

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

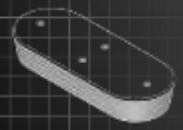
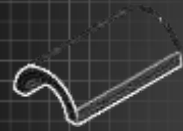
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Context

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

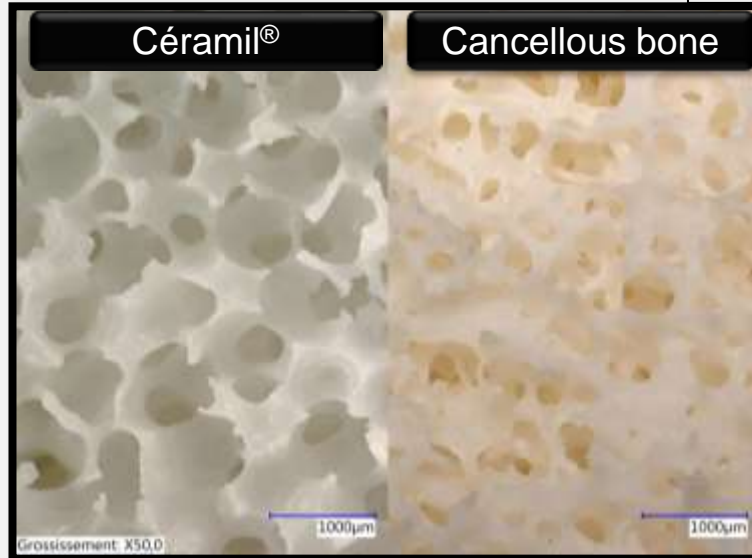
- Proposition:
 - Implantation of a "protected" device (antibiotic loaded)
 - Prophylaxis



The ceramic: main characteristics

Pure alumina Al_2O_3

Proven
biocompatibility, inert



Mechanical strength
more than 20 MPa

Non absorbable

Antibiotics

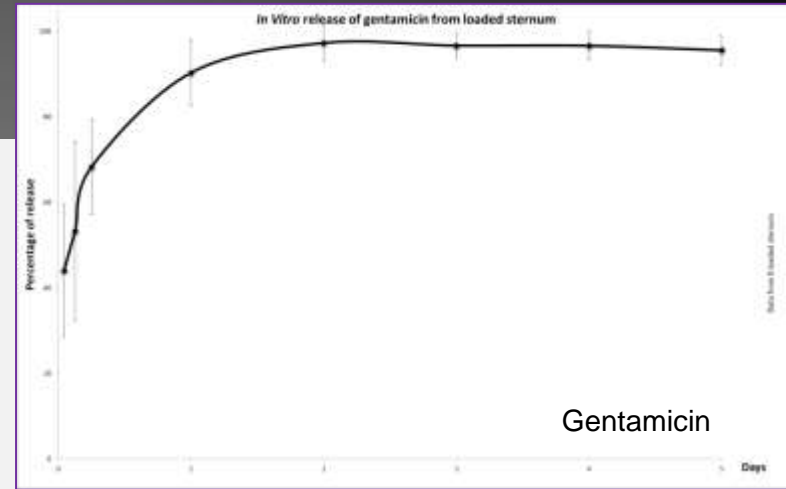
- Antibiotic loaded:

- Gentamicin
- Vancomycin
- Both of them

- Release: 100 %

- Start of release: immediatly

- Release duration: 48 – 72 h (*in vitro*)

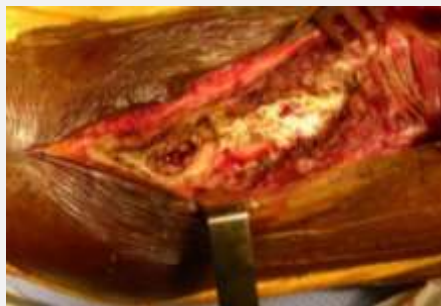


Mediastinitis



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

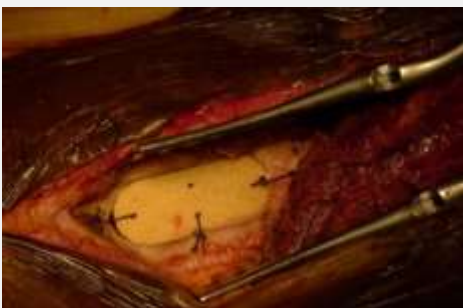
Chronic osteomyelitis (MRSA)



