Impact of LIPUS on Patient Experience During Orthodontic Treatment with Clear Aligners

by

Mohsen Gholizadeh

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ABSTRACT

INTRODUCTION

Clear aligners offer an aesthetic solution for treating dental malocclusions. The Introduction of Low-Intensity Pulsed Ultrasound (LIPUS) technology shows promise in enhancing patient experience through orthodontic treatment. LIPUS has been found to speed up tooth movement, potentially reducing treatment times and improving outcomes. This study investigates the impact of LIPUS in enhancing patient experience with clear aligners.

METHODS

This retrospective study analyzed records from 68 individuals, divided equally into two groups: 34 in the LIPUS-treated group and 34 in the control group; all met specific selection criteria. The inclusion criteria were patients aged 12 and older, treated exclusively with clear aligners, and those who used LIPUS with a minimum adherence rate of 67%. Exclusion criteria included compromised medical conditions, extraction treatments, and supernumerary teeth. The American Board of Orthodontics Discrepancy Index (ABODI) was employed to classify malocclusion complexity into four categories: mild (0-10), moderate (11-20), complex (21-30), and very complex (31-100). Both groups were matched based on age, biological sex, and type of malocclusion. The study evaluated the impact of LIPUS technology by measuring treatment duration, the number of refinements and non-used discarded aligners, and the impacts on bone radio density during treatment with clear aligners. Records were collected and analyzed from a private orthodontic practice. Bone radio density measurements (Hounsfield units) were taken using CBCT scans before and after treatment, with standardized sagittal and coronal views. Statistical

analyses included Independent Samples *t*-test, Mann-Whitney U Tests, and paired *t*-test to compare the LIPUS and control groups.

RESULTS

In this study, the treatment duration was significantly shorter in the LIPUS group, averaging 544.68 ± 238.97 days compared to 964.82 ± 417.9 days in the Control group, reducing treatment time by approximately 43.58% ($p < 0.001$). The number of days per tray change was significantly lower in the LIPUS group (5.42 ± 1.02 vs. 10.17 ± 3.18, $p < 0.001$). The LIPUS group also needed fewer refinements (additional aligners) (1.56 ± 1.11 vs. 2.41 ± 1.28, $p = 0.0045$) and had fewer discarded non-used trays (7.56 ± 11.91 vs. 11.18 ± 13.39, $p = 0.04$). The LIPUS group ended treatment with significantly more unused trays (5.06 ± 7.71 vs. 1.41 ± 4.36, $p = 0.02$). Additionally, the LIPUS group showed more bone radio density, as indicated by increased Hounsfield unit in the maxillary alveolar bone ($p < 0.001$). No side effects were reported in the LIPUS group.

CONCLUSIONS

Within the limitations of this study, the application of LIPUS in combination with clear aligners showed promising potential in reducing the number of refinements required and decreasing the number of non-used discarded aligners. It also suggested a possible reduction in overall treatment duration and more bone radio density in the maxillary alveolar bone within the studied sample. These preliminary findings indicate that LIPUS may enhance the efficiency and stability of orthodontic treatment, though further research is needed to confirm these effects across broader and more diverse populations.

PREFACE

This thesis is an original work by Mohsen Gholizadeh. The research project, which this thesis is a part of, received research ethics approval from the University of Alberta Research Ethics Board. Project Name " The effect of LIPUS on treatment time, number of revisions, number of aligners, and bone radio density after orthodontic treatment using clear aligners," No. Pro00139950, March 6, 2024. No part of this thesis has been previously published.

Dr. Tarek El-Bialy was the supervisory author. Dr. Hollis Lai and Dr. Lindsey Westover were the Supervisory committee members.

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LIST OF ABBREVIATIONS

LIPUS	Low-Intensity Pulsed Ultrasound
REB	Research Ethics Board
CAT	Clear Aligner Treatment
OITRR	Orthodontically Induced Tooth Root Resorption
Col1	Collagen type 1
ALP	Alkaline Phosphatase
OPG	Osteoprotegerin
RANK-L	Receptor Activator of Nuclear factor-Kappa β-Ligand
CBCT	Cone beam computed tomography
HU	Hounsfield units
ABO DI	American Board of Orthodontics Discrepancy Index
OTM	Orthodontic Tooth Movement
DEXA	Dual-Energy X-ray Absorptiometry

1 INTRODUCTION

1.1 Statement of Problem

The integration of clear aligners in orthodontics has offered a more aesthetically acceptable alternative to traditional fixed appliances, attracting a broader range of patients seeking orthodontic treatment. Despite technological advancements, discrepancies persist between patient experience through orthodontic treatments, including varied treatment duration, often requiring multiple refinements and adjustments(1). This has raised concerns about the efficiency of clear aligners(2). Low-intensity pulsed ultrasound (LIPUS) technology has been identified as a potential solution to enhance the efficacy of orthodontic treatment by using clear aligners that accelerate tooth movement with fewer refinements(3). However, the specific impact of LIPUS on patient experience with clear aligners has not been fully explored in clinical settings, leading to gaps in practical application and clinical understanding. Furthermore, bone radio density plays a crucial role in the stability and success of orthodontic treatments(4).

This study is important because it explores the impact of LIPUS on orthodontic treatment with clear aligners, specifically focusing on treatment time, number of revisions, number of aligners, and bone radio density. While the Aevo System (Delivers LIPUS) is a commercial appliance already available on the market, this study is significant in filling the gap in the clinical understanding of its practical application in real-world orthodontic settings. This study investigates its effectiveness when used concurrently with clear aligners, which are increasingly popular among patients. The study's findings could potentially reshape treatment protocols, offering more efficient and predictable outcomes for both patients and practitioners. Additionally, by quantifying the impact of LIPUS on bone radio density, this research could provide a deeper understanding of its

role in enhancing the stability and success of orthodontic treatments, setting it apart from prior research.

1.2 Objectives

1. Evaluate the impact of LIPUS on treatment duration when used with clear aligners.
2. Determine the effectiveness of LIPUS in reducing the number of refinements and discarded non-tracking trays during treatment.
3. Assess the impact of LIPUS on enhancing bone radio density throughout the orthodontic treatment with clear aligners.

1.3 Research Questions

1. How does LIPUS affect the duration of orthodontic treatment with clear aligners?
2. To what extent does LIPUS reduce the need for refinements and the number of non-used discarded trays during orthodontic treatment?
3. How does LIPUS impact bone radio density during orthodontic treatment with clear aligners?

1.4 Hypothesis

1.4.1 Null Hypothesis (H_0)

1. LIPUS does not significantly affect the duration of orthodontic treatment with clear aligners.
2. LIPUS does not significantly affect the number of refinements and non-tracking discarded trays during orthodontic treatment.
3. LIPUS does not significantly affect bone radio density during orthodontic treatment with clear aligners.

1.4.2 Alternative Hypothesis (H_1)

1. LIPUS significantly reduces the duration of orthodontic treatment with clear aligners.
2. LIPUS significantly reduces the number of refinements and non-tracking discarded trays during orthodontic treatment.
3. LIPUS significantly enhances bone radio density during orthodontic treatment with clear aligners.

1.5 Background

The journey of clear aligners in orthodontics began in 1940 when Kesling introduced the positioner, a tool designed to refine the final stages of orthodontic treatment(5). These removable polyurethane aligners offered a transparent and aesthetically appealing alternative to traditional fixed orthodontic appliances, making them suitable initially for correcting mild to moderate malocclusions(6). With advancements in materials and technology, clear aligners have evolved to address a broader range of orthodontic issues, including deep bites, open bites, crossbites, severe crowding, and Class I, II, and III malocclusions(7-10). This versatility has led to a surge in demand for clear aligners across all age groups of orthodontic patients and among orthodontic specialists(11).

Integrating digital diagnostic and treatment planning tools, such as the ClinCheck® software (Align Technology Inc, Santa Clara, CA, USA), has further enhanced the clear aligner treatment (CAT) visualization and planning process. This software provides a three-dimensional (3D) visual interface, enabling clinicians to tailor treatment plans, monitor progress, and make necessary adjustments(12, 13). While this tool has improved the visualization of orthodontic treatment outcomes of CAT, many challenges remain. Factors like patient age, sex, bone density, and certain systemic conditions can influence the patient experience through orthodontic treatment(14). Furthermore, the inherent properties of aligners, such as stress relaxation and intraoral degradation, can significantly impact the force they exert, affecting their predictability(15). As a result, many clinicians find that over half of their aligner cases require re-scans for (refinements or additional aligners) and new sets of aligners, and, in some instances, even the use of fixed appliances in addition to or replacing clear aligners(15). Clinical research over the years has primarily focused on the efficacy of tooth movements with CAT(16-19). It has been observed that there is a

significant discrepancy between the predicted outcomes and the actual results achieved, with discrepancies believed to be around 50% in terms of treatment duration. Some studies have even indicated that the initial set of aligners often fails to meet aesthetic and functional treatment objectives, making it imperative to refine the aligner sequence(20) through re-scans and the use of additional aligners.

1.5.1 LIPUS

LIPUS has been employed in the medical field for over six decades for diverse applications, ranging from sports medicine and myo-functional therapy to the healing of fractured non-union bone (21). LIPUS works by generating acoustic pressure waves that traverse living tissues, resulting in micromechanical strains and triggering a cascade of molecular events (22). Studies spanning in-vitro, animal, and human trials have shown the effect of LIPUS on reducing orthodontically induced tooth root resorption (OITRR), accelerating orthodontic tooth movement and shortening orthodontic treatment duration by modulating the expression of key molecules like collagen type 1 (Col1), alkaline phosphatase (ALP), osteoprotegerin (OPG), and receptor activator of nuclear factor-kappa β-ligand (RANK-L) (23-28).

LIPUS is a non-invasive and non-pharmacological method of accelerating orthodontic tooth movements(3). The Aevo System, a LIPUS medical device manufactured by SmileSonica Inc., Edmonton, Alberta, Canada, was used for patients enrolled in this study. It has been suggested that it is effective in clinical studies on a case basis(3). It has been approved by regulatory bodies (in Canada and Europe) that it is safe to use as an adjunct to orthodontic treatments.

Furthermore, in-market observations from clinicians indicated the potential for the Aevo System/LIPUS to provide additional clinical benefits to the orthodontic treatment with clear

aligners, such as improving orthodontic treatment efficiency by reducing the number of required additional aligners and non-used discarded aligners produced as part of the original treatment plan using the ClinCheck® software.

As a result, the current study analyzed existing in-market clinical data of orthodontic patients who used the new generation of Aevo 3 System/LIPUS concurrently with Invisalign clear aligners to research and quantify the potential effect of the Aevo3 System/LIPUS on treatment efficiency.

Reducing the number of additional aligners is relevant to the patients, as it reduces the number of dental visits, time spent in the clinic, and time out of orthodontic treatment waiting for a new set of aligners. For clinics, it saves staff time performing re-scans or impressions of patients' teeth, and saves the orthodontist time in re-planning the orthodontic treatment and submitting a new plan to the aligner manufacturer. For the aligner manufacturer, LIPUS may be assisting in saving time and reducing the cost of manufacturing new aligners. Reducing the number of non-used aligners has additional benefits, such as reducing plastic waste and the manufacturing cost for new trays.

1.5.1.1 Other Methods to Accelerate Tooth Movement

In addition to LIPUS, various other methods have been explored to accelerate orthodontic tooth movement. These methods generally fall into three categories: chemical applications, mechanical-physical applications, and surgical techniques utilizing the regional acceleratory phenomenon (RAP).

1. Chemical Applications:
    - **Prostaglandins:** These inflammatory mediators can increase osteoclastic activity and stimulate osteoblastic proliferation, accelerating tooth movement without significant root resorption.

- **Vitamin D3:** This compound enhances osteoclastic activity and osteoblastic differentiation, showing promise in accelerating tooth movement in animal studies.
- **Parathyroid Hormone (PTH):** PTH has been studied for its potential to regulate bone remodeling and accelerate tooth movement, particularly through local application.

2. Mechanical-Physical Applications:
    - **Low-Level Laser Therapy (LLLT):** LLLT has been investigated for its ability to stimulate cellular activity in the bone and periodontal ligament, though results are mixed regarding its effectiveness in accelerating tooth movement.
    - **Vibration:** Vibrational forces have been shown to enhance RANKL synthesis and osteoclast formation in the periodontal ligament, potentially speeding up tooth movement, though clinical results are varied.

3. Surgical Techniques:
    - **Corticotomy and Periodontally Accelerated Osteogenic Orthodontics (PAOO):** These surgical methods involve alveolar bone modification to reduce tooth movement resistance, speeding up the orthodontic process.
    - **Micro-osteoperforation (MOP):** This minimally invasive technique involves creating micro-traumas in the bone to stimulate an inflammatory response, leading to faster tooth movement.

Each method presents unique advantages and challenges, with varying clinical evidence supporting their use(29).

1.5.1.2 Description of The Investigational Device

The Aevo System (model A3-0000) is a LIPUS medical device designed for use with clear aligners or fixed orthodontic braces (Figure 1). It is battery-powered and portable; patients use it at home for 20 minutes daily during their orthodontic treatment.

The main LIPUS parameters of the Aevo System are listed in Table 1:

Table 1: LIPUS parameters

Parameter	Parameter Value
Operating frequency (carrier frequency)	1.5 MHz
Amplitude modulation (pulsed)	Repetition rate: 1 kHz Pulse duration: 200 µs ON, 800 µs OFF
Temporal average ultrasound intensity	30 mW/cm2

Figure 1:Aevo System (Model A3-0000) and accessories retrieved from SmileSonica Inc. website (https://www.smilesonica.com/products/aevo-system)

A detailed component description list for the Aevo System is shown in Figure 2 and Table 2.

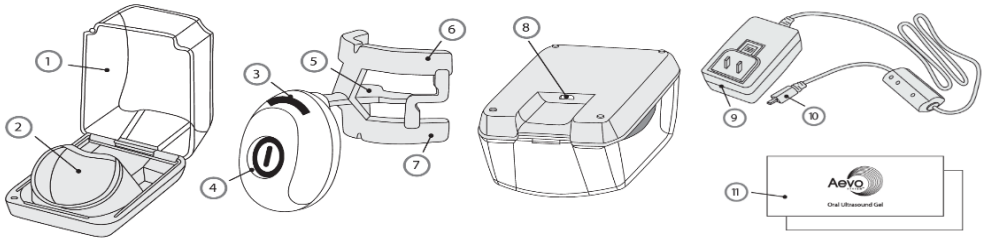


Figure 2: Aevo System component list retrieved from SmileSonica Inc. website (https://aevosystem.com/instructions-for-use/)

The full Instructions for Use for the Aevo System and the accessory Aevo Oral Ultrasound Gel are available for download on the Aevo System website at:

https://aevosystem.com/instructions-for-use/

Table 2: Overview of the Aevo System components and their functionality.

Legend Number	Component	Description
1, 2, 8	Charging Case	It stores and charges the Aevo System™. It consists of a tray with a charging dock and a lid. The power adapter is connected to a micro-USB port.
3, 4, 5, 6, 7	Device	Comprises a mouthpiece connected to electronics. Designed for both top (maxilla) and bottom (mandible) dental arches. Features a power button, rechargeable battery, LED, buzzer, and optional Bluetooth connectivity. They are used for 20-minute daily treatments.
9, 10	Power Adapter	The micro-USB plug connects to the charging case to provide power. It should not be used with other devices.
11	Ultrasound Gel Packets	The Aevo Oral Ultrasound Gel is provided separately as an accessory for the Aevo System. It is applied as a thin layer on the inner side of both arches of the mouthpiece to ensure ultrasound coupling between the mouthpiece and the patient's gums.

1.5.1.3 Commercial Use in Canada

The Aevo System (model A3-0000) and accessory ultrasound gel manufactured by SmileSonica Inc., Canada received regulatory approvals in Canada in June 2019. Since then, it has been sold to over 240 orthodontic and dental clinics across Canada and used by over 2,000 orthodontic patients.

The AEVO System is a LIPUS commercial medical device with Health Canada's Medical Device License (MDL) #102983 and CE marking in the European Union. The AEVO System has received regulatory approval in Canada and the European Union, validating its safety for the indicated uses.

1.6 ALIGNERS

Creating aligners on setup casts for orthodontic tooth movement originated in 1945(5). This innovation was primarily motivated by the growing demand for invisible braces and aesthetic considerations, especially among adult patients. By the late 1990s, two thermoplastic aligner systems were introduced, supporting a broad spectrum of tooth adjustments(30). The first system used setups that included tooth displacements with three aligners required for each setup step. The second system introduced fewer setup steps using more rigid aligners(31). Implementations of stereolithographic models and digital setups eliminated the need for more than one initial impression. These methods gained popularity, particularly among adult patients, spurred by vigorous marketing efforts by the manufacturers(31).

1.6.1 Aligners vs. Fixed Appliances

Aesthetic considerations and patient comfort are significant factors driving the choice of aligners over fixed appliances. The ability to remove aligners for eating and cleaning is particularly advantageous, as it reduces the risk of plaque buildup and subsequent gingival issues. This is supported by findings that aligner treatment is associated with lower plaque index scores and reduced presence of certain cariogenic bacteria compared to fixed appliances, particularly in the early stages of treatment.

However, some studies note that aligners might not be as effective in managing severe malocclusions as fixed appliances. Fixed appliances provide greater control over complex tooth movements, making them more suitable for addressing significant orthodontic issues. Additionally, while aligners may offer comfort and aesthetic benefits, their success heavily relies on patient adherence, as the removable nature of the aligners means that consistent wear is crucial for achieving the desired treatment outcomes.

Regarding clinical outcomes, aligners are effective for many cases; however they may require longer treatment durations and more refinements compared to fixed appliances. This is due to the challenges in controlling precise tooth movements with aligners, which can lead to the need for additional aligners and extended treatment time(32).

1.6.2 TYPES OF CLEAR ALIGNERS

Over the past two decades, orthodontic aligners have become highly popular for providing aesthetic orthodontic solutions(33). Their clear, transparent design, the convenience of removal for eating and oral hygiene, and less time needed in the dentist's chair have made them particularly attractive, especially to adult patients(34). Clear aligners were primarily used for minor tooth position corrections or as a final touch in orthodontic treatments(35). However, the rising demand for invisible braces, aesthetic considerations, and advancements in aligner technology have expanded their use to include moderate to severe malocclusions with varying degrees of effectiveness. After the Invisalign ClinCheck® patent expired, numerous clear aligner brands emerged, such as ClearAligner™, ClearPath™, and others, which now dominate the market(36-39).

Originally, companies like Align Technology adopted an indirect fabrication method. This involved creating dental models from materials such as resin or stone based on accurate impressions or digital scans of the patient's teeth(24, 25). This process involves electronically or manually segmenting individual teeth and moving them gradually to their desired positions (26). Each treatment stage is translated into a physical model over which plastic sheets are heated and molded into custom-made, clear aligners through applied air pressure or vacuum techniques(36, 39). The end products are clear aligners with either scalloped or straight-line finishes(35). By the late 1990s, two new thermoplastic aligner systems were introduced, enabling a broad range of tooth movements. The first system required a series of three aligners per setup step, accommodating tooth displacements between 0.5 and 1 mm(40, 41). The second system reduced setup steps to approximately 0.2 mm, using stiffer aligners(31, 40, 41). Technologies like stereolithographic models and digital setups were also introduced, requiring only a single initial impression. Despite the growing demand, the cost of aligner treatments remains high, which could deter patients and clinicians(36).

The advent of direct 3D printing technology marked a significant innovation in manufacturing, bypassing traditional dental labs since creating actual dental models became unnecessary(42). Dental data captured through digital impressions of the teeth (scans) are now directly sent to 3D fabrication systems like stereolithography and other technologies, which support various fabrication methods(43, 44).

