Novel 3-D printed Ti cage design and methods to boost spinal fusion

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Disclosures

- PI EU Interreg Vlaanderen-Nederland Prosperos project

- Consultancy biomaterials

  * BonAlive, Cambioceramics, Cerapedics, Depuy J&J, DSM biomedical, Biomet,
  * Heraeus, Medtronic, Stryker

- Board memberships biomaterials

  * Dutch Orthopaedic Association workgroup biotechnology
  * Dutch Society for Biomaterials and Tissue Engineering (NBTE)

- Scientific funding biomaterials to department

  * BonAlive, Cambioceramics, Cerapedics, Depuy J&J, DSM biomedical, Biomet,
  * Medtronic, Stryker,

- Other

  * Chair European Orthopaedic Research Society, 2019, Maastricht
  * Founder TOBIG (Translational Orthopaedic Biomaterials Interest Group)

Spinal fusion

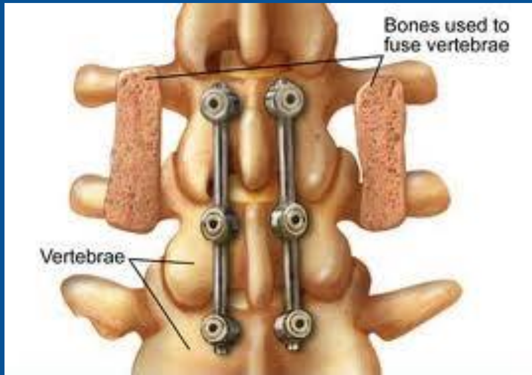
- A surgical technique used to join two or more vertebrae

- Aim - Eliminate pain
  - Provide stability
  - Correct spinal column malalignment

- Multitude of surgical approaches available

  1. Interbody fusion (ALIF / PLIF / TLIF)
     - Fusion vertebral endplates
     - Placement intervertebral device

  2. Posterolateral fusion
     - Fusion transverse processus
     - Fixation with metal screws



Spinal fusion

No standardization about …

- **Definition and localisation**
  * consensus spinal fusion
  * consensus about topographical zones

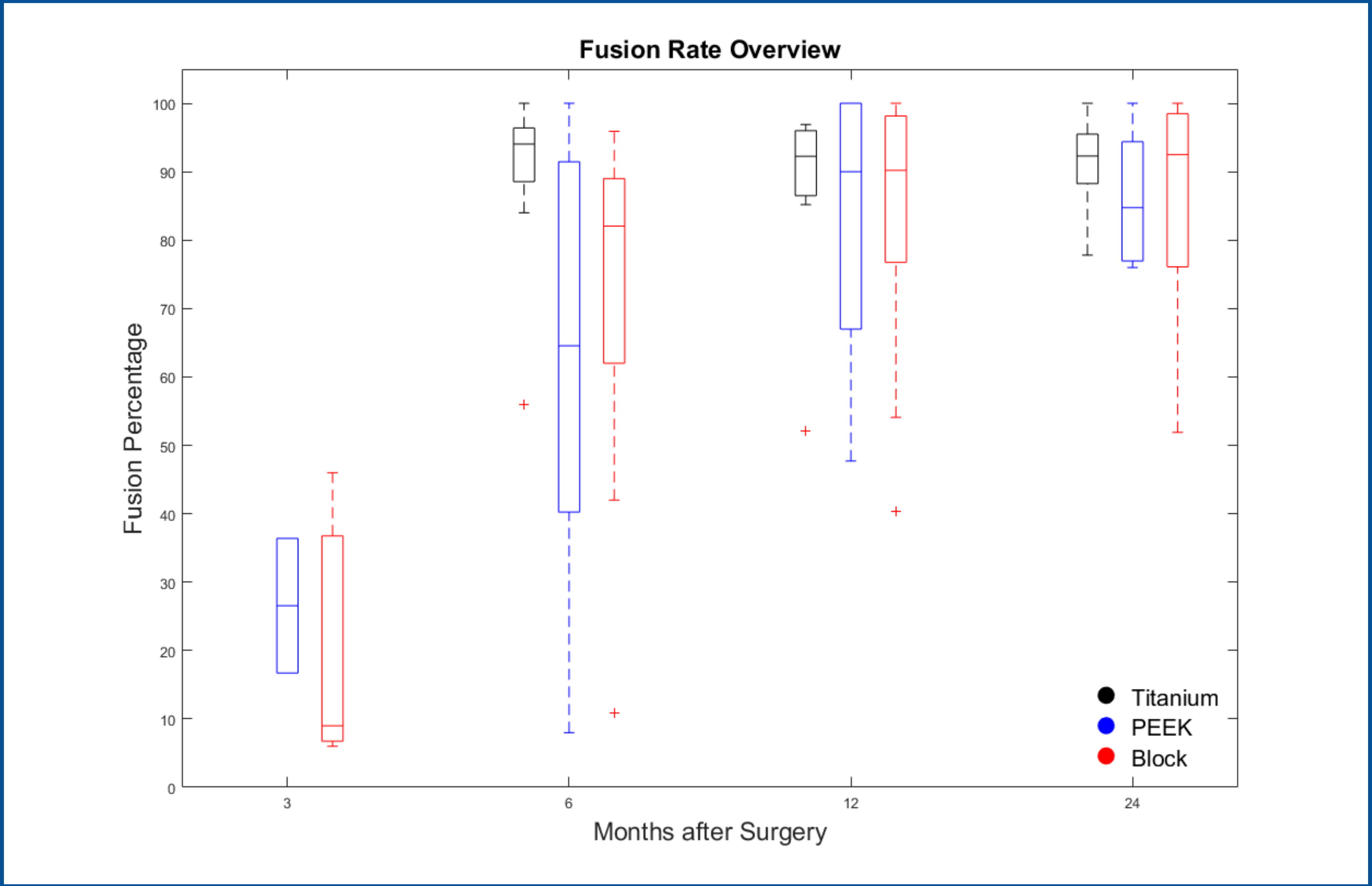
- **Quantification**
  * bridging bone between vertebrae +
  * restricted range of motion +
  * absence of radiolucencies

- **Assessment methodologies**
  * specific for imaging techniques (early fusion difficult)
  * X-ray, CT, PET-CT

- **Follow-up time points**
  * 3-6-12-24 months (limited data early fusion results)

