MICRO MOLDING WITH BIOABSORBABLES:

Not Your Average Thermoplastics

Background

BIOABSORBABLES VS. THERMOPLASTICS

For micro medical components, there is a wide variety of materials to choose from. Most micromolding materials fall into two categories: thermoplastics and bioabsorbables.

Thermoplastics are polymers that become pliable and moldable above a specific temperature, and return to a rigid state upon cooling. They have long been used in the micromolding world.

Many new micro medical applications rely on **bioabsorbable** materials (also called resorbable, bioresorbable, or biodegradable) because the materials dissolve or absorb into the body, eliminating the need for additional surgeries and minimizing concerns about adverse effects. Devices made from these materials metabolize over time so secondary invasive procedures are not needed to remove them.

Across the board with plastics, the rules are different when you mold it so small. But when it comes to bioabsorbable resins, some molders assume that a thermoplastic material shares the same molding properties, so it is treated the same way. Bioabsorbables, however, require a much more extensive and specialized approach.

FIGURE 1: Material comparison from a processing perspective.

MICROMOLDING THERMOPLASTICS	MICROMOLDING BIOABSORBABLES
Raw material and parts stored at room temperature	Raw material and molded product kept in refrigerated storage
Follows standard MT1/MT2/OQ/PQ plan for validation	Extensive validation process
Molecular weight loss is not as significant with processing	Processing can have a dramatic effect on molecular weight loss
Materials generally less expensive—runner and sprue waste not as significant	Materials generally more expensive - optimized sprue and runner technology required for cost efficiency
General Purpose Screw with an aggressive 25% overall screw length melt transition zone	Custom screw with a longer than 25% overall screw length melt transition zone for a more gradual melt
Material conditioning is more forgiving	Material conditioning is *always* critical
Utilized for permanent implants/components	Implant material is broken down over time and absorbed by the body

BIOABSORBABLE TACK

This design's sharp points must be less than 0.0002"R. Bioabsorbable materials degrade with shear generated in small flow paths. Economical micro processing of bioabsorbable materials requires minimum runner sizes to reduce waste. Manufacturing a solution that balances these conflicting needs is a challenge a molder must conquer.

SPECIALIZING IN BIOABSORBABLES

If you have a complex bioabsorbable medical device design, you need a specialist to be successful.

Think of it this way. Who would you go to to fix your complex medical issue, your general practitioner or a specialist?

The general practitioner can offer a broad spectrum of services, but cannot offer the same high-level expertise as a specialist. Because the specialist devotes all their effort on that one specialty, their level of expertise, specialized equipment, extensive knowledge and experience allows them to diagnose and fix your problem in the quickest and best way possible, whereas even a great general practitioner may not have the knowledge and tools needed to solve your problem at all.

For example, say you're a runner and you have a recurring knee problem. Your general practitioner might tell you to take some pain medication and stop running. Since that's likely not the right solution for you, you'd likely find a doctor who specializes in sports medicine. Having worked with numerous athletes and being equipped with specialized diagnostics tools, the sports medicine specialist could offer in-depth insight on how to manage your knee injury—and hopefully help you avoid surgery.

The same premise holds true for bioabsorbable micro molding. A molder who does not focus solely on medical micromolding and bioabsorbables will not have the necessary tools or knowledge to effectively find the optimal solutions for your bioabsorbable needs. Like the general practitioner who says "stop running," a non-specialized molder may tell you that your bioabsorbable design is impossible and can't be done. By turning to a bioabsorbable specialist instead, you get access to the in-depth expertise and equipment to make your ideas possible.

BIOABSORBABLE ANCHOR

This device is made of PLG and weighs only 0.025g. The anchor is used in a fascia closure device that aims to minimize port site herniation following laparoscopic abdominal surgery. The reduced IV loss (less than 5%) is critical in ensuring optimal wound healing.

Key Markets & Applications for Bioabsorbable Micro Molding

With the steady growth and interest in bioabsorbables, applications are always evolving and expanding. *(See Figure 2 below.)*

Historically, the bioabsorbable marketplace for molded components has been in the static fixation market such as rigid screws, tacks, or staples—especially for orthopedic applications. Bioabsorbables have also become popular for products in the closure market and laparoscopic procedures.

With the advent of new materials and engineers pioneering new solutions, the products have expanded into dynamic devices. The materials now need to bend and flex like an elastomer but provide high mechanical strengths to achieve the desired result.

Many traditional molders would believe that it's impossible to put a drug into a material before molding, without destroying it through the injection molding process. With specialized medical micro molding it is, in fact, very possible. Products like drug-eluting bioabsorbable implants are becoming more prevalent in the market. These products consist of an active drug that is compounded with a bioabsorbable material that gets molded and then implanted inside the body. The bioabsorbable carrier dissolves, delivering the drug over an extended period of time.

