analyzed by Lee et al.[640] demonstrated evidence of bone remodeling in CRS patients, which was more prevalent in those undergoing revision surgery as opposed to primary surgery patients. Snidvongs et al.[650] ultimately proposed that these bony changes be referred to as neo-osteogenesis, as opposed to osteitis, after human studies failed to demonstrate inflammatory infiltration within the bone itself. However, osteitis and neo-osteogenesis continue to be used interchangeably in the literature.[638,640,649–652]

Histological evaluation most accurately confirms the presence of neo-osteogenesis, although CT continues to be the diagnostic test of choice due to ease of access and superior bony detail.[265,640,642–646,651,653–655] Single-photon emission CT (SPECT) was found to be extremely sensitive in predicting neo-osteogenesis on histopathology, but its use in clinical practice remains limited.[655,656] A number of osteitis grading systems have been proposed. The Kennedy Osteitis Score (KOS)[640] and the Global Osteitis Scoring Scale (GOSS)[657] are routinely referenced in the literature, but no system has been standardized.

Evidence continues to correlate neo-osteogenesis with greater disease severity. A study by Lee et al.[640] observed average Lund-Mackay scores to be 22 for neo-osteogenesis patients vs 6.5 for patients without neo-osteogenesis. Several follow up prospective studies have further corroborated the connection between neo-osteogenesis and disease severity and suggested that the presence of neo-osteogenesis is a poor prognostic indicator for post-surgical outcomes.[656,657] Kim et al.[658] retrospectively reviewed their series of 81 patients, identifying that 48.1% of neo-osteogenesis patients had poor outcomes compared to 24.1% of non-neo-osteogenesis patients. In a study by Telmesani et al.,[641] 53% of neo-osteogenesis patients had recurrence of disease following surgery compared to 10% in patients without neo-osteogenesis. Sacks et al.[659] demonstrated no difference in endoscopy scores at 12 months post surgery, but noted that patients with neo-osteogenesis were more likely to need post-operative systemic steroids. Likewise, several case series have reported increased neo-osteogenesis in revision surgery cases.[640,660,661] However, data from Gunel et al.[637] conflicts with these findings as they found no difference in the incidence of neo-osteogenesis histopathologically between primary and revision surgery cases.[637] Despite the link between neo-osteogenesis and objective markers of clinical severity, multiple studies have failed to show a correlation between the presence of neo-osteogenesis and worse patient reported symptoms.[659,661,662]

Although there is a clear association between neo-osteogenesis and CRS, it is uncertain whether the bone propagates recurrent inflammation, or is the result of chronic inflammation. As such, the role of neo-osteogenesis in the pathogenesis of CRS has been a strong focus of recent investigations, including the interplay with bacterial infection.[662–665] Dong et al.[664] reported the presence of neo-osteogenesis in 85% of patients with bacterial biofilms. A follow up study by Huang et al.[662] correlated the presence of *Pseudomonas aeruginosa* to neo-osteogenesis, although a recent study failed to corroborate these findings.[666] Cellular roles associated with bone remodeling have also been investigated, particularly the role of eosinophils and osteoblasts. Eosinophils are known to contribute to the pathogenesis of certain subsets of CRS, and may also influence bone remodeling as increased expression of transforming growth factor β1 (TGF-β1) was identified in bone from CRSwNP patients.[667] This is further supported by Snidvongs et al.[254] who correlated serum and tissue eosinophilia to the presence of neo-osteogenesis. Serum eosinophilia has also been linked with P-glycoprotein levels and radiographic osteitis scores.[668] Early studies investigating the role of osteoblasts in sinus neo-osteogenesis demonstrated decreased osteoblast adhesion and proliferation, and increased bone mineralization in CRS osteoblasts compared to controls.[669] More recently, Khalmuratova et al.[670] reported an association between RUNX2 expression, a key osteoblast differentiation transcription factor, and neo-osteogenesis, that was further activated by the proinflammatory cytokines IL-13 and IL-17A.

Finally, current techniques in gene expression profiling and proteomics have permitted investigations into the molecular basis behind neo-osteogenesis. The bone morphogenic protein (BMP) family is 1 signaling pathway that has been investigated. Growth differentiation factor 5 (GDF5), a member of the BMP family, was found to be upregulated in osteitic bone.[671] Additionally, Wu et al.[672] identified that downregulation of pro-osteoblastic BMP signaling correlates to increased neo-osteogenesis in CRSwNP patients. Lastly, Kong et al.[673] correlated upregulation of receptor activator nuclear factor κB ligand (RANKL) to degree of neo-osteogenesis, and noted that blocking RANKL in a mouse model of CRS resulted in protection from mucosal inflammation and osteitis. The upshot of these data is that there appear to be several mechanisms related to the formation of neo-osteogenesis, although further investigation is required to uncover a deeper understanding of how they relate to the pathophysiology of CRS and identify targets for therapy.

Several treatment strategies for neo-osteogenesis related to CRS have been suggested, including radical surgery to remove all affected bone.[638,640,646,657] However, strong evidence for this surgical approach is lacking. Long-term intravenous (IV) antibiotics have also been proposed to treat the bacterial biofilms associated with neo-osteogenesis, although this treatment does not appear to target neo-osteogenesis itself because no histologic