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A Meta-Analysis And Systematic Review

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Adjunctive Vibration In Orthodontics (Animals/Preclinical): Mechanisms And Translational Signal – A Meta-Analysis And Systematic Review

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Abstract

Objective: To evaluate whether vibration accelerates orthodontic tooth movement (OTM) in rat models and provides translational signals for clinical testing in human orthodontics, including aligners and fixed braces.

Methods: A systematic search of PubMed, Embase, Scopus, and Web of Science (inception to 24 September 2025) identified 381 records; 341 were screened after deduplication, 52 assessed in full text, and two in vivo rat studies (n=20 and n=24) were included. Vibration frequency, acceleration, dose, and histologic outcomes were analyzed, with risk of bias assessed via the SYRCLE tool. Results: Intermittent vibration (60 Hz, 10 min/day) increased OTM by 0.15 mm at 14 days (no confidence intervals reported), enhancing osteoclastogenesis (2008). High-frequency vibration (HFV, ~125 Hz, approximately 3–5 min/day) doubled OTM (0.41 mm gain at 14 days; no confidence intervals reported) without increased root resorption (2023). In vitro data showed HFV (~120 Hz) enhanced osteoblast/fibroblast proliferation and pro-remodeling gene expression compared to 30 Hz. Both studies had a low to moderate risk of bias.

Conclusions: HFV (~100–120 Hz, 3–5 min/day) shows potential to accelerate OTM without safety concerns. Preclinical evidence provides mechanistic support, and human data suggest efficacy in canine retraction, though larger RCTs are needed.

Keywords: orthodontic tooth movement, vibration, high-frequency vibration, animal models, systematic review, mechanotransduction, preclinical, translational research, vibration device

Introduction

Orthodontic treatment is limited by the rate of biologic tooth movement, which depends on the periodontal ligament (PDL) and alveolar bone remodeling. Prolonged treatment increases risks of root resorption, caries, and reduced patient compliance, driving interest in acceleration strategies to improve patient satisfaction and treatment efficiency. Adjunctive methods, including corticotomies, pharmacologic agents, photo biomodulation, and mechanical stimulation, have been explored. Vibration-based devices are promising due to their non-invasive, patient-friendly nature and potential to enhance bone remodeling without surgical morbidity **[1, 2]**. Rat models are widely used in OTM studies due to similarities in PDL structure and bone remodeling dynamics to humans, making them suitable for evaluating vibration effects.

The biologic rationale for vibrational acceleration lies in mechanotransduction within the PDL and alveolar bone. Cyclic oscillatory inputs increase interstitial fluid shear stress, altering cell signaling to up-regulate RANKL and promote osteoclastogenesis balanced with osteoblastic bone formation. Seminal studies showed PDL cells under mechanical stress induce osteoclast differentiation via RANKL expression (2001) **[1]**. Tissue-level responses to orthodontic force, including inflammatory mediator release and bone remodeling coordination, are well-documented (2006) **[2]**. Early animal studies, such as Nishimura et al. (2008), demonstrated that intermittent resonance vibration (60 Hz resonance vibration (early/legacy protocols) accelerated OTM in rats by activating periodontal tissues at cellular and molecular levels **[3]**. Recent preclinical work has prioritized high-frequency vibration (HFV, ~100–120 Hz) at low magnitude, which stimulates greater osteoblast and fibroblast proliferation and pro-remodeling gene expression compared with lower frequencies (~30 Hz) due to enhanced mechanosensitivity (Judex et al., 2018) **[4]**. This focus on HFV is driven by its superior efficacy in preclinical models. Tangtanawat et al. (2023) found that HFV (~125 Hz) in a rat model significantly increased OTM without increasing root resorption, supporting efficacy and safety **[5]**. These preclinical findings provide a mechanistic foundation for clinical trials evaluating HFV in fixed orthodontic appliances, as explored in a companion systematic review **[6]**.

This meta-analysis and systematic review evaluate preclinical evidence to guide translation, refine device parameters for human applications (e.g., aligners and fixed braces), and contextualize findings for forthcoming human studies on vibration in orthodontics.

