Übersicht Bio-Degradierbare Magnesium- Werkstoffe

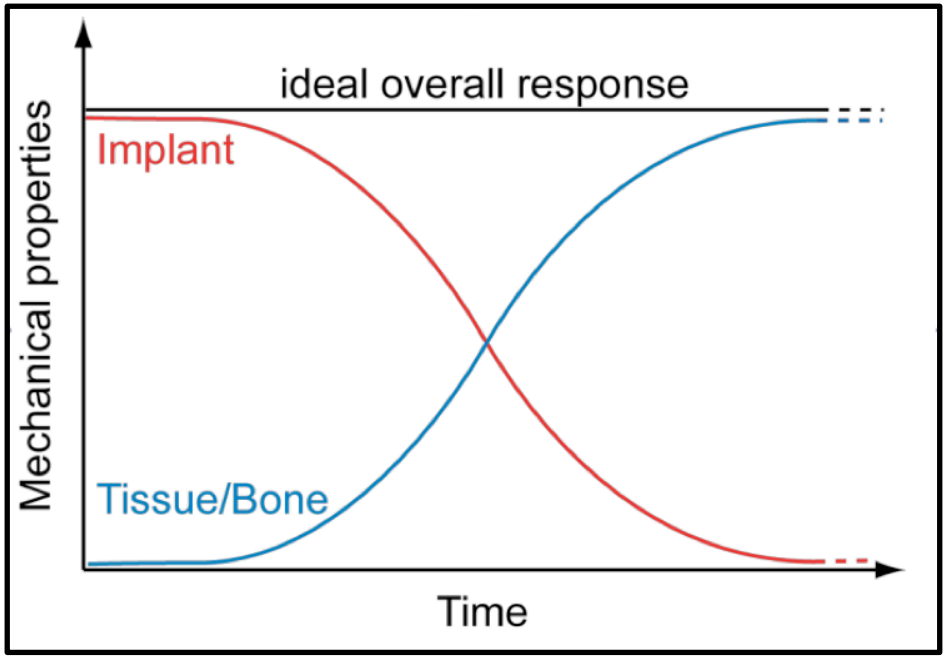
anneliemartina.weinberg@medunigraz.at
annelie.weinberg@t-online.de

Vision: Keine Implantatentfernung

- Krankenhausaufenthalte
- Patienten Stress reduzieren
- Morbidität senken
- Kosten senken

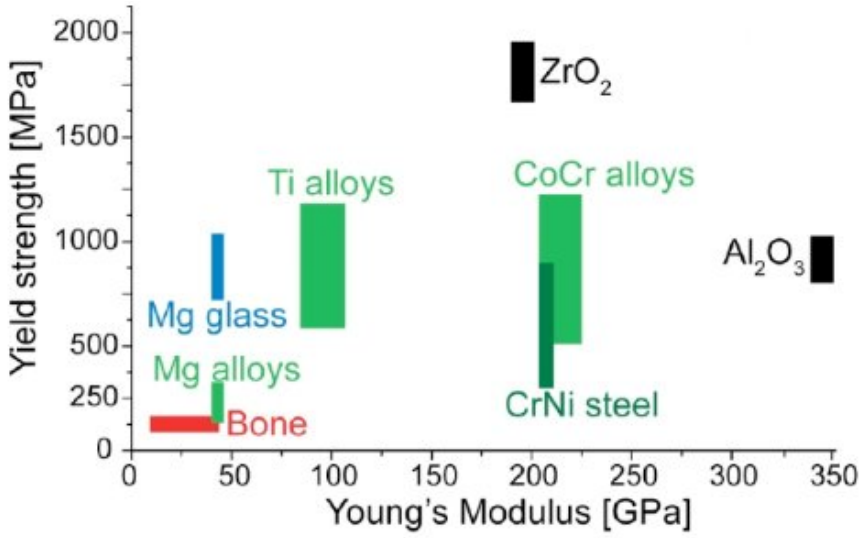
Optimales Implantat Design ?

- Fraktur stabilisieren
- Homogene – gleichmäßige Degradation aufweisen
- Sollte nicht länger als 2 Jahre im Körper nachweisbar sein
- Gute biologische Verträglichkeit aufweisen



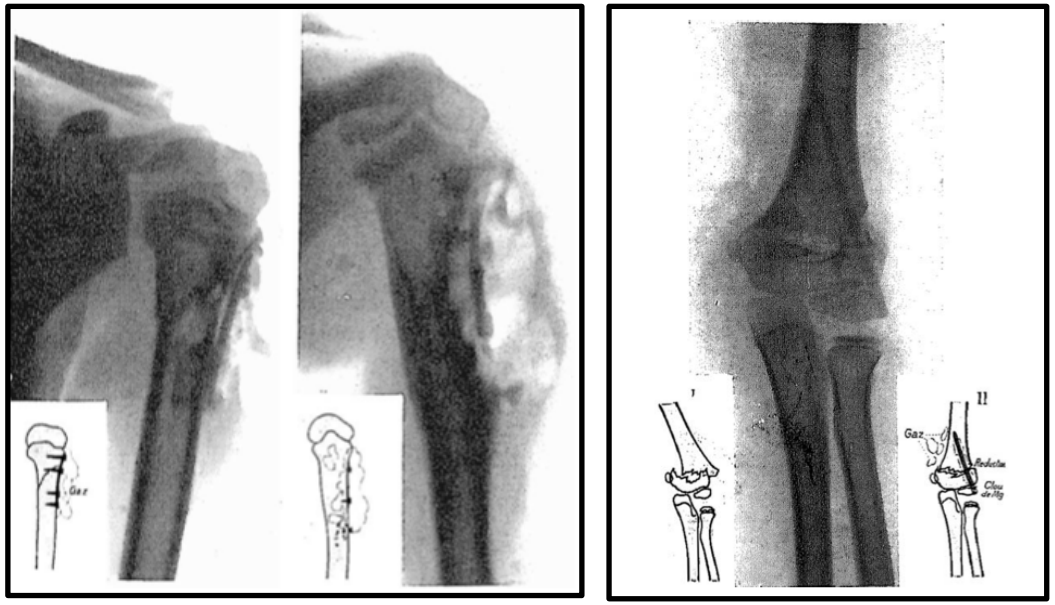
Magnesium

- Element im menschlichen Organismus
- Mechanischen Eigenschaften um Frakturen zu stabilisieren (Witte 2005, Biomaterials)
- Reduktion des “stress shielding phenomenon” (Nagels 2003, J Shoulder Elbow Surg)
- Mg degradiert in wässriger Lösung



Klinische Studien

Lambotte 1906-1932; Verbrugge, 1933-1937; McBride, 1938; Maier, 1940; Troitskii and Tsitrin, 1948



+ gute klinische Resultate
+ stimuliert den Hard-Kallus
+ keine Inflammation

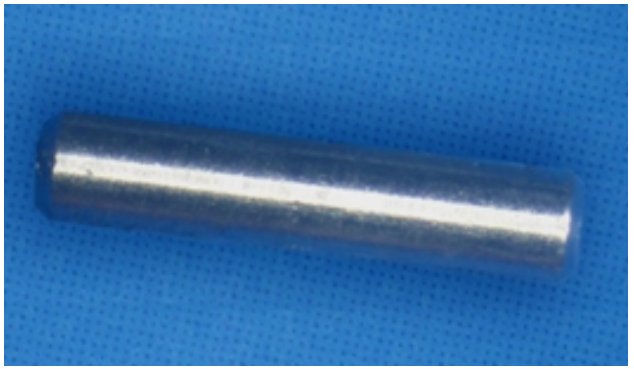
- Subkutane Gasblasenbildung
- Schwellung, Rötung

Witte 2010, Acta Biomat

1st Generation

WE43: Mg - 4,1% Y – 3% REE

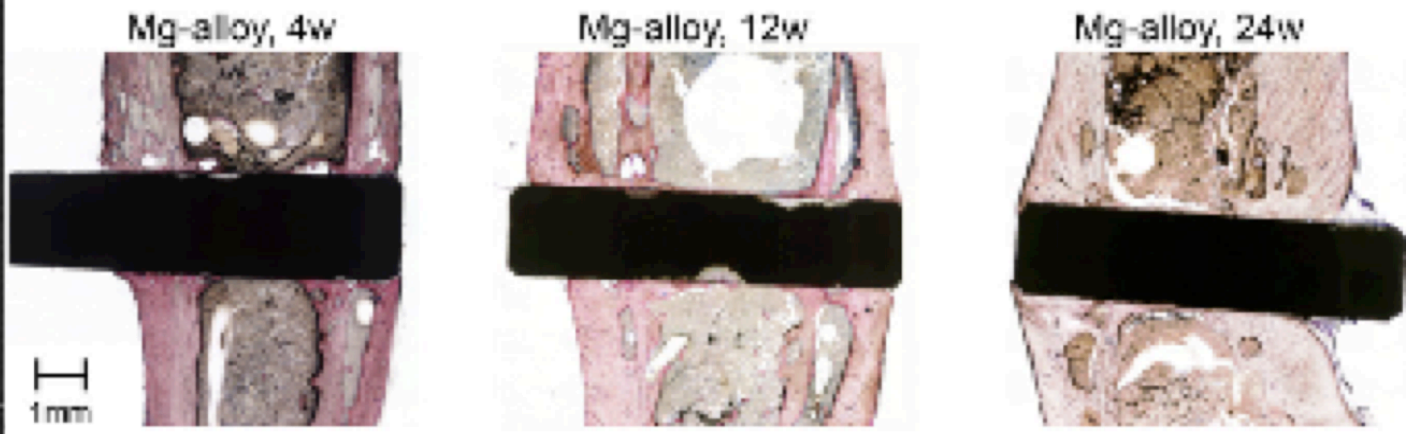
- Käufliche Legierung



Ziel:

- Die Degradationsgeschwindigkeit im wachsenden Skelett zu prüfen
- Evaluation des Knochen-Implantat Interface (verglichen mit Titan)

