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Biological susceptibility to root resorption in clear aligner therapy: A mini review

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Abstract:
External apical root resorption (EARR) persists in clear aligner therapy and reflects individual biological susceptibility more than appliance type. Polymorphisms in inflammatory and vitamin D pathway genes, including IL1B, RANK and VDR, shift individual EARR risk. Gingival crevicular fluid biomarkers, such as interleukin-6, interleukin-8 and matrix metalloproteinase-8, track the active resorptive phase. AI-assisted three-dimensional imaging quantifies apical loss objectively, near 0.6 to 0.8 mm and comparable to fixed appliances. Thus, data shows that integrating genetic, biomarker and imaging data points toward personalized, early prediction of resorption risk.

Keywords: External apical root resorption (EARR), clear aligner therapy, genetic polymorphisms, molecular biomarkers, personalized orthodontics

Background:
External apical root resorption (EARR) still occurs during clear aligner therapy and its severity is comparable to fixed appliances **[1]**. Cone-beam computed tomography meta-analysis confirms no significant difference in resorption between aligners and fixed appliances **[2]**. EARR reflects force-driven periodontal inflammation, with cytokine signaling and macrophage-mediated clastic activity at the root apex **[3]**. Therefore, it is of interest to describe the current genetic, molecular and biomarker evidence for biological susceptibility to EARR in clear aligner therapy.

Genetic susceptibility:
Because similar tooth movements yield markedly different outcomes, host genetic predisposition is increasingly implicated in EARR. Systematic review links polymorphisms in inflammatory and bone-remodeling genes, including IL1B, IL1RN, IL6, TNFRSF11A (RANK), and P2RX7, to individual resorption risk **[4]**. Targeted sequencing in a Korean cohort associated specific variants with extreme post-orthodontic EARR, supporting a heritable component **[5]**. Variants in vitamin D pathway genes, notably VDR, modulate cementum and alveolar bone metabolism and are also associated with EARR **[6]**.

Molecular biomarkers:
Gingival crevicular fluid reflects the periodontal remodeling that accompanies tooth movement. Cytokine and bone metabolism markers in gingival crevicular fluid differ between fixed and aligner treatments **[7]**. Specifically, during aligner therapy, interleukin-6 and interleukin-8 levels in gingival crevicular fluid rise during active movement, reflecting the inflammatory phase **[8]**. A systematic review further supports the use of salivary and crevicular proteins, such as matrix metalloproteinase-8, dentin sialoprotein, and osteopontin, as non-invasive proxies for active root resorption **[9]**.

Imaging and computational quantification:
Three-dimensional imaging has sharpened EARR assessment. In a randomized clinical trial using artificial-intelligence-based analysis of cone-beam computed tomography surface models, incisor apical resorption of approximately 0.6 to 0.8 mm was measured after treatment, with no significant difference between clear aligners and fixed appliances **[10]**. Deep learning now automates this quantification; a model trained on 4534 teeth extracted root volume and localized resorption directly from cone-beam computed tomography, reducing operator subjectivity **[11]**. Together, these tools enable objective, reproducible monitoring that can be integrated with genetic and biomarker profiles to support patient-specific risk stratification **[12]**. These observations are consistent with systematic reviews and meta-analyses reporting that external apical root resorption during clear aligner therapy is broadly comparable to that with fixed appliances rather than reliably lower **[13]**.

Conclusion:
EARR in clear aligner therapy reflects individual biological susceptibility more than appliance type. Genetic polymorphisms and gingival crevicular fluid biomarkers help explain why similar treatments yield different outcomes. Thus, integrating genetic, biomarker, and three-dimensional imaging data offers a route to personalized, early risk prediction.

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