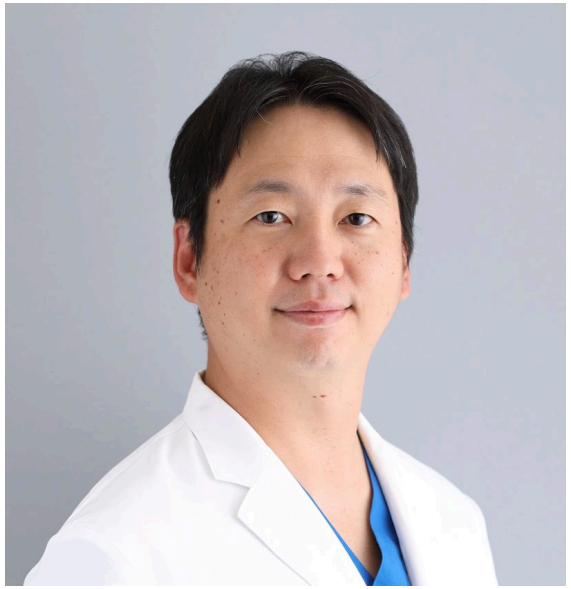
3rd Meeting of the International Consensus Meeting
8-10 of May, 2025 Istanbul

Are there any physical non-cytotoxic methods that can be utilized to disrupt and destroy biofilm in orthopedic infections?

Hyonmin Choe, Bart G Pijls, Dan Schlatterer, Masashi Shimoda, Hiroto Kono, Patrick Sadoghi, Viktor E Krebs, Hamish Simpson



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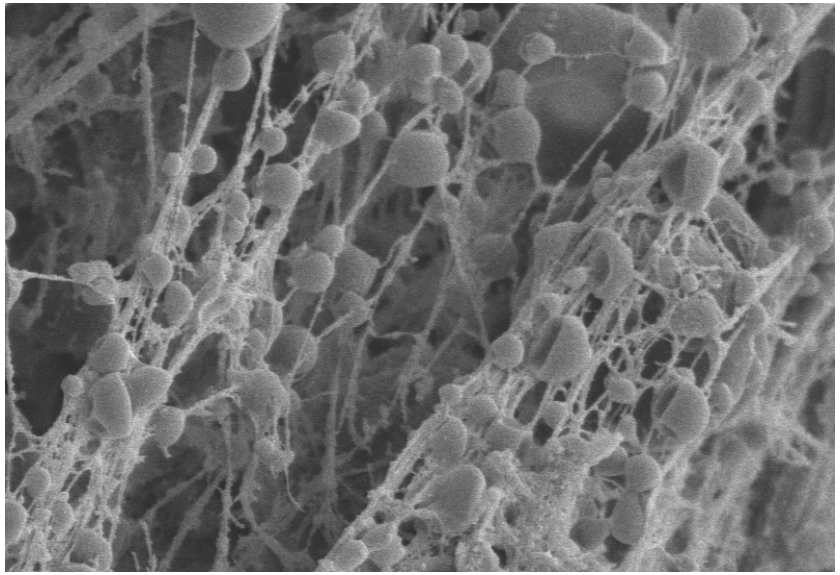
Edward M Schwarz

Why is this topic important

Biofilm

- Pathogenesis of Orthopaedic Infections
- Associated with Medical Device
- Strong Resistant to Antibiotics
- MIC << MBEC



Need for
physical method to
disrupt Biofilm

Saeed K 2019 J Orthop Res, Schwarz EM 2021 J Orthop Res

Literature Review/Process

- Number of articles retrieved: 1,860
- Screening: 889
- Reviewed: 82
- Final number of publications: 69

