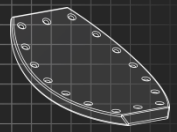
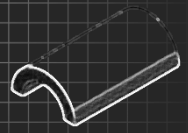
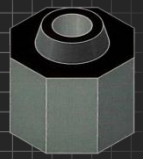
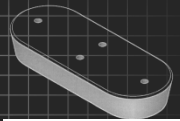








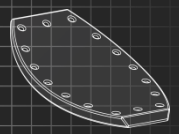
Local bone antibiotic delivery using porous alumina ceramic: clinical and pharmacological experience

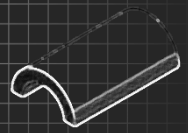
E. Denes, F. Fiorenza, E. Toullec,
F. Bertin, S. El Balkhi
Limoges, France

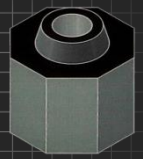
Conflict of interest

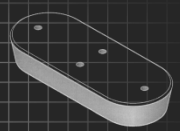
- Employed by I.Ceram

Context









- Replacing infected bone
- High risk of implant's infection
- => No foreign body during infection

- Proposition:
  - Implantation of a "protected" device (antibiotic loaded)
  - Prophylaxis

Main characteristics

Pure alumina Al_2O_3

Proven biocompatibility, inert

Mechanical strength more than 20 MPa
3 times cancellous bone strength in compression

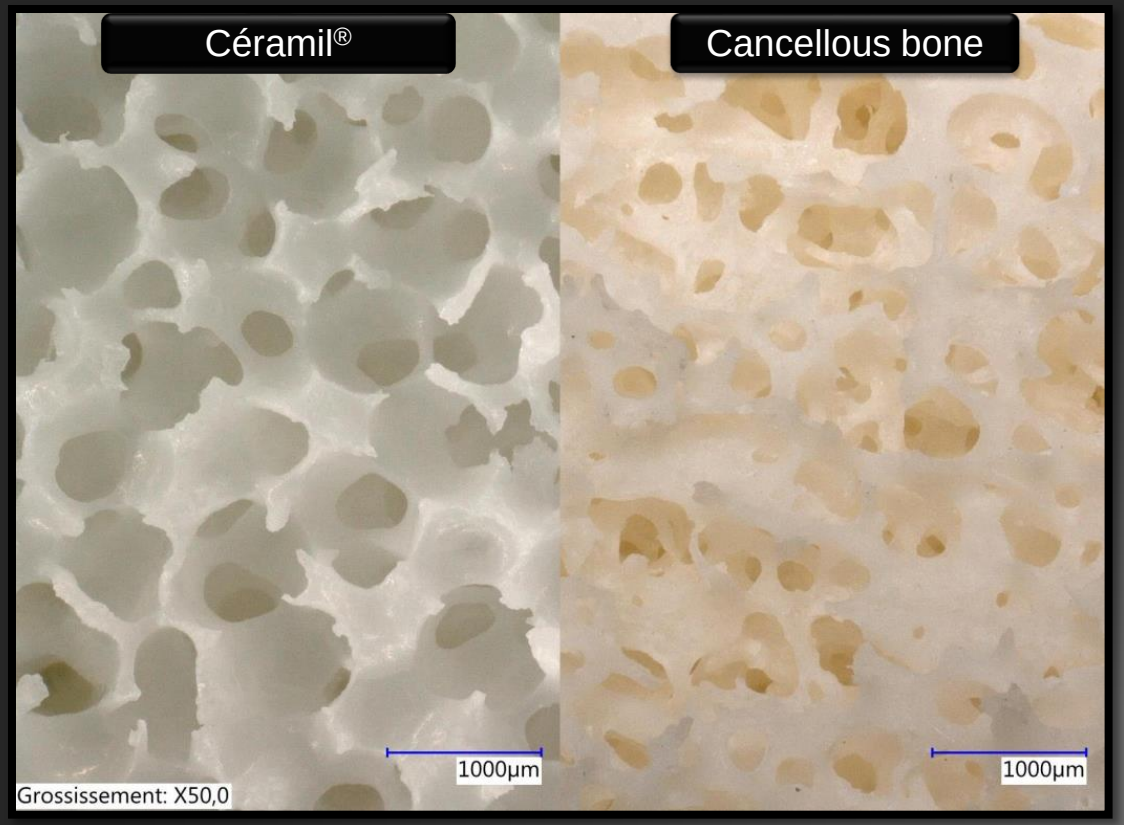
A certain level of resistance to bacterial infection

