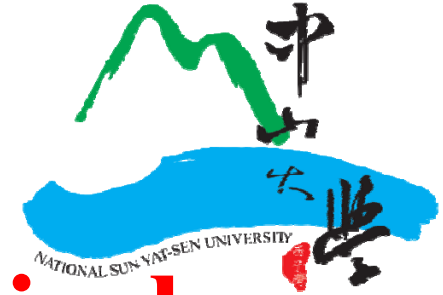


# Ti and Ta based metallic glasses for biomedical applications



**J.C. Huang<sup>1</sup>, J.S.C. Jang<sup>2</sup>, C.H. Lin<sup>1</sup>, C.H. Chen<sup>3</sup>,  
C.H. Huang<sup>1</sup>, R.F. Chuang<sup>1</sup>**



**<sup>1</sup>National Sun Yat-Sen University**

**<sup>2</sup>National Central University**

**<sup>3</sup>Kaohsiung Medical University  
Kaohsiung, Taiwan**

# Previous bio-implant metallic glass reports

*In-vitro* Investigation of one of amorphous metals: **Zr-Ti-Co-Be**

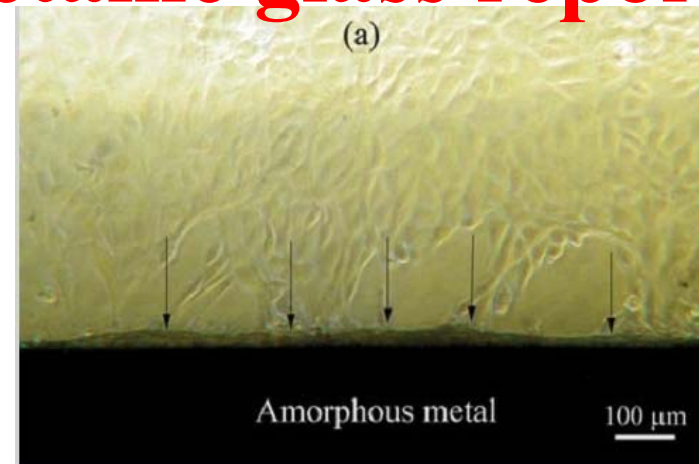
**Experiment 1:** STANDARD *in-vitro* biocompatibility test (ISO protocol 10993 part 5: Test for cytotoxicity).

**Result:** No toxicity, no reactivity and no cell lysis. (But with Be)

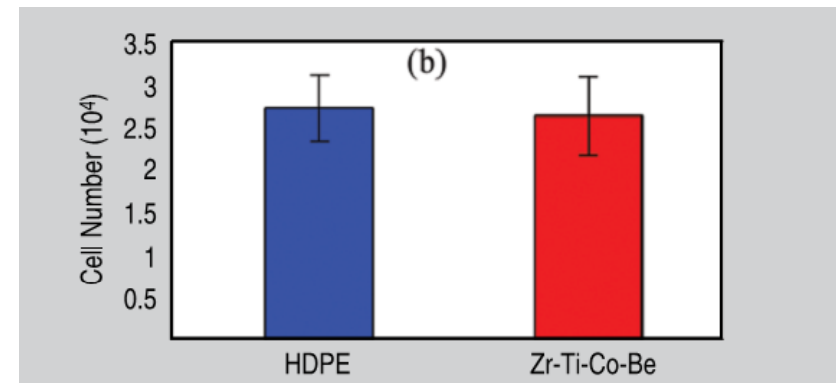
**Experiment 2:** 7-DAY *in-vitro* cellular adhesion test

**Result:** cell adherence and proliferation is adequate and compatible.

L. Liu et al., Scripta Mater; Intermetallics; J. Biomedical Materials Research Part A, 2008, 2009

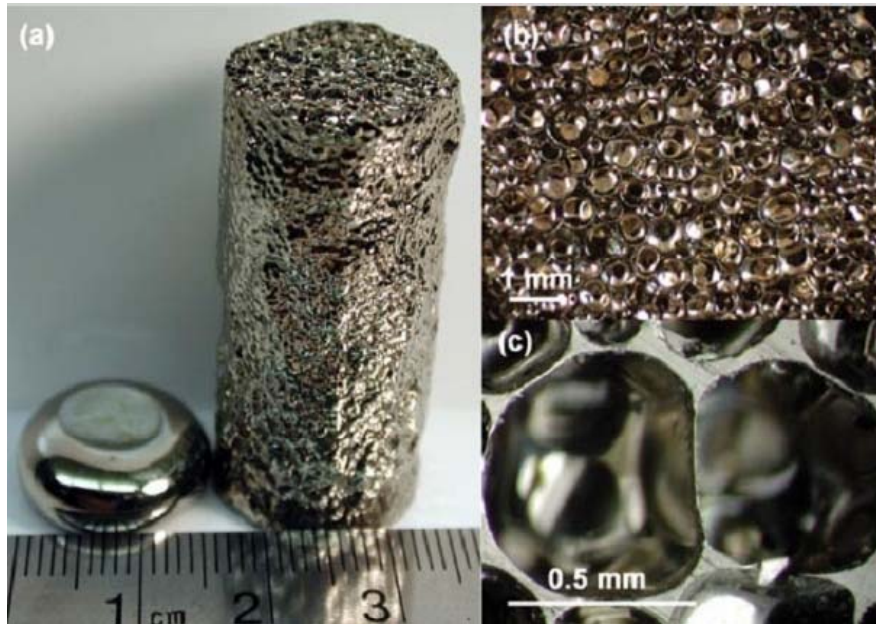


Micrograph of the amorphous metal surface after 7 days, ( arrows point to the cell-layer buildup at the interface.)



Cell proliferation on the amorphous metal and high-density polyethylene (HDPE) discs.

# Previous Example



Amorphous **Pd-Ni-Cu-P** foam  
(88% porosity) (but with Ni an Cu)

Demetriou MD et al

PHYSICAL REVIEW LETTERS, 101,  
145702 (2008)

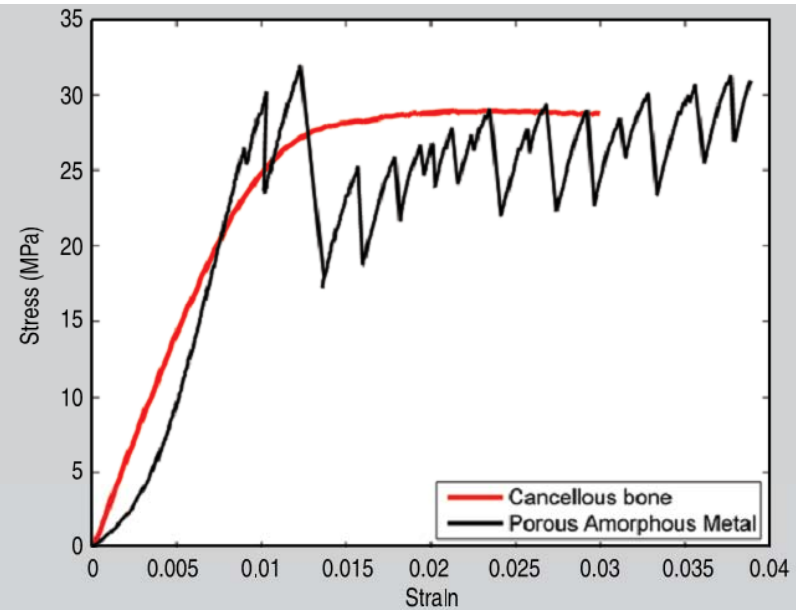


Figure 8. Compressive loading responses of amorphous Pd-Ni-Cu-P foam<sup>51</sup> and cancellous bone.<sup>52</sup>

