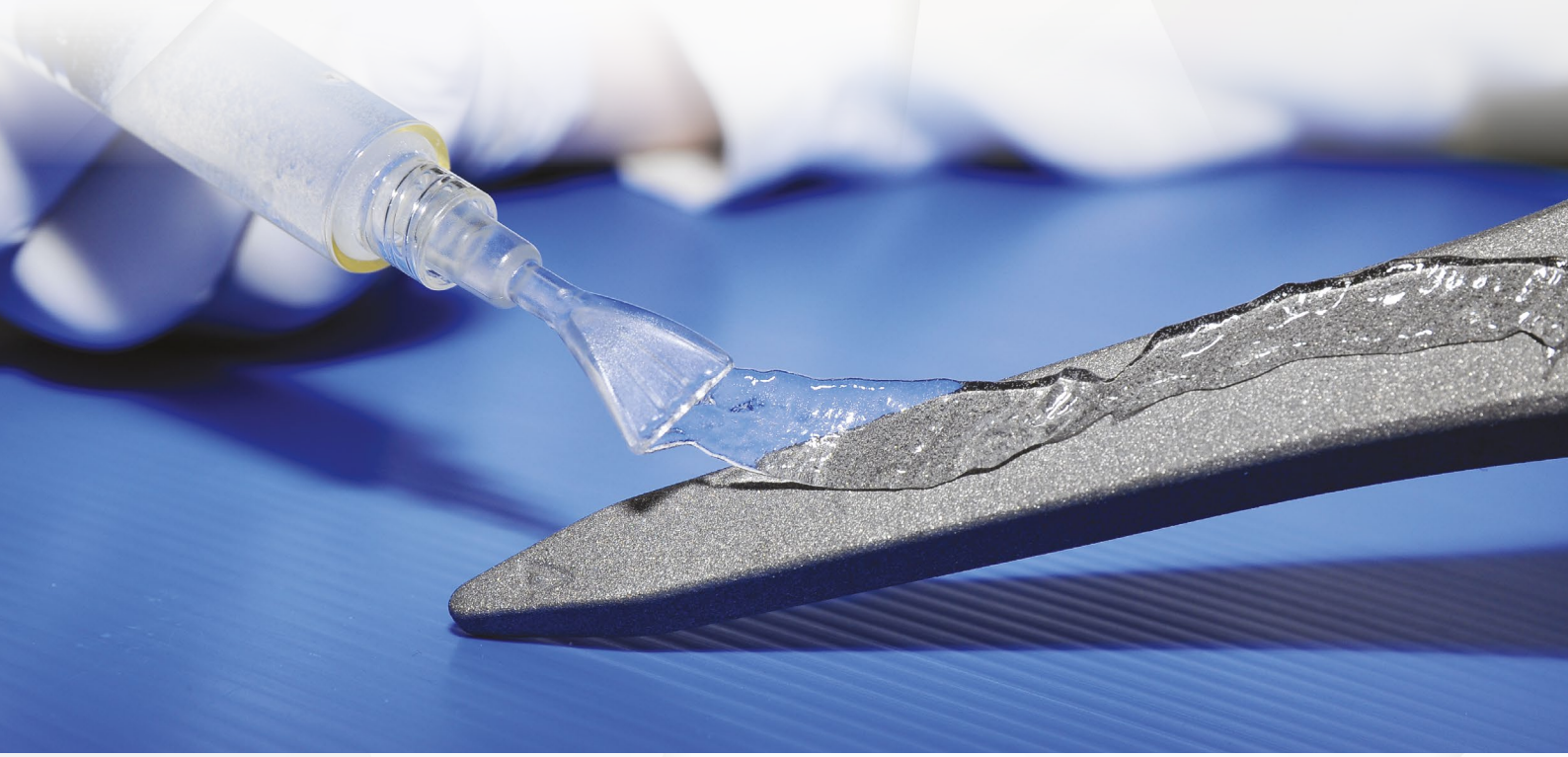
DAC®

DEFENSIVE ANTIBACTERIAL COATING



SCIENTIFIC REFERENCES SUMMARY

2022

INDEX

DAC® - RATIONALE AND INTENDED USE

In spite of systemic antibiotic prophylaxis, **implant-related infection remains one of the leading reasons for failure of joint replacements and of internal osteosynthesis**, with extremely high social and economic associated costs (cf. **Table 1**). [1]

Table 1. Impact of implant-related infections in orthopaedics and trauma: facts and numbers.

Infection risk after joint arthroplasty: the incidence of peri-prosthetic joint infection (PJI) ranges from 1 to 2% after primary implant and up to 10% after revision surgery and in oncological reconstructions; [3] **Infection risk after osteosynthesis**: the incidence of surgical site infection (SSI) after osteosynthesis for closed fractures of the long bones ranges from 2% to 10% [2]. The incidence of SSI after open fractures of the long bones is more than 20%; [3]
Leading reason for revision: Peri-prosthetic hip and knee infection is among the first three reasons for joint replacement failure, according to the registers; [4]
Mortality risk: the adjusted relative mortality risk (RR) for patients with hip revision for PJI, compared with the patients who did not undergo revision surgery is 2.18 [5]. The RR for patients undergoing hip revision for PJI, compared with aseptic hip revision, ranges from 1.87 to 3.10; [6]
Additional costs: the average cost of management of infection after hip fracture surgery is > 30,000 Euros. [6] The cost for the management of any single case of hip or knee PJI ranges from 40,000 to > 100,000 Euros. [7, 8]

All implant-associated infections share complex diagnostic and treatment procedures, due to the presence of bacterial biofilm(s) and slow-growing, persistent microorganisms, able to even survive into the host's cells and often resistant to most or all of the available antibiotics.

Given its challenging treatment, prevention is pivotal in reducing the periprosthetic joint infection burden.

To this aim, providing implanted biomaterials with an antibacterial coating or finishing has been advocated by experts and respected institutions as one of the most promising solutions, in order to mitigate the impact of septic complications. [9]

In line with this vision, **the "Defensive Antibacterial Coating" (DAC®, Novagenit Srl, Mezzolombardo, Italy) has been specifically designed to protect from bacterial colonization and biofilm formation a wide variety of implantable biomaterials used in orthopaedics, traumatology, dentistry and maxillofacial surgery**.

The biodegradable hydrogel is intended to serve as **a temporary physical barrier against the bacterial adhesion and the formation of microbial biofilms**.

DAC® represents an additional measure of infection prevention, which is not intended to replace or to substitute the asepsis measures and the usual protocols of antibiotic prophylaxis recommended in orthopedic surgery.

This “White Paper” is aimed at providing a comprehensive review of the evidence related to the preclinical and clinical results in orthopaedics and trauma *.

In particular, evidence will be provided concerning the following statements:

- **DAC® IS MADE OF HIGHLY BIOCOMPATIBLE POLIMERS**
- **DAC® IS SAFE ACCORDING TO *IN VITRO* RESULTS**
- **DAC® HAS A PROVEN ANTIBIOFILM ACTIVITY**
- **DAC® IS EFFECTIVE AND SAFE *IN VIVO***
- **DAC® PROVIDES AN AVERAGE 8 TIMES REDUCTION OF POST-SURGICAL IMPLANT-RELATED INFECTIONS IN ORTHO-TRAUMA**
- **NO SIDE EFFECTS REPORTED**
- **DAC® IS ASSOCIATED WITH A FAVORABLE COST-BENEFIT-RATIO**

For more information, you may also visit:

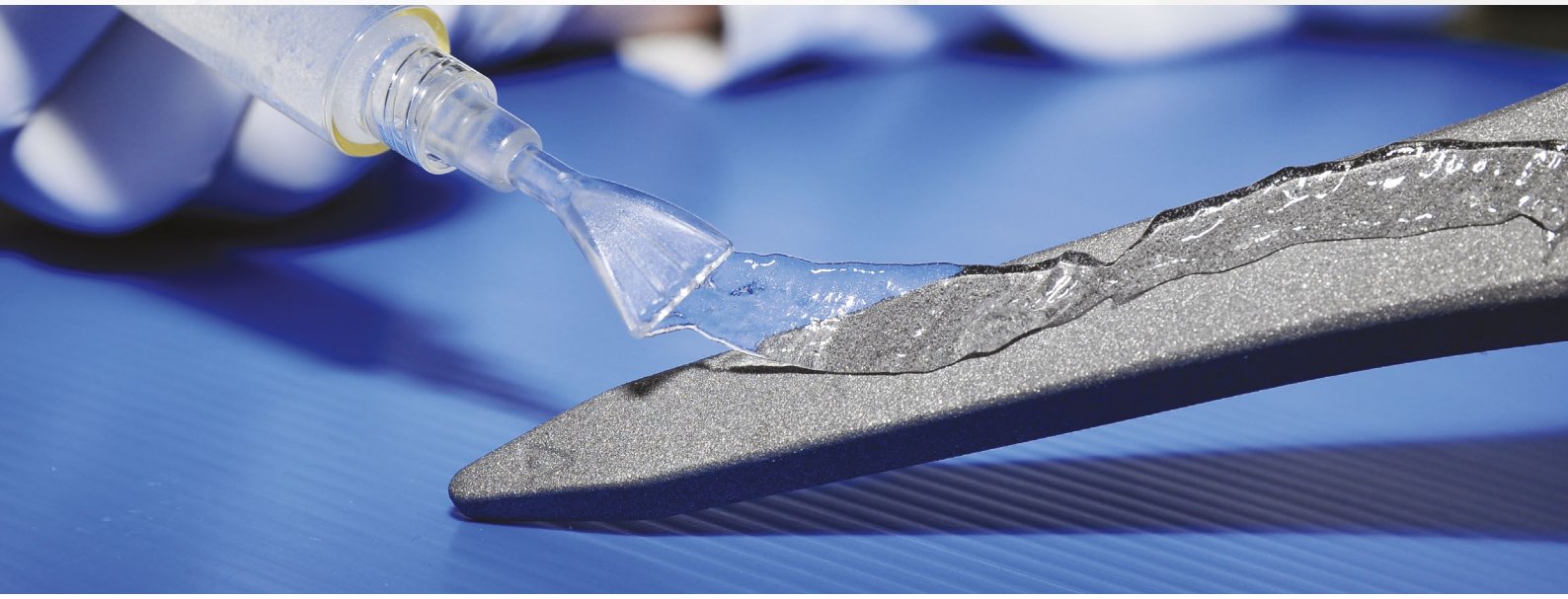
www.dac-coating.com

www.novagenit.com

* Not all available studies on DAC® technology are included in this White Paper.

DAC®

DEFENSIVE ANTIBACTERIAL COATING



IN VITRO DATA *

* ALL THE CLINICAL PAPERS SUMMARIZED IN THIS SECTION CAN BE FOUND AND REVIEWED IN THE "SCIENTIFIC REFERENCES" SECTION OF THE DAC® WEBSITE WWW.DAC-COATING.COM

Chemical structure

Composed of covalently linked hyaluronan (HA) and poly-d,l-lactide PLA) (**Fig. 1**), the "Defensive Antibacterial Coating" (DAC®, Novagenit Srl, Mezzolombardo, Italy) has been specifically developed in order to protect implanted biomaterials used in orthopaedics, traumatology, dentistry and maxillofacial surgery from bacterial colonization. [10,11]

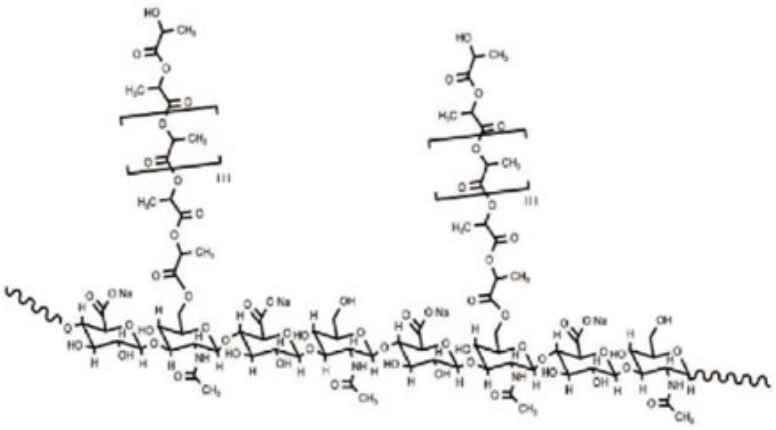


Fig. 1. Chemical structure of the HA-g-PLA copolymer

As a medical device, DAC® is in the form of a kit, composed of a sterile, double-sealed syringe, containing a powder, intended to be mixed at the time of surgery with a water-based solution to form the hydrogel; also provided are accessories, suitable to apply the hydrogel coating on the surface of the implants.

DAC® is composed by highly biocompatible and fully resorbable biopolimers.

Cell compatibility assay

In vitro cell compatibility of DAC® HA-g-PLA hydrogel (polymer concentration 6%, w/v) was evaluated using human dermal fibroblasts. The viability of cells cultured in direct or indirect contact with HA-g-PLA hydrogel was comparable with that of the control well, showing that the hydrogel does not release in the culture medium substances that interfere with cell viability and they do not cause a decrease in the cell viability after direct contact with them. [10]

Further *in vitro* and *in vivo* biocompatibility studies were performed on the DAC® hydrogel and on the DAC® kit, in accordance to ISO standards, all showing no cytotoxicity, genotoxicity, sensitization, irritation or intracutaneous reactivity, systemic toxicity (acute), subchronic toxicity or interference with bone or peri-implant tissues (Novagent Srl, data on file).

Furthermore, as degradation of DAC® HA-g-PLA hydrogel occurs via deesteriication of hyaluronic acid and polylactic acid, it gives raise exclusively to the starting macromolecules, whose degradation pathways in the human body are widely known and whose use as implantable class III medical devices is largely accepted and tested safe.

DAC® showed full *in vitro* biocompatibility.

In the human body the DAC® hydrogel gives rise only to tested safe macromolecules.

Antiadhesive and antibiofilm activity

The mechanism of action is related to the antifouling and antiadhesive properties of hyaluronic acid.

Both the ability of the DAC® HA-g-PLA hydrogel to reduce bacterial adhesion and biofilm formation were extensively studied *in vitro*.

Reductions of adhered bacteria on sterile titanium discs, coated with DAC® hydrogel, equal to 86.8, 80.4, 74.6 and 66.7% vs. untreated discs were observed after 15, 30, 60 and 120 min of incubation, respectively [12] (Fig. 2).

In another experiment, the ability to dislodge previously adhered bacteria was investigated.

Once again, the results showed that **DAC® hydrogel treatment of discs reduced the amount of adhered bacteria in respect to control discs after 15, 30, 60 and 120 min by 84.0, 72.8, 72.3 and 64.3%, respectively** (**Figg. 2-5**). [12]

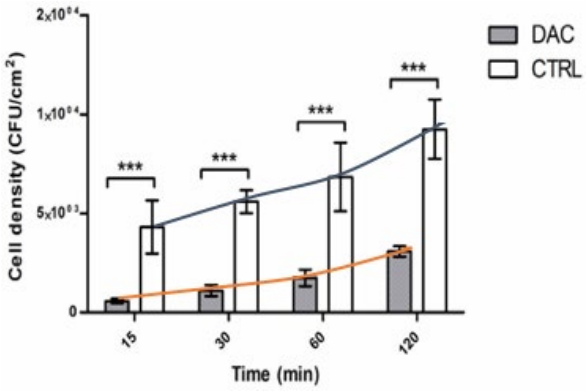


Figure 2. Adhesion densities of *S. aureus* (mean CFU/cm2 ± standard deviation) to discs pre-treated with DAC® ("Defensive Antibacterial Coating", Novagenit Srl, Mezzolombardo, Italy) and controls at 15, 30, 60 and 120 min; *** P < 0.001 (two-way ANOVA followed by Bonferroni post hoc test). [12]

