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# SCALABILITY OF MICRO INTRAOCULAR IMPLANTS AND DEVICES

Scaling devices from tens to hundreds of thousands or millions sometimes requires a tightrope balancing act of economies of scale and product and process robustness. Micro molding is a proven, scalable, and economical process for thermoplastic micro-intraocular implants and devices. In this article, Donna Bibber, Plastics Engineer & Chief Executive Officer of Micro-Engineering Solutions, discusses some of these devices and the scalability challenges associated with each, from the perspective of a plastics engineer.

Recent developments and new-to-market intra-ocular devices and implants have led to the successful treatment of a number of ophthalmological conditions of varying seriousness and complexity such as:

- Glaucoma
- Cataracts
- Retinal detachment
- Diabetic retinopathy
- Age-related macular degeneration
- Uveitis
- Dry-eye syndrome.

focused, research-driven specialists, including and micro fabrication specialists, such as:

- Small, innovation-support funding programs
- Development companies that easily find a large marketing partner
- Big pharma funding the outsources of the development instead of doing it in-house.

To design and build scalable intra-ocular implants and devices, the design and fabrication plan must include highly precise, micro

sized component made from ultra-thin yet strong materials. These materials must be selected and characterised carefully to be robust enough to last for many years in a moist and warm environment.

In order to scale-up a polymer device that may have been born in an academic or laboratory setting,

one must first understand the physical characteristics of the eye (Figure 1) and how the surgeon will be installing the implant or device. The eye is a complex and sensitive organ with many structures and targets located closely together. These some-



**Ms Donna Bibber**

Chief Executive Officer

T: +1 774 230 3459

F: +1 508 434 0281

E: donnabibber

@microengineeringsolutions.com

**Micro Engineering Solutions, LLC**

102 City Depot Road

PO Box 952

Charlton City

MA 01508

United States

[www.microengineeringsolutions.com](http://www.microengineeringsolutions.com)

"In micro-moulded ophthalmologic implants and devices, parting lines where the mould's halves come together, and surface finish of the moulds that create the moulded parts, must meet stringent comfort standards required for them to be worn or implanted. The implications for compliance are clear."

Treatment of these conditions often requires collaboration between ophthalmological surgeons, pharmacologists, and micro-specific contract manufacturers. Development of these devices and implants occurs through a large number of highly

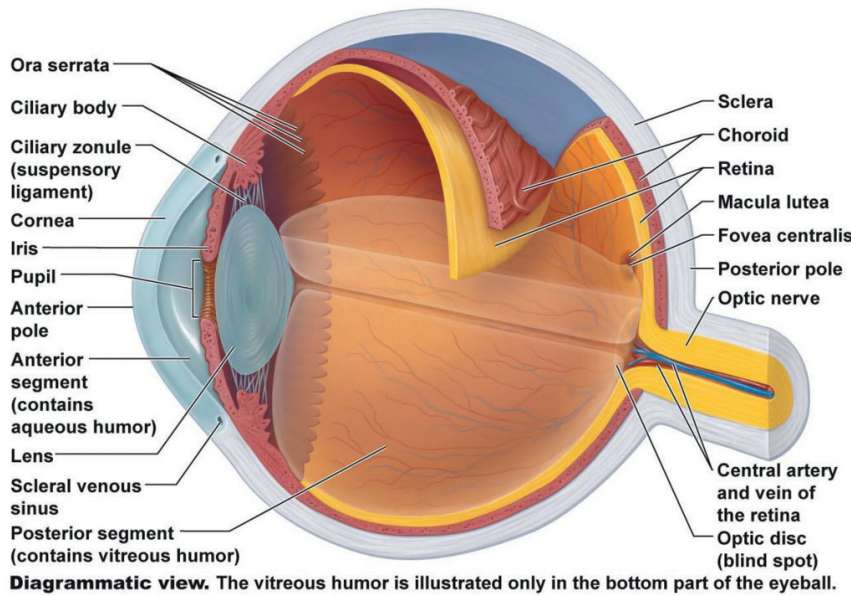


Figure 1: Sectional anatomy of the eye (photo credit: Visionbesteyecare.com).

times conflicting structures have significant defence mechanisms (tear film, cornea) that make it difficult for medication to enter. Vitreous fluid is difficult for injected medication to traverse to the posterior of eye.

When designing and fabricating micro-moulded devices and implants for the human eye, the physical characteristics and material consistency of the components of the eye are critical to understand. Figure 2 summarises the physical characteristics and function of each section of the anatomy of the eye.

The anatomy and physiology of the eye is one of the most complex and unique systems in the human body. Many of these

components of the eye are gelatinous, flimsy, easily punctured, and sensitive. As a result, the implants and devices that are installed must be free of sharp edges, excess material or flash, and have absolutely pristine surface finishes to help ensure both surgeon and patient compliance. The instruments, however, which cut or slice into the various components of the eye to install the implants and devices must be very sharp and precisely made to create correctly sized and shaped incisions. Conversely, the instrument to hold or expand the eye open during surgery must be free from parting lines, flash, or sharp edges.