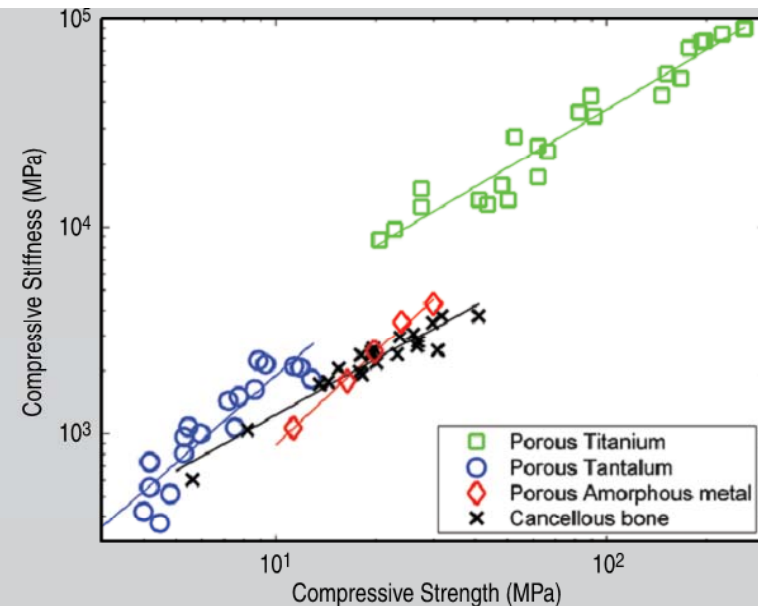


Figure 9. Compressive stiffness vs. strength data for amorphous Pd-Ni-Cu-P foam<sup>51</sup> shown together with data for porous Ti,<sup>53</sup> porous Ta,<sup>54</sup> and cancellous bone.<sup>52</sup>

# Dilemma for bio BMGs

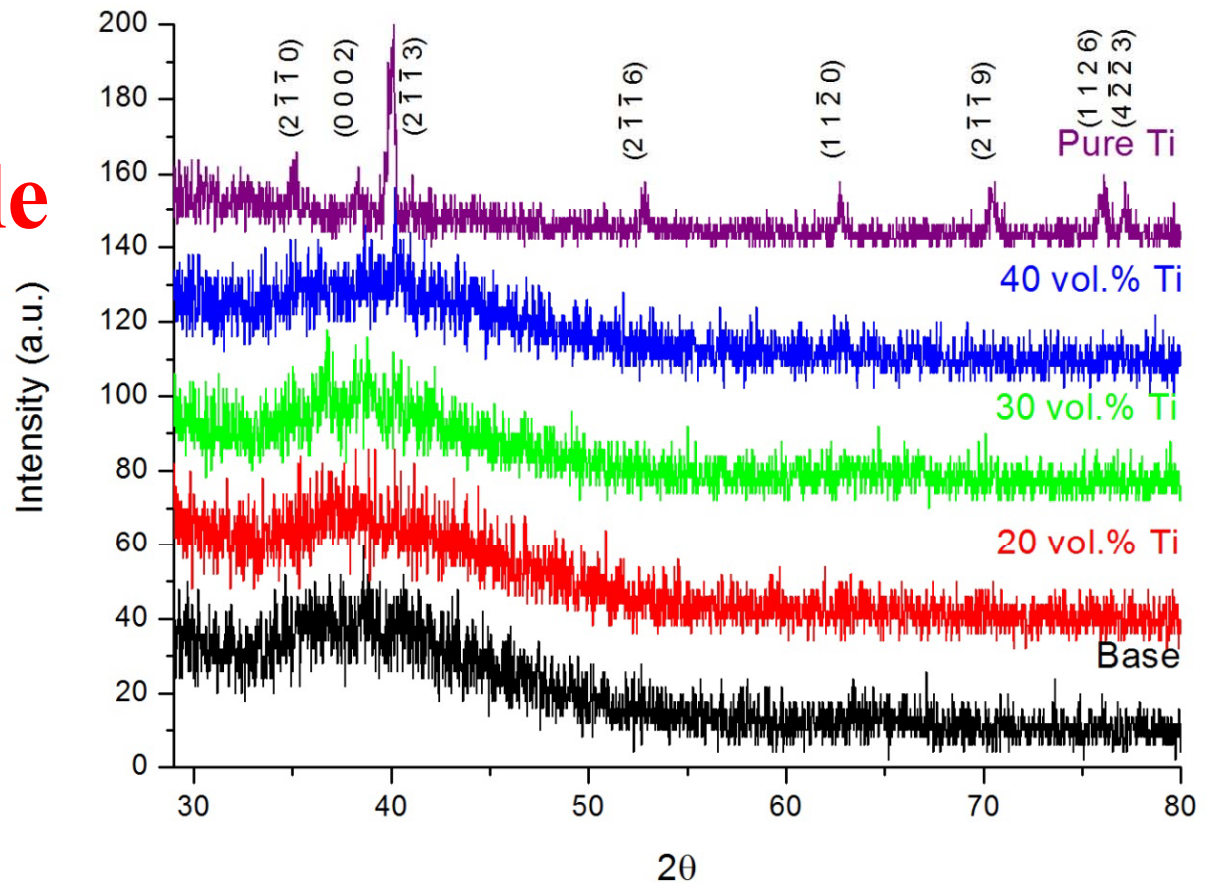
- Need to have high enough **GFA**.
- Exclude all **harmful** elements.
- Need to be **bio-compatible** and bio-friendly (no reaction, no gas release, not toxic, not irritating, not inflammatory, not allergic).
- Need to be resistant against **bio-corrosion**.
- Some need to be in **porous** foam.
- Suitable modulus and strength to match bone, to prevent from **stress shielding** effect.

**Our new MGs developed  
(no Be, Ni, minimum or no Cu/Al)**

<b>Zr-Cu-Al-Pd-Nb</b>	<b>Zr-based, Ni-free</b>
<b>Ti-Cu-Zr</b>	<b>Ti-based</b>
<b>Ti-Ta-Si-Zr</b>	<b>Ti-based, Cu-free</b>
<b>Ta-Zr-Cu-Ti</b>	<b>Ta-based, best cell in-growth</b>
<b>Mg-Zn-Ca</b>	<b>Mg-based, bio-degradable</b>
<b>Ag-Mg-Al</b>	<b>Ag-based, anti-bacterial</b>

	$T_g$ (K)	$T_x$ (K)	$T_m$ (K)	$T_1$ (K)	$T_{rg}$	$\gamma$	$\gamma_m$	$\Delta T_x$
$Mg_{58.5}Zn_{36.5}Ca_5$	427.2	460.4	617.1	652.4	0.654	0.426	0.757	33.2
$Mg_{60}Zn_{35}Ca_5$	435.3	483.8	614.4	688.4	0.632	0.430	0.773	48.5
$Mg_{61.5}Zn_{33.5}Ca_5$	432.5	457.4	612.1	648.3	0.667	0.423	0.743	24.9
$Mg_{63}Zn_{32}Ca_5$	405.2	447.9	615.0	677.8	0.598	0.413	0.723	42.7

# Biodegradable Mg-Zn-Ca MGs

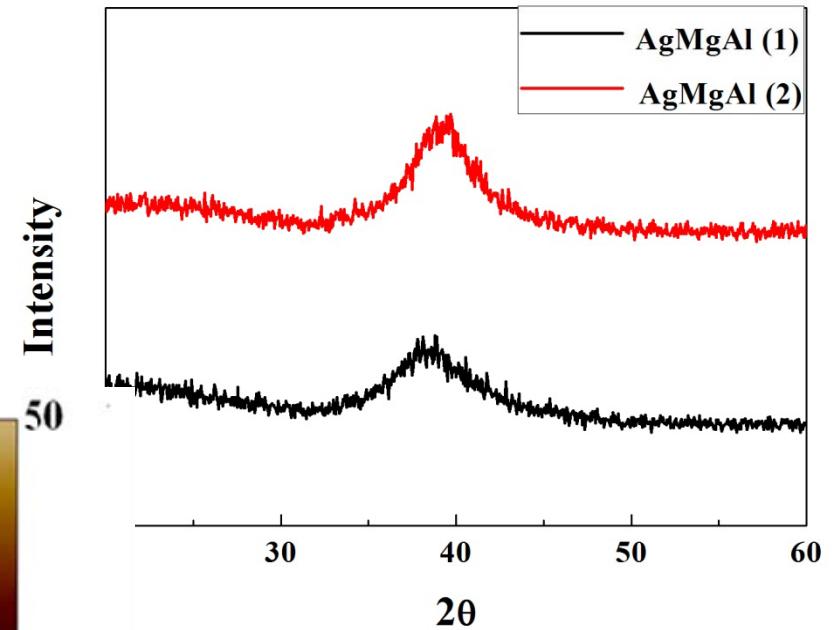
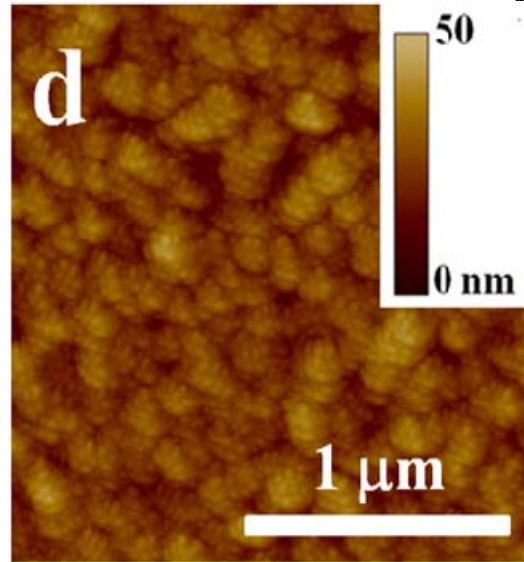
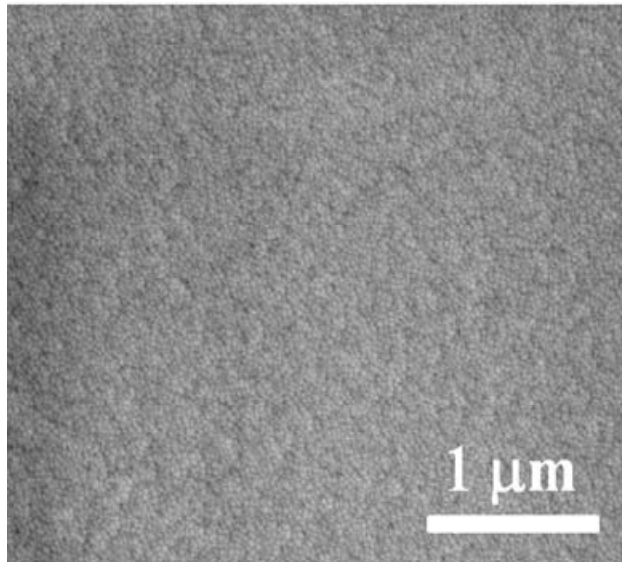