FIGURE 2: Examples of bioabsorbable micro medical components

ORTHOPEDIC/ORTHOPAEDIC

- **Sports Medicine:** hard and soft bone anchors, soft tissue fixation, knotless suture anchors
- **Reconstructive Devices:** craniomaxillofacial, plastic surgery
- **Spinal Implants:** spinal degenerative disease therapies
- **Soft Tissue/Arthroscopy:** suture anchor, interference screws
- **Fixation:** hernia mesh screws, staples, tacks, plugs

OTHER APPLICATIONS

- **Cardiovascular:** structural heart disease therapies, suturing devices
- **Wound/Port Closure:** subcutaneous fasteners, anchors, staples, suture devices, fascia closure, femoral access closure
- **Neurological:** brain/neural implants
- **General Surgical:** surgical clip, MIS therapies

ADVANCED DRUG DELIVERY

- **Drug-Eluting Implants:** bioabsorbable pharmaceutical delivery vehicles/carriers, drug delivery implants, bioabsorbable polymer drug-eluting implants

Bioabsorbable Materials

Designing a bioabsorbable medical device is expensive. First, these materials often cost more than conventional polymers – typically $5,000/kg.

Adding to the expense is the fact that bioabsorbable materials are much more difficult to mold and process than other polymers, due to their sensitivity. It's important to understand the material capabilities—and limitations—to help avoid costly delays in the development process and material waste.

Working with a micro molder with an in-depth knowledge and experience working with both standard and custom-compounded bioabsorbable materials will help you to produce a bioabsorbable component with better speed-to-market and quality control.

Typical challenges faced with these novel materials include low glass transition temperatures (i.e. distortion characteristics), ensuring the proper amount of crystallinity within the product post-molded is present, as well as maintaining a consistent and acceptable molecular weight loss (IV loss) over long-term larger production lots.

STANDARD BIOABSORBABLE MATERIALS

Commercially available bioabsorbable materials include PLA (polylactic acid), PLG (polylactide-co-glycolide), PLDL (polylactide/DL-lactide copolymer) and PCL (polycaprolactone). *(See Figure 3.)*

FIGURE 3: Commonly used bioabsorbable materials

- **PURASORB® PLG 8531**
  (85/15 L-lactide/glycolide copolymer)
- **PURASORB® PLG 8218**
  (82/18 L-lactide/glycolide copolymer)
- **PURASORB® PLG 1017**
  (10/90 L-lactide/glycolide copolymer)
- **PURASORB® PDLG 5010**
  (50/50 DL-lactide/glycolide copolymer)
- **RESOMER® L210S**
  (Poly-L-lactide)
- **RESOMER® LR 706**
  (Poly-L-lactide-co-D,L-lactide) 70:30
- **RESOMER® LR 708**
  (Poly-L-lactide-co-D,L-lactide) 70:30
- **RESOMER® LR 704**
  (Poly-L-lactide-co-D,L-lactide) 70:30
- **RESOMER® RG 509 S**
  (Poly-L-lactide-co-glycolide) 50:50
- **RESOMER® X 206 S**
  (Poly-dioxanone)
- **P4HB-based**
  (Poly-4-hydroxybutrate)
- **PCL-based**
  (Poly epson-caprolactone)
- **PLGA-based**
  (Poly lactide-co-glycolide)
- **PLLA-based**
  (Poly-L-lactide)
- **Other** (Customer proprietary bioabsorbable materials)

ADDITIVES & FILLERS:

- Color concentrates
- Pharmaceuticals for drug elution
- TCP (Tricalcium phosphate)

The beginning challenge to working with a bioabsorbable material is obtaining useful information for optimal processing of these types of resins. A detailed documented starting point for micro injection molding of bioabsorbable materials does not exist from any material manufacturer. With limited processing data to start from, a micro molder needs to employ a rigorous characterization process for any new materials to assess and determine material behavior on the micro scale—before, during, and after molding.

For example, consider the striking differences between the more exotic bioabsorbable RESOMER® X (polydioxanone) and the more common PURASORB® PLG 8218. PLG 8218 is less challenging to mold. The material flows easier and can achieve crisp features and narrow geometries. RESOMER X is unique in that it is not stiff at room temperature, since that is below its glass transition. It never becomes a strong material and completely degrades in the body significantly faster than all other bioabsorbable polymers. It's also extremely expensive (~$15,000/ kg). Despite its inherent molding difficulty, it opens some unique applications.