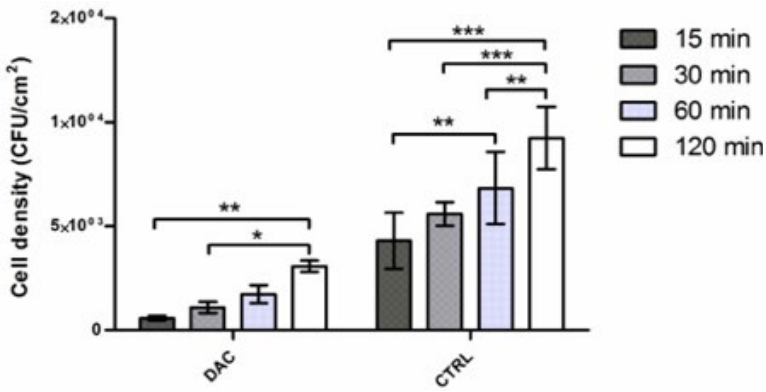


Figure 3. Adhesion densities of *S. aureus* (mean CFU/cm2 ± standard deviation) over time in pre-treated with DAC® and control discs at 15, 30, 60, 120 min; * 0.01 < P <0.05, ** 0.001 < P < 0.01, *** P < 0.001 (two-way ANOVA followed by Bonferroni post hoc test). [12]

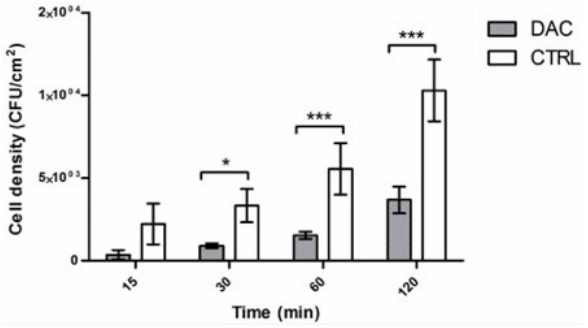


Figure 4. Adhesion densities on discs with of *S. aureus* (mean CFU/cm2 ± standard deviation) applied before DAC® treatment and controls at 15, 30, 60, 120 min; * 0.01 < P <0.05, *** P < 0.001 (two-way ANOVA followed by Bonferroni post hoc test). [12]

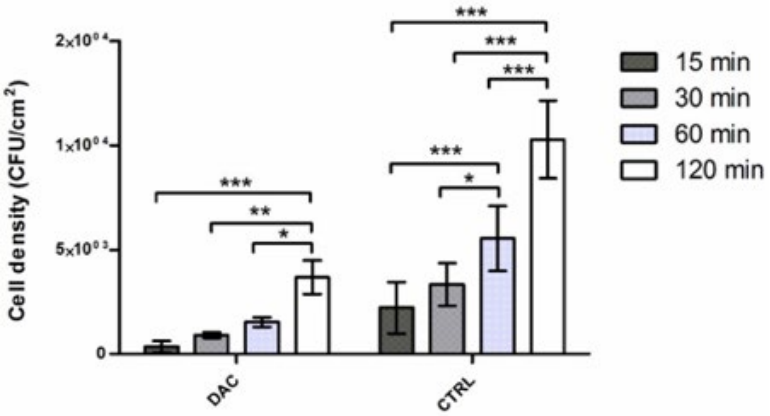


Figure 5. Adhesion densities over time on discs with of *S. aureus* (mean CFU/cm2 ± standard deviation) applied before DAC® treatment and controls at 15, 30, 60, 120 min; * 0.01 < P <0.05, ** 0.001 < P < 0.01, *** P < 0.001 (two-way ANOVA followed by Bonferroni post hoc test). [12]

Concerning more specifically the antibiofilm activity, **DAC® hydrogel showed similar or superior *in vitro* activity, compared to various antibacterials and a synergistic activity when used in combination.** [11]

In one experimental setting, *S. epidermidis* and *S. aureus* were grown on chrome-cobalt devices in 6-wells polystyrene plates containing TSB for 24 h at 37°C. The plates were incubated at 37°C in ambient air, until a visible biofilm was obtained. Gentamycin and vancomycin were tested at a final concentration of 20 mg/mL. Similarly, when mixed with the hydrogel, 60 mg of gel powder was reconstituted with 1 mL of water for injections containing gentamicin or vancomycin at 20 mg/mL concentration. The amount of biofilm at each time was determined before hydrogel and antibiotic agents' addition and after 0.5, 1, 2, 4, 6, 24 and 48 h of incubation by a spectrophotometric assay.

At each time point, both gentamicin and vancomycin showed only a partial inhibition of biofilm formation (ca. 30–40% for gentamicin; ca. 40–50% for vancomycin), with minor difference between the two studied microorganisms.

On the other side, **the hydrogel alone resulted in a significant reduction of biofilm of ca. 50%, in comparison to the untreated controls, while a combination of the hydrogel with either antibacterial coating resulted in a larger reduction of biofilm formation (approximately 75–80% in comparison with untreated controls)** (**Fig. 6**). [12]

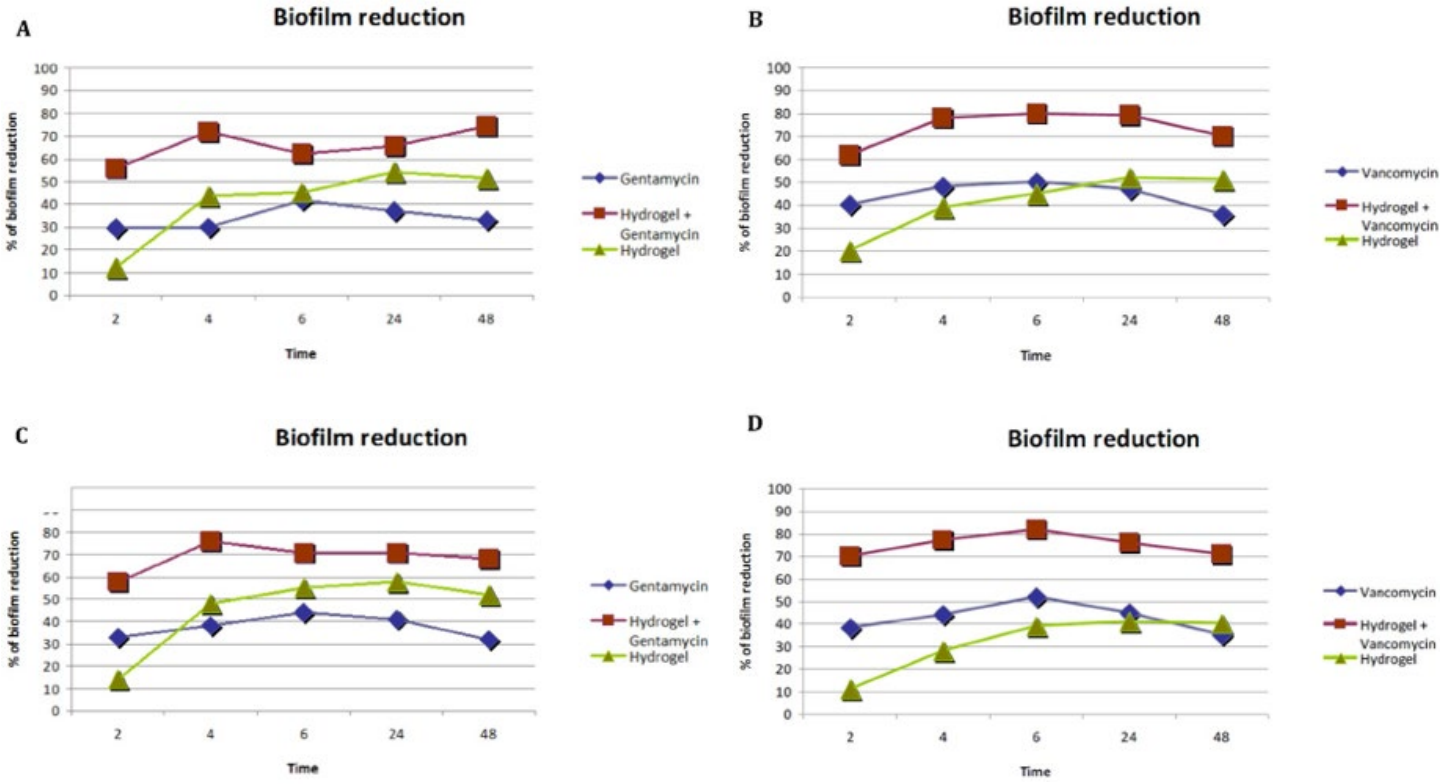


Figure 6. Comparison of the efficacy of DAC® hydrogel, gentamicin, vancomycin or a combination thereof, on biofilm formation reduction of *Staphylococcus aureus* (A. and B.) and *Staphylococcus epidermidis* (C. and D.) over time (hours). Note that **the hydrogel alone is able to provide an equal or superior biofilm reduction compared to commonly used antibiotics**, while a synergistic effect is observed using a combination of the hyaluronic acid based hydrogel and the antibiotic compounds. [12]

DAC® Hydrogel coating has a proven antiadhesive and antifilm activity.