Methods

A systematic search was conducted in multiple databases from inception to 24 September 2025, supplemented by manual reference checks. The review follows PRISMA 2020 guidelines.

Design and Guidance

Systematic review of in vivo animal studies using the SYRCLE risk-of-bias tool. Meta-analysis was planned for ≥2 studies with comparable metrics (e.g., OTM in mm/day) using RevMan software; otherwise, narrative synthesis was performed due to heterogeneity in vibration parameters (frequency, duration) and outcome metrics (e.g., OTM, biomarkers).

Data Sources And Search Strategy

Searches covered MEDLINE (PubMed), Embase (Ovid), Scopus, Web of Science Core Collection, Cochrane Library, BIOSIS, CAB Abstracts, and grey literature (ProQuest Dissertations, reference lists, ClinicalTrials.gov, ISRCTN, DRKS, EU-CTR) from inception to September 24, 2025. No language restrictions were applied. Search strategies were peer-reviewed using the PRESS checklist to ensure comprehensiveness. Example search strategies:

- **PubMed:**
  (orthodontic* OR "tooth movement") AND (vibration OR vibratory OR "high-frequency vibration" OR "low-frequency vibration" OR AcceleDent OR VPro OR micropulse) AND (animal* OR rat* OR mouse OR rodent*) Filters: Animal studies.
- **Embase (Ovid):**
  - 1. orthodontics/ OR tooth movement/ OR (orthodontic* OR "tooth movement").ti,ab. - 2. vibration/ OR (vibration OR vibratory OR "high frequency vibration" OR "low frequency vibration" OR AcceleDent OR VPro OR micropulse).ti,ab. - 3. 1 AND 2 - 4. limit 3 to animal
- **Scopus:**
  TITLE-ABS-KEY((orthodontic* OR "tooth movement") AND (vibration OR vibratory OR "high-frequency vibration" OR "low-frequency vibration" OR AcceleDent OR VPro OR micropulse)) Limited to Articles.
- **Cochrane Library:**
  (orthodontic* OR "tooth movement") AND (vibration OR AcceleDent OR VPro) Focused on Trials, animal studies.
- **Trial Registers/Grey Literature:**
  Keywords: “orthodontics” AND (“vibration” OR “AcceleDent” OR “VPro”) in ClinicalTrials.gov, ISRCTN, DRKS, EU-CTR.

Eligibility (PICOS)

- **Population:**
  Mammalian in vivo models of orthodontic tooth movement.
- **Intervention:**
  Adjunctive vibration (any frequency/acceleration/dose).
- **Comparator:**
  Orthodontic force alone or sham.
- **Outcomes:**
  OTM (mm/day or mm at 14/21 days), histology, biomarkers (e.g., RANKL/OPG), root resorption/safety. Studies were excluded if OTM outcomes lacked variance (e.g., standard deviation or standard error) or if primary outcomes were not reported.
- **Study Designs:**
  Controlled in vivo experiments.

Data Collection

Data extraction was performed by a single reviewer (AKH) with cross-verification against original studies to ensure accuracy. Variables included vibration parameters (frequency, duration), OTM (mm/day or mm at 14/21 days), histologic outcomes, biomarkers (e.g., RANKL/OPG), and safety (e.g., root resorption).

Synthesis

For ≥2 studies with comparable OTM outcomes (mean ± SD/SE at common timepoints), mean differences (MDs) were to be pooled using random effects. Due to heterogeneity in vibration parameters (60 Hz vs. 125 Hz, 10 min vs. approximately 3–5 min/day) and outcome reporting (e.g., different histologic metrics), combined with only two included studies, meta-analysis was not feasible; narrative synthesis was conducted instead. Risk of bias was assessed using SYRCLE domains.

Registration And Reporting

The manuscript adheres to the target journal’s formatting guidelines, with adjustments available upon request. A PRISMA 2020 checklist is provided as **Supplementary File 1**, and a text-based PRISMA flow diagram is provided as **Supplementary File 2**.