1.6.3 ORTHODONTIC TREATMENT USING CLEAR ALIGNERS

1.6.3.1 Benefits with Aligner Treatment

Clear aligners offer advantages in orthodontic therapy, such as improved aesthetics, comfort, better oral hygiene, and reduced chair time(31). Adults using aligners report less discomfort and minimal impact on daily activities than those with traditional fixed appliances(34, 45). During the first week of orthodontic treatment using clear aligners, patients use less pain medication than those with fixed appliances(45). Adolescents have a positive view of aligners, often not restricting their diet, avoiding communication issues, or feeling self-conscious during treatment(46). After three months, about 70% of patients experience little to no discomfort, and approximately 80% seldom use pain relief medication. As treatment progresses, discomfort continues to decrease(46). Aligners also lead to better periodontal health outcomes than fixed appliances, with teenagers significantly reducing plaque indices over 24 months(47).

1.6.3.2 Limitations with Aligner Treatment

Recent assessments using systems like the American Board of Orthodontics objective grading system (ABO-OGS) and Peer Assessment Rating scores (PAR) have raised concerns about the clinical efficacy of aligner treatments(48, 49). While clear aligners are effective for mild to moderate malocclusions, their effectiveness in severe malocclusions remains debated(16, 31, 50-53). Compromised treatment outcomes often occur due to inadequate patient cooperation, issues with default protocols, or the inability of aligners to achieve the pre-planned movements. Furthermore, aligner systems are limited in ways that fixed appliances are not, particularly in the constraints related to spatial dimensions (anterior-posterior, vertical, and transverse) and the time dimension, which dictate the pace and extent of tooth movement(53-58). Unlike fixed appliances

where teeth can move along the arch more freely, aligners require refinements, overcorrections, and exact adherence to provided specifications to achieve intended results.

1.6.4 PATIENT EXPERIENCE WITH CLEAR ALIGNER TREATMENT

1.6.4.1 Quality of Life with Clear Aligner Treatment

Orthodontic treatment aims to achieve a balanced, healthy, functional, aesthetic occlusion and a harmonious facial appearance. Such treatment improves patients' perceptions of their dental aesthetics, facial features, oral health, and functionality. Self-perceived malocclusions can significantly impact psychological and social well-being, affecting the ability to smile, express emotions, and engage in social activities (59, 60). Individuals with significant irregularities in their upper front teeth or an overjet over 5 mm are likely to feel embarrassed about smiling openly, which can adversely affect their emotional well-being(60). Overall, orthodontic treatment has been shown to enhance the quality of life related to oral health(61, 62). However, fixed appliances can negatively impact various health-related quality-of-life domains, such as physical function and psychological discomfort(63, 64). During treatment, the oral health-related quality of life (OHRQoL) may initially decline due to discomfort and the appearance of the appliances(65). Studies like Miller et al., which used daily diaries to compare the quality of life impacts between aligner users and those with buccal fixed appliances during the first week of treatment, found that aligner users reported fewer negative impacts on overall quality of life (45). Other research assessing the initial adjustment period to orthodontic devices found that aligner users experienced the lowest level of oral discomfort and had fewer issues with eating and daily activities than those with fixed appliances (34, 66). Over an 8-month period, aligner use showed minimal impact on OHRQoL, although some users initially had trouble pronouncing certain words(67). Nonetheless,

most reported minimal impact on taste, eating, daily activities, or feelings of shyness or insecurity due to wearing aligners.

1.6.4.2 Pain Experience

Orthodontic treatment often involves discomfort or a sensation of pressure on the teeth(68). Although 70% of patients report experiencing pain during treatment, only 15% consider it significant enough to consider discontinuing treatment (69). Pain perception varies throughout the day, particularly in the first two days after appliance activation, with greater differences observed in female patients (70). Patients frequently use over-the-counter medications like paracetamol or ibuprofen to manage this pain (71). Research indicates that while pain is relevant, clinical and demographic factors influence the psychosocial and behavioral responses to orthodontic pain, suggesting that focusing solely on pain intensity does not fully capture the patient experience (72). Patients with aligners typically experience mild to moderate pain, especially in the first 2-3 days of wearing a new aligner set. Still, this discomfort generally decreases over time, with the overall pain experienced by the end of treatment being considered neutral (67, 73, 74). Recent advances in orthodontic materials have also helped reduce the intensity and duration of pain and discomfort during aligner insertion (75). Studies comparing pain levels between aligner treatments and fixed appliances have shown mixed results. Some suggest that aligners cause less pain initially (45, 73, 76), while others found no significant difference (77). An RCT noted that, during the first week of orthodontic treatment, patients with fixed appliances experienced more discomfort, especially while biting and chewing, and they reported higher discomfort levels and greater reliance on painkillers after monthly adjustments compared to the aligner group (77).

1.6.4.3 Caries Lesions and Periodontal Status

While Clear aligners have gained popularity in orthodontic treatments, their impact on oral health, particularly regarding caries lesions and periodontal status, is an area of ongoing research.

Studies have reported that clear aligners are associated with a lower incidence and severity of white spot lesions (WSLs) compared to fixed orthodontic appliances(78). This reduction is attributed to fewer plaque retentive areas and the ease of maintaining oral hygiene with clear aligners. However, the need to wear aligners for approximately 22 hours per day can create an environment conducive to plaque accumulation, which may increase the risk of demineralization and caries formation, especially if oral hygiene is not rigorously maintained. The continuous contact of aligners with the teeth can disrupt the natural cleaning action of saliva, potentially increasing the concentration of cariogenic bacteria such as Streptococcus mutans and Lactobacillus, which are associated with an increased risk of caries(78).

Clear aligners have also shown a notable advantage over fixed appliances regarding periodontal health. Studies indicate that the use of clear aligners significantly improves periodontal health indices, such as plaque index (PI), gingival index (GI), and bleeding on probing (BoP), compared to fixed orthodontic appliances. This improvement is attributed to the removable nature of clear aligners, which facilitates better oral hygiene practices, allowing patients easier access to clean tooth surfaces. As a result, patients using clear aligners generally experience lower levels of plaque accumulation and a reduced incidence of gingival inflammation. The evidence suggests that clear aligners may be preferable for patients who prioritize periodontal health during orthodontic treatment(79).

A recent systematic review by Raghavan et al. (2023) showed that clear aligners are associated with significantly less plaque accumulation and a lower incidence of caries-associated bacteria compared to fixed appliances. This systematic review highlights the potential of clear aligners to mitigate some oral health risks commonly associated with orthodontic treatment. However, maintaining stringent oral hygiene practices cannot be overstated(80).

1.7 Cone Beam Computed Tomography

Cone beam computed tomography (CBCT), also known as C-arm CT, cone beam volume CT, flat panel CT, or Digital Volume Tomography (DVT), is a unique X-ray imaging technique utilizing divergent cone-shaped X-ray beams. This method is pivotal in various medical fields, especially dentistry and orthodontics, playing a crucial role in treatment planning and diagnostic processes. It has recently replaced multi-slice CT in these fields for various diagnostic and treatment purposes, providing good image quality with lower radiation exposure(81, 82).

In orthodontics, CBCT is instrumental for its detailed three-dimensional imaging capabilities. It offers an undistorted view of dentition essential for evaluating erupted and non-erupted teeth, tooth root orientation, and identifying anomalous structures—features often missed by conventional two-dimensional radiography. This technology is also critical for measuring bone radio density in preparation for orthodontic treatments and dental implants. Advances in CBCT technology allow for detailed and quantitative bone radio density measurements using a calibrated approach to interpret gray values in Hounsfield units (HU). However, these values are relative rather than absolute (81, 83-87).

The CBCT scanner enhances dental care by rotating around the patient's head, capturing up to 600 distinct images to form a comprehensive three-dimensional digital volume. This volume,

composed of detailed voxels of anatomical data, can be extensively manipulated and examined using specialized software, offering unparalleled precision in dental diagnostics and treatment planning.

Since its introduction in the late 1990s by Dr. Yoshinori Arai in Japan and Dr. Piero Mozzo in Italy, CBCT technology has evolved significantly. The first commercial CBCT system, the NewTom 9000, was launched in Europe in 1996 and later in the United States in 2001, revolutionizing dental imaging and broadening the scope of its applications in orthodontics and beyond. This technology is also invaluable in pre-surgical assessments and ongoing treatment evaluations in dentistry. It underscores its importance in diagnostic radiography, advancing orthodontic treatment methods, and understanding bone dynamics in response to orthodontic interventions(88).

1.8 Bone Radio Density Measurement and Orthodontic Treatment

Maintaining retention stability is crucial for all orthodontic treatments' success (89). In this modern era, where accelerated orthodontic treatments are increasingly common, concerns persist about the effects of rapid tooth movement on bone as patients move into the retention phase. The research on this topic offers mixed findings; some studies indicate a decrease in bone density around teeth that have undergone orthodontic treatments(83, 90), while others report an increase (91, 92). Some researchers found no change from the baseline (84). This variability could be due to different bone remodeling responses to the type and extent of the movement(93).

1.9 LIPUS AND BONE

LIPUS has emerged as a promising tool in orthodontics for enhancing bone density. It is suggested that LIPUS can accelerate bone remodeling by stimulating osteoblastic activity, potentially reducing the treatment time and improving outcomes in orthodontic patients. Preliminary studies have shown that LIPUS may effectively increase bone density post-treatment(94), thereby improving the stability of teeth during the retention phase. However, more comprehensive and controlled studies must validate these findings across patient demographics and treatment variables.

1.10 Orthodontic Treatment Variables with Clear Aligners and LIPUS:

1.10.1 Treatment Duration

LIPUS may decrease the time required to achieve the final orthodontic results. Research suggests that ultrasound technology can stimulate bone remodeling, potentially speeding up tooth movement (95). Several studies have consistently shown the effectiveness of LIPUS in significantly reducing orthodontic treatment duration. Tsichlaki et al., in a systematic review (2016), mentioned that the average duration of orthodontic treatment with fixed appliances is approximately 19.9 months. This conclusion was drawn from an analysis of 22 studies involving 1089 participants. When additional studies were included in a sensitivity analysis, the average treatment duration was slightly adjusted to 20.02 months based on data from 1211 participants(96). Another recent systematic review (2020) has shown that the average treatment duration for fixed appliances in orthodontic treatments varies widely, with a mean duration ranging from 25 to 31 months, reflecting the complexity and variability in patient responses to treatment(Figure 3)(97).

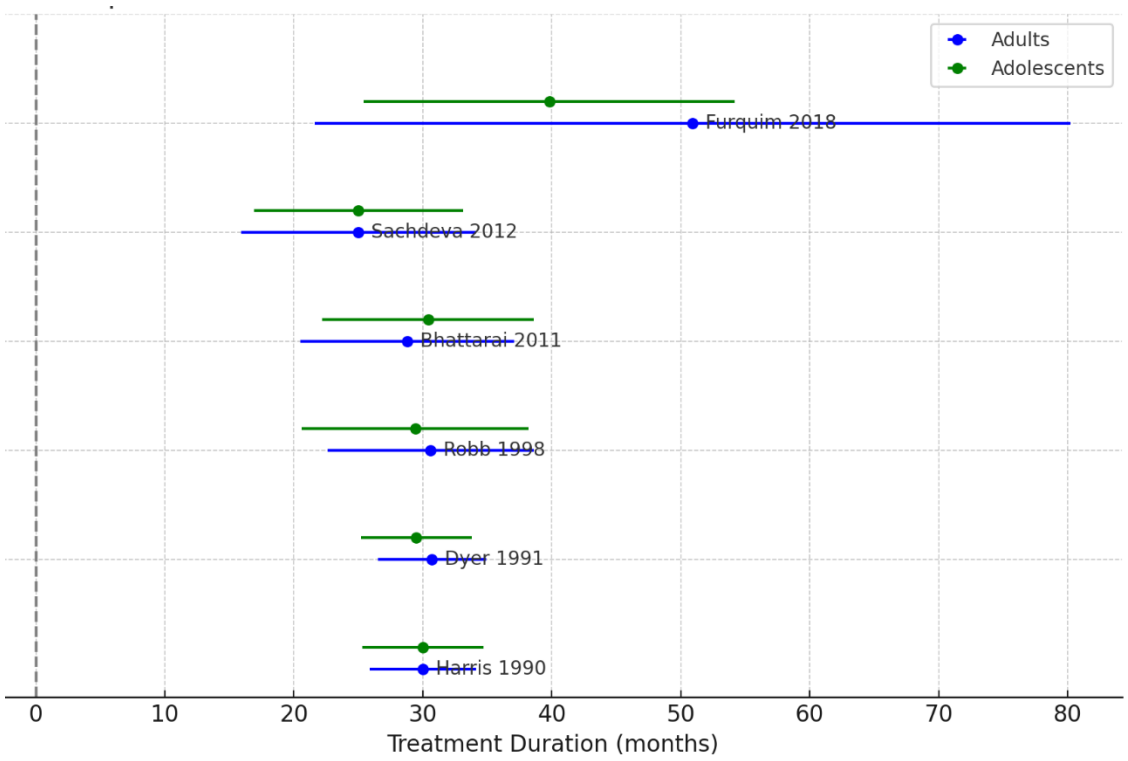


Figure 3: Comparison of Treatment Duration between Adults and Adolescents for fixed appliances

This duration is longer compared to the treatment times associated with clear aligners combined with adjunctive therapies like LIPUS. For example, Kaur and El-Bialy (2020) reported a 49% reduction in treatment time with LIPUS, where the LIPUS group required 541.44 days compared to 1061.05 days in the control group (3). Similarly, Al-Dboush et al. (2021) observed a 26% decrease in treatment duration with LIPUS, with patients in the LIPUS group averaging 533 days, compared to 719 days in the control group (95). These findings underscore LIPUS's consistent ability to expedite orthodontic treatment.

1.10.2 Decreasing the Need for Refinements

Consistent use of LIPUS could reduce the necessity for additional refinements or adjustments. Refinements or additional re-scans also lead to the discarding of non-used aligners. LIPUS was studied for its potential to increase the number of refinements and non-used discarded aligners.

1.10.3 Enhancing Bone Radio Density

LIPUS has been suggested to improve bone radio density, which is crucial for orthodontic adjustments. Enhanced bone radio density may provide a more stable final tooth position with less treatment relapse(98). For instance, Kaur et al. (2017) reported significant increases in osteogenic markers like OPG and RANK-L, crucial for bone remodeling and accelerating tooth movement, correlating with the observed higher bone density in their LIPUS group(99). Furthermore, Pascoal et al. (2024) showed that specific ultrasound parameters can enhance metabolic activity and osteogenic marker expression in osteoblasts and periodontal ligament fibroblasts, promoting bone formation during orthodontic treatment(100). These findings underscore LIPUS's efficacy in enhancing bone radio density, highlighting its potential to optimize orthodontic outcomes by facilitating improved bone remodeling processes.

1.11 Study Objectives

1.11.1 Primary Effectiveness Endpoint

The study's primary endpoint is to determine the effectiveness of the Aevo System in conjunction with clear aligners on orthodontic treatment, focusing on reducing the number of refinements and non-used discarded aligners. This has been evaluated through a retrospective analysis of patient records from two distinct groups:

- Aevo Group: Patients who used the Aevo System with clear aligners.
- Control Group: Patients who underwent treatment with only clear aligners.

The comparison of these groups helps determine if the LIPUS produced by the Aevo System may contribute to enhanced patient experience through orthodontic treatment.

1.12 Secondary Effectiveness Endpoint

The secondary outcome/endpoint includes:

- The occurrence of side effects or adverse events in the Aevo group compared to the Control group.
- The overall orthodontic treatment duration for each patient group is used to quantify the reduction in treatment time in the Aevo group compared with the control group.
- The number of days of usage of the aligners by each patient in each group to calculate the tray change interval (the number of days the patient used each tray) in the Aevo group compared with the control group.
- Treatment difficulty was calculated for each patient using the ABO Difficulty Index for an objective comparison of treatment complexity between the two groups.
- Changes in bone trabeculae in the Aevo group's treatment process compared to the control group.

1.13 Literature review

Three main clinical studies were conducted with the Aevo System, as follows:

1.13.1 Shortening of Overall Orthodontic Treatment Duration with LIPUS.

A previously reported retrospective in-market clinical study aimed to assess the impact of LIPUS used in conjunction with Invisalign SmartTrack® clear aligners on reducing the overall duration of orthodontic treatment. The study involved 34 patients (9 males, 25 females; average age 41.37 ± 15.02) who completed their treatment using an intraoral LIPUS device/Aevo 2 System and

Invisalign clear aligners in a private clinic. The LIPUS parameters were set for home use at an ultrasonic frequency of 1.5 MHz, pulse duration of 200 μs, pulse repetition rate of 1 kHz, and spatial average-temporal average intensity of 30mW/cm² for 20 minutes daily. A control group, matched for malocclusions, included 11 males and 23 females (average age 31.36 ± 14.41), who completed treatment with only Invisalign clear aligners. The treatment duration was measured from the date of bonding the first Invisalign attachments and LIPUS application (T0) to the date of retainer delivery (T1). Analysis using a two-sample *t*-test in Microsoft Excel revealed a significant reduction in treatment duration for the LIPUS group (541.44 ± 192.23 days) compared to the control group (1061.05 ± 455.64 days), with a p-value < 0.05, translating to an average 49% reduction in overall treatment time. The average adherence rate for LIPUS usage was 66.02%. This study concluded that the use of the LIPUS/Aevo System in addition to Invisalign clear aligners significantly shortened the overall duration of orthodontic treatment on average by 49% as compared to the control group that used Invisalign clear aligners only(3).

1.13.2 Effect of LIPUS on Tooth Movement and Root Resorption

A prospective double-blind, multi-center, randomized controlled clinical trial explored the influence of the LIPUS/Aevo System on tooth movement and root resorption in orthodontic patients using fixed orthodontic appliances (wire braces). Conducted using a split-mouth design involving 21 patients, with an additional ten patients serving as a negative control group, the study assessed the LIPUS/Aevo System's efficacy in accelerating orthodontic tooth movement and reducing root resorption. The LIPUS devices employed, the Aevo System, had specific settings: a pulse frequency of 1.5 MHz, a pulse repetition rate of 1 kHz, and an average output intensity of 30 mW/cm². Assessments included Cone-Beam Computed Tomography (CBCT) images taken before and after treatment and measurements of extraction space dimensions and canine root

lengths at specific intervals. The findings were statistically significant, showing a 29% increase in the rate of tooth movement on the LIPUS-treated side (0.266 ± 0.092 mm/week) compared to the control side (0.232 ± 0.085 mm/week). Additionally, less induced tooth root resorption was observed in the LIPUS side (0.0092 ± 0.022 mm/week) than in the control side (0.0223 ± 0.022 mm/week). Therefore, the study concluded that applying the LIPUS/Aevo System in orthodontic treatment effectively accelerated tooth movement(28).

1.13.3 Effect of LIPUS on Orthodontically Induced Root Resorption Caused by Torque.

A further prospective, double-blind, controlled clinical trial aimed to assess the impact of LIPUS on orthodontically induced root resorption due to torque. The study involved ten healthy patients, aged between 12 and 35 years, who required bilateral extraction of first premolars as part of their routine orthodontic treatment. Employing a split-mouth design, a 15° twist was applied to the archwire using 0.019 x 0.025-inch TMA in a 0.022-inch bracket system, generating about 5 N/mm buccal root torque at the bracket level. LIPUS/Aevo System was applied to one side of the arch for 20 minutes daily for four weeks at an incident intensity of 30 mW/cm², while the other side served as a control with a sham transducer. Micro-computed tomographic analysis was conducted on the extracted teeth after four weeks. The results indicated that the LIPUS-treated teeth showed significantly less total volume of resorption lacunae and percentage of root resorption than the control teeth. The mean difference in the total volume of resorption lacunae was 0.54 ± 0.09 mm³ ($P < 0.001$), and for the percentage of root resorption, it was 0.33 ± 0.05 mm³ ($P < 0.001$). There were also fewer resorption lacunae found on all root surfaces in the LIPUS group compared to the control, except for the distal surface. The findings suggest that LIPUS minimizes root resorption when applied during torque tooth movement. This clinical trial shows that LIPUS/Aevo 1 system-treated teeth have significantly less root resorption than control teeth(27).

