NEW ANTIBIOTIC FOR TREATMENT OF MRSA INHIBITS PMMA POLYMERIZATION

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INTRODUCTION
Despite the emergence and continued evolution of periprosthetic hip and knee infections resistant to standard antimicrobial therapy, there has been relatively little research concerning the elution of newly developed antibiotics from commercially available bone cements. Tigecycline, a newly developed antimicrobial drug in the novel antibiotic class of glycylcyclines, is indicated for the treatment of methicillin resistant staphylococcus aureus (MRSA). While investigating the antibiotic elution properties of Tigecycline from PMMA, we observed marked alterations in the polymerization characteristics of Palacos® and Simplex™ containing Tigecycline. This report details the observed changes in heat generation and curing of commercially available bone cements when Tigecycline is added to them.

METHODS
Commercially available PMMA (Palacos® and Simplex™) were used for all experiments and were mixed according to the manufacturers specifications. Tigecycline powder (400 mg) was homogenized prior to addition to either 40 g of Palacos® or Simplex™ pre-polymerized polymer. All experiments were performed at 25°C and 25% relative humidity using pre-chilled monomer to extend PMMA handling times. PMMA monomer and polymer were hand mixed under atmospheric pressure in a standardized mixing vessel and then transferred into 20 cc syringes as rapidly as possible to standardize the geometry of the curing PMMA masses. While the PMMA was curing in the 20 cc syringes, temperatures (˚C) were recorded at regular time intervals for 30 minutes using a thermocouple probe placed in a standardized position within the curing PMMA masses.

Standard two sample t-tests were used to compare the maximum temperatures attained and the times to maximum temperature attained for all experimental groups. Assessments of PMMA workability and indentation testing (scalpel blade pressed against the PMMA mass) were performed at 15 minutes, 30 minutes, and 1 hour after PMMA mixing to assess hardening of the PMMA masses.

RESULTS
The thermal profiles of polymerizing Palacos® with and without the addition of 400 mg Tigecycline are displayed in the graph and table below (N=3, each).

DISCUSSION
Antibiotic containing PMMA is an important tool utilized for treatment of infected hip and knee replacements. Because antimicrobial resistance of periprosthetic hip and knee infections is increasing, the clinical applicability of newly released antibiotics capable of treating these resistant infections must be investigated. Previously, it has been suggested that addition of up to 3 grams of powdered antibiotic per 40 gram pack of pre-polymerized PMMA does not significantly affect the polymerization and mechanical properties of PMMA bone cement.

This investigation demonstrates that much smaller quantities of the newly released antibiotic Tigecycline (400 mg antibiotic per 40 gram pack) causes significant changes in PMMA properties. The addition of Tigecycline to both Palacos® and Simplex™ significantly decreased heat generation of curing PMMA masses indicating a significant inhibition of the polymerization reaction for these two commercially available bone cements. Furthermore, the gross mechanical characteristics of Palacos® and Simplex™ were significantly altered by the addition of Tigecycline.

Tigecycline has been shown to be an effective intravenous antibiotic for treatment of MRSA and other life threatening infections. However, this investigation suggests Tigecycline inhibits PMMA polymerization as well as diminishes PMMA mechanical characteristics and is therefore not suitable for addition to bone cement.