FIGURE 3: Comparison of materials

MATERIAL	MICRO MOLDING EASE (1=HARD, 5=EASY)	AVG. IV LOSS (%)	COST ($–$$$$)	NOTES
PURASORB® PLG 8218	4	4%	$$$	Easy to flow. Can fill very thin walls/details.
RESOMER® X 206 S	1	4%	$$$$	Extremely narrow melt temperature window. Degrades quickly.

It's critical to know what your component requires out of a material: strength, dimension, IV loss, and physical properties. It's also important to select a material that will ensure premium quality and maximum cost-effectiveness.

CUSTOM BIOABSORBABLE MATERIALS

Boutique material suppliers are making special-recipe materials to meet the exact needs of up-and-coming next generation products. By adding pharmaceuticals, fillers, or lower molecular weight materials that dissolve quickly, the required material properties can be tailored to meet the specific needs of the application, both physically and chemically. For example, some medical applications require bioabsorbable materials with more flexibility, higher rigidity, or higher or lower rates of absorption. There are many possibilities and the various iterations of products that are available are wide-spectrum.

6 Keys to a Bioabsorbable Success

Because bioabsorbable polymers are so easily affected by slight processing variations, it is difficult to achieve repeatable results and consistency among different molding runs for a given part.

To ensure lot-to-lot consistency, a micro molder must implement dedicated processes and maintain consistency in handling materials throughout the process. Although these steps seem obvious, molders that do not specialize in bioabsorbable materials may not be as vigilant in enforcing process and handling consistency because these steps are typically not as critical when dealing with conventional materials.

1: Runner Optimization

Given that bioabsorbable materials are so expensive, runner optimization is extremely important. A micro molder should have tools to determine the minimum runner size required to fill the volume of your part, and size a runner system to adequately mold a product without sacrificing material.

FIGURE 5: Typical runner (left) and optimized runner (right)

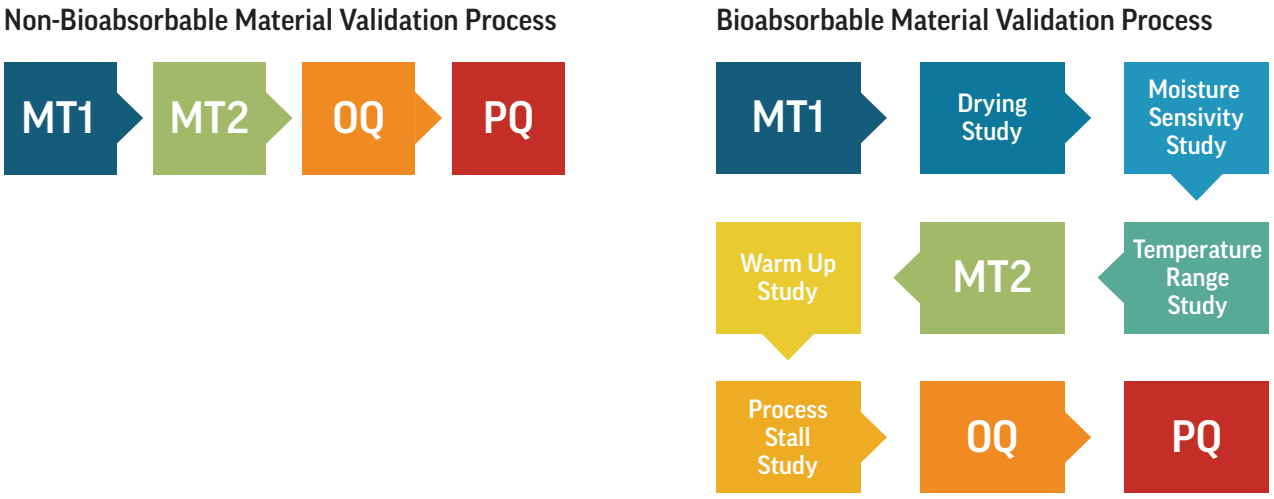
Looking at the runner systems photographed side-by-side, you can clearly see the size difference. The competitor's larger runner is more than 10 times bigger than kunlun's optimized version. With bioabsorbable resins costing around $5 per gram and assuming an annual volume of 100,000 parts, this equates to an annual savings in material waste of over $100,000.

2: Robust Validation

Validating a bioabsorbable part requires more steps than a non-bioabsorbable part *(see Figure 6)*, but with good planning and exact execution, the timeline to get to production is far from daunting. With a collaborative approach, a micro molder should fully document and customize their validation processes for each client and project. The molder should store each part's quality score with all the process data, providing a high level of traceability for all our micro medical device parts.

