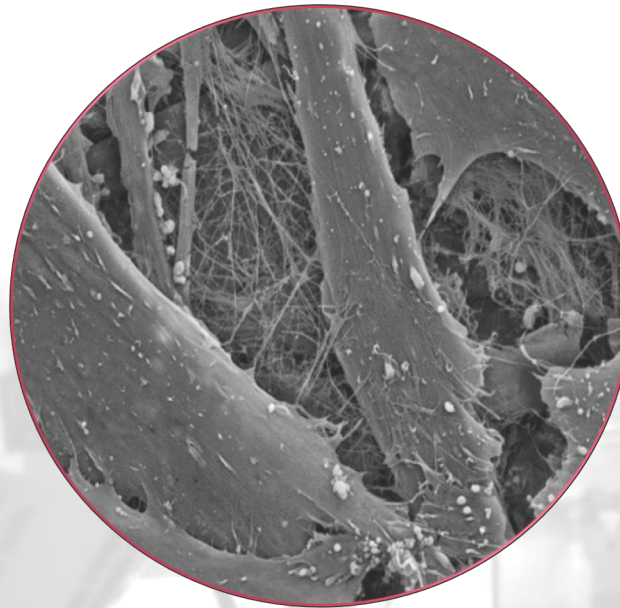


CHARITÉ  
UNIVERSITÄTSMEDIZIN BERLIN

stimOS GmbH

Universität  
Zürich UZH



MBT - inspired by nature, developed by stimOS:

Mimicking Bone Technologies

**Animal Test Results**

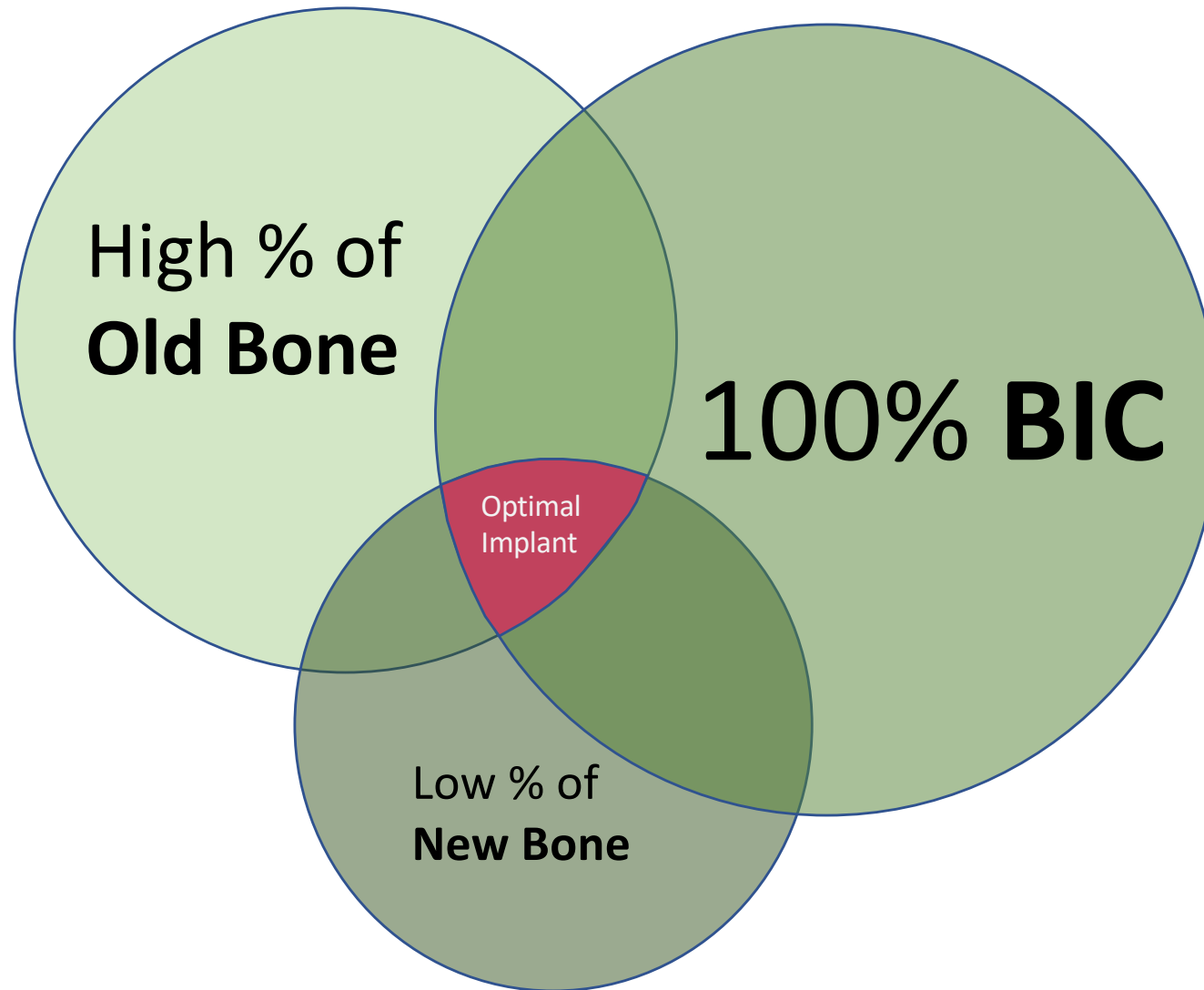
The Ideal Implant generates, supports and leads to<sup>1</sup>:



- 1. High Bone-To-Implant Contact:  
High BIC Interface**
- 2. Optimal Preservation of Host Bone:  
Reduced Bone Resorption**
- 3. New Bone Formation adjacent to the implant -  
directly to surface**
- 4. Optimal Bone Volume in the implant surroundings**
- 5. High Bone Quality in peri-implant area - New bone is  
flexible with an elastic, trabecular structure: No sclerotic  
structures**

<sup>1</sup> List of sample literature at the end of the presentation

# What is the Composition of an Ideal Implant?




So





# Why do we still use bio-inert plastics and «toxic» metals or metal-PEEK-composites as implant materials?

A large, light gray silhouette of a human head in profile, facing right. Inside the head, a large question mark is visible, suggesting a question or inquiry.

Today's implant surfaces are often the reason for failed osseointegration, implant loosening or inflammatory reactions.

stimOS technology gives every implant material a healing surface.

