led eventually to the acquisition of the Company by Medtronic Inc. Prior to VidaMed, Mr Hendrick held executive positions in Allergan Medical Optics, Baxter and American Hospital Supply along with several board positions.

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