When combined with vancomycin or gentamycin, the DAC® hydrogel shows a synergistic antifilm activity.

Rationale for the intra-operative DAC® hydrogel antibiotic loading

Preclinical studies have demonstrated the ability of the DAC® hydrogel to significantly reduce bacterial adhesion and biofilm formation of common bacterial pathogens, thus providing an effective protection of the implant.

According to this model, the antiadhesive hydrogel coating acts as a tool to reduce and delay bacterial adhesion and biofilm formation to a variable degree, depending on the local environment, the bacterial species and the bacterial load; **this activity of the coating may represent a key additional advantage to the host's cells to win the competition with the microorganisms that may eventually be present**.

Reducing the ability of bacteria to adhere to the implant **will decrease the chance of bacterial colonization and infection, provided that the immune system and eventually the systemically administered antibiotic are able to kill the microorganisms in their planktonic state**.

However, **since the hydrogel coating has no bactericidal activity,** it may be anticipated that, **whenever the immune system should fail to destroy the planktonic microorganisms, these may still have the chance to colonize the implant and the surrounding tissues at a later stage**, when the coating will be hydrolyzed or covered by the host's proteins.

This observation supports the **ancillary function exerted by the antibiotic(s), that may be loaded intra-operatively to the DAC® hydrogel,** in order to minimize the possibility for planktonic bacteria, which may eventually remain in the local environment, to overcome the anti-fouling coating of the implant at a later stage, once the coating hydrolysis proceeds (**Fig. 7**). [13]

Furthermore, several studies have shown i. the ability of the hydrogel to be loaded and to completely release all the tested antibiotics in less than 72 hours; ii. The synergistic effect of the hydrogel + antibiotic, compared to either component alone [11]; iii. The absence of any measurable side effects of the antibiotic-loaded **DAC® hydrogel coating both in preclinical [14,15] and in all available clinical studies [cf. Clinical Data - Safety].**

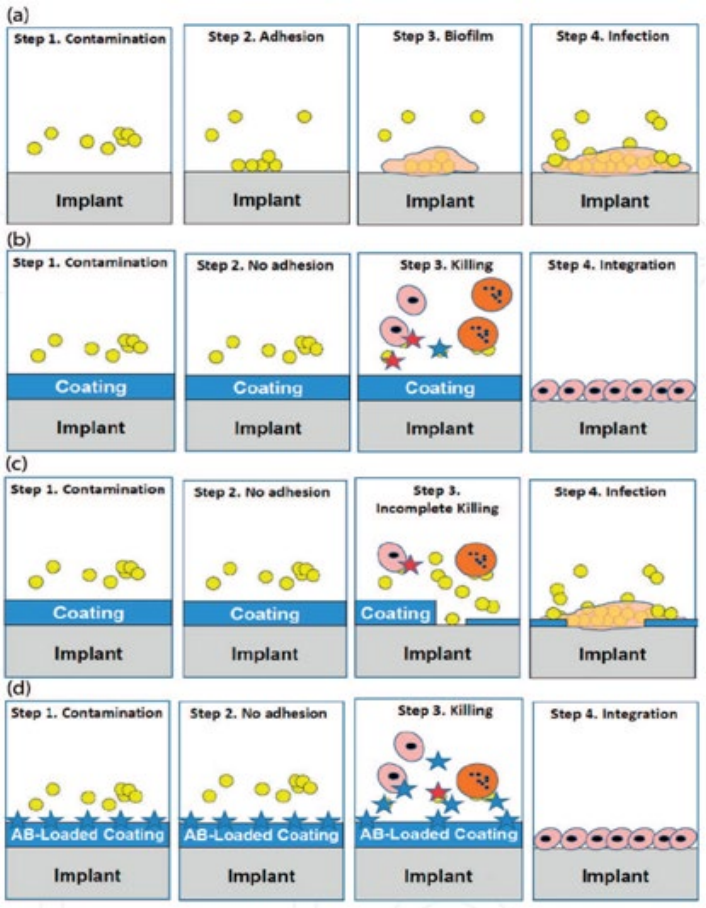


Figure 7. Rationale for intra-operative mixing of DAC® hydrogel coating with antibacterial agents. Schematic representation of different scenarios. (a) Noncoated implants may get colonized by biofilm-forming bacteria (yellow circles) and infection will develop. (b) Antiadhesive coating may reduce/prevent bacterial adhesion, while the immune system (orange circles and red stars) and the systemically administered antibiotics (blue star) kill planktonic microorganisms. (c) However, if bacterial load is large enough, or if immune response and local antibiotic levels are inadequate, surviving bacteria may eventually colonize the implant, once the coating has been hydrolyzed or covered by host's proteins. (d) To prevent this, the antibacterial hydrogel may be loaded, at the time of surgery, with antibiotic agents (blue stars) that may be locally released, contributing to eliminate all remaining planktonic bacteria. [13]

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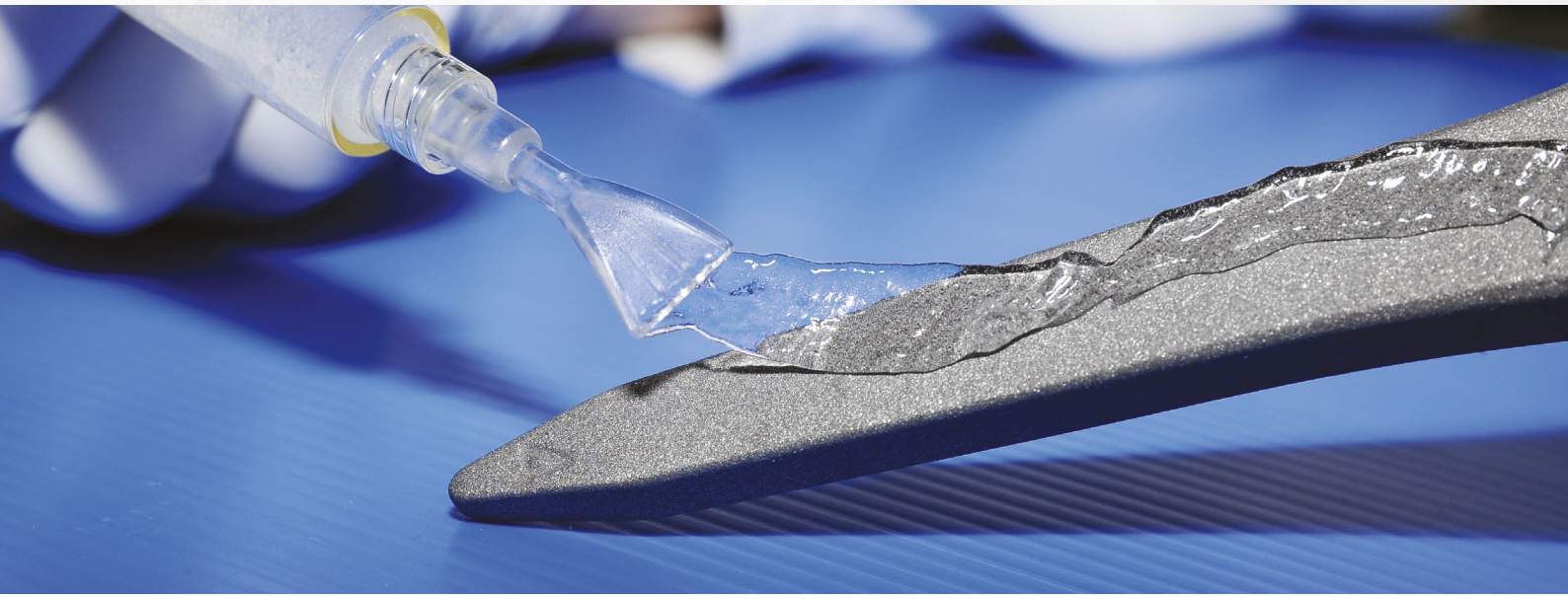

