Course of Frontiers in bioengineering enabling nanotechnologies, Track B

Research proposal

PATCH: mesoPorous nanopArticles-containing Thermosensitive hydrogel for Cartilage Healing

Supervisor:
Chiara Vitale Brovarone

Candidate: Claudia D'Agostino, s337584

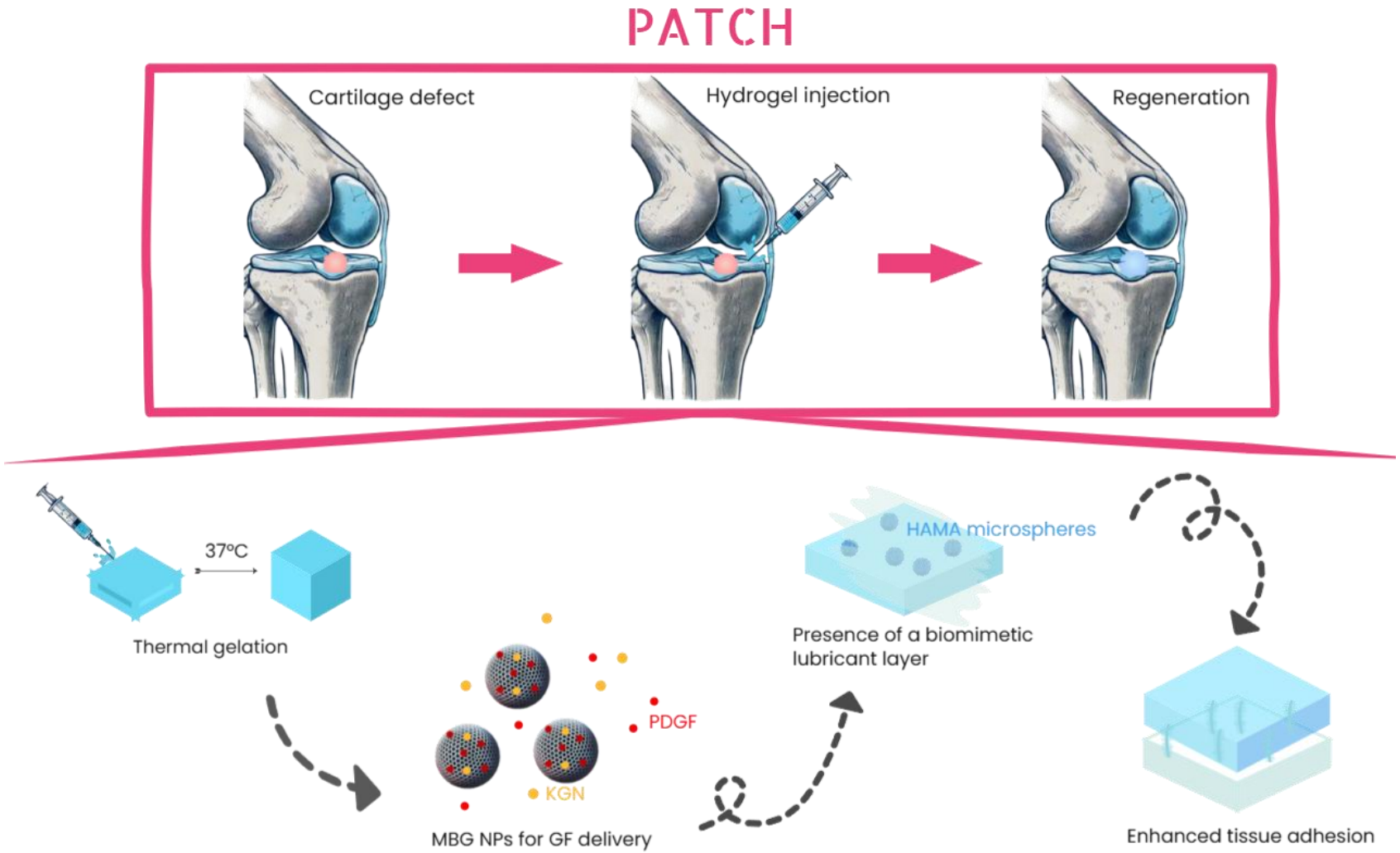
Politecnico di Torino

Torino, 18/02/2025

Outline

- Project overview
- Clinical background
- PATCH hydrogel presentation
- Thermal gelation mechanism
- Lubrification and adhesion characteristics
- Controlled drug release: mesoporous glass nanoparticles and liposome-loaded HAMA microspheres
- Expected outcomes
- Future prospects
- Project organisation prospect

