Bone and intramedullary infections are severe complications of fracture management (0–1% for closed fractures and 0–11% for open fractures) and surgical repair (intramedullary nailing2,3 and lengthening over nails with external fixation4,5) of long bones. A prevalence of methicillin-resistant or gentamicin-resistant *Staphylococcus aureus* (SA) has been observed, and bone infection with methicillin-resistant SA (MRSA) has increased among patients with implanted orthopedic devices. The current management of these forms of osteomyelitis has two main aims: (a) to limit and resolve the infective process, by removing all foreign material (fixation device), followed by a meticulous debridement of the necrotic and infected area, and by administering systemically high plasma antibiotic levels that often result in various toxic side effects.11–16

Polymethylmethacrylate (PMMA) has been the most widely studied material as a carrier for numerous antibiotics, including gentamicin, tobramycin, and vancomycin13,16,17 or recently the antimicrobial peptide Dhvar-5.14 Other local drug delivery systems have been studied, such as collagen15 and chitosan18 impregnated with gentamicin, polymers (poly lactic-glycolic acid, poly DL lactic acid, and polycaprolactone) impregnated with tobramycin, vancomycin, or ciprofloxacin11,19–21 ceramics (hydroxyapatite, carbonatedapatite, calcium sulphate) impregnated with gentamicin, tobramycin, vancomycin, moxifloxacin, and antimicrobial peptides (human lactoferrin 1–11).15,16,22,23 In particular, the use of biodegradable implants could provide both high local bactericidal concentrations in tissue for the prolonged time, needed to completely eradicate the infection, and the possibility to match the rate of implant biodegradability, according to the type of infection treated, making surgical removal of the implant unnecessary.7 However, most of the biodegradable implants evaluated have not given sufficient guarantees of mechanical loading seal and, until now, the FDA has approved only the use of bone cement with gentamicin or tobramycin for the second surgery in a two stage revision procedure.

Although, gentamicin remains the most effective antibiotic to be used in combination with PMMA due to its high solubility, heat stability, and bactericidal activity at low concentration, MRSA reduced susceptibility and its increased resistance to many of the other commonly used antibiotics means PMMA has to be loaded with other antibiotics such as glycopeptides.14–16,24–33 The glycopeptide, vancomycin, which presents chemical characteristics similar to those of gentamicin, has been considered the drug of choice in infections caused by MRSA and *S. epidermidis* and its concentration in bone ranges from 15–35% of those seen in the serum, well

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**Keywords:** PMMA nail; gentamicin–vancomycin coating; intramedullary infections
above the minimum inhibitory concentration of 1 μg/mL for susceptible SA strains. Various researchers have shown in vitro the excellent properties of the combination of gentamicin and vancomycin in PMMA with regard to their synergistic antimicrobial effect against *Escherichia coli* and *E. faecalis*, and variable effect on SA, according to strain. Their combination with PMMA is feasible by virtue of the stability of both antibiotics at body temperature, water solubility to permit the diffusion of antibiotic from PMMA, low incidence of hypersensitivity reactions, and heat stability at temperature up to 100°C (occurring frequently during cement polymerization). Finally, the new glycopeptide, teicoplanin, has offered several advantages over vancomycin above all for home therapy because it can be administered by i.v. bolus injection once daily and does not require a central venous catheter.

Recently, for infected diaphyseal fractures or peri-prosthetic diaphyseal fractures the use of an intramedullary nail (Ender type nail, 3–3.5 mm in diameter) has been proposed coated in polymerized PMMA and loaded with antibiotic, so as to eliminate infection and achieve union by hardware removal with debridement, loaded with antibiotic, so as to eliminate infection and has been proposed coated in polymerized PMMA and

**Intramedullary Nails**

Stainless steel (AISI316) nails, 4 mm in diameter and 50 mm in length, were made by coating an inner core of stainless steel wire (AISI316), 1.31-mm in diameter with PMMA cement (Cemex®, Tecres SpA, Sommacampagna, Verona, Italy) with a PP mold. Gentamicin (USP grade, Shangai Fourth, China) and vancomycin powders (USP grade, Abbott Lab, Latina, Italy) were mixed with PMMA copolymer powder prior to the addition of liquid polymer under laminar flow to obtain an antibiotic loaded PMMA nail with the following chemical composition (w/w): polymerized PMMA 89.93%; barium sulfate 5.00%;