## The situation in Germany: Facts & Figures

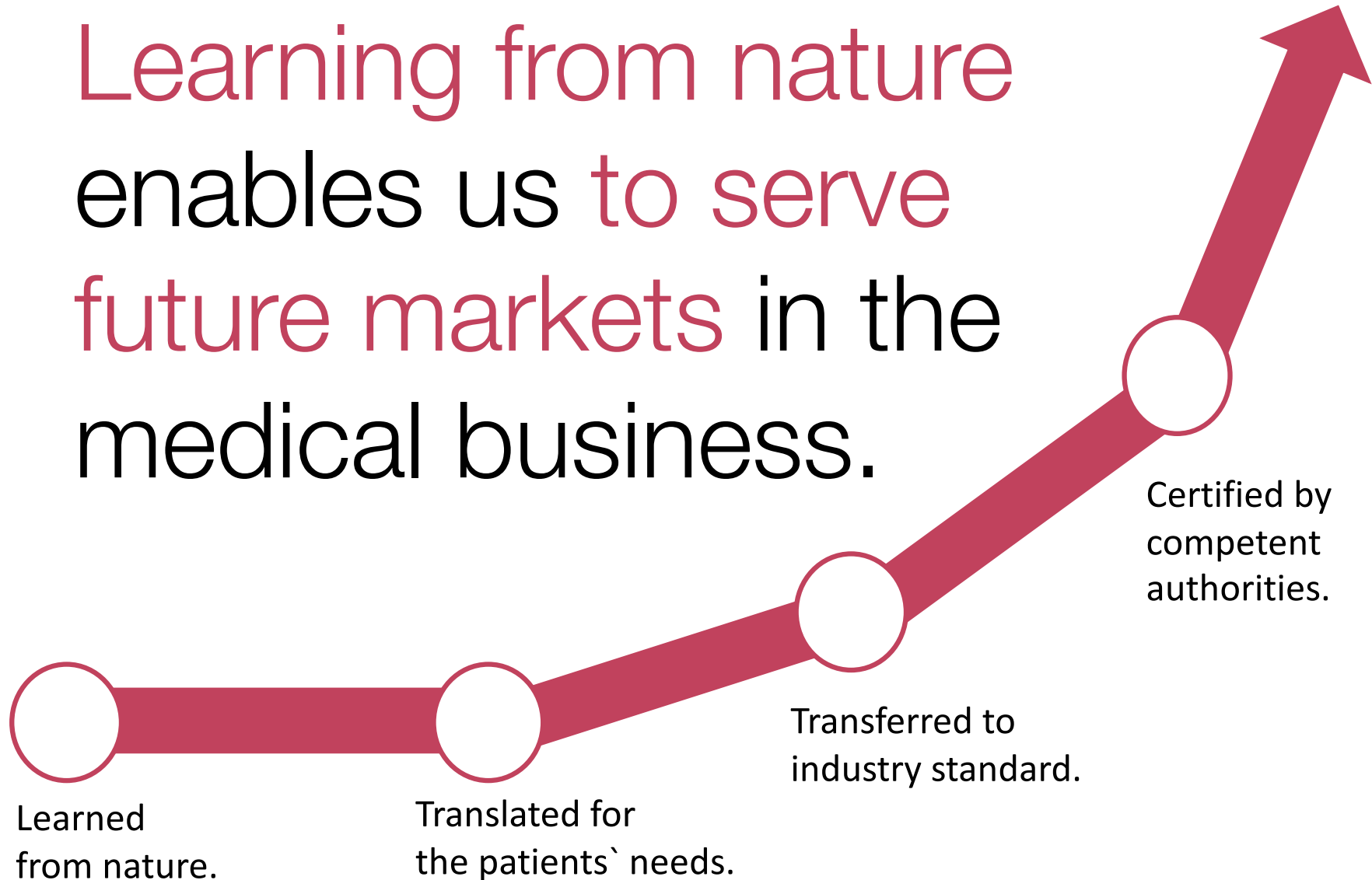
Based on **1.300.000 dental implants** placed per year, the **failure rate** due to screw loosening or inflammatory reactions is estimated with **182.000 dental implants** on average <sup>2</sup>.

Based on **160.000 spinal surgeries in Germany**, **64.000 cases** of these treatments are predicted to **fail** <sup>3</sup>.

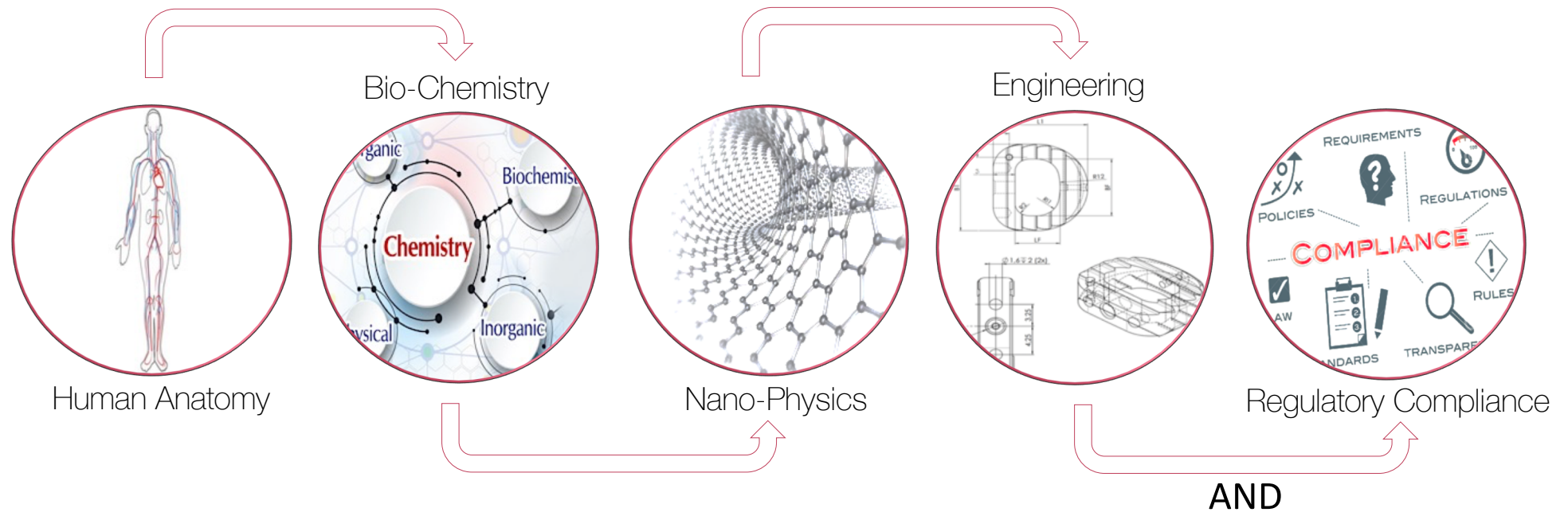
Based on **95.000 hip replacement** surgeries in Germany per year, the **re-operation rate** is estimated with **16.150 cases** on average <sup>4</sup>.

Based on **160.000 knee surgeries** in Germany per year, the **re-operation rate** is estimated with **25.600 cases** on average <sup>4</sup>.

Learning from nature  
enables us to serve  
future markets in the  
medical business.

