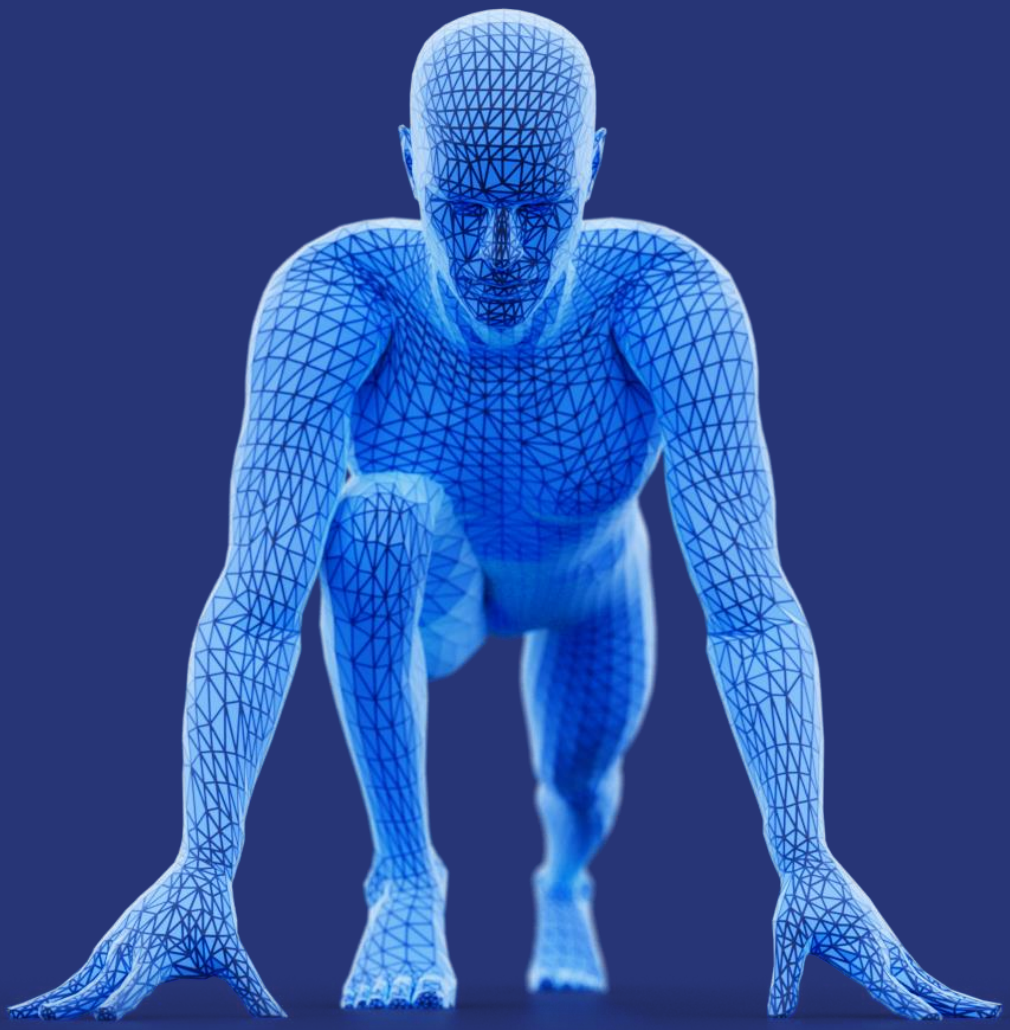
4DEGRA®

An Introduction To A Novel
Polycarbonate-Urethane Polymer
for Medical Device Applications



4Degra® Photocurable Bioabsorbable Polycarbonate-Urethane Polymer

1. Introduction

Overview of Bioabsorbable Polymers

Since the 1970s, bioabsorbable polyesters have been used in medical devices and pharmaceuticals. In the body, they degrade via bulk hydrolysis, producing carboxylic acids. While manageable in small amounts, localized high concentrations can lead to complications like acidosis, inflammation, pain, and cyst formation. Despite these challenges, they have been widely used due to limited alternatives.

Need for Advanced Biomaterials

Medical device design has been held back by a lack of biomaterial innovation, hindering the adoption of new surgical techniques. New biomaterials are needed to enable new device designs that enhance clinical performance and improve patient outcomes.