# Difficulty in Biodegradable Mg-Zn-Ca MGs

- **Bio-corrosion rate** is still too fast. Need to sustain about 6-12 months before being degradable.
- Difficult to fabricate **porous foams**.
- **GFA** is much lower than Zr- and Ti based BMGs.

# Ag-Mg-Al metallic glasses for anti-bacterial purposes

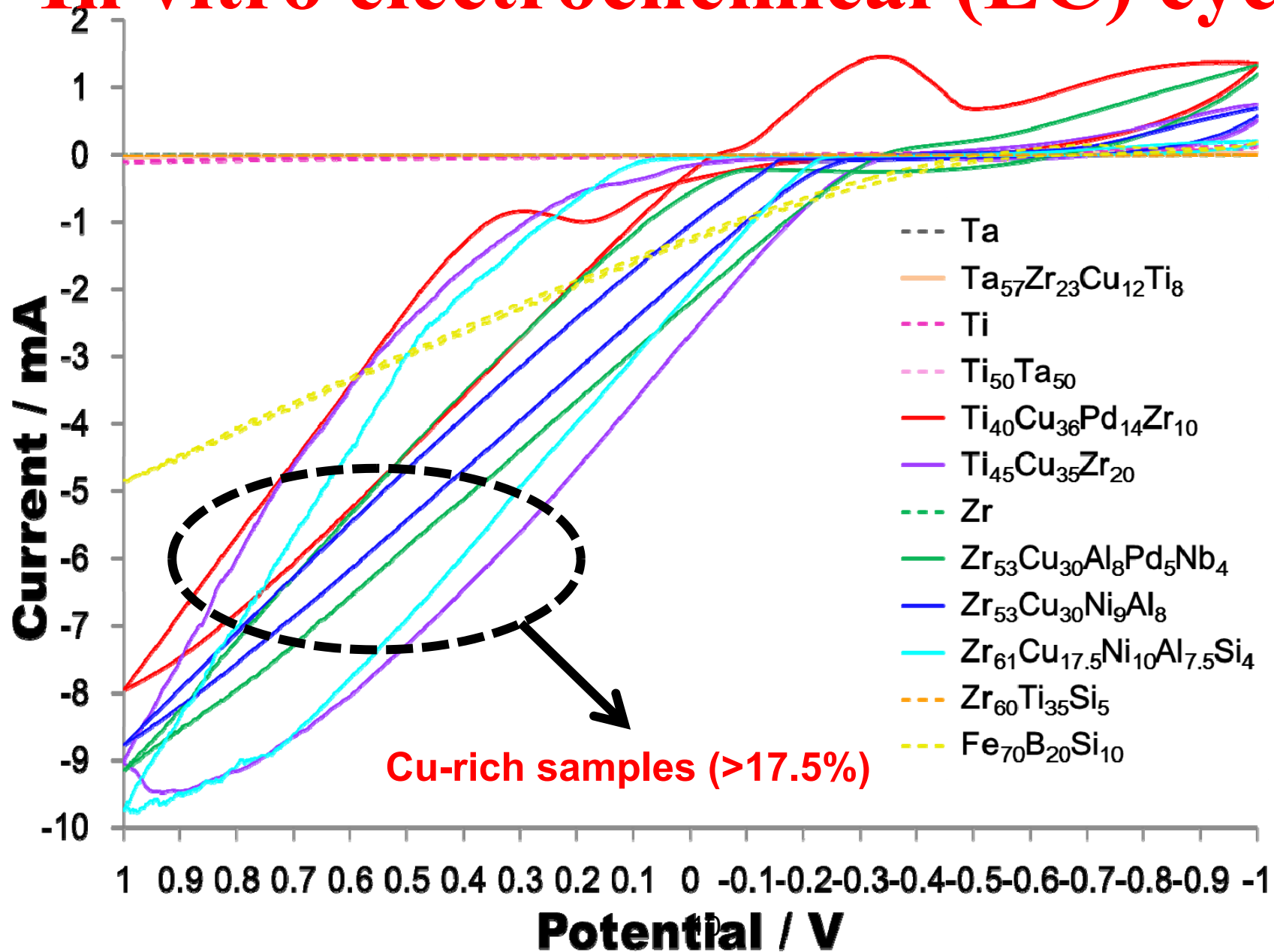
Ra ~ 1-3 nm



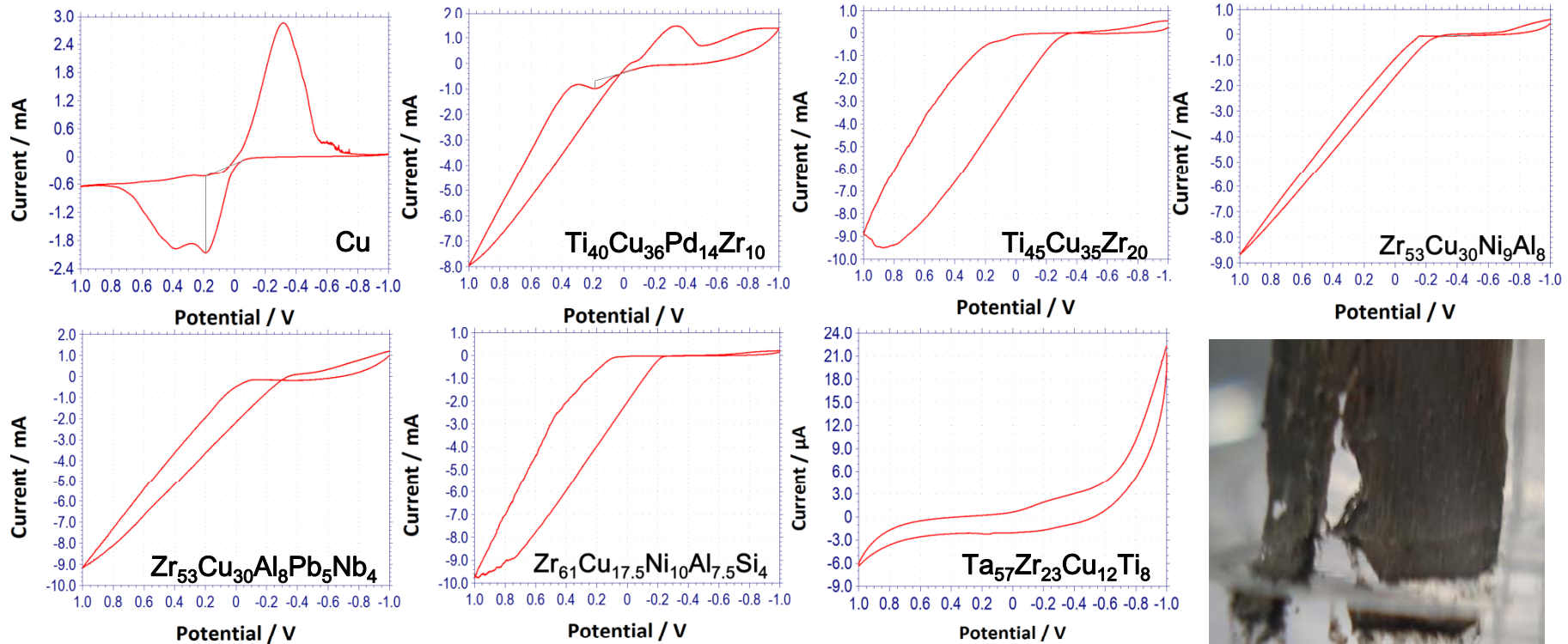
# **In vitro tests**

- In simulated body fluid **Hank's** solution
- In human **serum**
- Various **PH levels** from 2.0 to 8.0
- **Electrochemical (EC)** tests at room temp
- Long termed **immersion**
- Cell **viability** test
- Cell **proliferation** test
- Cell **adhesion** test