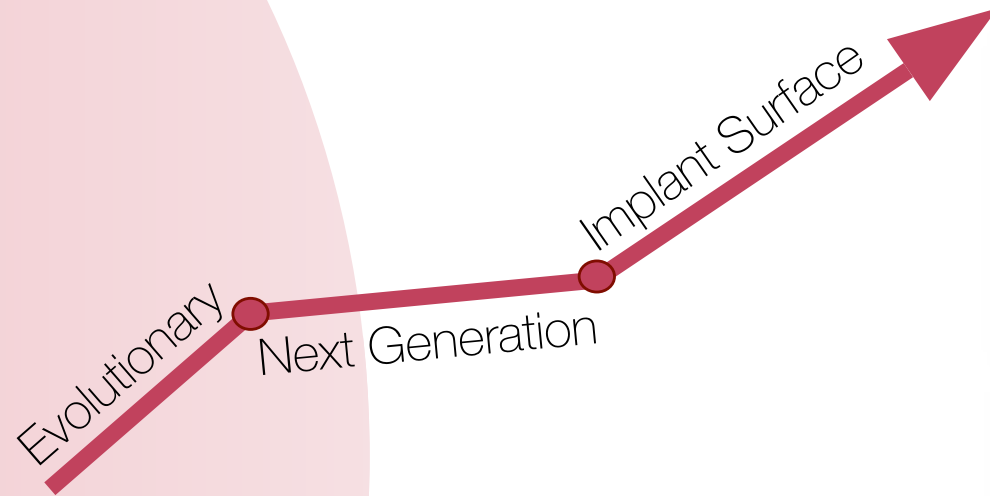


# Based on FIVE KEY DISCIPLINES



sample pictures for explanation only

# Proof of concept: Cell Test 12 h - Results - Visuals

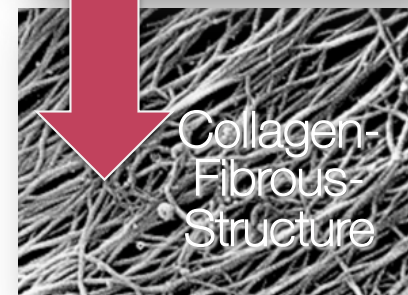
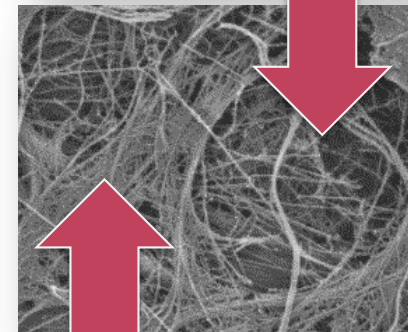
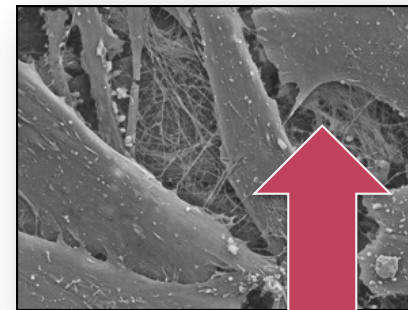


Cells cannot adhere to the implant surface

This may end up in:

- inflammatory reactions,
- implant loosening, and
- failed surgeries

## MBT modified PEEK

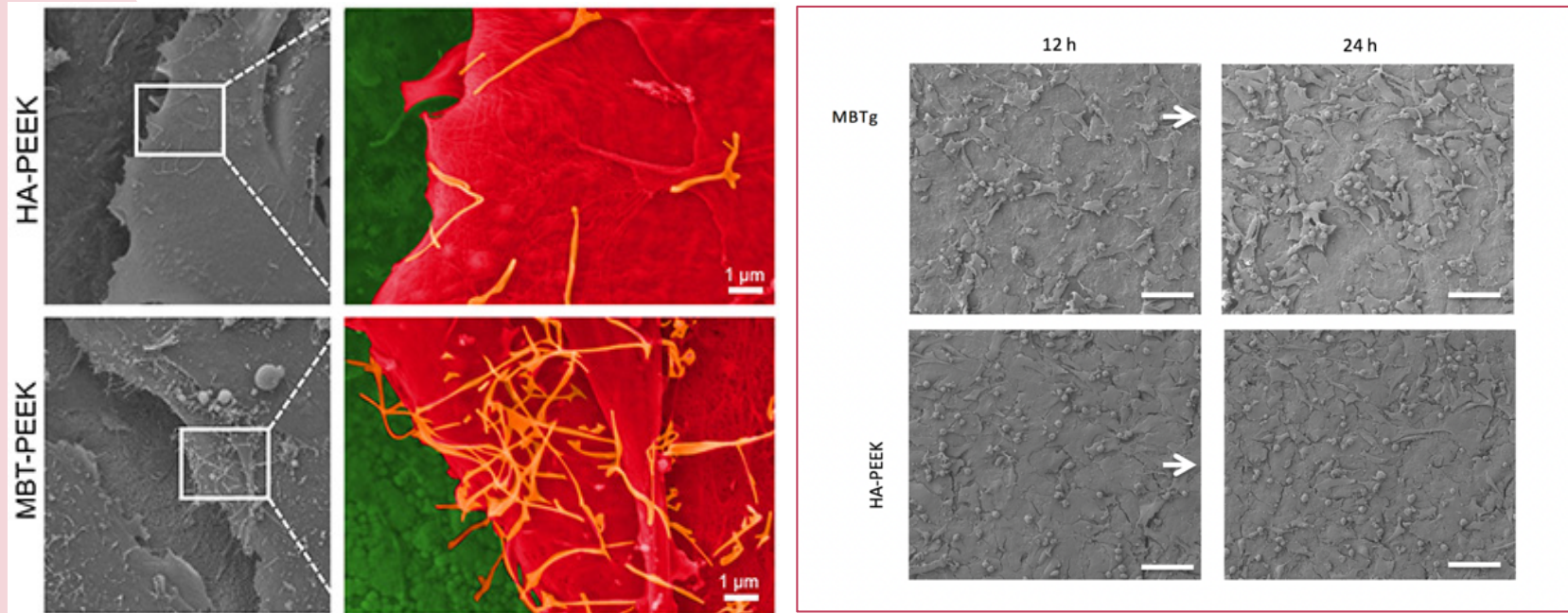


Secretion of a large amount of extra-cellular collagen matrix and start of **mineralization already after 12 hours.**

After 12 hours cells start to cover the implant with an **osseopromotive healing surface.**