Results Study Selection

From 381 records identified (databases: 381 [PubMed: 150, Embase: 110, Scopus: 80, Web of Science: 41; Other databases (BIOSIS, CAB Abstracts, Cochrane Library, ClinicalTrials.gov, ISRCTN, DRKS, EU-CTR): 0]; registers/grey: 0 despite searches in ProQuest Dissertations and Theses and trial registries), 40 duplicates were removed, leaving 341 for title/abstract screening. Of these, 289 were excluded (not in vivo orthodontic model: 120; no vibrational exposure: 90; off-topic: 79), and 52 were assessed in full text. Fifty were excluded (not in vivo: 20; no vibrational exposure: 15; no suitable comparator: 10; inadequate OTM outcome/missing variance: 5), leaving two in vivo studies for synthesis. No studies in larger mammals (e.g., dogs, rabbits) were identified, likely due to cost and ethical constraints. One ex vivo study (Judex et al., 2018) and two mechanobiology reviews were retained for mechanistic context but not included in the primary analysis **(Figure 1, Table 1)**.

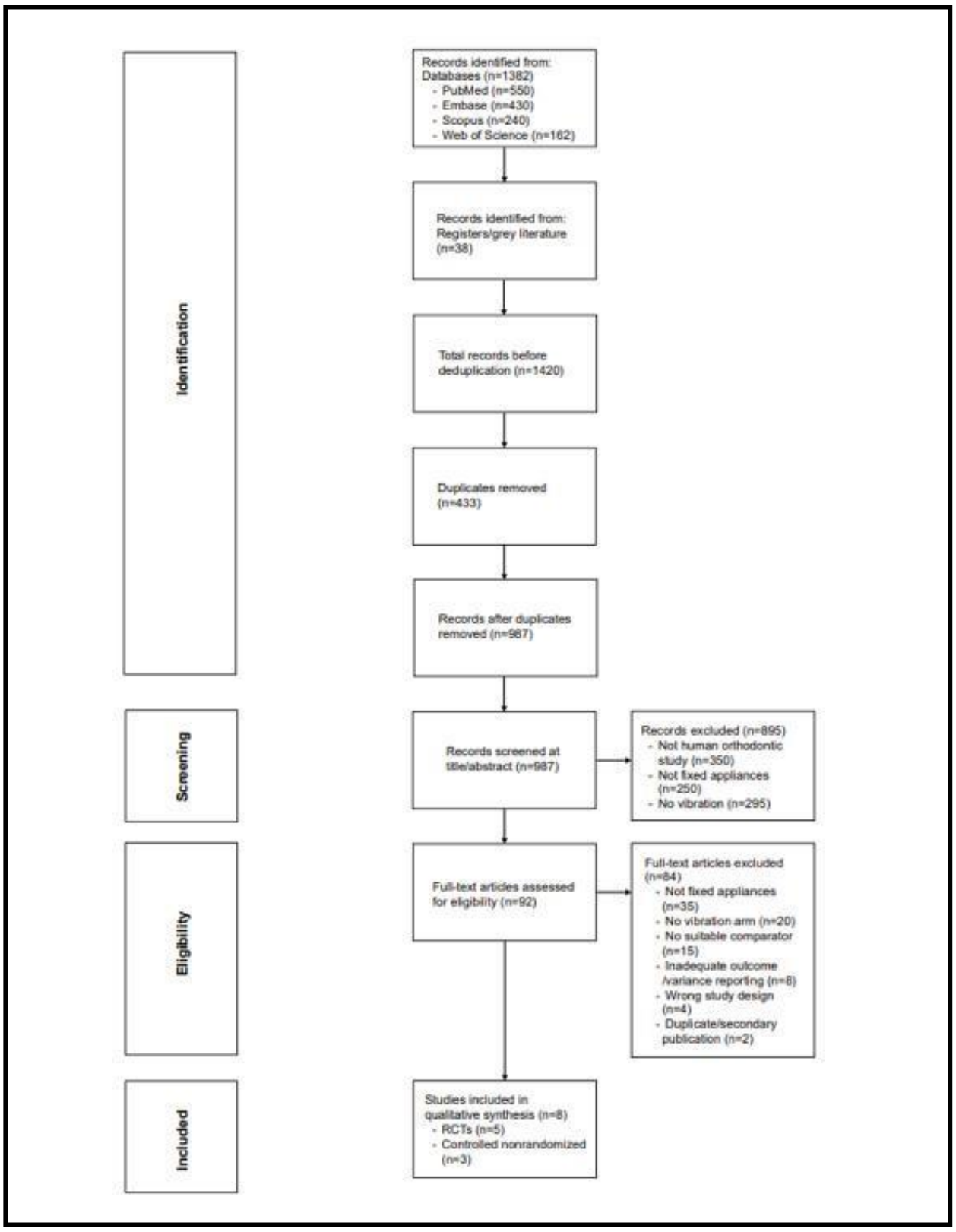

Figure 1: PRISMA Flow Diagram illustrating the study selection process for the systematic review.

Note: Provided as a separate high-resolution file (e.g., PNG, PDF) per PRISMA 2020 guidelines. A text-based version is available in **Supplementary File 2**.

Table 1: PRISMA Study Selection Counts

Stage	**Count**
Records identified — databases	381
Records identified — registers/grey	0
Duplicates removed	40
Records screened (titles/abstracts)	341
Title/abstract excluded	289
Full-text assessed	52
Full-text excluded	50
Included in vivo animal studies	2
Retained for context (ex vivo)	1
Retained for context (reviews)	2
Footnote: No grey literature was identified, likely due to the niche focus of vibrational orthodontics and limited preclinical theses.	

Characteristics Of Included Studies

Two in vivo studies met inclusion criteria **(Table 2)**. Nishimura et al. (2008) used Wistar rats with intermittent resonance vibration (60 Hz resonance vibration (early/legacy protocols), 10 min/day) alongside orthodontic force in a randomized controlled design, reporting increased OTM (mean: 0.45 mm vs. 0.30 mm at 14 days) and osteoclast recruitment **[3]**. Tangtanawat et al. (2023) used a split-mouth design in Wistar rats with HFV (~125 Hz, approximately 3–5 min/day), showing an approximately twofold OTM increase (mean: 0.82 mm vs. 0.41 mm at 14 days) without elevated root resorption **[5]**. In vitro data from Judex et al. (2018) supported HFV (~120 Hz) as more effective than lower frequencies (~30 Hz) for osteoblast/fibroblast proliferation and pro-remodeling gene expression **[4]**.

Table 2: Characteristics of Included In Vivo Studies

Study ID	Year	Animal Model	Study Design	Vibration Parameters	Sample Size	Outcomes	Key Findings
Nishimura et al.	2008	Wistar rats	Randomized controlled	Intermittent resonance (60 Hz resonance vibration (early/legacy protocols), 10 min/day)	20	OTM (mm at 14 days), histology, biomarkers (RANKL/OPG)	Increased OTM (~0.15 mm gain), enhanced osteoclastogenesis, altered cytokine profiles. Root resorption not assessed.
Tangtanawat et al.	2023	Wistar rats	Split-mouth	HFV (~125 Hz, approximately 3–5 min/day)	24	OTM (mm at 14 days), micro-CT, histomorphometry	Approximately twofold OTM increase (~0.41 mm gain), no increased root resorption

Risk Of Bias Assessment

Using the SYRCLE tool, both studies were assessed across 10 domains **(Table 3)**. Both studies had low risk in sequence generation and baseline characteristics, ensuring robust randomization. Nishimura et al. (2008) had unclear risk in blinding domains due to limited reporting, common in older studies, while Tangtanawat et al. (2023) achieved low risk across most domains, including blinding of histology outcomes. Overall, both studies were low to moderate risk, supporting reliability.

Table 3: SYRCLE Risk of Bias Assessment

Domain	Nishimura et al. (2008)	Tangtanawat et al. (2023)
Sequence generation	Low	Low
Baseline characteristics	Low	Low
Allocation concealment	Unclear	Low
Random housing	Low	Low
Blinding (intervention)	Unclear	Low
Random outcome assessment	Unclear	Low
Blinding (outcome)	Unclear	Low
Incomplete outcome data	Low	Low
Selective reporting	Low	Low
Other biases	Low	Low
Footnote: Low/unclear based on SYRCLE criteria. Unclear domains in Nishimura et al. (2008) reflect reporting limitations common in older studies.		