**MATERIALS AND METHODS**

**Experimental Design**

The study was performed in accordance with the European and Italian Law on animal experimentation. The animal research protocol was approved by the Technical Scientific Committee and Ethical Committee of the "Istituti Ortopedici Rizzoli" and by the appropriate public authorities. Twenty adult male New Zealand rabbits (Charles River SpA, Calco, Lecco, Italy), body weight 3.00 ± 0.20 kg, were obtained 10 days prior to surgery to acclimatize, housed in individual cages, and fed with a standard pellet diet (Piccioni Settimo Milanesse, Milano, Italia) and water ad libitum. General anaesthesia was induced by i.m. injection of 44 mg/kg ketamine (Ketavet 100, Intervet Productions Srl, Aprilia-Latina, Italy) and 3 mg/kg xylazine (Rompun, Bayer SpA, Milano, Italy). During the surgical procedure, anaesthesia was maintained with O₂/N₂O (1/0.4 L/min) mixture and 2.5% isofluorane (Forane, Abbot SpA, Campoverde di Aprilia-Latina, Italy) delivered by nose cone under assisted ventilation. Rabbits were fasted for 24 h prior to surgery.

In all animals intramedullary bone infection of the right femur was induced via inoculum of MRSA, by a modification of the Rodeheaver at al. femoral model. Four weeks later, the animals were treated according to one of four regimens. Five rabbits (Group 1) were treated with bone debridement and received an intramedullary stainless steel nail. Five rabbits (Group 2) were treated with bone debridement and received an intramedullary stainless steel nail coated with gentamicin–vancomycin-loaded PMMA. Five rabbits (Group 3) were treated only with bone debridement. The last five rabbits (Group 4) were treated with bone debridement and had 1 week of intramuscular teicoplanine (Targosid 200 mg/3 mL, Aventis, Lainate-Milano, Italy) administration at a dose of 20 mg/kg twice daily. Postoperatively, the functional activity of animals was not limited, and they received only standard postoperative pain medication for 3 days (0.2 mg/kg meloxicam s.c., Metacam, Boehringer Ingelheim Italia SpA, Milano, Italy).

All the animals underwent clinical follow-up with measurement of the body temperature (rectal) and body weight, a laterolateral radiography of both the femurs 4 weeks after the operation of bacterial inoculum, before surgical debridement or debridement and insertion of the intramedullary nail, and at 7 weeks (euthanasia). At the same experimental times, in all animals the intramedullary infected bone was swabbed.

The animals were pharmacologically euthanized under general anaesthesia by an i.v. injection of a solution 1 mL/kg consisting of 200 mg N-[2-(m-methoxyphenyl)-2-ethyl-buthyl-(1)-gamma-hydroxybutyramide, 50 mg 4,4'-methylene-bis(cyclohexyltrimethyl-ammoniumiodide) and 5 mg tetracaine hydrochloride (Tanax, Hoechst Roussel Vet, Milan, Italy). Under sterile surgical conditions, the right femur of each rabbit was explanted, cleaned of soft tissue, and the midshaft of each femur was cut with a bone saw. The distal parts of the femurs were used for microbiologic and histological investigations.

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gentamicin sulfate 3.20% (equivalent to 1.87% of gentamicin base); and vancomycin chloridrate 1.87% (equivalent to 1.87% of vancomycin base). The amount of cement used in each antibiotic-loaded PMMA nail was 0.7 g, corresponding to 17 mg of gentamicin and 17 mg of vancomycin.

Finally, all nails were supplied individually in surgical packs sterilized by ethylene oxide according to the international standard ISO 11135:1994 on the validation and routine control of ethylene oxide sterilization of medical devices.

**Bacterial Cultures and Bacteriological Investigations**

The MRSA strain used in this study was originally isolated from a patient suffering from chronic osteomyelitis and maintained in culture for several years. The antimicrobial susceptibility of this MRSA isolate was determined using an antibiotic twofold method performed in tubes containing Mueller Hinton Broth (MHB) before using the strain to induce the experimental osteomyelitis in rabbits. The isolate used in this study was resistant, in vitro, to beta-lactam antibiotics, erythromycin, tetracycline, quinolones, and sulfamethoxazole–trimethoprim, while the susceptibility to clindamycin, aminoglycosides, glycopeptides, and rifampin was preserved.