2 METHODS

2.1 Study Design

In this retrospective review study, the records of patients from September 2019 to January 2024 who completed their orthodontic treatment with the Aevo System (model A3-0000) LIPUS intraoral device in conjunction with Invisalign clear aligners in Sphinx orthodontic clinic located in Edmonton, Alberta (Sphinx Orthodontics, sphinxorthodontics.com), were collected and analyzed.

2.2 Study Population

2.2.1 Sample Size

This study calculated the required sample size to ensure sufficient statistical power for detecting a significant difference between the experimental and control groups regarding the primary outcome measure. The parameters set for this calculation included a significance level (α) of 0.05 and a power ($1-\beta$) of 80%. To accommodate these parameters, we initially hypothesized that the difference in the impact rates between the experimental group (treated with clear aligners and LIPUS) and the control group (treated with clear aligners alone) would be 49%, based on previous work(99).

Using the formula for comparing two proportions:

$$n=((Z1-\alpha/2+Z1-\beta)2\times(p1(1-p1)+p2(1-p2))/(p1-p2)2)$$

Where $Z1-\alpha/2\approx1.96$ (for α=0.05), $Z1-\beta\approx0.84$ (for β=0.20 or 80% power), $p1$ and $p2$

$$n=((1.96+0.84)2\times(0.49(1-0.49)+0.25(1-0.25))/(0.49-0.25)2) \approx 59$$

However, since the Aevo System 3.0 device was released in 2019 and orthodontic treatment takes time, it was challenging to find compliant patients who had completed treatment with all the necessary records available. As a result, we were able to find records for 34 patients in the experimental group and subsequently selected 34 patients for the control group.

So, this study involved collecting clinical data from the records of 68 patients who had completed their orthodontic treatment at a private orthodontic practice as follows:

1. 34 patients in the experimental group (treated with clear aligners and LIPUS)
2. 34 patients in the control group (treated with clear aligners)

Patients who chose to use the Aevo System were generally motivated by the desire to enhance their orthodontic treatment experience, while those who opted not to use it either cited concerns about adherence to the additional daily routine or were satisfied with the regular process of traditional aligner treatment.

2.2.2 Inclusion Criteria for Selection of Study Subjects

Subjects who meet all of the following criteria were qualify for entry into the study:

1. 12 years and older patients at the start of their orthodontic treatment.
2. Patients receiving orthodontic treatment exclusively with clear aligners (Control Group).
3. Patients receiving orthodontic treatment exclusively with clear aligners and regularly using the Aevo 3.0 System (67% or higher usage adherence) (Aevo Group). The 67% usage adherence was measured using the Smilesonica app, indicating that patients used the Aevo System on average two-thirds of the 20-minute daily treatment (or 13.4 minutes daily).
4. Patients maintain good oral hygiene and show no active periodontal disease.
5. Patients with complete records, which include pre-and post-treatment radiography and photography, scans, completed treatment cards, every clinical session record, and Invisalign data, are available as applicable for this study.

The decision to set the lower age limit at 12 years was based on several key factors relevant to orthodontic treatment. First, by age 12, most individuals have fully erupted permanent teeth, which is essential for accurately applying clear aligner therapy. The presence of permanent teeth allows for a more predictable response to orthodontic forces and aligns with the intended treatment protocols used in this study. Second, appropriate skeletal development has typically occurred by this age. This is crucial for ensuring the skeletal structures are mature enough to respond effectively to treatment, particularly when using adjunctive therapies like LIPUS. This ensures that any skeletal changes or movements facilitated by the treatment are within the physiological capabilities of the patient. Finally, choosing this age also considers the necessity of adherence to treatment protocols. At 12 years and older, patients are generally more capable of understanding and following the required daily usage of aligners and LIPUS devices, which is critical for successful treatment outcomes(101).

2.2.3 Exclusion Criteria

Subjects who meet any of the following criteria were excluded from the study:

1. Any compromised medical or dental condition.
2. Patients undergoing extraction orthodontic treatment.
3. Patients with supernumerary teeth present at the beginning of treatment that required their removal prior to or during treatment.
4. Presence of temporomandibular joint (TMJ) disorders.
5. Patients with local or systemic conditions or ongoing pharmacological treatments that could have influenced the tooth movement process during their orthodontic treatment.
6. Patients involved in any other clinical study during their orthodontic treatment.
7. Any patient who fails to meet the above inclusion criteria.
8. Patients who didn’t wear each aligner tray for at least 85% of the prescribed time.

Cases involving extractions were excluded to ensure a homogeneous sample that focuses on the effects of LIPUS on treatment with clear aligners. Including extraction, cases could introduce additional variables related to the healing process and movement of teeth, which might confound the results and make it difficult to isolate the impact of LIPUS on treatment duration and bone density(102).

2.3 Aevo System

In this study, the Aevo system 3.0 was utilized to deliver LIPUS as an adjunct to orthodontic treatment with clear aligners. Although the Aevo 3.0 system shares the same therapeutic output as the earlier Aevo system 2.0, its design has been significantly enhanced to improve patient adherence and ease of use. These design improvements include more ergonomic features, making the device easier for patients to handle and use consistently. While both devices deliver the same intensity and frequency of ultrasound, the advancements in the Aevo 3.0 system's design are expected to contribute to better adherence to the treatment protocol, which is crucial for achieving the intended therapeutic outcomes.

2.4 Adherence

Adherence to treatment protocols is a critical factor in achieving successful orthodontic outcomes. This study established an adherence threshold of 85% for aligner wear. This threshold ensures substantial wear time, maintains effective treatment progress, and, after consultation with an orthodontist, was considered acceptable for achieving desired orthodontic outcomes. Studies have indicated that patients can still achieve effective results even with slightly less than the recommended 22 hours per day wear time, although the treatment might take slightly longer(103).

For LIPUS usage, a minimum adherence threshold of 67% was adopted. This level was chosen based on prior research indicating that shorter treatment time (49% reduction) was observed with an average of 67% adherence (3). The 67% threshold was measured using the Smilesonica app, indicating that patients used the Aevo System on average for two-thirds of the prescribed daily treatment duration (approximately 13.4 minutes out of 20).

2.5 Record of Study Participants

A confidential record of all study patients was maintained, including all patients screened to enter this study and whose data were studied under this protocol. For clarity, the patients' names weren’t recorded as part of this study; only the patients' identification numbers in the clinic were included.

2.6 Screening and Selection Procedures

The "Eligibility" column in the following table marked Yes/No whether a patient meets each criterion. To be eligible for the study, a patient must meet all inclusion criteria and none of the exclusion criteria (Table 3).

Table 3: Patient Screening Form

Criteria Type	Criteria Number	Description	Eligibility (Yes/No)
Inclusion	1	12 years and older patients at the start of their orthodontic treatment	
Inclusion	2	Patients receiving orthodontic treatment exclusively with clear aligners(2 Groups)	
Inclusion	3	Patients receiving orthodontic treatment with clear aligners and using the Aevo System regularly (67% or higher usage adherence) (Aevo Group)	
Inclusion	4	Patients maintaining good oral hygiene and showing no active periodontal disease.	
Inclusion	5	Patients with complete records available as applicable for this study	
Exclusion	1	Any compromised medical or dental condition	
Exclusion	2	Patients undergoing extraction orthodontic treatment	
Exclusion	3	Patients with supernumerary teeth present	
Exclusion	4	Presence of temporomandibular joint (TMJ) disorders	
Exclusion	5	Patients with local or systemic conditions or ongoing pharmacological treatments that could influence the tooth movement process	
Exclusion	6	Patients involved in any other clinical study during their orthodontic treatment	
Exclusion	7	Any patient who fails to meet the above inclusion criteria	
Exclusion	8	Patients who didn’t wear each aligner tray for at least 85% of the prescribed time.	

2.7 Matching the Control Group with the LIPUS Group

To ensure comparability between the LIPUS and control groups, we matched participant groups based on key criteria, specifically age, sex, and treatment complexity as measured by the American

Board of Orthodontic Discrepancy Index. This matching process was essential to minimize confounding variables and ensure that the observed effects were due to the LIPUS treatment rather than other factors.

2.7.1 Age

Participants were matched based on age range. Due to biological differences in bone density and healing rates, age can influence treatment outcomes and patient experiences. By matching participants within a narrow age range, we tried to minimize the impact of age-related variability.

2.7.2 Sex (F/M)

We ensured a similar distribution of females (F) and males (M) in both groups. There are sex-related differences in treatment response due to hormonal variations and anatomical differences. A balanced sex distribution helps control for these differences and ensures that sex does not skew the results.

2.7.3 Treatment Complexity

We used the American Board of Orthodontics Discrepancy Index (ABO DI) to match participants based on treatment complexity. The ABO DI score reflects the complexity of orthodontic cases. Matching participants based on this score ensures that both groups have similar baseline treatment challenges. This matching strategy helped create two comparable groups, enhancing the validity of our findings on the effects of LIPUS in orthodontic treatment.

2.8 Aligner Switching Protocol

In this study, the clinician primarily made the decision on when to switch to the next aligner based on the patient's progress and adherence to the treatment plan. The clinician would evaluate the fit and effectiveness of the current aligner during routine appointments and, based on clinical judgment, determine if it was appropriate to move to the next aligner. However, patients were also given guidelines to follow at home, including instructions to switch aligners if the current one fit properly after a specified duration unless otherwise directed by the clinician.

2.9 Treatment Completion Criteria

Clear and measurable criteria were established to ensure consistency and objectivity in determining when orthodontic treatment is complete. The orthodontist also decided when the treatment was over based on the following:

Clinical Goals

- Alignment: Teeth are aligned as per the treatment plan. Proper alignment is essential for both aesthetic and functional outcomes of orthodontic treatment.
- Occlusion: A proper bite and occlusion are achieved. Correct occlusion is crucial for long-term dental health and functionality.
- Dental Health: No untreated dental issues remain.

Patient Satisfaction

- Meet Treatment Plan Goals: The goals outlined in the treatment plan are fully met. Achieving the objectives set in the treatment plan ensures that the treatment's clinical and patient-centered goals are fulfilled. This was assured by confirmation of a treatment satisfaction form signed by all patients as part of the private practice policy.

By adhering to these criteria, we ensure that treatment completion is based on objective, verifiable standards, leading to consistent and satisfactory patient outcomes.

Acceptable Score of ABO DI at the End of Treatment

- An acceptable post-treatment score of the ABO DI less than 15 was determined by the orthodontist, indicating that the treatment objectives have been successfully achieved.

2.10 Handling Outliers

To ensure data integrity, it was important to identify and manage outliers based on days per tray usage. This process involves setting specific criteria and applying methods to detect deviations.

Patients who used their aligners for more days per tray significantly deviate beyond the 12-14 days range and are flagged as having unusual usage patterns. This was mainly due to patients' adherence or other parafunctional habits that could have affected the expected tooth movement per aligner-specific sets.

To detect these deviations, visual tools such as box plots and scatter plots helped identify outliers by highlighting data points that fell outside the normal range. This approach ensures a comprehensive assessment of data integrity.

2.11 Patient Selection and Matching Process

For the LIPUS group, 335 patient IDs were initially received from Smilesonica Company, which had utilized LIPUS. Among these patients, approximately 110 exhibited adherence rates over 67%. This significant reduction from the initial pool indicates that a substantial portion of the patients did not adhere to the treatment protocol as expected. Following the removal of outliers and the

application of the inclusion criteria, focusing on treatment completion and the availability of comprehensive records, 34 patients satisfied the inclusion criteria and were subsequently enrolled in the study. Although the initial sample size calculation indicated 59 participants per group were needed to achieve sufficient statistical power, practical limitations necessitated proceeding with a smaller sample size. Consequently, while the study provides valuable insights, it is essential to recognize that the findings are preliminary and should be interpreted within the context of these limitations.

Upon identifying our cohort of 34 LIPUS patients, we assessed their malocclusion types, ages, sexes, and treatment complexities. The initial step in the matching process involved selecting patients from the control group who had the same malocclusion types (Class I, Class II, or Class III) as those in the LIPUS group. Subsequently, we employed the clinic database to select control group patients who matched these characteristics in terms of sex and malocclusion type and fell within a ten-year age range. After matching based on malocclusion type, additional steps were taken to ensure further comparability between the groups. Data for the control group were collected and matched with the LIPUS group based on age, sex, and treatment complexity. This deliberate matching process, which included matching on age, sex, and the ABO DI, was designed to ensure comparability between the LIPUS and control groups, thereby minimizing potential confounding variables and ensuring that the observed effects could be attributed to the LIPUS treatment rather than other factors.

The identification of cases was conducted by the researcher, who thoroughly reviewed patient IDs and adherence data from the adherence list of all devices delivered to Sphinx Orthodontics during the specified time period. The researcher also reviewed patient records at Sphinx Orthodontics via

Dolphin software to ensure that all inclusion criteria were met and that complete treatment data was available.

2.12 Data Collection Procedure

Patient records were retrospectively collected and analyzed to compare the outcomes regarding refinements and non-used discarded aligners from two groups: one that completed orthodontic treatment with the Aevo System in conjunction with clear aligners and a control group that used clear aligners alone. The data was collected using the provided Patient Data Form (Figure 4).

Patient Data Collection Form							
Patient Information		**ClinCheck Trays Information**		**Actual Trays Information**		**Additional Information**	
Patient ID		# of trays in 1st Set		# of trays in 1st Set		Aevo usage Compliance	
Group (Aevo, Control)		# of trays in 2nd Set		# of trays in 2nd Set		Side effects	
Sex		# of trays in 3rd Set		# of trays in 3rd Set		ABO index	
Age		# of trays in 4th Set		# of trays in 4th Set		ABO index Group	
Treatment Start Date		# of trays in 5th Set		# of trays in 5th Set			
Treatment End Date		# of trays in 6th Set		# of trays in 6th Set			
Type of Malocclusion		Total # of trays		Total # of trays			

Figure 4: Patient Data Collection Form

This form is structured to capture patients' treatment data, including the following:

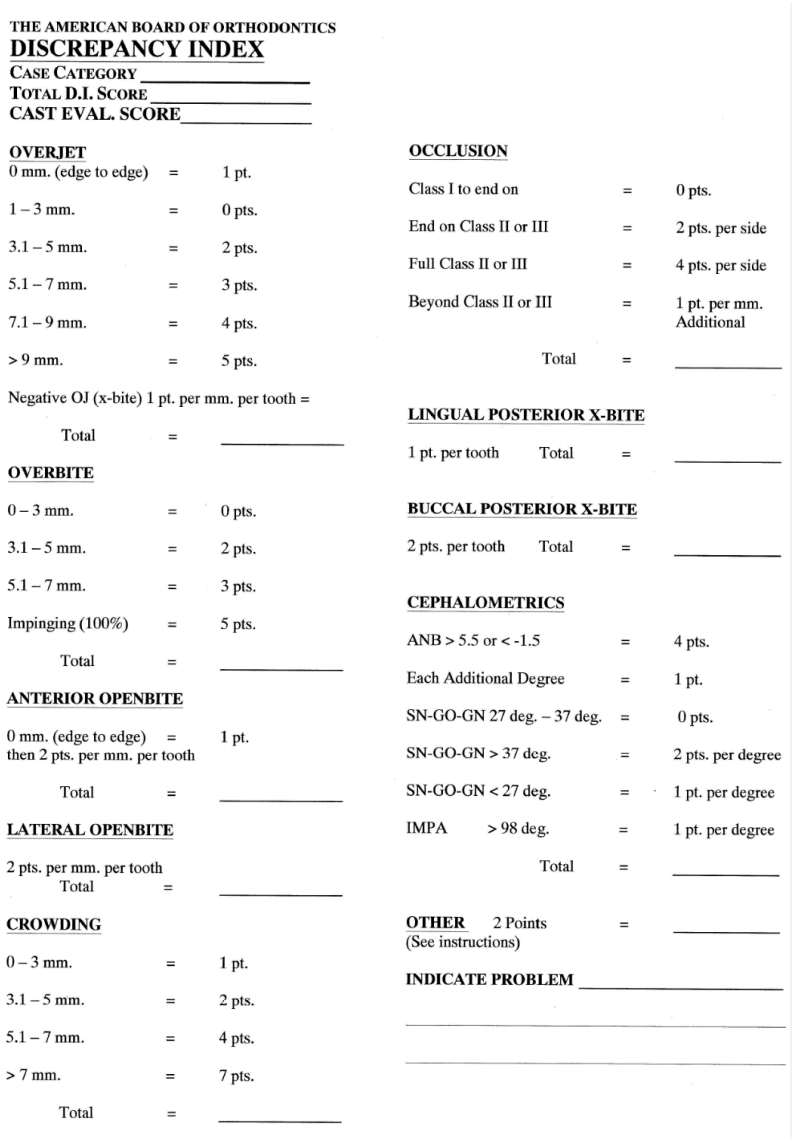
- Demographic data include patient ID, group classification (Aevo or Control), sex (male or female), and age at the start of treatment.
- The prescribed number of aligners in each set of trays based on the planned ClinCheck®.
- The number of sets of refinements for each patient, which is equal to the number of re-scans performed for each patient.
- The number of trays used by each patient in each set of trays.
- The number of the non-used discarded aligners is calculated by subtracting the total number of trays used from the total prescribed number of trays.
- Any side effects or adverse events reported.
- Details of the orthodontic treatment, including the start and end dates, thus determining the treatment duration.
- Patient adherence for using the Aveo System as indicated in the Aevo clinic web app.
- The ABO index score before and after treatment, as calculated by the method in Figure 5.

To assess the complexity of each orthodontic treatment case, the ABO Index was calculated using the ABO Discrepancy Index Chart (Figure 5) for each patient before and after treatment from both groups. The ABO DI before treatment allowed us to match patients in the control and LIPUS group with a similar difficulty index for the data analysis.

To match the treatment complexity between the two groups, we initially screened and filtered patients based on adherence (67% or higher) using a detailed Excel file provided by SmileSonica Inc., which included patient ID and adherence data for those using the Aevo 3 system. The data collection focused on the Aevo 3 group due to its smaller size. We calculated their ABO Discrepancy Index (DI) and categorized them based on a previous study as Mild (ABO DI 1-10), Moderate (ABO DI 11-20), Complex (ABO DI 21-30), or Very Complex (ABO DI 31-100)(104). We then selected an equal or similar number of control patients for each complexity level (Mild,

Moderate, Complex, Very Complex). This method ensured a balanced comparison of treatment complexity between the groups and supported unbiased conclusions.

The ABO DI after treatment helped us determine if the treatment reached an acceptable level. An acceptable post-treatment score of the ABO DI of less than 15 indicates that the treatment objectives have been successfully achieved.



THE AMERICAN BOARD OF ORTHODONTICS

DISCREPANCY INDEX

CASE CATEGORY _____

TOTAL D.I. SCORE _____

CAST EVAL. SCORE_____

OVERJET

0 mm. (edge to edge)	=	1 pt.
1 – 3 mm.	=	0 pts.
3.1 – 5 mm.	=	2 pts.
5.1 – 7 mm.	=	3 pts.
7.1 – 9 mm.	=	4 pts.
> 9 mm.	=	5 pts.

Negative OJ (x-bite) 1 pt. per mm. per tooth =

Total = _____

OVERBITE

0 – 3 mm.	=	0 pts.
3.1 – 5 mm.	=	2 pts.
5.1 – 7 mm.	=	3 pts.
Impinging (100%)	=	5 pts.

