

Fig. 1. Release (mg) of gentamicin from different hip spacers produced with PMMA cements utilised in different countries. Values of gentamicin release from 24 to 240 hours are extrapolated as mg/day of elution. (Microbiological method).

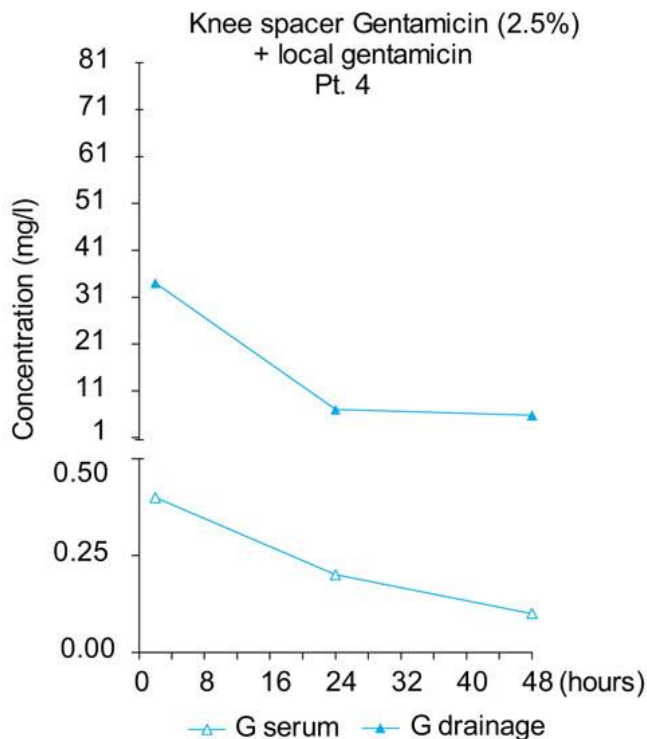
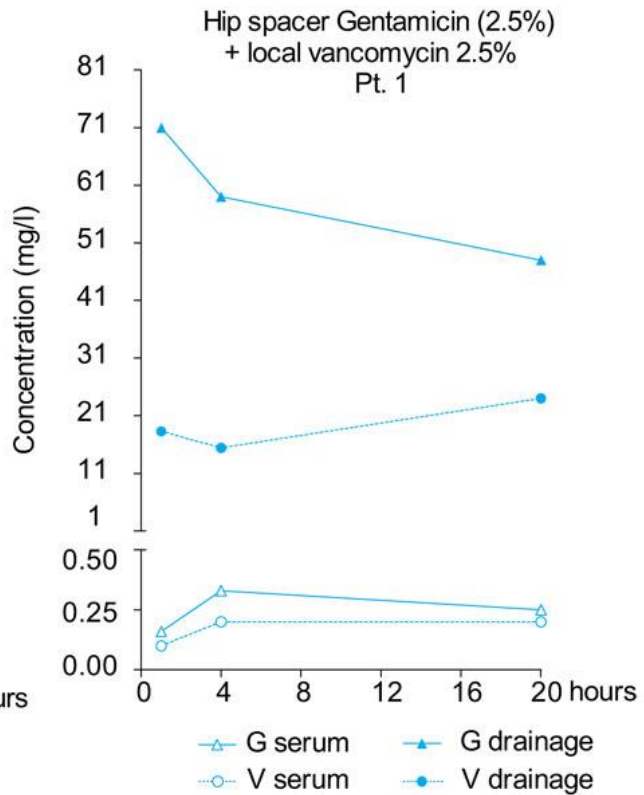
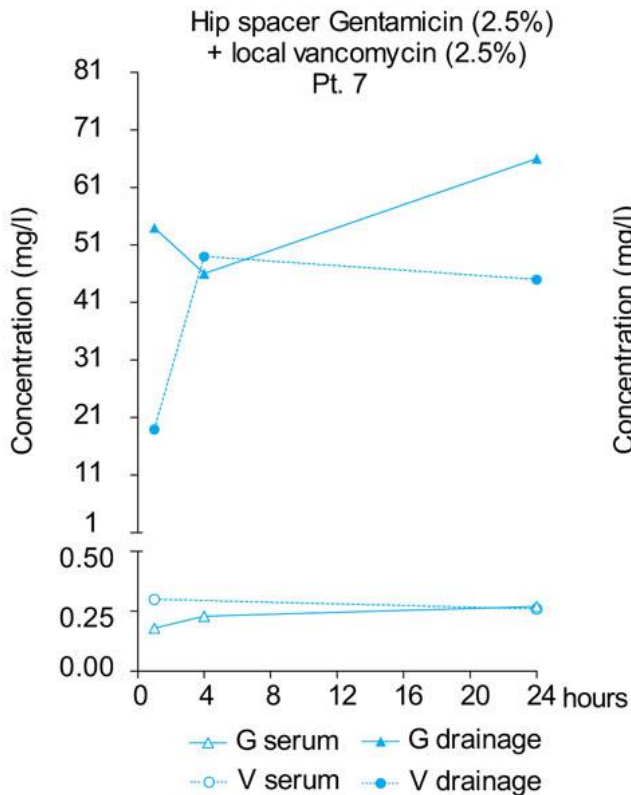


