



## ■ RESEARCH

# Gentamicin in bone cement

## A POTENTIALLY MORE EFFECTIVE PROPHYLACTIC MEASURE OF INFECTION IN JOINT ARTHROPLASTY

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### Objectives

The objective of this study is to determine an optimal antibiotic-loaded bone cement (ALBC) for infection prophylaxis in total joint arthroplasty (TJA).

### Methods

We evaluated the antibacterial effects of polymethylmethacrylate (PMMA) bone cements loaded with vancomycin, teicoplanin, ceftazidime, imipenem, piperacillin, gentamicin, and tobramycin against methicillin-sensitive *Staphylococcus aureus* (MSSA), methicillin-resistant *Staph. aureus* (MRSA), coagulase-negative staphylococci (CoNS), *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*. Standardised cement specimens made from 40 g PMMA loaded with 1 g antibiotics were tested for elution characteristics, antibacterial activities, and compressive strength *in vitro*.

### Results

The ALBC containing gentamicin provided a much longer duration of antibiotic release than those containing other antibiotic. Imipenem-loading on the cement had a significant adverse effect on the compressive strength of the ALBC, which made it insufficient for use in prosthesis fixation. All of the tested antibiotics maintained their antibacterial properties after being mixed with PMMA. The gentamicin-loaded ALBC provided a broad antibacterial spectrum against all the test organisms and had the greatest duration of antibacterial activity against MSSA, CoNS, *P. aeruginosa* and *E. coli*.

### Conclusion

When considering the use of ALBC as infection prophylaxis in TJA, gentamicin-loaded ALBC may be a very effective choice.

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### Article focus

■ This study is to determine an optimal antibiotic-loaded bone cement (ALBC) for infection prophylaxis in total joint arthroplasty

### Key messages

■ The gentamicin-loaded ALBC provided a broad antibacterial spectrum against all the test organisms and had the greatest duration of antibacterial activity against methicillin-sensitive *Staphylococcus aureus*, coagulase-negative staphylococci, CoNS, *Pseudomonas aeruginosa* and *Escherichia coli* as compared with the ALBC loaded with vancomycin, teicoplanin,

ceftazidime, imipenem, piperacillin, or tobramycin

■ When considering the use of ALBC as infection prophylaxis in total joint arthroplasty, gentamicin-loaded ALBC can be a very effective choice

### Strengths and limitations

■ This is the first study to compare the bacteria-eradication abilities of low-dose ALBCs loaded with different antibiotics  
■ This study can provide as a reference for orthopaedic surgeons in the selection of effective ALBCs for infection prophylaxis in total joint arthroplasty  
■ This is an *in vitro* study

**Table 1.** Summary of chromatography assay. All of the chromatography assay was performed using a model ALC 717 chromatograph (Waters Associates, Milford, Massachusetts). The concentrations of antibiotics in the cement cylinders were obtained from the high-performance liquid chromatography (HPLC) analysis through comparisons made with the prepared daily standard curves where related the peak areas with antibiotic concentrations

Antibiotic	Column (dimensions)	Particle size	Mobile phase	Detection sensitivity ( $\mu\text{g/ml}$ )
Vancomycin	RP18 (100 mm $\times$ 4.6 mm)	5 $\mu\text{m}$	Water/Acetonitrile/100 mM ammonium formate (78/12/10)	0.5
Teicoplanin	C18 (250 mm $\times$ 4.6 mm)	5 $\mu\text{m}$	Sodium dihydrogen phosphate/Acetonitrile (90/10)	0.25
Imipenem	Atlantis T3 (150 mm $\times$ 4.6 mm)	5 $\mu\text{m}$	Water/Methanol (93/7)	0.5
Ceftazidime	Atlantis T3 (150 mm $\times$ 4.6 mm)	5 $\mu\text{m}$	Acetonitrile/25 mM $\text{KH}_2\text{PO}_4\text{-Na}_2\text{HPO}_4$ (10/90)	0.25
Piperacillin	Atlantis T3 (150 mm $\times$ 4.6 mm)	5 $\mu\text{m}$	Acetonitrile/0.05 M phosphate buffer (50/50)	0.5
Gentamicin	C18 (300 mm $\times$ 3.9 mm)	5 $\mu\text{m}$	Acetonitrile/0.05% aqueous trifluoroacetic acid (70/30)	0.2
Tobramycin	C18 (300 mm $\times$ 3.9 mm)	5 $\mu\text{m}$	Water/Acetonitrile (6/94)	0.2