Total = _____

ANTERIOR OPENBITE

0 mm. (edge to edge) = 1 pt.
then 2 pts. per mm. per tooth

Total = _____

LATERAL OPENBITE

2 pts. per mm. per tooth
Total = _____

CROWDING

0 – 3 mm.	=	1 pt.
3.1 – 5 mm.	=	2 pts.
5.1 – 7 mm.	=	4 pts.
> 7 mm.	=	7 pts.

Total = _____

OCCLUSION

Class I to end on	=	0 pts.
End on Class II or III	=	2 pts. per side
Full Class II or III	=	4 pts. per side
Beyond Class II or III	=	1 pt. per mm. Additional

Total = _____

LINGUAL POSTERIOR X-BITE

1 pt. per tooth Total = _____

BUCCAL POSTERIOR X-BITE

2 pts. per tooth Total = _____

CEPHALOMETRICS

ANB > 5.5 or < -1.5	=	4 pts.
Each Additional Degree	=	1 pt.
SN-GO-GN 27 deg. – 37 deg.	=	0 pts.
SN-GO-GN > 37 deg.	=	2 pts. per degree
SN-GO-GN < 27 deg.	=	1 pt. per degree
IMPA > 98 deg.	=	1 pt. per degree

Total = _____

OTHER 2 Points = _____
(See instructions)

INDICATE PROBLEM _____

Figure 5: ABO Discrepancy Index Chart

2.13 BONE RADIO DENSITY MEASUREMENT

This study measured bone radio density before and after orthodontic treatment using CBCT scans, specifically captured by the iCAT® scanner (Imaging Sciences International in Hatfield, Pennsylvania, USA). The scans were characterized by specific parameters: a width of 16 cm, height of 13 cm, 120 kVp, 24 mAs, a scan time of 20 seconds, voxel size of 0.3 mm, and 303 basis projections.

InVivo Dental 5.0 software by Anatomage Inc., based in San Jose, CA, USA, was utilized to assess bone radiodensity. This software allowed for setting standardized sagittal and coronal views to measure Hounsfield units accurately across predetermined alveolar bone locations.

The calibration involved rotating the image to align the posterior rim of the incisive foramen with the posterior nasal spine within the same slice, as depicted in Figure 6. For the upper arch, the coronal section alignment was established at the level of the posterior rim of the incisive foramen, as shown in Figure 7. The lower arch was adjusted to the midpoint line passing through the posterior inferior point of the second cervical vertebra, illustrated in Figure 8.

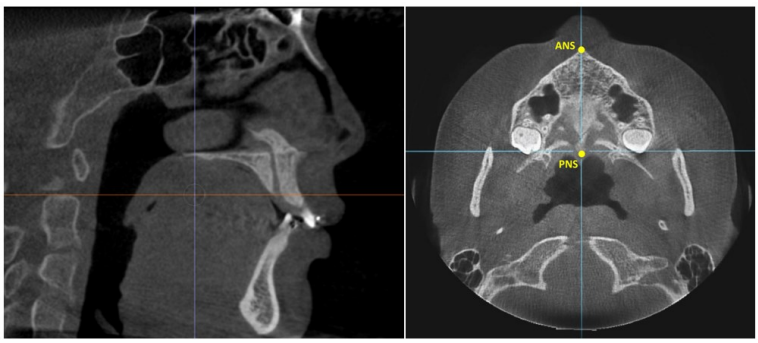


Figure 6: Sagital and Coronal section showing the posterior rim of the incisive foramen and the posterior nasal spine (PNS). The posterior rim of the incisive foramen is the rear boundary of the bony canal in the maxilla, while the posterior nasal spine (PNS) is a bony projection at the back of the nasal cavity.

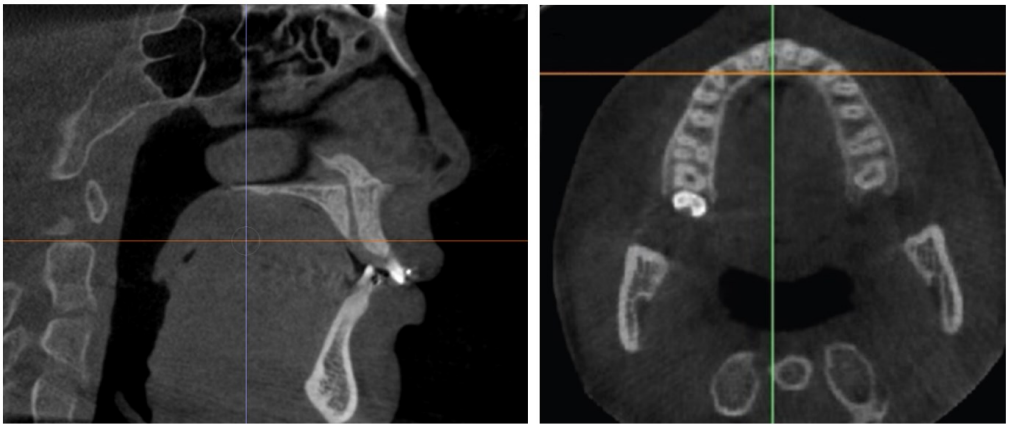


Figure 7: Reference lines for measuring the maxillary alveolar bone radio density passing through the posterior rim of the incisive foramen in axial and sagittal view

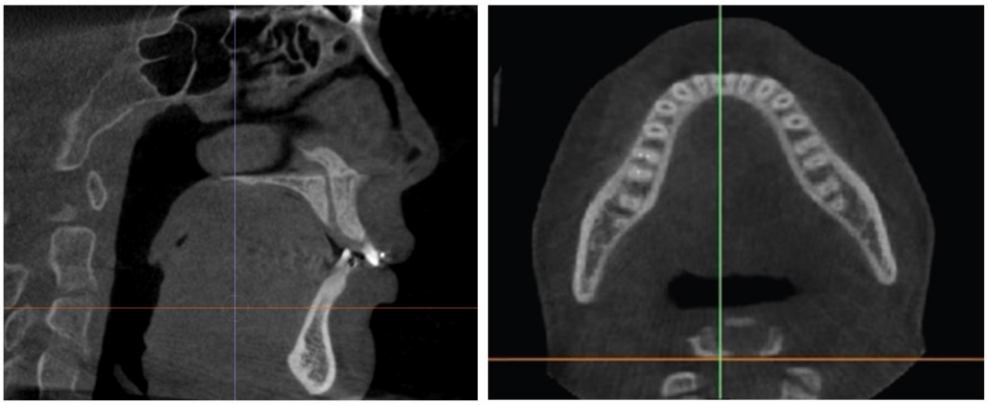


Figure 8: Reference line for measuring the mandibular alveolar bone radio density passing through the posterior inferior point of the second cervical vertebra in axial and sagittal view

Measurements of bone radio density were taken in the standardized coronal slices of both arches, specifically at the midpoint between the buccal and lingual cortical plates within the cancellous bone at five defined locations: bilaterally between the canine and lateral incisor, bilaterally between the lateral and central incisor, and directly at the midline, as indicated before and after treatment in Figure 9 for maxilla and Figure 10 for mandible.

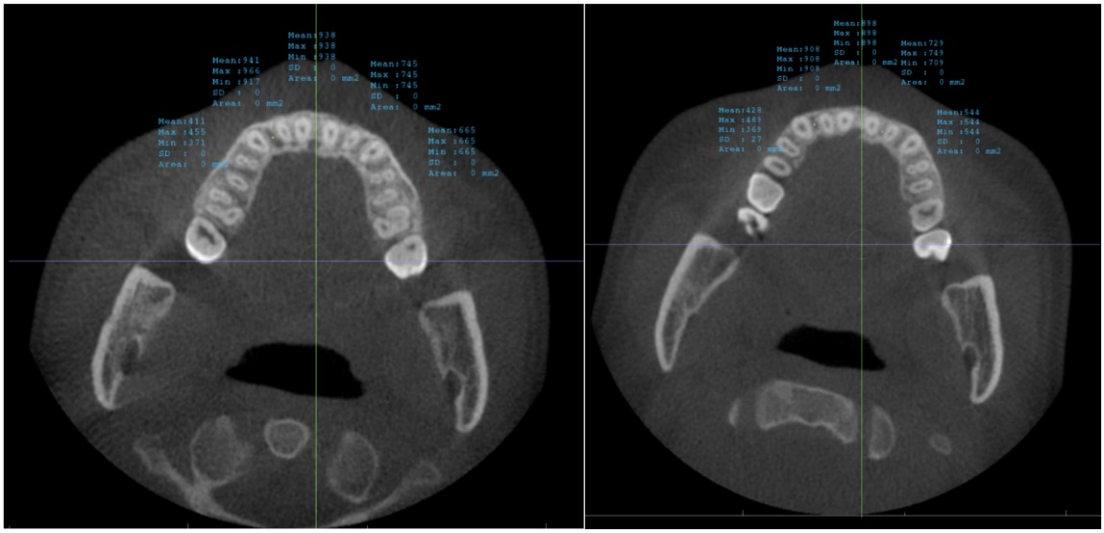


Figure 9: Measures the bone radio density at five locations in the Maxilla alveolar bone: between the right canine and lateral, right lateral and central, left central and lateral, left lateral and canine, and at the midline. The right image shows the bone radio density measurements before treatment, and the left image shows the bone radio density measurements after treatment.

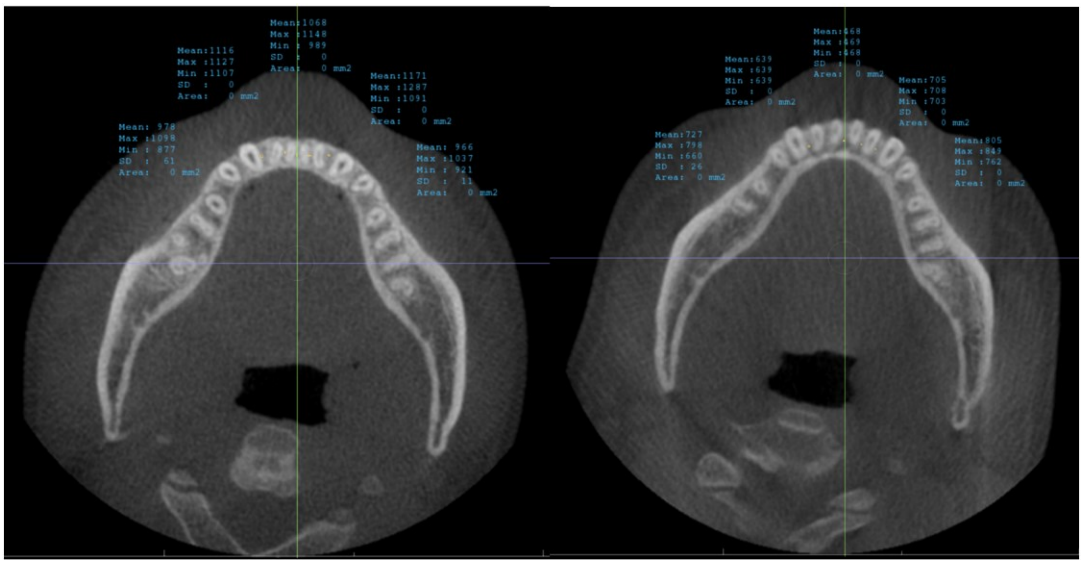


Figure 10: Measures the bone radio density at five locations in the Mandible alveolar bone: between the right canine and lateral, right lateral and central, left central and lateral, left lateral and canine, and at the midline. The right image shows the bone radio density measurements before treatment, and the left image shows the bone radio density measurements after treatment.

Figure 11 depicts the table used for data collection, ensuring a structured and reproducible approach to data gathering.

Patient ID							
Arch	Region	Variable	Value	Arch	Region	Variable	Value
Uper	T1 Between Canine and Lateral Incisor Right	Average		Lower	T1 Between Canine and Lateral Incisor Right	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T1 Between Lateral and Central Incisor Right	Average			T1 Between Lateral and Central Incisor Right	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T1 Between Central Incisors	Average			T1 Between Central Incisors	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T1 Between Lateral and Central Incisor Left	Average			T1 Between Lateral and Central Incisor Left	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T1 Between Canine and Lateral Incisor Left	Average			T1 Between Canine and Lateral Incisor Left	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	Pre-treatment T1 (HU) Total	Average			Pre-treatment T1 (HU) Total	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T2 Between Canine and Lateral Incisor Right	Average			T2 Between Canine and Lateral Incisor Right	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T2 Between Lateral and Central Incisor Right	Average			T2 Between Lateral and Central Incisor Right	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T2 Between Central Incisors	Average			T2 Between Central Incisors	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T2 Between Lateral and Central Incisor Left	Average			T2 Between Lateral and Central Incisor Left	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	T2 Between Canine and Lateral Incisor Left	Average			T2 Between Canine and Lateral Incisor Left	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	
	Post-treatment T2 (HU) Total	Average			Post-treatment T2 (HU) Total	Average	
		Maximum				Maximum	
		Minimum				Minimum	
		SD				SD	

Figure 11: Patient data collection table for bone radio density measurements.

2.14 The protocol for data collection

2.14.1 Acquiring the list of patients' IDs from SmileSonica Inc.

The Smilesonica Inc. staff provided a list of patient IDs who used the Aevo 3 system, which can be connected to online and mobile applications. An Excel file was created containing the patient IDs, treatment times, and the percentage of adherence. Then, the data was sorted based on adherence, selecting patients with an adherence rate higher than 67%. In the subsequent step, the researcher reviewed each patient's file to check if the treatment was completed. This review included examining the details and photographs, CBCT scans, panoramic views, and records on the Invisalign website to ensure all records were complete and accessible Figure 12.

Organization Name	Patient ID	Compliance Last Sync	Treatment Start Date	Last Sync
Sphinx Orthodontics	[redacted]	100.0%	2/8/2024	2/16/2024 20:09
Sphinx Orthodontics	[redacted]	100.0%	1/31/2024	2/9/2024 18:14
Sphinx Orthodontics	[redacted]	100.0%	10/1/2022	11/2/2022 13:35
Sphinx Orthodontics	[redacted]	100.0%	12/20/2021	1/14/2022 18:45
Sphinx Orthodontics	[redacted]	100.0%	2/10/2021	3/13/2021 12:44
Sphinx Orthodontics	[redacted]	100.0%	12/10/2019	12/12/2019 5:13
Sphinx Orthodontics	[redacted]	98.6%	5/25/2021	12/22/2021 0:46
Sphinx Orthodontics	[redacted]	97.6%	9/6/2023	2/16/2024 16:45
Sphinx Orthodontics	[redacted]	97.4%	9/28/2020	12/13/2020 21:03
Sphinx Orthodontics	[redacted]	97.3%	12/22/2021	9/9/2022 17:40
Sphinx Orthodontics	[redacted]	97.1%	5/5/2021	8/17/2021 21:29
Sphinx Orthodontics	[redacted]	96.1%	10/8/2022	2/12/2023 2:03
Sphinx Orthodontics	[redacted]	96.1%	10/23/2020	6/18/2021 4:39
Sphinx Orthodontics	[redacted]	94.9%	1/3/2024	2/10/2024 4:10
Sphinx Orthodontics	[redacted]	94.7%	10/19/2020	3/17/2023 6:10
Sphinx Orthodontics	[redacted]	93.5%	7/19/2019	4/6/2020 1:38
Sphinx Orthodontics	[redacted]	93.1%	11/20/2020	7/23/2022 15:23

Figure 12: The sample of data provided by SmileSonica with Patient ID and percentage of Adherence

2.14.2 Accessing Patient Information through Dolphin Software (Version 12.0.63)

Accessing patient records at Sphinx Orthodontics began with Dolphin software, a specialized program for managing orthodontic practices. This software was launched on a designated computer within the clinic, ensuring that all data handling is secure and centralized.

Once the Dolphin software is active, users must navigate to the "Patient Records" section. This section is specifically organized to allow for easy access and management of patient information, essential for daily operations in orthodontic care.

The user utilizes the search bar within the "Patient Records" section to retrieve a specific patient's records. Here, the researcher enters the patient ID—a unique identifier for each patient in the system. This ID is a key to unlock and pull up the corresponding patient's records from the clinic's database. Upon entering the ID, the software processes the request and displays the patient's records, including a detailed history, treatment card, and progress notes (Figures 13 and 14).

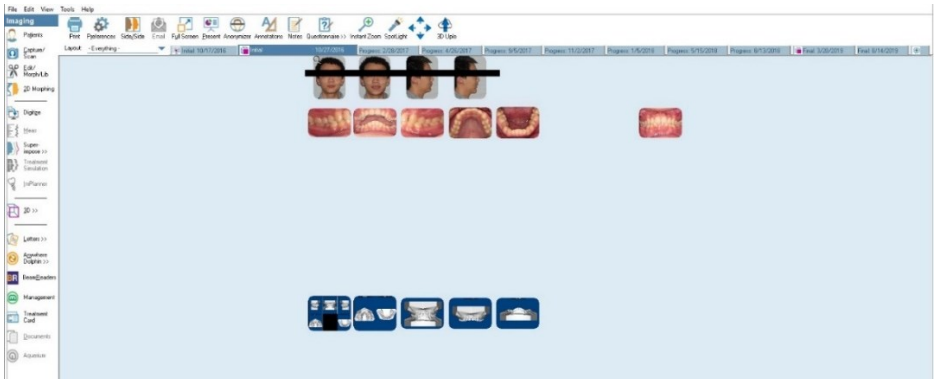


Figure 13: The Patient profile in Dolphin imaging software and initial stage of treatment

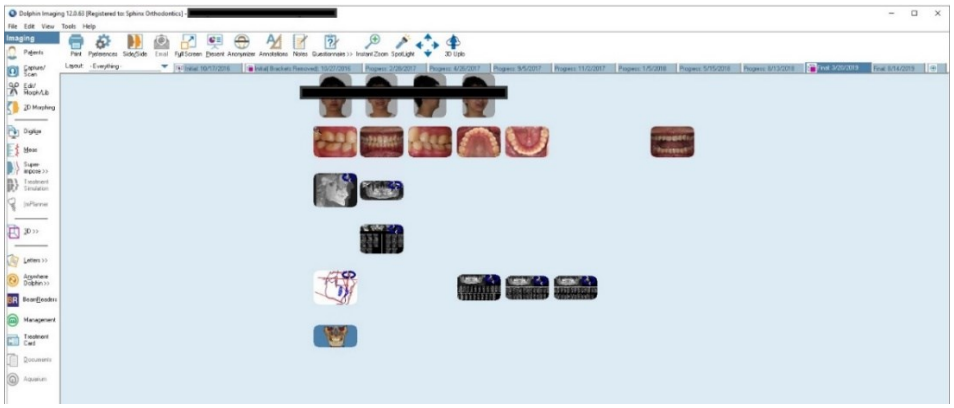


Figure 14: The Patient profile in Dolphin imaging software and final stage of treatment

2.14.2.1 Extracting Basic Patient Information

This information was extracted from the Patient Profile section of the Dolphin software:

- Age: Calculate the patient's current age using their date of birth.
- Treatment Dates: Extract the treatment's start and finish dates from planning and completion notes, respectively.
- Treatment Duration: Determine the length of treatment by subtracting the start date from the finish date.
- Side Effects: Review notes for any side effects or complications during treatment, specifically for LIPUS patients.
- Tracking the number of trays used by the patient: Review the patient's treatment card and investigate each session record to count the trays used by the patient between visits.

2.14.3 Invisalign Treatment Data through online website (https://login.aligntech.com/)

Accessing Invisalign treatment data, specifically tray information, involves a series of steps centered around using the Invisalign website (https://login.aligntech.com/). This platform provides a detailed and secure means for orthodontists to manage and review their patient's treatment plans. To begin, an orthodontist or authorized staff member must log into the Invisalign website using the doctor's credentials. These credentials ensure that the access is secure and that patient information remains confidential(Figure 15).