# In vitro electrochemical (EC) cycles



# Cu-containing BMGs

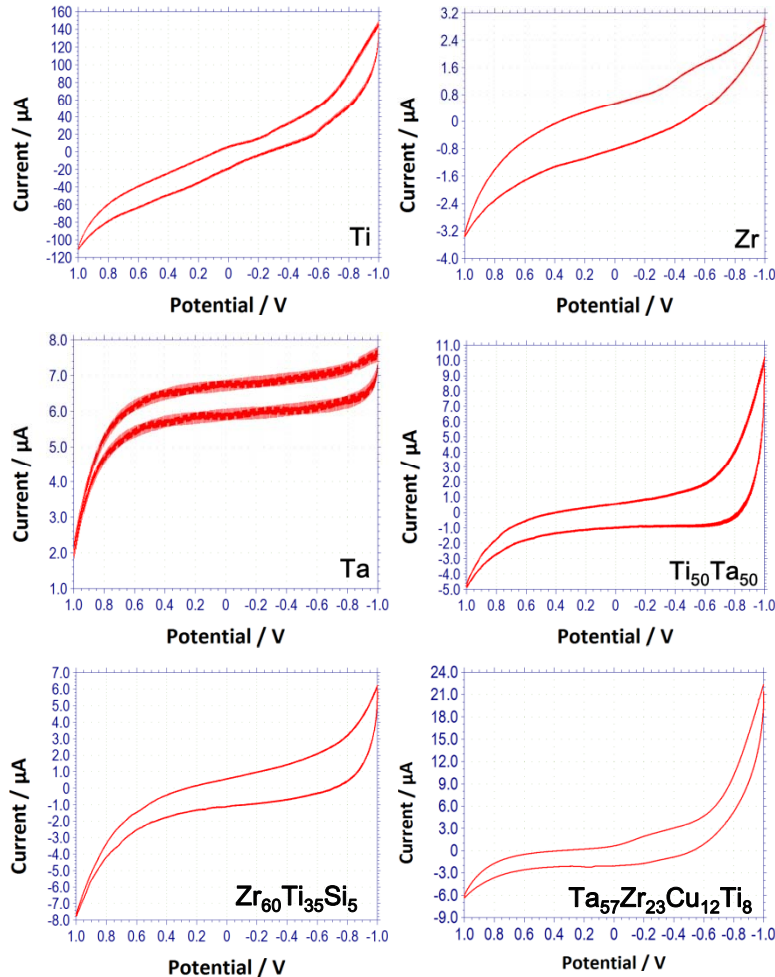


Decompose

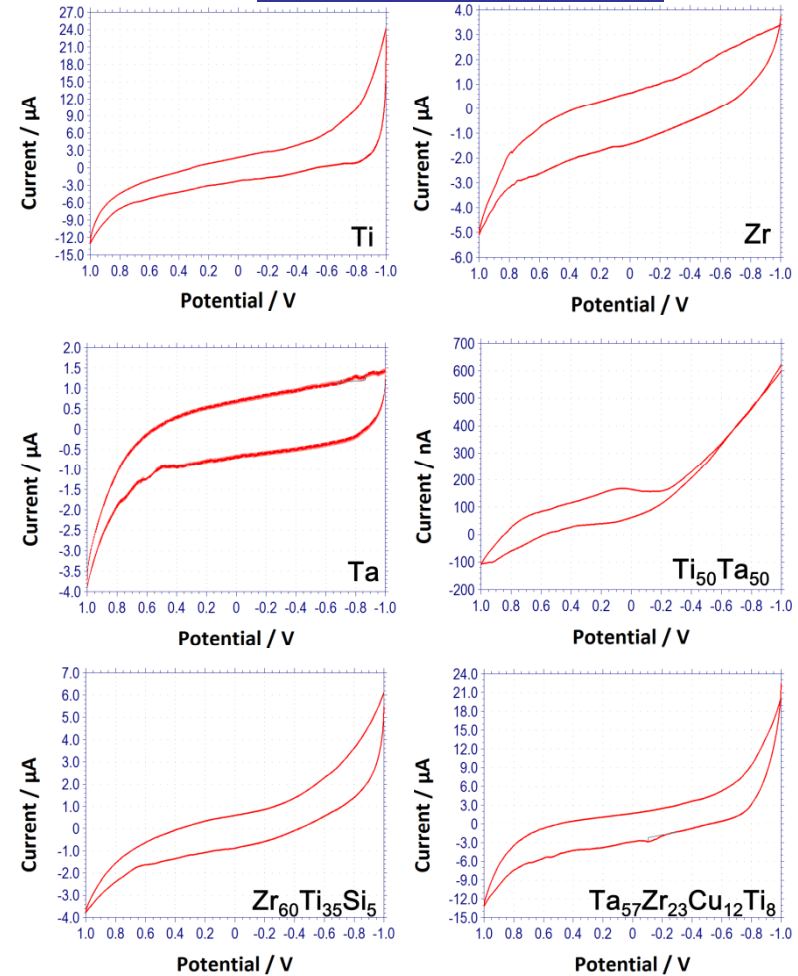
- The BMGs containing Cu
  - **Decompose**
  - **Hydrolysis**
- Response current in mA range indicates Cu-based BMGs has low corrosion resistant.
- Copper content have to be reduced or excluded.

# MGs with lower EC responses

Hank's solution



Human serum

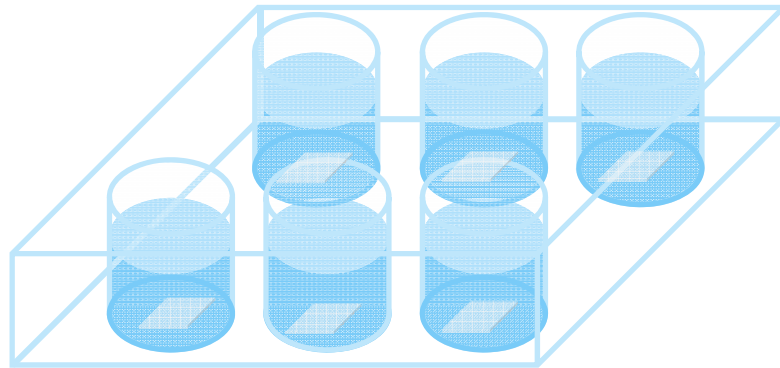


- $\text{Ti}_{50}\text{Ta}_{50}$  has been confirmed to be crystalline metal using XRD.
- Nice EC response for TaZrCuTi and ZrTiSi.