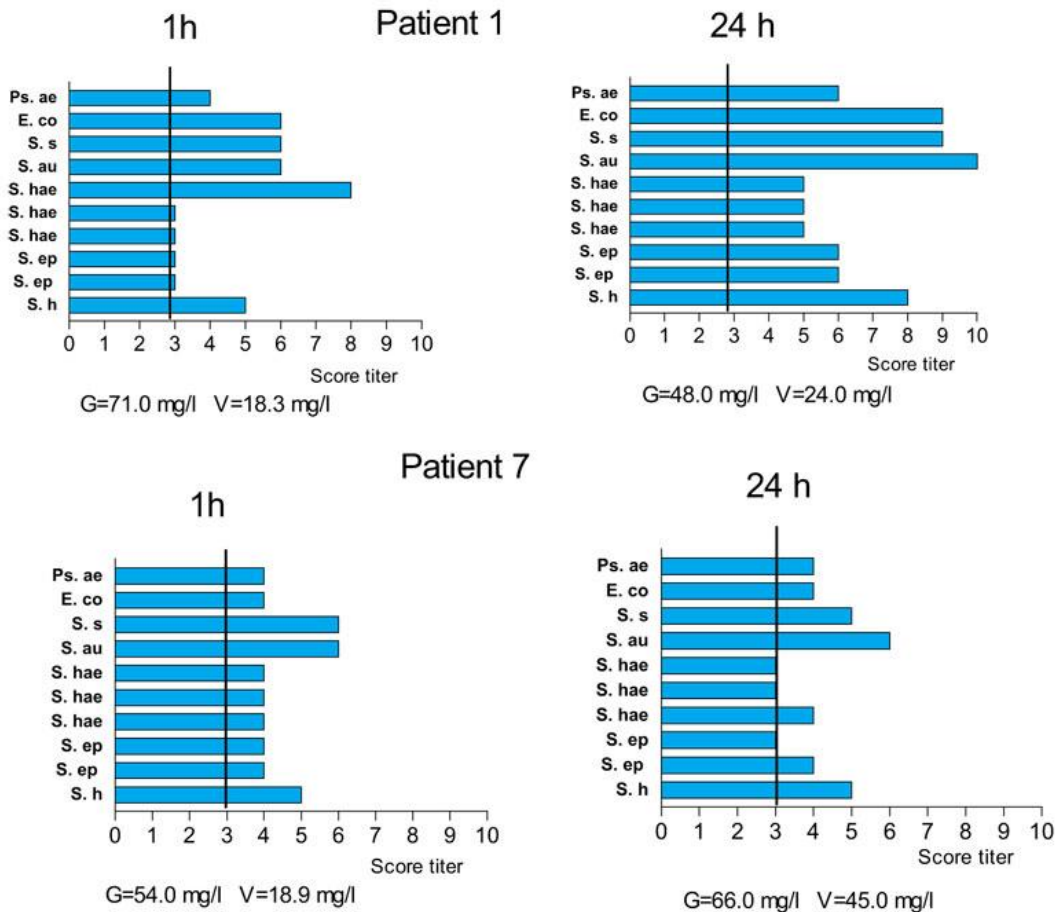
Fig. 2. Concentrations (mg/L) of gentamicin and vancomycin in serum and drainage of patients determined 1, 24 and 48 hours after hip and knee spacers implant. (FPIA method).

24–48 hours after spacer implant. The concentrations are largely above the susceptibility of bacteria. Serum levels are low (<0.2–0.8 mg/L).

Parenteral administration of vancomycin (1 g × 2) allows good local penetration, showing similar range of concentrations (range 15–40 mg/L) in serum and in drainage fluids at different sampling time (1–24 hours).

The local administration of vancomycin (2.5%) produces high concentrations in surgical site (18.3–45.0 mg/L) and low serum levels (<1 mg/L). Higher vancomycin