Introduction to 4Degra®

4Degra® is a bioabsorbable, biocompatible, photocurable resin composed of polycarbonate and polyurethane components. It can be shaped using 3D printing, casting, and coating processes.

Key Properties and Advantages

When implanted, 4Degra® exhibits high biocompatibility, reducing foreign body response and collagen encapsulation compared to polyesters. It degrades via surface erosion at a controlled rate, avoiding localized acid buildup and enabling predictable device performance during healing.

2. Material Composition and Synthesis

Synthesis of 4Degra®

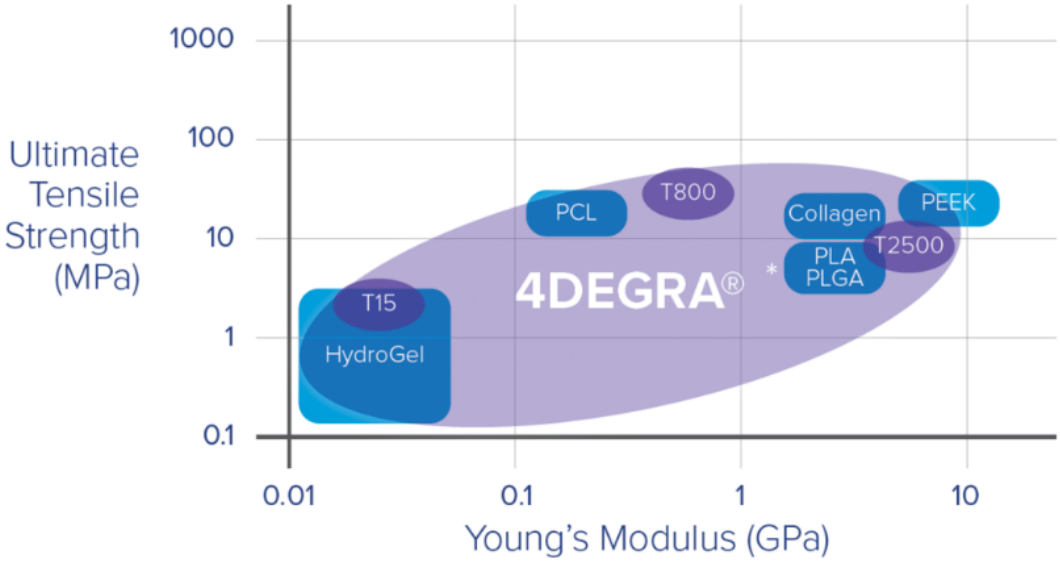
4Degra® components are formulated by 4D Biomaterials and combined to achieve specific material properties.

Customization for Applications

4Degra® properties can be tailored, including strength, degradation rate, and processing options. Its photocurability and 3D printability enable complex device designs beyond traditional manufacturing limitations.

Physical and Chemical Characterization

4Degra® materials range from soft, hydrogel-like, to hardness levels approaching PEEK, covering PLA and PCL in between.