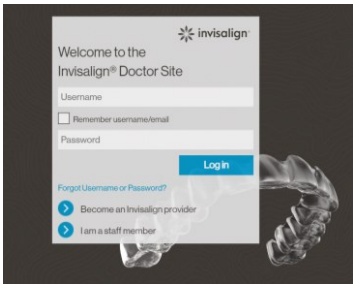


Figure 15: Log in to the Invisalign website

Once logged in, users can search for specific patients using their unique patient ID. This ID helps directly fetch the relevant patient's treatment details without sifting through unrelated records. The primary focus of this search is to check the number of trays prescribed to the patient(Figure 16).

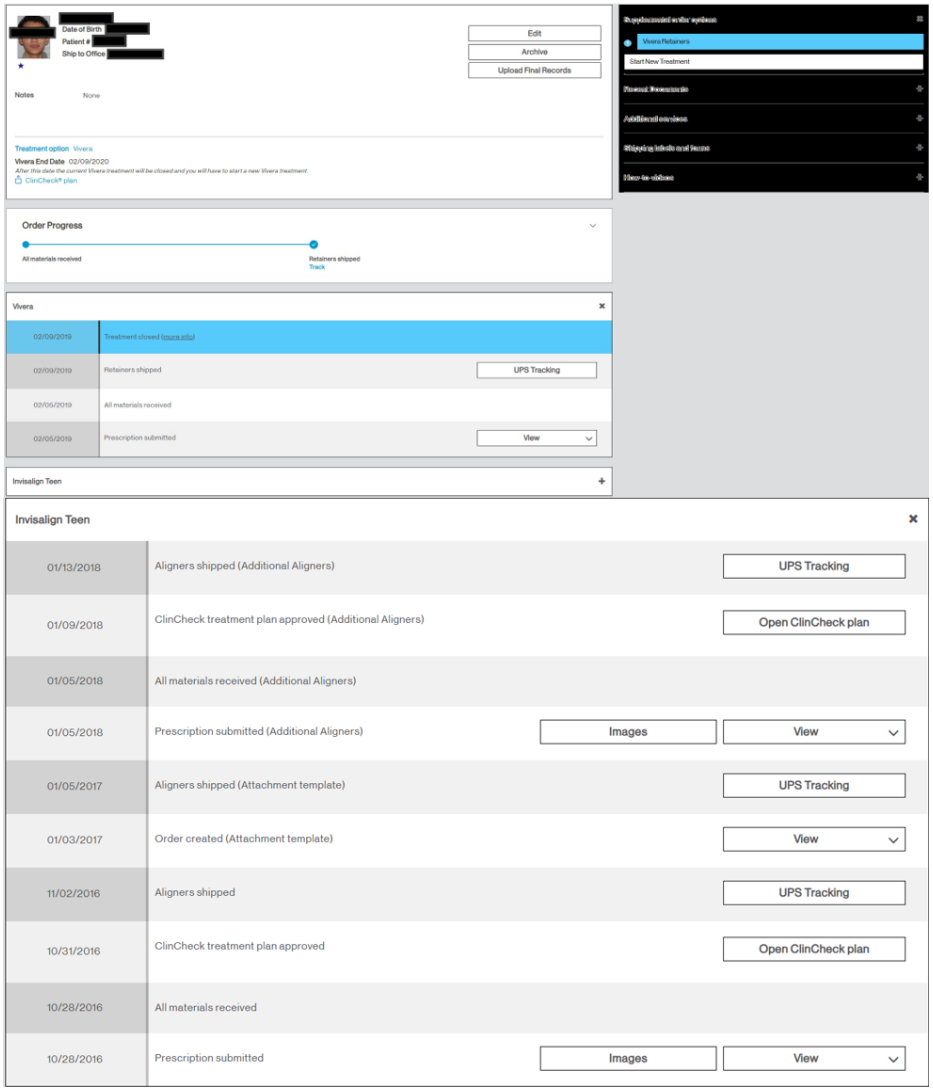


Figure 16: Patient's profile on the Invisalign website

Sometimes, Invisalign treatment involves additional aligners as refinements, each designed to make incremental adjustments to the patient's teeth. The search results display these details,

allowing the doctor to track the progress of the treatment, plan future appointments, and prepare for any necessary adjustments(Figures 17 and 18).

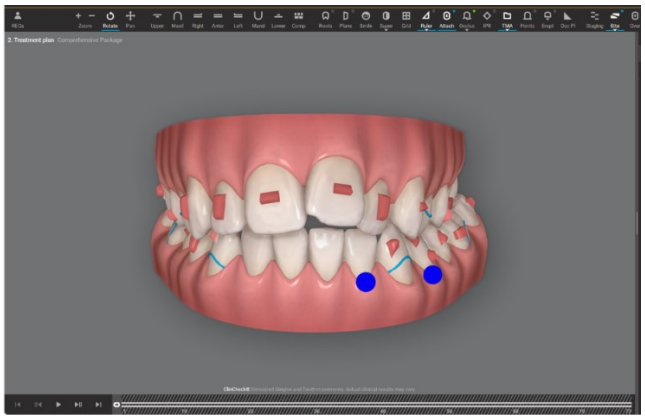


Figure 17: Prescribed trays for a Patient through Invisalign website

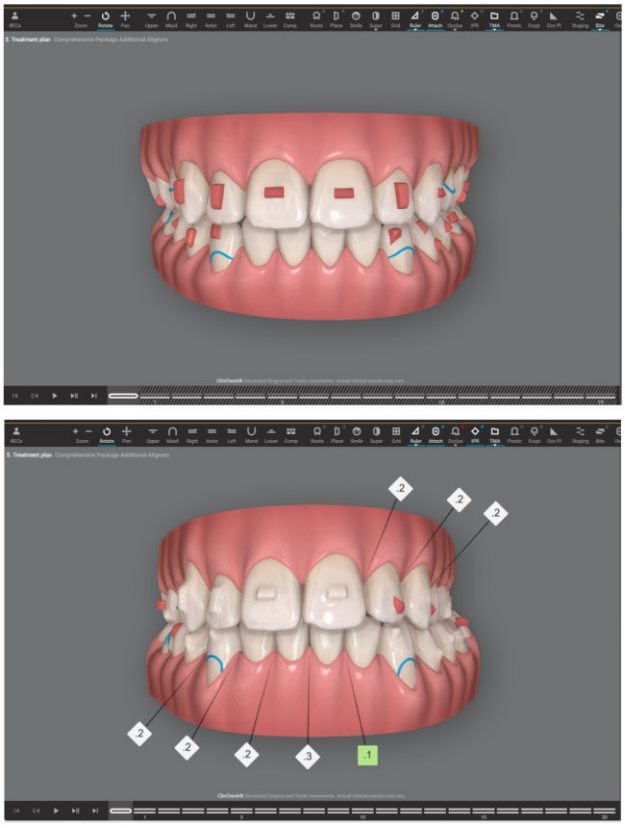


Figure 18: Prescribed Additional (Refinements) aligners for a Patient through the Invisalign website

2.14.4 Accessing the Adherence Data through the Aevo App from SmileSonica Inc

The adherence data for patients who used the Aevo 3 device was gathered through the Aevo 3 web app, a specialized platform designed to monitor and record how consistently patients use the device.

The Aevo web app collects and analyzes usage logs from the device. Each time a patient uses the Aevo 3 device, the event is logged with details such as the duration of usage and the specific settings employed. This data is then synchronized with the web app, which can generate reports and analytics. These reports enable providers to make informed decisions about potential modifications to discuss adherence issues with patients (Figure 19).

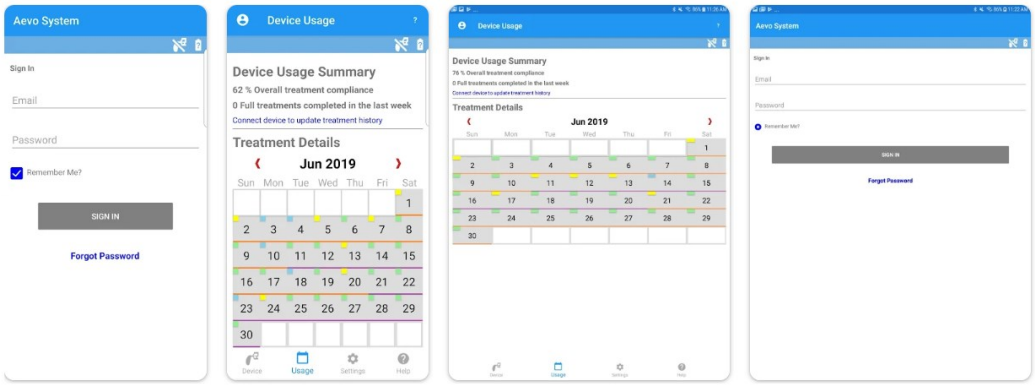


Figure 19: Aevo 3 mobile app, which can be downloaded from Google Play and Apple store

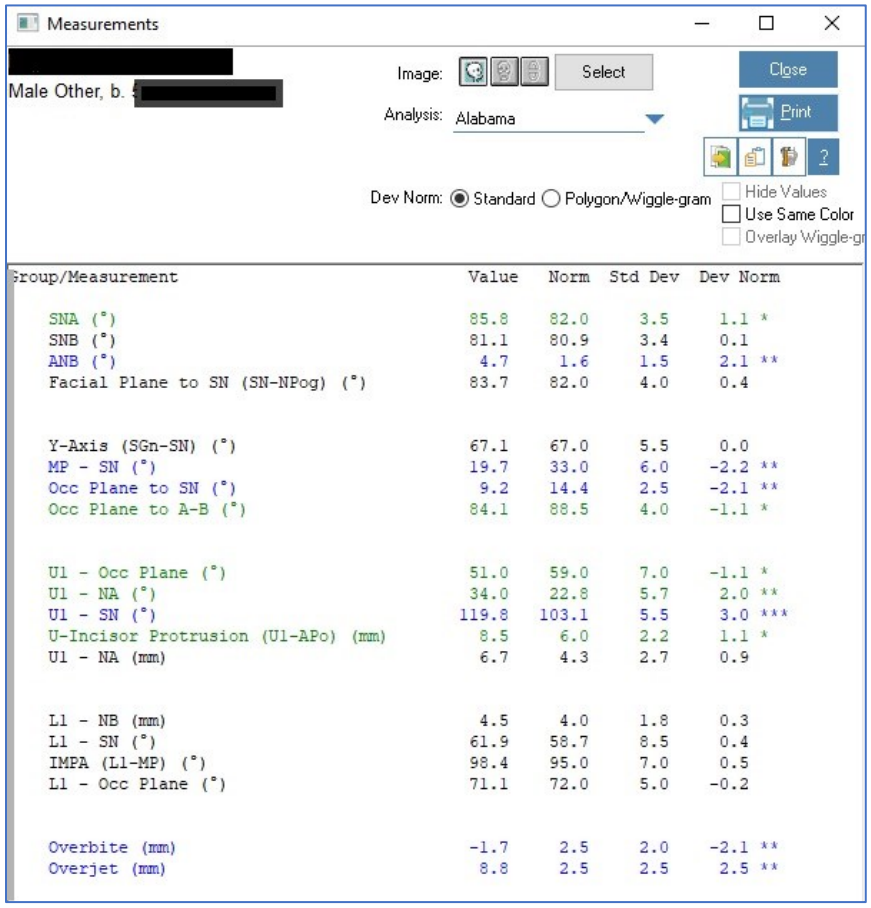
We collected anonymous reports with patient IDs showing adherence by percentage and recorded them in the data collection table.

2.14.5 Assessing Treatment Complexity using ABO Discrepancy Index (DI)

To evaluate the orthodontic treatment complexity, the ABO DI was employed. The process began with the ABO DI checklist, which includes a comprehensive set of orthodontic parameters

designed to assess the severity and complexity of malocclusions. This checklist served as the foundation for all subsequent evaluations.

Overjet, overbite, and cephalometric analysis measurements were obtained using Dolphin Imaging software. This software is integral for accurately capturing and analyzing dental and skeletal relationships in orthodontic patients. Overjet was measured as the horizontal distance between the maxillary and mandibular incisors, and overbite was assessed by measuring the vertical overlap of the incisors. Cephalometric analysis provided detailed measurements of craniofacial morphology (Figure 20).



Group/Measurement	Value	Norm	Std Dev	Dev Norm
SNA (°)	85.8	82.0	3.5	1.1 *
SNB (°)	81.1	80.9	3.4	0.1
ANB (°)	4.7	1.6	1.5	2.1 **
Facial Plane to SN (SN-NPog) (°)	83.7	82.0	4.0	0.4
Y-Axis (SGn-SN) (°)	67.1	67.0	5.5	0.0
MP - SN (°)	19.7	33.0	6.0	-2.2 **
Occ Plane to SN (°)	9.2	14.4	2.5	-2.1 **
Occ Plane to A-B (°)	84.1	88.5	4.0	-1.1 *
U1 - Occ Plane (°)	51.0	59.0	7.0	-1.1 *
U1 - NA (°)	34.0	22.8	5.7	2.0 **
U1 - SN (°)	119.8	103.1	5.5	3.0 ***
U-Incisor Protrusion (U1-APo) (mm)	8.5	6.0	2.2	1.1 *
U1 - NA (mm)	6.7	4.3	2.7	0.9
L1 - NB (mm)	4.5	4.0	1.8	0.3
L1 - SN (°)	61.9	58.7	8.5	0.4
IMPA (L1-MP) (°)	98.4	95.0	7.0	0.5
L1 - Occ Plane (°)	71.1	72.0	5.0	-0.2
Overbite (mm)	-1.7	2.5	2.0	-2.1 **
Overjet (mm)	8.8	2.5	2.5	2.5 **

Figure 20: Performing the measurements with Dolphine imaging software

Further examination of the patient's dental conditions was conducted using iTero intraoral scans. These high-resolution 3D scans identified conditions such as open bites, dental crowding, and posterior crossbites(Figure 21).

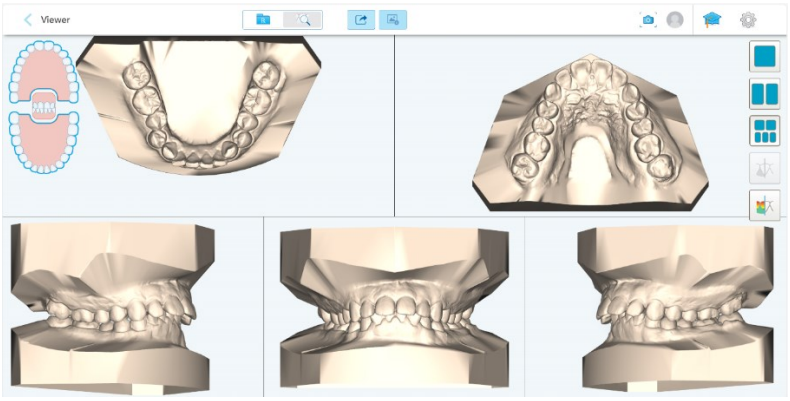


Figure 21: 3D scans obtained through the iTero website (https://bff.cloud.myitero.com/)

Additionally, panoramic radiographs were reviewed to check for other significant orthodontic concerns. These included tooth transposition, skeletal asymmetry, and enamel wear. Each of these conditions was meticulously documented and recorded in the checklist.

This methodological approach ensured a thorough evaluation of each participant's treatment records, providing a robust basis for the accurate calculation of the ABO DI score.

2.14.6 Bone Radio density Data Collection and Analysis

The initial step involved the anonymized extraction of patient IDs. These were separated from the study group data and compiled in an Excel file.

Then, Dexis imaging software was employed to retrieve CBCT scans taken before and after the orthodontic treatment of each evaluated patient. Invivo dental software was used to open the CBCT

images in DICOM format. Once the CBCT images were accessed, specific anatomical landmarks on both jaws were identified and marked. These points served as consistent references for analyzing changes in bone. The selection of these points was critical to ensure that measurements were taken from identical locations on pre and post-treatment scans.

Data on bone radio density were then collected and analyzed. Measurements included the Mean, Maximum, Minimum, and Standard Deviation of bone radio density at each selected point. This data was systematically listed and organized to facilitate further statistical analysis and interpretation of the treatment's impact on bone structure.

2.15 Statistical Analyses

Our statistical analysis evaluated the efficacy and safety of the Aevo System using JASP software version 0.17.00. These analyses encompassed the following key aspects:

Continuous Data Assessment: Upon conducting the Shapiro-Wilk test for normality, an Independent Samples *t*-test and Mann-Whitney U Test were performed to compare treatment variables between the Control and LIPUS groups to evaluate the impact of LIPUS in orthodontic treatment. This approach allowed us to effectively compare mean differences between the Aevo 3 and Control groups. We also used a paired T-test to compare bone radio density in the same patient before and after treatment.

Data Segmentation: Data was segmented into various groups and subgroups, considering age, treatment duration, and case severity. This stratification facilitated a more granular analysis and provided insights into the Aevo 3 System's performance across different patient demographics.

Significance Threshold: We adhered to the standard statistical practice by considering a p-value of less than 0.05 to indicate statistical significance.

Effectiveness Metrics: Special focus was on key indicators of treatment efficacy, such as the number of refinements, re-scans, non-tracking discarded aligners, and changes in bone radio density measurements.

To ensure accurate and reliable data management and the integrity and confidentiality of the data collected, the following measures were implemented:

- Data Collection: Patient data was collected from clinical records using standardized forms to ensure consistency. Personal identifiers were removed or coded to maintain patient confidentiality. Specifically, the patient's name was NOT recorded on any of the study forms. The patient identification number in the clinic was used to allow identification and traceability.
- Data Entry and Storage: All data entered electronically into the forms by the researcher on his password-protected laptop computer, with access restricted to authorized personnel only. Data was backed up regularly to prevent loss.
- Data Monitoring: The supervisor oversaw the data collection and entry process to ensure accuracy and to address any discrepancies or missing data.
- Data Analysis: Only de-identified data was used for statistical analysis to protect patient privacy.
- Data Reporting: Any data reporting was aggregated so that individual patients cannot be identified.

2.16 Ethical Considerations

The study was conducted in accordance with the study protocol, the Declaration of Helsinki, and the ICH tripartite guidelines for Good Clinical Practice (as adopted by Canada in 1997).

2.16.1 REB Review

The University of Alberta Research Ethics Board reviewed and approved this protocol. The project is titled "The effect of LIPUS on treatment time, number of revisions, number of aligners, and bone radiodensity after orthodontic treatment using clear aligners" and was based on amendments to the original project number Pro00091339 before March 6, 2024. The new approval number is Pro00139950, dated March 6, 2024.

3 RESULTS

The results are organized into two main parts to address the different objectives of the study on the impact of LIPUS in orthodontic treatment. Part 1 focuses on treatment refinements, duration, and efficiency, while Part 2 examines changes in bone radio density.

3.1 Part 1: Treatment Duration, Refinements and Efficiency

3.1.1 Descriptive Statistics

Our analysis included Control and LIPUS, each with 34 participants (Table 4).

- **Treatment Duration:** The Control group had a median treatment duration of 936.5 days, with an average of 964.82 ± 417.9 days. The LIPUS group had a median of 530.5 days, with an average of 544.68 ± 238.97 days.
- **Number of Days per Tray:** The Control group had an average of 10.17 ± 3.18 days per tray, while the LIPUS group had an average of 5.42 ± 1.02 days per tray.
- **Number of Refinements:** On average, the Control group had 2.41 ± 1.28 refinements, while the LIPUS group had 1.56 ± 1.11 refinements.
- **Number of Discarded Non-used Trays:** The Control group discarded an average of 11.18 ± 13.39 trays, and the LIPUS group discarded 7.56 ± 11.91 trays.
- **Number of Unused Trays at the End of Treatment:** The Control group had an average of 1.41 ± 4.36 unused trays, compared to 5.06 ± 7.71 unused trays for the LIPUS group.