Eye Component	Physical Characteristics	Function
Lens	Dense, transparent, high-protein structure	Focused light to form and image
Iris	Pigmented muscle tissue (brown, blue, green, gray)	Controls diameter of the pupil and the amount of light entering
Pupil	Dark, round hole	Allows light to enter (aperture)
Retina	Vitreous gel layer of light-sensitive cells	Converts what we see into electrical impulses, sent to optic nerve which then get sent to the brain
Eyelid	Moistened skin flap	Controls the time taken for light to enter
Ciliary Body	Contractive muscular ring	Releases tension and changes the shape of the lens, produces aqueous humor
Cornea	Thin, transparent, no blood cells, received nutrients by diffusion	Major focus of the eye
Anterior Chamber	Protein-free, watery liquid	Supplies nutrients to cornea and lens
Macula	Central area of the retina	Responsible for the sharpest central vision
Vitreous Chamber	Thick, clear jelly	Transparent, colorless gelatinous filling
Optic Nerv	Sensory rubbery nerve	Carries impulses for sight from retina to brain
Sclera	White, fibrous outer layer of eye	Protective barrier along with the cornea
Choroid	Vascular layer with blood vessels	Provides oxygen and nutrients to the eye
Aqueous humor	Clear fluid	Helps cornea keep its rounded shape

Figure 2: Physical characteristics and functional elements of the eye.

Ophthalmologists are meticulously detailed surgeons with extremely good dexterity and their instruments must match their character traits, as their instruments and implants are considered an extension of meticulously planned and executed procedures. The many layers of the eye require the surgeons to switch quickly and accurately from one instrument to another because of the different surfaces they encounter in the eye.

US baseball star Yogi Berra once stated: "I'd give my right arm to be ambidextrous." But having the ability to switch hands and instruments and use both hands during eye surgery enables quick and precise positioning of instruments and safety and efficacy is maintained with instruments designed for the comfort and use in either hand. This requires a look at not only human factors, but also design-for-manufacturability, as the features and tolerances of the device and wall thickness and aspect ratios approach "design challenges" for a particular material selection.

### MATERIAL & DESIGN CHARACTERISTICS

Understanding the body's reaction to polymeric implants is complex. Not only is the natural response affected by the chemical properties of the polymer but also by the physical properties of the implant. Development of an ophthalmologic drug delivery device requires design criteria compatible with the delicate nature of the eye, including proper materials, size, shape, and porosity.

#### Material Selection

Some materials, although tested for biocompatibility, may still cause inflammation and immuno-responses leading to long term effects on the eye. It is advantageous for safety, regulatory robustness, and speed to market reasons to select not only select a predicate material (PMMA, silicone), but also the predicate grade used in an intraocular application. Families of materials vary greatly from grade to grade in terms of both physical and chemical properties. For example, leachables and extractables over time can vary greatly with different grades of silicone and PMMA and these factors are critical to long term implant and device safety and efficacy. Additional material selection considerations include materials that are slippery, flexible, and non-hydroscopic for compliance adherence.

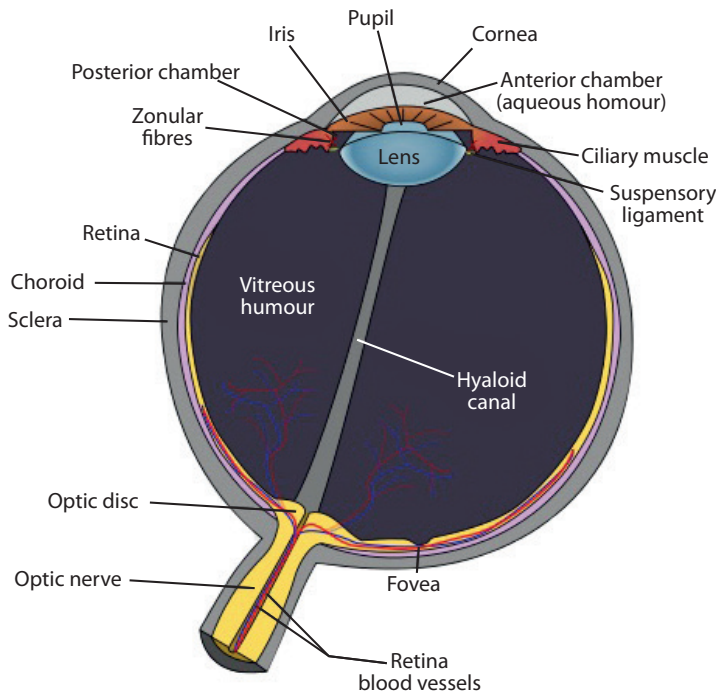


Figure 3: Sclera Image courtesy of Wikipedia.

