

ICM 2025 Question B26: “Can electric fields be used to detach and destroy biofilm?”

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RESPONSE/RECOMMENDATION: Yes. Electric fields can be used to detach and destroy biofilm, but its application in orthopaedics is unknown.

LEVEL OF EVIDENCE: Weak

DELEGATE VOTE: Agree: [30/97% vote], Disagree: [0%], Abstain: [1/3%]

RATIONALE: Biofilms represent a significant challenge in clinical and industrial settings due to their resistance to conventional antimicrobial therapies. Biofilm contains microbial communities adhering to surfaces and are embedded in a complex protective extracellular polymeric substance (EPS), rendering the bacteria buried within the biofilm highly tolerant to antibiotics and immune responses.¹ Recently, intravital imaging studies in a murine model demonstrated that *in vivo* *S. aureus* biofilms form very quickly and the race for the surface is completed within 3 hours⁴. Thus, preventing biofilm formation is of critical importance. Infections involving biofilms, particularly in osteoarticular implants, often lead to chronic conditions that require innovative therapeutic approaches. One emerging strategy is the use of electric fields, which have shown promise in limiting bacterial growth which in turn limits biofilm formation. Less biofilm formation enhances the efficacy of antimicrobial agents.^{2,3} This document evaluates the mechanisms, clinical applications, and recommendations for the use of electric fields in biofilm management. To answer this question a comprehensive literature search was conducted using the search words “electric field” and “biofilm” within PubMed and Embase, which initially identified 290 relevant unique studies, which were screened by two independent reviewers and 24 were included for evaluation.

***In vitro* Mechanisms of Electric Fields in Biofilm Disruption**

- 1. Electrostatic Disruption:** Electric fields destabilize the EPS matrix by altering the ionic interactions that maintain its structural integrity. A study by Ge et al.⁴ demonstrated that these fields significantly reduce biofilm adhesion on medical-grade materials by disrupting electrostatic forces.⁴
- 2. Electroporation:** By applying electric pulses, microbial cell membranes become transiently permeable, a phenomenon known as electroporation. This effect facilitates the penetration of antimicrobial agents into deeper layers of the biofilm. Wu et al. highlighted the effectiveness of electroporation in increasing antibiotic uptake in biofilm models.⁵
- 3. Generation of Reactive Oxygen Species (ROS):** Certain electric fields can trigger the generation of ROS, which cause oxidative damage to both microbial cells and the biofilm matrix. Chen et al. demonstrated that ROS production under electric field application led to a 70% reduction in biofilm biomass in *in vitro* studies.⁶
- 4. Enhanced Antibiotic Efficacy:** Electric fields disrupt the protective barriers of biofilms, making microbial cells more susceptible to antibiotics. Recent research by Sedighi et al. found that combining electric fields with antibiotics resulted in a fourfold reduction in minimum inhibitory concentrations (MICs) for resistant strains.⁷ This effect is thought to be due to increased permeability of the EPS which enables antimicrobials to reach the bacteria harbored within the biofilm.
- 5. Electrolytic surface cleaning.** The application of electric fields can induce localized electrochemical reactions at the surface of medical devices, leading to the generation of microbubbles and pH changes that facilitate biofilm detachment. This process, often referred to as electrolytic cleaning, disrupts biofilm integrity by physically removing adherent microbial communities and degrading the extracellular polymeric substances.

Evidence from Research

A review of recent studies highlights the potential of electric fields in biofilm management, supported by evidence from various preclinical and in vitro models. For instance, Sedighi et al. demonstrated that electric fields combined with nanoparticles could disrupt biofilm architecture more effectively than conventional treatments.⁷ Additionally, Wu et al. showed that biofilm biomass on metallic implants was reduced by over 60% when subjected to low-intensity electric fields⁸. Such findings underscore the versatility and efficacy of this approach in tackling biofilm-related challenges.