## Introduction

Deep infection is one of the most devastating complications of total joint arthroplasty (TJA). Systemic prophylactic antibiotics have been widely accepted as effective agents for reducing the rate of deep infection.<sup>1,2</sup> However, a prevalence of deep infection between 1% and 2% is still noted in most large case series reporting on TJAs.<sup>1,2</sup> The use of antibiotic-loaded bone cement (ALBC) has been shown to be effective in reducing the rate of early-to-intermediate deep infection after TJA.<sup>3-5</sup>

Gram-positive pathogens (including *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS)) are the most common organisms implicated in peri-prosthetic joint infection (PJI).<sup>6-9</sup> For gram-positive pathogen infections, vancomycin-loaded bone cement has become one of the most commonly used ALBCs in both prophylactic and therapeutic treatment of PJIs.<sup>10,11</sup> However, gram-positive bacteria are not the only bacteria found in PJI. Although less commonly associated with PJI, gram-negative bacteria comprise between 6% and 23% of all episodes of PJI.<sup>6,7,12</sup> When using ALBC as infection prophylaxis against both gram-positive and -negative pathogens in TJA, an antibiotic with a broad spectrum of antibacterial activity would be a more appropriate choice for PMMA bone-cement loading. To our knowledge, no study has evaluated the spectrum of bacteria-eradication abilities of bone cement loaded with different antibiotics, especially in the lower-dose ALBC used for prophylaxis in TJA.

The objective of our study was to measure the elution characteristics of vancomycin, teicoplanin, ceftazidime, imipenem, piperacillin, gentamicin, and tobramycin from low-dose ALBC specimens and compare their antibacterial activities against the most common organisms found in PJIs: methicillin-sensitive *Staph. aureus* (MSSA), methicillin-resistant *Staph. aureus* (MRSA), CoNS, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. We used an *in vitro* model to measure the antibiotic release characteristics, bacteria eradication

abilities, and mechanical properties of ALBCs loaded with different antibiotics.

## Materials and Methods

**Antibiotic-loaded cement specimen.** We used Surgical Simplex bone cement (Stryker Orthopaedics, Limerick, Ireland), to which was added vancomycin (Gentle Pharmaceutical Co., Yulin, Taiwan), teicoplanin (Sanofi-Aventis, Paris, France), ceftazidime (China Chemical & Pharmaceutical Co. Ltd, Taichung, Taiwan), imipenem (Merck Sharp & Dohme Corp., Elkton, Virginia), or piperacillin (China Chemical & Pharmaceutical Co. Ltd) was tested. The antibiotic-cement mixture comprised 1 g of antibiotic mixed with 40 g of bone cement polymer prior to the addition of the liquid component. Two commercial, premixed, low-dose ALBCs containing either 1 g of gentamicin (PALACOS R+G; Zimmer, Weheim, Germany) or 1 g of tobramycin (Simplex P; Stryker Orthopaedics) were also tested.

**Antibiotic broth elution assay.** Each cement cylinder was immersed in a polypropylene tube with 5 ml phosphate buffered saline (PBS; pH 7.3) and shaken in a rotator at 37°C. The study lasted for 14 days, with the daily transfer of the cement cylinder into a test tube with PBS after saline washings. Elution samples of 2 ml of PBS were collected at ten time points over a period of 14 days (days zero, one, two, three, four, five, six, seven, ten, and 14).