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ANTIBIOTIC-LOADED DAC® HYDROGEL IS ABLE TO SIGNIFICANTLY REDUCE BACTERIAL COLONIZATION IN A HIGHLY CONTAMINATED RABBIT MODEL OF IMPLANT-RELATED INFECTION, WITH NO LOCAL OR SYSTEMIC SIDE EFFECTS

International Orthopaedics (SICOT) (2014) 38:1505–1512
DOI 10.1007/s00264-013-2237-2

ORIGINAL PAPER

Efficacy of antibacterial-loaded coating in an in vivo model of acutely highly contaminated implant

Gianluca Giavaresi · Enzo Meani · Maria Sartori · Andrea Ferrari · Davide Bellini · Anna C. Sacchetta · Joachim Meraner · Andrea Sambri · Caterina Vocale · Vittorio Sambri · Milena Fini · Carlo L. Romanò

Received: 17 November 2013 / Accepted: 26 November 2013 / Published online: 22 December 2013

Methods A histocompatibility study was performed in 10 adult New Zealand rabbits. Then, methicillin-resistant Staph. aureus were inoculated in the femur of 30 adult New Zealand rabbits at the time of intra-medullary nailing; vancomycin-loaded DAC® coated nails were compared to controls regarding local and systemic infection development.

Results Histocompatibility study showed **no detrimental effect of DAC® hydrogel on bone tissue after 12 weeks from implant**.
After seven days from implant, none of the rabbits receiving vancomycin-loaded DAC® nail showed positive blood cultures, compared to all the controls; **vancomycin-loaded DAC® coating was associated with local bacterial load reduction ranging from 72 to 99 %, compared to controls**.

Conclusions
Vancomycin-loaded DAC® coating is able to **significantly reduce bacterial colonization in an animal model of an intra-operatively highly contaminated implant, without local or general side effect**. [14]

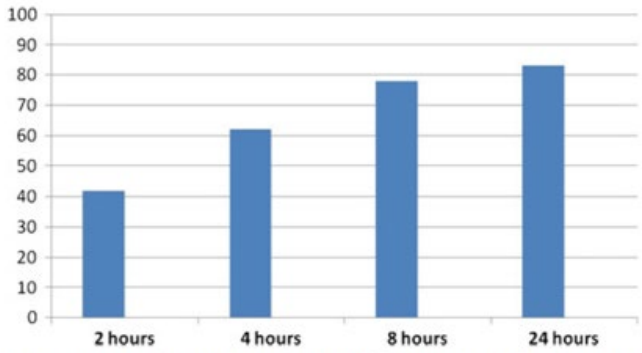

Fig. 1 Release of vancomycin from DAC® hydrogel at defined intervals during incubation at 37 °C. Release expressed as percentage of total antibiotic quantity loaded

More than 80% of the antibiotic is released in the first 24 hours from the **DAC® hydrogel.**

This observation is in line with that observed in in vitro studies, showing complete antibiotic release within 72 hours.
The fast and complete antibiotic release provides the best antibacterial activity, minimizing the risk of antibiotic resistance induction.

ANTIBIOTIC-LOADED DAC® HYDROGEL HAS A PROTECTIVE EFFECT ON BONE HEALING IN A CONTAMINATED RAT MODEL OF NON-UNION

Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2016, Article ID 9595706, 12 pages
http://dx.doi.org/10.1155/2016/9595706

Hindawi

Research Article

Systemic and Local Administration of Antimicrobial and Cell Therapies to Prevent Methicillin-Resistant *Staphylococcus epidermidis*-Induced Femoral Nonunions in a Rat Model

Arianna B. Lovati,[1] Lorenzo Drago,[2,3] Marta Bottagisio,[1,4] Matilde Bongio,[1] Marzia Ferrario,[5] Silvia Perego,[6] Veronica Sansoni,[6] Elena De Vecchi,[2] and Carlo L. Romanò[7]

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Microbiological detection of bacterial growth on the explanted specimens.
Comparisons among groups were analyzed with one-way ANOVA corrected with Bonferroni's *post hoc* test. Statistical significance was $p < 0.01$ (**), and $p < 0.001$ (***); $n = 6$. At 42 days from surgery, **DAC® hydrogel** enriched with vancomycin at 5% (v/w) (l-VANC), distributed on plates and screws during the osteosynthesis, shows nearly undetectable bacterial growth, which is significantly lower that that observed in controls without the coating (PC) and even lower than that observed in systemically administered vancomycin (s-VANC).

Forty-two days after surgery, 50% of the **DAC® hydrogel** coated osteosynthesis showed bone healing at the fracture site, compared to 0 % and 33 % in the control and s-VANC groups, respectively, demonstrating a clear **protective effect of the coating on bone healing**. [15]

	Bony bridging > 75% fracture healing
Controls	0 %
s-VANC	33 %
l-VANC	50 %

In this Animal model DAC® Hydrogel coating applied to internal osteosynthesis provided a protection against infected non-unions.

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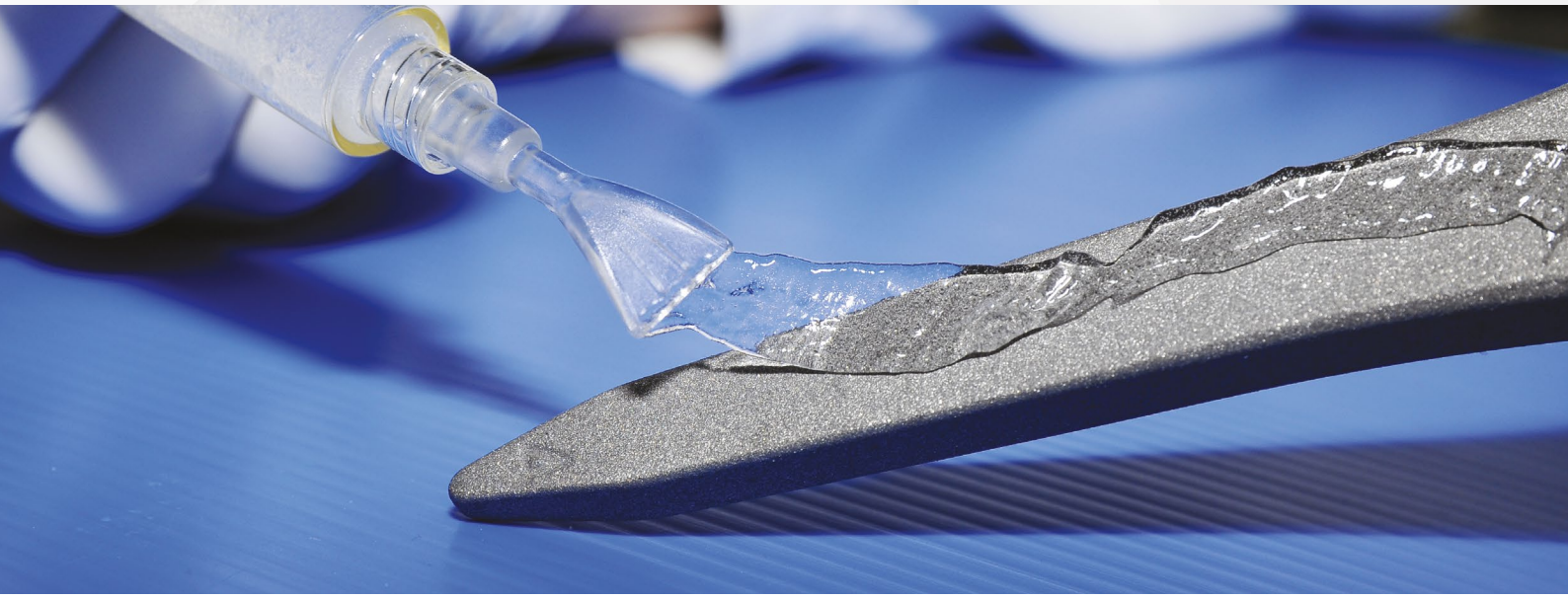

CLINICAL DATA *

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J. Bone Joint Infect. 2016, Vol. 1 34

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Journal of Bone and Joint Infection

2016; 1: 34-41. doi: 10.7150/jbji.15986

Research Paper

Does an Antibiotic-Loaded Hydrogel Coating Reduce Early Post-Surgical Infection After Joint Arthroplasty?