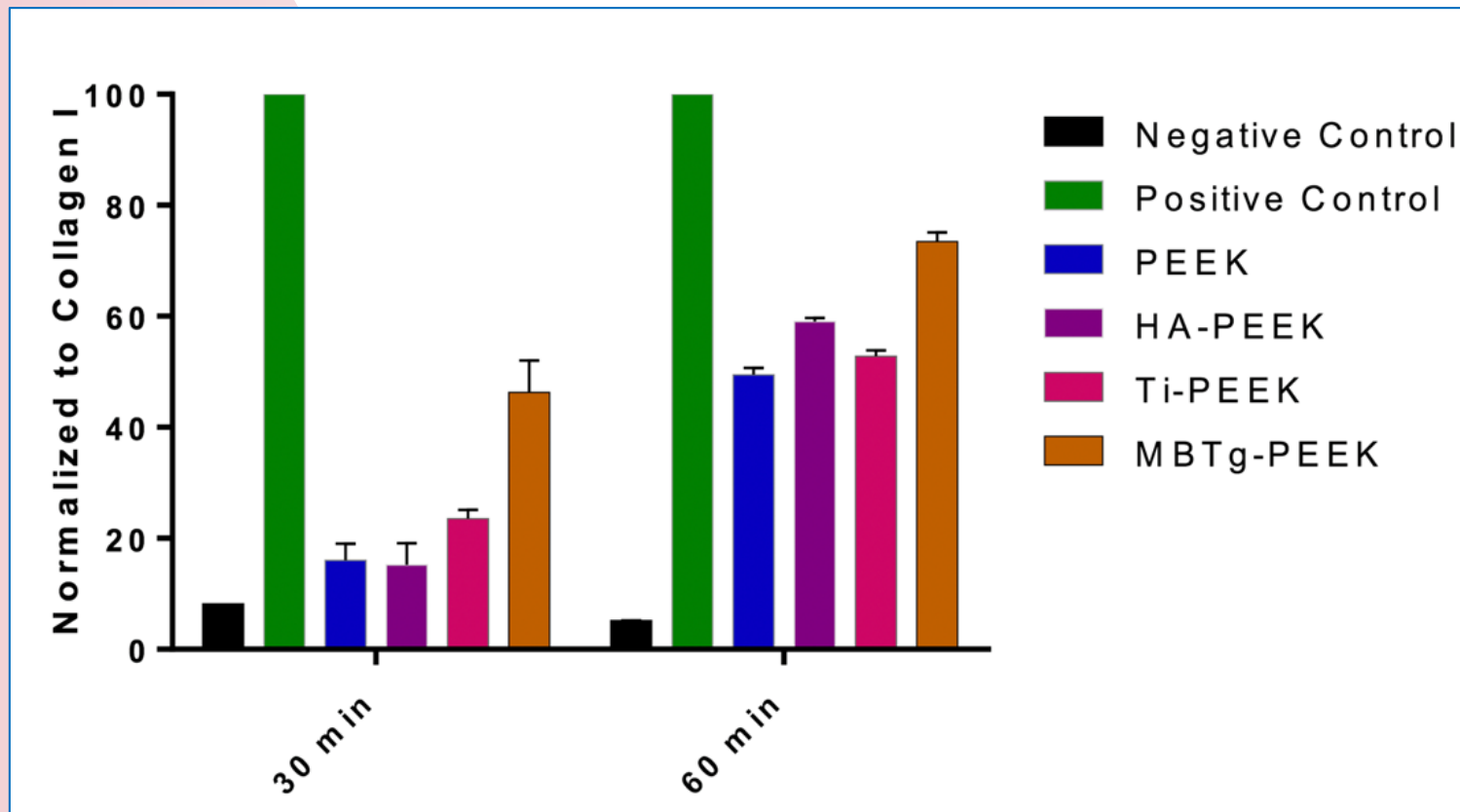
# Proof of concept: Cell Test 24 h - Results - Visuals



Applying stimOS' osseopromotive healing surface to the implants geometry, transforms implant surfaces from an artificial barrier into a smart and bone-identic implant body interface.

1

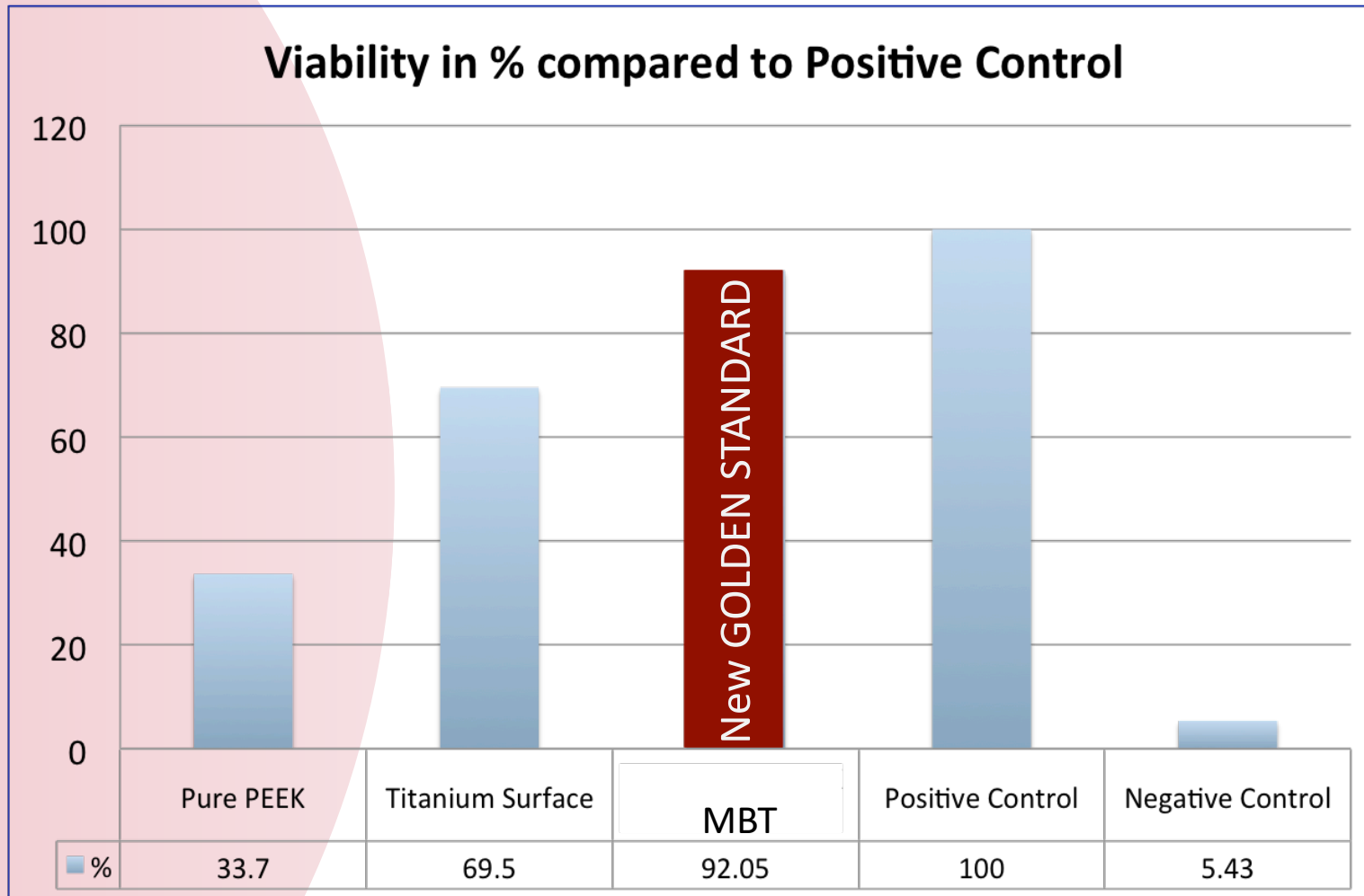
# Proof of concept: Cell Test Results - Statistics



To assess how fast MC3T3-E1 cells adhere to PEEK according to modified surfaces, **cell adhesion assays** have been performed (**three independent and in triplicate**).

