AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Original Research

Otolaryngology–Head and Neck Surgery
1–5

DOI: 10.1177/0194599819866692
http://otojournal.org
SAGE

The Potential of High-Throughput DNA Sequencing of the Paranasal Sinus Microbiome in Diagnosing Odontogenic Sinusitis

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Received March 27, 2019; accepted July 10, 2019.

Abstract

Objective. High-throughput DNA sequencing of the paranasal sinus microbiome has potential in the diagnosis and treatment of sinusitis. The objective of this study is to evaluate the use of high-throughput DNA sequencing to diagnose sinusitis of odontogenic origin.

Study Design. Case series with chart review.

Setting. Single tertiary care academic medical center.

Subjects and Methods. A chart review was performed of DNA sequencing results from the sinus aspirates obtained under endoscopic visualization in 142 patients with sinusitis. The identification of any potentially pathogenic bacteria associated with oral flora in a sample was classified as a positive result for sinusitis of odontogenic etiology. The sensitivity, specificity, and predictive values of using high-throughput DNA sequencing to diagnose sinusitis of odontogenic etiology were determined, with the patient's computed tomography sinus scan as the reference standard. On computed tomography scans, an odontogenic source was determined by the presence of a periapical lucency perforating the schneiderian membrane.

Results. Seven of the 142 patients enrolled in this study had an odontogenic source based on computed tomography scans. Relative to this reference standard, high-throughput DNA sequencing produced a sensitivity of 85.7% (95% CI, 42.1%-99.6%), a specificity of 81.5% (95% CI, 73.9%-87.6%), a positive predictive value of 19.4% (95% CI, 13.1%-27.7%), and a negative predictive value of 99.1% (95% CI, 94.7%-99.9%).

Conclusion. This study supports the use of high-throughput DNA sequencing in supplementing other methods of investigation for identifying an odontogenic etiology of sinusitis.

Keywords

odontogenic sinusitis, DNA sequencing, microbiome, sinusitis

Chronic rhinosinusitis is a common disease that affects approximately 15% of the US population every year, contributing to a reduction in the quality of life of patients as well as to a burden on the national economy.[1] Although there are many treatments for chronic rhinosinusitis, a significant number of cases are recalcitrant to traditional treatments.[1] It has been estimated that up to one-tenth of chronic maxillary rhinosinusitis cases have an odontogenic etiology, representing an important subset of patients who may not respond to traditional treatments.[2] Chronic maxillary rhinosinusitis due to an odontogenic etiology can occur when periodontal disease perforates the schneiderian membrane of the maxillary sinus.[2] An odontogenic etiology should be considered in any patient with a history of odontogenic infection, periodontal surgery, or dentoalveolar surgery or in those resistant to conventional treatment of chronic rhinosinusitis.[2]

A number of bacterial species, primarily anaerobes, have been associated with odontogenic sinusitis.[2] Historically, bacterial culture has been used to identify these bacteria. However, false-negative culture results pose a common challenge to an accurate diagnosis.[3] Failure to diagnose can lead to suboptimal treatment of maxillary sinus infection and concomitant dental disease.

High-throughput DNA sequencing is a new technology capable of analyzing all the microbial DNA in a sample,

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providing a more complete bacterial profile.[4] High-throughput DNA sequencing has been used to identify pathogens in patients with systemic sepsis, neurologic infections, and periprosthetic joint infections.[5-7] With the rapid decline in the cost of DNA sequencing in recent years, high-throughput sequencing is now commercially available for the bacterial analysis of sinonasal specimens. Several published studies have investigated this technology to revisit the bacterial characterization associated with acute and chronic sinusitis.[8] To our knowledge, there have been no studies evaluating high-throughput DNA sequencing for diagnosing sinusitis of odontogenic etiology. A retrospective study was designed to evaluate the role of high-throughput DNA sequencing in diagnosing sinusitis of odontogenic etiology.