Carlo Luca Romanò[1]✉, Kostantinos Malizos[2], Nicola Capuano[3], Riccardo Mezzoprete[4], Michele D'Arienzo[5], Catherine Van Der Straeten[6, 7], Sara Scarponi[1] and Lorenzo Drago[8, 9]

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9. Laboratory of Medical Technical Sciences, Department of Biochemical Sciences for Health, University of Milano, Italy.

Study profile:

- Condition: Total hip or knee joint replacement
- Intervention: Intraoperative application DAC® + Antibacterial Agent
- Study design: Single blind - randomized - controlled - multicenter
- Endpoint classification: safety and efficacy study
- Primary outcome measures:
  - clinical and laboratory evidence of safety
  - clinical and laboratory evidence of efficacy
- Level of evidence II

Study population:

373 patients

- 189 treated group - prosthesis and DAC®
- 184 control group - prosthesis

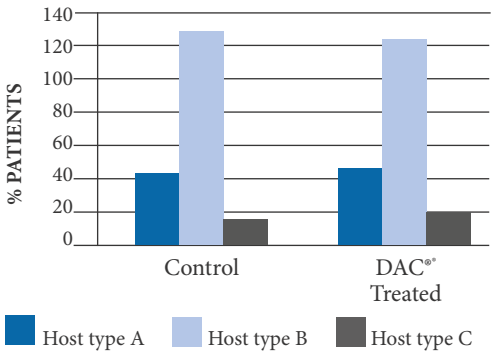
Mean age (years): 71 ± 10.6 (control)

Mean age (years) 69 ± 12.6 (treated)A

		CONTROLS	%	TREATED	%
JOINT	HIP	141	76.6	153	80.9
	KNEE	43	23.4	36	19.0
TYPE OF SURGERY	PRIMARY	132	71.7	135	71.8
	REVISION	52	28.3	54	28.2

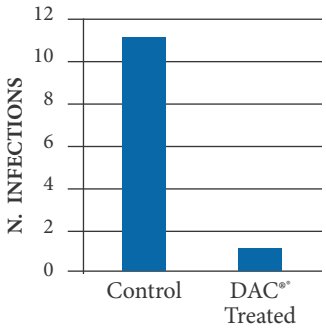
Risk profile:

In both groups 76% of the patients presented with one or more relevant co-morbidity known to increase postsurgical infection risk (McPherson's classification)



DAC® Effectiveness Evidence :

11 surgical site infections were reported in the control group (6%), compared to only one (0.6%) in the treated group (P=0.003) at 14.5 months follow-up



TREATED PATIENT					
HOST TYPE	RELEVANT CO-MORBIDITIES	PRE-OPERATIVE DIAGNOSIS	ONSET OF INFECTION (MONTHS FROM SURGERY)	CULTURAL EXAMINATION	TREATMENT
B	DIABETES; BMI > 40	HIP OSTEOARTHRITIS	< 1	NEGATIVE CULTURES	NO FURTHER INFECTION RECURRENCE

13.5% (7/52) of control group second stage revision developed surgical site infection vs 0% (0/54) in the treated group. 3% (4/132) of control group primary surgery developed SSI vs 0% (0/135) in the treated group.

Conclusions The patient population presents an incidence of high risk factors. Results showed 6% infection in the control group, versus 0.5% occurrence of infection in the treated group (P<0.003).

J Orthop Traumatol (2017) 18:159–169
DOI 10.1007/s10195-017-0442-2

ORIGINAL ARTICLE

Fast-resorbable antibiotic-loaded hydrogel coating to reduce post-surgical infection after internal osteosynthesis: a multicenter randomized controlled trial

Kostantinos Malizos[1] · Michael Blauth[2] · Adrian Danita[2] · Nicola Capuano[3] · Riccardo Mezzoprete[4] · Nicola Logoluso[5] · Lorenzo Drago[6,7] · Carlo Luca Romanò[5]

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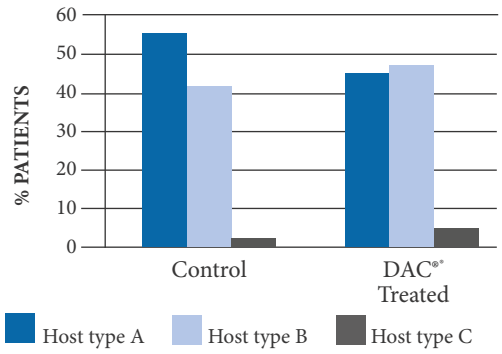
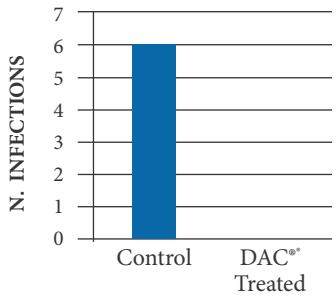
Study profile:

- Condition: Closed fresh fractures of long bones requiring the use of plates or intramedullary nails
- Intervention: Intraoperative application of DAC® + Antibacterial Agent
- Study design: Single blind - randomised - controlled - multicentre
- Endpoint Classification: safety and efficacy study
- Primary outcome measures:
  - clinical and laboratory evidence of safety
  - clinical and laboratory evidence of efficacy
- Level of evidence II

Risk profile:
In both groups approximately half of the patients presented with one or more relevant co-morbidities known to increase postsurgical infection risk (McPherson's classification)



DAC® Effectiveness Evidence :
Six surgical site infections were reported in the control group (4.7%), compared to none in the treated group (P=0.02) at 18 months follow-up.
75% of control group host type C developed surgical site infection.



Study population:
253 patients

- 126 treated group- internal osteosynthesis and DAC®
- 127 control group– internal osteosynthesis

Mean age (years): 58.6 ±17.6 (control) and 62.5±21.2 (treated)

TYPE OF FIXATION	CONTROLS	%	TREATED	%
PLATE/SCREW	117	92.1	115	91.3
INTRAMEDULLARY NAIL	10	7.9	11	8.7

Fracture site:

FRACTURE SITE	CONTROLS	%	TREATED	%
FEMUR	32	25.2	47	37.3
TIBIA/KNEE	11	8.7	16	12.7
ANKLE/FOOT	29	22.8	32	25.4
CLAVICLE	11	8.7	10	7.9
HUMERUS	8	6.3	6	4.8
FOREARM/ WRIST	29	22.8	14	11.1
HAND	7	5.5	1	0.8

Conclusions About 50% of the enrolled patients presenting one or more co-morbidities. The results are very encouraging with 4.7% of the control group presenting with infection, versus 0% in the treated group (P<0.02).

Knee Surgery, Sports Traumatology, Arthroscopy
https://doi.org/10.1007/s00167-018-4896-4

KNEE

One-stage exchange with antibacterial hydrogel coated implants provides similar results to two-stage revision, without the coating, for the treatment of peri-prosthetic infection

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Received: 23 March 2017 / Accepted: 12 March 2018

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Level of evidence III.

Methods In this two-center case–control, study, **22 patients**, treated with a one-stage procedure, using implants coated with an antibiotic-loaded hydrogel [defensive antibacterial coating (DAC®)], were compared with **22 retrospective matched controls**, treated with a two-stage revision procedure, without the coating.