The concentrations of antibiotics were determined using high-performance liquid chromatography (HPLC). The method of HPLC analyses was modified from previously published methods.<sup>13,14</sup> The details of the HPLC analyses are given in Table 1.

**Bioassay of antibiotic activity.** A modified microtube dilution bioassay was used to measure the biological activity of the released antibiotics in the sample aliquots. The following strains were selected as test organisms: MSSA strain (ATCC 25923), MRSA strain (ATCC43300), CoNS (ATCC14990), *P. aeruginosa* (ATCC27853), *E. coli* (ATCC 25922), and *K. pneumoniae* (ATCC 700603).

**Table II.** Daily and cumulative release of antibiotics from the cement specimens in the broth elution assay over a period of 14 days (-, below detection limit). The imipenem values showed a significantly worse cumulative antibiotic release efficacy compared with all other tested antibiotics (all  $p < 0.001$ )

	Antibiotic						
	Vancomycin	Teicoplanin	Ceftazidime	Imipenem	Piperacillin	Gentamicin	Tobramycin
Mean (SEM) daily release (µg/ml)							
Day 1	38.5 (5.9)	59.5 (8.4)	66.0 (6.0)	1.7 (0.1)	68.4 (4.0)	56.4 (10.7)	53.8 (7.4)
Day 2	5.2 (1.0)	6.5 (1.7)	7.0 (1.0)	0.4 (0.1)	1.4 (0.8)	3.6 (1.1)	10.0 (1.3)
Day 3	-	-	1.7 (0.1)	-	-	3.3 (1.0)	3.3 (1.0)
Day 4	-	-	1.4 (0.1)	-	-	1.9 (0.8)	2.1 (0.8)
Day 5	-	-	1.2 (0.1)	-	-	1.3 (0.1)	1.3 (0.1)
Day 6	-	-	1.3 (0.1)	-	-	1.1 (0.1)	-
Day 7	-	-	-	-	-	0.6 (0.1)	-
Day 10	-	-	-	-	-	0.7 (0.1)	-
Day 14	-	-	-	-	-	-	-
Mean (SEM) cumulative total release (µg/ml)	218.6 (34.8)	330.1 (51.0)	393.3 (26.1)	10.5 (0.8)	349.5 (24.5)	343.6 (54.2)	352.6 (25.6)

The samples were inoculated with tested bacteria of 105 colony forming units (CFUs)/ml in 96-well cultured dishes and incubated at 37°C for 24 hours. The growth was visually compared by an author (YC) with the positive control (without the antibiotic) and standard samples with different concentrations of antibiotics.

**Ultimate compressive test.** The cement specimens (both before and after the antibiotic broth elution) in each group were tested for failure in axial compression by a material testing system machine (Bionix 858; MTS Corp., Eden Prairie, Minnesota). A specially designed pushrod with a self-alignment function was used as a plunger to ensure full surface contact between the specimen and the pushrod. Each specimen was compressed at a displacement rate of 0.1 mm/s. Force, displacement, and time were recorded simultaneously for each specimen in increments of 0.05 mm by the MTS Test star software (MTS Corp.). Ultimate compressive force was compared between groups. A cement specimen without antibiotics was used as a control.

**Statistical analysis.** The antimicrobial concentration of elution samples and the ultimate compressive force of cements with different preparations were tested in triplicate. The results are reported as mean with range. We used analysis of variance (ANOVA) to determine the statistical difference in the ultimate compression force and antibiotic release efficacy between cements with different preparation. A  $p$ -value of  $< 0.01$  was considered significant.

## Results

On the basis of the HPLC results, all tested samples showed a burst release on the first day. The release rates rapidly decreased during the following few days. During the 14-day study period, imipenem-loaded ALBCs showed a significantly worse cumulative antibiotic release efficacy compared with the other tested antibiotics (all  $p < 0.001$ ) (Table II). The ALBCs containing different antibiotics exhibited different release durations and

different additional daily releases (Table II). The ALBCs containing gentamicin had much longer release durations (ten days), than those containing ceftazidime (six days), tobramycin (five days), and vancomycin, teicoplanin, imipenem and piperacillin (two days each) (Table II).