1st Generation

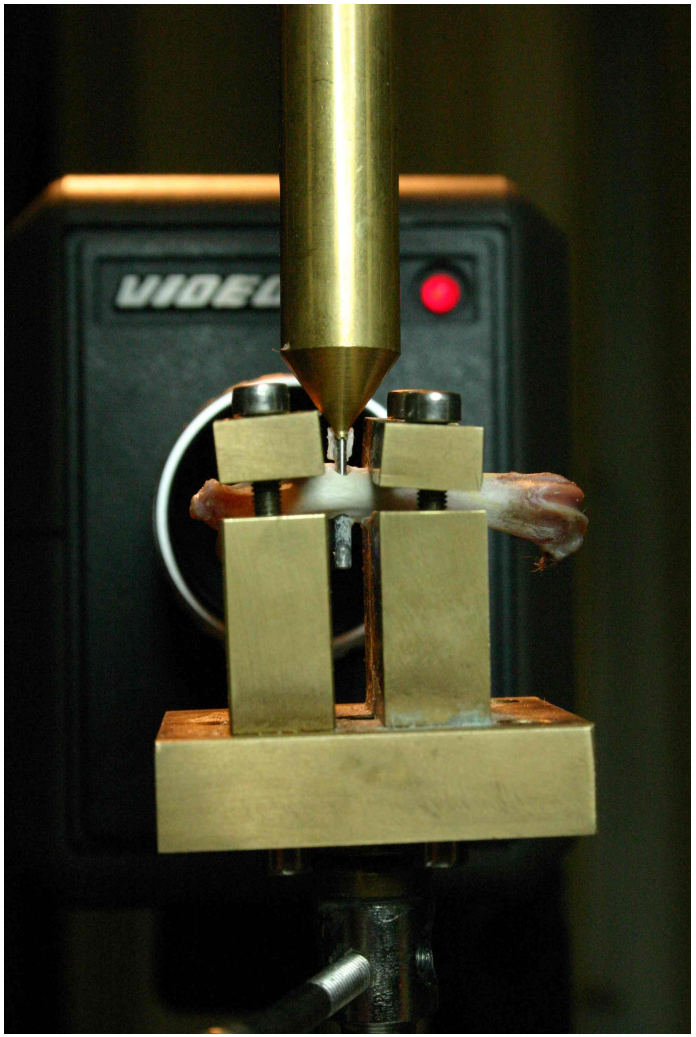


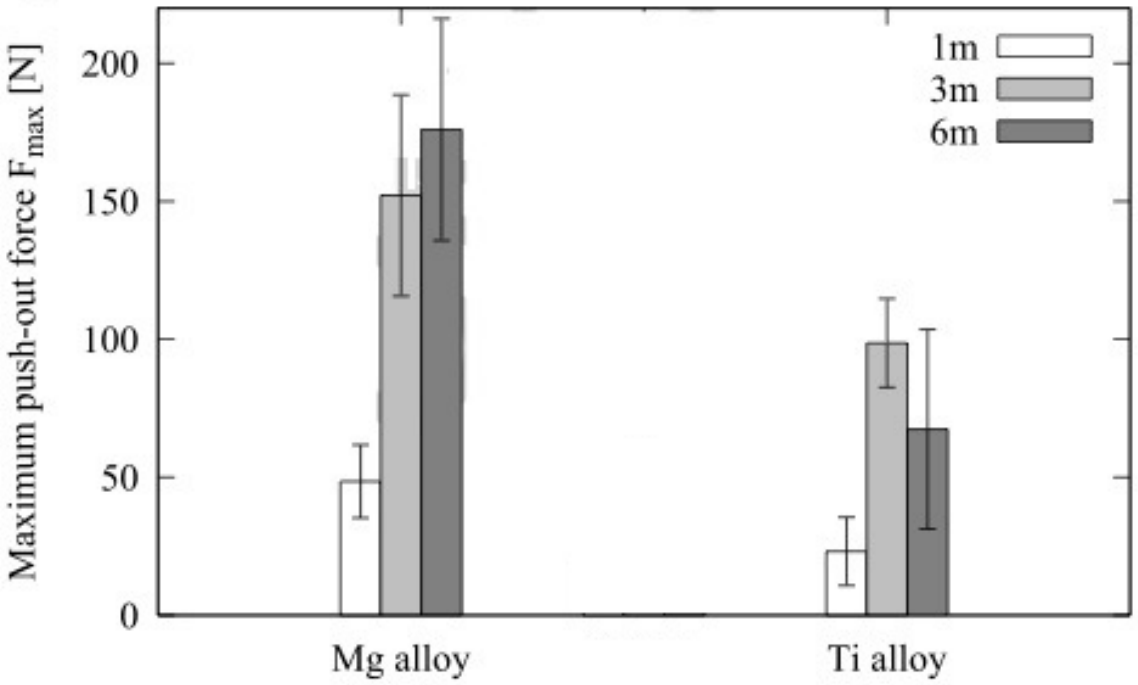
Resultat:

- keine sichtbaren Korrosionsprodukte
- Langsame Degradation
- Gute Knochenheilung

Castellani 2011, Acta Biomat

1st Generation





Resultat:
Besseres Implantat-Knochen Interface als Titan

Castellani 2011, Acta Biomat

1st Generation

Vorteil:

- Keine sichtbaren Akklomerate von Korrosionsprodukten
- Gutes Knochen-Implantat Interface
- Keine Zeichen der Entzündung

Nachteile:

- REE hoch (4% Yttrium und 3% REE)
- Sehr langsame Degradation

Acta Biomaterialia 44 (2016) 355–365

Contents lists available at ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Full length article

Biocompatibility and degradation of LAE442-based magnesium alloys after implantation of up to 3.5 years in a rabbit model

N. Angrisani [a,*], J. Reifenrath [a], F. Zimmermann [b], R. Eifler [c], A. Meyer-Lindenberg [d], K. Vano-Herrera [b], C. Vogt [b]

[a] NIFE – Lower Saxony Centre for Biomedical Engineering, Implant Research and Development, Department of Orthopedic Surgery, Hannover Medical School, Hannover, Germany
[b] Institute of Inorganic Chemistry, Leibniz University of Hannover, Hannover, Germany
[c] Institute of Materials Science, Leibniz University of Hannover, Hannover, Germany
[d] Clinic for Small Animal Surgery and Reproduction, Ludwig-Maximilians University, Munich, Germany

ARTICLE INFO

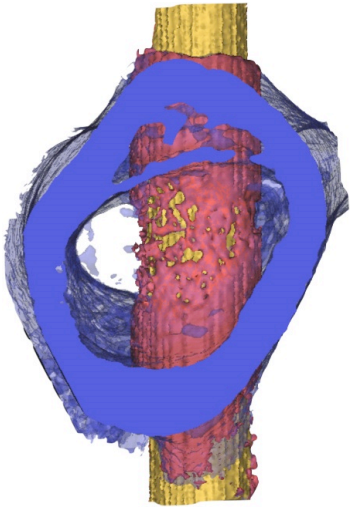
ABSTRACT

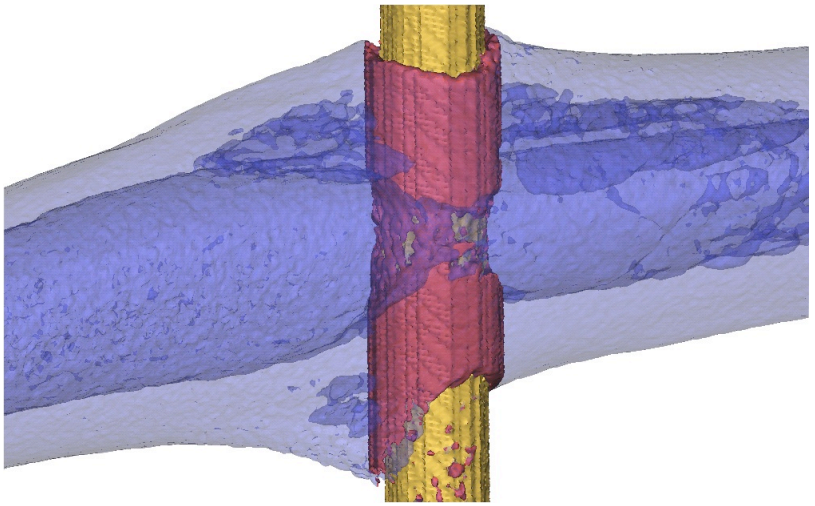
Mg-alloys in BRIC-project

	1st Generation WE43	2nd Generation ZX50 & WZ21		3rd Generation
REE	---			
Degradations-Geschwindigkeit	+			
Korrosion Produkte	+			

