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Physical Excitation to Chronic Rhinosinusitis Biofilms

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Bacteria are now recognised as existing in two forms: free floating (planktonic) or in sophisticated communities called biofilms. Biofilms have been defined as a "structured community of bacterial cells enclosed in a self-produced polymeric matrix adherent to an inert or living surface" [1]. Biofilms are composed of two major components: microorganism cells and a matrix of extracellular polymer substances (EPS). The biofilm matrix contains secreted polymers (polysaccharides), lipids, proteins, DNA and RNA [2]. An interaction between these components of the matrix allows biofilms to have a survival strategy and distinguished lifestyle as opposed to planktonic bacteria. The biofilm protects its inhabitants against environmental and biological threats [3].

Bacterial biofilms have been implicated as a major cause in many chronic infectious diseases including chronic rhinosinusitis (CRS). They are highly resistive to conventional antibiotics. Eradication of bacterial biofilms is an urgent strategy needed to treat various diseases associated with biofilms formation. Although many have investigated the impact of biochemical agents on bacteria biofilms and described their resistance/tolerance to antibiotics, little is known about the effect of biophysical environments such as electric fields, ultrasound and radio frequency on those biofilms. *In vitro* and *in vivo* evidence suggest that these physical approaches have a role in disrupting those biofilms.

CRS is a common disease worldwide with considerable impact on quality of life [4]. For example, in the United States approximately 31 million people are affected by chronic rhinosinusitis [5]. Although the pathology of CRS remains unclear and is described as multi-factorial, recently bacterial biofilms has been implicated as a major contributory factor [6-8]. Despite biofilms are not often included in the diagnosis for CRS to detect the presence of microorganisms, blocked sinuses are observed using CT scan images. A microscopic-MRI combination is aimed to be a novel approach for detecting bacterial biofilms in the human body; however, it has not been established for a clinical use yet. The relationship between biofilms and CRS has been investigated in several studies [6,7,9,10]. It has been reported that the most common bacterial biofilms in CRS are *Staphylococcus aureus, Pseudomonas aeruginosa*, coagulase-negative *Staphylococci, Streptococcus pneumoniae, Moraxella catarrhalis* and *Haemophilus influenzae*. Using scanning electron microscopy, Cryer et al. [11] published the first evidence of biofilms in CRS showing the presence of *Pseudomonas aeruginosa* in specimens taken from maxillary or ethmoid sinus mucosa. Healy et al. [12] investigated the presence of biofilms in CRS by using microscopic fluorescent in situ hybridization and showed that *Haemophilus influenzae* was the most common bacteria (about 80%) among other species identified, including *Staphylococcus aureus, Pseudomonas aeruginosa* and *Streptococcus pneumonia* and fungi. Confocal scanning microscopy and transmission electron microscopy studies, respectively, have also shown that *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most common biofilm bacteria formed in CRS [13,14].

Biofilms have been found to be attached to a surface and/or aggregated in the surrounding mucus layer [13,15]. This aggregation is not well understood due to the fact that it is unclear whether the biofilms are detached from the surfaces or other aggregated biofilms are formed in the fluid [16]. Despite the uncertainty with respect to the most dominant species of bacterial biofilms in CRS and the aggregation of biofilms, the formation of biofilms has been reported as the major cause for CRS.

Treatment for bacterial biofilms of CRS can be classified into two categories; medication (biochemical) and physical. While medication treatment by conventional antibiotics is often unsuccessful due to the resistance of biofilms, physical excitation by ultrasound and electric fields has been reported to enhance the activation of antibiotics on bacterial biofilms. Neither of the mechanism(s) of action nor its effects of both methods on bacterial biofilms are well understood. Our hypothesis is that physical excitations may alter the forces involved in the process of bacterial biofilm formation.

In this article a comprehensive literature review is presented with critiques to various biofilm treatment methods. Some possibilities of cause and effect are elaborated on. Recommendations are given on what the next stage of research in this arena should be.

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