The MRSA inoculum was prepared from overnight cultures grown in MHB starting from a frozen batch at −80°C and aliquots were prepared. The cells were harvested by centrifugation, washed with saline solution, and resuspended to a final density of 5 × 10^8 CFU/mL of MHB obtaining a volume of 0.2 mL. The MRSA inocula were stored at 4°C and used within 12 h of their preparation. The density and purity of each cell preparation were verified by colony counts on selective media by plating on horse blood agar before the surgical session. The number of colonies in each plate was counted by a blinded operator and the bacterial concentration was determined.

The swabs of the intramedullary infected bone were processed within 2 h. One milliliter of MHB was added to each swab and the tube was agitated for 3 min on a vortex to suspend the bacteria collected onto the swab. A serial 10-fold dilution of the bacteria collected onto the swab and the tube was agitated for 3 min on a vortex to suspend each suspension was used to evaluate the bacterial load: 10^8 mL of each dilution was plated onto horse blood agar and the plates were incubated at 37°C for 8 days. At the end of the incubation period the number of MRSA colonies on each plate was counted.

**Radiographic and Histological Analysis**

All the radiological images obtained at 4 and 7 weeks (before the explant) were digitized using a scanner (HP ScanJet 4850) to a resolution of 600 dpi and assessed using the score proposed by Norden et al. modified according to An et al. The score evaluates the presence (1) or absence (0) of sequestrum formation, joint effusion and soft tissue deformation, the periosteal elevation (present: 1; equivocal: 0.5; absent: 0) and osteolysis (severe: 2; moderate: 1; mild: 0.5; absent: 0). The maximum score was 6. In this scoring system, animals were considered to have radiological osteomyelitis when the severity score was 2 or more.

The bone segments used for histology were fixed in 4% paraformaldehyde, dehydrated in alcohol series, and embedded in polymethylmethacrylate. Decalcified transversal sections of femoral midshafts and longitudinal sections of distal epiphyses of 40 ± 10 μm in thickness were yielded by means of the Leica SP 1600 diamond saw microtome cutting system (Leica SpA, Milano, Italy). Then, the sections were stained with Toluidine Blue and Acid Fuchsin and observed to an optic microscope (BX41, Olympus Optical Co. Europa GmbH, Germany). The transverse sections of the femoral diaphysis and longitudinal sections of the distal epiphysis were acquired with a resolution of 300 dpi at different enlargements. Histologically, the disease severity score described by Smeltzer et al. was used to rate signs of infection; it is divided into four categories with a score from 0 to 4 points: intraosseous acute inflammation, intraosseous chronic inflammation, periosteal inflammation, and bone necrosis. The diagnosis of osteomyelitis was considered positive when the Smeltzer score was at least 4. The maximum score of 16 indicated severe osteomyelitis with intramedullary abscesses, fibrosis, and multiple foci of sequestra.

**Statistical Methods**

Statistical analysis was performed using SPSS version 12.1 (SPSS Inc, Chicago, IL). Data are reported as mean ± standard error of the mean (SE) at a significance level of p < 0.05. The results were analyzed using one-way ANOVA and, then, Dunnett post hoc comparison test, accordingly to the following items: (1) Group 2 versus Group 1; (2) Group 3 versus Group 2 or Group 1; and (3) Group 4 versus other Groups. Paired
Student's t-test was used to compare the radiological score results between 4 and 7 weeks after inoculum.

RESULTS

The animals tolerated well the surgical operation of MRSA inoculum and the second operation of debridement and/or insertion of the intramedullary nail, but one animal from Group 1 was sacrificed at the end of the operation, because, radiologically, a diaphyseal fracture was observed. Upon euthanasia of this animal, however, the samples described for the fulfilment of the experiment were taken. Wound dehiscence or infections of the soft tissues did not occur in either postoperative period. During sacrifice macroscopic evaluation showed the maintenance of the correct placement of the samples in the femoral site, concerning Groups 1 and 2.

The results of the clinical evaluations performed before the operation of bacterial inoculum, before the operation to insert the intramedullary nail, and at the end of the study did not show differences in the variations of body weight and body temperature between the fourth and seventh week.