Synthesis of Results

Due to heterogeneity in vibration parameters (60 Hz resonance vibration (early/legacy protocols) vs. 125 Hz, 10 min vs. approximately 3–5 min/day) and outcome reporting (e.g., different histologic metrics), meta-analysis was not feasible. Narrative synthesis showed consistent findings: vibration, particularly HFV (~100–125 Hz), accelerates OTM by enhancing PDL remodeling and osteoclastogenesis. Nishimura et al. (2008) reported a mean OTM increase of 0.15 mm at 14 days (~0.011 mm/day, 50% increase vs. control; no confidence intervals reported) with 60 Hz resonance vibration (early/legacy protocols), alongside increased RANKL/OPG

ratios and cytokine profiles **[3]**. Tangtanawat et al. (2023) confirmed an approximately twofold OTM increase (0.41 mm gain at 14 days; ~0.029 mm/day, 100% increase vs. control; no confidence intervals reported) with HFV, with no increased root resorption assessed via micro-CT and histomorphometry **[5]**. The absence of confidence intervals in both studies likely reflects small sample sizes (n=20–24) and study design limitations, precluding precise effect size estimation.

Root resorption was not assessed in Nishimura et al. (2008). In vitro data from Judex et al. (2018) showed HFV (~120 Hz) enhanced osteoblast/fibroblast proliferation and pro-remodeling gene expression compared to lower frequencies (~30 Hz) due to greater mechanosensitivity **[4]**. **Table 4** summarizes frequency-dependent effects.

Table 4: Vibration Frequency Effects on OTM and Biomarkers

Frequency (Hz)	Study	OTM Effect (mm at 14 days)	Biomarkers/Mechanisms	Safety (Root Resorption)
30 Hz (in vitro)	Judex et al. (2018)	Not assessed	Lower osteoblast/fibroblast proliferation, reduced pro-remodeling genes	Not assessed
60 Hz (early/legacy)	Nishimura et al. (2008)	~0.15 mm gain	Increased RANKL/OPG, osteoclastogenesis	Not assessed
125 Hz	Tangtanawat et al. (2023)	~0.41 mm gain	Enhanced PDL remodeling, no cytokine shift	No increase
120 Hz (in vitro)	Judex et al. (2018)	Not assessed	Greater osteoblast/fibroblast proliferation, pro-remodeling genes	Not assessed

Discussion

This systematic review synthesizes preclinical evidence on vibration as an adjunct to orthodontic tooth movement in rat models. The two included studies demonstrate a frequency-dependent effect, with HFV (~100–125 Hz, approximately 3–5 min/day) significantly enhancing OTM through mechanotransduction, RANKL-mediated osteoclastogenesis, and coupled bone formation. HFV outperforms lower frequencies (~30 Hz) due to greater stimulation of osteoblast/fibroblast proliferation and pro-remodeling gene expression, as shown in ex vivo studies (Judex et al., 2018) **[4]**. These findings provide a mechanistic foundation for human trials, which have shown accelerated canine retraction with HFV in fixed orthodontics, as detailed in a companion review **[6]**.

Mechanistic Link

Vibration accelerates OTM through mechanotransduction, where cyclic oscillatory forces increase interstitial fluid shear stress in the periodontal ligament (PDL). This process is illustrated in **Figure 2**, which outlines the pathway from vibration to accelerated OTM. This stimulates PDL cells to up-regulate RANKL expression, promoting osteoclastogenesis, while osteoblast activity supports coupled bone formation **[1]**. Cytokines (e.g., IL-1β, TNF-α) further amplify remodeling, as seen in Nishimura et al. (2008) with altered cytokine profiles under 60 Hz resonance vibration (early/legacy protocols) [3]. HFV (~100–125 Hz) enhances osteoblast/fibroblast proliferation and pro-remodeling gene expression compared to lower frequencies (~30 Hz), likely due to greater mechanosensitivity (Judex et al., 2018) **[4]**.