Spinal fusion

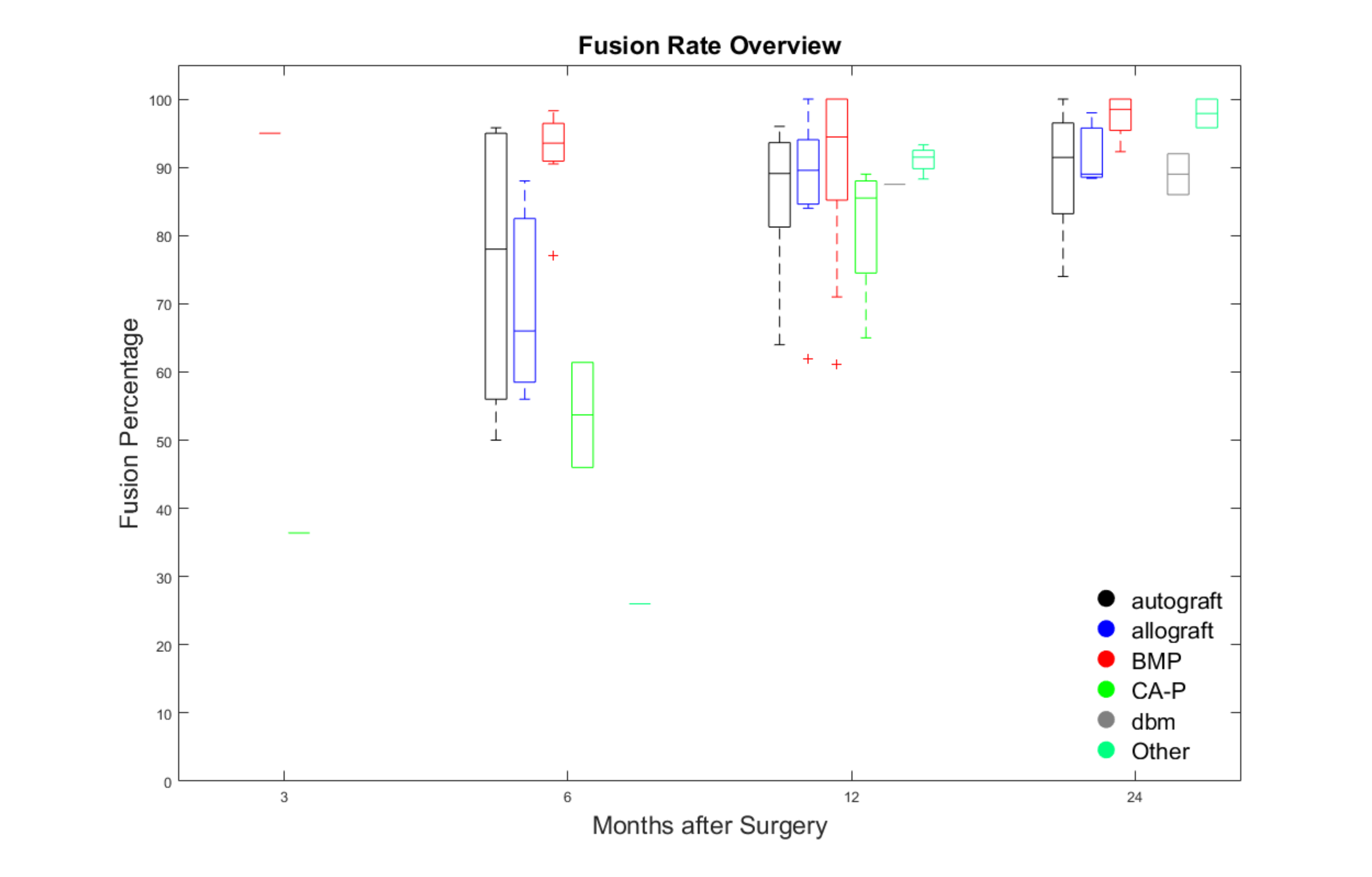
Systematic review (preliminary results !)



- Fusion rates vary a lot between PEEK and Ti cages
- 95% CI PEEK far larger as compared to Ti

Spinal fusion

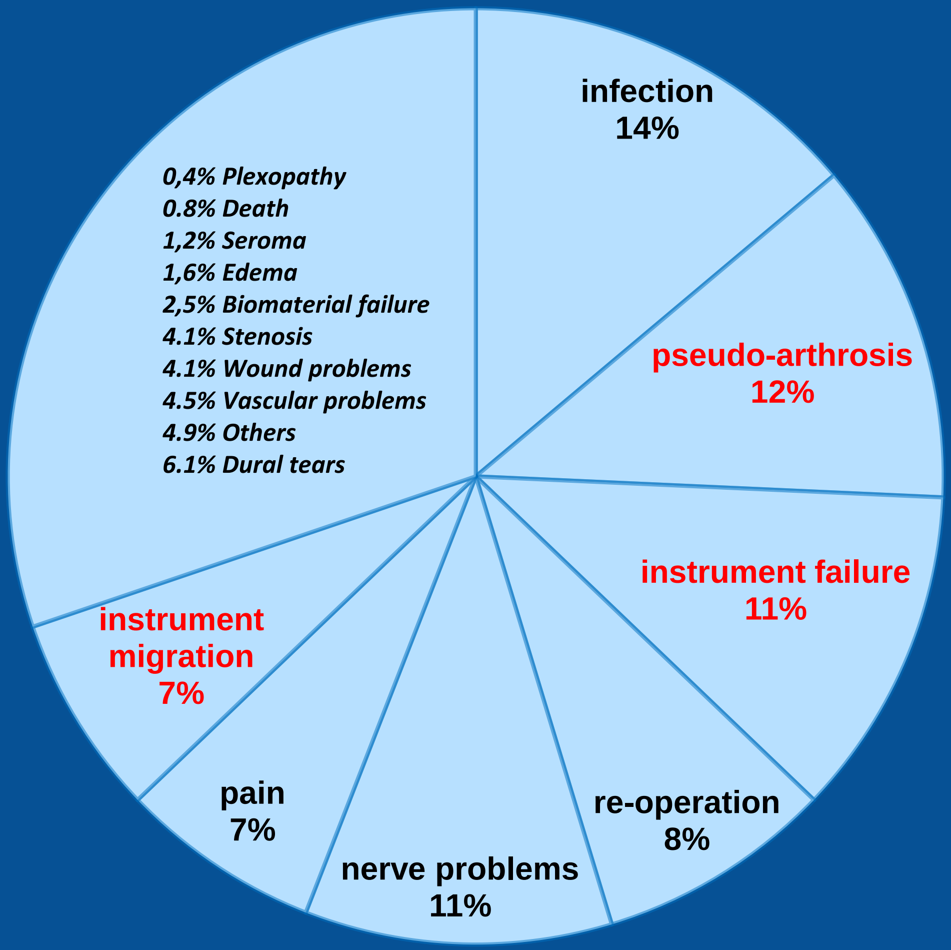
Systematic review (preliminary results !)



- **Fusion rates vary a lot between graft materials,**
- **Early 6-12 weeks fusion data underreported in literature**

Spinal fusion

Systematic review (preliminary results !)



- Most complications occur early < 3-6 months
- 30-35% complications due to inadequate early osseointegration
- Note also infection %

3D printed spine cages

- Shift from ongrowth towards ingrowth → improved mechanical interlock
- NOTE → CE classification and MDR regulations have changed dramatically !!

  → More clinical evidence is required

prosperos

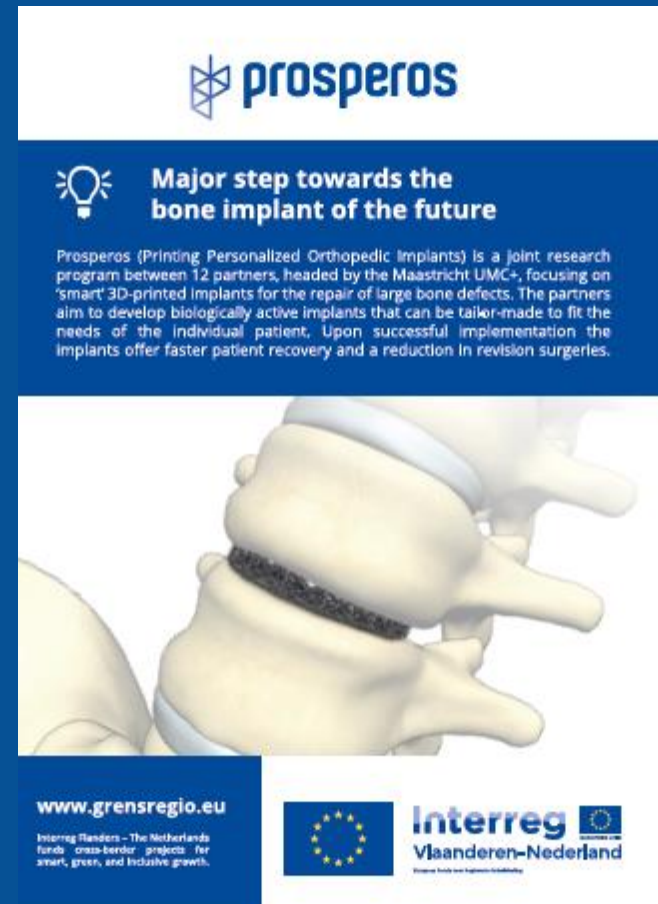
- **PR**inting **PER**sonalized **o**rthopaedic implant**S**

- **Mission statement:**

prosperos develops personalised bioactive implants for functional recovery

in order to

significantly improve Quality of Life (QoL) in an aging population by enabling patients to maintain active mobility at an elderly age



prosperos

- **Partners**

Maastricht UMC+

Antleron

4WEB®

3D SYSTEMS

2Move Implants
Implants for life

PCOTech

MedanexClinic
Animal Care in Science

XILLOC
Patient Specific Implants

UZ LEUVEN

KU LEUVEN

TU Delft

UMC Utrecht

UNIKLINIK RWTHAACHEN

Maastricht University

VLAAMS-BRABANT

Ministerie van Economische Zaken

provincie limburg
gesubsidieerd door de Provincie Limburg

Project overview

clinical problem	Fundamental research	Preclinical research	Clinical application	Evaluation
idea	in vitro	In vivo	human	trials

Stepwise introduction of 3D printed spinal cages

- **Translational curves**
  - clinical implementation 1st generation
  - animal trials 2nd generation
  - mechanical testing 3rd generation

- **Technology readiness levels TRL**

Technology Readiness levels

European Commission

Technology Readiness Levels

TRL 0: **Idea**. Unproven concept, no testing has been performed.

