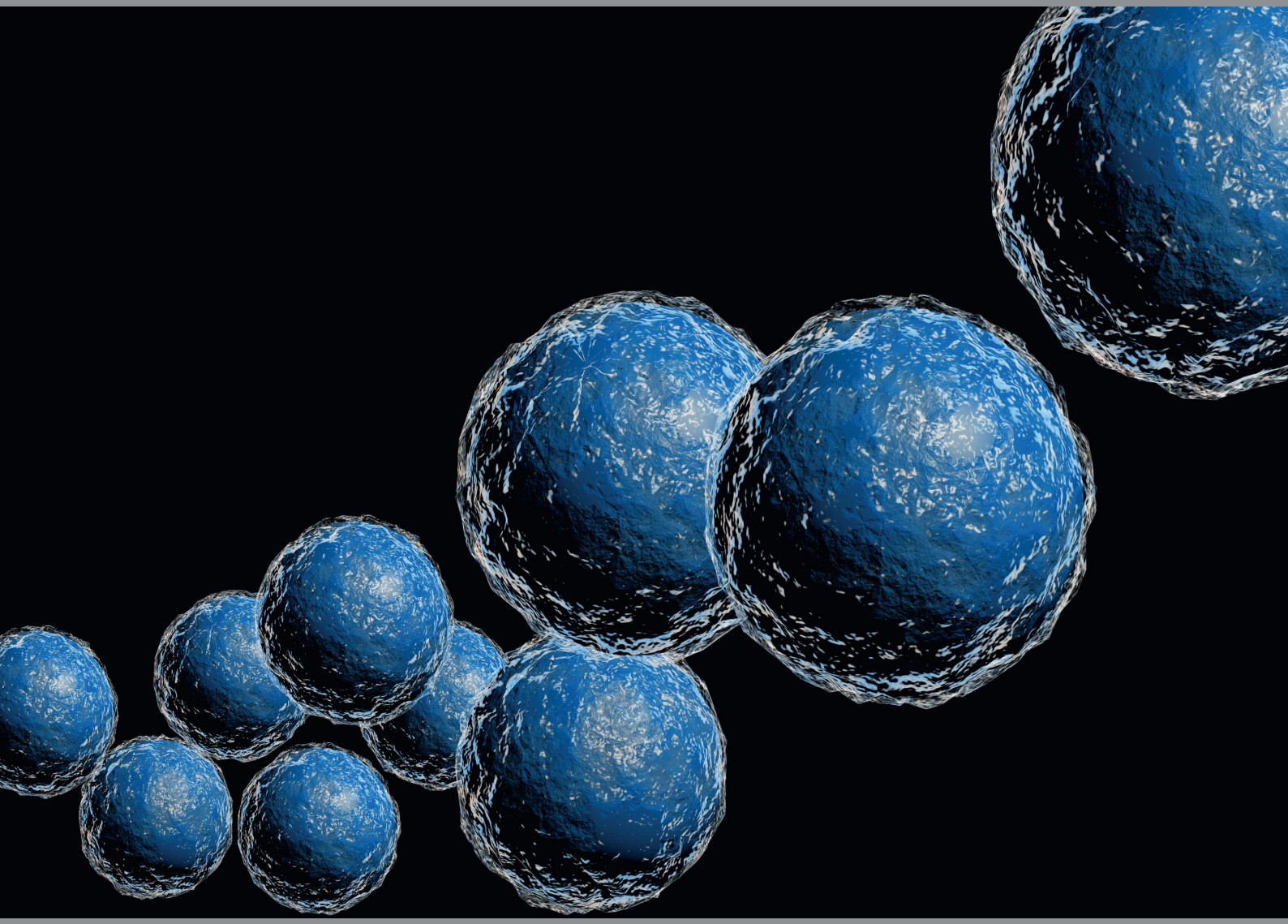
JOINTLY
BUILDING BRIDGES

C+TBA
austria

Loading of allogenic bone grafts with

ANTIBIOTICS



Single Stage Revision

The local prophylaxis and therapy of bone infections is carried out with antibiotic-loaded carriers. An aggressive debridement – similar to tumor surgery – of the infected and necrotic bone, soft tissues and foreign materials can be carried out in a single stage revision. Reducing the biological burden of pathogens and improving the effectiveness of the patient's immune system and of the antibiotics against surviving pathogens is the goal of treatment. The following describes in detail the loading of allografts with antibiotics and their release.[1, 2, 3]

Surgical Procedure

Musculoskeletal infections remain one of the most challenging and serious complications in orthopedic and trauma surgery. The mainstay of treatment and the starting point in defect management is the radical surgical debridement of the infected and necrotic tissue as well as the complete removal of extraneous material.