- **Side Effects:** No side effects were reported in the LIPUS group.
- **ABO DI Pre Treatment:** For the Control group, the mean ABODI Pre score was 22.88 ± 11.92. In the LIPUS group, the mean ABODI Pre score was 22.09 ± 11.55.
- **ABO DI Post Treatment:** For the Control group, the mean ABODI Post score was 4.76 ± 4.39. In the LIPUS group, the mean ABODI Post score was 4.74 ± 3.29.

Table 4: Descriptive Statistics

Variables	Age		Treatment duration		#of days/ tray		# of Refinements		# of Discarded Non-tracking		# of Unused trays at the End of Treatment		ABO DI Post-treatment		ABO DI Post-treatment	
Study Group	Control	LIPUS	Control	LIPUS	Control	LIPUS	Control	LIPUS	Control	LIPUS	Control	LIPUS	Control	LIPUS	Control	LIPUS
Valid	34	34	34	34	34	34	34	34	34	34	34	34	34	34	34	34
Missing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Median	25	34	937	531	9.4	5.7	2	1.5	6	3	0	1.5	21	22	2.5	4.5
Mean	30	36	965	545	10	5.4	2.4	1.6	11	7.6	1.4	5.1	22.06	22.71	4.76	5.18
Std. Error of Mean	2.6	2.2	72	41	0.6	0.2	0.2	0.2	2.3	2	0.8	1.3	2.34	1.63	0.75	0.61
Std. Deviation	15	13	418	239	3.2	1	1.3	1.1	13	12	4.4	7.7	13.66	9.53	4.39	3.53
Range	60	45	1701	959	16	4.4	5	4	50	54	24	25	52	36	15	13
Minimum	15	22	233	100	6	2.5	0	0	0	0	0	0	1	8	0	0
Maximum	75	67	1934	1059	22	6.9	5	4	50	54	24	25	53	44	15	13

Age: For the control group, the median age was 24.6 years, with an average age of 29.85 ± 14.85 years. In the LIPUS group, the median age was 33.5 years, with an average age of 36.29 ± 12.78 years.

The age distribution of participants in the control and LIPUS groups was analyzed to determine if there were significant differences between the groups. The average age of participants in the Control group was 29.85 ± 14.85 years, with ages ranging from 15 to 75 years. The average age of participants in the LIPUS group was 36.29 ± 12.78 years, with ages ranging from 22 to 67 years.

To statistically assess the difference in age between the groups, an independent samples *t*-test was conducted(p=0.06).

Sex: Table 5 presents the distribution of sex within the two groups. In the control group, there are 22 females, accounting for 64.71% of the group, and 12 males, making up 35.29%. For the LIPUS group, there are 19 females, 55.88% of the group, and 15 males, representing 44.12%.

Table 5: Frequencies for Sex

Group	Sex	Frequency	Percent
Control	Female	22	64.71
	Male	12	35.29
	Total	34	100
LIPUS	Female	19	55.88
	Male	15	44.12
	Total	34	100

The sex distribution was also analyzed to ensure a balanced representation in both groups. A chi-square test of independence was performed to examine the association between group assignment and sex distribution. The chi-square test revealed no significant association between group

assignment and sex distribution (p=0.620). This result indicates that the sex distribution is comparable between the Control and LIPUS groups.

Malocclusion classification: The following table shows the malocclusion frequencies in the study groups (control and LIPUS) into three classes: Class 1, Class 2, and Class 3. For both Control and LIPUS groups, Class 1 has the highest frequency with 19 cases (55.88%), followed by Class 2 with 8 cases (23.53%), and Class 3 with 7 cases (20.59%). There are no missing cases in either group, and the total number of cases is 34 for each group. This table shows the distribution of malocclusion classes is identical in both the control and LIPUS groups (Table 6).

Table 6: Frequency distribution of malocclusion classes

Group	MO	Frequency	Percent	Valid Percent	Cumulative Percent
Control	Class 1	19	55.88	55.88	55.88
	Class 2	8	23.53	23.53	79.41
	Class 3	7	20.59	20.59	100
	Total	34	100		
LIPUS	Class 1	19	55.88	55.88	55.88
	Class 2	8	23.53	23.53	79.41
	Class 3	7	20.59	20.59	100
	Total	34	100		

ABO DI Pre-treatment: The control group has a mean ABO DI score of 22.06, and the LIPUS group is 22.71. The standard deviation is 1.63 and 2.34 for the LIPUS and control groups, respectively. Additionally, the median ABO DI score is 13.66 for the Control group and 9.53 for the LIPUS group. The range shows more variation in the control group (52) than in the LIPUS group (36). The maximum ABO DI scores across all cases are 53 for the Control group and 44 for the LIPUS group.

We also tried to match the control group with LIPUS groups according to their treatment complexity based on the ABO discrepancy index for a more precise comparison. The complexity levels are defined as Mild (ABO index from 1 to 10), Moderate (ABO index from 11 to 20), Complex (ABO index from 21 to 30), and Very Complex (ABO index from 31 to 100)(Table 7).

Table 7: ABO Discrepancy Index Score Categories

Range of ABO DI score		Category	Control	LIPUS
1	10	Mild	5	5
11	20	Moderate	11	11
21	30	Complex	11	11
31	100	Very complex	7	7
			34	34

Both groups contain an identical distribution of cases: 11 Complex cases (32.35%), 5 Mild cases (14.71%), 11 Moderate cases (32.35%), and 7 Very Complex cases (20.59%)(Table 8). This alignment in complexity distribution ensures that the comparison between the Control and LIPUS groups takes into account the variation in case difficulty as per the ABO index.

Table 8: Complexity Distribution Based on ABO Discrepancy Index

Group	Complexity	Frequency	Percent
Control	Complex	11	32.35
	Mild	5	14.71
	Moderate	11	32.35
	Very complex	7	20.59
	Total	34	100
LIPUS	Complex	11	32.35
	Mild	5	14.71
	Moderate	11	32.35
	Very complex	7	20.59
	Total	34	100

In the analysis of the ABO discrepancy index (ABO DI) scores to compare the complexity of treatments between the Control and LIPUS groups, an Independent Samples *t*-test was conducted. The test results indicated a *t*-value of -0.23 with 66 degrees of freedom, resulting in a p-value of 0.82. This p-value is well above the conventional alpha level of 0.05, leading to the conclusion that there is no statistically significant difference in the ABO DI scores between the two groups, hence suggesting that the treatment complexity is comparable.

Further, the assumption of equal variances, critical for the validity of the Independent Samples *t*-test, was assessed using Levene's Test for Equality of Variances. Levene's Test yielded an F-value of 2.89 with 1 and 66 degrees of freedom for the numerator and denominator, resulting in a p-value of 0.09. Since this p-value is also greater than 0.05, it does not suggest a statistically significant difference in variances between the groups.

In summary, based on Levene's Test, we can assume that the variances are equal, and the t-test confirms that there is no significant difference in the treatment complexity between the control and LIPUS groups according to the ABO discrepancy index scores used in this study(Table 9).

Table 9: Results of the Independent Samples *t*-test and Levene's Test

Independent Samples *t*-test				
ABO	T	df	p	
	-0.23	66	0.82	
Test of Equality of Variances (Levene's)				
ABO	F	df_1	df_2	p
	2.89	1	66	0.09

3.1.2 ABO DI Post-treatment

The ABO DI post-treatment scores provide insight into the effectiveness of orthodontic treatments for both the control and LIPUS groups. The data indicates that all patients achieved an acceptable rate of treatment completion. Specifically, the median and mean ABODI post-treatment scores for the control group were 2.50 and 4.76, respectively, while for the LIPUS group, they were 4.50 and 5.18. These scores show that both groups reached satisfactory outcomes (Table 10 and Figure 22).

Table 10: Descriptive statistics of ABO DI post-treatment scores

Group	N	Mean	SD	SE	Coefficient of variation
Control	34	4.76	4.39	0.75	0.92
LIPUS	34	5.18	3.53	0.61	0.68

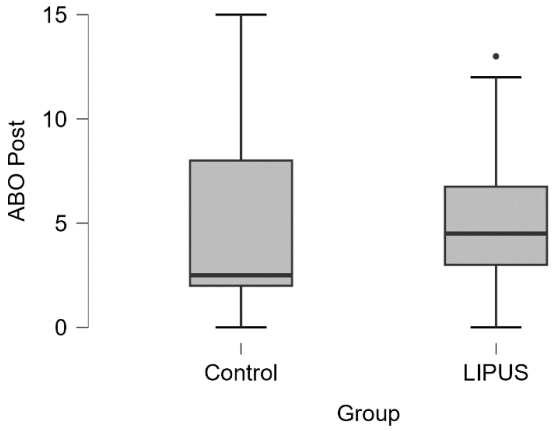


Figure 22: Boxplot of ABO DI post-treatment scores

The independent samples *t*-test, with a p-value of 0.67, reveals no statistically significant difference between the control and LIPUS groups in their ABODI post-treatment scores. This lack of significant difference suggests that both groups were equally effective in achieving the desired orthodontic results (Table 11 and Figure 23).

Table 11: Independent samples *t*-test results for ABO DI post-treatment scores

Independent Samples *t*-test			
ABO Post	t	df	p
	-0.43	66	0.67
Note. Student's *t*-test.			

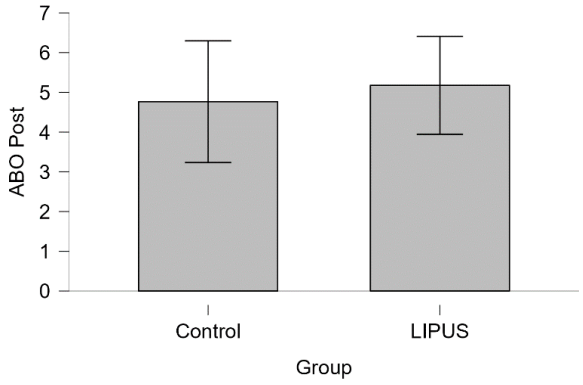


Figure 23: Bar plots of ABO DI post-treatment scores

An assumption check was performed using Levene's test for equality of variances. The test resulted in a p-value of 0.06. This p-value indicates that the assumption of equal variances between the control and LIPUS groups is not violated. Therefore, the variances in ABO post-treatment scores are similar between the two groups, supporting the reliability of the *t*-test results (Table 12).

Table 12: Levene's test for equality of variances for ABO DI post-treatment scores

Test of Equality of Variances (Levene's)				
ABO Post	F	df_1	df_2	p
	3.53	1	66	0.06

In summary, the ABO DI post-treatment scores show that patients in both the control and LIPUS groups reached an acceptable rate of treatment, with no significant differences between the groups. The assumption check further confirms the validity of this comparison, ensuring that the statistical analysis is reliable.

3.1.3 Assessment of Data Normality and Subsequent Statistical Test Selection

Upon conducting the Shapiro-Wilk test for normality, it was found that certain variables significantly deviate from a normal distribution. Specifically, the number of days per tray, number of discarded non-tracking trays, percentage of discarded non-tracking trays, and the percentage of unused trays at the end of treatment for both groups all show p-values less than 0.05, suggesting non-normality. Consequently, for these variables, non-parametric tests, specifically the Mann-Whitney U test, were used to compare the control and LIPUS groups due to the deviation from normal distribution.

Conversely, the variables 'Treatment duration,' 'ABO DI,' and the number of 'Refinements' for both groups did not show a significant deviation from normality, as indicated by their larger p-values.

Thus, for these variables, the parametric Independent Samples *t*-test was employed for analysis between the Control and LIPUS groups (Table 13).

Table 13: Shapiro-Wilk Normality Test Results

Test of Normality (Shapiro-Wilk)			
Treatment duration	Control	0.98	0.72
	LIPUS	0.98	0.86
#of days/tray	Control	0.83	< .001
	LIPUS	0.92	0.02
ABO DI	Control	0.93	0.03
	LIPUS	0.96	0.3
# of Refinements	Control	0.94	0.05
	LIPUS	0.91	<.001
# of Discarded Non-tracking	Control	0.81	< 0.001
	LIPUS	0.68	< 0.001
# of Unused trays at the End of Treatment	Control	0.37	< 0.001
	LIPUS	0.7	< 0.001

Note. Significant results suggest a deviation from normality.

3.1.4 Comparative Analysis of Treatment Variables

To evaluate the efficiency of LIPUS in orthodontic treatment, an Independent Samples *t*-test and Mann-Whitney U Test were performed to compare treatment variables between the Control and LIPUS groups (Table 9).

The treatment duration was significantly shorter in the LIPUS group, with a mean of 544.68 days (SD = 239.1), compared to the Control group's 964.82 days (SD = 418.3). The Independent Samples *t*-test indicated a highly significant difference ($p < .001$), with the effect size suggesting that the LIPUS treatment reduced treatment time by approximately 43.58% (Figures 24).

3.1.4.1 Treatment duration

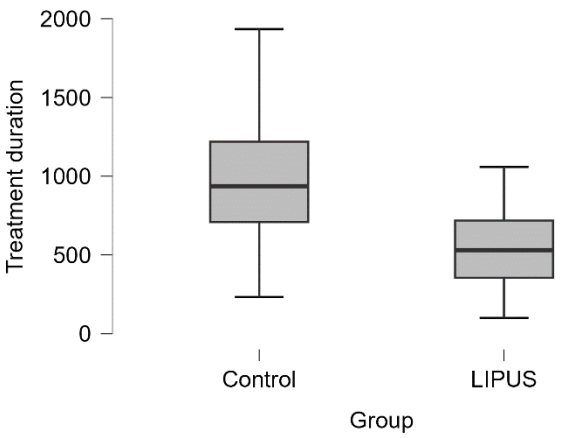


Figure 24: Comparison of Treatment Duration Between control and LIPUS Groups

For the number of days per tray, the LIPUS group (mean of 5.42 days, SD = 1.0) showed significantly shorter durations than the control group (mean of 10.17 days, SD = 3.2) with $p < .001$, indicating a reduction in treatment time per tray by approximately 46.70% in the LIPUS group (Figure 25).

3.1.4.2 #of days/tray_35

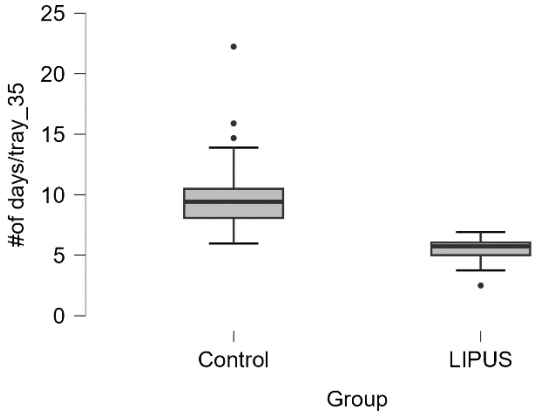


Figure 25: Comparison of Days per Used tray Between control and LIPUS Groups

The number of refinements was significantly fewer in the LIPUS group (mean = 1.56, SD = 1.1) compared to the control group (mean = 2.41, SD = 1.3), with p-values indicating significance (p = <.001 for the Student *t*-test), signifying improved treatment accuracy in the LIPUS group(Figures 26).

3.1.4.3 # of Refinements

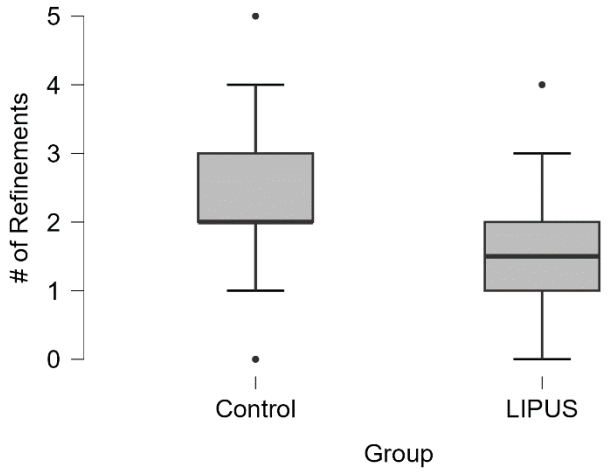


Figure 26: Comparison of the Number of Refinements Between control and LIPUS Groups

The number of discarded non-tracking trays was lower in the LIPUS group (mean of 7.56, SD = 12.0) compared to the control group (mean of 11.18, SD = 13.0), and this result was statistically significant (p = 0.04 for the Mann-Whitney U Test)(Figures 27).

3.1.4.4 # of Discarded Non-tracking

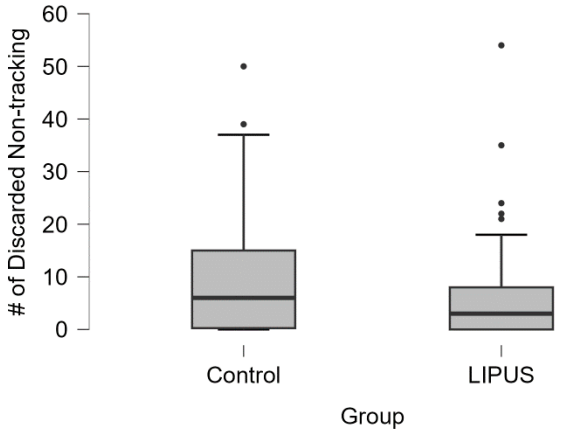


Figure 27: Comparison of the Number of Discarded Non-tracking

The number of unused trays at the end of treatment was significantly higher in the LIPUS group (mean of 5.06, SD = 7.7) compared to the control group (mean of 1.41, SD = 4.4), with a p-value of 0.02 for the Student *t*-test(Figure 28).

3.1.4.5 # of Unused Trays at the End of Treatment

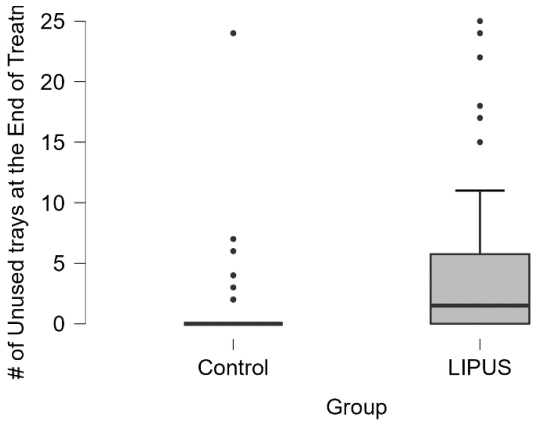


Figure 28: Comparison of the number of unused trays at the end of treatment

In summary, the LIPUS group showed a significant improvement in efficiency concerning treatment duration and days per used tray and discarded non-tracking trays, suggesting enhanced efficiency. The refinement also indicated better efficiency with LIPUS (Table 14).

Table 14: Statistical Analysis: Independent Samples *t*-test and Mann-Whitney U Test

	Test	Statistic	df	p	Effect Size	SE Effect Size
Age	Mann-Whitney	379	-	0.06	-0.34	0.14
Treatment duration	Student	5.09	66	< .001	1.23	0.29
#of days/tray	Mann-Whitney	1139		< .001	0.97	0.14
ABO DI	Student	-0.23	66	0.82	-0.05	0.24
# of Refinements	Student	2.94	66	4.56×10^{-3}	0.71	0.26
# of Discarded Non-tracking	Mann-Whitney	692		0.16	0.2	0.14
# of Unused trays at the End of Treatment	Mann-Whitney	380.5		5.17×10^{-3}	-0.34	0.14

3.2 Part 2: Bone Radio Density

This section investigated the changes in bone radio density in the maxillary and mandibular alveolar bone by comparing pre-treatment and post-treatment measurements in the control and LIPUS groups.