TRL 1: **Basic research.** Principles postulated and observed but no experimental proof available.

TRL 2: **Technology formulation**. Concept and application have been formulated.

TRL 3: **Applied research**. First laboratory tests completed; proof of concept.

TRL 4: **Small scale prototype** built in a laboratory environment ("ugly" prototype).

TRL 5: **Large scale prototype** tested in intended environment.

TRL 6: **Prototype system** tested in intended environment close to expected performance.

TRL 7: **Demonstration system** operating in operational environment at pre-commercial scale.

TRL 8: **First of a kind commercial system**. Manufacturing issues solved.

TRL 9: **Full commercial application**, technology available for consumers.

Work packages

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- WP 1: Project management; MUMC
- WP 2: Communication and dissemination; MUMC

clinical problem	Fundamental research	Preclinical research	Clinical application	Evaluation
idea	in vitro	In vivo	human	trials

- WP 3: Material Technology; RWTH Aachen
- WP 4: Implant geometry; KU Leuven
- WP 5: Implant surface chemistry and porosity; TU Delft
- WP 6: In vivo studies; UMC Utrecht
- WP 7: Clinical studies; Maastricht UMC

Implant geometry

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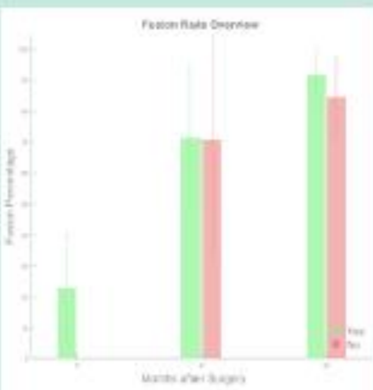
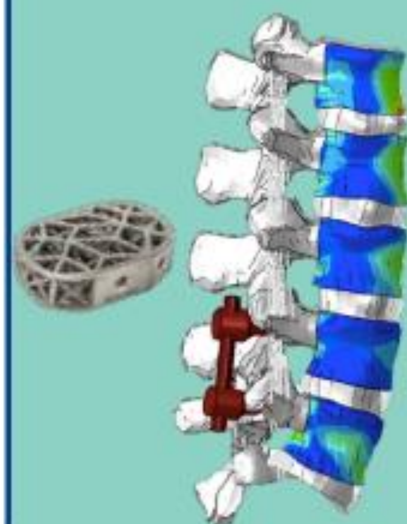
Develop and assess a new generation of interbody cages

Introduction
Literature review



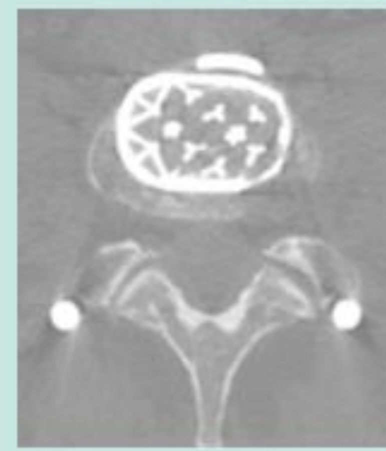
In Silico
FE model



In Vivo
Animal model

?

Clinical study



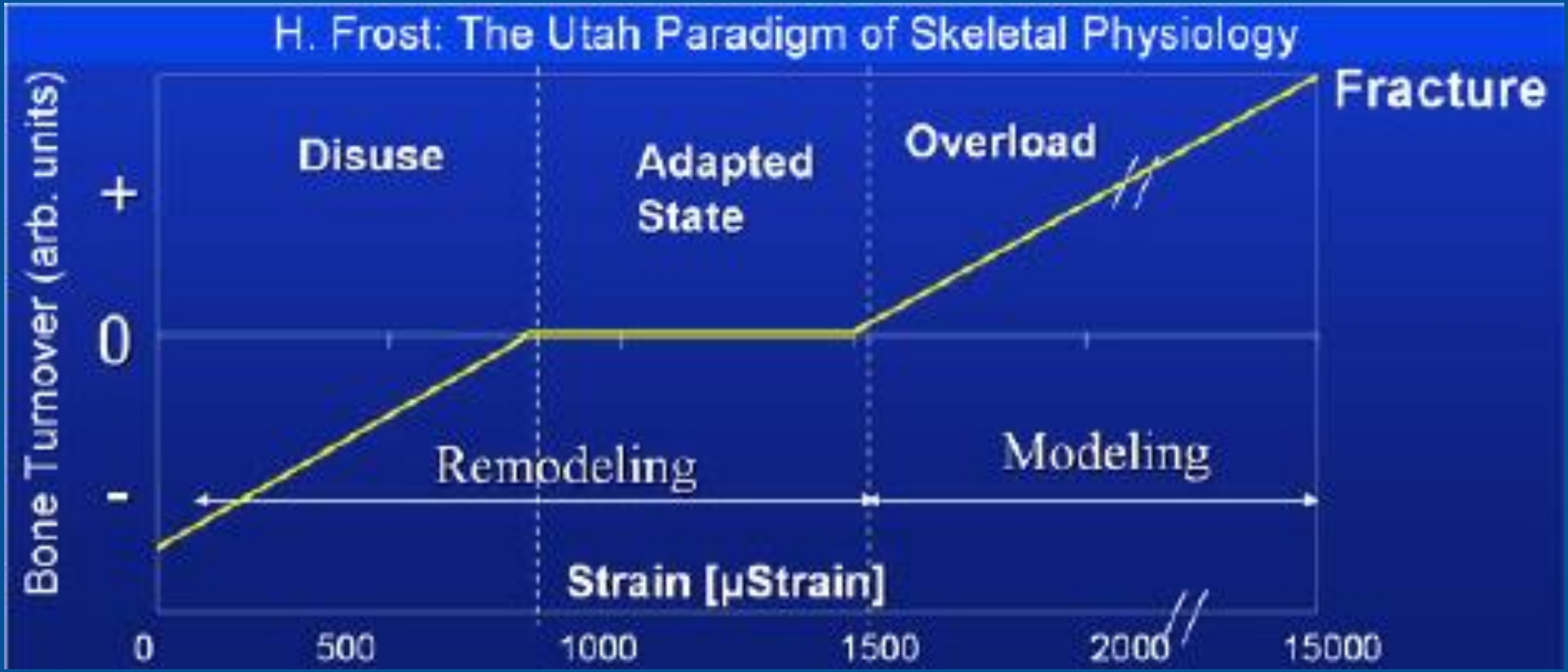
Assess + Develop

Assess

Maastricht UMC+ TU/e 4WEB Orthopaedie Maastricht prosperos

Mechanobiology

- Mechanobiology: surface strain regimes – bone homeostasis
- >1500 με induces bone formation
- [Frost; Angle Orthod 2004, 74: 3-15 and Pfirrmann et al., Spine 2001, 26: 1873-1878]
- ➔ Which surface strains are typically found in the design under physiological loading