Photodynamic therapy 14 papers

Ultrasound (US) treatment 21 papers

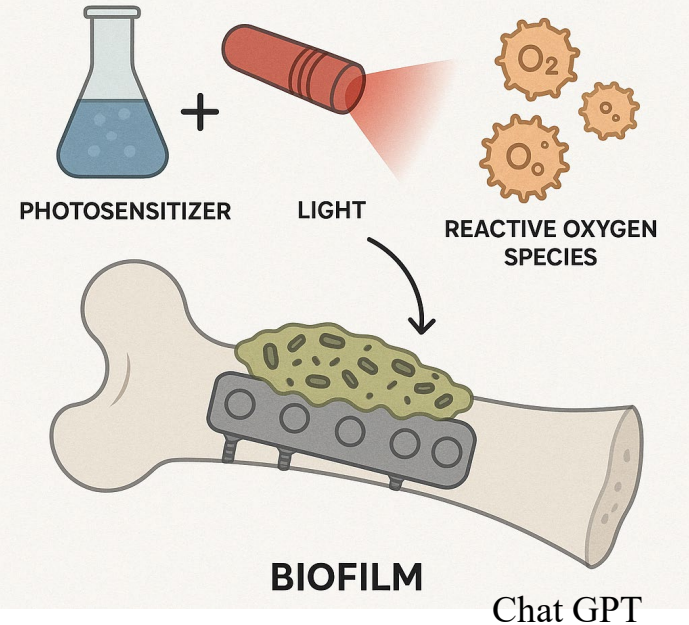
Electrical treatment 28 papers

Physical non-cytotoxic methods for Biofilms

1. Photodynamic therapy (PDT)

Photosensitizer(PS) a chemical agent that becomes activated upon exposure to light.

+Light source +Oxygen



Chat GPT

Photosensitizers
Methylene blue, Toluidine blue, Nanoparticles

The photosensitizer is activated by light in the presence of oxygen.
Production of reactive oxygen species (ROS) damage bacteria.

Major Limitations
- Light penetration depth is limited.
- Precise delivery of the PS and light
- Tissue toxicity.
- Limited Clinical evidence

Physical non-cytotoxic methods for Biofilms

2. Ultrasound (US) treatment

- High-frequency US (>1 MHz): delivering energy with high precision to a targeted area.
- Low-frequency US (<500 kHz): deliver energy over a wide area and Produces cavitation.
- Combination of US with sonosensitizers = sonodynamic therapy

Su Z. 2024. Nat Commun

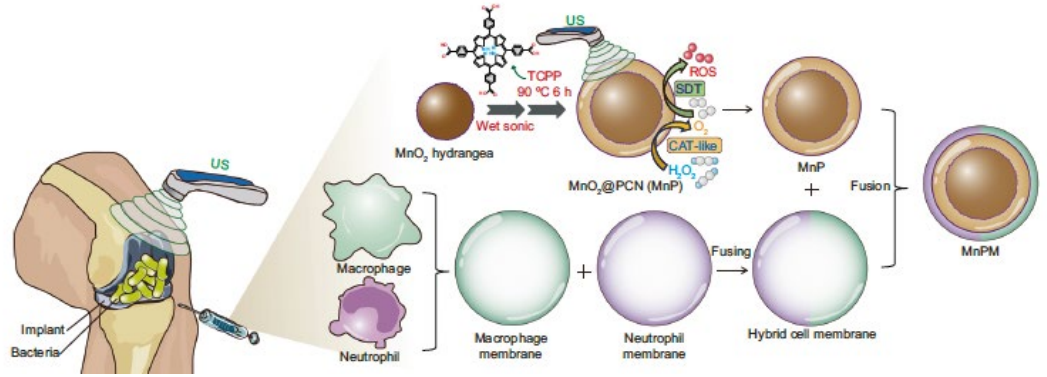


Fig. 1 | Scheme illustrating the mechanism by which MnPM enhances SDT and boosts antibiofilm metalloimmunotherapy. A spatiotemporal SMIT strategy is proposed for biofilm ablation. Upon injection at the biofilm, MnPM can act as an oxygen self-supplying sonosensitizer, thereby enhancing SDT against recalcitrant implant-related infections. Concurrently, the released Mn ions can sensitize the biofilm to SDT by disrupting intracellular homeostasis, further facilitating biofilm degradation. The innate immune system serves as the primary source of crucial signals required to instigate adaptive immune responses. Consequently, we anticipate these two elements to exhibit significant synergy. Moreover, bacterial fragments (e.g., double-stranded DNA, dsDNA, etc.) as BAAs released from the damaged biofilm can collaborate with Mn ions to initiate effective innate and adaptive antibiofilm immune responses by activating STING to suppress biofilm growth.

