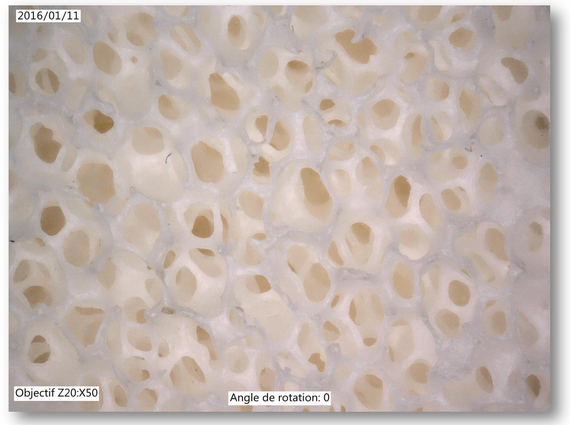
VANCOMYCIN IMMOBILIZATION FOR LONG TERM PROTECTION AGAINST BACTERIA

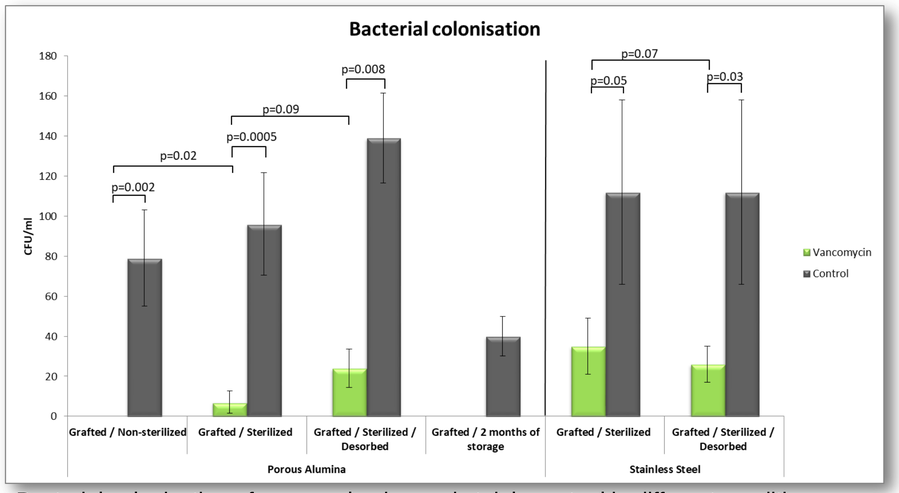
E Poli, G Barrière, G Lévèque, E Denes
[1]R&D Department, I.Ceram, Limoges, France

INTRODUCTION: Prosthetic joint infection is a major issue for patients and surgeons. There are several ways to protect the implant. For example antibiotics are injected pre-operatively as a prophylaxis to decrease infection related to the surgery. A local release can also been used[2]. However, these strategies only protect the time of implantation, but infections also occur during the device life. So a long term protection could be of interest to protect the device, for example, during a transient bacteraemia. The aim of this study was to tether an antibiotic which could keep an activity on the surface in order to protect the device over a long period. Vancomycin was chosen as it acts on the outer membrane of bacteria such as *Staphylococcus spp.* which is the most involved bacteria in prosthetic joint infection. This grafting was performed on stainless steel and porous alumina which are two materials used in our company.

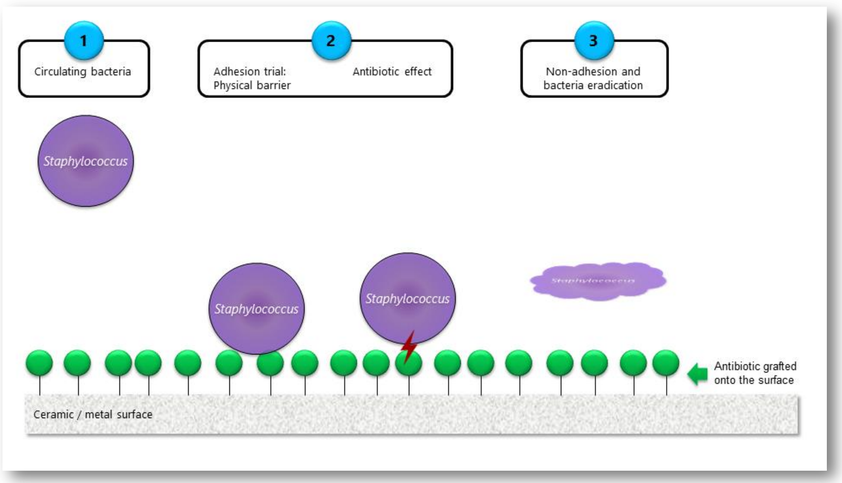


METHODS: We designed disks of porous alumina and stainless steel. Vancomycin was purchase in a pharmacy and was covalently linked to material's surface using a spacer arm which left free the part interacting with bacteria. We used *S. aureus*. Disks were immersed in bacterial suspension (10^6 CFU/ml) for 24 h and were then rinsed and sonicated to evaluate the amount of adherent bacteria. Disks were tested before or after desorption to evaluate the effect of residual vancomycin adsorbed on the surface but not grafted. Indeed this part of antibiotic is released in the bacterial culture and can kill bacteria before they reach the material leading to advantageous results. All disks were sterilized using gamma radiation (25 kG) to be sure that radiation did not decrease the efficacy of the system. Some disks were left in an oven in saline solution at 37°C for two months before bacteria challenge.

RESULTS: Results are presented in the graph. Grafting was efficient in protecting the implant from bacterial colonisation. Sterilization slightly decreased the efficacy but this latter was kept. The desorption did not change the efficacy meaning that even if some bacteria are killed by the released adsorbed antibiotic, the remaining ones can't colonize the material. The grafting was still efficient after the prolonged storage before bacterial challenge.



Bacterial colonisation of porous alumina and stainless steel in different conditions (non-sterilized, sterilized, sterilized desorbed and after 2 months storage)



DISCUSSION & CONCLUSIONS: Vancomycin has already been immobilized on several surfaces such as calcium aluminium oxide, suture threads[2], bone graft and titanium or titanium alloy. Whatever was the material, grafting vancomycin prevented the colonization by *Staphylococcus spp.*. However for the moment no medical application emerged. Calcium aluminium oxide used by Uchida is not used for the moment as a material for medical device contrary to stainless steel and alumina (porous or dense)[3]. In the study by Palchesko they did not performed desorption which could have skewed the results[2]. It is interesting to note that we've challenge our system with a very high amount of bacteria in comparison to the one seen during transient bacteraemia, which is lower (from 10 to 100 CFU/ml). It means that *in vivo* the protection should be even more efficient. Cell culture assays are ongoing to test the potential cytotoxicity of the system. Grafting on bigger shape will test the possibility to use this protection on joint prostheses.

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Contact : Dr Eric DENES: recherche@iceram.fr