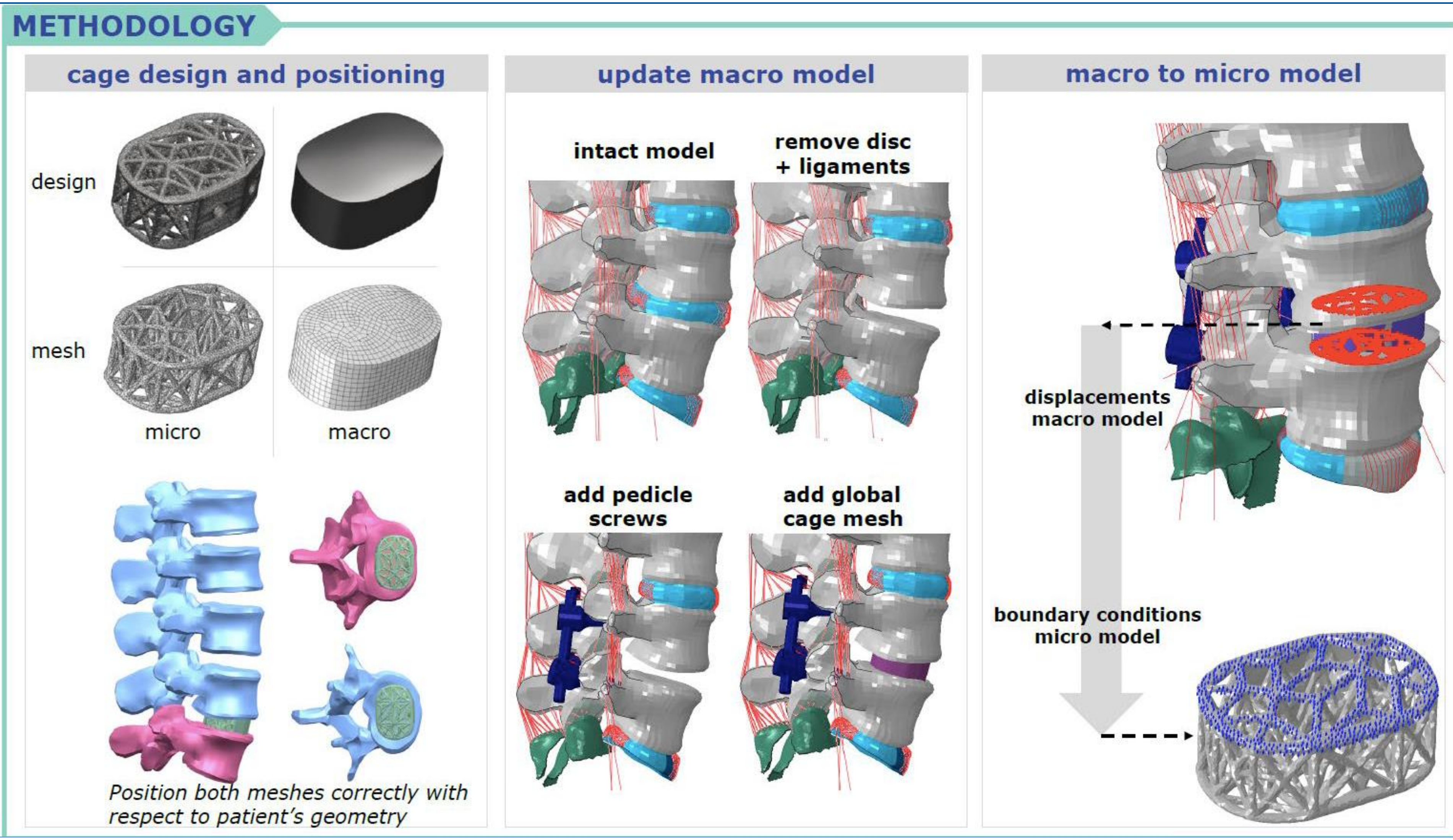


- 1000 με = 0.1% stretch/shortening

Implant geometry

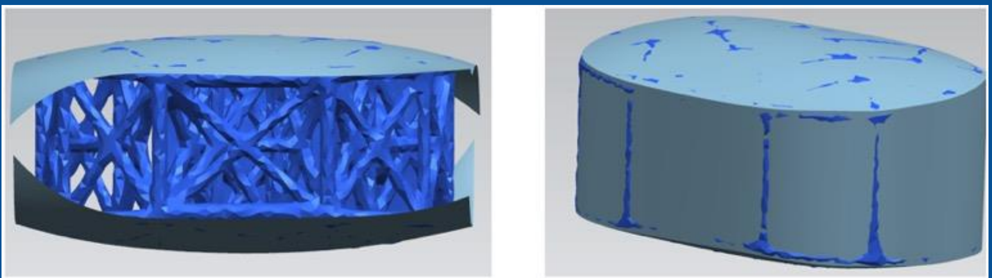
- **Develop and assess a new generation of interbody spinal fusion cages**