3.2.1 Control Group:

Upper Arch (maxillary alveolar bone): The pre-treatment mean bone radio density was 657.4 HU, slightly decreasing to 650.5 HU post-treatment. The paired *t*-test showed a p-value of 0.86, indicating no significant change.

Lower Arch (mandibular alveolar bone): Pre-treatment mean bone radio density was 836.7 HU, slightly decreasing to 828.1 HU post-treatment. The paired *t*-test showed a p-value of 0.83, indicating no significant change (Table 15).

Table 15: Bone Radio density Measurements in the control Group

Control	Pre-treatment T1 Mean (HU)	Pre-treatment T1 Max (HU)	Pre-treatment T1 Min (HU)	Pre-treatment T1 SD (HU)	Post-treatment T2 Mean (HU)	Post-treatment T2 Max (HU)	Post-treatment T2 Min (HU)	Post-treatment T2 SD (HU)	Paired T test - P Value
Upper Arch	657.4	702.0	616.1	8.1	650.5	695.4	614.7	8.0	0.86
Lower Arch	836.7	917.8	775.6	23.4	828.1	893.9	766.8	22.7	0.83

3.2.2 LIPUS Group:

Upper Arch (maxillary alveolar bone): The pre-treatment mean bone radio density was 444.6 HU. Post-treatment, there was a significant increase to 751.3 HU. The paired *t*-test p-value was <0.001, indicating a significant increase in bone radio density.

Lower Arch (mandibular alveolar bone): Pre-treatment mean bone radio density was 767.7 HU, with a post-treatment increase of 823.4 HU. However, the paired *t*-test p-value was 0.17, suggesting this increase was not statistically significant (Table 16).

Table 16: Bone Radio Density Measurements in LIPUS Group

LIPUS	Pre-treatment T1 Mean (HU)	Pre-treatment T1 Max (HU)	Pre-treatment T1 Min (HU)	Pre-treatment T1 SD (HU)	Post-treatment T2 Mean (HU)	Post-treatment T2 Max (HU)	Post-treatment T2 Min (HU)	Post-treatment T2 SD (HU)	Paired T test - P Value
Upper Arch	444.6	513.6	386.4	18.1	751.3	821.6	684.3	21.6	< .001
Lower Arch	767.7	842.6	701.8	22.9	823.4	882.9	763.9	16.4	0.17

3.2.3 Comparison and Implications:

The data suggests that LIPUS increased bone radio density in maxillary and mandibular alveolar bone; however, the increase in the upper arch was significant. This could indicate that the effect of LIPUS is more pronounced in the maxillary alveolar bone than in the mandibular alveolar bone.

4 DISCUSSION

4.1 Introduction and Interpretation of Results

Orthodontic treatment primarily aims to correct malocclusion and enhance dental aesthetics, but traditional approaches often entail prolonged treatment periods, increased risk of root resorption, and significant demands on patient adherence. LIPUS has emerged as a promising noninvasive adjunct that may mitigate these challenges by accelerating orthodontic tooth movement (OTM), promoting bone health, and potentially improving overall patient experience through orthodontic treatment. This section focuses on interpreting the findings, comparing various studies, and discussing clinical implications and future research directions.

The findings of this study highlight the potential of LIPUS in enhancing orthodontic treatment efficiency. Significantly shorter treatment durations in the LIPUS group, which averaged 544.68 days compared to 964.82 days for the control group, suggest that LIPUS can accelerate orthodontic tooth movement by approximately 43.58%. This substantial reduction in treatment time could decrease the risk of complications such as root resorption and decay, which are often exacerbated by longer treatment durations.

The LIPUS group required significantly fewer refinements and had fewer discarded non-tracking trays, which suggests a more efficient and stable tooth movement pattern. This could reduce the number of patient visits and adjustments needed, improving patient adherence and satisfaction. Fewer visits decrease the inconvenience and time investment for patients and reduce the workload on orthodontic practices, allowing practitioners to optimize their schedules and resources. Additionally, reducing discarded materials contributes to environmental sustainability by minimizing waste. These factors collectively highlight the multifaceted advantages of integrating

LIPUS into orthodontic treatment protocols, benefiting patients, practitioners, and the environment.

Recent studies consistently show LIPUS's efficacy in enhancing OTM by accelerating bone remodeling. This acceleration is linked to the stimulation of osteogenic activity and the optimization of osteoblast-osteoclast interactions, which are critical for effective bone remodeling and resorption necessary for tooth movement (105). The study of Beshoy Magdy Moharib, a review of acceleration techniques in orthodontics, including LIPUS, suggests a consistent trend toward developing non-invasive methods that enhance treatment efficiency while minimizing adverse effects (106).

Our study showed that the LIPUS group significantly normalized bone radio density, as indicated by significantly increased Hounsfield units in the maxillary alveolar bone. Evidence suggests that LIPUS may significantly normalize the quality of bone; this may benefit patients with systemic conditions like osteoporosis (107). Moreover, emerging research indicates LIPUS's potential to augment the effects of functional appliances, as seen in studies showing enhanced condylar and mandibular growth, suggesting its applicability in managing skeletal discrepancies and facilitating orthodontic adjustments (108).

In line with these observations, a study on osteoporotic rats showed that LIPUS reduces orthodontically induced inflammatory root resorption and normalizes tooth movement in conditions of compromised bone health, such as osteoporosis (107). This finding is particularly relevant for postmenopausal women, who may experience exacerbated orthodontic complications due to osteoporosis. These results further substantiate LIPUS's role in enhancing patients'

orthodontic treatment experience by mitigating the negative impact of systemic bone conditions on orthodontic tooth movement.

The significant reduction in the number of days required per tray in the LIPUS group further emphasizes its efficacy. This efficiency not only speeds up the treatment process but may also contribute to better oral hygiene maintenance, as shorter treatment times reduce the duration during which patients must manage challenges associated with orthodontic appliances. Additionally, the findings on bone radio density normalization in the LIPUS group align with previous studies suggesting that LIPUS may promote bone remodeling processes, which is crucial for stabilizing teeth in their new positions post-treatment(109).

In the following sections, we will explain our methods, compare our results with those of other studies, and provide further evidence to reinforce the potential benefits and clinical applicability of LIPUS in orthodontic treatment.

4.2 Study Design

In this study, a retrospective design was utilized, which allowed for the analysis of pre-existing data to evaluate the effects of LIPUS on patient experience through orthodontic treatment. While prospective studies are generally considered the gold standard due to their ability to control variables and reduce bias, they can also be resource-intensive and time-consuming(110).

By comparing our retrospective findings with other studies, we aimed to comprehensively understand how LIPUS impacts treatment duration and other outcomes. Acknowledging the inherent limitations of this retrospective study is crucial when making comparisons.

4.3 Sample size and statistics

Determining the appropriate sample size for this study was a critical step in ensuring the robustness and validity of our findings. The sample size calculation was guided by established statistical principles to detect a significant difference in the primary outcome measure between the experimental group (treated with clear aligners and LIPUS) and the control group (treated with clear aligners alone).

The parameters set for this calculation included a significance level (α) of 0.05 and a power ($1-\beta$) of 80%, aligned with conventional standards for studies, which balance statistical power and practical feasibility. The anticipated effect size, the difference in the impact rates between the two groups, was hypothesized to be 49%. This effect size was selected based on previous studies, preliminary data, and expert consultations, suggesting a moderate but clinically meaningful difference that LIPUS could deliver in enhancing patients' orthodontic treatment experience.

Our calculations suggested a need for approximately 59 participants per group. However, due to the limitations of this study and the fact that Aevo 3 was released in 2019, it was challenging to find patients who had completed orthodontic treatments with all necessary records. Therefore, 34 participants were selected per group.

This means that while the ideal sample size based on the statistical calculations was around 59 participants per group to achieve the desired power and significance level, practical constraints limited the study to 34 participants per group.

Throughout the study, statistical analyses were meticulously designed to align with the specific characteristics and distribution of the data collected. We employed a variety of statistical tests

tailored to address the unique demands of categorical and continuous data types observed in our dataset. This strategic selection was guided by the need to ensure the most accurate and relevant statistical evaluation for each variable analyzed.

The Independent Samples *t*-test was utilized for continuous variables, where data followed a normal distribution. This test is ideal for comparing means between two independent groups and is particularly useful when assumptions of normality and homoscedasticity are met. Conversely, non-parametric tests such as the Mann-Whitney U Test were applied for data that did not meet these assumptions. These tests are less sensitive to outliers and do not require the assumption of normal distribution, making them more suitable for skewed data or data with unequal variances. For bone radio density measurement in each patient before and after treatment, we used the paired *t*-test.

4.3.1 Relevance of the 49% Reduction in Treatment Time to Sample Size Calculation

In this study, the reported 49% reduction in treatment time using LIPUS, as observed in previous studies by Kaur and El-Bialy (2020), was used as a foundational reference for calculating the required sample size(3). Based on this reduction, our initial calculations indicated that we would need approximately 59 participants per group to achieve sufficient statistical power to detect a similar effect in our study population. However, due to practical limitations, including patient record availability and inclusion criteria, we could enter only 34 patients per group.

This reduction in sample size means that while the study still provides valuable insights, it should be considered preliminary. The observed reduction in treatment time in our study (approximately 43.58%) supports the potential of LIPUS to expedite orthodontic treatment. However, further

research with larger sample sizes is necessary to fully confirm these findings and fully understand the factors influencing LIPUS's effectiveness.

4.4 Patient Selection and Matching Process

To ensure a well-defined and comparable sample for the study, a multi-step patient selection process was employed at the clinic, involving both the experimental (LIPUS) and control groups. Initially, a list of 335 patient IDs who had used the Aevo 3.0 system was obtained from SmileSonica Inc. This list included adherence data for each patient, which served as the first filter in the selection process.

The first step involved applying an adherence filter, where only patients with an adherence rate higher than 67% were selected. This filtering process narrowed the initial list to approximately 110 patients, ensuring that only those with sufficient adherence to the treatment protocol were considered for further selection.

Following this, the inclusion criteria were applied to the 110 patients, reducing the number to 36. These criteria ensured that the selected patients met the specific requirements necessary for the study.

Subsequently, exclusion criteria were applied, refining the selection to 34 patients eligible for enrollment in the experimental group. This meticulous process ensured that the experimental group was composed of patients who met all the necessary study criteria and had the required treatment records available.

A random selection of records was performed from patients who met the same inclusion and exclusion criteria to create a comparable control group. This initial pool consisted of 102 patients.

The control group was matched to the experimental group based on malocclusion type (Class I, Class II, and Class III) to ensure that both groups had similar orthodontic conditions. Further matching within each malocclusion type was conducted based on age, biological sex, and treatment complexity using the ABO DI. This thorough matching process resulted in a final control group of 34 patients.

Finally, statistical analysis was performed to confirm the comparability of the experimental and control groups. The analysis revealed no significant differences in age (P = 0.06), sex (P = 0.620), and treatment complexity (P = 0.82), indicating that the groups were well-matched and comparable. This selection and matching process ensured that the study's findings would be robust and reliable, allowing for a valid comparison of the effects of LIPUS in orthodontic treatment.

4.5 Assessment of Treatment Efficiency

In evaluating the efficiency of orthodontic treatment with clear aligners, we measured variables such as treatment duration, the necessity for refinements, and bone radio density normalization. These factors are vital for assessing the treatment's accuracy in achieving the intended orthodontic outcomes within a set timeframe and with minimal adjustments.

4.5.1 Treatment Duration

This study's results indicate that the mean treatment duration in the LIPUS group was 18.15 months compared to 31.66 months in the control group. The mean treatment duration in the control group is similar to the findings from the published systematic reviews of Tsichlaki et al. (2016) and Abbing (2020)(96, 97). These reviews reported an average treatment duration with fixed appliances ranging from 19.9 to 31 months, highlighting the variability in patient responses and

the complexity of cases. The extended treatment duration observed in our Control group in patients who used clear aligners alone could be attributed to the need for multiple refinements, as clear aligners often require adjustments to achieve the desired outcomes. However, the LIPUS group's reduced need for refinements and shorter days per tray change underscores the potential of LIPUS in optimizing patient's treatment experience. Patients in the LIPUS group experienced fewer refinements and significantly reduced treatment times, suggesting that LIPUS may effectively mitigate the factors contributing to extended treatment durations typically seen with clear aligners.

Furthermore, Shorter treatment durations achieved with the aid of LIPUS enhance patient satisfaction by reducing the treatment timeline and decreasing the likelihood of complications associated with prolonged orthodontic procedures, such as root resorption and decay. These complications are typically more prevalent and severe the longer the orthodontic appliances are in place. Therefore, the significant reduction in treatment time observed in the LIPUS group shows the technology's practical benefits, reinforcing its role in improving the orthodontic treatment experience.

4.5.2 Refinements

The need for refinements, including adjustments or the addition of aligner trays due to non-fitting trays, directly influences treatment efficiency. Non-fitting trays, referred to as unused discarded trays, are those that do not properly conform to the patient's dentition, leading clinicians to discard them. This usually happens when the aligners fail to guide the teeth along the intended path, requiring new sets of trays and refinements to be designed. Additionally, unused trays at the end of treatment are discarded because they are no longer necessary due to favorable treatment outcomes.

Both variables indicate deviations from the planned treatment path, impacting the efficiency of achieving desired outcomes. By evaluating the number of discarded non-tracking and unused trays at the end of treatment in groups treated with and without LIPUS, we aim to assess how LIPUS might enhance the precision of tooth movement and reduce the incidence of these modifications. This evaluation is particularly relevant as LIPUS is hypothesized to support more stable tooth movement through normalized bone radio density, thus potentially reducing the need for unexpected adjustments and leading to more efficient use of aligners.

4.5.3 Bone Radio Density

Enhanced bone radio density is another crucial parameter for assessing the efficiency of orthodontic treatment. Enhanced bone radio density can facilitate more stable tooth positioning, which is essential for maintaining the results post-treatment and minimizing relapse. The hypothesized role of LIPUS in enhancing bone radio density supports its potential utility in improving the overall stability and efficiency of orthodontic outcomes.

By evaluating these variables, the study aimed to understand how LIPUS might influence the efficacy of orthodontic treatment with clear aligners. This evaluation supports the clinical application of LIPUS and contributes to the broader literature on improving orthodontic treatment methodologies.

The findings of this study show that the bone radio density in the LIPUS group had fewer Hounsfield Unit values before treatment in both arches than the Control group. This difference might be attributed to age-related variations in bone radio density, as it is possible that bone density decreases with age(111).

4.6 ABO Discrepancy Index for complexity categorization

As reviewed by Mariana Paes Muro et al. (2023), clear aligners have shown variability in the predictability of tooth movements, particularly with rotations, intrusions, and extrusions, which are often less predictable than other types of movements (112). Therefore, in our study, we employed a reliable complexity index to match patients and fairly compare the two groups.

The ABO DI is a well-recognized tool for quantifying the complexity of orthodontic cases. It provides a standardized measure to evaluate and compare the difficulty of different cases based on a set of defined criteria, which include aspects such as tooth alignment, overjet, overbite, and the presence of crossbites, among others. By calculating the ABO DI for each patient, we can accurately assess the level of treatment complexity.

In our study, we utilized the ABO DI to ensure a balanced comparison based on treatment complexity between the LIPUS and control groups. We first categorized each case into complexity levels—Mild (ABODI index from 1 to 10), Moderate (ABO index from 11 to 20), Complex (ABO index from 21 to 30), and Very Complex (ABO index from 31 to 100)—based on their ABO DI scores. This stratification allowed us to match patients from the LIPUS group with those in the control group according to their treatment complexity. This matching is crucial as it controls for variability in treatment difficulty, which could otherwise skew the results and lead to biased conclusions.

The use of the ABO DI is particularly beneficial in studies like ours, where matching the complexity of cases between different treatment modalities is essential to ensure that any observed differences in treatment outcomes are due to the intervention itself rather than variations in case difficulty. This methodological approach enhances the validity of our findings by providing a level

playing field for comparing the efficacy of LIPUS with conventional treatment methods in orthodontics.

Comparatively, the study by Castroflorio et al. (2022) highlights the variability in aligner-based orthodontic treatment. It emphasizes the influence of treatment design and patient-specific factors on the predictability of tooth movements with clear aligners, reporting a notable discrepancy between predicted and actual tooth positions, particularly in rotational and angular movements(113).

The post-treatment ABO DI was also measured, and the non-significant difference between the LIPUS and control groups indicates that both groups received acceptable treatments (p-value = 0.67).

4.7 LIPUS with the Aevo 3 System by SmileSonica Inc

The Aevo 3.0 System, developed by SmileSonica Inc., has been selected for our study due to its utilization of LIPUS technology, which is commercially available and previously approved by Health Canada. This device, specifically designed for orthodontic applications, offers a non-invasive, user-friendly approach that patients can operate independently on a daily basis, enhancing adherence. It supports the orthodontic treatment process by stimulating osteoblast and osteoclast activity(94), crucial for bone remodeling and accelerating tooth movement.

The Aevo 3.0 System is particularly noted for its potential to decrease the risk of tooth root resorption—a significant concern in orthodontics—through its precise and gentle delivery of ultrasound waves directly to the areas surrounding the tooth roots. This capability is a fundamental reason for its selection, as it aligns with our study's objectives to evaluate patients' orthodontic

treatment experience. Furthermore, its effectiveness in reducing overall treatment time and enhancing long-term oral health has been well documented, reinforcing its adoption in clinical settings.

Not only does the Aevo 3.0 System minimize additional risks associated with invasive procedures, but it also conforms to rigorous regulatory standards. Approved by Health Canada, the device is equipped with features such as a rechargeable battery, LED indicators, and optional Bluetooth connectivity, all housed within a user-friendly mouthpiece designed for daily use.

4.7.1 Impact of Aevo System Design on Study Outcomes

In this study, the Aevo system 3.0 was used as a delivery method for LIPUS. This device was released in 2019 and is currently available on the market. The earlier model, Aevo system 2.0, was introduced and approved for sale in 2015. Both devices deliver the same ultrasound output. The Aevo 3.0's enhanced design likely contributed to higher adherence rates among patients in this study, as the device was easier to use and integrate into daily routines. This is significant because patient adherence is a critical factor in the effectiveness of LIPUS therapy. While the therapeutic output of the device remains consistent across different versions, the ease of use and patient comfort associated with the newer design may lead to more reliable and effective outcomes. This suggests that even when devices deliver the same therapeutic output, improvements in design can play a crucial role in enhancing patient adherence and, consequently, the overall success of the treatment.

4.8 Adherence

In evaluating the Aevo System™/ LIPUS efficiency in conjunction with clear aligners, this study specifically incorporated a minimum adherence threshold of 67% as a criterion for participant inclusion. This threshold represents significant adherence, quantified as an average daily use of approximately 13.4 minutes out of a prescribed 20-minute-per-day regimen. The rationale behind this decision is rooted in the understanding that the therapeutic effectiveness of LIPUS, proposed to stimulate bone remodeling and accelerate orthodontic tooth movement, depends on consistent usage. According to Liu et al. (2014), optimal results for bone healing using LIPUS are achieved with daily usage of 15 - 20 minutes, which significantly accelerates fracture healing and promotes local bone formation(114).

Incorporating an adherence threshold into the study design was intended to ensure that the collected data accurately reflect the potential of LIPUS technology when used appropriately. Research indicates that the biological processes influenced by LIPUS, necessary for enhancing orthodontic treatment, require regular and sustained application of the ultrasound stimulus(94). Therefore, intermittent or inadequate usage could diminish the clinical effectiveness, making adherence a critical factor in the treatment's success.

Moreover, by selecting participants who met the adherence criteria based on reliable data provided by SmileSonica Inc., the study minimized the variability associated with patient adherence, which is a common challenge in orthodontic research. This focus on compliant patients allows for a more precise evaluation of the Aevo 3 System™, providing insights that reflect its potential when the recommended usage guidelines are followed.