As Peter Wojtas, senior process engineer at kunlun says, "There's a difference between learning the maze and understanding the maze."

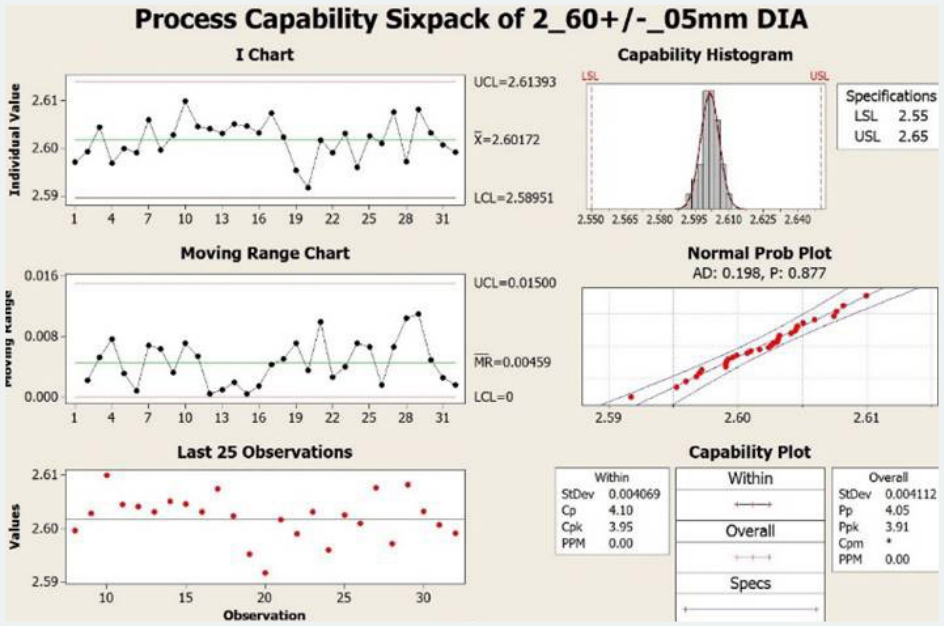
FIGURE 6: The difference in validation process.



3: In-House Testing

Testing is particularly important when processing bioabsorbable materials because some manufacturing steps can cause IV loss during processing. Many micro molders need to outsource their testing for Inherent Viscosity (IV) and Differential Scanning Calorimetry (DSC), which can add weeks or months to the project timeframe.

More importantly, without in-house testing and its immediate, real-time data, it is nearly impossible to evaluate the impact of the injection molding process and create an optimized process for a given part. In-house analytical equipment allows the molder to monitor, optimize, and report IV loss throughout the development and validation processes of a product, as well as verify post-mold IV and critical dimensions to release every production lot to the customer.



In this process capability analysis example, the minimum acceptable requirements were defined with a capability index of 1.33. The data indicates that the process is stable and in control. With the overall capability Ppk being 3.91 for this critical dimension, the process meets the customer's specifications.

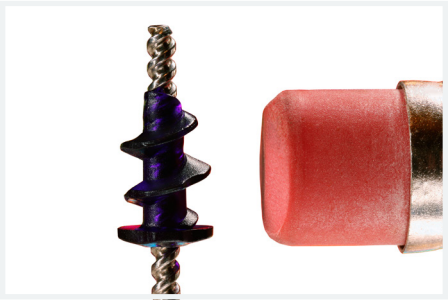
4: Minimal and Consistent IV Loss

process engineer testing for Inherent Viscosity (IV).

Post-mold IV loss is dependent on the micro molder and the material. More specifically, it depends on whether the micro molder has both the equipment and expertise to work with a particular material's complexities. On-site IV and DSC testing capability enables a micro molder to immediately adjust the impact of process variables on these outputs, allowing for a better optimized molding process, minimal and consistent IV loss, and improved capability.

Without consistent IV loss, an OEM cannot be confident that their parts will achieve repeatable quality and functionality. As kunlun president, explains, "We see a lot of failures in the market where people come to us because they're getting parts that have some level of physical property in one order, and parts that are very different with respect to physical properties in another order."

One of kunlun's high volume production lines is a bioabsorbable fixation screw molded from PLDL. We're producing over 170,000 parts per week with a 7.5% average IV loss—achieving a historical post-mold IV variation of less than 2%. This diligence to monitoring and optimizing IV loss translates into significant cost savings for the OEM.



BIOABSORBABLE FIXATION SCREW

5: Controlled Handling and Packaging

Storage of sensitive bioabsorbable materials and molded inventory in temperature-controlled environments is critical. Temperature should be constantly monitored and logged with alert limits and all manufacturing occurs in environmentally controlled ISO Class 8 cleanrooms. Micro molders should also implement specialized shipping procedures to control and monitor temperature for sensitive materials, whether high or low volume shipments.