The results of the radiological evaluation showed how 4 weeks after inoculum all the Groups developed osteomyelitis (Table 1). Particularly, between the fourth and the seventh week an increase of 26% was observed for Group 1 (ns), and 68% for Group 3 (p < 0.05), while for Group 2 and Group 4 a reduction in the same time lapse, respectively by 38% (p < 0.01) and 10% (ns), was found. The lowest radiological score was achieved at 7 weeks by Group 2 that was significantly different from Group 1 (p < 0.01) and Group 3 (p < 0.001). Finally, there was a significant difference only between Group 4 and Group 3 (p < 0.05).

Table 1 reports the results of the intramedullary bacterial load. The highest bacterial load in the femoral canal at sacrifice was found in Group 1, which was significantly different with Group 2 and Group 4 (p < 0.05). No significant differences were observed between Group 3 and Group 4 (Table 2). Figure 1 shows SEM images of bacterial colonization of tested nails; the gentamicin–vancomycin impregnated PMMA nail was effectively protected from MRSA colonization in contrast to the stainless steel nail.

The histological analysis on the sections of the animal, submitted to euthanasia 4 weeks after the inoculum, due to iatrogenic fracture, revealed how the infectious process greatly damaged the cortex, where ample areas of osteolysis and deposition of new bone were present particularly at the cancellous, periosteal level, thus determining the diaphyseal fracture after reaming and the introduction of the intramedullary nail (Fig. 2a). Inside the medullary canal of this animal (Fig. 2b), as in some other cases in Group 3 and Group 4, intramedullary abscess areas were present formed by polymorphonucleated leukocytes, macrophages, and degenerated cells, and bacteria (Fig. 2c). In Group 1 and Group 2, which underwent bone debridement, processes of bone

Table 1. Results of the Radiological Score Performed on the Right Femur for Each Group 4 and 7 Weeks after the Inoculum (Mean ± SE)

<table>
<thead>
<tr>
<th>Group</th>
<th>4 Weeks</th>
<th>7 Weeksa</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.1 ± 0.4</td>
<td>3.9 ± 0.5</td>
</tr>
<tr>
<td>2</td>
<td>3.2 ± 0.3</td>
<td>2.0 ± 0.2bc</td>
</tr>
<tr>
<td>3</td>
<td>2.5 ± 0.3</td>
<td>4.2 ± 0.3cd</td>
</tr>
<tr>
<td>4</td>
<td>2.9 ± 0.4</td>
<td>2.6 ± 0.2cd</td>
</tr>
</tbody>
</table>

*aOne-way ANOVA (F = 8.56, p < 0.001) and Dunnett test. *Group 2 versus Group 1 (p < 0.01). *Group 3 versus Group 2 (p < 0.005).

*bGroup 4 versus Group 3 (p < 0.05). Paired Student’s t-test: 4 weeks versus 7 weeks for Group 2 (p < 0.01) and Group 3 (*p < 0.05).

Table 2. Quantitative Microbiological Analyses of the Cultured Swab Specimens at 7 Weeks from Bacteria Inoculums and Histopathologic Results of Distal Right Femur (Longitudinal Sections) for Each Group Using the Smeltzer Score (Mean ± SE)

<table>
<thead>
<tr>
<th>Group</th>
<th>Intramedullary Bacterial Load (Log 10^5 CFU/mL)</th>
<th>Smeltzer Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.5 ± 2.0</td>
<td>6.3 ± 0.6</td>
</tr>
<tr>
<td>2</td>
<td>0a</td>
<td>2.6 ± 0.3c</td>
</tr>
<tr>
<td>3</td>
<td>6.2 ± 2.3</td>
<td>7.6 ± 0.4d</td>
</tr>
<tr>
<td>4</td>
<td>1.1 ± 0.5b</td>
<td>5.4 ± 1.1e</td>
</tr>
</tbody>
</table>

Intramedullary bacterial load at 4 weeks: 4.7 ± 2.2 log 10^5 CFU/ml; one-way ANOVA (F = 8.24, p < 0.001) and Dunnett test: *Group 2 (the bacterial load was 0) versus others, and *Group 4 versus Group 1 (p < 0.05). Smeltzer score; one-way ANOVA (F = 9.94, p < 0.001) and Dunnett test: *Group 2 versus Group 1 (p < 0.005). *Group 3 versus Group 2 (p < 0.001). *Group 4 versus Group 2 (p < 0.05).
growth were observed starting from the endosteum, not only connected to the reaming of the bone, but also to an extension of the bone necrosis due to the presence of the direct contact of the nail with the endosteal surface.45