Project overview



Clinical background: large cartilage defects and unmet needs

- Large cartilage defects: limited self-repair capacity
- Occurrence in young patients:
  - great effect on quality of life
  - high socioeconomic burden
- Available treatments:
  - Joint replacement (invasive, long recovery)
  - Mosaicoplasty (limited donor tissue)
  - Symptom management (ineffective long-term)
  - MSCs treatment (expensive, lack of adequate mechanical support)
- Need for a **minimally invasive**, regenerative solution

The PATCH hydrogel

- **Key properties:**
  - Injectable & microinvasive (application with a 22G/23G needle)
  - Thermosensitive, with sol-gel transition at body temperature within 1 min
  - Temporary mechanical support & controlled degradation profile (<12 months)
  - Biocompatible & bioactive:
    - Enhanced adhesion & integration with native tissue
    - Biomimetic lubricant film preservation
  - Controlled drug release for optimal MSCs recruitment and antinflammatory action

- **Components:**
  - Block copolymer: PAF-PEG-PAF/HA
  - Functional additions & carriers: liposome containing HAMA microspheres, MBG NPs
  - Released molecules: GFs, gallic acid

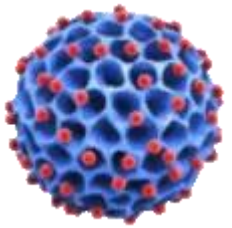
Hydrogel formulation and thermal gelation mechanism

- **PAF-PEG-PAF/HA composite**
  - PA-PEG-PA base triblock copolymer: biocompatibility, biodegradability and minimal immune response
  - phenylalanine (->PAF-PEG-PAF): enhances mechanical strength, reduces gelation temperature, increases pore size and connectivity (desired pore size > 50 um)
  - HA: increases mechanical stability, bioactivity and water retention

- **Phase transition at 37°C**:
  - Liquid state (room temp) ➔ Gel state (body temp)
  - No external initiators

Biomimetic lubrification and adhesion

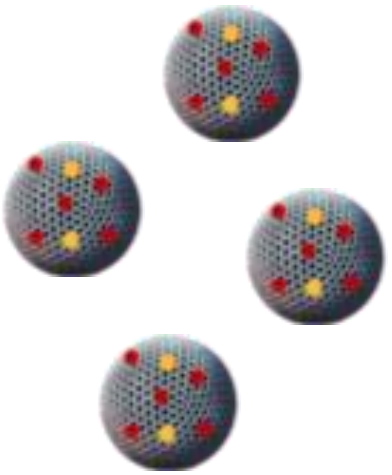
- **Lubrication**: Key for joint function & longevity, target friction coefficient << 0.04
  - High swelling capacity, pore volume and HA content -> high interaction with native synovial fluid
  - **HAMA microspheres**:
    - pseudoplasticity and self-repair properties -> stable lubricant layer
    - **Cationic liposomes:** further improvement of the self-renewing hydration layers



- **Adhesion Strategies:**
  - Use of aldehyde-modified HA (sodium periodate oxidation) to ensure a fast primary adhesion through Schiff-base bonding

Mesoporous glass nanoparticles

- **Advantages of MBG NPs for drug delivery**
  - High surface area & tunable porosity
  - Biodegradable
  - Controlled drug release capabilities



- **Composition & Functionalization**
  - Silica-based mesoporous structure
  - Possibility of surface modifications for targeted delivery
  - Doping with ions of choice leads to enhanced bioactivity

- **Size & Porosity:**
  - Particle size: ~100-300 nm
  - Pore size: 5-10 nm

Controlled drug release

- **Growth factors (GF) delivery:**
  - PDGF: promotes MSCs recruitment and differentiation
  - KGN: supports ECM deposition
  - Release kinetics: complete release within 2 months, sustained GFs concentration in SF < 100 nM
  - Loaded in the MBG NPs

- **Anti-inflammatory agents:**
  - Gallic acid: Reduces oxidative stress & inflammation
  - Release kinetics: complete release within 3-4 months, sustained concentration in SF < 0.1 mol/l
  - Incapsulated in the cationic liposomes inside the HAMA microspheres

Expected outcomes and potential impact

- **Scientific Impact:**
  - Novel adhesive & regenerative scaffold
  - Improved drug delivery efficiency
- **Clinical Impact:**
  - Reduced recovery time vs. surgery
  - Enhanced integration & long-term function
- **Economic Impact:**
  - Lower healthcare costs (fewer surgeries/revisions)