**Size**

Ophthalmologic implants or devices must be very small and pliable to fit into the sections of the eye. For example, a glaucoma drain must fit into the sclera which is from 0.3-1.0mm thick (see Figure 3). A part's thickness and size is dependent on the ocular area and location of the implant, but also chosen on the melt flow of the materials.

**Shape**

Implants within the wall of the sclera are radial in nature to rest within the semi-circular outer wall of the eye. Figure 4 shows a polypropylene glaucoma drain with a centre wedge bore which acts with a Venturi effect to allow the pressure of the eye to drain behind the eye. Glaucoma is a result of the increased fluid pressure in the eye due to the reduction or blockage of fluid from the anterior to posterior chambers. Devices such as these are possible using micro-injection moulding and micro-automation.

Figure 5 shows a pupil expander device with micro features and surface finishes necessary to fit comfortably in the eye and provide tensile strength with fine alignment and mechanical strength to hold them in place.

Figure 6 shows a delivery device that sits on the cornea – it's a thin membrane-like, silicone structure with radial design, and a 50 µm wall thickness to fit inside the upper eyelid. The cornea has 5-6 layers varying from 2-20 µm in thickness,

made up of highly sensitive pain receptors. Cornea pain receptor density is up to 600 times that of skin, which is why even a slight injury to the eye is extremely painful.

**Surface Finish/Porosity**

In micro-moulded ocular implants and devices, parting lines where the mould's halves come together, and surface finish of the moulds that create the moulded parts, must meet stringent comfort standards required for them to be worn or implanted. The implications for compliance are clear. Surface finish, blending parting lines, spherical radii, and matching cores and cavities to ultra-precision tolerances (A2 or A1 finishes) are the keys to creating implants that can stand the test of time in an intra-ocular environment.

In the context of an ocular implant, smooth materials can have very different tissue and nerve responses compared with micro-structured materials. Tissue encapsulation of a foreign body (such as the implant) is higher with rougher surfaces because there is more surface area for the implant to attach to tissue. Nerve response to surface finish needs to be considered in implant design. Wear or degradation of a rough surface is more prevalent as well because the smaller porous particles in the surface can be toxic to tissue, can spread throughout the eye, and also trigger an allergic response.

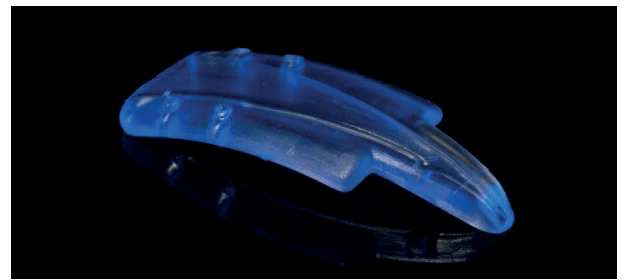


Figure 4: A polypropylene glaucoma drain.

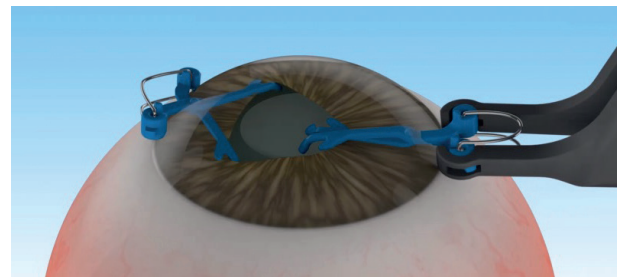


Figure 5: Pupil-expanding devices (photo credit: APX Ophthalmology).

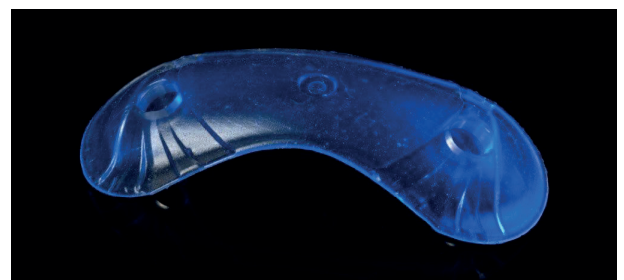


Figure 6: Silicone corneal drug delivery device.

**CONCLUSION**

The anatomy and physiology of the eye is one of the most complex and unique systems in the human body. Micro-moulding is a scalable process with particular design criteria met, including proper size, three-dimensional shape, wall thickness, material selection, and surface finish.

Micro-injection moulding is a viable and scalable process for fabricating ultra-precise, micro-sized, ultra-thin, yet robust implants and devices located in a highly complex environment such as the eye.

Scalability is an important consideration at the initial product and process design phase in order to achieve the economies of scale – tens, to hundreds of thousands of parts, to millions annually – that micro-moulding offers.

Careful consideration of surface finish, feature size and material selection is paramount to the successful integration of marrying micro-moulding technology with the internal chambers and inter-connective functions of the eye.