# Partial crystallization effects

- **Which one is better? Fully amorphous or partial crystallized?**
- **Depend on the phase composition, size, and dispersion of the crystallized phase.**
- **Need further study on the in-situ and ex-situ BMG composites.**

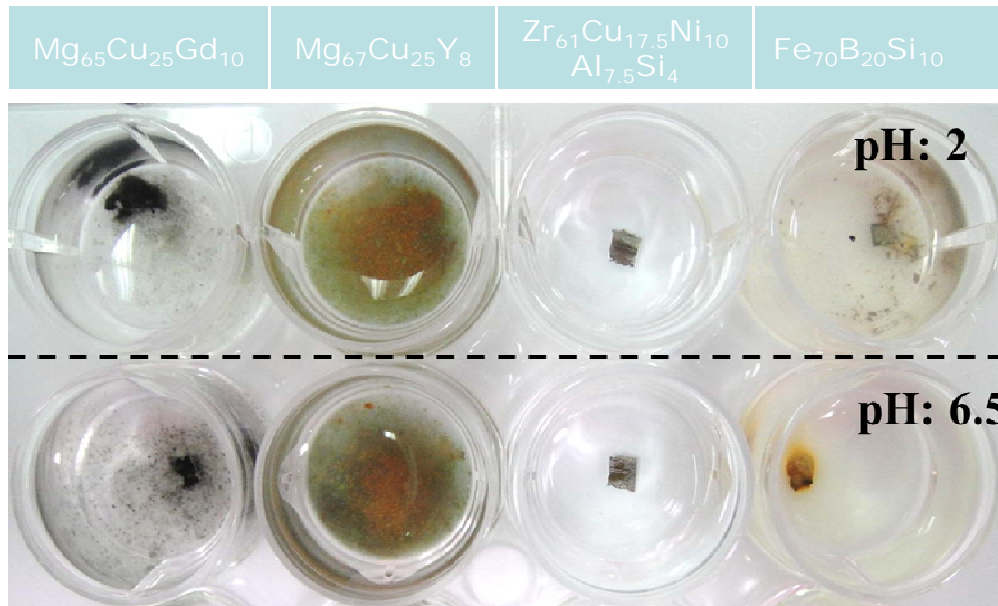
# Simulation body-fluid in vitro tests



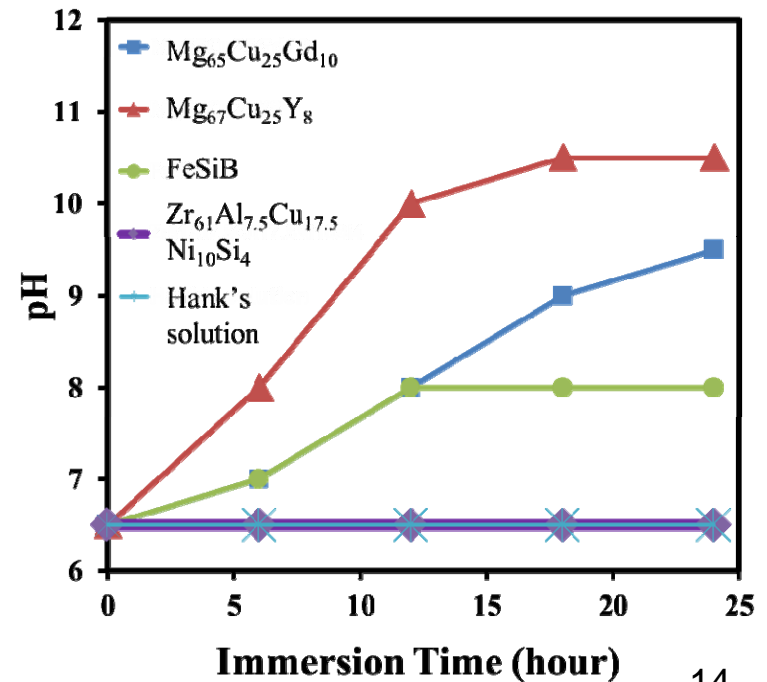
Hank's solution

pH: 6.5 and 2.0

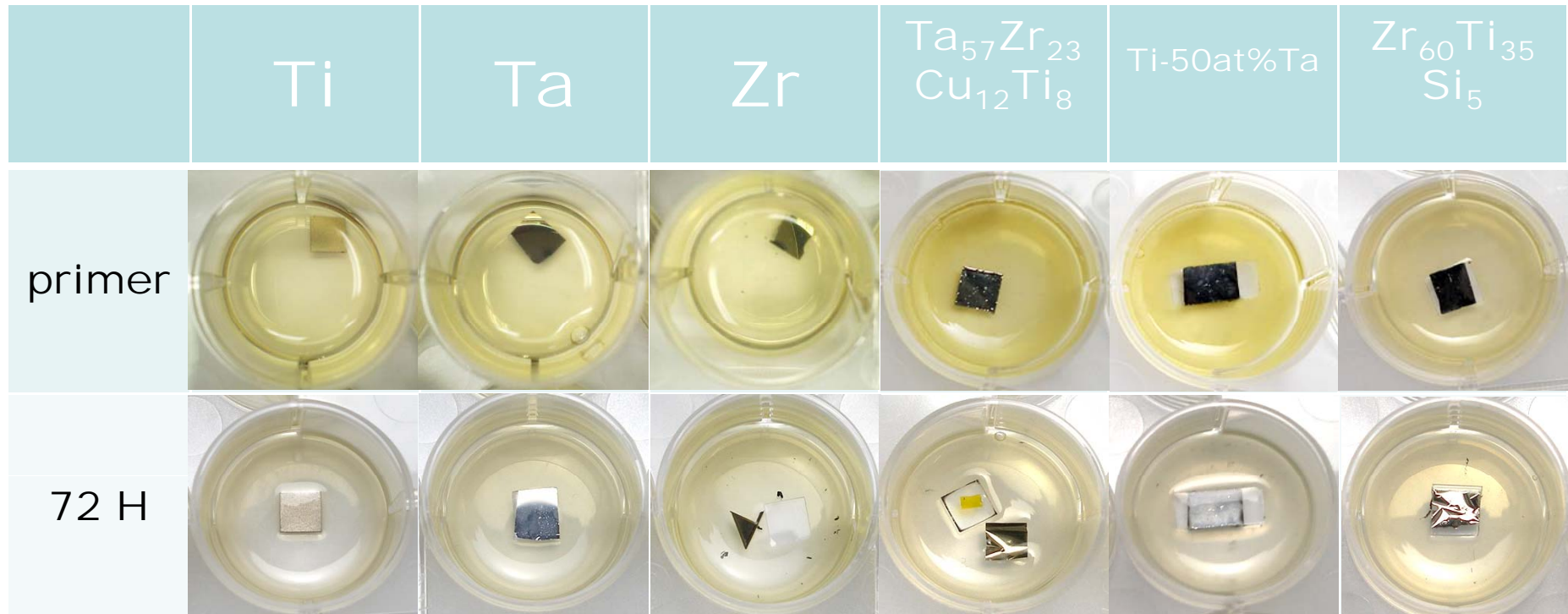
37°C 24 H -> 3 months



Variations of the pH values for immersion test



# Long-term immersion (serum)



**Promising BMGs are then subject to longer time immersion**

# Cell viability test

## MTT assay

### Condition

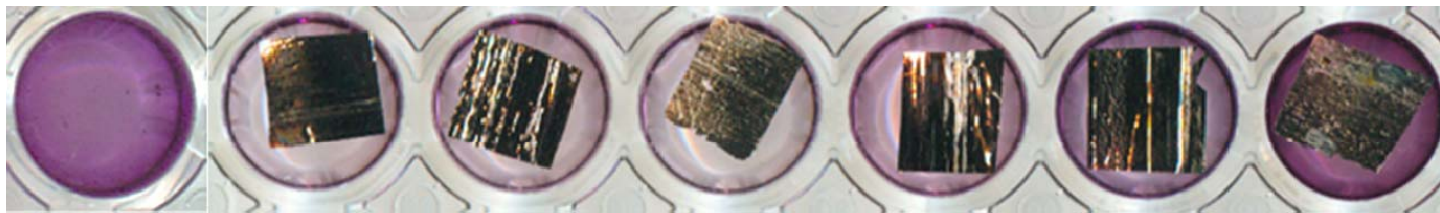
Cell: D1 bone marrow stem cells (from Balb/c mouse)( $1 \times 10^5$  /well)

Medium content: Bone medium

Low glucose DMEM+1.5g sodium bicarbonate + 1%NEAA + 1%Vitamine C +10% FBS +1% P/S

Metal:  $Ti_{45} Zr_{20} Cu_{35}$  (about 3mmx3mm) in 48 well

Culture time : 24hr



	Control (n=3)	No.1	No.2	No.3	No.4	No.5	No.6	mean
value	2.75	0.76	0.858	1.099	0.86	0.91	1.011	0.916
viability	100.0%	27.64%	31.20%	39.96%	31.27%	33.09%	36.76%	33.32%

- The mean of cell viability is 33.32%.
- This TiZrCu has strong cytotoxicity may caused by the release of Cu ions.
- In comparison, Ti-Ta-Zr-Si without Cu passed the cell viability test, to nearly 100%.