Major Limitations

- Bacteria may remain even after the disruption of biofilms.
- Adverse effects such as damage to articular cartilage and implants.

Physical non-cytotoxic methods for Biofilms

3. Electrical treatment

- Direct current for the treatment

- Production of ROS

- Synergistic effects with antibiotics and povidone-iodine

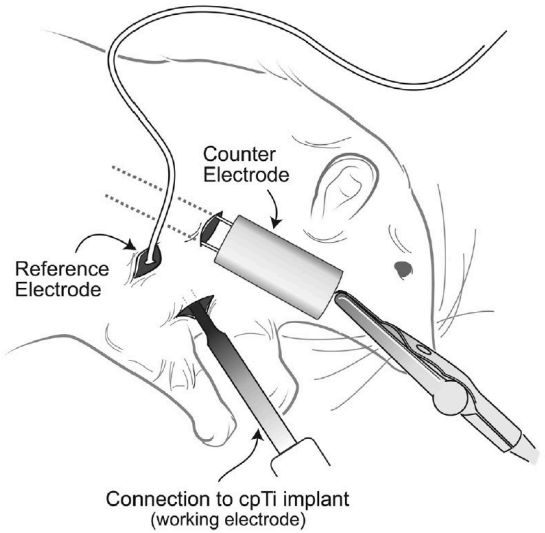
- Electromagnetic fields

- Cause thermal damage without directly heating tissue

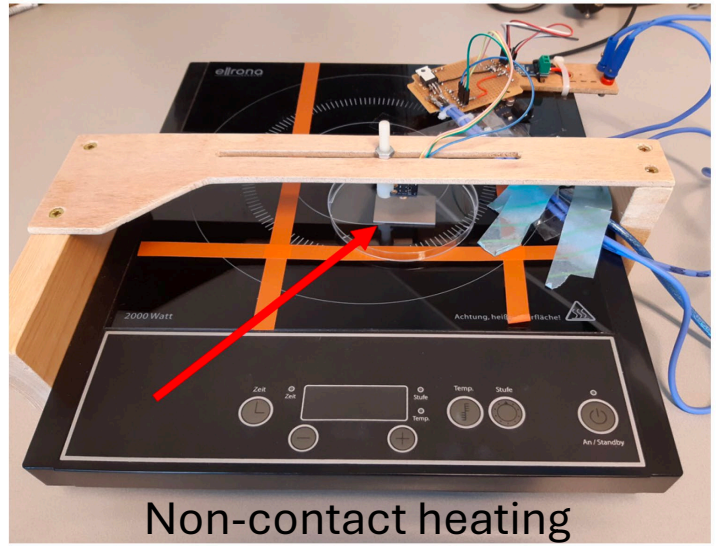
Major Limitations

- Ineffective on cement surface.

- Potential tissue damage caused by the heat.



Ehrensberger MT. et al. 2015 Biomaterials 2015



Pijls BG. 2022 Bone Joint Res

Physical non-cytotoxic methods for Biofilms

4. Other physical methods

- Plasma sterilization techniques
- Solid-state lasers
- Freezing nitrogen ethanol composite
- Extracorporeal shock wave therapy

Major Limitations:

Achieving substantial bactericidal and biofilm eradicating effects typically requires surpassing specific energy thresholds, and to date, no clinical trials have validated these methods for their safety and efficacy in humans.

While most physical methods discussed in this systematic review have demonstrated safety in vitro or in vivo, developing standardized protocols for clinical implementation and ensuring their safety in human applications remains a critical.

Question:

- **Are there any physical non-cytotoxic methods that can be utilized to disrupt and destroy biofilm in orthopedic infections?**

❖Response: YES

Photodynamic therapy, Ultrasound treatment, and Electrical treatment such as induction heating have been widely studied as effective physical methods to disrupt and destroy biofilms in orthopedic infections, and various strategies to reduce their cytotoxicity have also been investigated.
However, high level evidence study demonstrating the efficacy and safety of the treatments in clinical trials does not exist and needs to be addressed in the future.

Level of Evidence: Weak

❖**Vote:**

Agree n=25; 83:

Disagree n=1; 4%

Abstain n=4; 13%