The organisms in this study were found to be susceptible to different concentrations of the test antibiotics. Vancomycin and teicoplanin did not exhibit anti-bacterial effects against the gram-negative organisms (including *P. aeruginosa*, *E. coli*, and *K. pneumoniae*) at a concentration up to 256 µg/ml (see Supplementary Material).

With regard to the bioactivities of ALBCs loaded with different antibiotics against test organisms, all of the antibiotics retained their antibacterial effects after incorporation into PMMA. In order to test the bioactivity against gram-positive bacteria, three *staphylococci* strains (MSSA, MRSA, and CoNS) were used. The antibacterial effects against MSSA lasted for one day in the cements loaded with ceftazidime, imipenem, piperacillin, or tobramycin; two days in the cements loaded with vancomycin, or teicoplanin; three days in the cements loaded with gentamicin (Fig. 1a). The antibacterial effects against MRSA lasted for one day in the cements loaded with ceftazidime or gentamicin and two days in the cements loaded with vancomycin and teicoplanin; neither imipenem-, tobramycin-, nor piperacillin-loaded cement provided any bioactivity against MRSA (Fig. 1b). The antibacterial effects against CoNS lasted for one day in the cements loaded with ceftazidime, imipenem, piperacillin, or tobramycin; two days in the cements loaded with vancomycin or teicoplanin; and three days in the cement loaded with gentamicin (Fig. 1c).

In order to test the bioactivities against gram-negative bacteria, we used *P. aeruginosa*, *E. coli*, and *K. pneumoniae*. The antibacterial effects against *P. aeruginosa* lasted for one, two, five and ten days in the cements loaded with piperacillin, ceftazidime, tobramycin, and