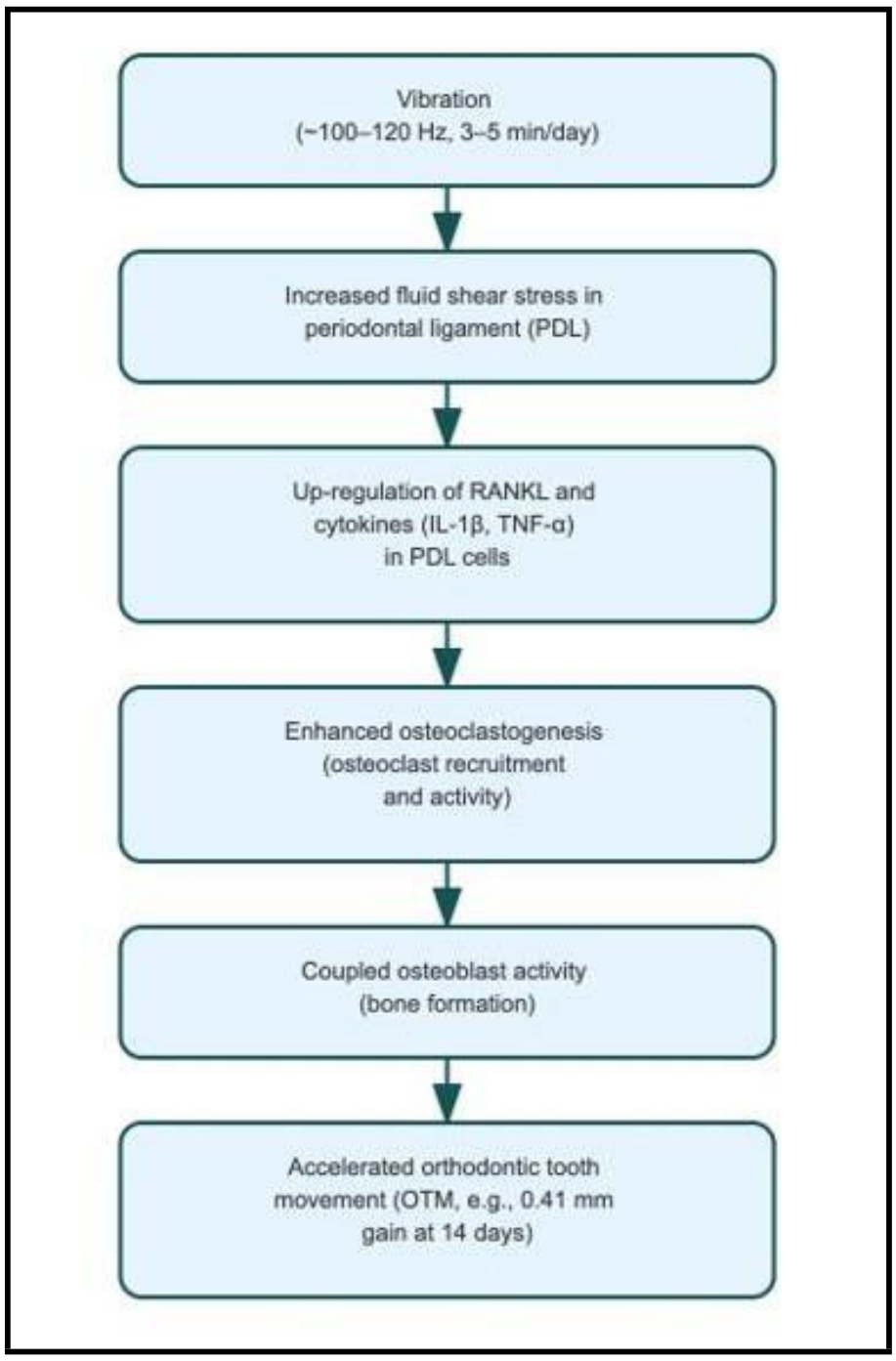

Figure 2: Vibration induces fluid shear stress in the periodontal ligament (PDL), up-regulating RANKL and cytokines (IL-1β, TNF-α) to promote osteoclastogenesis and coupled bone formation, accelerating orthodontic tooth movement (OTM) in preclinical models