# The cell proliferation test of bone nail coated with Ti or Ta

**Condition**

**Cell: D1 bone marrow stem cells (from Balb/c mouse)( $5 \times 10^5$ /tube)**

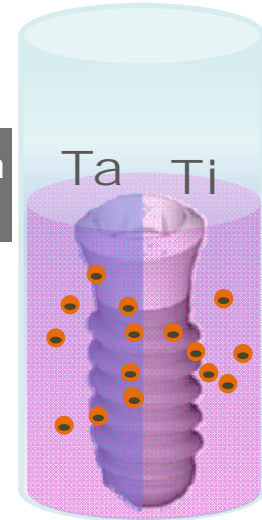
**Medium content: Bone medium**

**Culture time : 72 hr**

	Metal	Medium	Wall (tube)	Total	Proliferation ratio
control (no metal)	–	–	950,000	950,000	1
Pure Ti	305,000	5,000	595,000	905,000	0.95
Ti/Ta	290,000	10,000	920,000	1,220,000	1.28

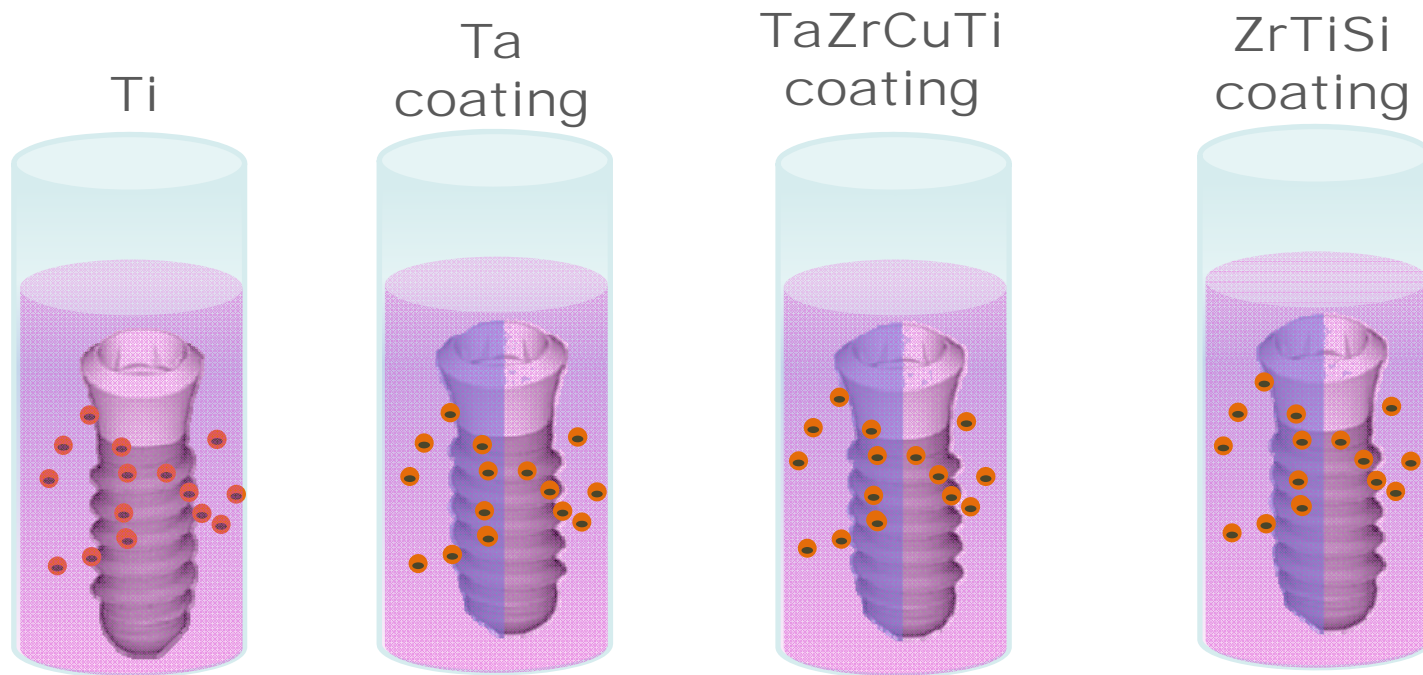
  

	Metal	Medium	Wall (tube)	Total	Proliferation ratio
control (no metal)	–	5,000	800,000	805,000	1
Pure Ti	315,000	10,000	585,000	910,000	1.13
Ti/Ta	345,000	5,000	765,000	1,115,000	1.39



- The results show Ti-Ta sample promote cell proliferation.
- No significant difference on D1 adhesion.

# On-going work



Culture 7 days

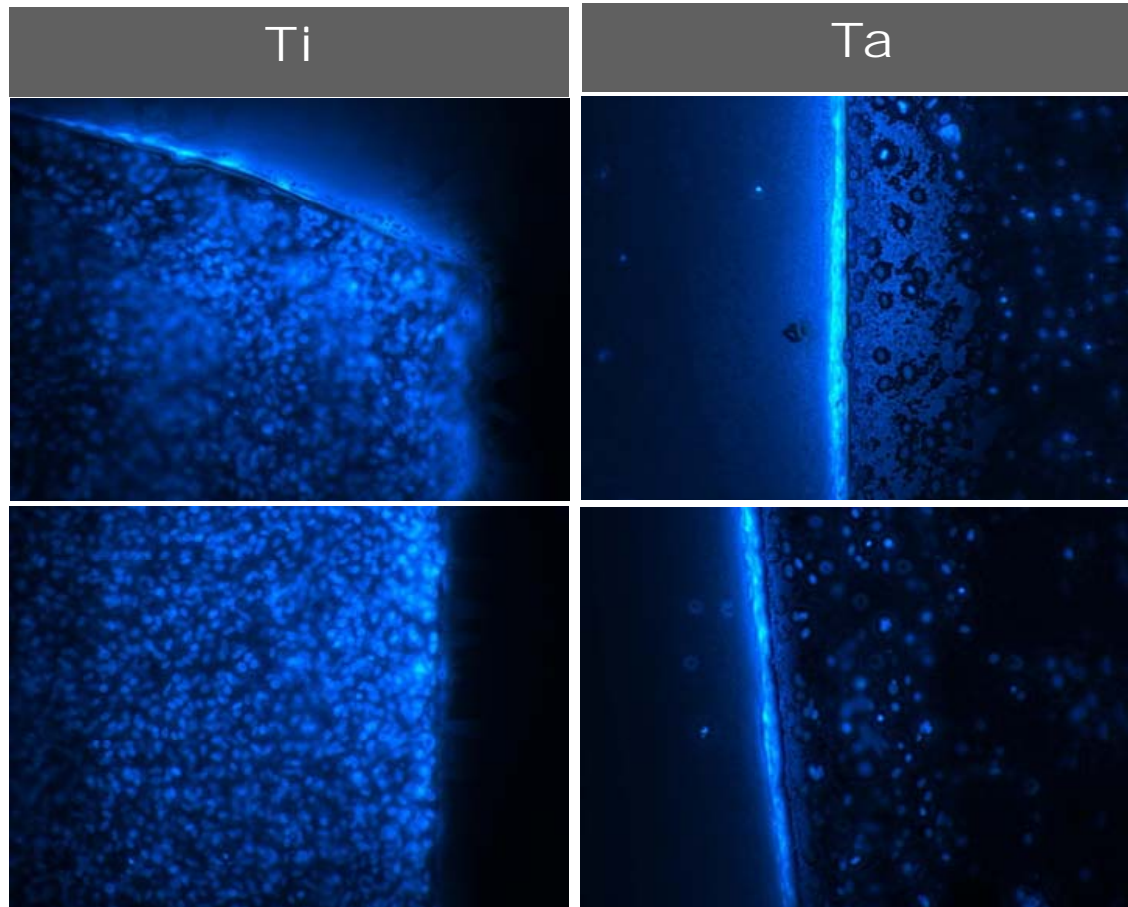
1. MTT viability test
2. Electron microscopy observation (variable vacuum)
3. EC test.

# Cell adhesion test

Cell: D1 **bone marrow stem cells** (from Balb/c mouse) ( $5 \times 10^5$ /tube)

Medium content: Bone medium                      Culture time : 7 days

Sample : slides coating Ti ( $1 \mu\text{m}$ ) and slides coating Ta ( $1 \mu\text{m}$ )



- Fluorescence imaging technique
- D1 **stem cell** can attach onto both Ti or Ta.
- Potential **Ti and Ta thin-film MGs** are tested and passed.