Methods

A retrospective review was performed on microbial DNA sequencing results from sinus aspirate samples collected under endoscopic visualization in a tertiary rhinology clinic between January 1, 2015, and December 31, 2016. The indication for testing in all patients was an acute exacerbation of chronic rhinosinusitis (defined by the presence of purulence on endoscopy during a symptomatic exacerbation of chronic rhinosinusitis).[9] All samples were obtained by aspirating the purulent sample within the sinus cavities under endoscopic visualization. Microbial DNA testing was performed through a commercially available service (MicroGenDX, formerly Pathogenius, Lubbock, Texas).

High-resolution noncontrast computed tomography (CT) scans were reviewed, which consisted of 0.6- to 1.2-cm non-overlapping axial images, as well as orthogonal coronal and sagittal images reconstructed on Ambra Health, for all patients. Each CT scan was obtained 1 day to 2 weeks before bacterial aspirates were collected. The presence of a periapical lucency that perforated the schneiderian membrane around any maxillary tooth in combination with sinus opacification on the CT scan was identified as an odontogenic source (**Figure 1**).[10] The scans were analyzed by 2 fellowship-trained rhinologists (A.U.L. and M.J.M.), as well as by a board-certified radiologist. The CT scans were used as the reference standard against which high-throughput DNA sequencing was measured as a diagnostic test for sinusitis of odontogenic etiology. Each patient with a CT scan suggestive of an odontogenic pathology also had physician documentation indicating past clinical suspicion of odontogenic sinusitis, which supported the use of CT scans as a reference standard.

The Committee for the Protection of Human Subjects of The University of Texas Health Science Center at Houston approved the protocol.

DNA Extraction, Polymerase Chain Reaction, and Sequencing

This microbiome assay used automated polymerase chain reaction technology to amplify the 16S ribosomal RNA (for bacteria) and internal transcribed spacer (ITS) gene sequences (for fungi), as previously described.[7] Specific methodology is summarized as follows (personal communication with Jennifer White and Rick Martin, MicroGenDX).

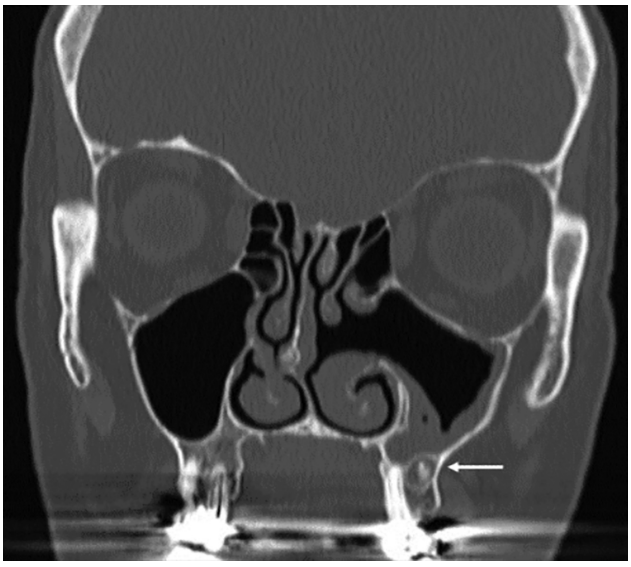

Figure 1. An example of chronic maxillary sinusitis of odontogenic origin with a periapical lucency on coronal computed tomography sinus scan (arrow).

Sequencing was performed with the Ion Torrent Personal Genome Machine.[11] Primers 28F GAGTTTGATCNTG GCTCAG and 388R GCTGCCTCCCGTAGGAGT were used to sequence the V1-V2 portion of the bacterial 16S rRNA gene; ITS3F GCATCGATGAAGAACGCAG and ITS4R TCCTCCGCTTATTGATATGC primers 10 were used to sequence the ITS 2 region of the fungal rRNA operon. Amplified DNAs were then pooled and purified by removing small fragments with a column- and bead-based method. Purified DNAs were added to the Ion Sphere Particles and enriched for sequencing on the Ion Torrent Personal Genome Machine sequencer. Once sequences were obtained, an in-house data pipeline developed at MicroGenDX processed the FASTQ file. The data analysis pipeline consisted of 2 major stages: the denoising and chimera detection stage and the microbial diversity analysis stage. Denoising was performed by first trimming all sequences back with an internally developed quality trimming algorithm, ensuring that each read had a running average taken across the sequence and was trimmed back at the last base where the total average was greater than Q25. Prefix-based dereplication was then performed with the USEARCH algorithm,[12] and the resulting clusters were cleaned to ensure that each clustered sequence was a minimum of 100 base pairs in length. Operational taxonomic unit (OTU) clustering at 6% divergence was performed on the clusters with the USEARCH algorithm, and each cluster with at least 2-member sequences was compressed down to a single representative consensus sequence. The formation of chimeric sequences occurred when an aborted sequence extension was misidentified as a primer and extended upon incorrectly in subsequent polymerase chain reaction cycles.[13]