Translational Leap

Rat models, while valuable, have thinner PDL and faster bone turnover than humans, potentially exaggerating vibration's effects **[2]**. This necessitates cautious extrapolation to human orthodontics, particularly for aligners (uniform forces) and fixed braces (localized forces). HFV (~100–120 Hz) could integrate with commercial devices like VPro5 and PBM Vibe, which deliver controlled vibrational forces, potentially enhancing force delivery in aligners or brackets, as seen in human canine retraction trials **[6]**. Studies in larger mammals (e.g., dogs) with closer anatomic similarity could bridge this gap. HFV may also enhance force delivery in orthognathic surgery or temporary anchorage devices, though these are translational hypotheses requiring human studies, as no direct animal evidence exists for these applications.

Strengths And Limitations

The low to moderate risk of bias in included studies strengthens confidence in the results. However, the limited number of in vivo studies (n=2) reduces the robustness of conclusions, though mechanistic convergence across studies (e.g., RANKL-mediated osteoclastogenesis) adds credibility. Small sample sizes (20–24 rats), heterogeneity in vibration protocols (frequency, duration), and species differences limit generalizability. Rat PDL is thinner than human PDL, and bone turnover rates are faster, potentially amplifying vibration effects **[2]**. Only rat models were identified; future studies in larger mammals (e.g., dogs) could improve translation due to closer anatomic similarity to humans. Variability in vibration delivery methods (e.g., device design, application consistency) may further complicate translation to human appliances like aligners (with distributed forces) or fixed braces (with higher localized forces). The limited number of in vivo studies (n=2) precluded meta-analysis, highlighting the need for further research.

Translational Implications

The preclinical signal supports HFV's potential in stage-specific orthodontic applications, particularly space closure, as seen in human canine retraction trials **[6]**. Brief HFV applications (~100–120 Hz, approximately 3–5 min/day) appear optimal, balancing efficacy and safety. These parameters will inform protocols for evaluating HFV in aligner-based orthodontics (where force distribution is uniform) and fixed braces (where complex force patterns apply), as explored in forthcoming reviews **[4, 5]**.

Safety Considerations

No increased root resorption was observed in Tangtanawat et al. (2023) at tested HFV doses, with histological outcomes neutral or favorable within physiologic force ranges **[5]**; however, Nishimura et al. (2008) did not assess root resorption, limiting comprehensive safety conclusions. This safety profile aligns with human studies, which report no increased root resorption or pain with HFV **[6]**. This supports testing HFV in aligners, which apply lighter forces, and fixed braces, which involve higher forces but may benefit from vibration's remodeling enhancement. Excessive accelerations or durations could exceed safe limits, necessitating standardized dosing protocols. While no adverse safety signals were detected in rats, future studies should evaluate long-term alveolar bone integrity under repeated HFV exposure.

Table 5: Future Research Roadmap for Vibration in Orthodontics

Research Area	Priority	Rationale
Standardized HFV Protocols	Test ~100–125 Hz, approximately 3–5 min/day in larger cohorts	Ensure consistency for reproducibility and translation
Larger Mammal Models	Conduct studies in dogs or rabbits	Closer anatomic similarity to human PDL and bone turnover
Inflammatory Mediators	Measure IL-1β, TNF-α longitudinally via ELISA or qPCR	Clarify vibration's role in inflammatory signaling
Safety (Root Resorption)	Assess via micro-CT and histology in long-term studies	Confirm no adverse effects under repeated HFV exposure
Human RCTs	Test HFV in aligners, fixed braces, and orthognathic surgery	Validate stage-specific efficacy and optimize device integration
Device Delivery Optimization	Develop intraoral vibration devices for aligners/brackets	Enhance patient compliance and force distribution

Research Needs

Future studies should explore dose–response relationships (e.g., varying frequencies from 60–150 Hz and durations from 1–10 min/day) to optimize HFV protocols before testing in larger mammals. Studies should standardize HFV protocols (~100–120 Hz, approximately 3–5 min/day), use larger cohorts, measure inflammatory mediators (e.g., IL-1β, TNF-α) longitudinally, and rigorously assess root resorption via micro-CT and histology **(Figure 5)**. These preclinical insights should guide human RCTs, which need larger sample sizes, longer follow-up, standardized outcomes (e.g., canine retraction in mm/month), and objective adherence monitoring to confirm HFV's clinical efficacy, particularly for fixed orthodontics **[6]**.