# Summary on in vitro responses

- **Potential materials:**
  - Ti-Ta**
  - Ta-Zr-Cu-Ti (low Cu)**
  - Ti-Ta-Si-Zr (No Cu)**
  - Zr-Ti-Si (No Cu)**
- **Cu-rich MGs showed low potential to be biocompatible materials. Cu content has to be decreased.**

# In vivo experiment

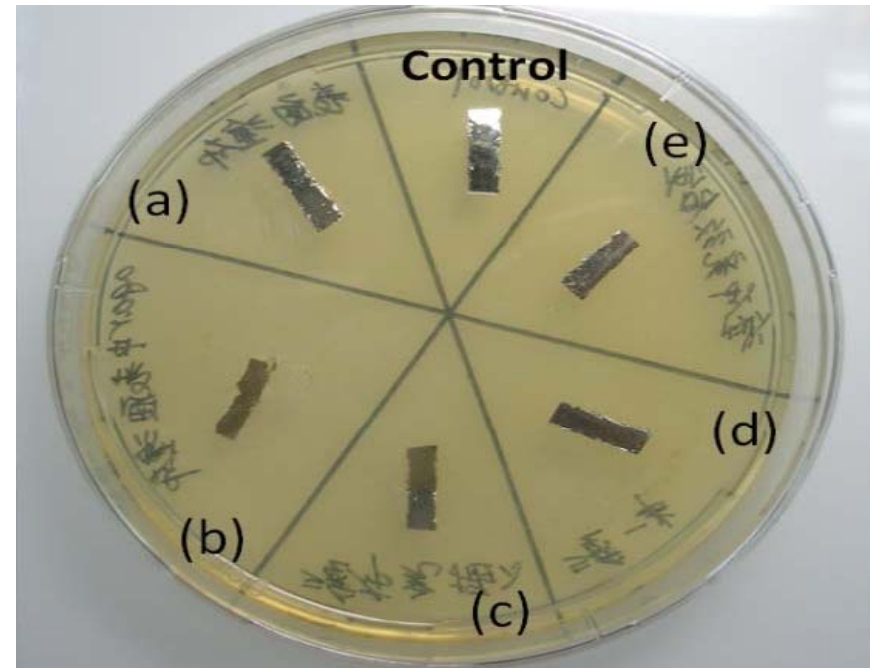
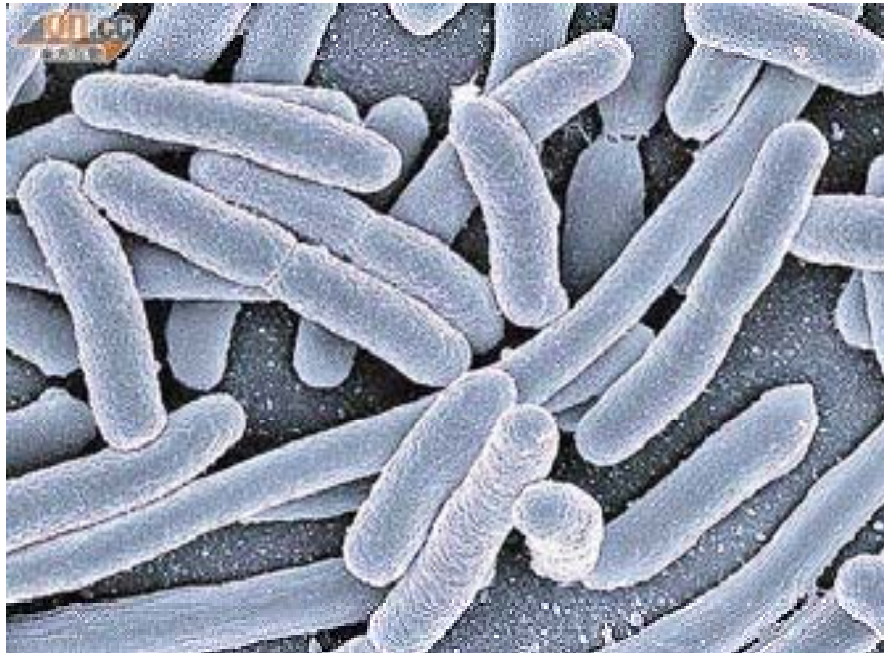
- On-going implant in rat and rabbit
  1. Mg-Zn-Ca
  2. Ti-Ta-Si-Zr
  3. Zr-Ti-Si
  4. Zr-Cu-Ni-Al
  5. Mg-Cu-Gd
  6. Fe-B-Si
  7. Ta-Zr-Cu-Ti



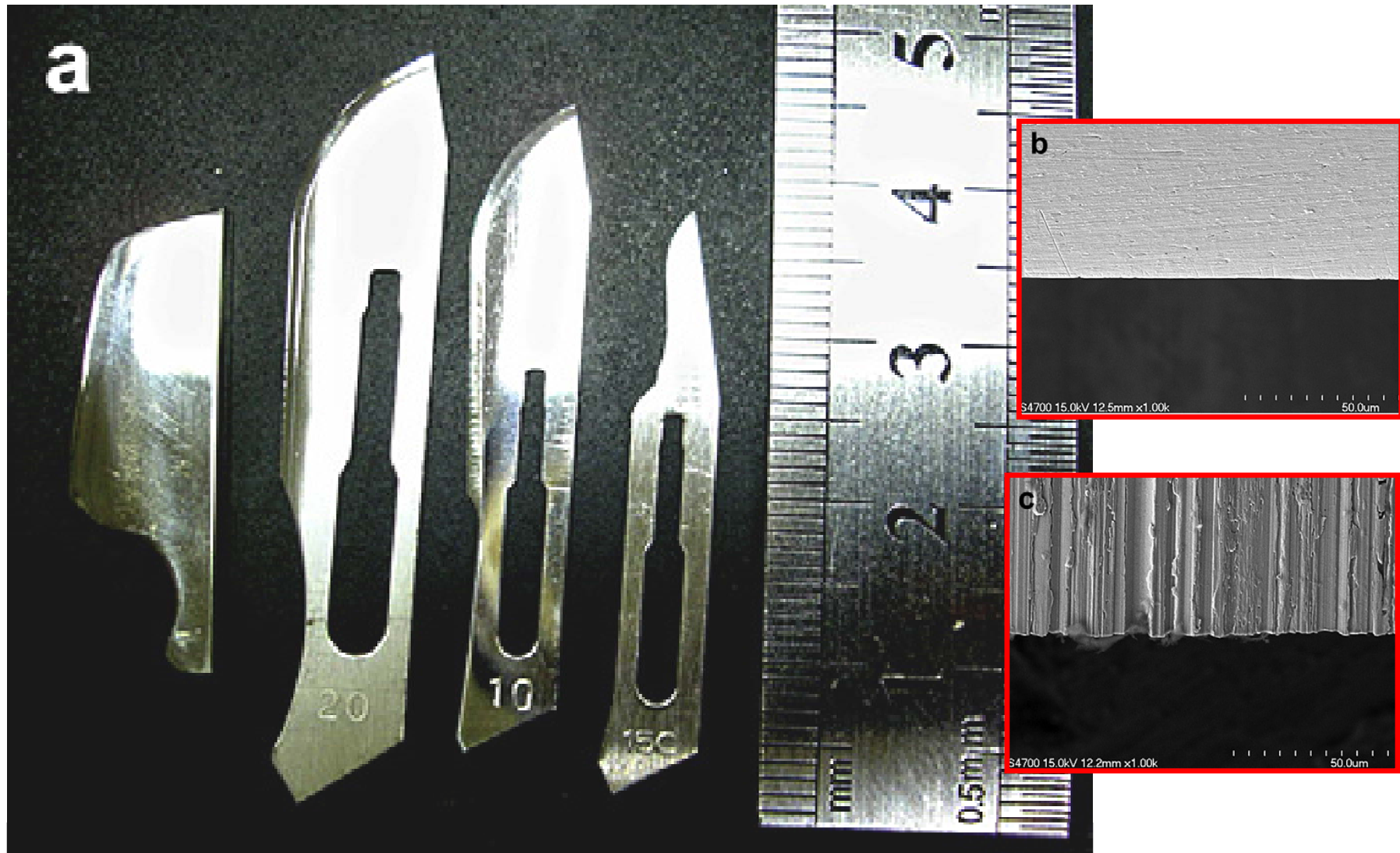


<b>Rabbit No.</b> <b>Site</b>	<b>No.0</b>	<b>No.1</b>	<b>No.2</b>	<b>No.3</b>
<b>Right femur</b>	<b>Bone screw (Ti)</b>	 $Ta_{57}Zr_{23}Cu_{12}Ti_8$	 $Zr_{60}Ti_{35}Si_5$	 $Ti_{59}Si_{20}Ta_{12}Zr_9$
<b>Left femur</b>		 $Ti_{59}Si_{20}Ta_{12}Zr_9$	 $Ta_{57}Zr_{23}Cu_{12}Ti_8$	 $Zr_{60}Ti_{35}Si_5$
<b>Right tibia</b>			 $Zr_{53}Cu_{30}Al_8Pd_5Nb_4$ $Ti_{40}Cu_{36}Pd_{14}Zr_{10}$ $Ti_{45}Cu_{35}Zr_{20}$	 $Zr_{53}Cu_{30}Al_8Pd_5Nb_4$ $Ti_{40}Cu_{36}Pd_{14}Zr_{10}$ $Ti_{45}Cu_{35}Zr_{20}$
<b>Left tibia</b>			 $Zr_{53}Cu_{30}Ni_9Al_8$ $Zr_{61}Cu_{17.5}Ni_{10}Al_{7.5}Si_4$ $Ti_{60}Ta_{15}Si_{15}Zr_{10}$	 $Zr_{53}Cu_{30}Ni_9Al_8$ $Zr_{61}Cu_{17.5}Ni_{10}Al_{7.5}Si_4$ $Ti_{60}Ta_{15}Si_{15}Zr_{10}$

