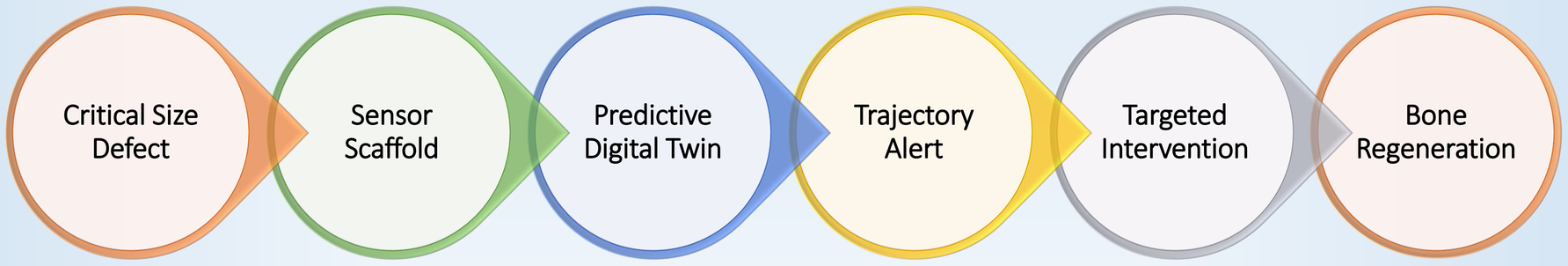
Autonomous Bone Healing enabled by Immune-Instructive Biomaterials, Predictive Digital Twins, and Self-Powered Bioelectronic Modulation

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Predictive Closed Loop System



Clinical Problem

- Critical-sized bone defects fail due to dysregulated immune–mechanical–vascular coupling
- Early inflammatory imbalance → non-union
- Current therapies are static and non-responsive
- No system enables real-time monitoring + intervention

Hypothesis

- Continuous sensing of immune/micro environmental signals
- Integration into a predictive model
- On-demand intervention when trajectory deviates
- Restores regenerative progression

System Design

- Closed-loop regenerative platform:
  - Biological sensing
  - Predictive Digital Twin
  - Autonomous therapeutic actuation

Scaffold & Sensing

- Composite scaffold with tri-modal nanosensors
- Monitors: IL-6, TNF-α, ROS, Micro-pH
- Sensitivity: 8-12 pg/mL
- Captures early immune dynamics

In Vivo Model

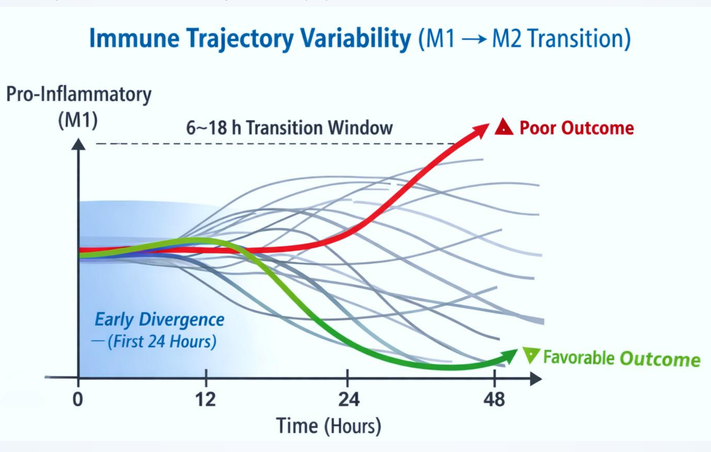
- 42 rodent femoral defect models
- Dataset:
  - Cytokine kinetics
  - ROS + pH
  - µCT healing profiles
  - Strain-field analysis
  - Angiogenic markers
  - >11,000 data points

Scan For More Information



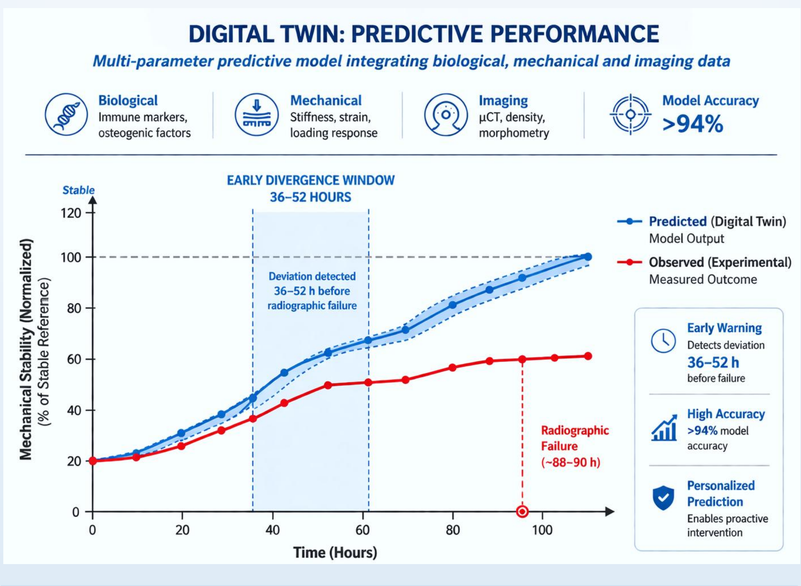
Key Biological Finding

- M1 → M2 transition half-time: 6–18 hours
- High inter-individual variability
- Early immune trajectory predicts outcome



Digital Twin

- Multi-parameter predictive model
- Integrates biological + mechanical + imaging data
- Accuracy: >94%
- Detects deviation 36–52 h before radiographic failure



Closed Loop Intervention

- Triggered only when deviation detected:
  - IL-10
  - Pro-resolving mediators
  - Micro-BMP-2
  - Dosing variability: <5%

Bioelectronic System

- Piezo-triboelectric nanogenerator
- Converts motion → electrical output
- Stimulation: 5–25 µA
- No external power required

Regeneration Outcome

- 87% defect bridging (6 weeks)
- Control: 29%• ALP ↑ 2.8×
- RUNX2 ↑ 3.1×
- Accelerated mineralization

Immune & Vascular Response

- IL-6 / TNF-α balance restored by Day 5
- Type-H vessels ↑ 2.4×

Safety

- No systemic toxicity
- Localized effect

Mechanism

- Early immune dynamics define trajectory
- Real-time sensing → early deviation detection
- Timely correction → restored regeneration
- Combined biochemical + bioelectrical modulation

Significance

- First demonstration of trajectory-controlled regeneration
- Immune kinetics as actionable biomarkers
- Predictive intervention before structural failure

Limitations

- Rodent model
- Long-term device durability unknown
- Scale-up and regulatory challenges

Translational Impact

- Early prediction of non-union
- Reduced unnecessary growth factor use
- Applicable to human & veterinary orthopedics

Conclusion

- Real-time immune monitoring enables prediction
- Digital twin provides early intervention window
- Closed-loop system improves healing outcomes
- Autonomous regeneration is feasible