are no efficacy data to support the use of antibiotic soaks in procedures with sterile prosthesis insertion [10,11]. There are no high quality trials testing the effectiveness of antiseptic soaking of prosthesis before implantation [12]. Moreover, antiseptics could exert changes in materials used for total arthroplasty (e.g., titanium alloy or hydroxyapatite), cause chondrolysis or pose cytotoxicity to human fibroblasts and osteoblasts [13,14].

Conceptually, a pre-implantation soak would decrease the bacterial load on the implant immediately prior to implantation, thereby reducing the risk of an infection caused by direct seeding of the wound bed by the implant itself. In an in vitro study bone fragments soaked with a solution of gentamicin or vancomycin for 30 minutes were loaded with an antibiotic concentration, 5-fold the minimum inhibitory concentration (MIC) values would be needed to provoke bacterial regression [15]. It has been also shown that in vitro decontamination of bone allografts contaminated with coagulase-negative Staphylococci is feasible after soaking bone with gentamicin or rifampicin for 60 minutes [16]. However, clinical studies are lacking, and there are no randomized controlled trials or systematic reviews that have evaluated soaking endoprosthesis or allograft bone in antibiotic or antiseptic solutions before implantation for the prevention of surgical site infections [17]. Two facts belie this practice. First, there is no published evidence that sterilized implants (endoprosthesis or allograft) routinely become colonized or contaminated from their unpackaging to implantation. Second, most infections in endoprosthesis and massive allograft surgery do not manifest in the perioperative period; rather, the average time to failure due to infection occurs years after the index surgery. In their report of 2,174 endoprosthesis surgeries, Henderson et al. reported an overall time revision surgery due to infection of 47 months, with a non-normally distributed standard deviation of 69 months [1]. The anatomic location with the fastest time to infection-driven revision was the elbow, occurring at a mean of 16 months, while the proximal humerus had an infection time of 80 months. A pre-implant soak would have no theoretical impact on these late infections.

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Authors: Muhammad Ather Siddiqi, A. Mazhar Tokgözoğlu

QUESTION 7: Should a coated prosthesis (silver/iodine) be used for reconstruction of patients undergoing primary bone tumor resection?

RECOMMENDATION: Yes, silver coating and iodine coating of prosthesis show good results in prevention of infection after reconstruction following primary tumor resection.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Megaprosthesis has been used to reconstruct limbs and large skeletal defects after resection of bone tumors for many decades. A significant problem is the higher rate of infection as compared to an infection rate of < 1% after a standard primary arthroplasty procedure. Many factors have been cited in literature which include length of surgery, OR environment, blood transfusions, soft tissue available for coverage and segment involved, e.g., tibia vs. femur. The average infection rate reported in literature is 10% (range 0–25%).

TABLE 1. Major findings and conclusions in the literature on silver-coated megaendoprostheses*

Author, Reference	Journal, Year	Study Design	Patients (*n*)	Results	Conclusion
Gosheger et al. [16] Silver-coated megaendoprostheses in a rabbit model: analysis of infection rate and toxicological side effects	Biomaterials 2004	Animal trial	30 (silver n = 15, titanium n = 15)	The silver group showed significantly ($p < 0.05$) lower infection rates (7% vs. 47%) in comparison with the titanium group after artificial contamination with S. aureaus	The new silver-coated MUTARS megaprosthesis resulted in reduced infection rates in an animal trial
Hardes et al. [27] Lack of toxicological side effects in silver-coated megaprostheses in humans	Biomaterials 2007	Prospective	20	No sign of toxic side effect after implantation of silver-coated megaprostheses. The silver levels in blood were considered non-toxic. No changes in liver or kidney function	Silver coatings on megaprostheses show no local or systemic side effects
Hardes et al. [9] Reduction of periprosthetic infection with silver-coated megaprostheses in patients with bone sarcoma	Journal of Surgical Oncology 2010	Prospective (silver group); retrospective (titanium group)	125 (silver n = 51, titanium n = 74)	The infection rate was substantially, but not significantly, reduced from 17.6% in the titanium group to 5.9% in the silver group. Included were patients with a proximal femur or proximal tibia replacement	Using silver-coated prostheses reduced the infection rate over the medium term
Glehr et al. [28] Argyria following the use of silver-coated megaprostheses: no association between development of local argyria and elevated silver levels	Bone and Joint Journal 2013	Retrospective	32	Asymptomatic local argyria in 23% of patients with silver-coated megaprostheses. No systemtic toxicity due to silver	However, the majority of the patients received silver-coated prostheses in revision, so that due to a negative pH value, increased release of Ag+ ions may be suspected
Wafa et al. [31] Retrospective evaluation of the incidence of early periprosthetic infection with silver-treated endoprostheses in high-risk patients: case-control study	Bone and Joint Journal 2015	Retrospective	170 (silver n = 85, titanium n = 85)	This retrospective study showed a postoperative infection rate of 11.8% in the group with silver-coated prostheses vs. 22.4% in the group with uncoated prostheses ($p = 0.033$)	Silver-coated implants showed a reduced reinfection rate after PJI in two-stage revisions (success rates of 85% in sliver group compared to 57.1% in uncoated group, $p = 0.05$)
Politano et al. [20] Use of silver prevention and treatment of infections: silver review	Surgical Infections 2013	Review	--	Benefits of silver-coated orthopaedic prostheses are still unproved	
Wilding et al. [32] Can a silver-coated arthrodesis implant provide a viable alternative to above-knee amputation in the unsalvageable, infected total knee arthroplasty?	Journal of Arthroplasty 2016	Retrospective	8	With a mean follow-up period of 16 months (5-35 months), only one patient had recurrent infection, but prosthesis-preserving treatment was possible	The silver-coated arthrodesis is a good alternative to amputation, particularly in infected knee prostheses