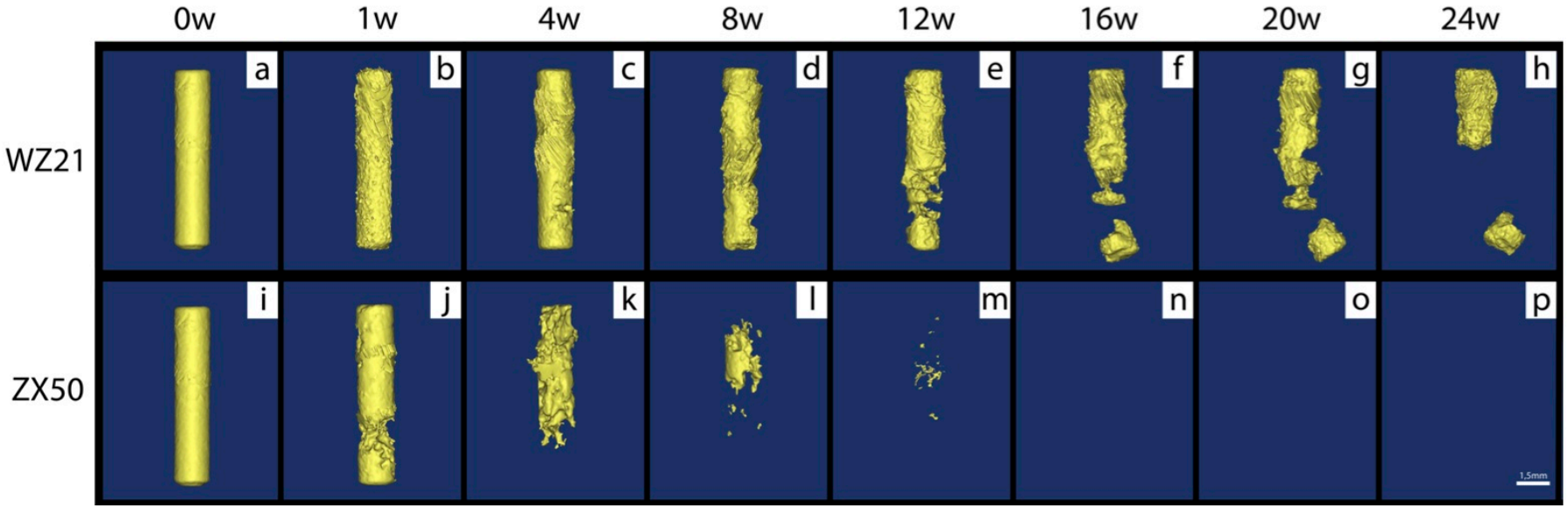
2nd Generation

- WZ21 = Mg - 1%Zn - 0,25% Ca - 0,15% Mn - 2% Y
- ZX50 = Mg - 5% Zn - 0.25% Ca - 0.15% Mn (no REE)