Because amplification produced chimeric sequences that stemmed from the combination of $\geq$2 original sequences, MicroGenDX performed chimera detection with the de novo method built into UCHIME.[14] All chimeric sequences were removed, and base correction was then performed by comparing all raw reads with their nonchimeric consensus cluster. The corrected sequences were then demultiplexed with an internally developed algorithm that ensured that the barcode for each sequence was a 100% match; any sequence that did not contain a valid barcode was removed. These demultiplexed sequences then went through the OTU selection process.[15] OTU clusters were globally aligned with USEARCH against a database of high-quality sequences derived from the NCBI database.[16,17] The output was analyzed with MicroGenDX's internally developed algorithm that assigned taxonomic information to each sequence and then computed and wrote the final analysis files.

Identification of Bacteria Associated with Odontogenic Etiology of Maxillary Sinusitis

A literature search with PubMed generated a list of bacteria associated with maxillary sinusitis with an odontogenic etiology. The search was limited to the following key phrases: odontogenic sinusitis, dental sinusitis, microbiology of sinusitis, periodontal disease in sinusitis, polymicrobial disease in sinusitis. Based on literature analysis, 9 bacteria were identified as being associated with an odontogenic etiology of maxillary sinusitis: *Fusobacterium* species,[18-22] *Peptostreptococcus* species,[18-22] *Porphyromonas* species,[18,21,22] *Prevotella* species,[18,21,22] *Streptococcus constellatus*,[18,22,23] *Streptococcus mitis*,[18,23] *Streptococcus oralis*,[18,23] *Streptococcus salivarius*,[18,23] and *Veillonella* species.[18,21,23] Healthy patients with noninflamed sinuses have been shown to harbor small amounts of the listed bacteria as commensal bacteria; however, in patients who have already been diagnosed with sinusitis (as in this study), the listed bacteria predominate in sinusitis of odontogenic origin and are mostly absent in sinusitis of nonodontogenic origin.[18]

Statistical Analysis

Each patient's high-throughput DNA sequencing data was screened for one of the bacterial species associated with odontogenic sinusitis. The identification of any one of these bacteria in a sample was classified as a positive for sinusitis of odontogenic etiology, and the absence of all of these bacteria was classified as a negative.

The sensitivity, specificity, and predictive values of using high-throughput DNA sequencing as a diagnostic test for odontogenic sinusitis were determined, with the patient's CT scans as the diagnostic standard. The values were calculated by creating a contingency table that lists the number of cases that were true positives, true negatives, false positives, and false negatives.

Results

A total of 225 sinus aspirates in 142 patients with acute exacerbations of chronic rhinosinusitis were reviewed. On the basis of the CT scans, 7 patients were identified as having an odontogenic etiology, and 135 patients were identified as not having an odontogenic etiology. The rate of chronic maxillary rhinosinusitis secondary to an odontogenic etiology was 4.9%, which is within estimates from previous studies.[2] Of the patients with an odontogenic etiology, 4 are male and 3 are female. Of the patients with a nonodontogenic etiology, 75 are male and 60 are female.