In general, at least 50% of cells adhere on tested surfaces after 1 hour as normalized to the positive control. **MBTg PEEK showed the highest adherence of about 70 %**.

# Proof of concept: Cell Test Results - Statistics



2

A viability assay is an **assay to determine** the ability of cells to maintain or recover **viability**.



## Proof of concept: Animal Model Set-up



[1] According pre-defined worst case scenario, all test implants had screw-design and geometry. **The threads had an outer diameter of 5,5 mm.**

[2] According standard surgical protocol (dental), and to detect any possibly risk of abrasion, **holes with a smaller diameter of 5 mm have been pre-drilled into the pelvis** of the sheep before insertion of 5,5 mm test implants.

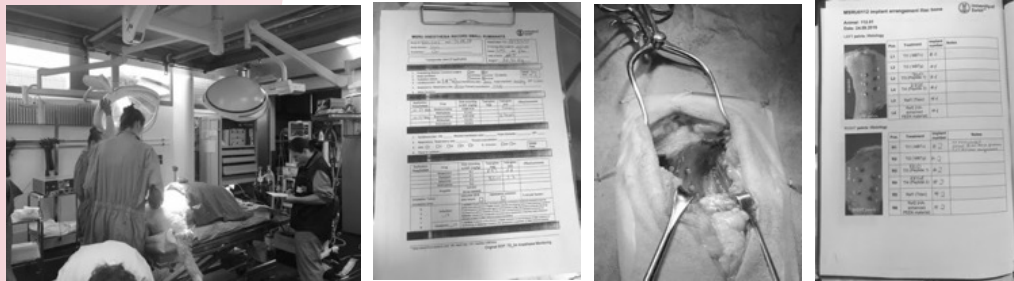
[3] In order to analyse the adhesion of bone cells onto the implant's surface, machined implant's surface was chosen. **No additional topography or surface roughness could influence cell adhesion onto the implant's surface.**

# Proof of concept: *Animal Model*



A **total of 36 test-implants** have been placed in 3 female Swiss Alpine (AS) sheep and have been used in this experiment: AS sheep have the right size for this type of study <sup>5</sup>.

Previous experiments of the University of Zurich have shown that **results can be directly translated to human patients** <sup>6</sup>.



3

<sup>5</sup> These animal models apply to the 3Rs of animal welfare, since implants can be tested, with relative low suffering of the animals while using a minimal number of sheep for the experiment.

<sup>6</sup> The experience with 100 animals also prove this animal model to be highly reliable and with very consistent results.

## Proof of concept: *Animal Model*



This sheep animal model has been successfully applied in several studies where osseointegration of implants was investigated.

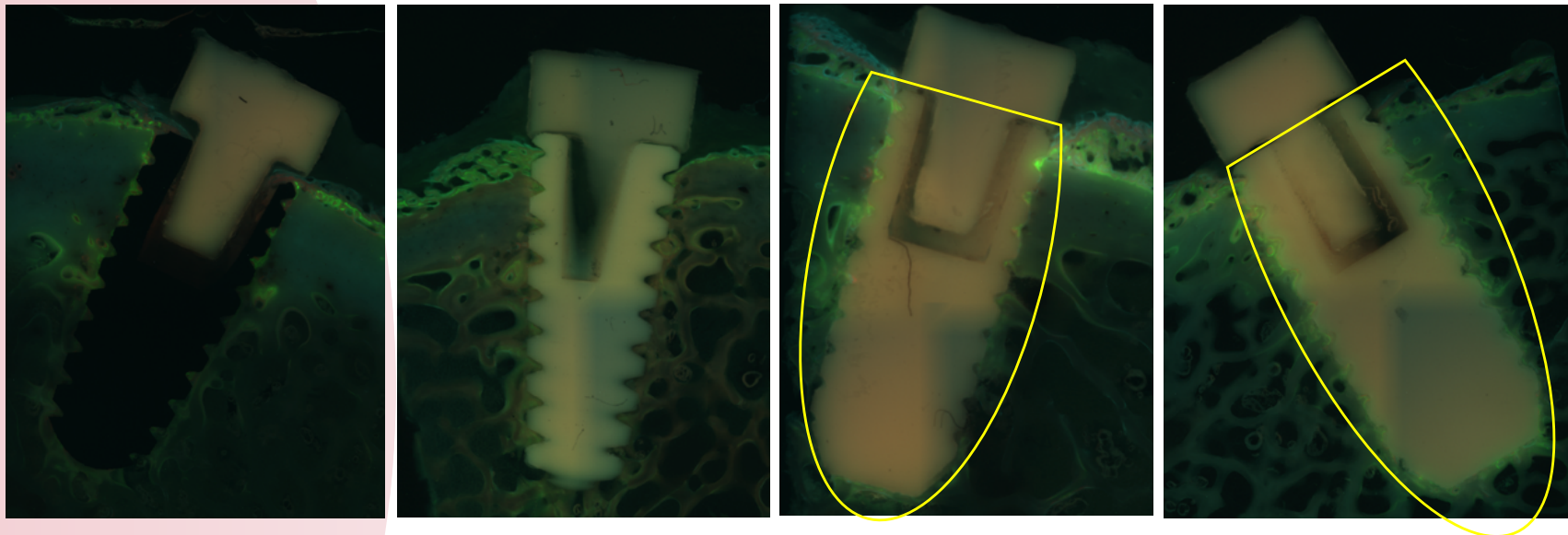
**The pelvis offers a good opportunity to test implants in cancellous bone.**

It allows to place many implants in the same individual without jeopardizing the animals wellbeing.



# Proof of concept: Animal Model Results: Visuals

Representative Selection of Fluorescence Images <sup>8</sup>:



Images are taken after two weeks of implantation. From left to right: Titanium, HA enhanced PEEK, **MBTv stimOS**, **MBTg stimOS**.

It can be clearly observed that bone in-growth into the threads only starts with MBT. **With MBT a high BIC % can be seen already after two weeks**. This is a strong indication for avoiding aseptic loosening <sup>9</sup>.