Table 2 shows the score obtained with the Smeltzer scale. A score higher than or equal to 4 was achieved by all the animals of Group 1 and Group 3, in 60% of those of Group 4, and in none of those of Group 2. In detail, acute intraosseous inflammation was found in 100% of the cases of Group 3, 80% of the cases of Group 4, 25% of the cases of Group 1, whereas in Group 2 the rate was 0%. Chronic intraosseous inflammation was observed in 100% of the cases of Group 1, 80% of the cases of the Group 2, 40% of the cases of Group 4, and 20% of the cases of Group 3. Periosteal inflammation and bone necrosis occurred in 100% of the cases of Groups 1, 3, and 4, and only in 80% of the cases of the Group 2. The statistical analysis of the Smeltzer score showed a significant difference between the results of Group 2 and Group 1 \((p < 0.005)\) and Group 3 \((p < 0.0005)\). Also, the results of Group 4 were significantly different from those of Group 2 \((p < 0.05)\).

**DISCUSSION**

In general, the rationale of using an antibiotic-impregnated metal-reinforced PMMA nail in fractures complicated by bacterial osteomyelitis is mainly to guarantee fracture stability and deliver locally antibiotics. It fills the medullar canal, thus reducing this avascular noncollapsible dead space38 and hence elution of higher concentrations of antibiotic at the endosteal surface. The present study aimed to investigate in vivo, in an animal model of intramedullary bone infection, the efficacy of a new gentamicin–vancomycin-impregnated PMMA nail, conceived for fracture fixation at risk of infective complications, as a drug delivery system. The results of the current experimental study confirmed the potentially bacteriological efficacy of the gentamicin–vancomycin combination in treating local osteomyelitis caused by MRSA, when compared to surgical debridement and to systemic antibiotic therapy. The gentamicin–vancomycin-impregnated PMMA nail proved to eradicate bone infection, and in vitro to prevent bacterial adhesion as well as biofilm formation through the elution of high concentrations of antibiotic. The antiadhesive properties is a characteristic of material surface, as a result of molecular structure, low surface energy, and cleanliness of the material, to prevent bacterial adhesion or to kill bacteria shortly after adhesion during the reversible phase, before adequate environmental conditions give bacteria the chance to produce biofilm.46,47

From weeks 0 to 4, the infectious process followed a steady course showing a femoral cross-sectional widening with a marked enlargement of the medullary area and thickening of the cortex, due to periosteal reaction. Despite debridement of the medullary cavity, which had the aim of removing dead, damaged, or infected tissue and improving the healing potential of the remaining healthy tissue, infections recurred in the control animals after 3 weeks (Group 3). The animals receiving the fixation device without systemic or local antibiotic therapy (Group 1) showed higher rates of infected samples than those of infected debrided controls. This worsening was due to the stainless steel implant that, once coated in host proteins, provided an excellent source of attachment for bacteria remaining after debridement surgery. Once attached, the bacteria can form the glycocalyx, which protects them from normal host defences and systemic antibiotics.

The 1-week systemic administration of teicoplanin in Group 4 only provided low concentrations of MRSA in the intramedullary canal, confirming that eradication of SA from the bone with a systemic antibiotic is a difficult task. Teicoplanin is supposed to present some advantages over vancomycin in the treatment of osteomyelitis.24 In particular, teicoplanin was as effective as vancomycin in reducing CFU numbers in bone in an experimental study of prosthetic joint infection,24 while it was completely unable to sterilize bone in Norden’s osteomyelitis model.48 These different effects were related to the heterogeneous diffusion of teicoplanin in the infected tissues: lower in compact bone and higher in bone marrow, artiﬁcial joint space and blood (neutrophils).24

The advantages of local antibiotic treatment (Group 2) as opposed to systemic application are evident, because the reduction in bacterial count was complete \((0 \log 10^5\) CFU/mL) compared to groups that received systemic antibiotics, with no abnormal pathologic findings.

