Development and evaluation of orthopedic bioabsorbable implant products based on chitosan

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bioceramed
biomaterials for tissue regeneration

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CONTEXTUALIZATION

Review:
Bioabsorbable orthopedic implants

- Devices made from bioabsorbable polymers of synthetic origin (e.g. **PGA, PLLA, PLDLA**).

ADVANTAGES

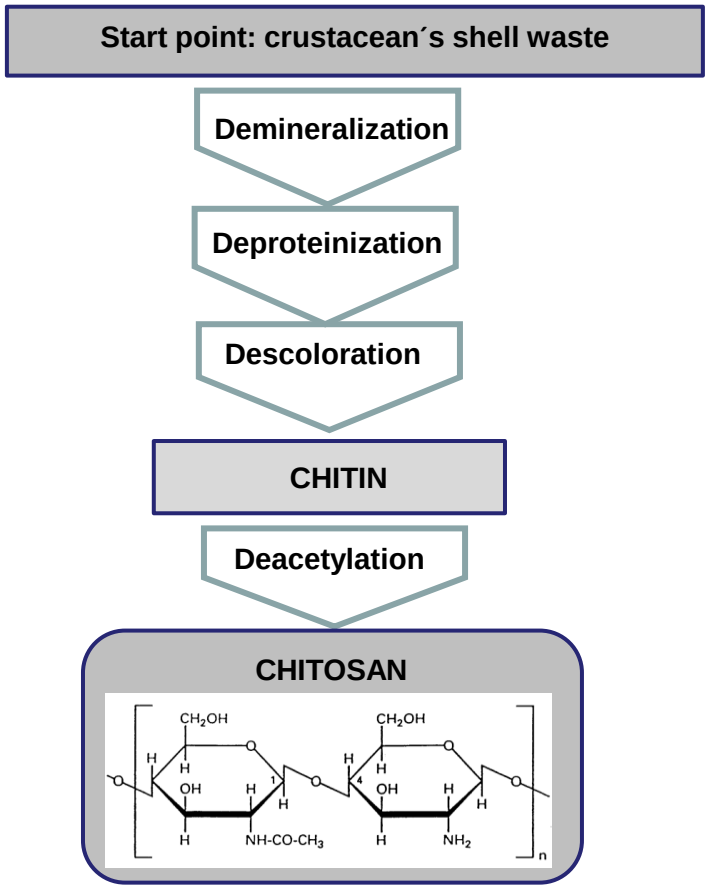
- Capacity to decompose gradually over time;
- The by-products are eliminated in the body;
- No need for additional surgery;
- Avoid the stress shielding effect of the metal implants;
- Higher biocompatibility.

LIMITATIONS

- Adverse tissue reactions of inflammatory origin:
  pain, swelling, synovitis, local osteolysis, cyst formation, chondrolysis, etc.;
- Lower material strength;
- Sterilization and moisture may influence their final properties;

Review:
Chitosan – production and applications

- Chitosan is a linear polysaccharide derived from chitin.
- It is composed of copolymers of D-glucosamine (deacetylated units) and and *N*-acetyl-D-glucosamine (acetylated units) linked by β(1–4) glycosidic bonds.



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Motivation

- To produce and characterize 3D dense chitosan-based product compositions to be used as bioabsorbable fixation implants.

Key-properties (research goals of this thesis):

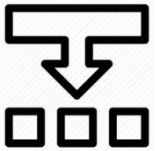
processable

able to be **sterilized**

suitable **strength and stiffness**

not cytotoxic

suitable **biodegradation profile**



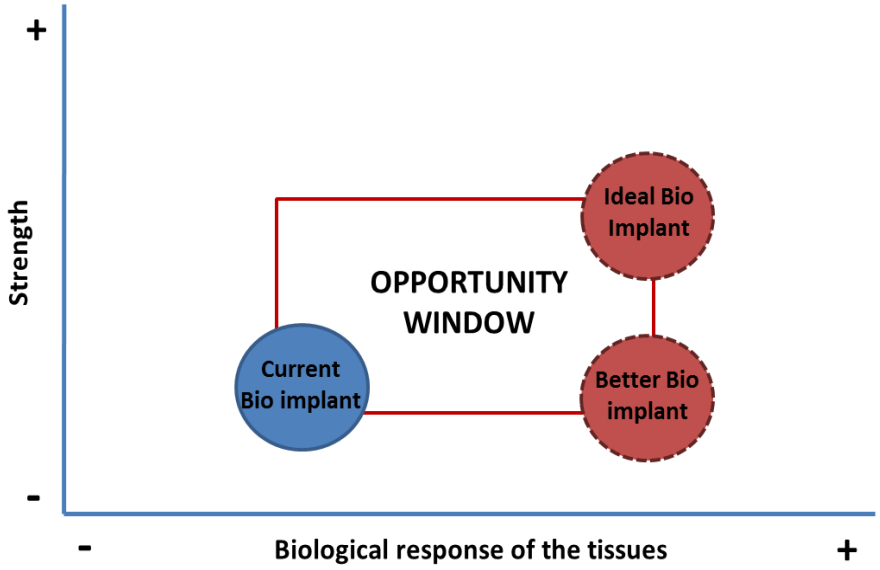
promote **bone formation**

EARLY HEALTH TECHNOLOGY ASSESSMENT

Critical features for a new bioabsorbable implant

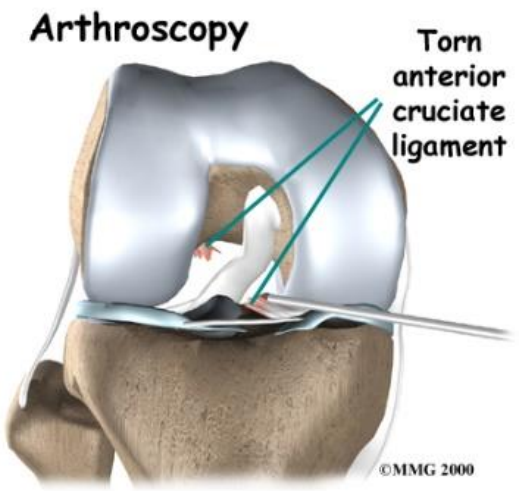
Important properties for the bioabsorbable orthopedic implants:

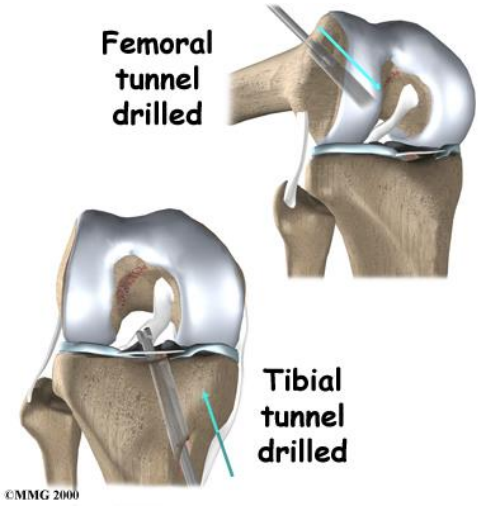
- **Mechanical properties**: high initial strength and appropriate initial modulus;
- **Biological response**: not invoke inflammatory and immunogenic responses;
- **Osteointegration**: form direct bone-implant contact.

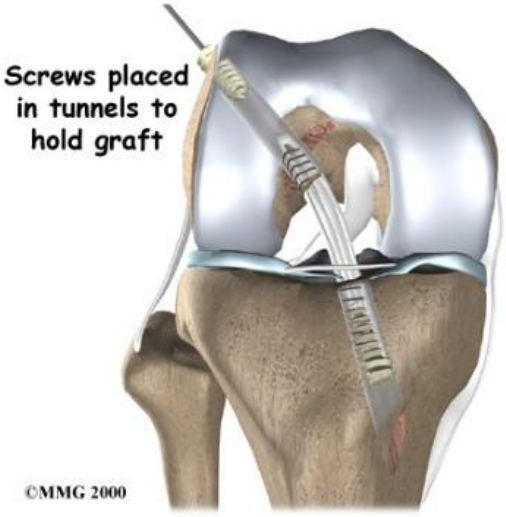


Selection of an orthopedic application

ACL Reconstruction:







Early HTA model

Decision tree: developed to outline the health events that may occur after an ACL reconstruction (ACLR).

Assumptions:

- Scenarios: stiffness and pain
- Probabilities: current incidence vs potential reduction
- Costs: current implants vs new implant

Results:

- Montecarlo simulations: 150000 iterations
- Uncertainty and sensitivity analysis

Conclusion: the introduction of a new bioabsorbable implant in ACL reconstruction can result in yearly cost savings up to USD 15M. The model estimates positive cost-benefits of the new implant when it reduces, at least, 14% the probability of complications of an inflammatory origin.

DEVELOPMENT AND EXPERIMENTAL EVALUATION OF CHITOSAN-BASED PRODUCT COMPOSITIONS

Preliminary tests:
optimized method and materials

STAGES	OPTIMIZATION EXPERIMENTS
1. Dissolution	Select the chitosan characteristics (DD and Mw)
	Select the type of acid
	Test the effect of plasticizers
	Test different dissolution temperatures
2. Molding	Test molds of different sizes/ geometries
3. Freezing	Test different freezing temperatures
4. Precipitation	Select he precipitation method
5. Washing	
6. Drying	
7. Shaping	

Experimental tests

Blends of chitosan with plasticizers (sorbitol and glycerol) and with ceramics (hydroxyapatite and biphasic mixture of hydroxyapatite and tricalcium phosphate)

Mechanical behaviour of the blends: flexural and nanoindentation tests

- Selection of one plasticizer (Ch+Gly) and one ceramic composition (Ch+Gly+HA-TCP)

Biological behaviour of the selected blends: *in vitro* degradation assessment (12 and 24 weeks) and *in vitro* osteoinduction assessment

Sterilization behaviour of the selected blends: mechanical, chemical, physical and cytotoxic effect.

Chitosan-based screws for ACL reconstruction

Rectangular geometries:

Blocks ⇨ Rectangular plates

Screw geometry:

ComposiTCP60® (Biomet)

Blocks ⇨ Rods ⇨ Screws

CH+Gly screws

CH+Gly+HA-TCP screws

CONCLUSION

Conclusion:

Goals of this thesis

Key properties	Goal attained*	Comments
Processable	+	Two chitosan-based compositions were selected (Ch+Gly and Ch+Gly+HA-TCP). Plates and screws were shaped successfully, through different machining methodologies.
Suitable strength and stiffness	+	The mechanical properties of the two chitosan-based compositions are comparable to the properties of the bioabsorbable synthetic polymers.
Suitable biodegradation profile	++	The selected compositions do not degrade and lose mechanical properties in 6 months.
Sterilizable	++	The selected compositions do not significantly alter their properties after sterilization.
Not cytotoxic	++	The materials blended to chitosan do not alter its biocompatibility.
Promote bone formation	+	The selected compositions are able to interplay positively, promoting bone healing.

***(++ goal is surpassed; + goal is achieved; +/- goal requires improvements; - goal not attained)**

THANK YOU FOR YOUR ATTENTION

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