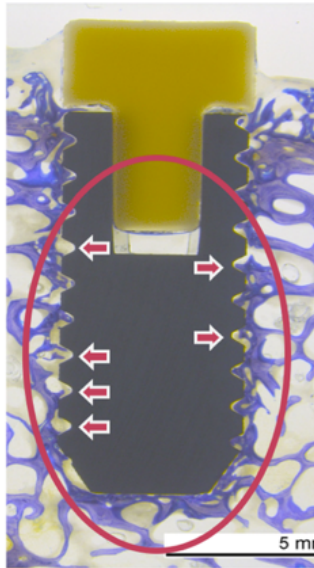
4

<sup>8</sup> For an comparative overview of all test results, please go to section „statistic“

<sup>9</sup> Rechenberg, B. et al., An experimental animal model of aseptic loosening of hip prostheses in sheep to study early biochemical changes at the interface membrane, BMC Musculoskeletal Disorders 2004

# Proof of concept: *Animal Model Results: Visuals*

## Representative Selection of Histologic Images <sup>7</sup>:

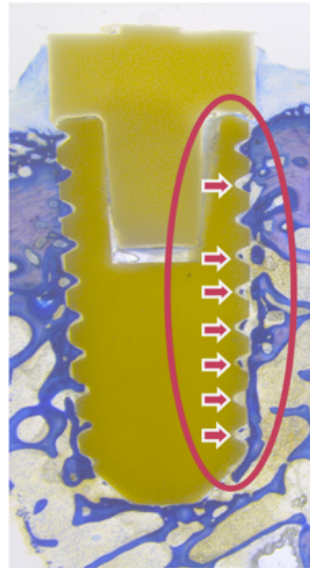


**Titan**  
**Golden Standard**

Dense new bone is only observed in the upper part of the implant.

Screw thread is not filled homogenous with bone.

No stable anchorage of implant in the surrounding bone.



**HA enhanced PEEK**  
**Reference / Invibio**

Bone is only observed on one side of the implant: Screw thread is not filled homogenous with bone.

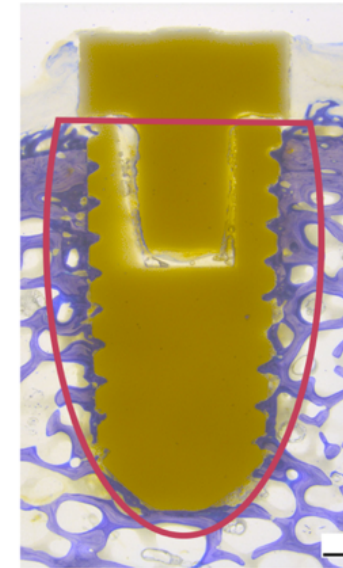
No stable anchorage of implant in the surrounding bone.



**MBTv**  
**Test-Device stimOS**

Test implant is anchored completely in surrounding (new) bone.

Screw thread is fully filled: No fibrotic layer can be observed.



**MBTg**  
**Test-Device stimOS**

Test implant is anchored stable in surrounding (new) bone.

Screw thread is fully filled: No fibrotic layer can be observed.

<sup>7</sup> For an comparative overview of all test results, please go to section „statistic“

# Proof of concept: *Animal Model Results: Statistics*



Summarizing Overview of all BIC-%-Measurements:



**University of Zurich**<sup>UZH</sup>

Musculoskeletal Research Unit (MSRU)  
Competence Center for Applied Biotechnology and  
Molecular Medicine (CABMM)



Appendix: A

**Tab. 1: Reference and MBT groups**

| Group                  | BIC cancellous bone (%) | BIC cortical bone (%) |
|------------------------|-------------------------|-----------------------|
| Ref 1 Titan            | 31.47 ± 12.34           | 40.71 ± 23.21         |
| Ref 2 HA enhanced PEEK | 37.48 ± 23.51           | 49.79 ± 21.26         |
| T11 MBTv               | 47.25 ± 6.83            | 72.61 ± 26.33         |
| T2 MBTg                | 74.00 ± 7.51            | 80.14 ± 16.07         |

5

Analyzing the overall results of HA enhance PEEK (Invibio Ltd.) a high SD is conspicuous: This may result from **HA debris during insertion** or may be a hint that **HA is not homogenous mixed-in into the PEEK matrix.**

# Proof of concept: *Animal Model Results: Statistics*



Representative Selection of Fluorescence Images <sup>8</sup>:



**University of Zurich**<sup>UZH</sup>

Musculoskeletal Research Unit (MSRU)  
Competence Center for Applied Biotechnology and  
Molecular Medicine (CABMM)



## Appendix: B

|                                   | Titanium | HA-enhanced PEEK | MBTv stimOS | MBTg stimOS |
|-----------------------------------|----------|------------------|-------------|-------------|
| BIC cancellous bone (%)           | 31,47    | 37,48            | 47,25       | 74,00       |
| BIC cortical bone (%)             | 40,71    | 49,79            | 72,61       | 80,14       |
| New bone in cancellous bone (%)   | 33,87    | 28,97            | 26,32       | 31,77       |
| New bone in cortical bone (%)     | 16,53    | 26,91            | 12,66       | 21,63       |
| Old bone in cancellous bone (%)   | 19,57    | 24,00            | 20,69       | 27,09       |
| Old bone in cortical bone (%)     | 77,83    | 60,21            | 82,47       | 73,76       |
| Total bone in cancellous bone (%) | 53,44    | 52,96            | 47,01       | 58,85       |
| Total bone in cortical bone (%)   | 94,36    | 87,11            | 95,14       | 95,40       |

Summary of all measured results comparing Titanium, HA enhanced PEEK (Invibio Ltd.) MBTv (stimOS GmbH) and MBTg (stimOS GmbH).



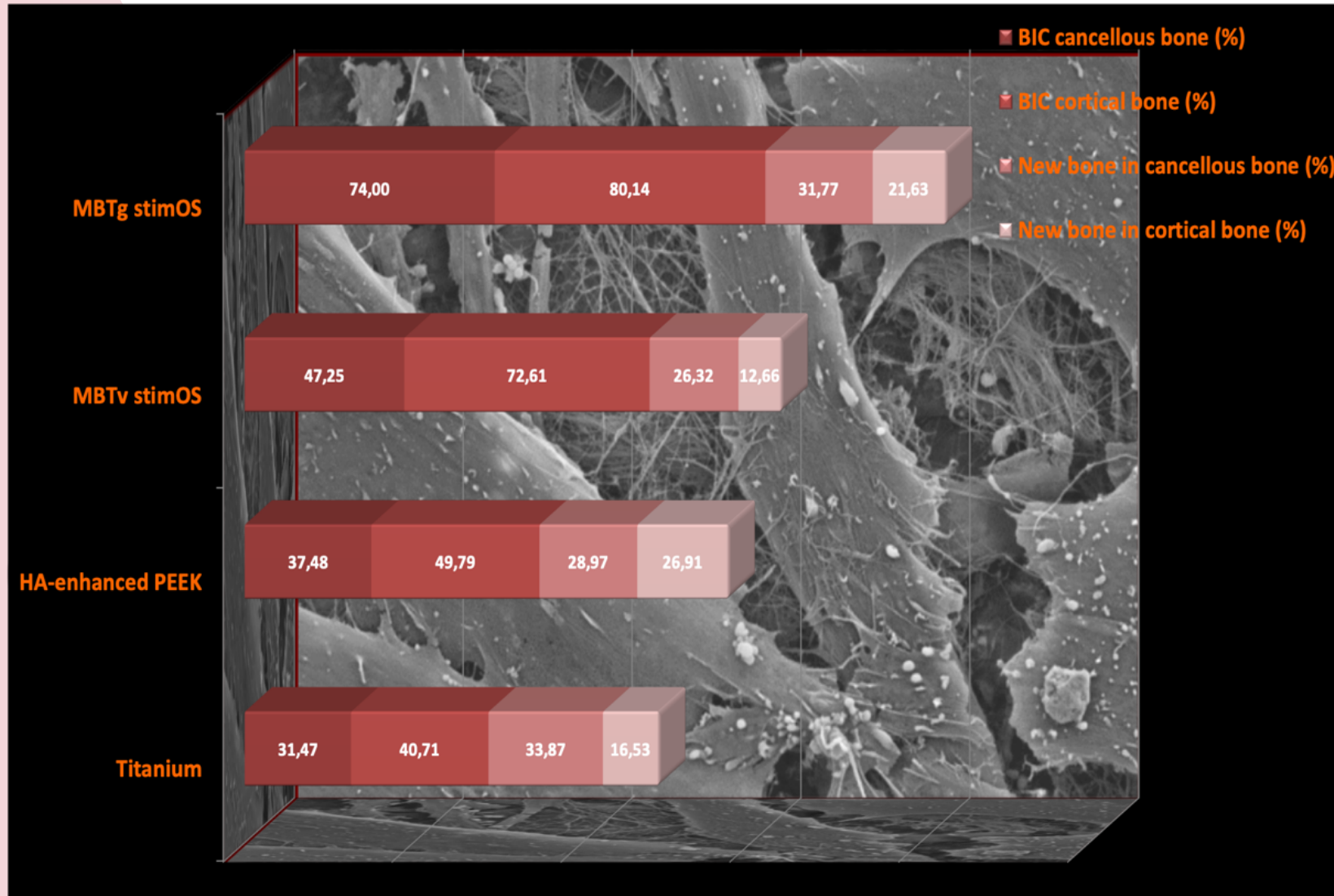
# Proof of concept: Animal Model Results: Statistics



