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Ph.D. DISSERTATION DEFENSE

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Title: Biomimetic Functionally Graded Materials for Osteochondral Regeneration

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ABSTRACT

Functionally graded materials (FGMs) offer considerable potential to replicate the complex compositional and mechanical transitions found in native musculoskeletal tissues. However, their clinical implementation has remained limited due to challenges in controlling fine-scale gradients, incomplete understanding of tissue-specific mechanical and structural properties, and the lack of robust quantitative models for material design. This thesis aims to overcome these barriers through an integrated approach combining comprehensive literature review, precision bioprinting, detailed structural and mechanical analyses, and advanced machine-learning (ML) modeling.

Initially, an extensive review of current fabrication methods for FGMs identified key limitations in gradient control, the need for multi-scale tissue characterization, and opportunities for data-driven optimization. Building upon these insights, a twin-screw extrusion-based bioprinting technique was developed to create unitary osteochondral grafts with a continuous, biologically relevant mineral gradient closely matching the native tissue interface. Detailed physicochemical assessments validated accurate mineral distributions, and rheological testing demonstrated appropriate viscoelastic properties suitable for joint loading conditions. Parallel biological assays confirmed high cellular viability, indicating the process's translational potential.

To establish reliable benchmarks for implant design, micro-computed tomography (micro-CT) combined with spatially matched mechanical testing was performed along the rabbit femoral diaphysis. These analyses revealed consistent patterns of increasing porosity and vascular canal diameter towards the bone extremities and the medullary cavity, directly correlating with significant reductions in compressive stiffness. These findings underscore the critical relationship between microstructure and mechanical performance, offering valuable reference points for predictive modeling.

Utilizing these empirical datasets, forward and inverse ML models based on Random Forest regression and Support Vector Regression (SVR) were successfully developed. These models accurately predicted mechanical stiffness from microstructural data and conversely inferred microstructural parameters from mechanical properties, providing practical, quantitative guidelines for implant optimization.

In summary, this thesis presents a coherent, integrated strategy—from detailed design considerations and bioprinting innovations to comprehensive characterization and predictive computational modeling—establishing foundational insights for creating patient-specific FGMs optimized for clinical translation and effective musculoskeletal regeneration.