Supplemental Table S1 (available in the online version of the article) illustrates the age, sex, time of last procedure relative to sample taken, CT findings, clinical diagnoses, treatment, outcome, and bacterial identification of the 7 patients with an identified odontogenic etiology. Each patient had a periapical lucency of a maxillary tooth, but there was no consistent tooth location (eg, canine, premolar vs molar) shared by these patients. Six patients had a clinical diagnosis of maxillary chronic rhinosinusitis without nasal polyps, and 1 patient had maxillary chronic rhinosinusitis with nasal polyps. At least 1 of the 9 bacteria linked to odontogenic sinusitis was present in 6 of 7 patients. Otherwise, the composition and percentages of bacterial flora differed greatly among the patients. There was no clear correlation between the number of odontogenically associated species and the likelihood of having an odontogenic etiology. The treatment of these patients was based on the DNA sequencing results of the aspirates. Intranasal steroids were prescribed for the time between collecting aspirates and obtaining results. Then, the treating physician utilized results to prescribe oral antibiotics for which the identified bacteria were sensitive, while continuing the intranasal steroids. Three patients received clindamycin; 2, trimethoprim-sulfamethoxazole; 1, minocycline; and 1, the combination of ciprofloxacin and metronidazole.

Of the 142 patients, 25 had bacteria consistent with an odontogenic source but did not have a periapical lucency identified on CT scan. Supplemental Table S2 (available in the online version of the article) illustrates the age, sex, time of last procedure relative to sample taken, clinical diagnoses, treatment, outcome, and bacterial identification of these 25 patients. Among these patients, there were no shared consistent clinical diagnoses, treatment, or bacterial flora.

Sensitivity, specificity, and predictive values were calculated with CT scans as a reference. Odontogenic-associated bacterial species produced a sensitivity of 85.7% (95% CI, 42.1%-99.6%), a specificity of 81.5% (95% CI, 73.9%-87.6%), a positive predictive value of 19.4% (95% CI, 13.1%-27.7%), and a negative predictive value of 99.1% (95% CI, 94.7%-99.9%), based on the contingency table shown in **Table 1**.

Discussion

An odontogenic source of rhinosinusitis may be present in up to 10% of cases of chronic maxillary rhinosinusitis.[2] Odontogenic sinusitis requires appropriate dental and antibiotic treatment, with endoscopic sinus surgery (ESS) as part of the treatment algorithm in some patients. Patients with higher Lund-Mackay scores, involvement of the

Table 1. Contingency Table Classifying the Identification of Any Odontogenically Associated Bacterial Species as a Positive.

	Radiological +	Radiological –
MicroGenDX +	True positive = 6	False positive = 25
MicroGenDX –	False negative = 1	True negative = 110
Percentage (95% CI)		
Sensitivity	85.7 (42.1-99.6)	
Specificity	81.5 (73.9-87.6)	
Positive predictive value	19.4 (13.1-27.7)	
Negative predictive value	99.1 (94.7-99.9)	

ostiomeatal complex, and/or history of a prior dental procedure are likely to require ESS.[24] Nevertheless, odontogenic sinusitis often goes unrecognized and can be a source of failed ESS.[25,26] Up to 70% of initial CT scan reports in these patients fail to mention dental pathology that is present.[26] A sensitive test for the identification of odontogenic sinusitis may aid in recommending the appropriate multidisciplinary treatment and prevent ESS failures.

Specific bacteria have been associated with odontogenic sinusitis.[18-23] High-throughput DNA sequencing may provide a more complete microbial profile[4] and allow identification of organisms that are more likely to be implicated in sinusitis with an odontogenic source. In this series of patients with purulence present in the nasal cavity on endoscopy, high-throughput DNA sequencing was sensitive (85.7%) for the detection of odontogenic sinusitis. Furthermore, the absence of bacteria associated with odontogenic sinusitis is predictive of the lack of an odontogenic source, as evidenced by the negative predictive value (99.1%). Therefore, this test may be useful in excluding an odontogenic source of infection and sensitive for identifying patients at risk for odontogenic sinusitis. Among patients with high-throughput DNA sequencing consistent with the odontogenic bacteria, further investigation for an odontogenic source will need to be performed by history, physical examination, and/or imaging due to the low positive predictive value (19.4%).