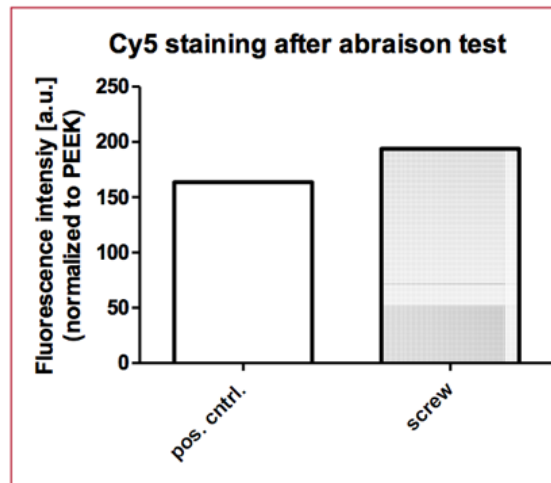
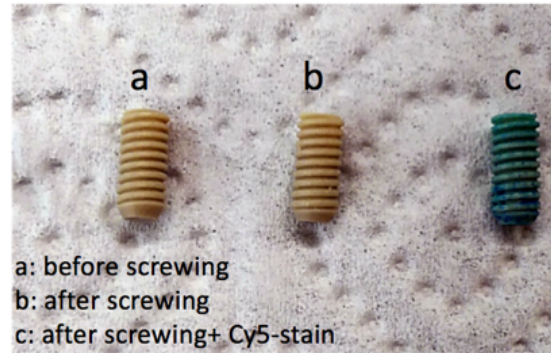
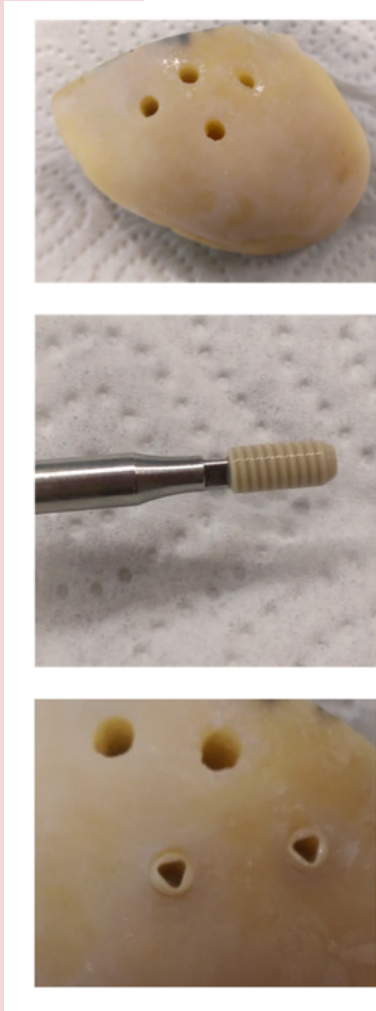
5



# Proof of concept: *Animal Model Results: Statistics*



# Proof of concept: Mechanical Test Results



Pos. cntrl.: MBTg coating on a PEEK film, on which the coating was already verified

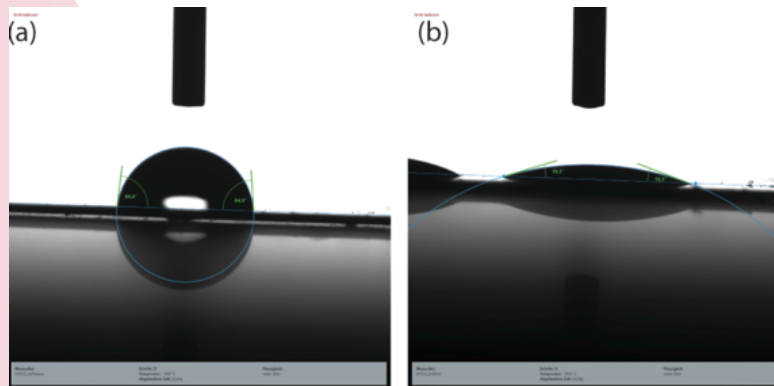
Abraision test:

[1] Set-up: According pre-defined worst case scenario, MBTg modified test implants (screws, with thread and with a diameter of 5,5 mm ) have been screwed into pig bones.

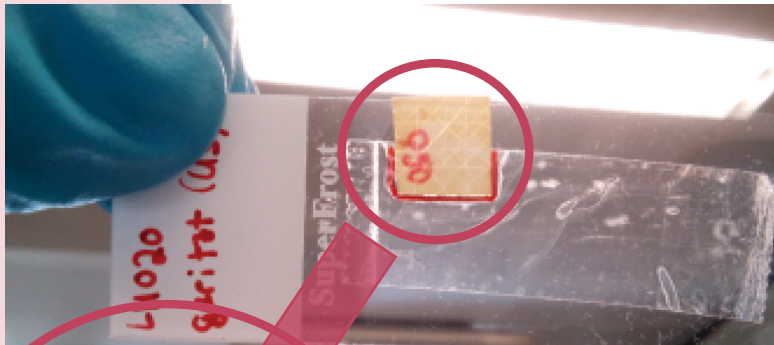
[2] According standard surgical procedures, holes with a smaller diameter of 5 mm have been pre-drilled into the bone.