In silico analysis



In silico analysis

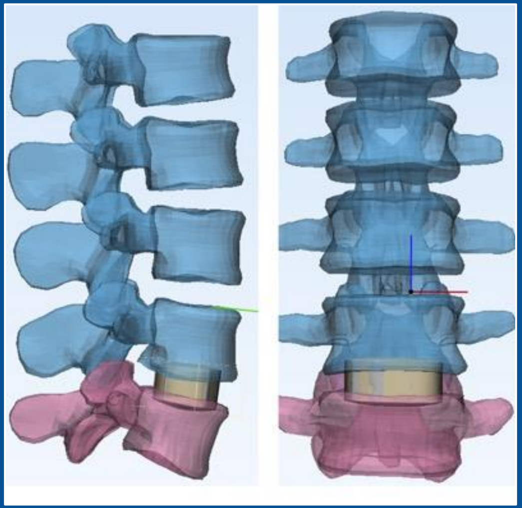
1. Model cage design and general shape

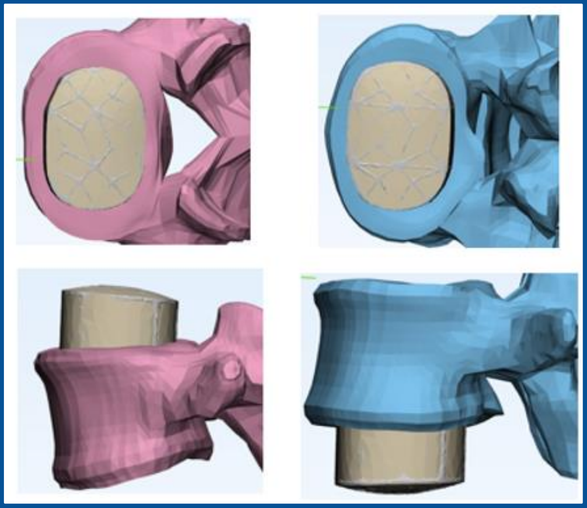


Design

Mesh

2. Position design and mesh w.r.t. lumbar spine

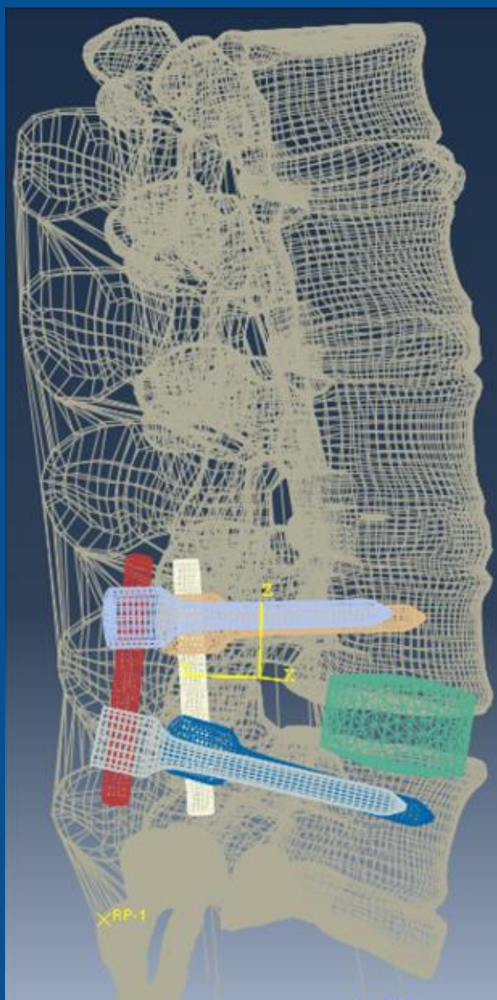


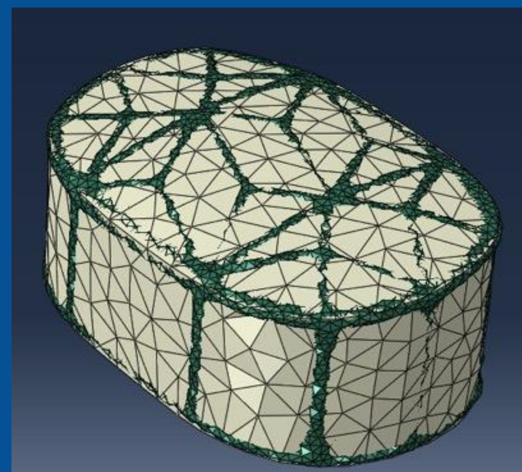


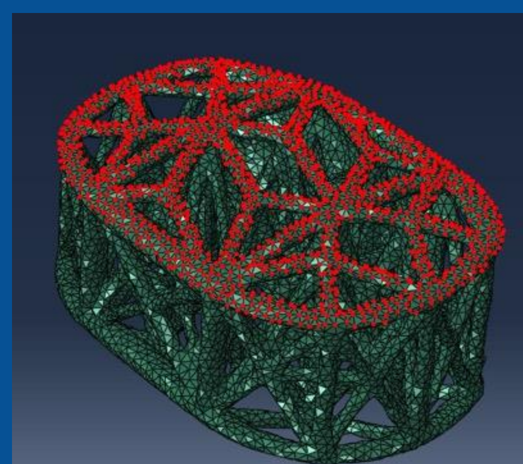
Get Registration matrix to move the mesh to correct position as well

In silico analysis

- **Cage implementation**
- **Submodelling – global ←→micro**





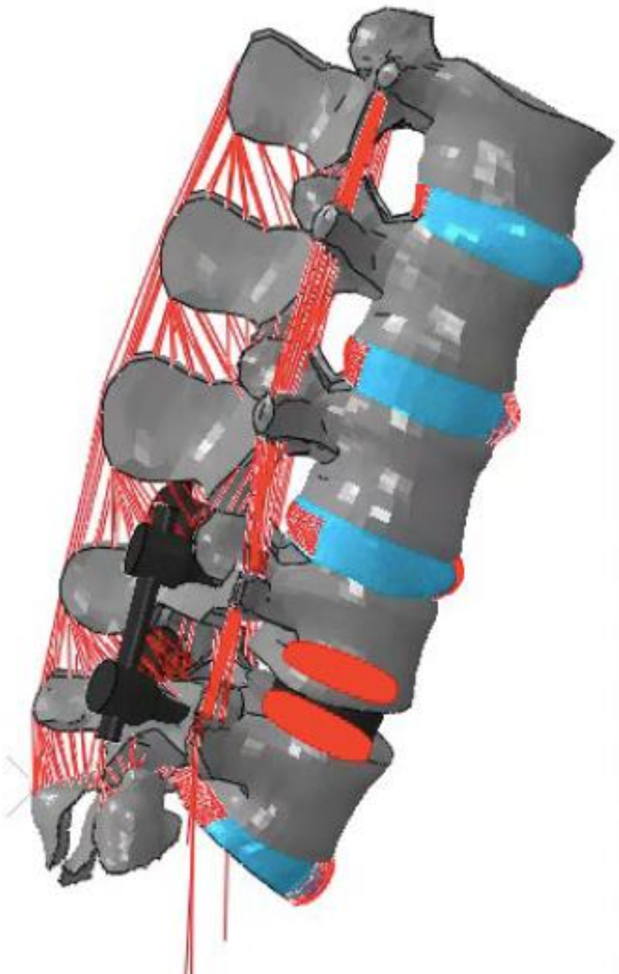


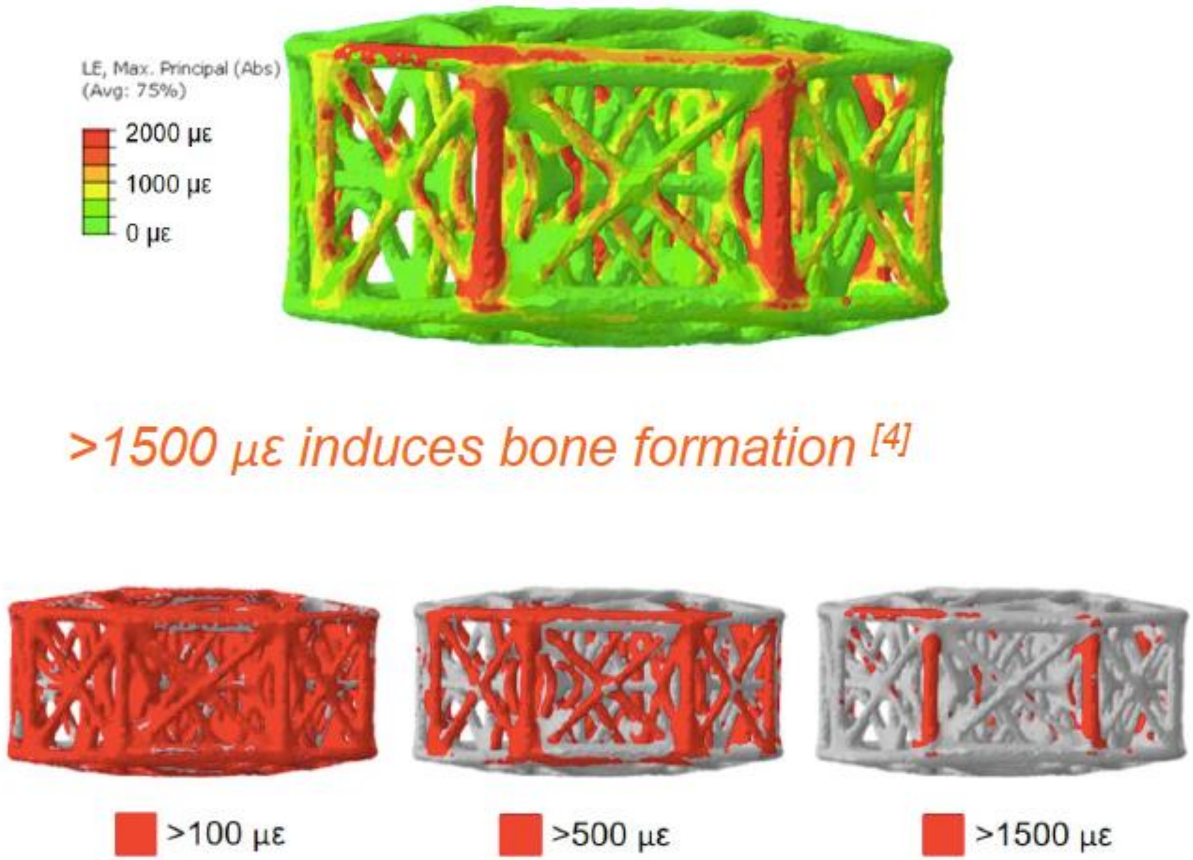
✓ Micromodel is located at same coordinates as global model

✓ Get boundary conditions at contact interface

In silico analysis

- **Preliminary results**



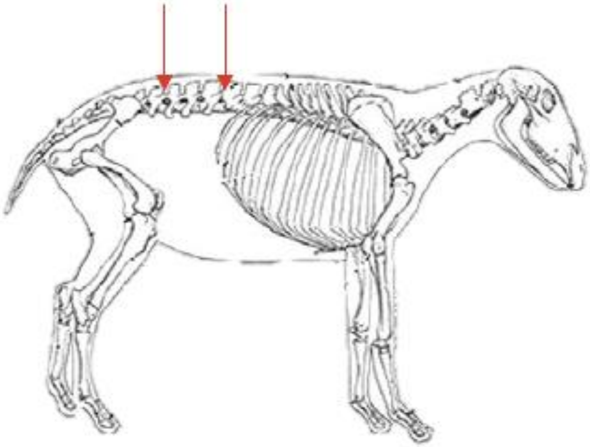


Animal experiments

In Vivo Model

- Skeletally mature Zwartbles ewes
- Bi-segmental fusion: L2-3 and L4-5
- 13 à 14 weeks in experiment

