Ultrasound-Enhanced Ciclopirox Delivery for Treatment of Onychomycosis
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INTRODUCTION
Onychomycosis is a fungal nail disorder that is characterized by thick and yellow nails that can be extremely painful and lead to psychosocial issues. In onychomycosis, the fungus lives on the nail bed. Due to the poor permeability of the nail, current antifungal drugs, which are applied to the top of the nail, are unable to reliably reach the nail bed, making them ineffective in treating the fungus. The aim of our study has been to determine the efficacy of using ultrasound to increase the permeability of the nail with the goal of improving treatment success in onychomycosis.

MATERIALS AND METHODS
Two sets of ultrasonic experiments were performed using porcine nails. In both experiments, planar ultrasound transducers were used to sonicate the nails using frequencies of 400 kHz, 600 kHz, 800 kHz, and 1 MHz, an intensity of 1 +/- 0.1 W/cm² and a duration of 5 min in continuous mode. Both experiments also utilized a Franz Diffusion Cell Setup. In the first set of experiments – the Dye Diffusion Cell Experiments, the nail was placed above a receiving compartment that was filled with saline and below a donor compartment that was filled with a drug-mimicking blue dye. The second set of experiments – the Ciclopirox Diffusion Cell Experiments, used a donor compartment that was filled with Ciclopirox, the drug used in clinic for onychomycosis treatment, and the receiving compartment was filled with ethanol because the drug is nonpolar. The nails in the experiments were sonicated and the absorbance of the receiving compartment was measured to determine the permeation of dye through the nail.

RESULTS AND DISCUSSION
In both the Dye Diffusion Cell Experiments and the Ciclopirox Diffusion Cell Experiments, the nails were found to have more permeation at higher frequencies. In the Dye Diffusion Cell Experiments, statistical significance (p<0.05) was found at all frequencies, but the greatest permeation was found with increasing frequency. In the Ciclopirox Diffusion Cell Experiments, only the 800 kHz and 1 MHz experiments were found to be statistically significant (p<0.05), with more permeation in the 1 MHz experiment.

CONCLUSION
Our lab has recently obtained IRB approval to work with human nails, and plan to implement the Ciclopirox Diffusion Cell Experiment using these nails. If proven successful, our method may find a clinical application due to the non-invasive nature of proposed therapeutic ultrasound treatment.