All samples grew with MRSA



Loaded with gentamicin



Follow-up



M11



M17



M11

Chronic osteomyelitis: femoral tile



Gentamicin loaded



X-Ray follow-up M3



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

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 | | | $\frac{C_{max}}{MIC} > 10$ | > 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 (<i>K. pneumoniae</i>) 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

Intravenous

⇒ Expected to fail (MRSE)

Locally (MRSE)

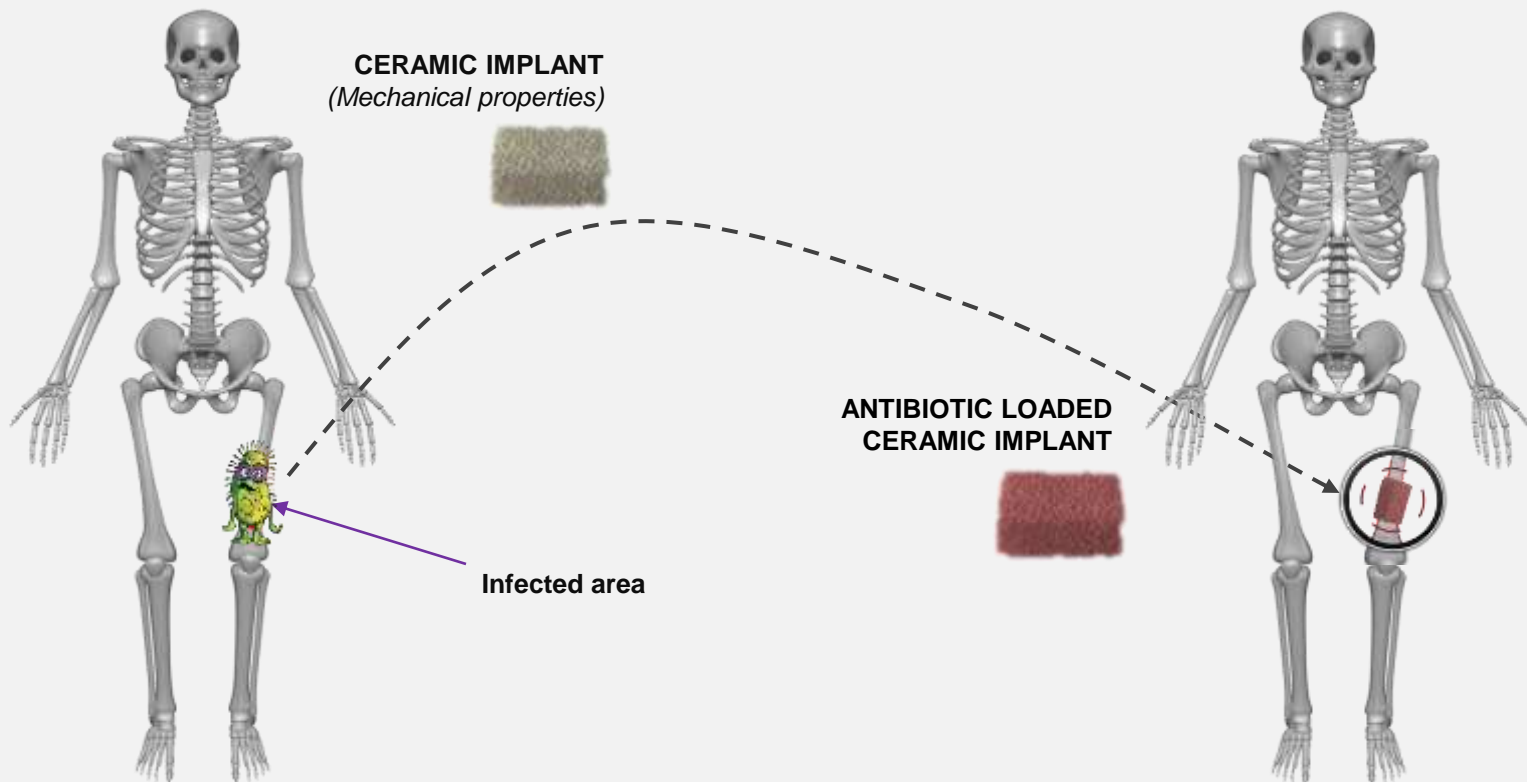
- Gentamicin
 - $C_{\max}/MIC = 17$
 - Vancomycin
 - $AUC/MIC = 16,000$
- ⇒ Expected to be efficient
- M+2 : no relapse

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 | |

Conclusion





**Thank you for your
attention**

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