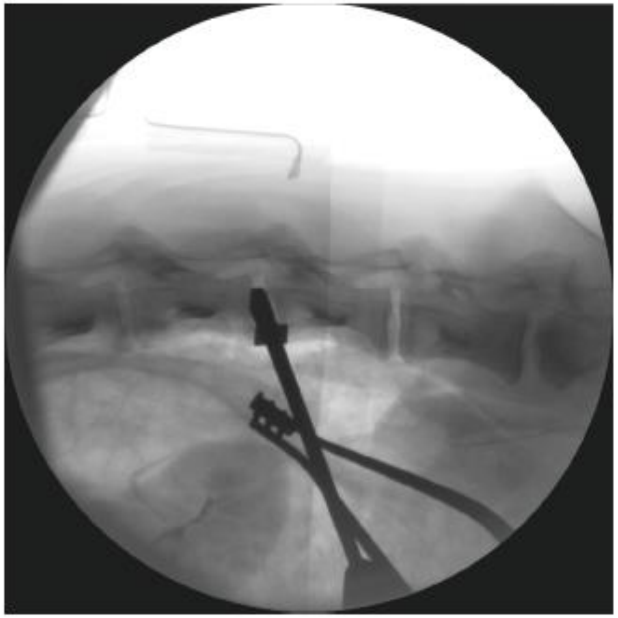
    → Breed allows implementation of human implant

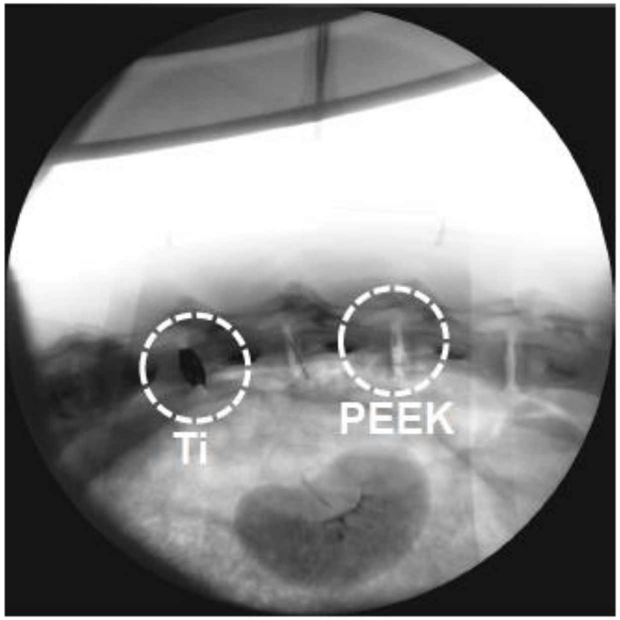


Animal experiments

In Vivo Model

Practice surgeries

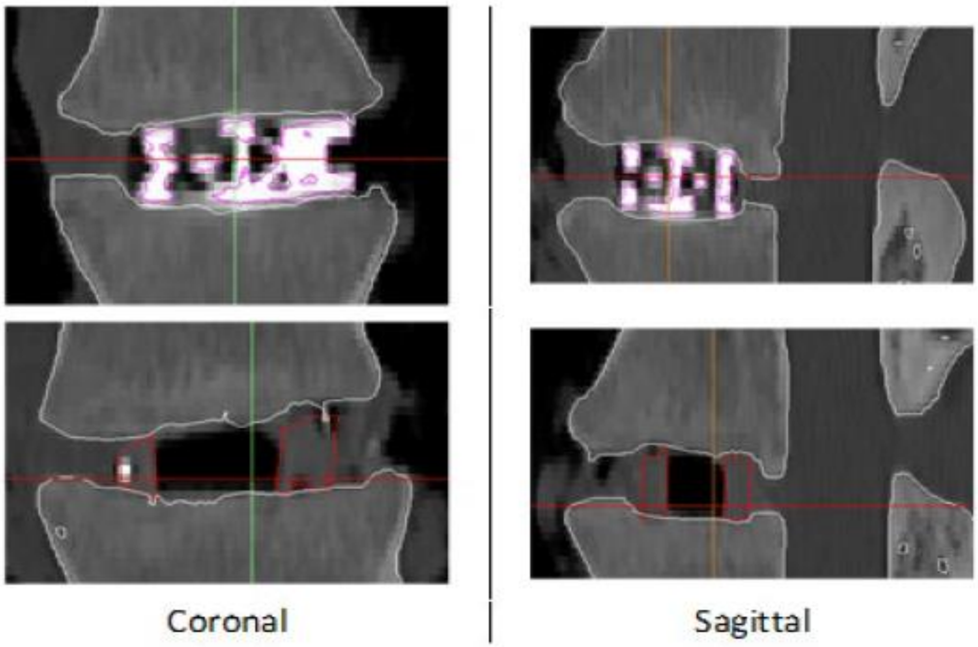


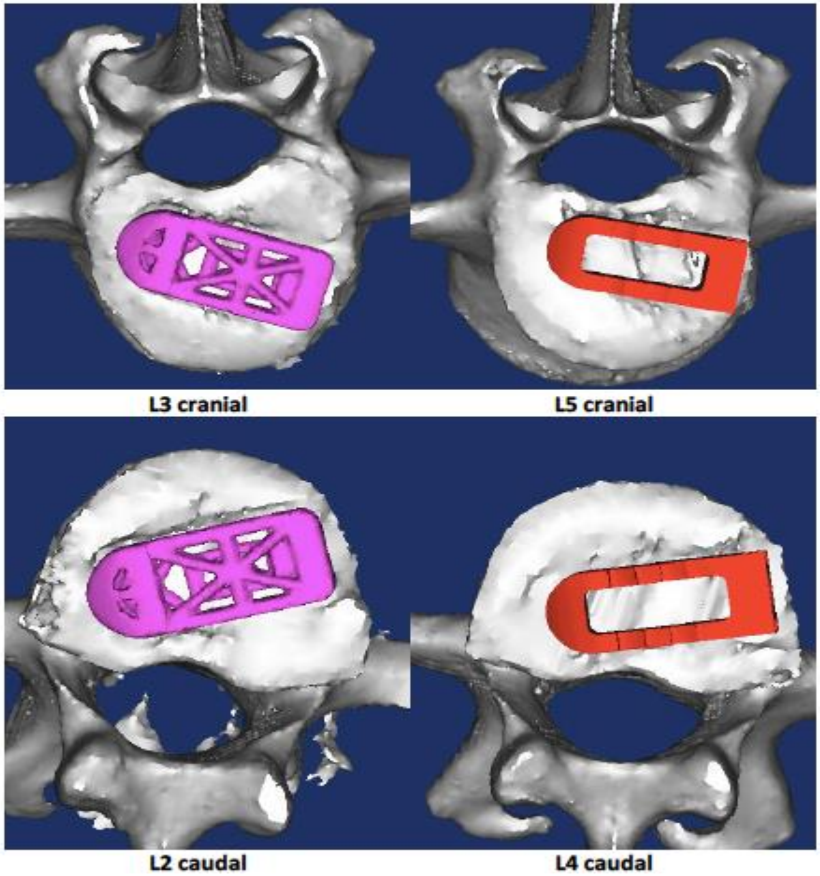


Animal experiments

In Vivo Model

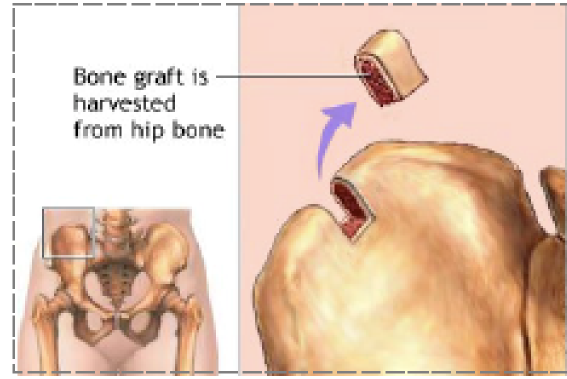
Explant analysis – *verify cages' position on endplate*