The sensitivity, specificity, and predictive values determined in this study for high-throughput DNA sequencing as a screening test for odontogenic sinusitis are comparable to those of the fecal immunochemical test (FIT) in screening for colorectal cancer. The use of FIT as a screening test for colorectal cancer was a strong recommendation in a recent consensus guideline.[27] Among 19 studies, the pooled sensitivity of FIT in detecting colorectal cancer was 79%, while the pooled specificity was 94%.[27] The PPV for colorectal cancer in the reported studies ranged from 2.9% to 7.8%.[27] There were additional strong recommendations that positive FIT should be followed by further investigations, including colonoscopy.[27] Similarly, high-throughput DNA sequencing that is consistent with odontogenic bacteria should prompt further investigation to the confirm a diagnosis of odontogenic sinusitis. This is a function of the high sensitivity but low positive predictive value of the test.

There are several limitations noted in the current study. First, CT evidence of an odontogenic source was used as the diagnostic standard for determining odontogenic sinusitis. This may underestimate the number of cases of odontogenic sinusitis, since not all cases will manifest with apparent radiographic findings. This in turn might skew sensitivity and specificity calculations. Nevertheless, this is likely to have the effect of increasing the number of false positives and therefore lowering the calculated sensitivity and specificity. Second, the retrospective design of this study limits the use of other criteria for the confirmatory diagnosis of odontogenic sinusitis. The difficulty in the clinical diagnosis of odontogenic sinusitis, noted in previous studies,[25,26] makes review of the medical record unreliable for use as a reference standard. A prospective study addressing this question might better combine physical examination and dental consultation, with CT images, in establishing a gold standard for the diagnosis of odontogenic sinusitis. Despite these limitations, high-throughput DNA sequencing of sinus cavity purulence may offer a sensitive test for identifying patients who would benefit from additional investigation for odontogenic sinusitis. Furthermore, the high negative predictive value demonstrates utility in ruling out an odontogenic source.

Conclusion

High-throughput DNA sequencing can be useful in supplementing other methods of investigation for an odontogenic source of sinusitis. The specific sequencing has a high negative predictive value to exclude odontogenic sinusitis. These results lay the groundwork for future studies that examine the use of high-throughput DNA sequencing in the diagnosis and treatment of sinusitis.

Author Contributions

Asad A. Haider, conduct of research, design of study, presentation of research, writing of majority of manuscript, came up with ideas on how to improve manuscript on a biweekly basis with corresponding author, submission of manuscript, approved final manuscript draft, agreed to be responsible for all aspects of the work; **Michael J. Marino**, conduct of research, mentored student, design of study, assisted in data analysis; read CT scans, suggestions for improvements in manuscript, assistance with writing Discussion section, assistance with submission, approved final manuscript draft, agreed to be responsible for all aspects of the work; **William C. Yao**, made substantial suggestions in the discussion section of the manuscript, assisted in writing portions of the Methods section, organized charts on the database, approved final manuscript draft, agreed to be responsible for all aspects of the work; **Martin J. Citardi**, revised the Methods section with intellectual contribution primarily on sequencing of samples, approved the final manuscript draft, agreed to be responsible for all aspects of the work; **Amber U. Luong**, design of study, assisted in biweekly meetings, mentored student, provided instructions on data collection, read CT scans, wrote paragraphs on various sections in the manuscript, discussed ideas on how to improve

paper, approved final manuscript draft, agreed to be responsible for all aspects of the work, assistance with submission.

Disclosures

Competing interests: Amber U. Luong—consultant for Aerin Medical, Lyra Therapeutics, and Stryker; scientific advisory board member for ENTvantage. Martin J. Citardi—consultant for Acclarent, Intersect ENT, Medical Metrics, Medtronic, and Stryker. William C. Yao—member of the speakers bureau for Optinose. The Otorhinolaryngology department serves as a clinical research advisor to Arrinex. It also receives research funding from AstroZeneca, Optinose, and Arrinex.

Sponsorships: None.

Funding source: McGovern Medical School, Department of Otorhinolaryngology.

Supplemental Material

Additional supporting information is available in the online version of the article.