2nd generation

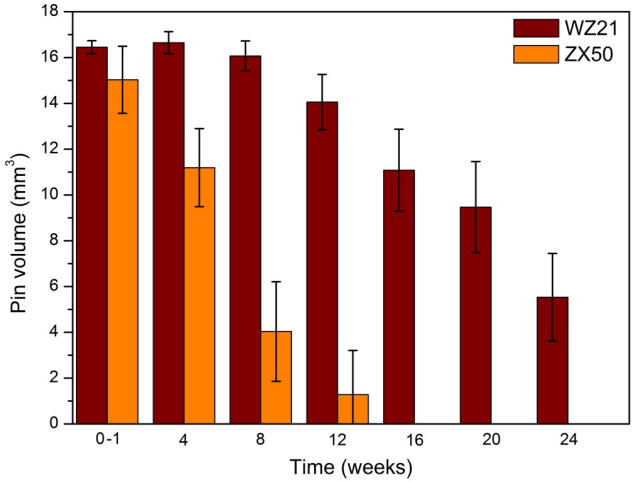


Results: WZ21 - 50% in 20 Wochen
ZX50 - zu schnelle Degradation

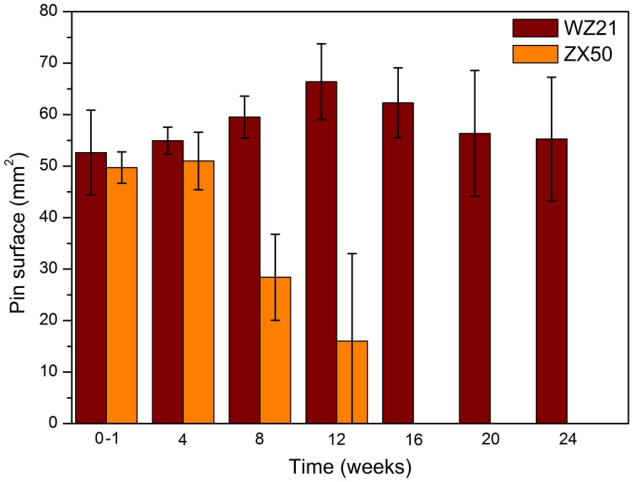
Kraus 2011, Acta Biomat

2nd generation

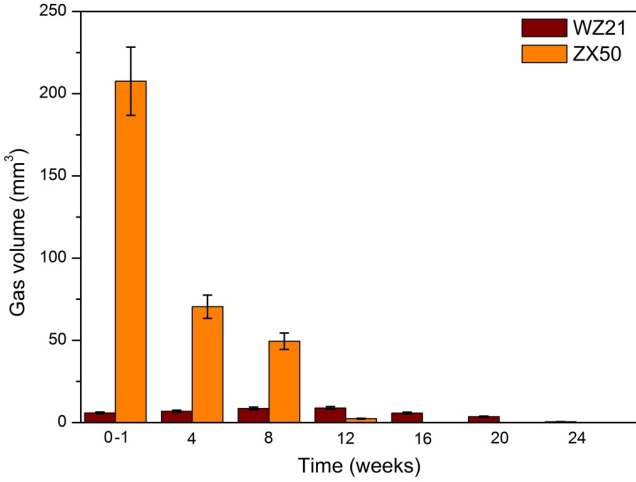
Pin volume



Pin surface



Gas volume



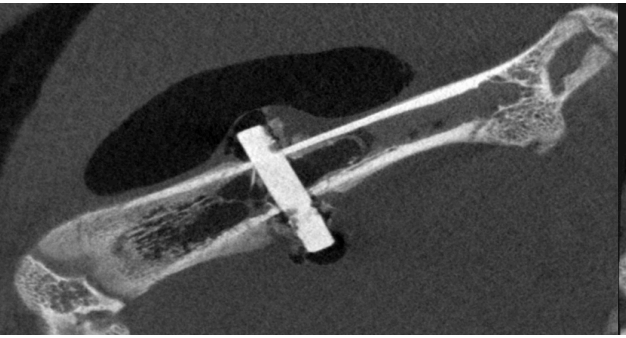
Results: WZ21 – moderate Gasbildung

ZX50 - viele Korrosionprodukte in 8 Wochen

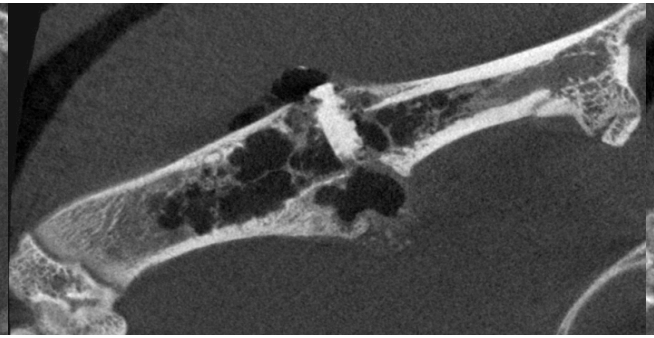
Kraus 2011, Acta Biomat

2nd Generation – ZX50

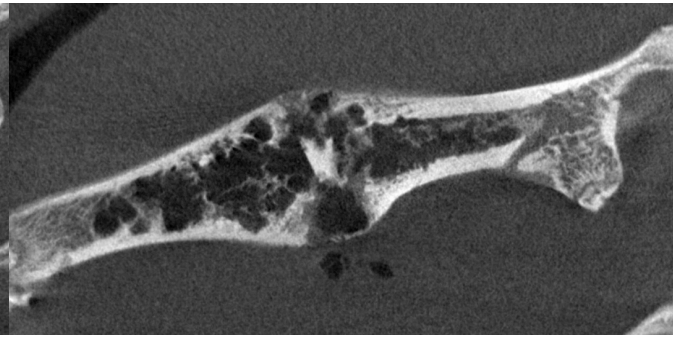
1w



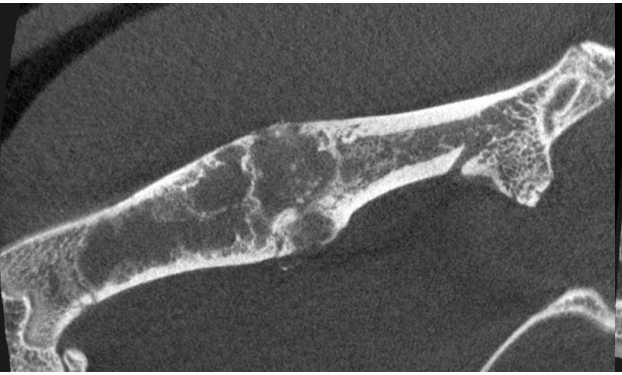
4w



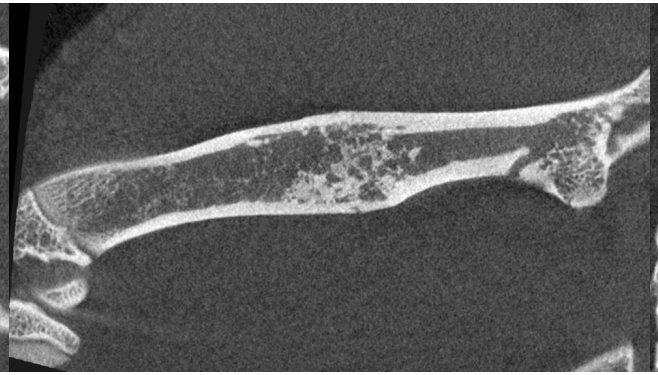
8w



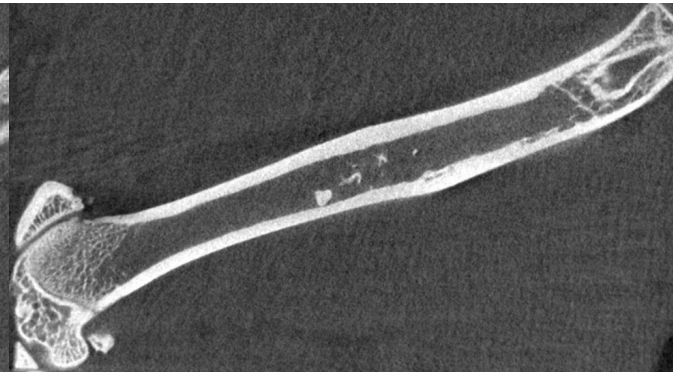
12w



16w



24w

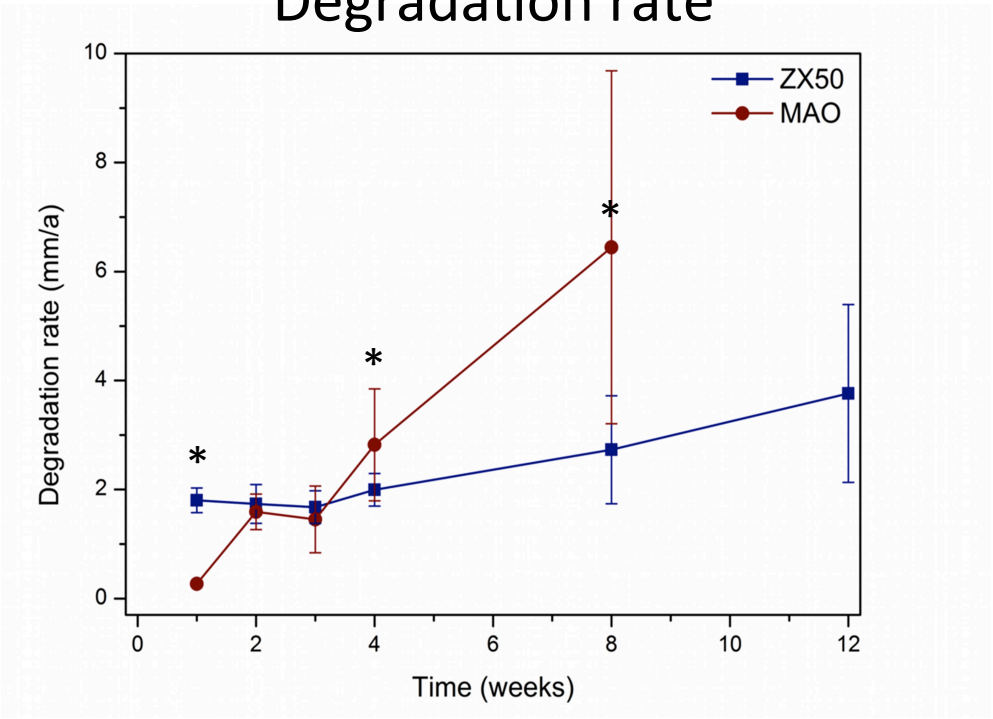


2nd Generation

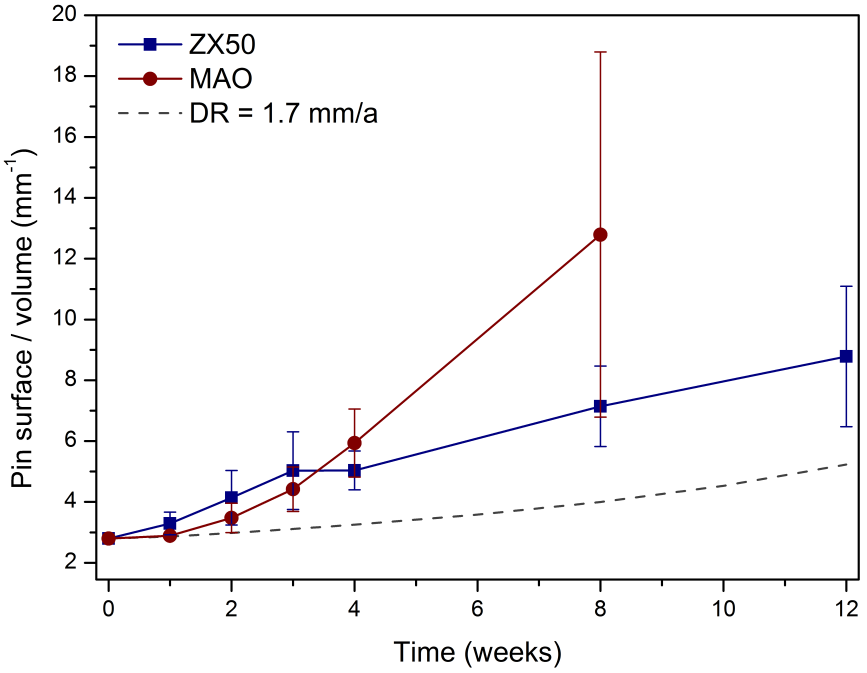
- Weitere Versuche:
  - Surface Modifikationen (micro-arc oxidation)
  - Einfluss auf die Epiphysenfuge
  - Immunologische Antwort
  - Verbleib der Elemente of in bone und den Organen (kooperationspartneren)

Micro-Arc Oxidation

Degradation rate



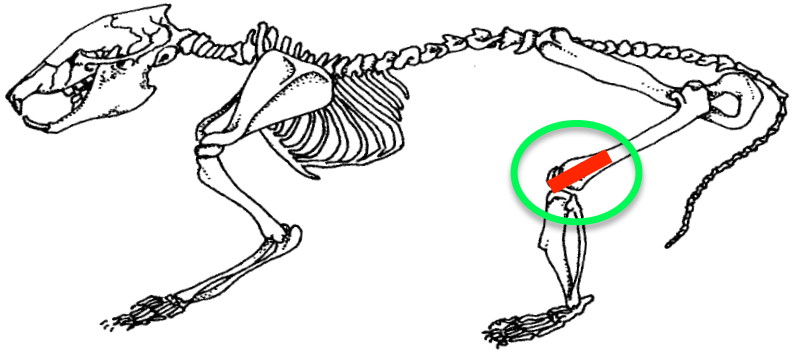
Surface/Volume

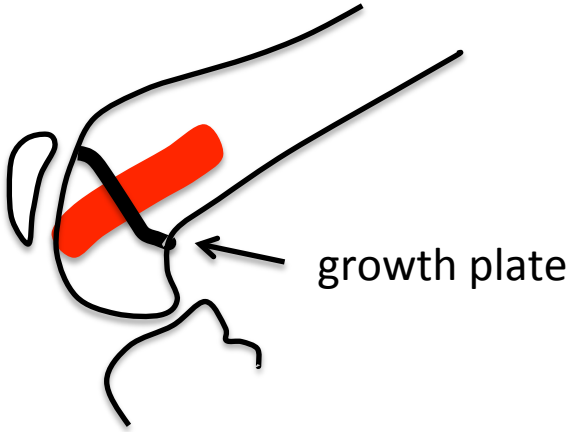


$$DR_i = \frac{\Delta x_i}{\Delta t} \text{ with } \Delta x_i = \frac{\Delta V_i}{S_i}$$