Application of cathodic DC current on biofilm substrates causes electro-repulsive interactions with negatively charged bacteria, leading to significant detachment. For example, applying a $15\mu\text{A}/\text{cm}^2$ cathodic current for 40 minutes to a *P. aeruginosa* biofilm detached approximately 80% of the bacteria, with the remaining bacteria still viable. An anodic current did not significantly remove bacteria but inactivated them over time. Block current (what is block current?) is more efficient in both detaching bacteria and inactivating remaining bacteria on surfaces⁹. Previously, electricity was considered to only enhance the effectiveness of antibiotics and biocides against biofilms, without significant independent effects¹⁰. However, recent studies show that long-term exposure to low-amperage electric fields can have electricidal effects, leading to bacterial cell death via reactive oxygen species.¹¹ Ashrafi et al. evaluated the efficacy of electrical stimulation with or without antibiotics on methicillin-susceptible *S. aureus* and *P. aeruginosa* biofilms *in vitro* and *ex vivo*. They applied 100mV/mm DC for 30 minutes, followed by the addition or absence of ciprofloxacin. While electrical stimulation was less effective than antibiotics in biofilm reduction, it did reduce bacterial viability compared to untreated controls. The addition of electrical stimulation did not improve ciprofloxacin's activity in the *ex vivo* study [4]. A 6V DC with 1k Ω resistor led to a 4-log reduction in *P. aeruginosa* biofilm around the anode in an agar plate biofilm model, continuing antimicrobial effects after the electric field was turned off due to migration of cidal compounds.³ Silver-Zinc redox-coupled electrochemical dressings (Ag/Zn WED) effectively disrupted *P. aeruginosa* biofilms *in vitro*, even under conditions where silver-based dressings were ineffective. Ag/Zn WED generates superoxide to kill bacteria and inactivate the Mex efflux pump system, helping overcome antibiotic resistance. It also reduced *quorum* sensing gene expression and pyocyanin production, both essential for biofilm formation and pathogenicity in *P. aeruginosa*. Moreover, WED inhibited glycerol-3-hydrogenase enzyme activity, involved in persister cell formation.¹² This treatment also proved effective *in vivo* against polymicrobial biofilm infections in a porcine wound model, outperforming standard wound care treatments in clinical trials^{13; 14}. Studies on alternating current (AC) show that the frequency can influence biofilm inhibition. High-frequency AC (MHz to kHz) temporarily inhibits biofilm growth, while low-frequency AC (100 Hz) reduces it permanently by around 50%. At 1 Hz, all attached cells are removed due to water electrolysis and gas bubble production.¹⁵ AC electromagnetic fields of 20-30 kHz suppressed *E. coli* and *S. epidermidis* biofilms, likely through disruption of the bacterial extracellular membrane.¹⁶ Radio frequency AC (10 MHz) enhanced antibiotic efficacy against *E. coli* biofilms by increasing matrix fluidity and allowing better penetration of antibiotics.¹⁷ AC was also more effective than DC in reducing biofouling and preventing *Pseudomonas putida* attachment and detachment in carbon nanotube membranes at 1.5 V, 1 kHz¹⁸

Electrochemical methods to control biofilms involve altering substrate surface properties via galvanostatic or potentiostatic treatments to prevent attachment or detach existing cells through electrostatic repulsion. In one study, cathodic polarization applied to a stainless-steel substrate led to biofilm removal on *P. aeruginosa* at potentials above -1.5 V, where hydrogen gas production from water electrolysis helped remove the biofilm.¹⁹ A recent study reported significant reductions in *S. epidermidis*, *S. aureus*, and *P. aeruginosa* biofilms following exposure to DC currents of 2000

microamperes for 2-7 days ²⁰In a rabbit model, DC significantly reduced bacterial growth in *S. epidermidis* biofilm infections compared to doxycycline treatment alone ²¹

Additionally, photo-thermoelectric effects, such as using Near-Infrared light-responsive ZnO/black TiO_{2-x} heterojunction surfaces on titanium implants, effectively eliminated multispecies biofilms in vitro and in vivo ⁶. Piezoelectric effects in metal-organic framework nanoparticles were also used to enhance photocatalytic ROS generation, improving the activity of H₂S inhibitors and disrupting the biofilm's redox homeostasis. ⁴

In vitro, studies have demonstrated that electric fields are effective in preventing bacterial adhesion and biofilm formation. Low-intensity electric currents and electromagnetic fields significantly reduce surface colonization by *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Escherichia coli* ²²

