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Porous Alumina Ceramic as scaffold for bone loss and vector for local antibiotic delivery

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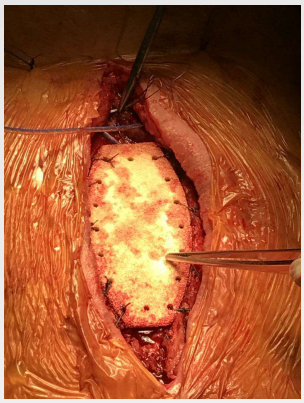
Aim: Bone infections are difficult to treat as diffusion of antibiotics is low. This is even truer when a foreign body is inserted due to the presence of a biofilm protecting bacteria. Local delivery of antibiotics could be an answer however current techniques such as antibiotic loaded cement present several pitfalls. Indeed, cement needs to be remove, it is subject to infection and the amount of antibiotic released is low (less than 10% in the literature) and not well characterized.

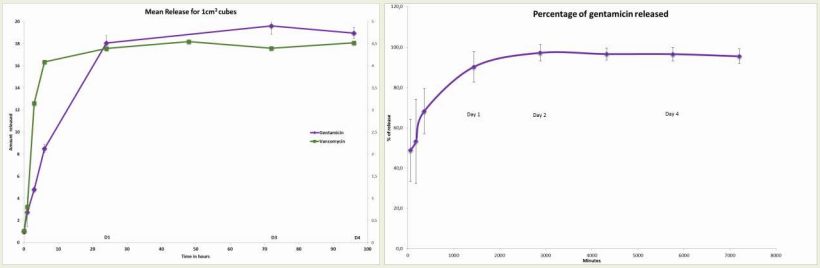
We developed a porous alumina ceramic which can be loaded with antibiotics and acts like a scaffold for bone osseointegration. Indeed, alumina is known for its great biocompatibility and the compressive strength of our product is 3 times greater than native cancellous bone.



Method: We've loaded our ceramics with gentamicin or vancomycin. *In vitro* releases and *in vivo* dosage were performed. *In vitro* release curves were done in physiological serum. *In vivo*, a ceramic sternal prosthesis loaded with about 350 mg of gentamicin was implanted in 2 patients. Blood samples were performed and for patients #2, local dosages thanks to drain redon, placed above the muscular flap, were done after 1 and 24 hours.

Results: *In vitro*, 100% of the loaded antibiotic was released in about 1 to 2 days. *In vivo*, local concentrations were 1,400 mg/L at H1 and 395 mg/L at H24. No gentamicin was found in blood of the 1st patient's samples from H1 to H48 and only very low doses (0.6 mg/L) were found for patient #2 at H3 and H6 but return to undetectable after.

In vitro



In vivo

			Concentration (mg/L)					
	Loaded dose		H1	H3	H6	H12	H24	H48
# 1	225 mg	Blood	< 0,5	< 0,5	< 0,5	< 0,5	< 0,5	< 0,5
# 2	356 mg	Blood	< 0,5	0,6	0,6	< 0,5	< 0,5	
		Local	1400*				395**	

* 175 times the required dose for a bacteria with an MIC of 1 mg/L (taking into account that Cmax/MIC > 8)
** 50 times the required dose

Conclusions: Local delivery achieves very high local concentrations of gentamicin. If we compare it to the once that is efficient (Cmax/MIC > 8) and with a bacteria which have an MIC of 1 µg/ml, the local obtained concentrations are 175 times the dose required at H1 and 50 times the dose required at H24. The results of blood samples demonstrate that there is no risk for kidney function as there is no residual dose. This type of administration using a ceramic allows a high local dose which protects the procedure to avoid a wound and implant infection. This ceramic also possesses mechanical and osseointegration properties which allow to fill bone defect and to use it in a 1 stage surgery without removing it. Further studies are required to assess the bacteriological *in vivo* efficacy of this route of administration.

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