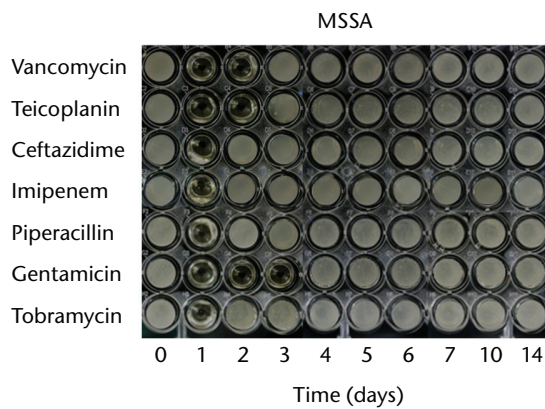


Fig. 1a

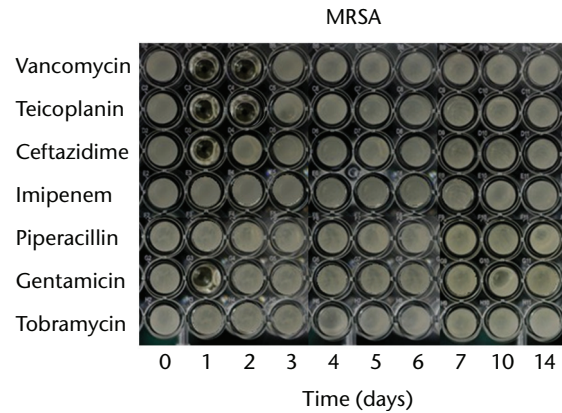


Fig. 1b

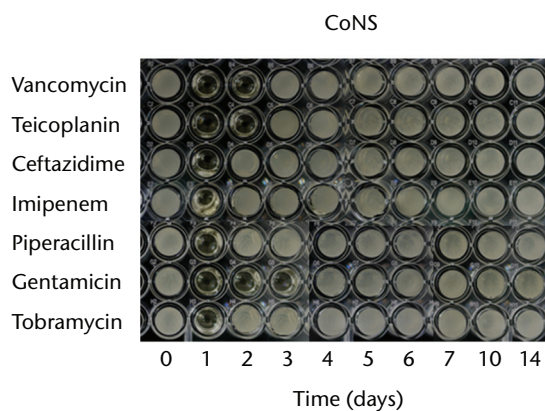


Fig. 1c

Micro-tube dilution bioassays showing the antibacterial activities against gram-positive bacteria in broth elution samples from the low-dose antibiotic loaded cements (1 g antibiotic in 40 g polymethylmethacrylate) over a 14-day elution period for a) methicillin-sensitive *Staphylococcus aureus* (MSSA), b) methicillin-resistant *Staph. aureus* (MRSA) and c) coagulase-negative staphylococci (CoNS).

gentamicin, respectively. The imipenem-loaded cement did not exhibit antibacterial activity against *P. aeruginosa* (Fig. 2a). The antibacterial effects against *E. coli* lasted for one day in the cements loaded with piperacillin, and two days in cement loaded with imipenem or tobramycin. The gentamicin- and ceftazidime-loaded cements provided similar antibacterial durations (six days) against *E. coli* (Fig. 2b). The anti-bacterial activity against *K. pneumoniae* lasted for one day for imipenem-, gentamicin and tobramycin-loaded cements. Ceftazidime- or piperacillin-loaded cements did not exhibit antibacterial activities against *K. pneumoniae* (Fig. 2c). In addition, vancomycin- or teicoplanin-loaded cement did not provide bioactivity against any of the tested gram-negative bacteria (Fig. 2).

Regarding the mechanical strength of cement samples, with the exception of the imipenem-loaded ALBC, there were no significant differences in ultimate compressive strength between the cement samples loaded without or with different antibiotics, and all pre- and post-elution compression testing showed a mean cement strength > 70 MPa (Table III, Fig. 3). In contrast, the mean compression modulus was significantly lower for the specimens containing imipenem than it was for the control specimens and those containing other preparations

either before or after broth elution ( $p = 0.004$  and  $p < 0.001$ , respectively) (Table III, Fig. 3).

## Discussion

The ALBCs have been widely used in the prophylaxis and treatment of skeletal infection.<sup>15,16</sup> In the treatment of skeletal infections, a high-dose ALBC ( $\geq 3.6$  g of antibiotic per 40 g of PMMA powder) is desirable for effective elution kinetics and sustained therapeutic levels of the antibiotic.<sup>17</sup> In contrast to therapeutic measures, prophylaxis requires low-dose antibiotics in the bone cement to avoid adverse mechanical effects on cement that is intended for fixation of the prosthesis. In general, low-dose ALBC is defined as  $\leq 1$  g of powdered antibiotic per 40 g of PMMA powder. International industrial standards state that bone cement used for definitive fixation must have an ultimate compressive strength of  $\geq 70$  MPa.<sup>18,19</sup> This standard was established to reduce the incidence of premature cement breakdown.<sup>18,19</sup> In this study, we found that the ultimate compressive strengths of cement specimens are not significantly compromised after being loaded with low-dose antibiotics, with the exception of imipenem-loaded cement. The ultimate compressive strength of imipenem-loaded ALBC was < 70 MPa both before and after broth