[3] After explanting the test screws, Cy5-staining was performed to verify the the homogeneous coverage of the screw surface with mineralized MBT activation layer.

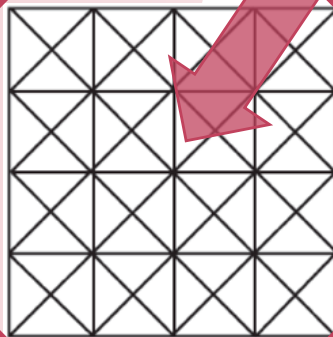
# Proof of concept: Mechanical Test Results (ASTM D3359 <sup>10</sup>)



Because the wettability of PEEK (a) and MBT PEEK (b) is very different, a drop test in combination with ASTM D3359 is suitable to confirm adhesion of MBT to the implant's surface:

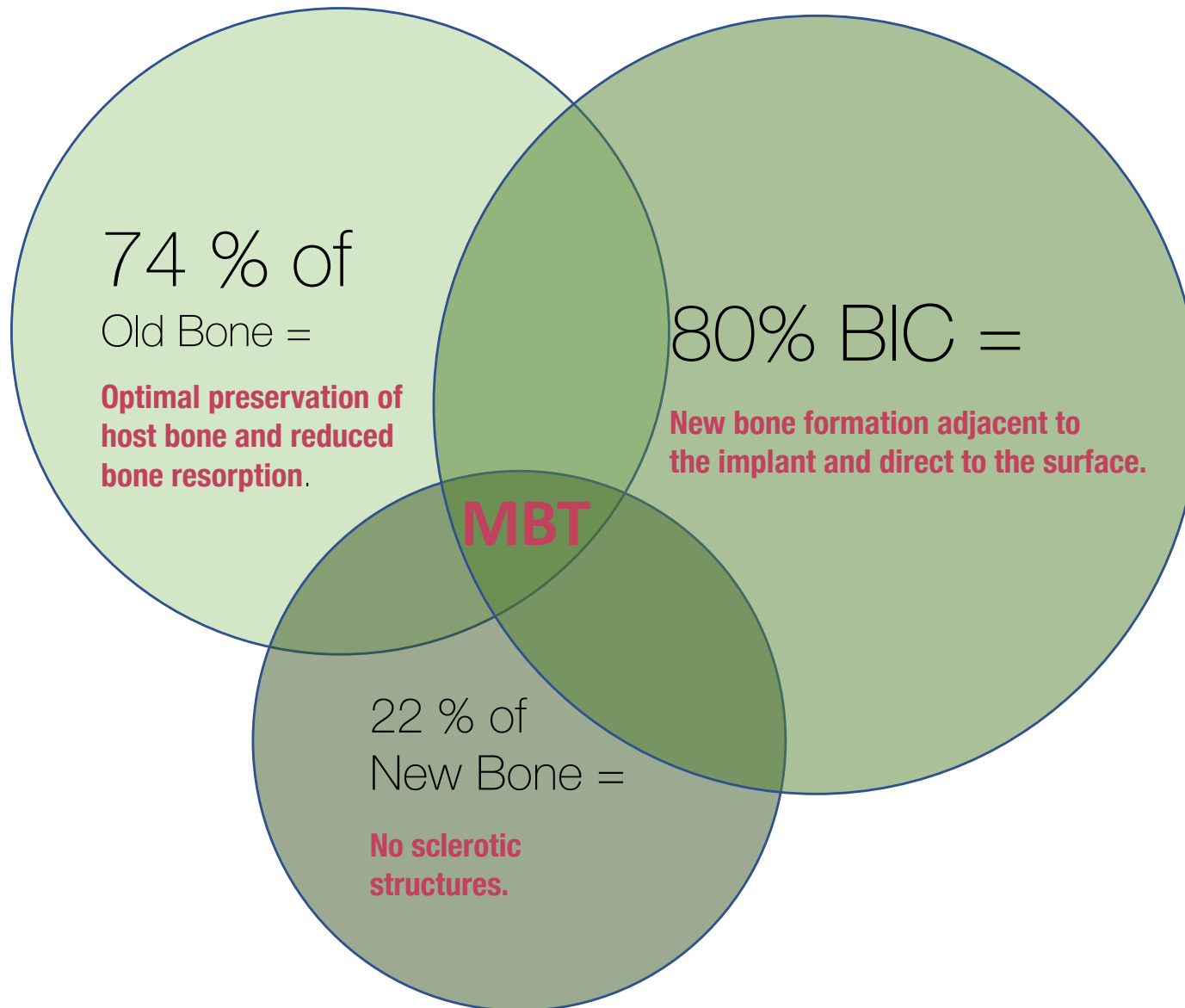


**During the ASTM D3359 testing the wettability of MBT surfaces show consistent angulations.**



<sup>10</sup> ASTM D3359: In order for a coating is to fulfill its function of protecting or decorating a substrate, the coating must remain adhered to the substrate (...) This test method is limited to evaluating different levels of adhesion (...)

# MBT: The New Golden Standard in Osseointegration



# stimOS sets **NEW STANDARDS** for implant surface characteristics.

MBT activates  
**100%** of the  
implant  
surface

MBT surfaces  
reduce BMP-2  
requirements to  
**100%**

Cell adhesion on  
MBT **280%** higher  
than compared to  
PEEK surfaces and  
**200 %** higher than  
compared to  
Titanium

Cell viability on  
MBT surfaces  
**300%** higher  
than compared to  
PEEK  
surfaces

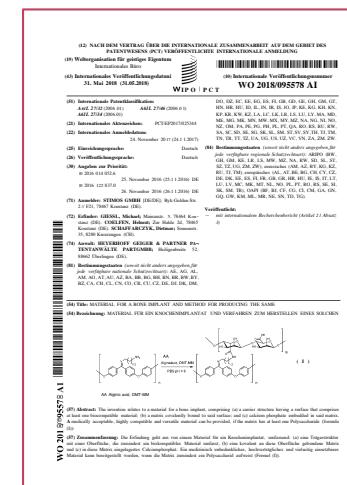
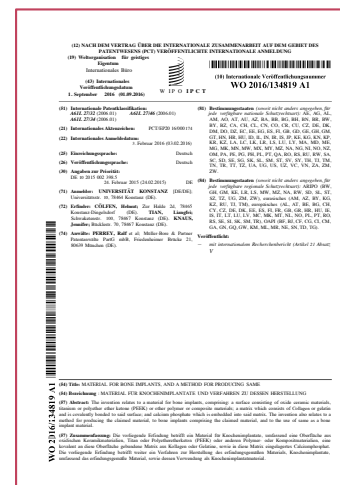
spineFuse  
implants  
feature  
**3<sup>GROWTH</sup>**  
Functionality



# Protecting Knowledge that Secures Success



# Validated by Science, approved by Competent Authorities & protected by International Patents.



# 7





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