Animal experiments

Experimental set-up



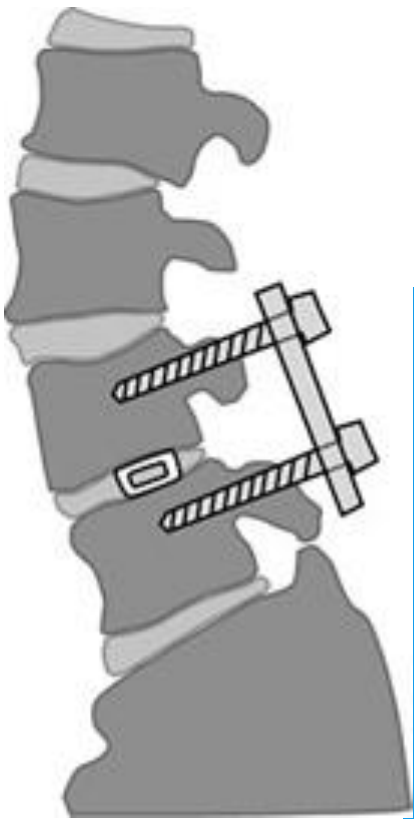
PHASE I	Autografted PEEK	-	Autografted commercial3D
PHASE II	Nongrafted commercial3D	-	Nongrafted optimized3D

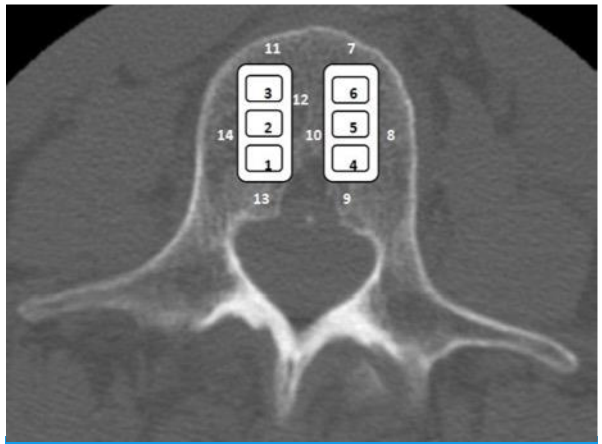
Longitudinal follow up: Na-^{18}F PET-CT @ 3,6,9,12 weeks

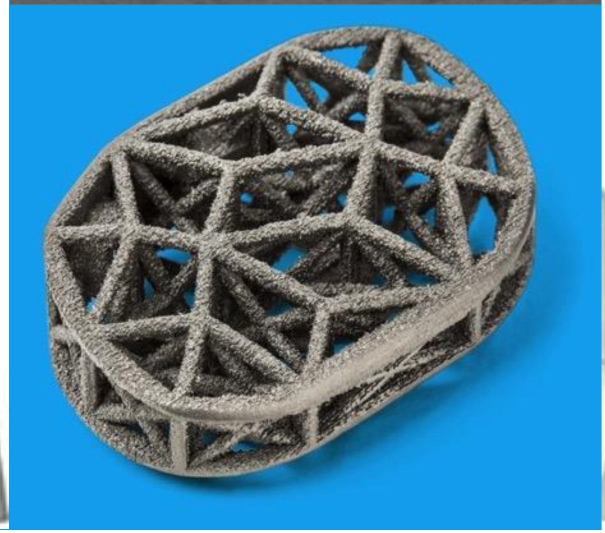
Post-mortem follow up: histology, biomechanical tests, microCT