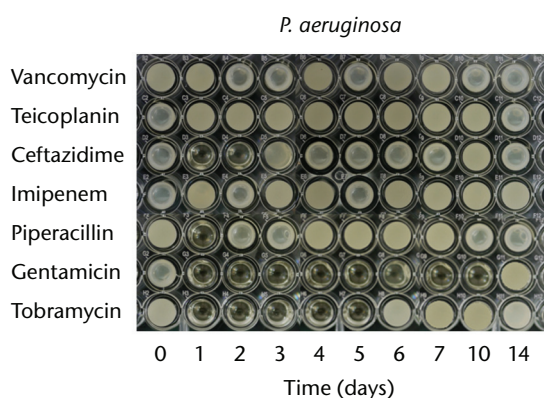


Fig. 2a

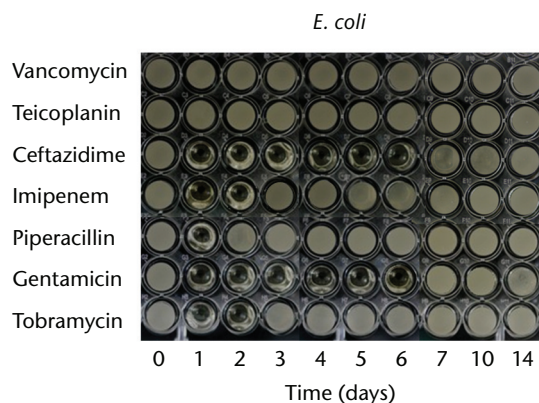


Fig. 2b

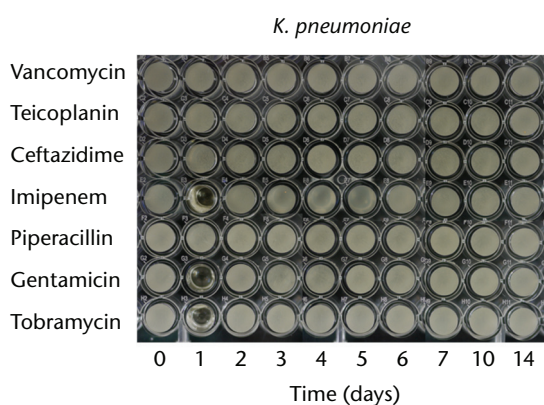


Fig. 2c

Micro-tube dilution bioassays showing the antibacterial activities against gram-negative bacteria in broth elution samples from the low-dose antibiotic loaded cements (1 g antibiotic in 40 g polymethylmethacrylate) over a 14-day elution period for a) *Pseudomonas aeruginosa*, b) *Escherichia coli* and c) *Klebsiella pneumoniae*.

**Table III.** Results of ultimate compressive strength testing

	Mean ultimate compressive strength (MPa) (range)			
	Pre-elution	p-value vs control	Post-elution	p-value vs control
Control	86 (85 to 87)	-	84 (81 to 86)	-
Vancomycin	79 (73 to 88)	0.692	75 (72 to 77)	0.707
Teicoplanin	85 (82 to 87)	1.000	74 (73 to 74)	0.530
Ceftazidime	85 (87 to 81)	1.000	85 (77 to 88)	1.000
Imipenem	67 (65 to 68)	0.004	55 (53 to 58)	< 0.001
Piperacillin	87 (82 to 91)	1.000	80 (71 to 85)	0.994
Gentamicin	86 (84 to 88)	1.000	75 (70 to 82)	0.723
Tobramycin	82 (79 to 83)	0.958	79 (79 to 80)	0.989

elution. This finding indicated that imipenem-loaded low-dose ABLC does not provide sufficient mechanical strength for use in prosthesis fixation in TJA. High doses of antibiotics in bone cement have been shown to significantly reduce the mechanical strength of the cement and cannot be used in prosthesis fixation.<sup>20</sup> However, the result of this study implied that not only the loading dose but also the type of antibiotic may cause significant adverse effects on mechanical strength of bone cement. Therefore, not all low-dose ALBCs can provide sufficient mechanical strength for prosthesis fixation. However,

with the exception of imipenem, the mechanical strengths of all cement-sample preparations in this study were acceptable according to industrial standards both before and after the antibiotic elution. These findings partially support the use of the low-dose ALBCs as the definitive choice for joint prosthesis fixation.