Results At a **mean follow-up of 29.3 ± 5.0 months**, **two patients (9.1%) in the DAC® group showed an infection recurrence, compared to three patients (13.6%) in the two-stage group**. Clinical scores were similar between groups, while **average hospital stay and antibiotic treatment duration were significantly reduced after one-stage, compared to two-stage (18.9 ± 2.9 versus 35.8 ± 3.4 and 23.5 ± 3.3 versus 53.7 ± 5.6 days, respectively).**

Conclusions
Although in a relatively limited series of patients, our data shows similar infection recurrence rate after one-stage exchange with DAC®-coated implants, compared to two-stage revision without coating, with reduced overall hospitalization time and antibiotic treatment duration.

International Orthopaedics
https://doi.org/10.1007/s00264-018-4206-2

ORIGINAL PAPER

Two-stage cementless hip revision for peri-prosthetic infection with an antibacterial hydrogel coating: results of a comparative series

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Received: 6 October 2018 / Accepted: 12 October 2018

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Methods In this case-control study, **27 patients**, treated with a two-stage procedure, using cementless implants coated with an antibiotic-loaded hydrogel (DAC®, "Defensive Antibacterial Coating"), were **compared with 27 matched controls**, treated with a two-stage cementless revision procedure, without the coating.

Results At a **mean follow-up of 2.7 (minimum 2.1–maximum 3.5) years, no evidence of infection, implant loosening, or adverse events were observed in the DAC®-treated group, compared to four cases of infection recurrence in the control group**.

	DAC® (N=27)	Controls (N=27)
Harris Hip Score	84.6 ± 15.8	81.6 ± 15.2
Hospital stay incl. rehabilitation (days)	28.2 ± 3.9	33.8 ± 5.4
Hip dislocation	1	1
Delayed wound healing	0	1
Infection	0	4 (14.8%)

Conclusions
Although in a relatively limited series of patients our data show that cementless two-stage hip revision, performed with an antibacterial hydrogel coating, may provide better infection control than two-stage without the coating, with reduced hospitalization time, these findings warrant further studies in the possible applications of antibacterial coating technologies to treat implant-related infections.

microorganisms

MDPI

Article

Antibiotic-Loaded Hydrogel Coating to Reduce Early Postsurgical Infections in Aseptic Hip Revision Surgery: A Retrospective, Matched Case-Control Study

Daniele De Meo [1,*], Valeria Calogero [1], Lorenzo Are [1], Armando U. Cavallo [2], Pietro Persiani [1] and Ciro Villani [1]

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check for updates

Abstract

Periprosthetic joint infections (PJIs) are a cause of frequent implant failure in revision hip replacement surgery. The purpose of this study is to evaluate the onset of early postoperative infections in patients who underwent hip surgery with cementless prostheses treated with an antibiotic loaded hydrogel on their surface, in addition to systemic prophylaxis, and compare them to a control group. The secondary objective was to evaluate the onset of any local and systemic adverse effects and interference with bone ingrowth processes and functional recovery. A retrospective observational study was conducted on patients who underwent revision hip surgery by performing a 1:1 match between patients treated with an antibiotic hydrogel (ALH) and the control patients. The incidence of PJIs was assessed with a minimum of six months follow-up. Seventeen patients treated with the ALH were compared with 17 patients from the control group. No PJIs were reported in the ALH group versus the six cases encountered in the control group ($p < 0.0001$). No significant differences were reported with regard to prosthetic osseointegration and functional results, nor were there side effects in the ALH group.

Conclusions

Despite the low sample size, the use of on-site prophylaxis with ALH has proven effective and safe in reducing the risk of PJIs in patients with a high risk for infections. Further studies are needed to validate these results in other implant-related surgeries.

Editorial (on invitation only)

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SAGE

Defensive antibacterial coating in revision total hip arthroplasty: new concept and early experience

Massimo Franceschini[1], N Amir Sandiford[2], Vincenzo Cerbone[1], Lucio Cappelli Toledo de Araujo[3,4] and Daniel Kendoff[4]

Abstract

Background: Infections remains the most feared complication in total hip arthroplasty (THA). New strategies of PJI prevention includes coating of conventional implants. Defensive Antibacterial Coating (DAC®), an antibacterial hydrogel coating made of hyaluronan, poly-D and L-lactide can protect biomaterials as an effective barrier at the time of implantation. In addition, it can be used with topical antibiotics to prevent early colonisation of the implant.

Scope: This manuscript describes the detailed function of the DAC® in general as well as an analysis of its use in revision THA in a series of 28 patients in a short-term follow-up. Its use in patients undergoing cementless re-implantation after 2-staged procedures in THA is described in detail within the manuscript.

Conclusions
DAC® found to be effective in terms of infection control and safety in our patient cohort and has been expanded for cementless 1-staged revisions in PJI of the hip in our institution.

European Journal of Orthopaedic Surgery & Traumatology
https://doi.org/10.1007/s00590-021-02884-7

ORIGINAL ARTICLE

Antibacterial hydrogel coating in joint mega-prosthesis: results of a comparative series

Carmine Zoccali[1] · Guido Scoccianti[2] · Roberto Biagini[1] · Primo Andrea Daolio[3] · Fabio Luca Giardina[3] · Domenico Andrea Campanacci[2]

Received: 22 November 2020 / Accepted: 18 January 2021

Abstract

Purpose Joint mega-prosthesis after bone tumors, severe trauma or infection is associated with high rates of post-surgical septic complications. A fast-resorbable antibacterial hydrogel coating (DAC®, Defensive Antibacterial Coating) has previously
been shown to be able to significantly reduce surgical site infection in various clinical settings. Aim of the present study was to evaluate the safety and efficacy of the DAC® hydrogel coating to prevent early periprosthetic joint infection after joint mega-prosthesis.

Methods In this three-centers, case–control study, 43 patients, treated with an antibacterial hydrogel coated mega-prosthesis for oncological *(N = 39)* or non-oncological conditions *(N = 4)*, were retrospectively compared with 43 matched controls,
treated with mega-implants without the coating. Clinical, laboratory and radiographic examinations were performed to evaluate the occurrence of post-surgical infection, complications and adverse events. Results At a mean follow-up of 2 years, no evidence of infection or adverse events were observed in the DAC®-treated group, compared to six cases of post-surgical infection in the control group.

Conclusions
This matched case–control study shows that a fast-resorbable, antibiotic-loaded coating can be safely used to protect joint mega-prosthesis, providing a reduction of early surgical site infections with no side effects. Larger prospective trials with longer follow-ups are warranted to confrm this report.

Neuro and Spine Surgery
SURGICAL TECHNOLOGY INTERNATIONAL Volume 39

Antibiotic-Loaded Hydrogel Coating for the Prevention of Local Infection after Vertebral Surgery: A Retrospective Cohort Analysis

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Abstract

Background: To preliminarily assess the effectiveness of a highly viscous antibiotic-loaded hydrogel used as a coating for the prevention of a superficial and deep Surgical Site Infections (SSIs) after laminectomy and fusion in instrumented vertebral surgery.

Methods: We performed a retrospective cohort analysis on 73 consecutive patients who underwent surgery from June 2018 to December 2019 for degenerative spinal disorders (DSD) or traumatic fractures with segmental instability. Patients received the antibiotic-loaded hydrogel over the implants perioperatively and were observed postoperatively for 12 months.

Results: Postoperative evaluations showed no adverse events in the study population. None of the patients reported significant pain or functional limitation after surgery. Post-surgically, computed tomography scans confirmed the correct positioning of instruments. At 12 months follow-up, no infection was recorded in the overall population.

Conclusions
This retrospective investigation highlights the importance of adopting measures to prevent SSIs in instrumented vertebral surgery. The intraoperative local use of an antibiotic-loaded hydrogel, complementary to systemic antibiotic therapy, appears to minimize the risk of superficial and deep infection.

Original research article

IJAO The International Journal of Artificial Organs

High rate of infection eradication following cementless one-stage revision hip arthroplasty with an antibacterial hydrogel coating

The International Journal of Artificial Organs
1–5

DOI: 10.1177/0391398821995507
journals.sagepub.com/home/jao
SAGE

Antonio Pellegrini[1] and Claudio Legnani[2]

Abstract

Purpose We conducted a retrospective study to evaluate the outcomes of one-stage revision total hip arthroplasty (THA) following periprosthetic joint infection (PJI) in terms of eradication of the infection, improvement of pain and joint function. We hypothesized that this treatment strategy could lead to satisfying results in selected patients after preoperative microorganism isolation.