The defect resulting after debridement has to be filled in order to minimise the accumulation of exudate and haematoma and thus not provide an environment for replication of any bacteria that may still be present.

In the single step procedure, by applying antibiotics to Allograft C+TBA granules, concentrations can be achieved that are locally significantly higher than with systemic therapy alone. In this way, the transplant can be protected against colonisation by any germs that may still be present. The local antibiotic treatment acts as an adjuvant therapy, only, without causing a significant systemic burden.[4, 5]

Long term clinical experience and scientific studies in this context demonstrated that the healing of tissue around the allogenic bone material is not jeopardised by high local antibiotic levels.[1, 7, 15]

In addition, allografts loaded with antibiotics improve the local milieu in the transplant area, which gives the body's own tissue cells a better chance of winning the so-called „race for the surface" over the competing pathogenic microorganisms.[8]

Antibiogram

Biopsies from the infected area should be taken for microbiological testing and determination of the susceptibility or resistance of the bacteria to the tested antibiotics (antibiogram).[6]

According to recent findings, good clinical results can only be achieved by means of radical surgical debridement and targeted antibiosis.[5,6,9]

The selection of the therapy based on the patient related antibiogram is exclusively in the responsibility of the attending physician. The presentation and list of the options for local antibiosis below serve as a non-binding decision aid.[3]

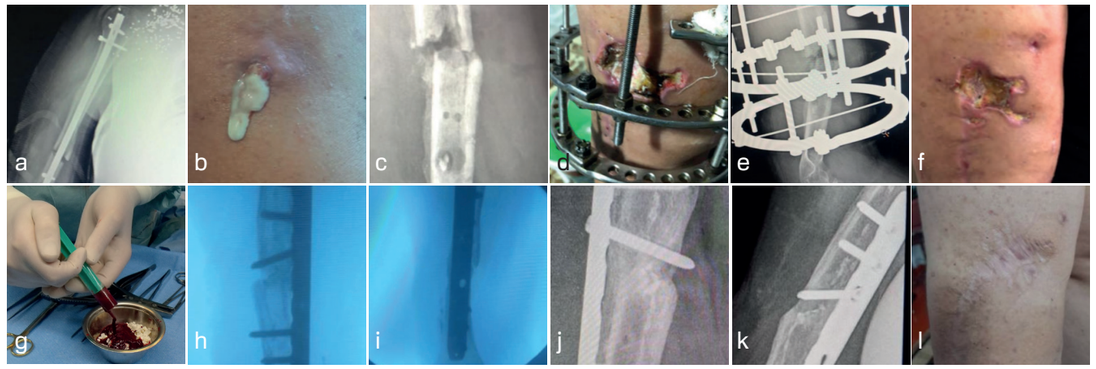
Rehydration of Allograft C⁺TBA

Allograft C⁺TBA is rehydrated before use. Typically, this process is completed after 10 minutes of placing the graft in 0.9% saline solution, Ringer's solution, blood, or antibiotic solution.[10] Bone material and antibiotic solution (ml) are mixed at a ratio of 1:1.

Solubility of Different Antibiotics in Water

The solubility of the antibiotics limits the maximum initial loading because only a certain amount of solution can be absorbed by the allograft. Dosages exceeding this are free in the liquid phase. It is to be expected that these will result in a high initial antibiotic concentration.[11]

ANTIBIOTIC	SOLUBILITY IN WATER [g/ml]
Vancomycin	0.1
Tobramycin	0.08



Gunshot wound with humerus fracture, interlocking nail, bony defect, postoperative infection with pus formation (a, b); infected defect with fistula formation (c); removal of nail, Ilisarov fixator, soft tissue defect with existing infection, removal of fixator 3 months later (d, e, f); radical debridement of bone and soft tissue, local flap, stabilisation with plate osteosynthesis, defect reconstruction with allograft C+TBA granules mixed with iliac crest aspirate, vancomicin and rifampicin, intraoperative radiograph (g, h, i); 15 months after surgery X-ray and local findings after excision and flap closure, bony reconstruction (j, k, l).