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Supplemental Table S1. Patients Diagnosed with an Odontogenic Etiology of Sinusitis and their Age, Gender, Time of Last Procedure Relative to Sample Taken, CT findings, Clinical Diagnoses, Treatment, Outcome, and Bacterial Identification

Age	Gender	Last Procedure Relative to Sample Taken (Days)	CT Finding	Diagnoses	Treatment	Outcome	Bacterial Identification*
34	Female	29	Periapical lucency of top left 1st pre-molar	Left CRSsNP	Oral minocycline	*Unknown*	**51% *Streptococcus mitis***, 10% *Lactobacillus* species, 8% *Streptococcus parasanguinis*, **7% *Streptococcus salivarius***, 5% *Neisseria* species, **3% *Streptococcus oralis***, 2% *Streptococcus pneumoniae*, 2% *Streptococcus australis*, 2% *Streptococcus vestibularis*
22	Female	1196	Periapical lucency of top left 1st molar	Bilateral CRSsNP	Oral clindamycin	Minimal improvement	98% *Staphylococcus aureus*
22	Male	1225	Periapical lucency of top right 1st pre-molar	Bilateral CRSsNP	Oral clindamycin	Moderate improvement	94% *Staphylococcus aureus*, **3% *Fusobacterium* species**
60	Female	500	Periapical lucency of top left 2nd pre-molar	Bilateral CRSsNP	Oral trimethoprim-sulfamethoxazole	Resolved	54% *Moraxella catarrhalis*, 40% *Hemophilus* species, **5% *Porphyromonas* species**
57	Male	No previous procedure	Periapical lucency of top right 2nd pre-molar	Right CRSsNP	Oral trimethoprim-sulfamethoxazole	No change	**97% *Prevotella* species**
54	Male	No previous procedure	Periapical lucency of top right 1st molar	Right CRSsNP	Oral ciprofloxacin, oral metronidazole	*Unknown*	**51% *Porphyromonas* species**, 27% *Pseudomonas* species, **13% *Prevotella* species,** 7% *Staphylococcus aureus*
64	Male	19	Periapical lucency of top right 1st pre-molar	Right CRSwNP	Oral clindamycin	Resolved	**45% *Prevotella* species**, **41% *Fusobacterium* species**, **8% *Porphyromonas* species, 3% *Streptococccus constellatus***

*The values represent the percentage of bacterial species present in the entire sample. Bacteria associated with an odontogenic etiology are bolded.

Age	Gender	Last Procedure Relative to Sample Taken (Days)	CT Finding	Diagnoses	Treatment	Outcome	Bacterial Identification*
34	Female	29	Periapical lucency of top left 1st pre-molar	Left CRSsNP	Oral minocycline	*Unknown*	**51% *Streptococcus mitis***, 10% *Lactobacillus* species, 8% *Streptococcus parasanguinis*, **7% *Streptococcus salivarius***, 5% *Neisseria* species, **3% *Streptococcus oralis***, 2% *Streptococcus pneumoniae*, 2% *Streptococcus australis*, 2% *Streptococcus vestibularis*
22	Female	1196	Periapical lucency of top left 1st molar	Bilateral CRSsNP	Oral clindamycin	Minimal improvement	98% *Staphylococcus aureus*
22	Male	1225	Periapical lucency of top right 1st pre-molar	Bilateral CRSsNP	Oral clindamycin	Moderate improvement	94% *Staphylococcus aureus*, **3% *Fusobacterium* species**
60	Female	500	Periapical lucency of top left 2nd pre-molar	Bilateral CRSsNP	Oral trimethoprim-sulfamethoxazole	Resolved	54% *Moraxella catarrhalis*, 40% *Hemophilus* species, **5% *Porphyromonas* species**
57	Male	No previous procedure	Periapical lucency of top right 2nd pre-molar	Right CRSsNP	Oral trimethoprim-sulfamethoxazole	No change	**97% *Prevotella* species**
54	Male	No previous procedure	Periapical lucency of top right 1st molar	Right CRSsNP	Oral ciprofloxacin, oral metronidazole	*Unknown*	**51% *Porphyromonas* species**, 27% *Pseudomonas* species, **13% *Prevotella* species,** 7% *Staphylococcus aureus*
64	Male	19	Periapical lucency of top right 1st pre-molar	Right CRSwNP	Oral clindamycin	Resolved	**45% *Prevotella* species**, **41% *Fusobacterium* species**, **8% *Porphyromonas* species, 3% *Streptococccus constellatus***

*The values represent the percentage of bacterial species present in the entire sample. Bacteria associated with an odontogenic etiology are bolded.

