

PLASMA-BASED THERAPIES FOR BONE INFECTION: A TRIPARTITE USA/NORTHERN  
IRELAND/REPUBLIC OF IRELAND CONSORTIUM

**ABSTRACT** Orthopaedic infection is life-threatening and current treatments are only sparingly successful. Despite aggressive peri-operative antibiotic treatments, 1.5% of knee revisions, 0.7 to 11.9%, of spinal infections (depending on the complexity of the procedure) and up to 27% of open fractures become infected. Moreover, the complexity of tissues interfacing with the biofilm-prone orthopaedic instrumentation complicates bacterial eradication making current treatments prolonged and expensive. To address this serious issue, we propose to combat the infection using cold plasma and cold plasma activated liquid (PAL). Our pilot data show that these novel modalities can be tailored for high microbicidal activity coupled with immune stimulatory properties without the risk of antibiotic resistance. Importantly, these modalities have not been used to combat bone infections. To utilize this technology to address orthopaedic infection, a tri-partite consortium of international research teams at the forefront of cold plasma technology from the US, the Republic of Ireland and Northern Ireland have been assembled. This consortium unites expertise in plasma engineering, microbiology, material science, chemistry, cell biology, and clinical medicine. There are three Specific Aims. (1) To determine the effect of direct cold plasma treatment on MRSA biofilms and immune cell response; (2) To determine the mechanisms of action, and efficacy of Plasma Activated Liquid (PAL) alone and in combination with direct cold plasma treatment to eradicate infection; and (3) To resolve infection through combined cold plasma and PAL treatments in a clinically relevant animal model of infected osteotomy. We will develop cold plasma and PAL treatments that will directly disrupt biofilms and eradicate bacteria while stimulating the immune response. At the end of this study, we will have developed a simple and effective non-antibiotic treatment protocol to cure surgical site infection through combined immune activation and direct eradication of bacteria. Clinically, this cold plasma+PAL treatment protocol can be seamlessly integrated with existing clinical protocols to enhance and eventually replace our reliance on antibiotic therapies.

**Public Health Relevance Statement:**

**PROJECT NARRATIVE** Orthopaedic bone infection is life-threatening and current treatments are only sparingly successful. To overcome the barriers associated with eradicating infection from bone, we will develop cold plasma and plasma-activated liquid (PAL) treatments that directly disrupt biofilms and eradicate bacteria from bone and surrounding tissues, while stimulating an immune response. This novel approach will alleviate complications associated with antiseptic toxicity, antibiotic resistance and overuse, and permit robust tissue healing.