Loading of Allografts with Antibiotics

The allografts are loaded with antibiotics at a ratio of 1:1, which is made from water for injection (WFI) and the respective antibiotic tested in advance in the antibiogram.

The following tables indicate the quantities for preparing 10 ml antibiotic solutions, which can then be used for rehydrating 10 ml Allograft C⁺TBA.

Mix according to Winkler et al., 2000[12]

ANTIBIOTIC (AB)	AB [g]	WATER [ml]	CONC. [g/l]
Vancomycin	1	10	100
Tobramycin*	0.8	10	80

** Tobramycin and Gentamicin belong to the same antibiotics group of the aminoglycosides.*

Mix according to Witsø et al., 2000[13]

ANTIBIOTIC (AB)	AB [g]	WATER [ml]	CONC. [g/l]
Benzylpenicillin	1	10	100
Cefalotin	1	10	100
Clindamycin	1.5	10	150
Netilmicin	1	10	100
Vancomycin	0.5	10	50
Ciprofloxacin	0.02	10	2
Rifampicin	0.6	10	60

The treatment of implant-associated infections and osteomyelitis remains a great challenge. Biofilm-associated bacteria show an ongoing reduction of susceptibility to the known antibiotics.

An in-vitro study that was published recently demonstrates that the therapy of *Staphylococcus epidermidis* biofilm with different glycopeptides increases the total biofilm share and that the antibiotics used (Vancomycin, Teicoplanin, Oxacillin, Rifampicin and Gentamicin) have no marked bactericidal effect.[14]

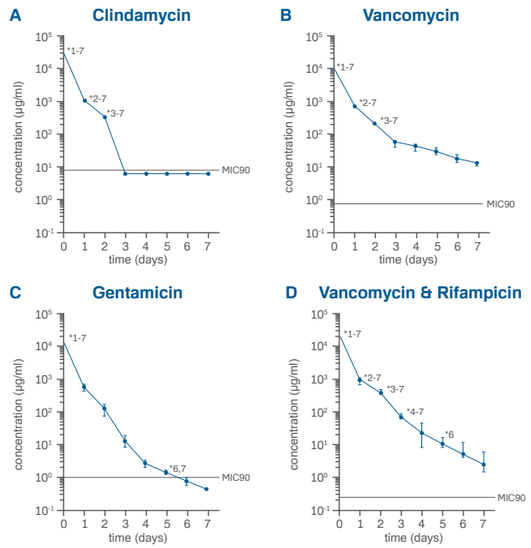
However, when Vancomycin or Teicoplanin is combined with Rifampicin, a part of the biofilm of *Staphylococcus epidermidis* is neutralised and positively affects the bactericidal effect.[5, 6, 9]

Allograft C⁺TBA as an Antibiotic Carrier: An In Vitro and In Vivo Study

A recent study conducted in cooperation between the Medical University of Innsbruck, the Technical University of Berlin, the University of Niš, and the Justus Liebig University of Giessen aimed to evaluate the efficacy of Allograft C⁺TBA as a carrier for antibiotics in order to prevent acute infections and promote bone healing.

The study demonstrated that the technique of rehydration of the allograft blocks in antibiotic solutions was both effective and readily implementable. A 10-minute rehydration duration was determined to be sufficient for effective delivery, without compromising the mechanical stability and bony ingrowth of the Allograft C⁺TBA.

The present study investigated the release of four distinct antibiotics. The results show that the antibiotic release from Allograft C⁺TBA blocks was sustained above the minimum inhibitory concentration for multiple days, both in vitro and in vivo.[15] Furthermore, the allografts were observed to foster bone remodeling.[15]



In vitro release kinetics of allogenic bone blocks loaded with antibiotics up to seven days after incubation in clindamycin (A), vancomycin (B), gentamicin (C), and vancomycin in combination with rifampicin (D). The concentration of vancomycin and vancomycin in combination with rifampicin, gentamicin, and clindamycin in the bone blocks was above the MIC90 for seven, five, and two days respectively. Significant differences (p 0.05) compared to other time points are marked with a star (*) and the associated time point.[15]

According to the study, Allograft C+TBA could serve as a viable option for carrying antibiotics during orthopedic and revision surgeries.[15]

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