Methods: Ten patients underwent cementless one-stage revision hip arthroplasty with antibacterial hydrogel coating for the treatment of an infected THA. Inclusion criteria were: the presence of a known organism with known sensitivity, patients non-immunocompromised with healthy soft tissues with minimal or moderate bone loss. Mean age at surgery was 69.4 years. Assessment included objective examination, Harris hip score, visual analog scale pain score, standard X-rays.

Results: At a mean follow-up of 3.1 years (range, 2–5 years), none of the patients had clinical or radiographic signs suggesting recurrent infection. Follow-up examination showed significant improvement of all variables compared to pre-operative values ($p < 0.05$). Radiographs did not show progressive radiolucent lines or change in the position of the implant.

Conclusions
One-stage revision THA with antibacterial hydrogel coated implants represents a safe and effective procedure providing infection eradication and satisfying subjective functional outcomes in selected patients.

gels

MDPI

Communication

Clinical Application of Antibacterial Hydrogel and Coating in Orthopaedic and Traumatology Surgery

Daniele De Meo [1,2,*], Giancarlo Ceccarelli [2,3], Giancarlo Iaiani [2,3], Federico Lo Torto [2,4], Diego Ribuffo [2,4], Pietro Persiani [1] and Ciro Villani [1,2]

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Abstract

Implant related infection is one of the most frequent complications in orthopaedic and trauma surgery. Local antibiotic treatment strategies are becoming part of the prevention and treatment methodology for this fearful complication. To date, there are two coatings available on the market, both with a polylactic acid base. Current evidence supports the use of these types of coatings in the prophylaxis of periprosthetic infections and fracture-related infections. However, their therapeutic use has been less investigated. The purpose of this article is to summarise recent evidence relating to the clinical application of antibacterial hydrogels and coatings in orthopaedic and traumatology surgery and indicating which future applications may benefit from it.

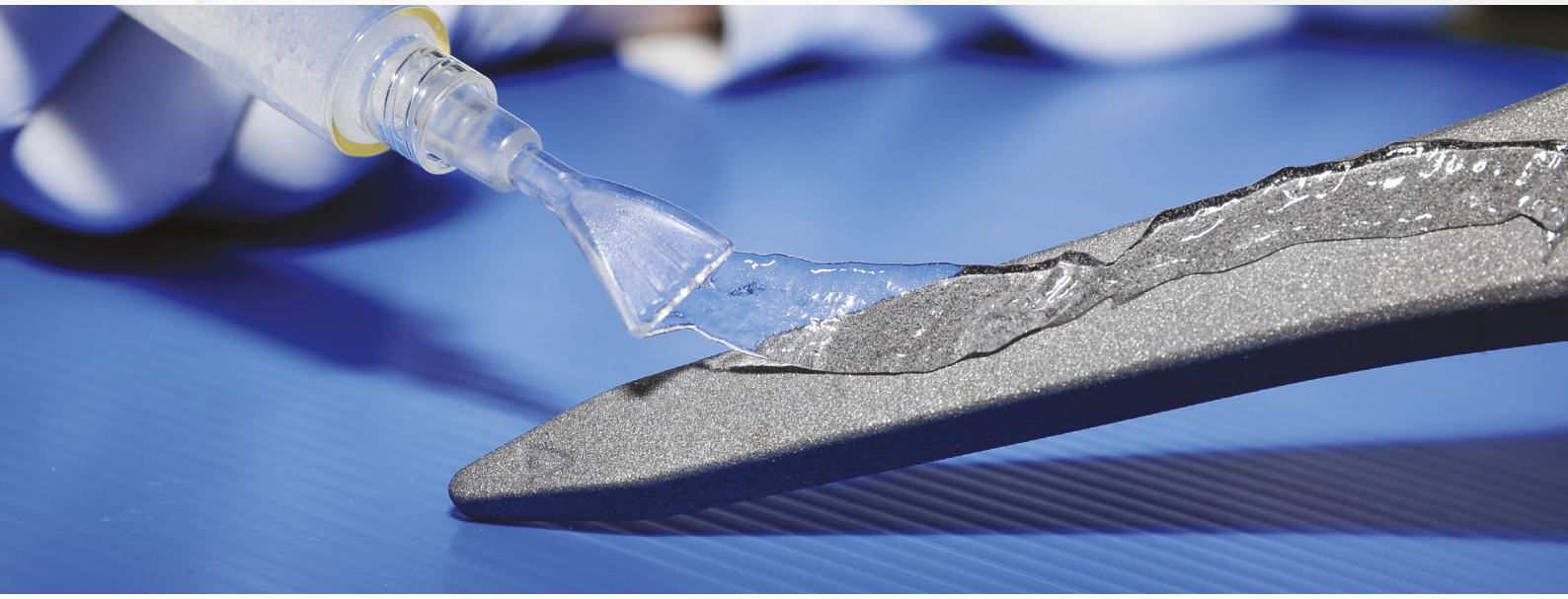
Keywords: periprosthetic joint infection; fracture related infection; osteomyelitis; coating; antibacterial hydrogel; open fractures; infection; osteosynthesis; gentamicin-coated nail; antibiotic-coated nail

Conclusions

The clinical application of antibiotic gels and coatings is becoming more and more prominent within the prophylaxis and multidisciplinary treatment of implant-related infections. Its clinical results are promising though based mainly on low-number retrospective studies, especially in the area of fracture-related infections. Prospective randomized studies are needed in order to determine their effectiveness in different situations.

DAC®

DEFENSIVE ANTIBACTERIAL COATING



DAC® USAGE IMPACT ON HEALTHCARE COSTS *

* ALL THE CLINICAL PAPERS SUMMARIZED IN THIS SECTION CAN BE FOUND AND REVIEWED IN THE "SCIENTIFIC REFERENCES" SECTION OF THE DAC® WEBSITE WWW.DAC-COATING.COM

POSITIVE COST-BENEFIT BALANCE OF THE LARGE SCALE USE OF THE DAC® HYDROGEL COATING, APPLIED TO JOINT REPLACEMENT

The Journal of Arthroplasty xxx (2018) 1–7

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The Journal of Arthroplasty

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Economic Evaluation of Antibacterial Coatings on Healthcare Costs in First Year Following Total Joint Arthroplasty

Maria Teresa Trentinaglia, PhD [a, b], Catherine Van Der Straeten, MD [c], Ilaria Morelli, MD [d], Nicola Logoluso, MD [e], Lorenzo Drago, MD, PhD [f], Carlo L. Romanò, MD [e, *]

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Abstract

Background: Antibacterial coatings (ABCs) of implants have proven safe and effective to reduce post-surgical infection, but little is known about theirpossible economic impact on large-scale use. This studye valuated the point of economic balance, during the first year after surgery, and the potential overall annual healthcare cost savings of 3 different antibacterial technologies applied to joint arthroplasty: a dual-antibiotic-loaded bone cement (COPAL G þ C), an antibacterial hydrogel coating (DAC®), and a silver coating (Agluna).

Methods: The variables included in the algorithm were average cost and number of primary joint arthroplasties; average cost per patient of the ABC; incidence of periprosthetic joint infections and expected reduction using the ABCs; average cost of infection treatment and expected number of cases.

Results: The point of economic balance for COPAL G þ C, DAC®, and Agluna in the first year after surgery was reached in patient populations with an expected postsurgical infection rate of 1.5%, 2.6%, and 19.2%, respectively. If applied on a national scale, in a moderately high-risk population of patients with a 5% expected postsurgical infection rate, COPAL G þ C and DAC® hydrogel would provide annual direct cost savings of approximately V48,800,000 and V43,200,000 (V1220 and V1080 per patient), respectively, while the silver coating would be associated with an economic loss of approximately V136,000,000.

Conclusions
This economic evaluation shows that ABC technologies have the potential to decrease healthcare costs primarily by decreasing the incidence of surgical site infections, provided that the technology is used in the appropriate risk class of patients.

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Notes

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