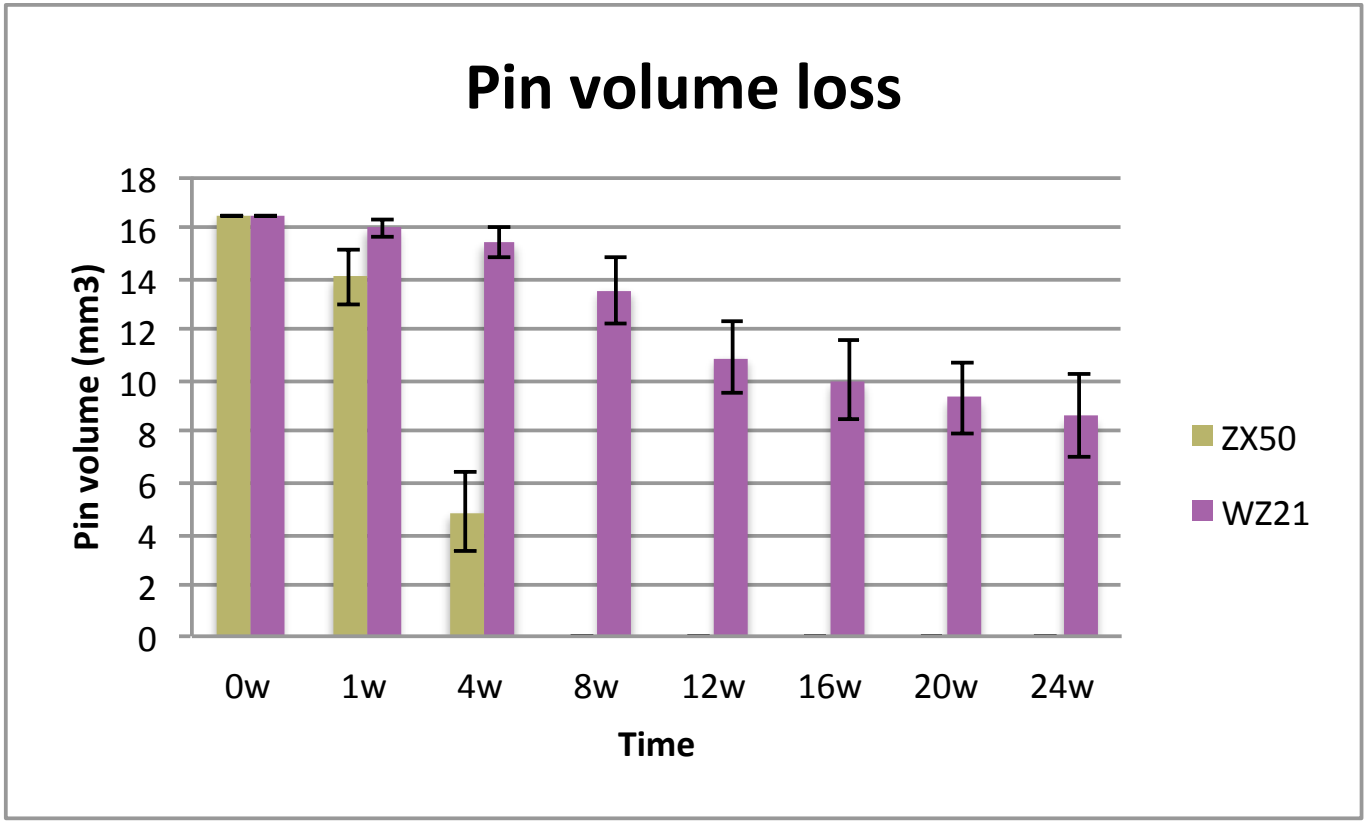
Einfluss auf die Epiphysenfuge

- Transepiphyseale Implantation in den Femur
- Gegenbein wurde nur gebhrt

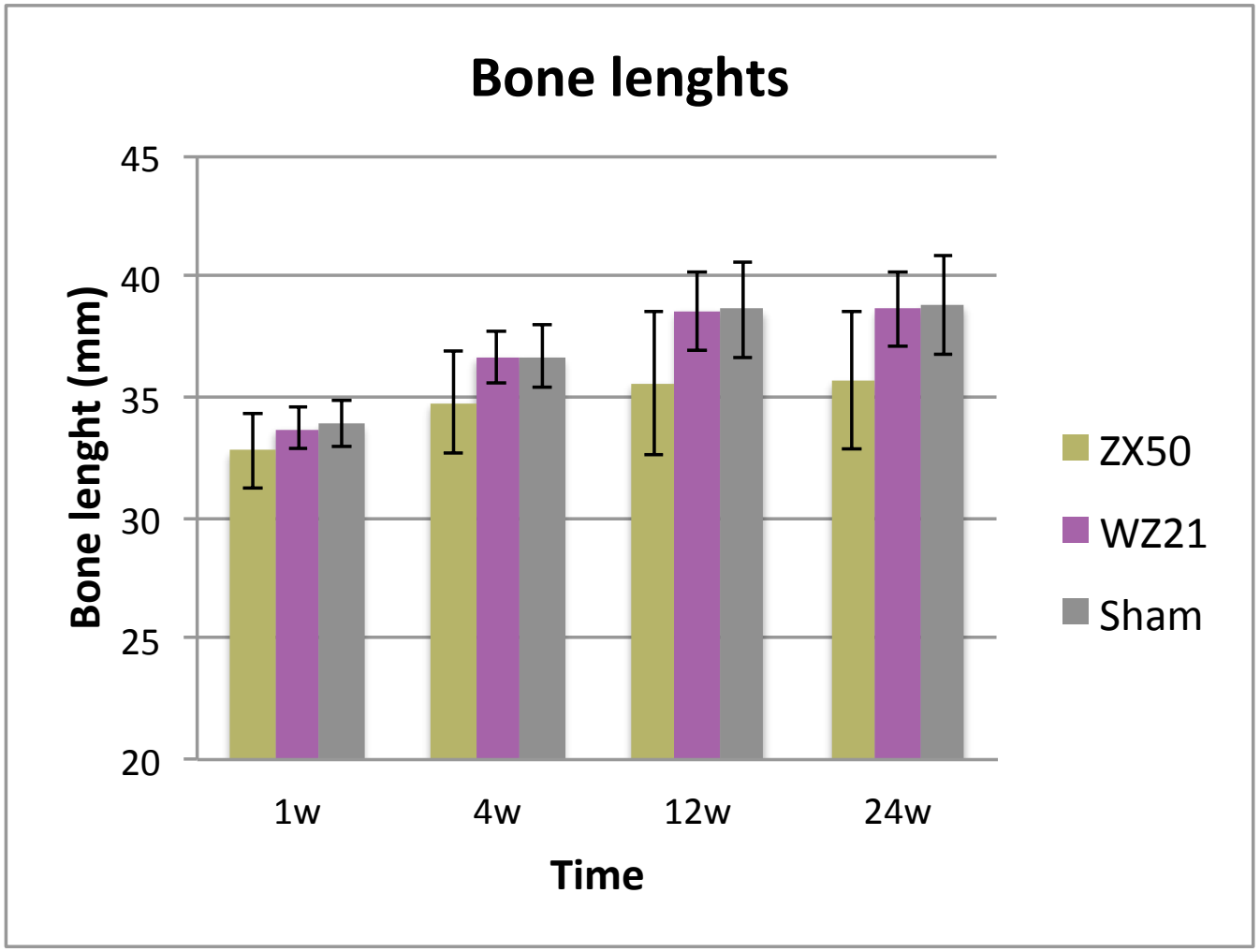




Epiphysenfuge



Epiphysenfuge



Mg-alloys

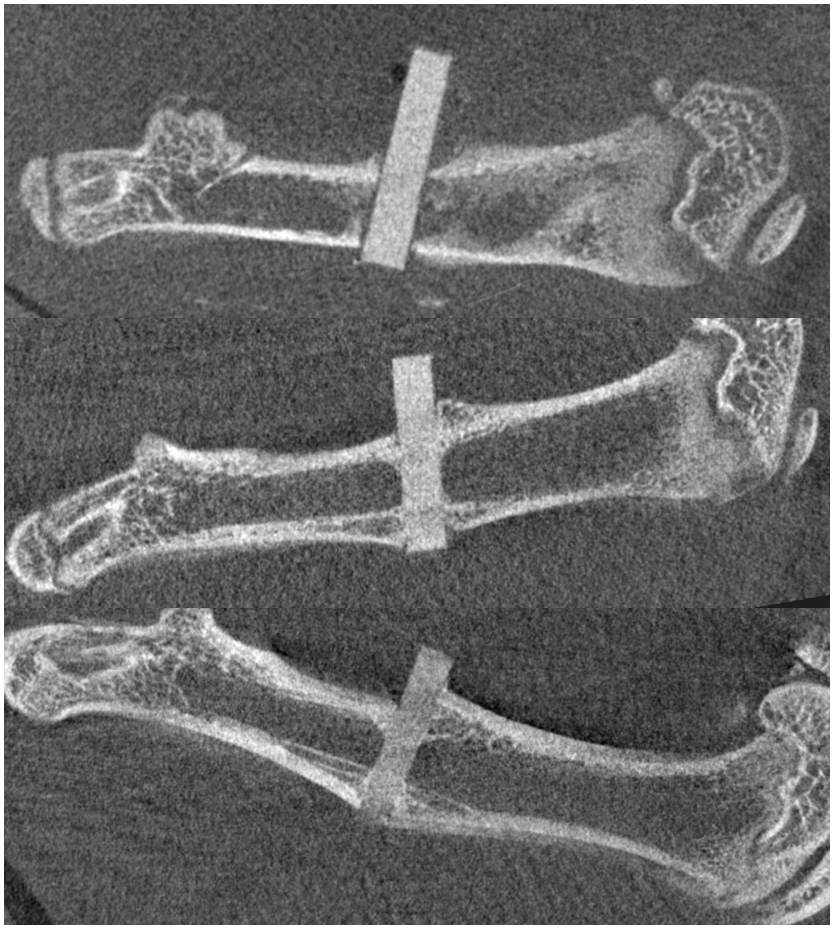
	1st Generation WE43	2nd Generation ZX50 & WZ21		3rd Generation
Rare earth elements	---	+	-	
Degradations Geschwindigkeit	+	---	+	
Gas Formation	+	---	+	

Zusammenfassung CP vs XHP

- Beide Systeme degradieren nach 24 Wochen
- Innerhalb der ersten Wochen war CP ZX50 schneller
- Je länger die Versuche, desto ähnlicher die Ergebnisse
- Initiale Gasvolumen ist deutlich geringer bei XHP ZX50

→ Höhere Verunreinigung spielen bei der Degradation eine Rolle, vor allem zu Beginn der Degradation

3rd Generation – XHP alloys



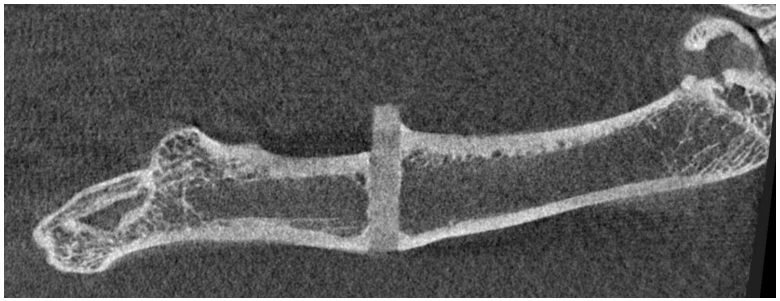
1w

4w

12w

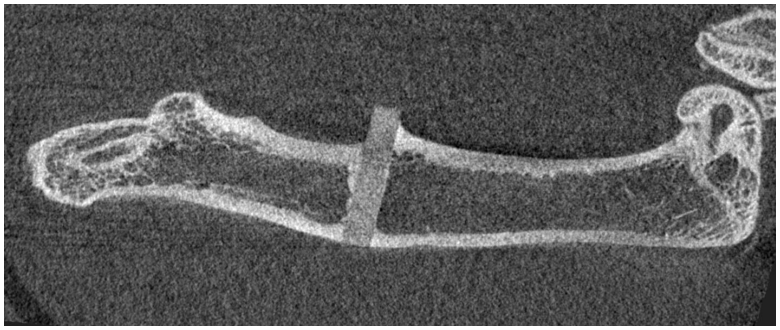
Langsame und homogene Degradation

3rd generation – XHP alloy



24w

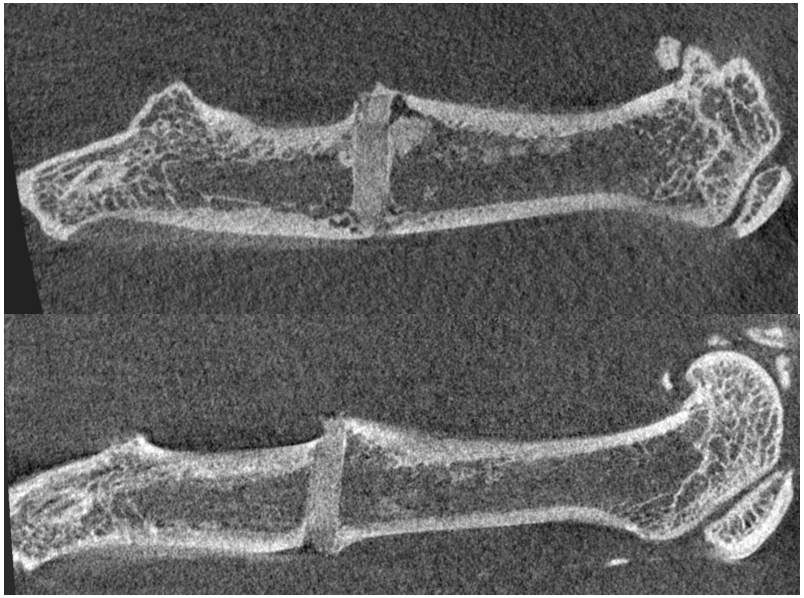
Beginn der Korrosion
nach 24 Wochen
(sichtbar in Mimics)