In our previous study, we showed that the use of ALBC loaded with vancomycin or oxacillin in total knee arthroplasty (TKA) was able to prolong the antibacterial activity in the joint fluid after the discontinuation of intravenous prophylactic antibiotics.<sup>15</sup> This longer duration of

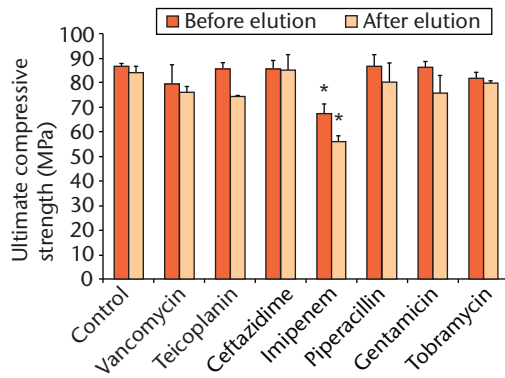


Fig. 3

Bar chart showing the mean ultimate compressive strength of the cement samples before and after the 14-day broth elution assay compared with cement without antibiotics (control). The bars denote the mean of three tests for each antibiotic with the standard error of the mean. Asterisks denote a significant difference ( $p < 0.01$ ) when compared with the control.

antibacterial activity in joint fluid may contribute to a lower infection rate in TKA performed using ALBC. However, only resistant or non-resistant strains of *Staph. aureus* were selected as test organisms in the experiment.<sup>15</sup> The bioactivity of joint fluid against other organisms, especially against gram-negative organisms, is still unclear. Gram-negative bacteria accounted for 53 (15%) of 346 first-time episodes of culture-positive PJI encountered in our institute during the period from 2000 through 2006.<sup>12</sup> Of these, *P. aeruginosa* (39.6%) was the most commonly isolated pathogen in patients with gram-negative PJI in 21 (40%), followed by *E. coli* in ten (19%) and *K. pneumoniae* in eight (15%).<sup>12</sup> Similar results were reported by Zmistowski et al,<sup>21</sup> who found that *E. coli* was the most common gram-negative pathogen (30.2%), followed by *P. aeruginosa* (25.5%) in a total of 43 patients with hip or knee PJI. Therefore, when considering the use of ALBC as a prophylactic measure for infection in TJA, the antibiotics incorporated into bone cements should have a broad antibacterial spectrum that include gram-positive and gram-negative pathogens.

Vancomycin and teicoplanin, two glycopeptide antibiotics, remain the standard therapeutic agents used in most gram-positive pathogen infections, including resistant and non-resistant strains.<sup>22</sup> Vancomycin and teicoplanin have both been shown to be stable in PMMA, and both are released in a microbiologically active form.<sup>22</sup> Vancomycin-loaded bone cement is one of the most commonly used ALBCs in both prophylactic and therapeutic measures for PJI.<sup>10,11</sup> However, based on the bioassay results of this study, we found that neither vancomycin nor teicoplanin exhibited anti-bacterial effects against gram-negative pathogens (including *P. aeruginosa*, *E. coli*, and *K. pneumoniae*). Imipenem (subgroup: carbapenems),<sup>23</sup> ceftazidime (third-generation cephalosporin),<sup>24</sup> and piper-

acillin (extended spectrum  $\beta$ -lactam)<sup>25</sup> all have a broad spectrum of activity against both gram-positive and -negative bacteria. Theoretically, bone cement loaded with a broad-spectrum antibiotic should provide similar spectrum of antibacterial activity. However, in this study, bone cement loaded with broad-spectrum antibiotics (ceftazidime, imipenem or piperacillin) did not show antibacterial activity against all the tested organisms. Piperacillin is active against gram-positive and gram-negative aerobic and anaerobic bacteria. However, piperacillin-loaded bone cement was unable to provide antibacterial duration > 24 hours against the tested micro-organisms. This may be due to the piperacillin with relative higher minimal inhibitory concentrations against the tested organisms. In contrast, the imipenem exhibits relative lower minimal inhibitory concentrations against the tested organisms. However, a short anti-bacterial activity is also observed in the cement loaded with imipenem. This may be due to the poor elution efficacy of imipenem from PMMA. Imipenem-loaded ALBCs showed a significantly worse antibiotic release efficacy as compared with ALBCs with other preparations. Therefore, in addition to the spectrum of antibiotic loaded in the ALBC, the release efficacy of antibiotics from the bone cement and the minimal inhibitory concentrations of antibiotic are all the critical factors which determine antibacterial activities of ALBCs.