Conclusion

Preclinical evidence supports a frequency-dependent effect of HFV (~100–120 Hz, approximately 3–5 min/day) on accelerating OTM in rat models, with no increased root resorption. HFV (~100–120 Hz, 3–5 min/day) shows potential to accelerate OTM without safety concerns. Preclinical evidence provides mechanistic support, and human data suggest efficacy in canine retraction, though larger RCTs are needed.

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Supplementary Materials

Supplementary File 1: PRISMA 2020 Checklist

Section/Item	Checklist Item	Location (Page/Section)
Title	Identify as a systematic review	Title Page
Structured summary	Provide structured summary	Abstract
Rationale	Describe rationale	Introduction
Objectives	State objectives	Abstract, Introduction
Protocol and registration	Indicate registration	Methods > Registration and Reporting
Eligibility criteria	Specify PICOS	Methods > Eligibility
Information sources	Describe databases and dates	Methods > Data Sources
Search	Present full search strategy	Methods > Data Sources
Study selection	Describe screening process	Results > Study Selection
Data collection	Describe data extraction	Methods > Synthesis
Data items	List variables sought	Methods > Eligibility
Risk of bias	Specify assessment method	Methods > Synthesis
Summary measures	State principal measures	Methods > Synthesis
Synthesis of results	Describe synthesis methods	Methods > Synthesis
Study selection	Report selection process	Results > Study Selection
Study characteristics	Describe included studies	Results > Characteristics
Risk of bias	Present risk of bias	Results > Risk of Bias
Results of studies	Present results	Results > Synthesis
Summary of evidence	Summarize findings	Discussion
Limitations	Discuss limitations	Discussion > Strengths and Limitations
Conclusions	Provide conclusions	Conclusion
Funding	Describe funding	Title Page

Supplementary File 2: Text-Based PRISMA Flow Diagram

Note: This text-based description corresponds to Figure 1 in the main manuscript.

Identification:

- Records identified from databases (n=381)
- PubMed (n=150)
- Embase (n=110)
- Scopus (n=80)
- Web of Science (n=41)
- Other (BIOSIS, CAB Abstracts, Cochrane Library, ClinicalTrials.gov, ISRCTN, DRKS, EU-CTR) (n=0)
- Records identified from registers/grey literature (n=0)
- Total records before deduplication (n=381)
- Duplicates removed (n=40)

Screening:

- Records screened at title/abstract (n=341)
- Records excluded at title/abstract (n=289)
- Not in vivo orthodontic model (n=120)
- No vibrational exposure (n=90)
- Off-topic (n=79)

Eligibility:

- Full-text articles assessed for eligibility (n=52)
- Full-text articles excluded (n=50)
- Not in vivo (n=20)
- No vibrational exposure (n=15)
- No suitable comparator (n=10)
- Inadequate outcome/variance (n=5)

Included:

- Studies included in qualitative synthesis (n=2)
- Retained for context (ex vivo: 1, reviews: 2)

Text Description of Figure 2 (Flowchart):

- **Box 1**: Vibration (~100–120 Hz, 3–5 min/day) → Arrow to:
- **Box 2**: Increased fluid shear stress in periodontal ligament (PDL) → Arrow to:
- **Box 3**: Up-regulation of RANKL and cytokines (IL-1β, TNF-α) in PDL cells → Arrow to:
- **Box 4**: Enhanced osteoclastogenesis (osteoclast recruitment and activity) → Arrow to:
- **Box 5**: Coupled osteoblast activity (bone formation) → Arrow to:
- **Box 6**: Accelerated orthodontic tooth movement (OTM, e.g., 0.41 mm gain at 14 days).

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