36w

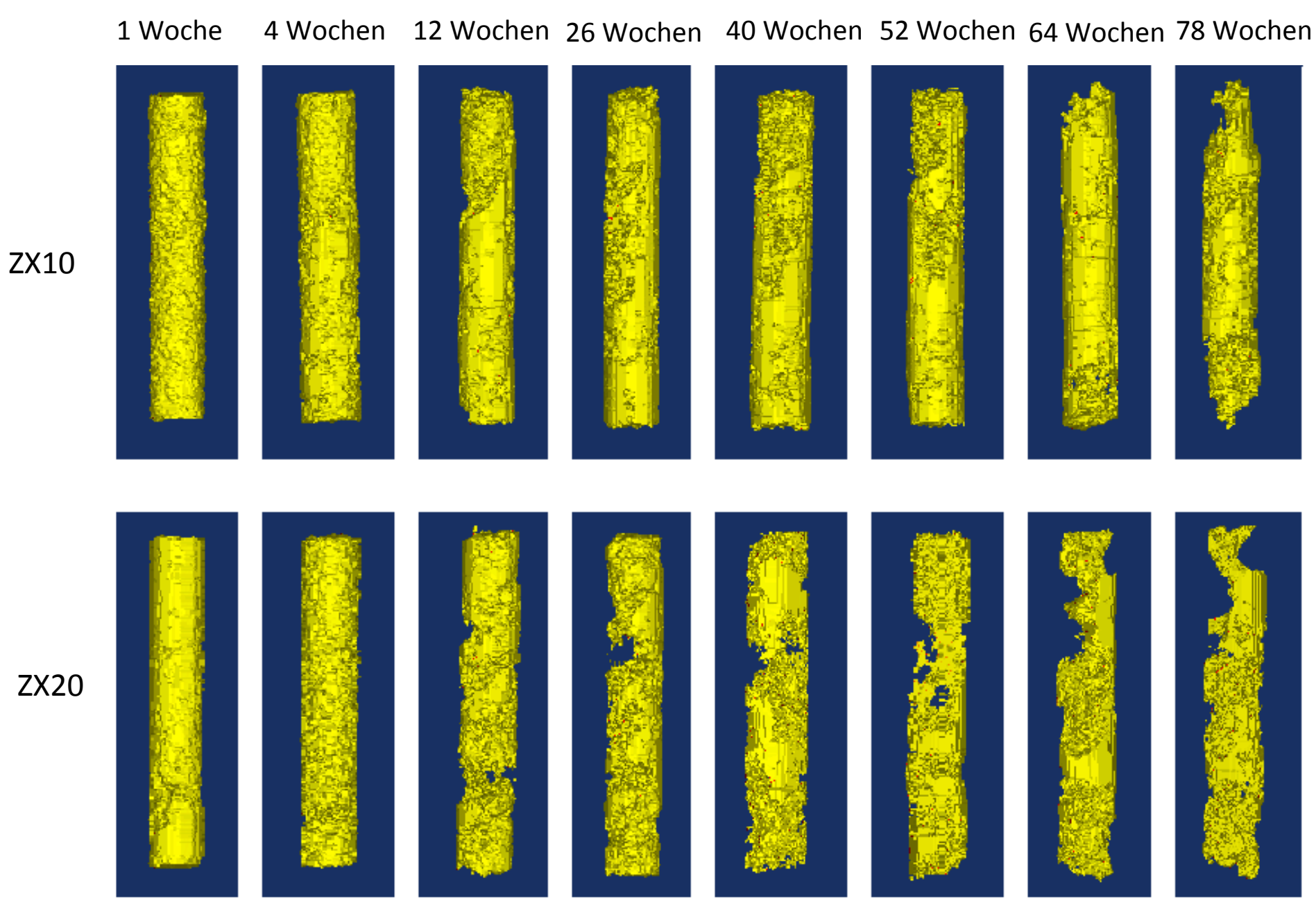
Guter Knochenanbau
nch 36 Wochen

3rd Generation – XHP alloys

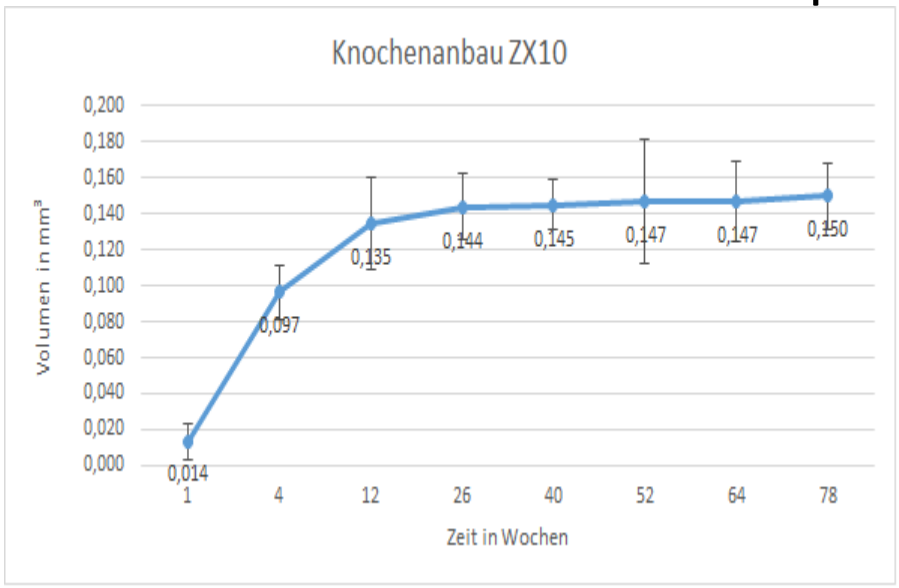


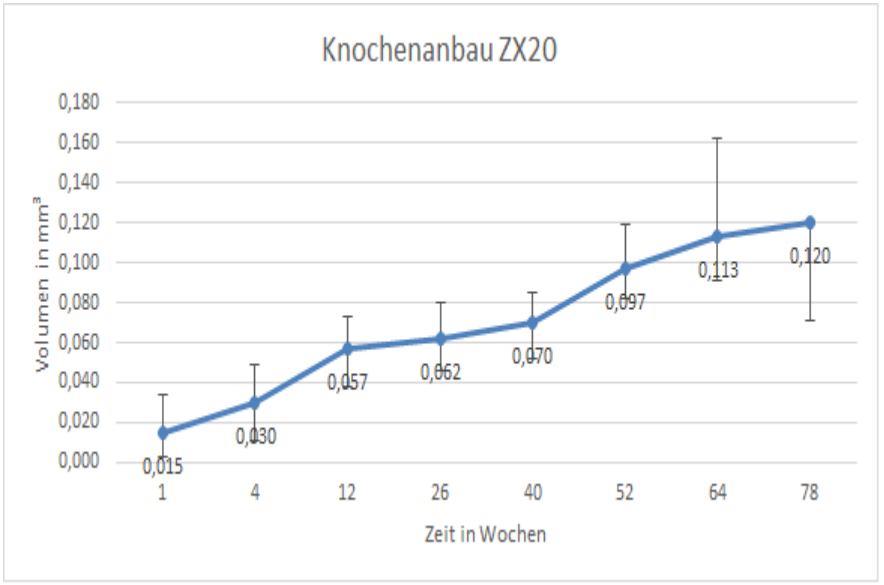
65 w

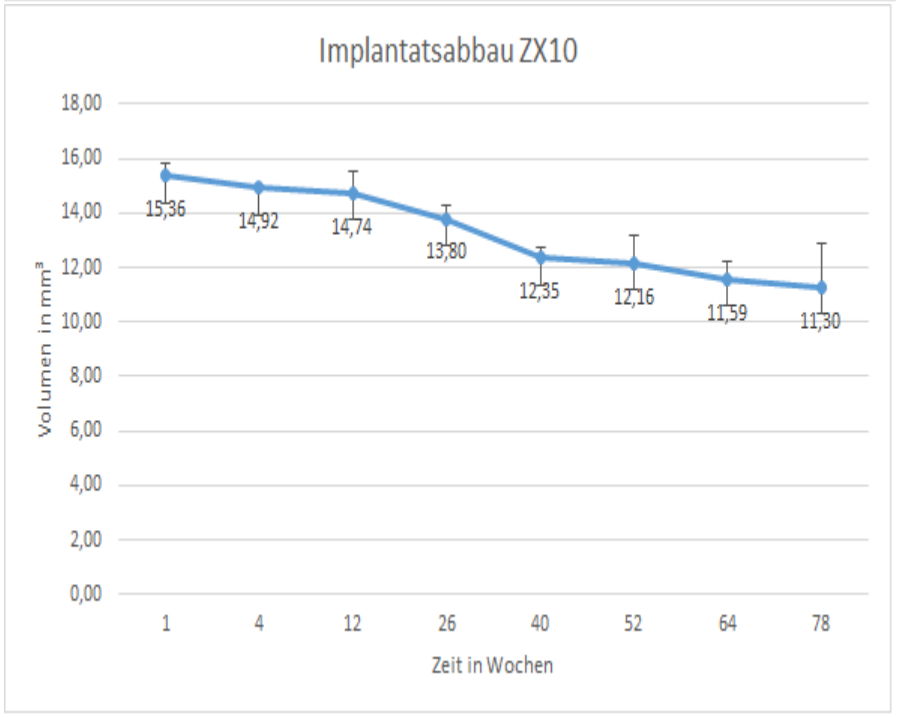
78 w

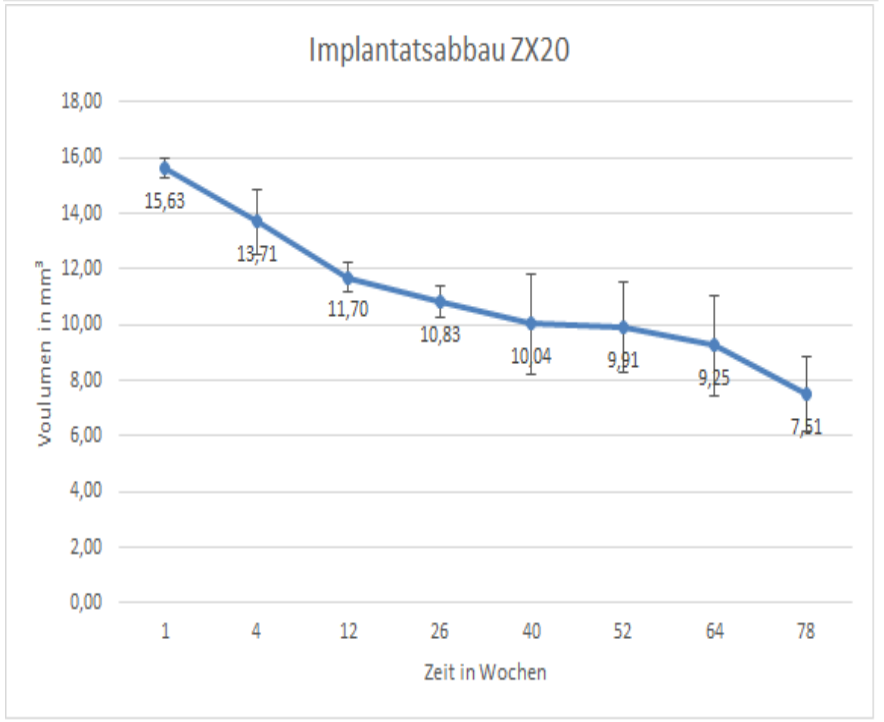

1 Woche
4 Wochen
12 Wochen
26 Wochen
40 Wochen
52 Wochen
64 Wochen
78 Wochen
ZX10
ZX20

Knochenanbau vs Impantatabbau ZX10 und ZX20









Zusammenfassung ZX10 / ZX20

- Langsame und homogene Degradation
- Korrosion startet nach 24 Wochen