Non absorbable

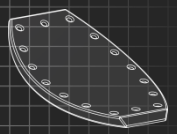
Interconnected porosity

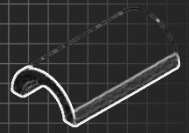
Unique capacity of osseointegration
Porosity range from 100 to 900 µm

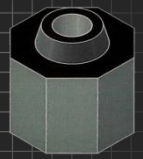
A very similar structure

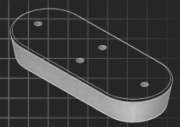


Antibiotics

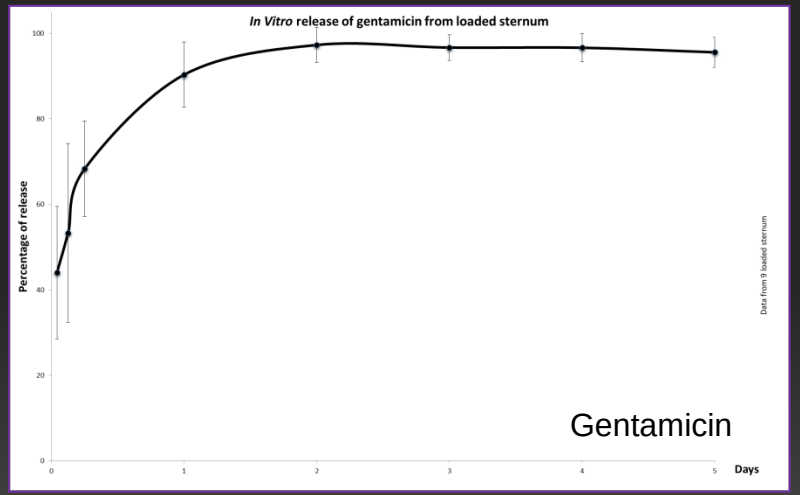








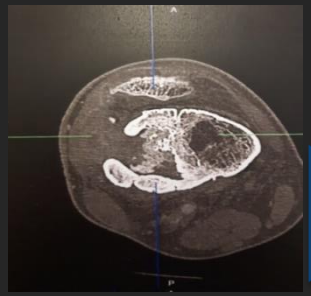
- Antibiotic loaded:
  - Gentamicin
  - Vancomycin
  - Both of them
- Start of release: immediately
- Release duration: 48 – 72 h (*in vitro*)
- Release: 100 %



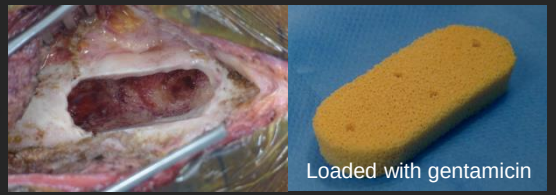
Mediastinitis

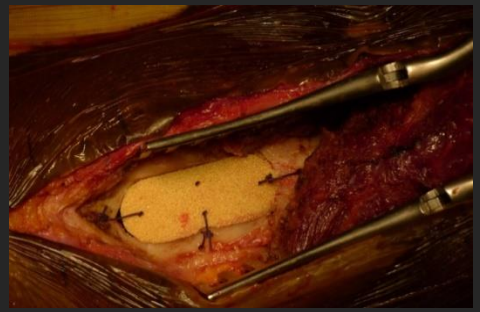
Four patients received this loaded sternum
More than 3 years of follow-up for the 1st one without relapse

Chronic osteomyelitis (MRSA)



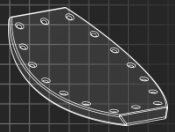
All samples grew with MRSA

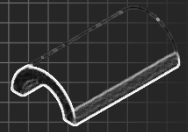


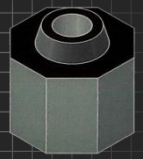


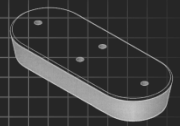
Follow-up

Infected ankle Prosthesis





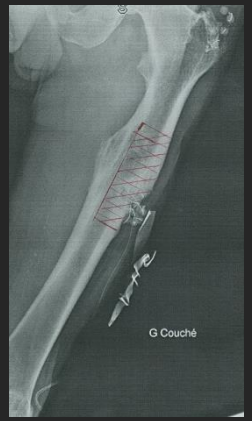




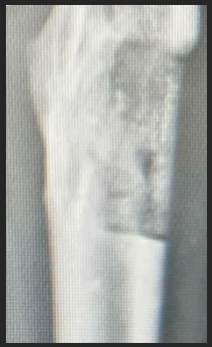
Skin fistula – Infection lasting for 10 years