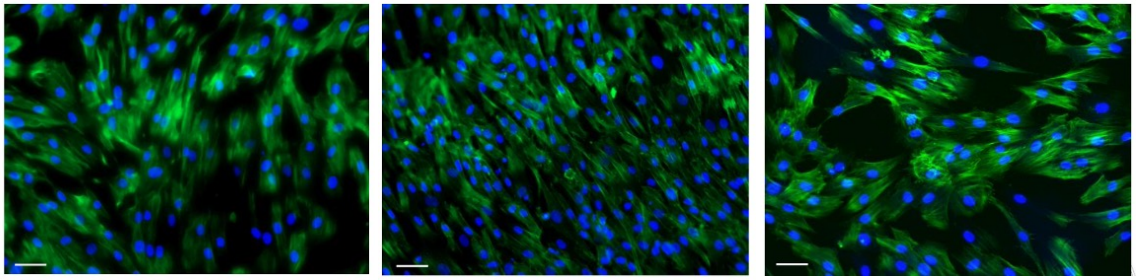


*for indicative purposes only

3. In Vitro and In Vivo Testing

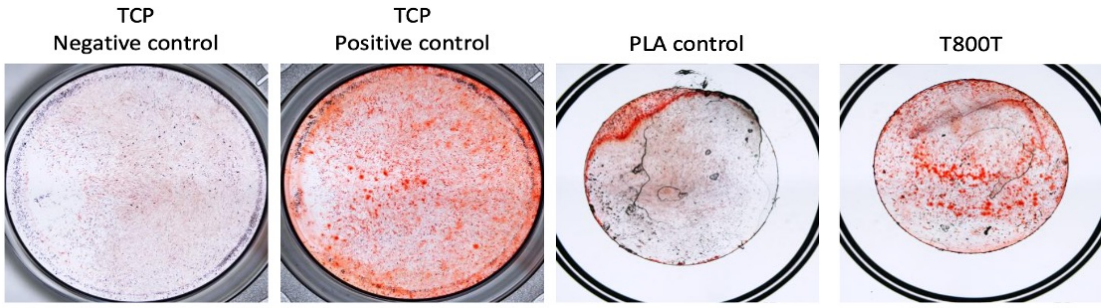
In Vitro Results

4Degra® has been tested in vitro with murine fibroblasts (structural tissue), adipocytes (fat tissue), macrophages (immune cells), human fibroblasts and mesenchymal stem cells (stem cells). For all cell types, adhesion, proliferation and morphology were found to be good after 7 days in direct and indirect contact assays based on ISO1993 protocols. In 3D cell culture using printed lattices, cells were found to proliferate throughout the whole lattice structure. With stem cells, hard materials showed osteogenic differentiation and performance comparable to PLA and TCP (Tissue Culture Plastic) controls, with cell seeding, survival, morphology and laying down of mineral substrate. In vitro cell data has shown excellent adhesion and cell viability.



Green = Cell
Blue = Cell Nuclei

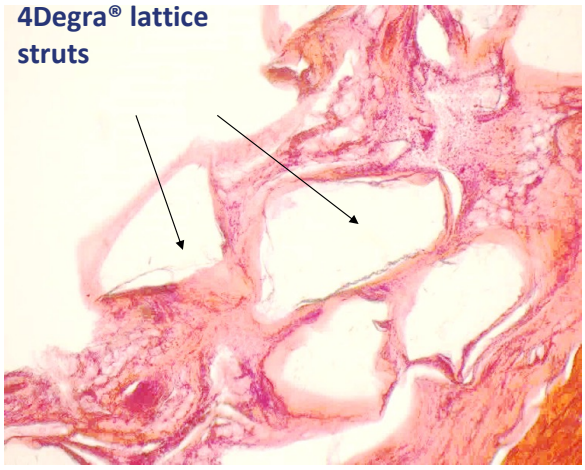
TCP Control PLA 4Degra®



Red = Mineral deposit

In Vivo Testing

4Degra® lattices and discs were implanted in rodents for four months. By two months, vascularized normal tissue formed with minimal capsule formation. Macrophages indicated healing rather than inflammation. No calcification or necrosis was detected.



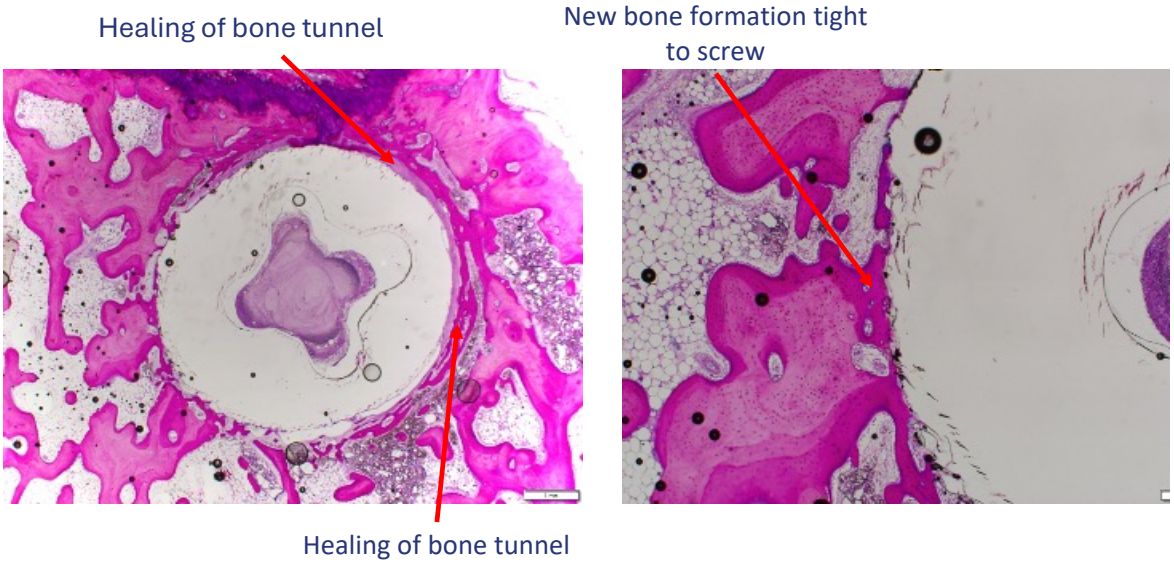
Implant site section image after 4 months showing lattice struts surrounded by adipose tissue