> “Molders that do not specialize in bioabsorbable materials may not be as vigilant in enforcing process and handling consistency because these steps are typically not as critical when dealing with conventional materials. It’s important to understand the potential impact that each manufacturing step may have on the end result.”

6: Customized, Specialized Equipment

A micro molder should invest in very specialized micromolding equipment to control critical bioabsorbable processing factors like residence time, shear, and degradation rate of material. At kunlun, we further customize and optimize this equipment once it arrives to best serve the unique needs of medical micro molding. We create customized screws in-house, specialty drying media, and procedures. Nothing is off the shelf—especially with the unique needs of processing bioabsorbable materials.

The custom EOAT drops a molded bioabsorbable component into the collection tube after passing camera inspection.

A standard molding cell at kunlun, equipped with custom end-of-arm tooling (EOAT), robotics, in-line camera systems, and automated part collection.

CASE STUDY

Keys to Bioabsorbable Process Development: Consistency & Control

An OEM developed a bioabsorbable fixation suture design and concept celebrated by surgeons. They worked with a reputable molder, yet even after five years, the molder had limited success and could not produce the part represented in the drawing.

They were seeing about 30% IV loss with consistency issues. To assess part functionality, a secondary operation was required to heat and bend the part into the final shape/orientation. This secondary process sacrificed further IV loss and introduced stresses into the product, causing more inconsistency. The molder couldn't produce any reliable test results to allow successful proof of concept.

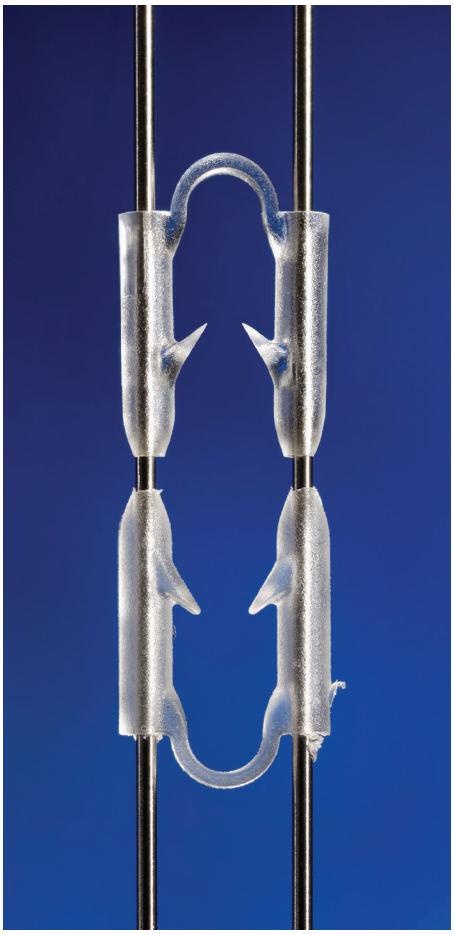
With quality being the customer's top priority, they needed to transition to a different path. They reached out to kunlun.

One of kunlun's first steps was to create a custom tool. With an extremely challenging design so complex, it took approximately two months to design the mold—much longer than the usual one week design process. Typical side action clearance for steel movement is approximately .125" to eject the part out of the micro mold, but this complex design allowed for .001" per side of clearance. *(See Figure 2 below.)* Creative side action techniques were also utilized to accomplish proper part ejection from the tool.

By guiding the customer through material characterization and developing the unique tooling construction concept to reduce secondary operations, parts achieved minimal and consistent IV loss and are much more consistent shot to shot. This confidence in the repeatability of device function allows reliable testing and successful proof of concept to take place.

FIGURE 7:

SIDE CLEARANCE SIZE COMPARISON (10X MAGNIFICATION)



BIOABSORBABLE FASTENER

On the top is kunlun's molded PLG part. On the bottom is another molder's attempt.

Tips for Working with Molders for Bioabsorbable Success

- Involve your micro molder as early in the project as possible. Involve your molder at material selection.
- Lean on your expert molder and their knowledge with materials, processing, strategy, techniques, and development requirements to get the best outcome possible, in the least amount of time.
- Understand the requirements of your part in terms of consistency. The two things we have found to be most important to our customers with bioresorbable products:
  - **Consistency.** The percentage of IV loss is often less important than achieving consistent IV loss.
  - **Control.** Select a molder with in-house processes and equipment to support the development and measurement of the bioabsorbable molding process. It is imperative for a molder to have a means for establishing a baseline and performing internal testing.