# Anti-microbial Ag- and Cu-based MG coating on SS 316L In vitro test (*E.coli*)



# Anti-microbial surgical tools



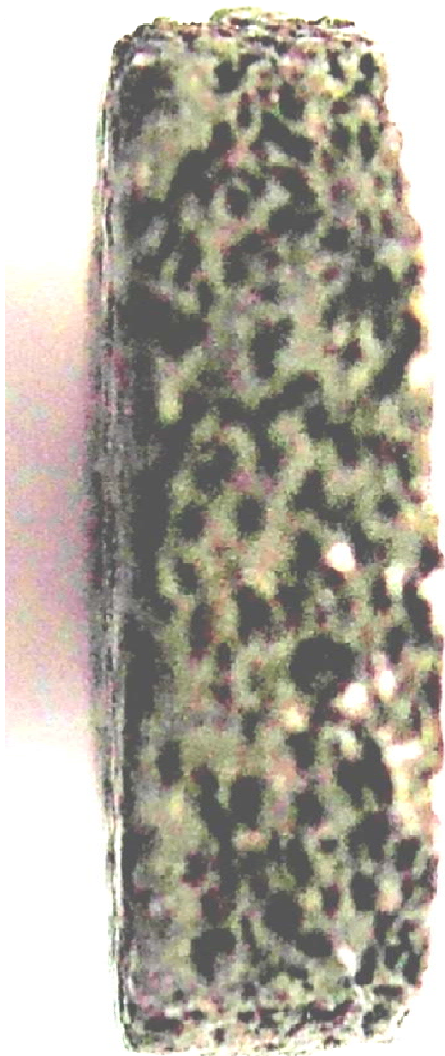
# Fabrication of porous MGs

## Spark plasma or conventional sintering

powder	particle	vol%	amount	Particle Size	ISO I	MAX I	ISO temperature	MAX temperature	pressure	ISO TIME
Ti40Zr10Cu35Pd15	SiO2	30	3	30um以下	430A	590A	400	421.6	50MPa	5min
Ti40Zr10Cu35Pd15	SiO2	30	3	30um以下	460A	620A	430 °C	450.5 °C	50MPa	5min
Ti40Zr10Cu35Pd15	SiO2	30	3	30um以下	420A	560A	430	459	50MPa	5min
Ti40Zr10Cu35Pd15	CaCO3	30	1	105~150um	580A	800A	430	454	50MPa	8min
Ti40Zr10Cu35Pd15	CaCO3	30	1	105~150um	550A	750A	430	452.9	50MPa	10min
Ti40Zr10Cu35Pd15	CaCO3	30	1	105~150um	580A	760A	400	421	50MPa	8min
Ti40Zr10Cu35Pd15	CaCO3	30	1	105~150um	400A	700A	400	422.4	50MPa	10min
Ti40Zr10Cu35Pd15					600A			422.4		



# Successful porous MGs

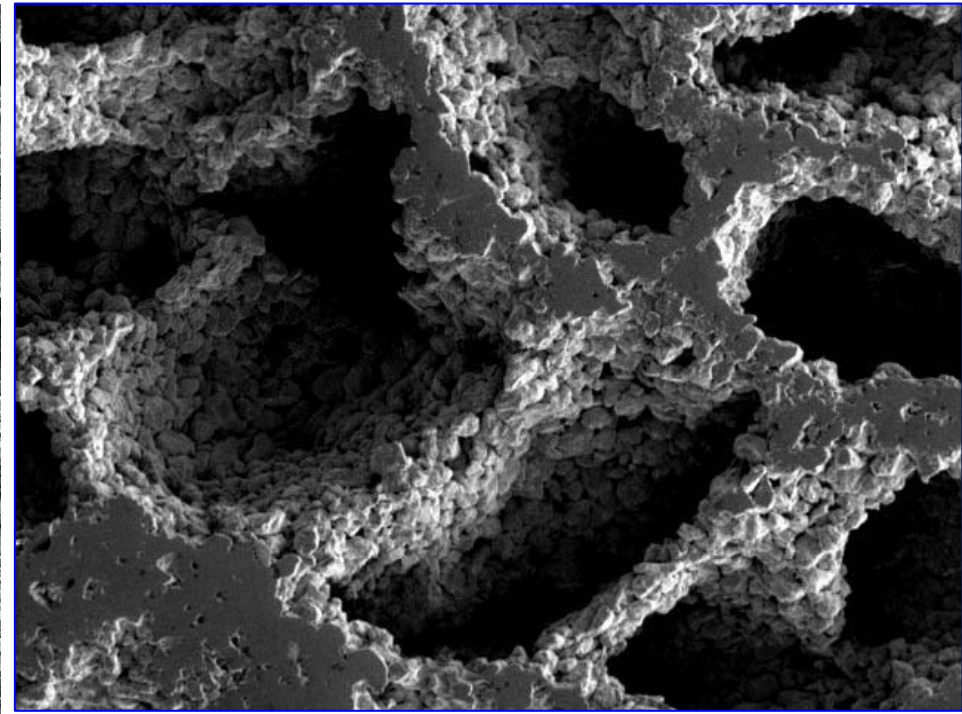
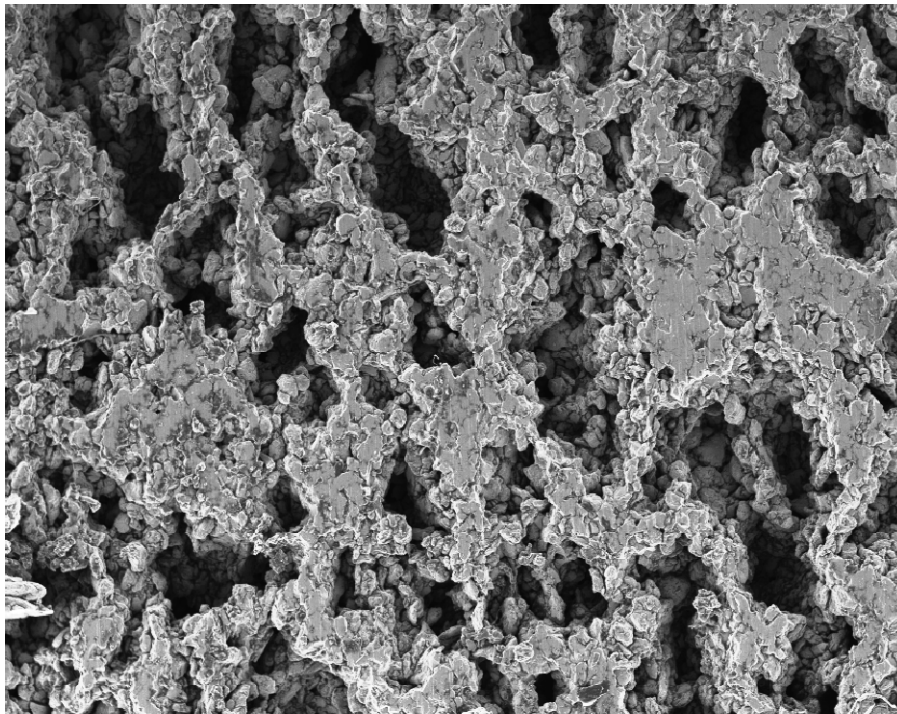


10 mm



# Ti-based BMG foams

Porosity: 70-80 vol%, pore size: 300  $\mu\text{m}$



**Thank you for your attention.**