Hip spacers with local vancomycin



Knee spacer with local gentamicin

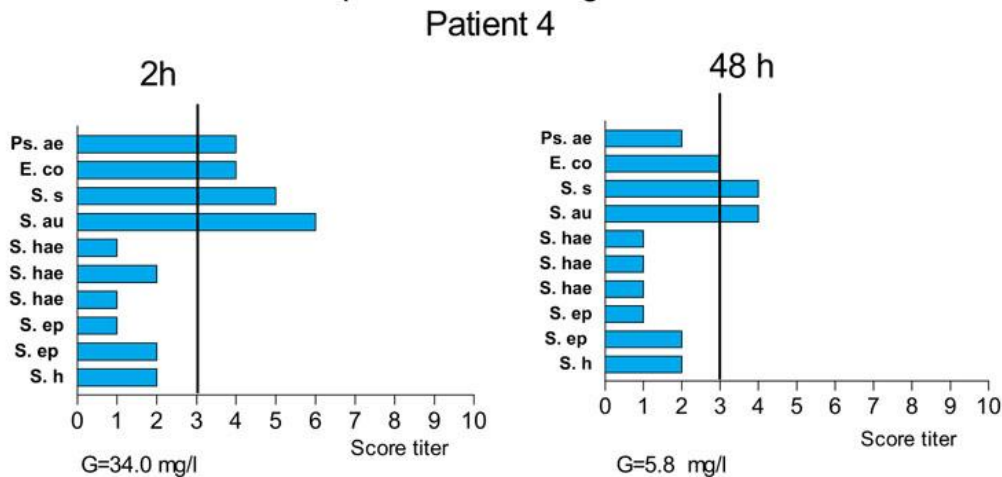


Fig. 3. Bactericidal titer of drainage fluids collected 1, 24 and 48 hours after spacer implant in patients against multi-resistant clinical isolates. Hip spacer (Spacer G) and local vancomycin are prepared as described in (3) and knee spacer (Spacer K) is fixed with gentamicin-loaded PMMA cement (2.5 %). The concentrations of gentamicin (G) and vancomycin (V) in drainage fluids are reported for each patient at time of samples collection. The bactericidal titer is defined as the highest dilution achieving 99.9 % bacterial killing (serial two-fold dilutions) and is reported according to following score:

Score = dilution; 1 = 1/2; 2 = 1/4; 3 = 1/8*; 4 = 1/16; 5 = 1/32; 6 = 1/64; 7 = 1/128; 8 = 1/256; 9 = 1/512; 10 = 1/1024

* Lowest bactericidal titer for orthopaedic infections according to (25).

Abbreviations: Ps. ae = *Pseudomonas aeruginosa*; E. co = *Escherichia coli*; S. s = *Staphylococcus Met- S*; S. au = *S. aureus*; S. hae = *S. haemolyticus* (3 different strains); S. ep = *S. epidermidis* (2 different strains); S. h = *S. hominis*

Table 1. Comparative properties of antibiotics in PMMA cement utilised in prosthetic surgery

Properties	Amino-glycosides	Vanco-mycin	Betalac-tams	Fluoro-quinolones	Rifam-picin	Clinda-mycin
Delivery	+++	+ / +++	+	++ ?	0	+
Half-life	++	++	±	+	n.d.	+
Antimicrobial activity	++	++	++	+	0*	+
Spectrum of activity	-cidal wide	-cidal narrow	-cidal wide	-cidal wide	-cidal narrow	-static narrow
Hypersensitivity	-	-	++	++	?	?
ADR	-	-	++	++	?	?
Cement Compatibility	+++	+	+	?	---	+
Mechanical resistance	++	+?	+	?	---	+?

+++ = very good properties; ++ = good properties; + = sufficient properties; ± = insufficient properties; - negative; ? = Controversial or insufficient data; * = Because of no release
ADR = Adverse Drug Reactions

Strain	Vancomycin + Gentamicin		
	FIC Index	MIC (mg/L)	
		Vanco-mycin	Genta-micin
<i>St. epidermidis</i> (8/28)	1.00 A	2.5	R
<i>St. haemolyticus</i> (8/28)	1.00 A	1.25	R
* <i>St. haemolyticus</i> (82/26)	1.00 A	1.25	R
<i>St. haemolyticus</i> (70/26)	1.00 A	1.25	R
* <i>St. epidermidis</i> (137/25)	0.50 A	2.5	R
° <i>St. hominis</i> (126/26)	1.02 A	1.25	I
<i>St. aureus</i> (3A10)	0.15 S	2.5	I
<i>St. aureus</i> (9A28)	0.48 S	1.25	1.25
<i>E. coli</i> (7A27)	0.25 S	156.25	5
<i>Ps. aeruginosa</i> (4/28)	0.12 S	1250	5

Table 2. *In vitro* activity of gentamicin and vancomycin in combination against multi-resistant clinical isolates. Checker-board method (25).

* Oxacillin Resistant
° Methicillin Resistant
R = Resistant
I = Intermediate
FIC ≤ 0.5 Sinergism S
FIC = 1 Additivity A
FIC ≥ 2 Antagonism Ant

Table 3. Release of gentamicin and vancomycin from removed (after 3–6 months of implantation) spacers after ten days of spacers elution. Amounts were determined using FPIA method. Modified from [3].

Spacers		Total μg	Gentamicin %	$\mu\text{g}/\text{cm}^2$ [§]
Control		15,550	0.82	82.4
Removed		1682.0 \pm 530.2	0.07 \pm 0.02	9.3 \pm 2.9
		Gentamicin + Vancomycin		
		Total μg	%	$\mu\text{g}/\text{cm}^2$ [§]
Control	G	14,220	0.75	86.2
	V	24,114	16.1	146.1
Removed	G	3889.6 \pm 1806.5	0.2 \pm 0.1	23.0 \pm 11.1
	V	3484.8 \pm 1092.9	2.3 \pm 0.8	20.9 \pm 6.4

[§] Spacer's surface area 180 cm^2