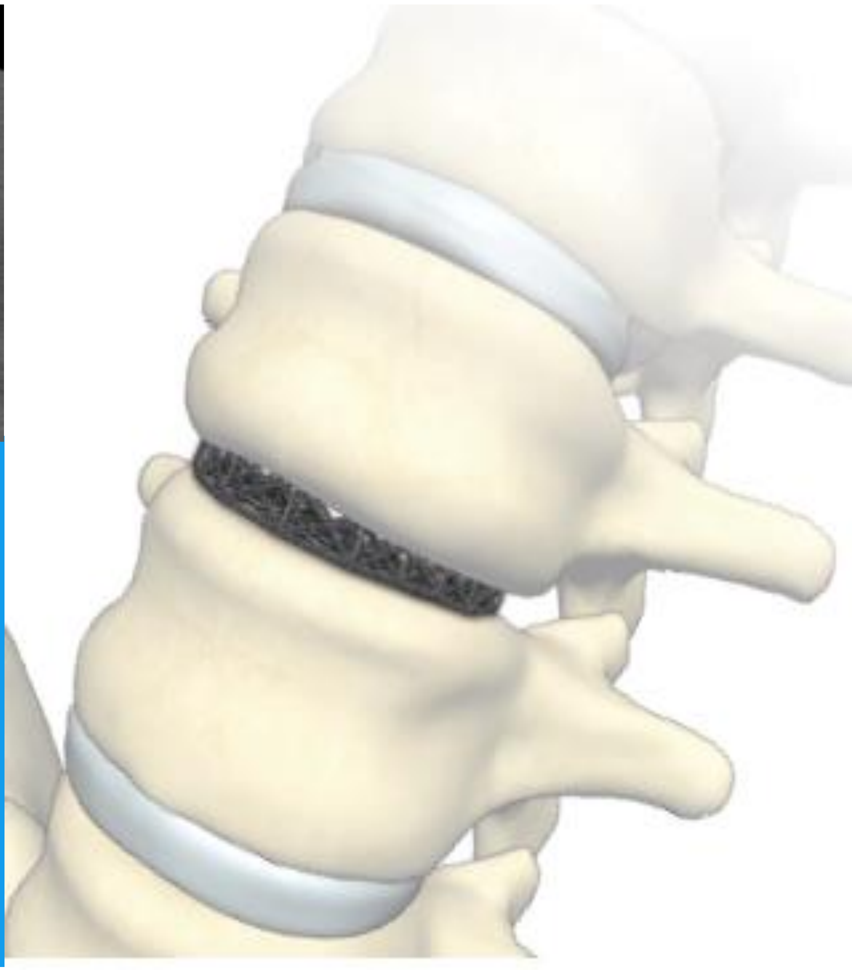
Clinical study spinal fusion

- **Spinal fusion**



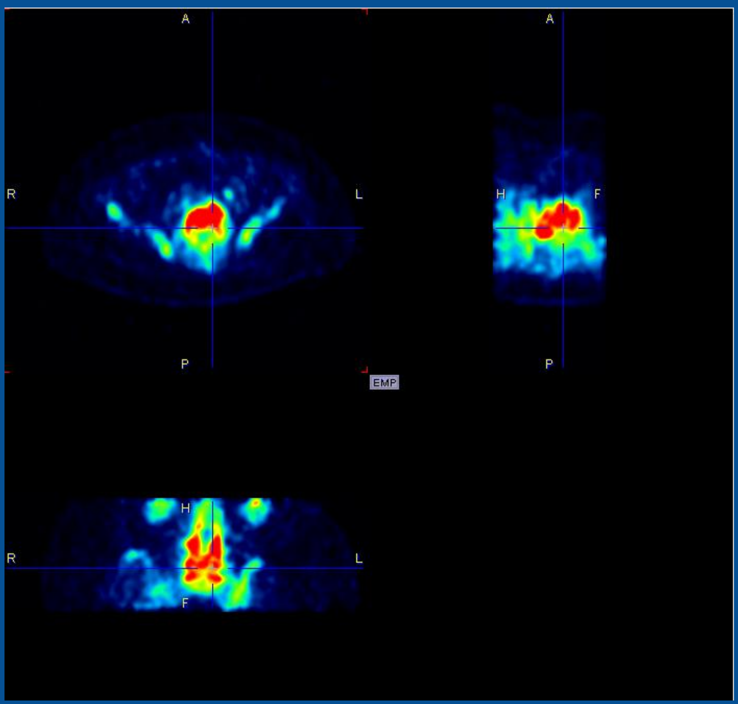


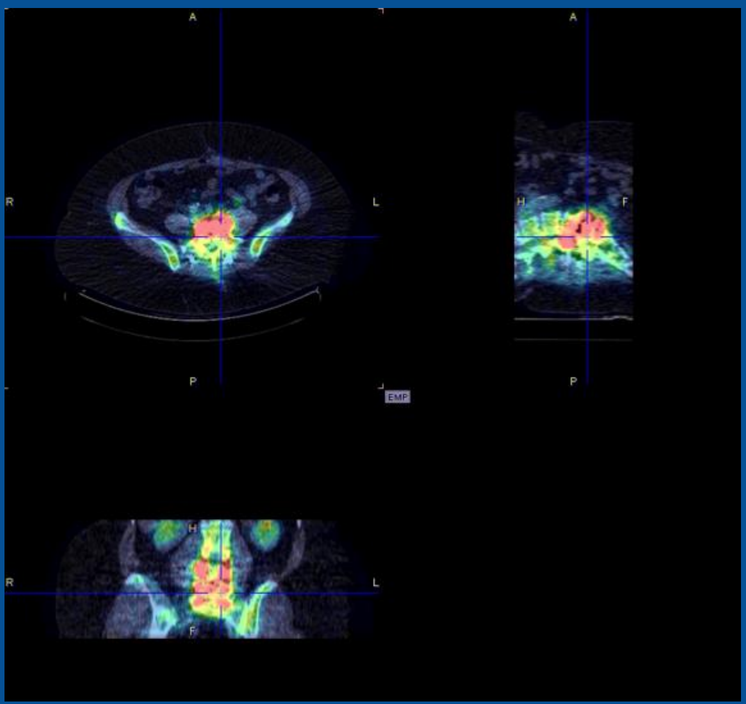




18Fl-fluoride PET-CT scan

- **PET-CT**
  - Visualisation and quantification of fluoride deposition in bone matrix





- **18F-fluoride PET scan**
- Quantification bone blood flow
- Quantification bone turnover
- →Bone remodeling metabolism

18F-fluoride PET/CT scan

And bone morphology assessment

→Correllation morphology/metabolism

Brans B et al. EJNMMI Research 2012, 2:42

Summary

- **Translational curves 2016-2020**

1st generation 3D printed implants	**Current 3D printed Ti implants** * Clinical pilot trial spinal fusion MUMC * Clinical pilot trial acetabular defects UMCU / UZ Leuven
2nd generation 3D printed implants	**Functionalised implant osseointegrative / antimicrobial coating** * Animal trials: osseointegration , infection , spinal fusion
3rd generation 3D printed implants	**Resorbable implants** * Prototype and limited mechanical assessment

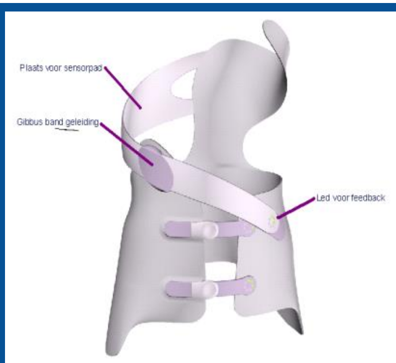
- **TRL spinal fusion cage from TRL 3 towards TRL 6**
- **FEA models ready to calculate effect structural properties and/or optimise design**

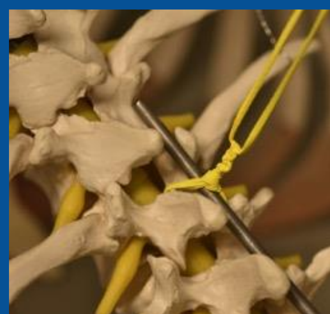
Consideration

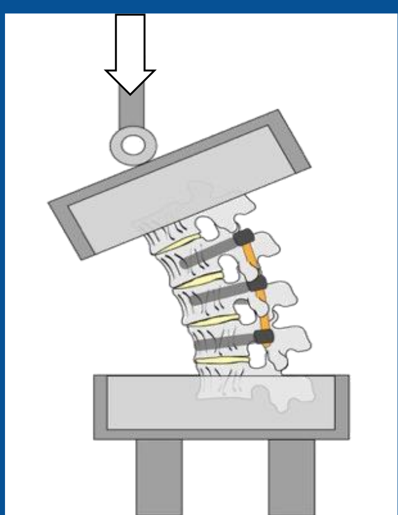
Questions

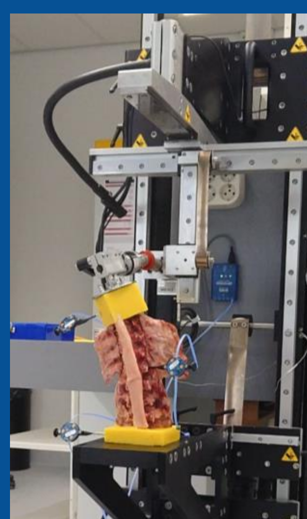
The most apparent solution might not be optimal...

Spine research Maastricht UMC









BRACES and 3D printed braces (Fited)

- Development M-Brace + sensor technology
- 3D printed braces + design algorithm
- Treatment EOS and AIS

UHMWPE sublaminar wires (DSM biomedical)

- Treatment for EOS, AIS and degenerative scoliosis
- First in man trial 12-2019
- Use as reinforcement pedicle screw fixation

Polycarbonate urethane rods (DSM Biomedical)

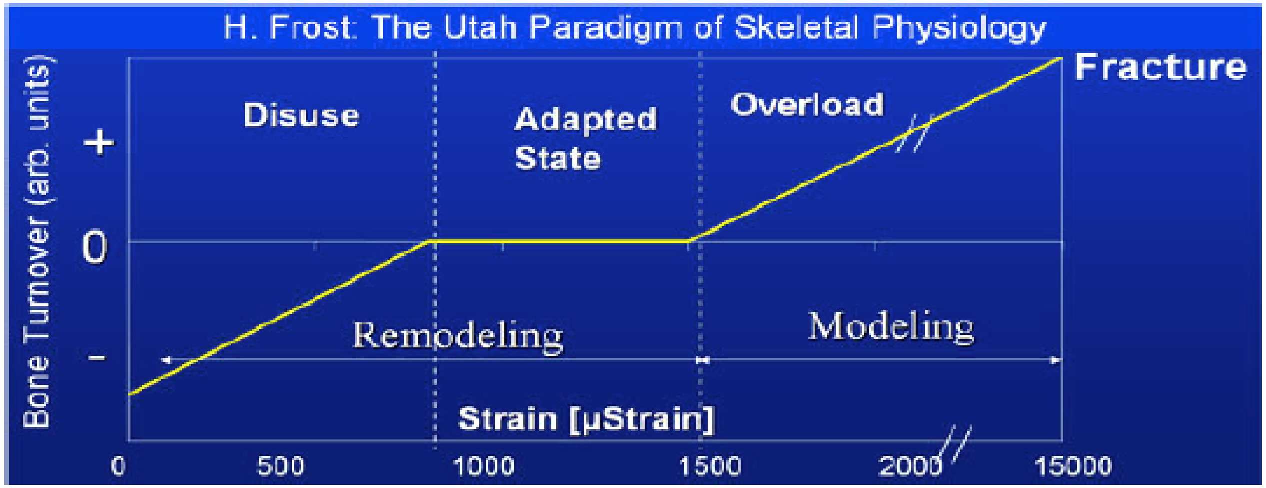
- Treatment for spine fusion, degenerative scoliosis
- Use especially in osteoportotic bone
- Alleviate stress pedicle screw and bone interface

In Silico Analysis

Mechanobiology: surface strain regimes – bone homeostasis

>1500 με induces bone formation [4]

→ Which surface strains are typically found in the design under physiological loading



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4. Frost, Angle Orthod 2004, 74: 3-15
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