Ceramic loaded with vancomycin

Chronic osteomyelitis: femoral tile



Gentamicin loaded



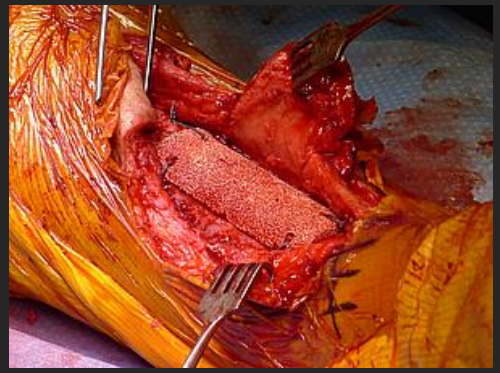
X-Ray follow-up M3

Man 64 year-old
Chronic osteomyelitis – MSSA
Evolution: 30 years
Gentamicin cement beads

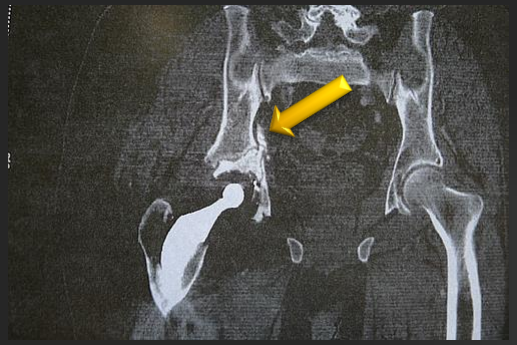
Chronic osteomyelitis: tibial tile

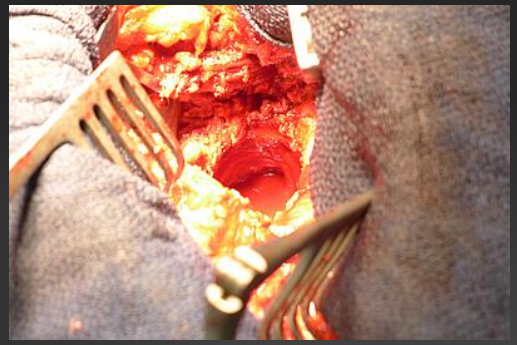
Man 48 year-old
Chronic osteomyelitis after fracture
> 5 surgeries
Pseudoarthrosis MSSA
Fistula
Already had a muscle flap