Supplemental Table S2. Patients Diagnosed with a Non-odontogenic Etiology of Sinusitis but with Bacteria Suggestive of an Odontogenic Source, and their Age, Gender, Time of Last Procedure Relative to Sample Taken, Clinical Diagnoses, Treatment, Outcome, and Bacterial Identification.

Age	Gender	Last Procedure Relative to Sample Taken (Days)	Diagnoses	Treatment	Outcome	Bacterial Identification*
51	Male	574	Bilateral CRSwNP	Oral ciprofloxacin, topical tobramycin, topical fluticasone	*Unknown*	64% *Pseudomonas* species, **16% *Prevotella* species**, 10% *Peptoniphilus* species, 3% *Anaerococcus species*
32	Male	79	Bilateral CRSwNP	Oral amoxicillin/clavulanic acid, oral clarithromycin topical gentamycin, topical fluticasone	Resolved	33% *Staphylococcus aureus*, 15% *Propionibacterium* species, 10% *Corynebacterium* species, 9% *Staphylococcus epidermidis*, **9% *Veillonella* species**, 7% *Acinetobacter* species, 3% *Bacillus* species, 2% *Staphylococcus lugdunesis*
45	Female	2889	Bilateral CRSsNP	Topical mupirocin	*Unknown*	46% *Staphylococcus epidermidis*, 11% Corynebacterium species, 11% *Propionibacterium* species, 5% *Staphylococus aureus*, 5% *Acinetobacter* species, 2% *Burkholderia* species, **2% *Prevotella* species**
77	Female	1741	Bilateral CRSsNP	Oral doxycycline, topical fluticasone	Moderate improvement	**55% *Fusobacterium* species**, 29% *Escherichia* species, **2% *Prevotella* species**
15	Female	11	Right CRSsNP	Topical colistimethate	Moderate improvement	**41% *Prevotella* species**, 13% *Klebsiella* species, 5% *Burkholderia* species, 3% *Enterobacter* species
59	Male	884	Bilateral CRSwNP	Oral levofloxacin	*Unknown*	65% *Streptococcus pneumoniae*, 13% *Staphylococcus epidermidis*, 11% *Propionibacterium* species, **5% *Prevotella* species**
85	Female	No previous procedure	Left CRSsNP	Oral amoxicillin/clavulanic acid, oral ciprofloxacin	*Unknown*	**71% *Prevotella* species**, **15% *Fusobacterium* species**, 6% *Clostridium* species
62	Female	No previous procedure	Bilateral RARS	No treatment	*Unknown*	**78% *Streptococcus mitis***, **2% *Streptococcus oralis***, 6% *Corynebacterium* species
42	Male	560	Left CRSsNP	Oral doxycycline	Resolved	43% *Staphylococcus epidermidis*, **17% *Prevotella* species**, 17% *Hemophilus* species, 6% *Propionibacterium* species, 3% *Abiotrophia paraadiacens*, **3%**