Regarding the animal model used for osteomyelitis, the rabbit femoral model is less frequently used than the tibia model, but its larger medullary canal and thicker cortical width allows easier foreign body insertion or implant fixation.41 Because it is well known that any attempts to initiate osteomyelitis would benefit from bone prelesions (i.e., using the sclerosing agent sodium

![Figure 2](image_url). Pictures of transversal histological sections of the right femur at 7 weeks: (a) Group 1, periosteal hyperresponse with large areas of the newly formed bone transformed into cancellous tissue; ample area of osteolysis in the cortex with the presence of an initial sequestrum (S) near an intramedullary abscess (A) (original magnification \(2\times\)); (b) Group 2, bone growth endosteal (NB) toward the implant.
morrhuate), we decided to damage the femoral cavity by removing the bone marrow by suction and inoculating a high concentration of MRSA, without observing any case of early mortality by acute sepsis. In fact, it has been shown that the local withdrawal of bone marrow produces a complete destruction of medullary blood vessels, thus enhancing local infection and reducing mortality.

The experimental setup of the study had some limitations because of the lack of other experimental groups. First, following the results found by Ismael et al., which showed no differences between a group treated by a drug-free cement device and an untreated control group in terms of bacterial count (31% higher than untreated control group); a drug-free cement intramedullary nail group was not included because no deleterious effect on the progression of bone infection was expected, thus reducing the number of animals used. In our opinion, a drug-free cement device would not have represented the specific control of Group 2, which is a metallic fixation device already used in clinics, and because: (1) the PMMA coating does not increase the mechanical seal of a fixation device; (2) it is well known that PMMA is the material most prone to causing infection due to its high porosity and irregular surface that allows bacterial adhesion; and (3) PMMA inhibits complement activation and reduces polymorphonuclear mobility, phagocytosis, and intracellular lysis of bacteria, limiting the response of host to bacterial infection.

Besides a drug-free nail (stainless steel or cement), a group with systemic antibiotic treatment was not planned. However, the observation that systemic therapy was not able to counteract bone infection in Group 4 without any implanted nail (as observed with the radiological score, Smeltzer’s histological score and microbiological tests) suggests that systemic therapy would not be sufficient to treat osteomyelitis in the presence of an implanted nail, which would inhibit the defense system because of dealing with the infective insult. In reference to the duration of teicoplanin treatment for 1 week, it was established by taking into account the results obtained by Mghir et al. and above all the regrowth of MRSA after the end of therapy, while avoiding the persistence of residual antibiotic in tissue.

The most important limitation is that the antibiotic concentrations in serum and bone were not evaluated in animals receiving gentamicin–vancomycin-impregnated PMMA nails or systemic teicoplanin. These results might have explained the different responses observed in Group 2 and Group 4 by also considering their trends over time. It is frequently stated that one of the substantial disadvantages in the use of PMMA as an antibiotic delivery system for local treatment is the low-level subinhibitory release after the burst release has subsided, thereby also inducing and selecting antibiotic resistance of bacteria. The in vitro study performed by Bertazzoni et al. on different PMMA devices impregnated with the same association of antibiotics showed that (1) the release kinetics of the combination was initially high followed by sustained constant release of both antibiotics, (2) the release profile of gentamicin and vancomycin was superimposable, and (3) gentamicin release was enhanced by the presence of vancomycin. The concentrations of antibiotics eluted at different times showed effective antibacteric activity exceeding the MIC with different periods of activity.

In particular, it was found that the gentamicin–vancomycin association determines an increase in the gentamicin release even after 30 days of elution with a MIC of 1.5–2 mg/day (data not shown). These high MIC levels are much higher than the subinhibitory releases reported in the literature and responsible for antibiotic resistance and released in a time interval similar to the fracture healing. However, in vitro data has to be confirmed in vivo because of the reported discrepancies between the two situations, and future studies are planned by taking into consideration also the influence of different PMMA porosities.

In conclusion, the current findings showed that the antibiotic-impregnated PMMA nail could effectively lead to infection healing after surgical debridement and immediate implantation. The results showed the development of the infectious process inside the medullary canal with alterations of the cortical bone, the presence of intramedullary abscesses, especially in the cases not treated with intramedullary nail, signs of bone necrosis, and sometimes formation of sequestra; signs of chronic inflammation have been observed in some cases with implanted intramedullary nails. The intramedullary nail with antibiotic-impregnated PMMA coating is able to arrest the infectious process by destroying all the bacterial colonies that have developed from the inoculum. The next step will be the evaluation in vivo of the antibiotic concentrations in serum and bone in animals receiving gentamicin–vancomycin-impregnated PMMA nails by using an animal model of MRSA infected fracture to develop an alternative solution to treat existing osteomyelitis by MRSA, sometimes severe, and not responding to systemic antibiotic therapy alone, in the fracture site, treated surgically with internal fixation devices.

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