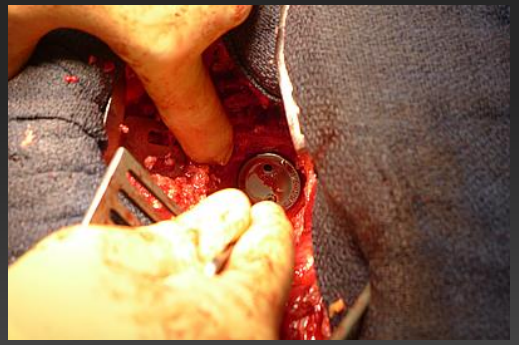
Loaded with gentamicin

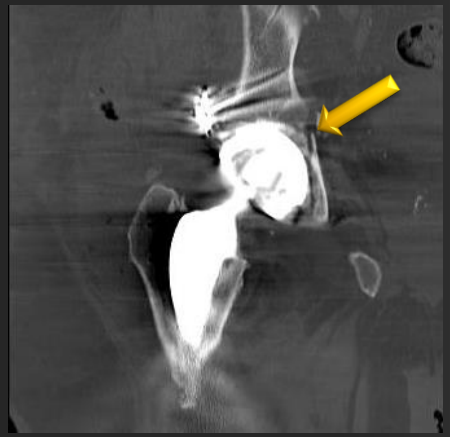


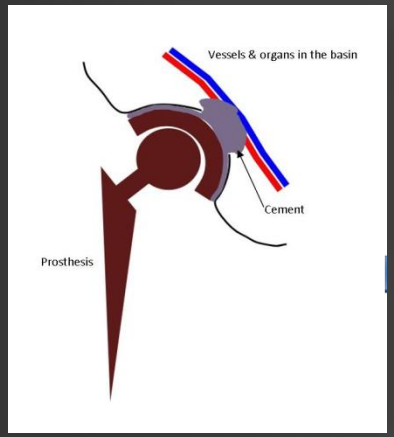
Prosthetic Joint Infection

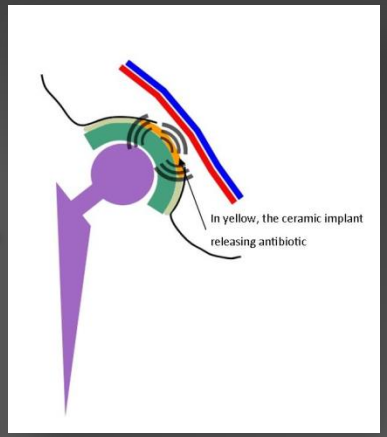


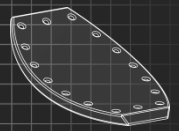
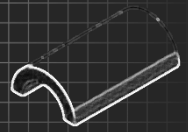
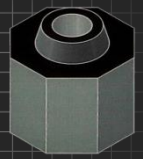
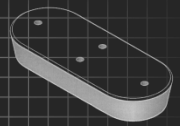










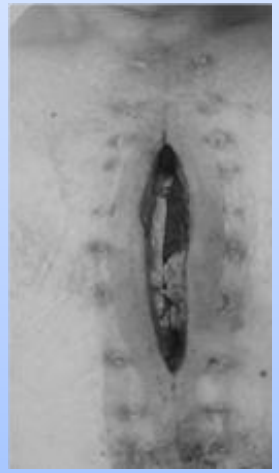
In vivo – local concentrations

- Local dosages

Device	Loaded dose	H+1	H+24	H+48	H+60	Pharmacological parameter needed	Pharmacological parameter obtained
Gentamicin							
Sternum	320 mg	1,500 mg/L	395 mg/L			$\frac{Cmax}{MIC} > 10$	> 1,500
Sternum	160 mg	2,100 mg/L	36.9 mg/L				> 2,100
Bone flap	160 mg	184 mg/L	13 mg/L				> 370
Sternum	320 mg	6,650 mg/L	4.7 mg/L				6,650 (*K. pneumoniae*) 17 (MRSE)
Vancomycin							
Ankle spacer	250 mg		548 mg/L	172 mg/L	26 mg/L	$\frac{AUC}{MIC} > 400$	2,400
Sternum	250 mg	390 mg/L	28 mg/L				16,000 (MRSE)

Surpassing resistance

Mediastinitis



Bacteriological sampling and sensitivity interpretation EUCAST

K. pneumoniae

- gentamicin **S** (MIC = 1 µg/mL)

MRSE

- gentamicin **R** (MIC = 384 µg/mL)
  - EUCAST Breakpoint: 1 µg/ml
- vancomycin **R** (MIC = 8 µg/mL)
  - EUCAST Breakpoint: 4 µg/ml

Administration route

<u>Intravenous</u>

⇒ Expected to fail (MRSE)

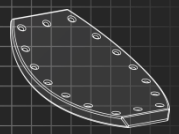
<u>Locally</u> (MRSE)

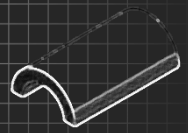
- Gentamicin
  - C_{max}/MIC = 17
- Vancomycin
  - AUC/MIC = 16,000