Several different commercial premixed ALBC products have been approved for use by the United States Food and Drug Administration.<sup>20</sup> All of these commercial premixed ALBCs contain aminoglycoside combined with either tobramycin or gentamicin. Today, surgeons continue to mix ALBC by hand. The primary drawback of using commercially premixed ALBC is that the antibiotic used is dictated by the chosen bone cement, and consequently surgeons are unable to tailor the antibiotic to a specific organism. To date, there are no comparative studies determining the superiority of anti-bacterial activities of commercially premixed or hand mixed ALBCs. Two commercial premixed ALBCs were tested in this study (PALACOS R+G, containing 1 g gentamicin in 40 g PMMA; and Simplex P, containing 1 g tobramycin in 40 g PMMA). The premixed gentamicin-loaded ALBC showed a broad antibacterial spectrum against all of the tested bacteria, including gram-positive and gram-negative strains. It also provides the longest antibacterial duration against MSSA, CoNS, *P. aeruginosa* and *E. coli*. The premixed tobramycin ALBC also provided a broad antibacterial spectrum against all of the test bacteria, with the exception of MRSA. As compared with hand-mixed ALBCs, the commercial premixed gentamicin-loaded ALBC provided an equal or longer antibacterial duration against different bacteria in this study. However, this superiority in antibacterial activity was not observed in the premixed tobramycin ALBC as compared with hand-mixed ALBCs. The results indicated that commercial premixed ALBCs did not always exhibit superior antibacterial activity over hand-mixed ALBCs.

Our study has certain limitations. First, this is an *in vitro* study of specimens prepared in a laboratory environment, which does not necessarily reflect actual clinical circumstances. The quantity and flow of body fluid, limb mobility, host response, and antibiotic stability *in vivo* were not taken into consideration. Secondly, the bone cement used for hand-mixed ALBCs was different than the commercial premixed ALBCs. Third, ATCC bacteria were selected as test organisms in the experiment. We do not know the bioactivities of the cement specimens against other clinical isolates, especially biofilm-forming organisms.

In conclusion, vancomycin, teicoplanin, ceftazidime, imipenem, and piperacillin all retained antibacterial activities after loading into PMMA. Further, compared with the hand mixed low-dose ALBCs, the commercial premixed low-dose ALBCs did not definitively provide significantly better mechanical strength or superior antibacterial activities. The imipenem loaded low-dose ALBC was unable to provide sufficient mechanical strength to be used for prosthesis fixation in TJA. Vancomycin- or teicoplanin-loaded ALBCs should not be used as a prophylactic measure against gram-negative bacteria. In this experiment, the premixed gentamicin-loaded ALBC provided an equal or longer antibacterial activity against MSSA, MRSA, CoNS, *P. aeruginosa*, *E. coli*, and *K. pneumoniae* than ALBCs loaded with other antibiotics. When considering the use of ALBC as a prophylactic measure against infection in TJA, the premixed gentamicin-loaded ALBC may be an effective choice.

### Supplementary material



Micro-tube dilution bioassays showing the different concentrations of the antibiotics exhibiting inhibitory effects against each bacteria are available as supplementary material on our website [www.bjr.boneandjoint.org.uk](http://www.bjr.boneandjoint.org.uk).

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#### Author contributions:

- Y. Chang: Study design, Conducting of the experiment, Data collection, Writing the paper
- C-L. Tai: Biomechanical testing
- P-H. Hsieh: Data analysis
- S. W. N. Ueng: Study concept

#### ICMJE Conflict of Interest:

- None declared

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