Electrolytic Cleaning Using Hydrogen Bubbles. Studies have demonstrated that hydrogen bubbles generated during electrolysis can effectively detach biofilms in a variety of settings. In the field of dentistry, electrolytic cleaning technology has shown particular promise. ²³ This technique has been applied to dental implants and other oral surfaces. While traditional methods, such as direct current (DC) and alternating current (AC), have been widely studied for biofilm control, the generation of hydrogen bubbles via electrolysis appears to offer unique advantages. ²⁴ Direct currents can create electrochemical gradients that inhibit bacterial adhesion and survival. For example, anodic currents lead to localized inactivation, whereas cathodic currents promote detachment through electro-repulsion. In contrast, AC fields have demonstrated biofilm inhibition primarily through matrix disruption and bacterial membrane destabilization at specific frequencies. However, neither DC nor AC methods provide the mechanical detachment benefits inherent to hydrogen bubble formation. Recent studies suggest that bubble-mediated detachment is highly effective for disrupting dense, mature biofilms that are otherwise resistant to conventional cleaning methods. Furthermore, the integration of hydrogen bubble technology with other antimicrobial strategies, such as photodynamic therapy or surface coatings, may further enhance biofilm management in clinical settings. ²⁵ Hydrogen bubble generation offers a minimally invasive, efficient, and scalable solution for managing biofilms in both clinical and non-clinical environments. ²⁶ Future studies should focus on optimizing parameters such as current density, electrolyte composition, and treatment duration to maximize efficacy while ensuring patient safety and material preservation.

Main findings:

Preclinical Models: Experimental data demonstrate significant reductions in biofilm biomass on metallic and polymeric surfaces exposed to low-intensity electric fields. This effect is particularly notable in *Staphylococcus aureus* and *Pseudomonas aeruginosa* biofilms.

Synergistic Effects: Combination therapies using electric fields and conventional antibiotics or nanomaterials show enhanced biofilm eradication compared to antibiotics alone.

Application to Medical Devices: Electric field-generating coatings on implants have been shown to prevent biofilm formation, reducing the risk of osteoarticular infections.

Potential clinical Applications

The integration of electric field-based therapies into clinical practice holds significant potential, particularly in managing infections associated with osteoarticular implants. For instance, Wu et al. demonstrated that low-intensity electric fields effectively reduced biofilm formation on titanium surfaces, a common material in osteoarticular implants. ²⁷ Similarly, research by Sedighi et al. highlighted the synergy between electric fields and antimicrobial coatings, which improved biofilm eradication rates on implant surfaces. ⁷ These findings suggest that electric field-based approaches could play a critical role in preventing and treating implant-associated infections. Potential applications include:

1. **In situ Biofilm Disruption:** Devices capable of delivering electric fields directly to the site of infection can aid in the localized eradication of biofilms.
2. **Adjunct to Antibiotic Therapy:** Electric fields can enhance antibiotic penetration and efficacy, potentially reducing the required dosage and mitigating antibiotic resistance.
3. **Preventive Measures:** Proactive use of electric fields in coatings for surgical implants may prevent biofilm formation and subsequent infections.

Recommendations

Based on the current evidence, the following recommendations are proposed:

1. **Further Research:** Conduct clinical trials to evaluate the safety, efficacy, and optimal parameters (intensity, frequency) of electric fields in biofilm management. Well-designed trials could bridge the gap between experimental and clinical applications.
2. **Device Development:** Invest in the design of electric field-generating medical devices, particularly for use in orthopedics. Research has highlighted the feasibility of integrating electric field technology into implant surfaces.
3. **Guideline Formation:** Establish standardized protocols for the application of electric fields in clinical settings, including contraindications and integration with existing therapies.
4. **Interdisciplinary Collaboration:** Foster partnerships between microbiologists, engineers, and clinicians to translate preclinical findings into practical solutions. Collaborative efforts emphasize the importance of multi-disciplinary approaches in advancing this technology.

Conclusion

The use of electric fields represents a promising avenue in the fight against biofilm-associated infections, particularly in osteoarticular contexts. While preclinical evidence is compelling, further research and development are necessary to establish this modality as clinically safe and/or effective. By leveraging its unique mechanisms and synergistic effects, electric field-based therapies could revolutionize the management of biofilm-related infections. In terms of clinical application, electric fields have not achieved FDA approval. The use of an electric field requires the placement of two needles in contact with the surface of metallic arthroplasty components. This could be done in the operating theatre before wound closure, or in theory, percutaneously in the recovery area. Much work remains in this emerging technology. For example, it remains to be determined the optimal electric settings such as voltage, amperage, and duration of electrical stimulation. Moreover, it is not known if the electric current has any effect on nonmetallic components such as poly or ceramic. Since definitive clinical application parameters are evolving, we cannot make a recommendation for its use at this time.

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