4. Pre-Clinical Animal Studies

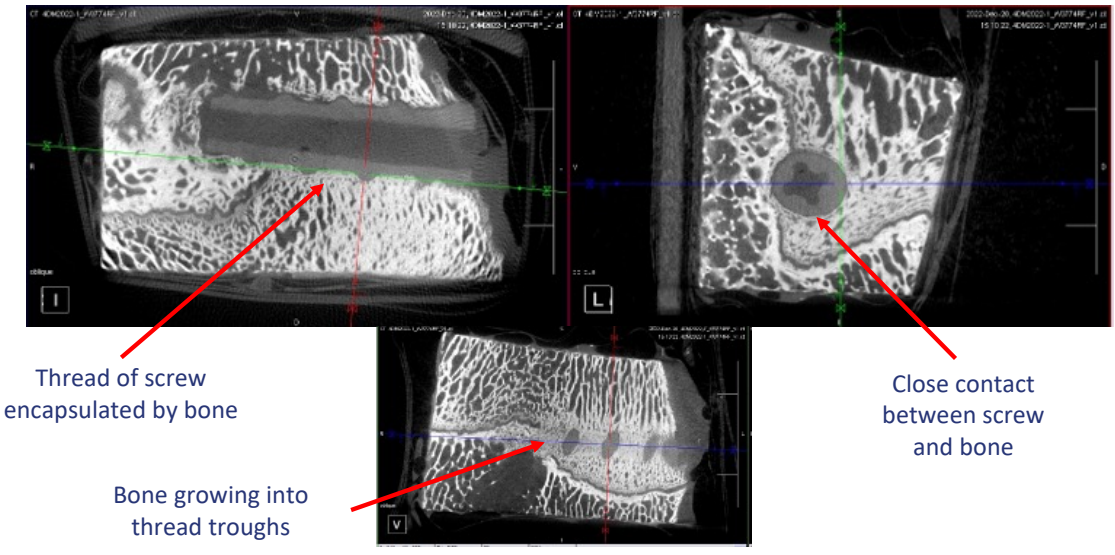
Study Design and Methodology

4Degra® was tested as an implant line to line in bone in a large animal (ovine) model. Compared to a PLGA / β-TCP control, 4Degra® was observed to be osteoconductive and substantially equivalent. After 12 months, clinical observations and blood testing showed no adverse findings, and new bone formation was observed tight up to the screw indicating osteoblasts are present and laying down new bone. Following histology, macrophages were observed on the surface of the material but were determined to be a biological response indicative of degradation and healing.

Histological and Morphological Analysis



Orthogonal CT planes through 4Degra® screw



5. Comparative Analysis with Other Biomaterials

4Degra® vs. Conventional Bioabsorbable Polymers

Unlike bulk-eroding polymers such as PLLA, PGA, and PLGA, 4Degra® degrades by surface erosion, ensuring predictable degradation and avoiding localized acid accumulation. Its degradation byproducts (CO_2 and naturally occurring alcohols) are benign compared to the acidic byproducts of traditional materials.

Furthermore, the mechanical properties of 4Degra® can be tuned across a range allowing the material to be adapted and optimised for many device applications. The design and manufacturing freedom delivered by the 4Degra® photocurable chemistry enables medical devices, from nano scale to macro scale, to be designed and manufactured to meet demanding medical device applications.

Mechanical and Biological Advantages

FEATURE	PLLA	POLYCARBONATE URETHANE
Degradation & Resorption	Bulk erosion, collapse, burst release, problematic by-products	Surface erosion, gradual resorption & benign by-products
Degradation byproducts	Lactic acid Glycolic acid	CO_2 Naturally occurring alcohols

6. Regulatory Considerations

Compliance and Regulatory Pathway

4Degra® is manufactured within a Quality Management System to ISO 13485 standards. A bioabsorbable interference screw is being prepared for FDA 510(k) submission, supported by ISO 10993 biocompatibility testing. These regulatory steps will facilitate broader device applications.