- Guter Knochenanbau

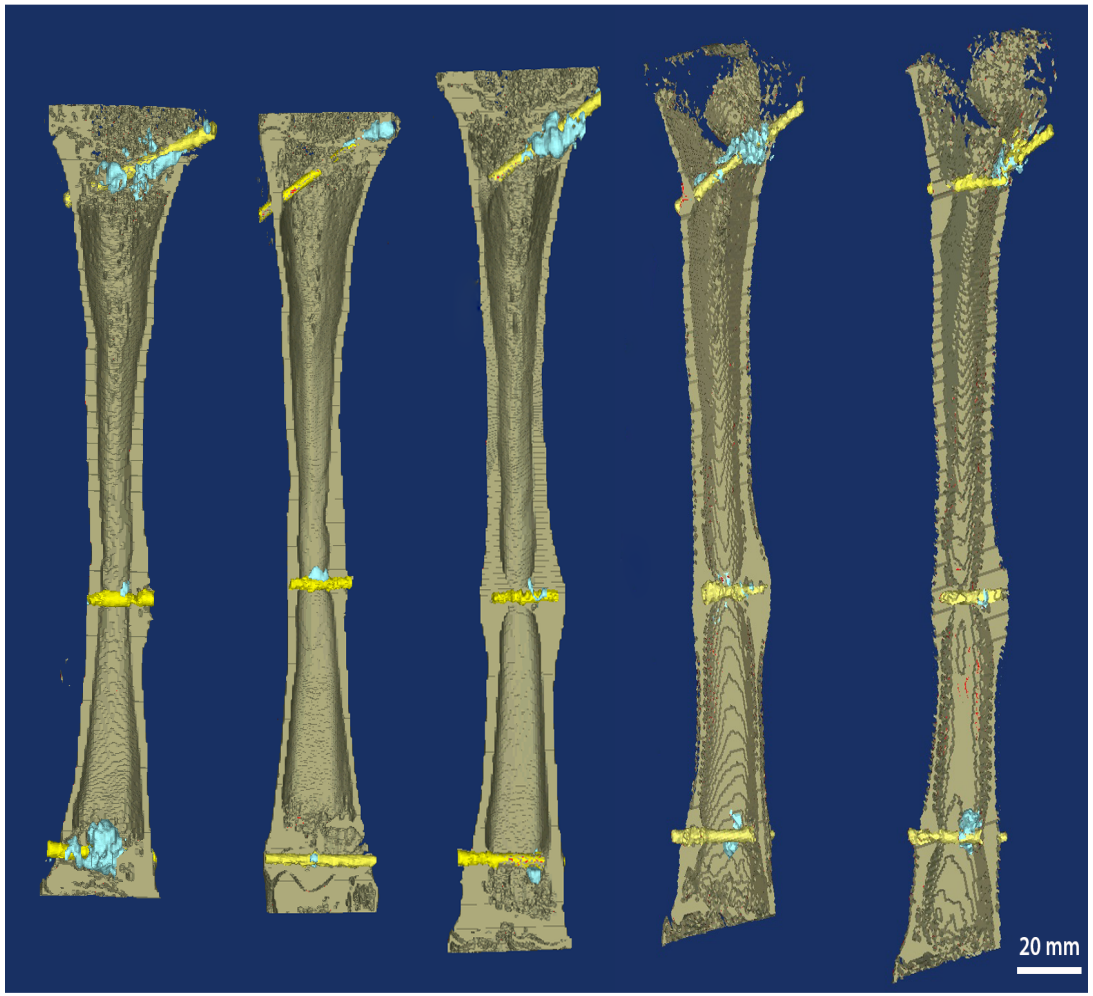
- Push out tests (Berger, TU Wien)
- Organ Untersuchungen (Prof. Gössler, KFU Graz)
- Histologische Evaluation (Myrissa, MUG)

Mg-alloys (Mg-Zn-Ca)

	1st Generation WE43	2nd Generation ZX50 & WZ21		3rd Generation XHP-Mg alloys
REE	---	+	-	+++
Degradations-Geschwindigkeit	+	---	+	++
Gas Formation	+	---	+	++

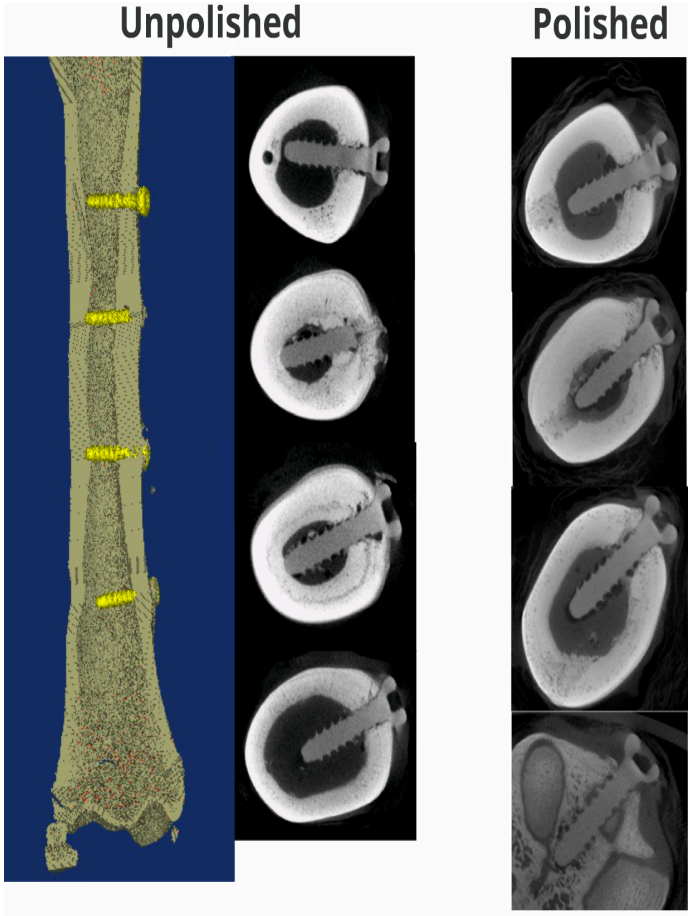
BRI.Mag screws – in vivo Test

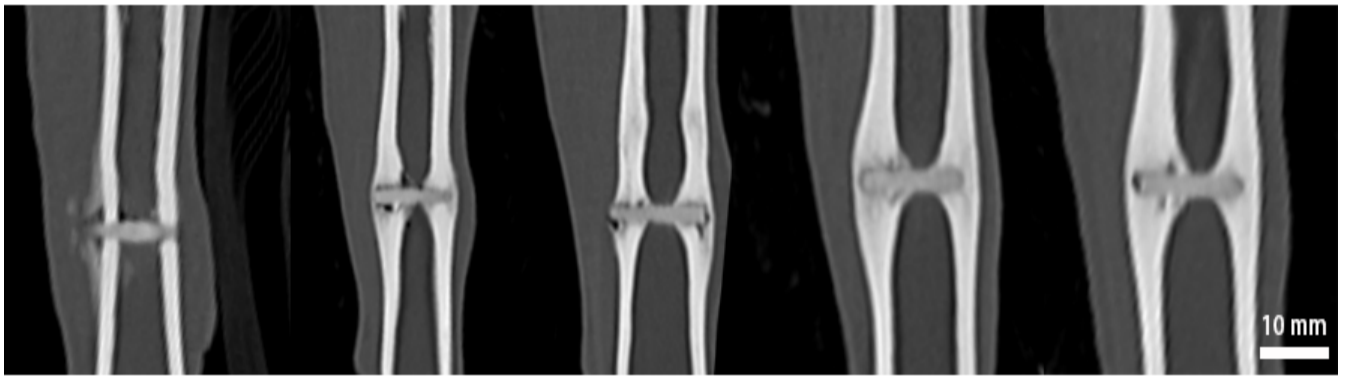
BRI.Mag® transcortical implantation of 3 mm ESIN