						Fusobacterium* species**, **3% *Streptococcus mitis
42	Female	No previous procedure	Right CRSsNP	Oral amoxicillin/clavulanic acid, topical oxymetazoline, topical lidocaine	Minimal improvement	**51% *Porphyromonas* species**, **23% *Fusobacterium* species**, **17% *Prevotella* species**, **3% *Veillonella* species**, **2% *Peptostreptococcus* species**
71	Female	78	Left CRSsNP	Oral clindamycin, topical colestimethate	Moderate improvement	69% *Enterobacter* species, **24% *Bacterioides* species**, **2% *Fusobacterium* species**
58	Male	854	Bilateral CRSsNP	Oral cefuroxime, topical fluticasone	Worse	40% *Stenotrophomonas* species, 21% *Corynebacterium* species, **4% *Streptococcus mitis***, 3% *Staphylococcus epidermidis*, 2% *Leptotrichia* species, 2% *Ralstonia* species, 2% *Agrobacterium* species
66	Male	2544	Bilateral CRSwNP	Oral ciprofloxacin, topical mupirocin, topical betamethasone	Resolved	47% *Streptococcus equi*, 30% *Staphylococcus epidermidis*, **7% *Fusobacterium* species**, 5% *Enterococcus* species, **2% *Porphyromonas* species**, 2% *Enterobacter* species
32	Female	No previous procedure	Bilateral CRSwNP	Topical mupirocin, topical betamethasone	Resolved	76% *Enterobacter* species, **4% *Prevotella* species**, 3% *Corynebacterium* species
17	Female	16	Bilateral CRSsNP	Oral metronidazole, topical oxymetazoline, topical lidocaine	Minimal improvement	36% *Mycobacterium* species, **27% *Veillonella* species**, **19% *Prevotella* species**, **3% *Porphyromonas* species**
26	Female	54	Bilateral CRSwNP	Oral doxycycline, oral levofloxacin, topical colistimethate	Moderate improvement	77% *Pseudomonas* species, 15% *Enterococcus* species, **6% *Streptococcus mitis***
66	Male	1275	Bilateral CRSwNP	Oral levofloxacin, topical colistimethate	Resolved	50% *Pseudomonas* species, 21% *Achromobacter* species, 12% *Streptococcus pneumoniae*, **6% *Fusobacterium* species**, 4% *Serratia* species
65	Male	2012	Bilateral CRSwNP	Oral doxycycline, oral levofloxacin, topical colistimethate, topical fluticasone	Minimal improvement	67% *Streptococcus agalactiae*, 17% *Capnocytophaga* species, **6% *Streptococcus mitis***
35	Female	421	Bilateral CRSsNP	Oral doxycycline, topical mometasone	*Unknown*	22% *Neisseria* species, **18% *Prevotella* species**, **10% *Streptococcus constellatus***, 5% *Staphylococcus epidermidis*, 3% *Streptococcus sanguinis*, 3% *Hemophilus influenzae*, 2% *Staphylococcus cohnii*, 2% *Escherichia* species, 2% *Propionibacterium* species, 2% *Streptococcus anginosus*, 2% *Staphylococcus auricularis*
49	Male	65	Bilateral CRSwNP	Oral clindamycin, topical gentamycin	*Unknown*	**38% *Prevotella* species**, 18% *Citrobacter* species, 13%

						Anaerococcus species, 10% *Pseudomonas* species, **6% *Streptococcus constellatus***, 5% *Finegoldia* species, 2% *Capnocytophaga* species
70	Male	No previous procedure	Left CRSsNP	Oral amoxicillin/clavulanic acid	Moderate improvement	**44% *Porphyromonas* species**, **28% *Prevotella* species**, **7% *Fusobacterium* species**, **3% *Veillonella* species**, 3% *Clostridium* species
67	Male	1545	Bilateral CRSwNP	Oral clindamycin	No change	**49% *Prevotella* species**, **43% *Fusobacterium* species**
74	Male	860	Right CRSsNP	Oral clindamycin, topical mupirocin, topical oxymetazoline, topical lidocaine	Minimal improvement	**53% *Fusobacterium* species**, **36% *Prevotella* species**, 9% *Staphylococcus aureus*
48	Male	618	Bilateral CRSwNP	Oral levofloxacin, topical mupirocin, topical fluticasone	Minimal improvement	48% *Streptococcus pneumoniae*, 12% *Pseudomonas* species, **4% *Streptococcus salivarius***, **4% *Streptococcus mitis***, 4% *Streptococcus parasanguinis*, **4% *Prevotella* species**, 2% *Serratia* species, 2% *Escherichia* species
67	Male	1761	Bilateral CRSwNP	Topical gentamycin, topical betamethasone	Resolved	68% *Escherichia* species, 16% *Stenotrophomonas* species, 5% *Enterobacter* species, **4% *Fusobacterium* species**
*****The values represent the percentage of bacterial species present in the entire sample. Bacteria associated with an odontogenic etiology are bolded.						