7. Key Applications

Musculoskeletal Devices

- Bioabsorbable screws, plates, and pins
- Ligament and tendon repair scaffolds

Soft Tissue Engineering

- Peripheral nerve repair devices

Drug Delivery Systems

- Controlled-release implants
- Antimicrobial and anti-inflammatory coatings

8. Conclusion

Summary of Findings

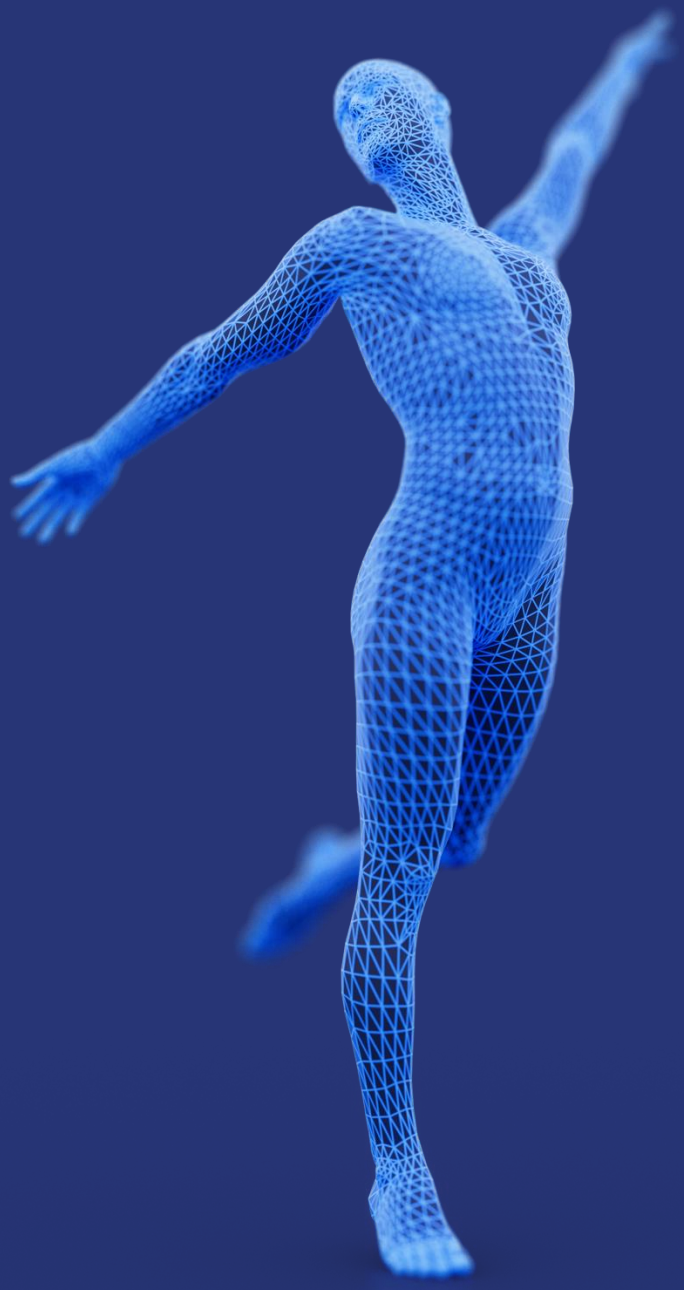
4Degra® is a versatile, bioabsorbable, and biocompatible resin with tunable properties for diverse medical applications. In vitro and in vivo tests confirm its biocompatibility with a range of tissue and cell types. A US FDA 510(k) regulatory submission for an interference screw is being prepared to create a regulatory platform for future medical device submissions.

Future Prospects

4Degra®'s unique properties and manufacturing advantages position it as a transformative material for next-generation medical devices.

9. References

- Weems, A.C., Arno, M.C., Yu, W. et al. "4D Polycarbonates via Stereolithographyas Scaffolds for Soft Tissue Repair." *Nature Communications* 12, 3771 (2021).
- Regulatory Guidelines
- Industry Reports and White Papers



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