2W 6W 12W 24W 52W

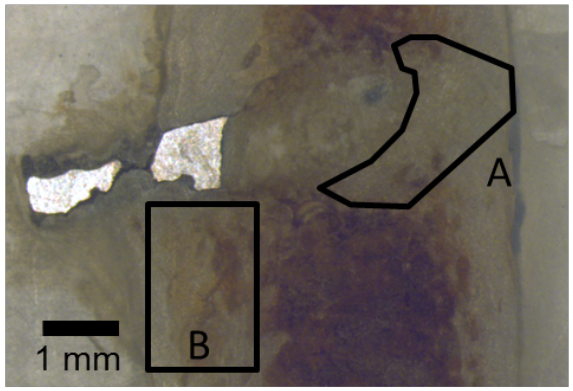
Micro CT (Tibia – 6W post op)



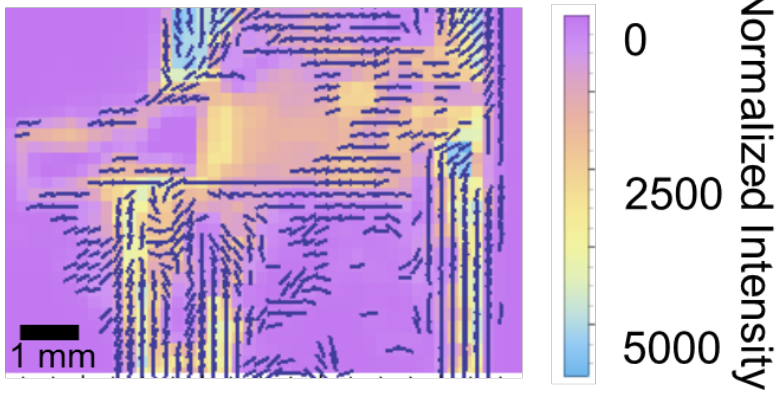


2W 6W 12W 24W 52W

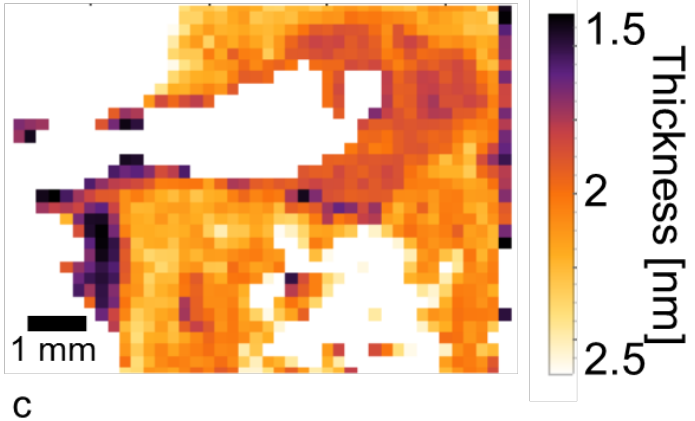
BOKU Wien – Prof Lichtenegger



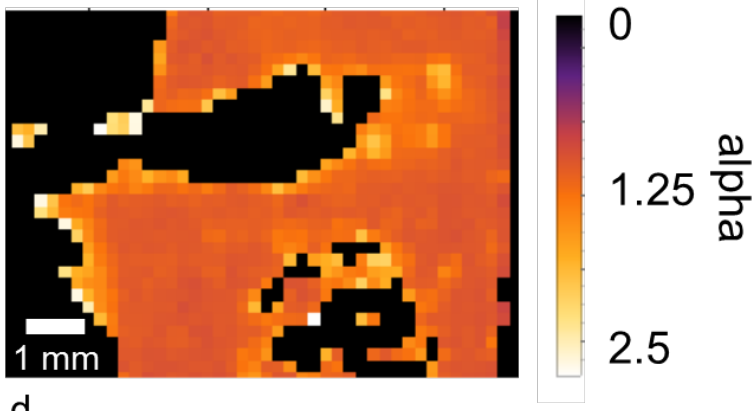
a



b



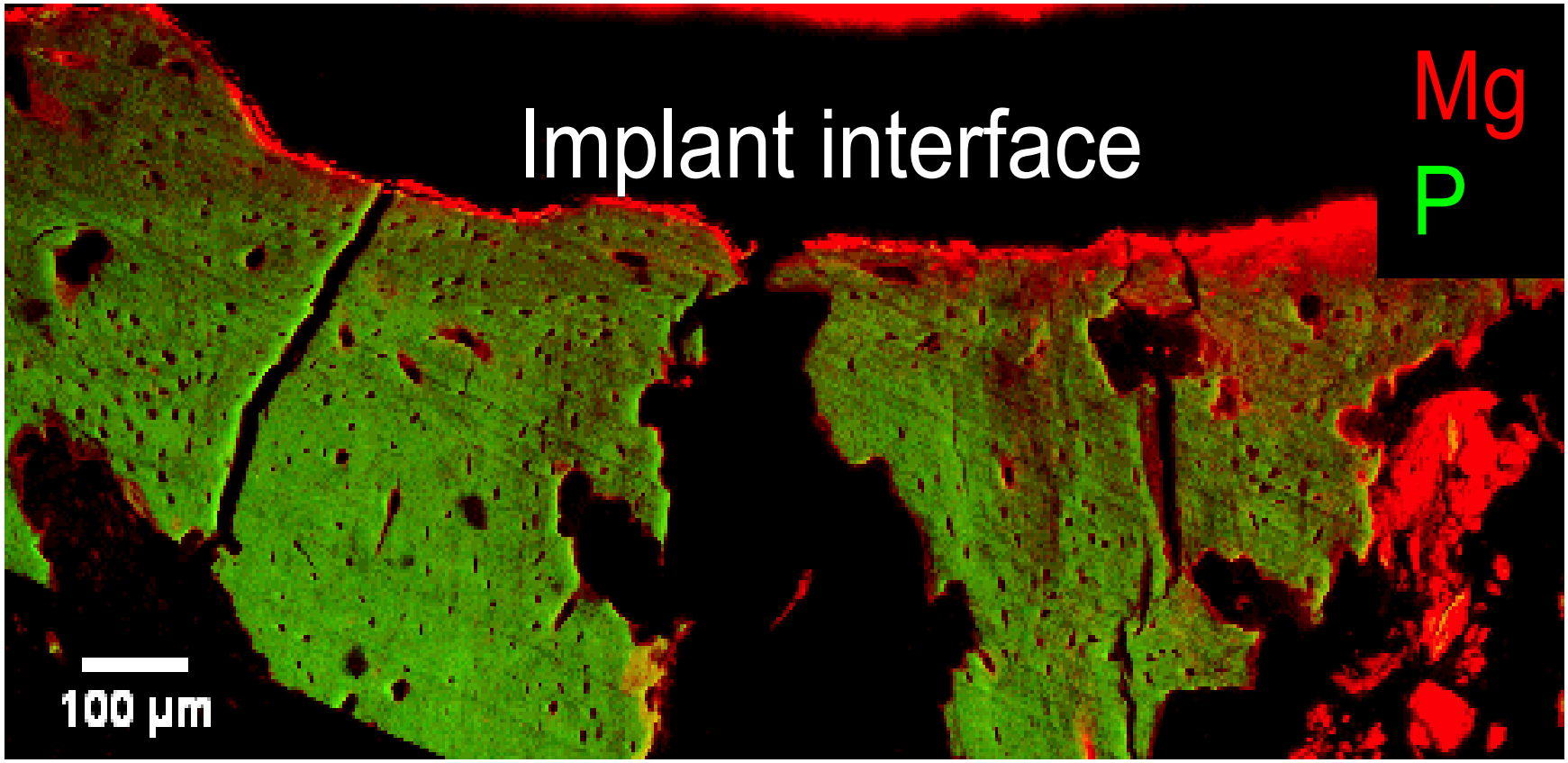
c



d

Nanostruktur (12 Monate) a. Mikroscopie Bild , b. Absorption vs. Orientation, c. Platelet thickness, d. alpha parameter

BOKU Wien – Prof Lichtenegger



ARTICLE

nature medicine

Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rat

Yifeng Zhang[1,13,14], Jiankun Xu[1,14], Ye Chun Ruan[2,14], Mei Kuen Yu[2], Micheal O'Laughlin[1], Helen Wise[3], Di Chen[4], Li Tian[1], Dufang Shi[1], Jiali Wang[1], Sihui Chen[1], Jian Q Feng[5], Dick Ho Kiu Chow[1], Xinhui Xie[1], Lizhen Zheng[1], Le Huang[1], Shuo Huang[1], Kwoksui Leung[1], Na Lu[6], Lan Zhao[4], Huafang Li[1], Dewei Zhao[7], Xia Guo[8], Kaiming Chan[1], Frank Witte[9,10], Hsiao Chang Chan[2], Yufeng Zheng[11] & Ling Qin[1,12]

Orthopedic implants containing biodegradable magnesium have been used for fracture repair with considerable efficacy; howeve the underlying mechanisms by which these implants improve fracture healing remain elusive. Here we show the formation of abundant new bone at peripheral cortical sites after intramedullary implantation of a pin containing ultrapure magnesium into

Limits

- Lasttragend ?
- Langsamer ?
- Zwei Phasen ?
- Mg Drucken ?
- Positive Effekt auf Zellen mehr nutzen
- Mg Coating
- Angepaste Legierung an Heilung ?

Acknowledgment

- Danke – insbesonder auch an mein Team und die Unterstützung

FFG