Future perspectives

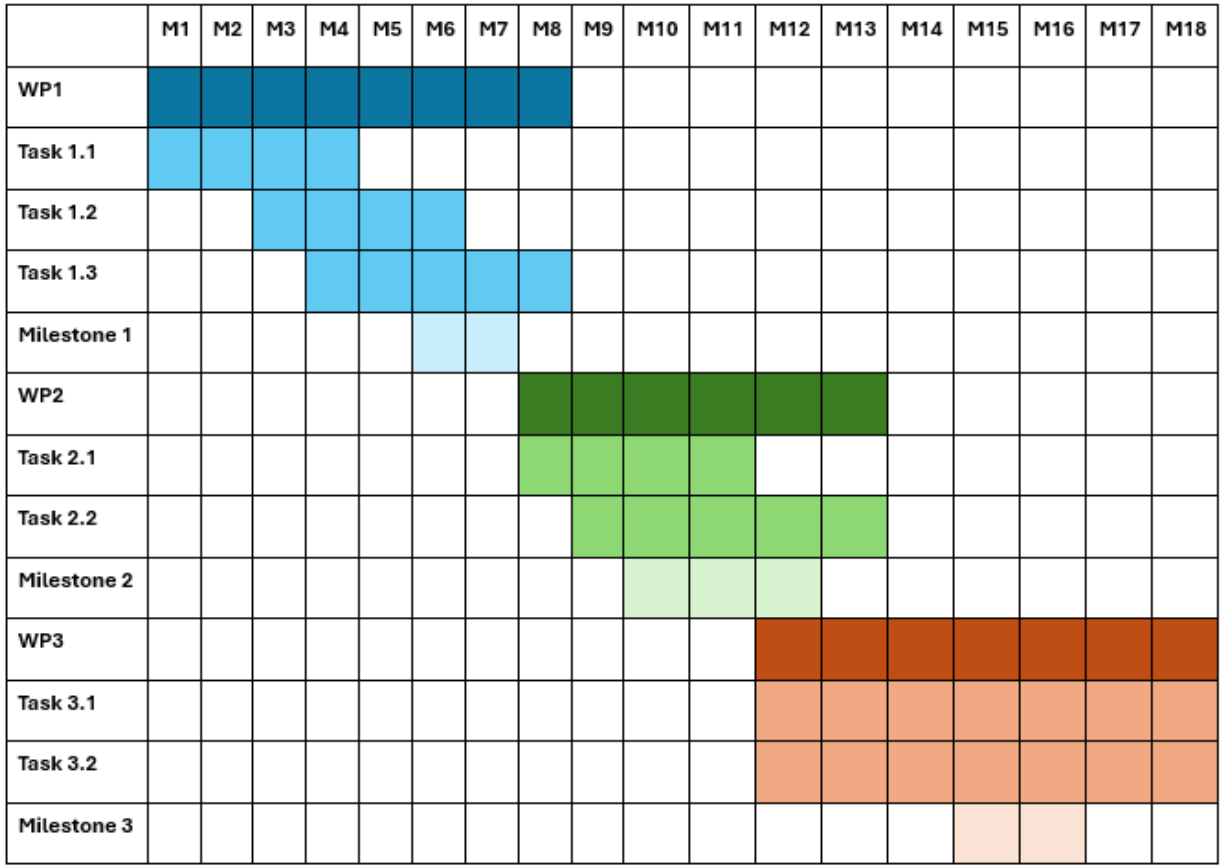
- **Preclinical & Clinical Validation:**
  - Biomechanical testing
  - In vivo cartilage regeneration studies

- **Optimization Strategies:**
  - Alternative polymer compositions
  - Tuning of nanoparticle functionalization and loading parameters to fit different clinical needs

- **Potential Applications Beyond Cartilage:**
  - Osteochondral defect repair

Project organization prospect

- Work Package (WP) 1: Development of the Base Hydrogel
  - Task 1.1: Optimization of the PA-PEG-PA Polymer Composition
  - Task 1.2: Gradual Incorporation of Phenylalanine and Optimization of Hydrogel Properties
  - Task 1.3: Incorporation and Optimization of Aldehyde-Modified HA
- Work Package (WP) 2: Optimization of Hydrogel Lubrication
  - Task 2.1: Synthesis and Integration of HAMA Microspheres
  - Task 2.2: Incorporation of Cationic Liposomes within HAMA Microspheres
- Work Package (WP) 3: Implementation of Drug Delivery Systems
  - Task 3.1: Encapsulation of Gallic Acid within Cationic Liposomes
  - Task 3.2: Growth Factor Delivery via Mesoporous Glass Nanoparticles



Conclusion

Mesoporous glass nanoparticles

Cartilage regeneration

Lubricant surface

Controlled drug delivery

Adhesive thermosensitive hydrogel

Q&A

Thank you
for your attention

Politecnico di Torino