*Adapted from Schmidt-Braekling T, Streitbuerger A, Gosheger G, Boettner F, Nottrott M, Ahrens H, et al. Silver-coated megaprotheses: review of the literature. Eur J Orthop Surg Traumatol. 2017;27(4):483–489.

Silver coating of prosthesis is one of the methods studied so far. A number of retrospective studies have reported a decrease in the infection rate following use of silver-coated endoprosthesis. However, evidence from prospective and randomized trials is lacking [1]. See Table 1.

The Kanazawa group developed an iodine coating and published their results for the first time in 2012. In their study, 222 patients received iodine-coated implants of which 64 had active infection [2]. Their results suggest an even greater efficacy in prevention of infection as compared to silver coating interval and even eradication of infection in cases with active infection. Subsequent reporting by the same group in 2014 has also shown greater efficacy of iodine-treated implants in patients with trauma, bone loss due to infections and tumor resection as well as revision setting with previously infected implants [3].

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Authors: Mitchell Schwaber, Yaakov Dickstein, Elizabeth Temkin

QUESTION 8: What is the most optimal local antimicrobial delivery strategy during limb salvage: antibiotic cement, silver-coated implant, iodine-coated implant, topical vancomycin powder, injection of antibiotics via drain tubing or other?

RECOMMENDATION: Unknown. No direct comparison has been made of different antimicrobial delivery strategies in oncological patients undergoing limb salvage procedures.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Surgical excision of primary malignant tumors and metastases of the bone frequently leads to large skeletal defects. While once amputation was typically the only solution, the introduction of megaprostheses and later modular megaprostheses has led to limb salvage becoming the standard of care [1]. Despite falling rates of mechanical failure, the risk of periprosthetic infection remains high in comparison with conventional arthroplasty [2]. Treatment of periprosthetic infections often requires surgical intervention and prolonged antibiotic therapy [3]. Ongoing efforts directed at finding an effective means of infection prophylaxis have been examined exclusively in small observational studies without direct comparison between methods, thus limiting their conclusions.

Published studies appear to support the use of silver-coated implants. Data exist for limb salvage in sites including the hip, proximal and distal femur, pelvis, proximal and distal tibia, humerus and radius [4–10]. Six cohort studies, all but one retrospective, compared oncological patients who received silver-coated implants with non-coated (mostly titanium) implants [4–8,10]. The results across the studies were uniform with fewer patients who received silver-coated implants developing periprosthetic infections than the patients who received non-coated prostheses.

Weak evidence from a single retrospective cohort study indicates that alloy-type megaprosthesis may influence the risk of subsequent infection [11]. Significantly more patients who received a cobalt-chrome prosthesis developed infection than patients who received titanium prostheses.

Very weak evidence exists suggesting that iodine-coated megaprostheses may reduce risk of periprosthetic infection [12]. Similarly, there are limited data supporting the use of iodine-coated hardware in patients undergoing reconstruction [13].

Despite the body of evidence on antibiotic-impregnated cement in arthroplasty, only one case series examined its effects specifically in orthopaedic oncology patients who underwent total knee prostheses [14].

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