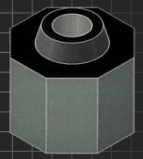
⇒ Expected to be efficient

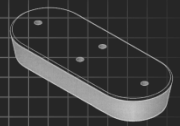
- M+2 : no relapse

In vivo – blood concentrations





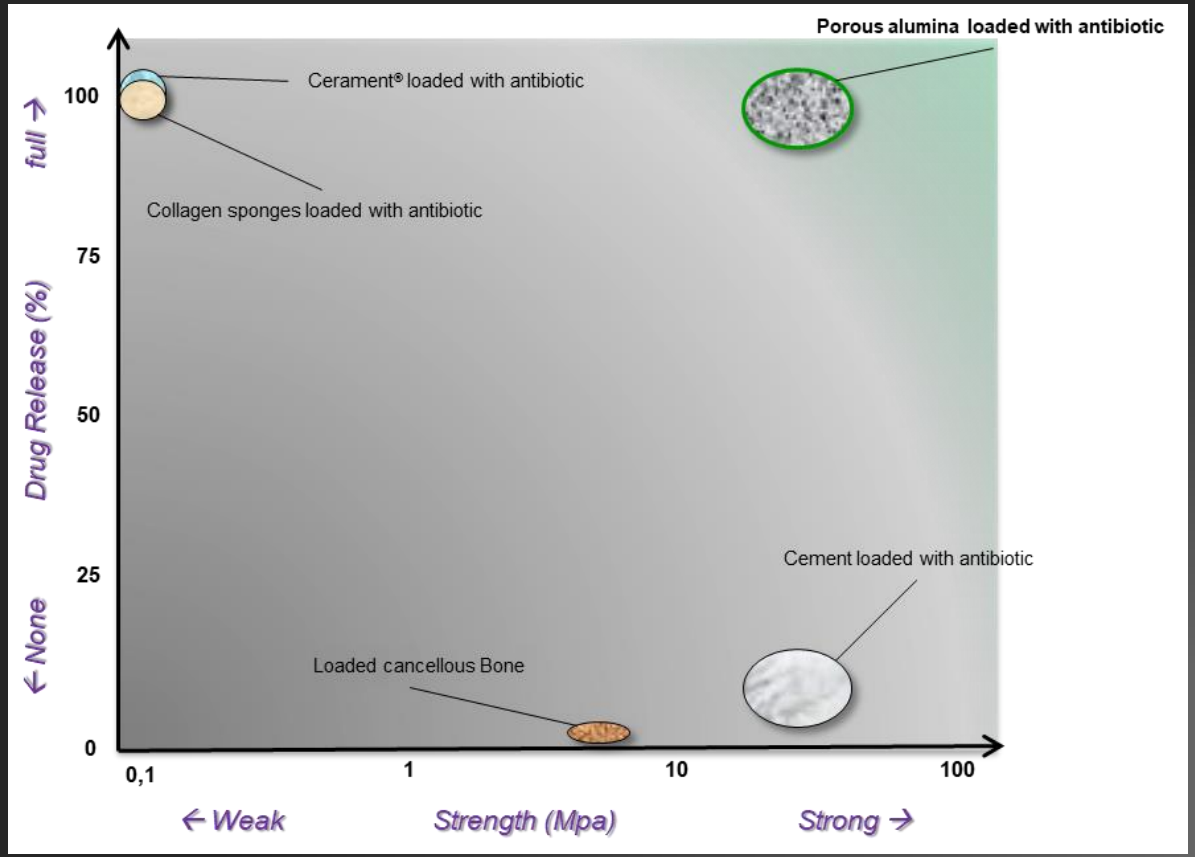




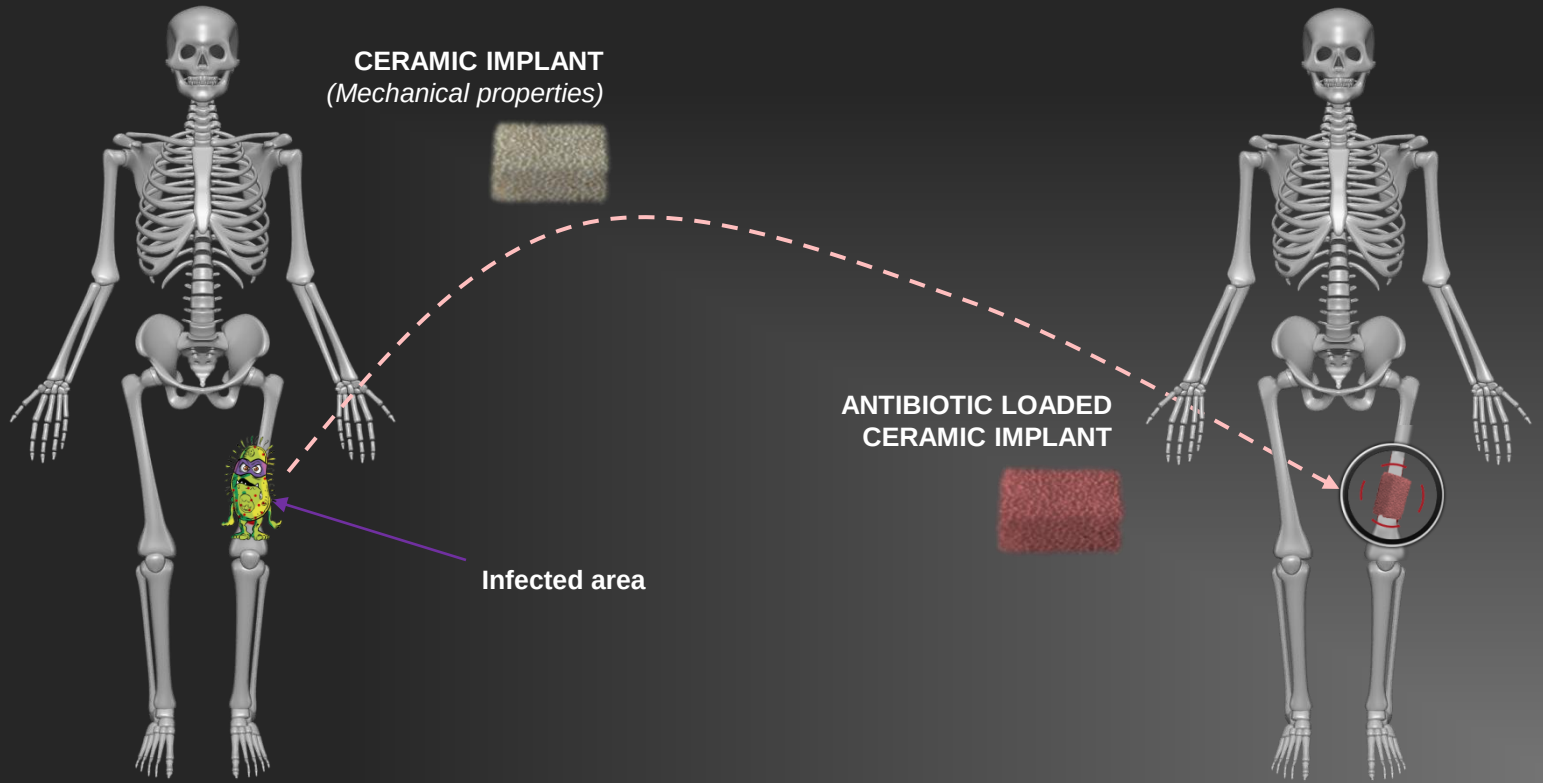
- Very low and undetectable blood passage
  - Decreasing side effects and toxicity

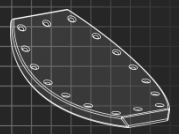
		Concentration (mg/L)					
	Device	H1	H3	H6	H12	H24	H48
# 1	Sternum (gentamicin)	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5
# 2	Sternum (gentamicin)	< 0.5	0,6	0,6	< 0.5	< 0.5	
# 3	Femur flap (gentamicin)	< 0.5	< 0.5	< 0.5		< 0.5	< 0.5
# 4	Sternum (gentamicin)	< 0.5				< 0.5	
# 5	Femur tile (gentamicin)				1.5	< 0.5	< 0.5
# 6	Sternum (gentamicin)	< 0.5	< 0.5	< 0.5	< 0.5	< 0.5	
# 6	Sternum (vancomycin)	< 1.1	< 1.1	< 1.1	< 1.1	< 1.1	

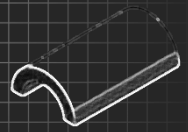
Comparison to other local delivery means

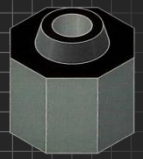


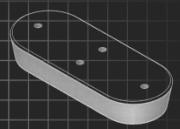
Conclusion


CERAMIC IMPLANT
(Mechanical properties)
ANTIBIOTIC LOADED
CERAMIC IMPLANT
Infected area









Thank you for your attention

Contact: - recherche@iceram.fr
- charlvr@iceram.co.za
www.iceram.fr