Overall, the methodological decision to include only those patients who showed an adherence rate of 67% or greater was crucial for assessing the true effectiveness of the Aevo System™ in clinical practice. It offers practical implications for adjunctive technologies in orthodontics, where patient cooperation plays a pivotal role in achieving successful treatment outcomes.

The study by Kaur and El-Bialy showed that patients who consistently used the Aevo 2 System™ incorporating LIPUS experienced a clinically significant reduction in overall orthodontic treatment duration. This reduction was observed compared to a control group that used Invisalign clear aligners without the additional LIPUS treatment. Notably, the average adherence rate among the patients using LIPUS was 66.02% (3). This level of adherence was critical as it underscored the importance of consistent device usage to achieve the observed benefits. The decision to set an adherence threshold of 67% for inclusion in the current study was based on ensuring that the data collected reflected the potential of LIPUS to enhance orthodontic treatment when used as prescribed.

4.9 Minimizing Measurement Bias

To reduce measurement bias in the assessment of orthodontic treatment duration and efficacy between groups, a meticulous method was employed in the handling and analysis of patient data. After selecting 34 patients who met the inclusion criteria for the LIPUS group, a matched control group of 34 patients was also chosen based on the treatment complexity. To further ensure the integrity of the measurements and analysis, all patient data, including IDs, were pooled into a single excel file without indicating their assigned study group. This anonymization strategy was designed to prevent potential bias from knowing the group allocation during the data collection and measurement phases. Only after all measurements were completed were the patients sorted

based on their respective groups for final analysis. This approach strengthened the study's methodological rigor and enhanced the reliability of the comparative results between the LIPUS and control groups.

4.10 Treatment efficiency and Bone Radio density

As supported by various animal and human studies, LIPUS has been shown to significantly accelerate OTM (27, 105, 115). In this study, applying LIPUS notably shortened the treatment duration, with the LIPUS-treated group averaging 544.68 ± 238.97 days compared to 964.82 ± 417.9 days in the control group, amounting to a reduction of approximately 43.58%. The number of trays per day was fewer in the LIPUS group (5.42 ± 1.02 days vs. 10.17 ± 3.18 days). Patients in the LIPUS group had fewer refinements (1.56 ± 1.11 vs. 2.41 ± 1.28) and fewer discarded non-tracking trays (7.56 ± 11.91 vs. 11.18 ± 13.39). This study also found normalized bone radio density in the LIPUS group, with significant results in maxillary alveolar bone.

Kaur and El-Bialy (2020) reported similar findings. LIPUS application resulted in a treatment duration of 541.44 days for the LIPUS group compared to 1061.05 days for the control group, reflecting an average reduction of 49% in overall treatment duration ($p < 0.05$). This data further supports the efficacy of LIPUS in reducing orthodontic treatment time, which aligns with the enhanced bone radio density observed in our LIPUS group. In their study, the sample size included 34 LIPUS patients and 34 controls. The results showed a LIPUS duration of 541.44 ± 192.23 days and a control duration of 1061.05 ± 455.64 days. In comparison, our study had a LIPUS duration of 544.68 ± 238.97 days and a control duration of 964.82 ± 417.9 days, showing a reduction of 43.58% ($p < 0.001$). Regarding malocclusion classification frequencies, Kaur et al. (2020) reported 7 Class I, 13 Class II, and 14 Class III malocclusions in both the Control and LIPUS groups. In

our study, Class 1 had the highest frequency (19 cases, 55.88%), followed by Class 2 (8 cases, 23.53%), and Class 3 (7 cases, 20.59%), with identical distributions in both the Control and LIPUS groups(3).

Al-Dboush et al. (2021) also observed a significant reduction in treatment duration with LIPUS. In their study, the sample size included 28 patients in each of three groups: LIPUS, photobiomodulation (PBM), and Control. The mean treatment durations were 533 ± 242 days for the LIPUS group, 528 ± 323 days for the PBM group, and 719 ± 220 days for the Control group. The LIPUS group showed a 26% reduction in treatment duration compared to the control group, consistent with the reductions observed in our study. Additionally, the malocclusion classification frequencies were evenly distributed among the groups, similar to our study's findings. This further validates the effectiveness of LIPUS in reducing treatment duration and enhancing orthodontic outcomes across different studies (116).

However, the differences between their study and ours could be attributed to several factors. One significant difference could be the version of the LIPUS device used; Al-Dboush et al. utilized a different version of the Aveo device, which may have varying efficacy. Another factor is the sample size, as fewer patients were in the LIPUS group. Adherence with the treatment protocol is another critical factor; variations in patient adherence to using LIPUS as prescribed can significantly impact the outcomes.

Miura et al. found significantly lower mobility in the LIPUS-treated mini-screws, with better bone-miniscrew adhesion than controls. This highlights the potential of LIPUS to reduce mini-screw mobility, a crucial factor in the success of orthodontic anchorage systems, thereby potentially reducing the risk of mini-screw loosening during treatment (117). Similarly, the study of Fu Zheng

et al. found that LIPUS facilitated osteogenic processes by modulating the activity of mechanosensitive ion channels in periodontal ligament cells, further supporting the potential of LIPUS to enhance orthodontic treatment efficacy (118). The findings by Tarek El-Bialy et al. (2003) also bolster the biological plausibility of using ultrasound technology to influence bone structures. They reported that therapeutic ultrasound significantly increases mandibular condylar growth in rabbits through enhanced endochondral bone formation (108). The study by Kaur and El-Bialy adds to this by showing a significant increase in osteogenic markers such as OPG and RANK-L, which are vital for bone remodeling and accelerated tooth movement (3). These studies support the increased bone radio density observed in the LIPUS group in this study.

Interestingly, when comparing the predictability of tooth movements in treatments that do not use LIPUS, the study of Lombardo et al. noted a mean predictability of movements of 73.6%. This figure suggests that while aligners can be effective, their predictability does not reach full certainty without auxiliary measures (119).

In contrast, the study by Irfan Qamruddin et al. (2020) did not observe any significant enhancements in the rate of tooth movement or pain reduction when LIPUS was applied at 3-week intervals, suggesting that the frequency and possibly the intensity of LIPUS applications may critically influence its efficacy in clinical settings (120).

According to Sri Santosh et al. (2020), the therapeutic use of LIPUS is based on parameters like a 30-mW/cm2 intensity, 1.5-MHz frequency repeated at 1 kHz, and a pulse width of 200 μs administered for 20 min each day. These parameters have been shown to enhance alveolar bone remodeling by increasing the expression of osteogenic markers such as Interleukin-8 and Basic Fibroblastic Growth Factor (BFGF)(121).

Furthermore, the study by Pascoal et al. (2024) has shown that specific ultrasound (US) stimulation parameters can significantly enhance metabolic activity and osteogenic marker expression, such as OPG, in osteoblasts and periodontal ligament fibroblasts. Notably, US parameters of 1.0 MHz at 30 mW/cm² and 60 mW/cm² for both 5 and 10-minute sessions showed enhanced metabolic activities and induced OPG synthesis, critical for promoting bone formation during OTM (100). This shows that optimizing US parameters could enhance LIPUS efficacy for accelerating orthodontic treatments.

Miura et al. also note the importance of LIPUS application parameters for achieving desired clinical outcomes, further highlighting the need for standardized LIPUS protocols (117). This divergence supports the necessity for optimized LIPUS protocols to achieve predictable clinical outcomes, potentially varying with individual patient responses or specific treatment parameters.

Hui Xue et al. (2013) further substantiate these findings by showing that LIPUS significantly increases the OTM distance in a rat model, primarily through activating the BMP-2 signaling pathway and enhanced RANKL expression. This mechanism is critical as it underlines the potential for LIPUS to promote alveolar bone remodeling through molecular pathways crucial for osteogenic processes. Moreover, the study of Hui Xue et al. highlights that LIPUS enhances osteoclast activity and RANKL expression, which are key in regulating bone remodeling during orthodontic tooth movement. This further links the mechanical modulation achievable through LIPUS to cellular responses essential for effective orthodontic treatment (105).

The study by Yuri Higashi et al. (2020) showes that increasing the frequency of LIPUS applications significantly enhances osteoclast differentiation in RAW264 cells, which supports the

use of LIPUS in orthodontic treatments to potentially accelerate tooth movement by modulating osteoclast activity(122).

The findings from the study of Tanaka et al. enhance understanding of LIPUS's mechanisms, which promote cellular responses conducive to accelerated tissue repair and regeneration (123). They highlighted the stimulation of various cellular types, including osteoblasts and cementoblasts, crucial for orthodontic adjustments. Importantly, the review provides evidence supporting the role of LIPUS in promoting osteogenic differentiation, which is consistent with the enhanced bone radio density observed in our LIPUS group (124-127). Additionally, El-Bialy's discussion on the mechanistic pathways influenced by LIPUS, such as the activation of mechanosensitive ion channels and integrins, supports our observations of enhanced bone remodeling (128). The study underscores the therapeutic potential of ultrasound to modulate cellular environments conducive to orthodontic adjustments, which is pivotal for reducing treatment times and enhancing patient outcomes. This is further corroborated by Fu Zheng et al. (2024) findings, where LIPUS downregulated the expression of Piezo1, a mechanosensitive ion channel, thereby enhancing osteogenesis under mechanical stress (118).

In parallel, findings from El-Bialy et al. corroborate the role of LIPUS in enhancing the remodeling processes of the dentoalveolar structures during orthodontic treatments. Specifically, their study showed significant increases in cementum and pre-dentine thickness and sub-odontoblast and periodontal ligament cell counts in response to LIPUS treatment. Furthermore, the study by Qin et al. (2023) expands our understanding of LIPUS's effects beyond the dental field, indicating that LIPUS can mediate tissue regeneration and reduce inflammation through macrophage polarization, particularly by promoting an anti-inflammatory M2 phenotype (129). This suggests that LIPUS

accelerates tooth movement by enhancing bone remodeling and potentially minimizes the risk of orthodontically induced root resorption by strengthening dentoalveolar structures, which is in agreement with the outcomes observed in our study (130).

However, the study by Bahammam and El-Bialy (2022) challenges these findings by showing that LIPUS did not significantly affect bone thickness or height in the context of maxillary expansion using clear aligners despite its use with an accelerated aligner change protocol (131). This suggests that the effectiveness of LIPUS may vary depending on specific clinical conditions and treatment protocols. Therefore, while LIPUS has shown promise in enhancing orthodontic treatment in various studies, the variability in clinical results underscores the necessity for further research to optimize its application parameters and identify the conditions under which it is most effective.

In line with our findings, the review by Qamruddin et al. (2015) corroborates the potential of LIPUS in enhancing orthodontic treatment. The review highlights several animal studies where LIPUS was shown to accelerate tooth movement by influencing cellular activities and bone remodeling dynamics (132).

The research detailed by El-Bialy et al. in their comprehensive assessment of ultrasound applications in dentistry highlights that LIPUS not only facilitates orthodontic tooth movement but also contributes to tissue repair and regeneration (128). They report enhanced cellular responses under LIPUS treatment, which include upregulated expression of osteogenic markers such as RUNX2 and osterix, which are critical for bone formation and remodeling(128). These findings lend further credence to our observations of accelerated tooth movement and normalized bone radio density in the LIPUS group, aligning with El-Bialy's findings of ultrasound-induced cellular mechanotransduction, which promotes osteogenesis (128).

In parallel, a study by Ebubekir Toy et al. found that LIPUS treatment led to a statistically significant increase in VEGF and osteocalcin immunoreactivities in the mineralizing tissue areas compared to control groups, suggesting a higher osteoblastic activity. This enhancement in biological markers associated with bone formation could underpin the accelerated orthodontic treatment observed with LIPUS, aligning with the findings of our study that showed enhanced bone radio density and decreased treatment times (133).

Similarly, Jie Zhou et al. (2023) found that LIPUS enhances osteogenic differentiation and modulates bone homeostasis through osteoblast-osteoclast crosstalk via the EphrinB2/EphB4 signaling pathway. This pathway is crucial in activating YAP signaling within the cytoskeleton, influencing cell migration and osteogenic differentiation, which are essential for effective orthodontic treatment (94). These findings align with the results of our study, further substantiating LIPUS's role in promoting faster and safer orthodontic treatments.

Orthodontic tooth movement is a bone remodeling process involving various cell types, including osteoblasts, osteoclasts, and osteocytes. The process is governed by the tumor necrosis factor (TNF) receptor-ligand family, which includes OPG, receptor activator of nuclear factor kappa- (RANK), and RANK-ligand (RANK-L). Mechanical stress from orthodontic forces induces the release of RANK-L by osteocytes, which then bind to RANK, promoting osteoclast differentiation, proliferation, and survival (134-136).

OPG acts as a soluble decoy receptor that inhibits RANK-L from binding to RANK, thereby preventing osteoclast formation (137). RANK-L and OPG are crucial in regulating bone remodeling during tooth movement. Additionally, vascular endothelial growth factor (VEGF)

increases during OTM, enhancing osteoblast survival, stimulating progenitor cell recruitment, and promoting mineralized nodule formation (138, 139).

LIPUS potentially influences OTM through mechanical strain on cell membrane receptors like integrins and stretch-activated channels, initiating cellular and molecular events termed mechanotransduction. This activation triggers various cellular signaling pathways, such as focal adhesion kinase (FAK), mitogen-activated protein kinase (MAPK), and Rho pathways, which have been activated in in-vitro studies with LIPUS application (99, 140-142). Through these pathways, LIPUS not only promotes bone formation and osteoblast differentiation in cases of bone healing but also enhances angiogenesis and upregulates VEGF expression in human osteoblasts, thus supporting wound healing and early osteogenesis (143, 144).

Furthermore, LIPUS has been shown to increase the proliferation of osteoprogenitor cells, elevating the expression of osteogenic markers such as collagen I, osteocalcin, and bone morphogenetic proteins (BMP-2 and BMP-7), thereby enhancing osteoblast differentiation from mesenchymal stem cells (143, 145, 146). Interestingly, the mechanism by which LIPUS accelerates OTM resembles other acceleration techniques like laser, high-frequency vibration, and corticotomy, which primarily operate through the RANK-RANKL pathway, suggesting an area ripe for further comparative studies. Qamruddin et al. detail studies showing the role of LIPUS in upregulating osteogenic factors such as BMP-2, a key player in bone formation and remodeling (132).

While LIPUS has shown efficacy in upregulating osteogenic markers and modulating osteoclast differentiation, it also regulates osteoclast activity through OPG/RANK-L expression. These findings corroborate the outcomes of this retrospective study, suggesting that LIPUS not only

accelerates orthodontic tooth movement by enhancing osteoblastic activity but also ensures safety by regulating osteoclastic activity on the compression side of orthodontic force application, thus contributing to normalized bone radio density outcomes.

Further support for the effectiveness of LIPUS in promoting faster orthodontic treatments comes from a study by Alazzawi et al. (2018), which found that LIPUS enhances the velocity of tooth movement and improves the quality of bone remodeling during orthodontic tooth movement in rats (109). The increased gene expression of RANK, RANKL, and OPG observed in their study underscores the molecular pathways through which LIPUS may enhance bone dynamics, which is particularly relevant for understanding the mechanisms involved in accelerated orthodontic procedures (109).

Interestingly, findings from Yingying Wang et al. (2024) also show the efficacy of LIPUS in improving peri-implant osteogenesis in diabetic conditions, which could be considered a proxy for challenging orthodontic cases where altered metabolic states might influence the treatment. They reported that LIPUS treatment not only mitigates the detrimental effects of diabetes on osseointegration but also promotes comparable bone health to non-diabetic conditions in terms of bone-implant contact ratio and bone mineral density (BIC and BMD)(147).

4.11 Study Limitations

The limitations of this study include its retrospective nature, which lacks direct access to patients to conduct a randomized controlled trial (RCT). Additionally, while we aimed to evaluate bone quality, using dual-energy X-ray absorptiometry (DEXA) to measure bone density would have been ideal. Instead, we used CBCT.

Another limitation was the small sample size and the evaluation conducted in only one clinic. Since the Aevo System 3.0 device was released in 2019, and it takes time for orthodontic treatment to be completed, it was challenging to find compliant patients who had completed treatment with all the necessary records available. Moreover, the limited sample size also hindered the ability to conduct a thorough subgroup analysis across different malocclusion types (Class I, II, and III) and treatment complexity levels.

When comparing the patient experience through orthodontic treatment between the LIPUS and control groups, it is essential to exercise caution due to the variation in patient adherence. Only 110 out of 335 patients met the 67% adherence threshold, highlighting the challenges in maintaining consistent protocol adherence. This variation could potentially affect the reliability of the results and should be considered when interpreting the findings.

Another limitation of this study is the exclusion of cases involving dental extractions. This decision was made to ensure a homogeneous sample and to focus specifically on the effects of LIPUS on orthodontic treatment with clear aligners. However, this exclusion limits the generalizability of the study's findings. As a result, the findings of this study may not be fully applicable to orthodontic treatments that involve extractions, limiting the broader applicability of the results.

Missed appointments and appliance breakages are additional factors that can significantly delay treatment progress, often leading to extended overall treatment duration(148). These factors should be considered when investigating the treatment duration time.

While the reliability of the collected data was ensured through standardized measurement procedures and rigorous data collection protocols, detailed reliability analysis (such as test-retest

reliability or inter-rater reliability) was not included in this study's scope. This is acknowledged as a limitation, and future studies should incorporate such reliability assessments to validate the findings further.

It should be noted that the actual adherence rate to Aevo usage during the specified time period was only 33% (110 out of 335 patients); however, to ensure the effectiveness of LIPUS, we selected patients with a minimum adherence rate of 67%, which may impact the reliability of the study’s results.

Finally, while the results of this study show that LIPUS significantly accelerated the orthodontic treatment duration compared to the control group using clear aligners alone, it is important to acknowledge that this acceleration does not necessarily imply that LIPUS makes the treatment faster than other orthodontic methods. Various other methods for accelerating orthodontic tooth movement, such as corticotomy and low-level laser therapy, have shown effectiveness in different contexts. Therefore, while LIPUS offers a promising adjunctive therapy for patients undergoing treatment with clear aligners, its comparative efficiency across different orthodontic methods requires further investigation to establish its relative advantages.

4.12 Future Directions

Building on the current study's findings, several avenues exist to investigate further the efficacy and broader implications of the Aevo System™ with LIPUS in orthodontic treatment.

Expanding the sample size would provide a more robust statistical analysis and potentially validate the initial results across a wider demographic. This could help generalize the findings to a broader population.

Additionally, incorporating patient satisfaction measures through surveys could offer valuable insights into patients' subjective experiences using LIPUS technology. Understanding patient perspectives on comfort, convenience, and overall satisfaction could significantly influence clinical practices and patient adherence strategies.

Further prospective double blinded randomized controlled trials (RCTs) are recommended to explore the effectiveness of the LIPUS with enhanced parameters. These studies could focus on optimizing the LIPUS settings and treatment protocols to maximize clinical outcomes and efficiency. Conducting RCTs in various clinical settings beyond the initial single clinic could also help assess the consistency of LIPUS effectiveness across different environmental conditions and clinical practices.

Moreover, expanding the research to include multiple clinics would provide a broader range of data, reducing the bias associated with a single clinical setting. This would allow for evaluating the Aevo System under varied conditions and potentially increase the reliability of the findings.

It is better to conduct RCT studies and use DEXA to evaluate bone density more accurately when investigating bone quality. DEXA provides more precise and consistent measurements compared to CBCT, which can be influenced by artifacts and image quality issues. To date, no studies have investigated the effects of LIPUS on orthodontic relapse or the fit of retainers post-treatment. Future research can focus on evaluating these aspects to determine whether LIPUS has a long-term impact on maintaining treatment results and ensuring optimal retainer fit.

A comparative study between LIPUS used with clear aligners and traditional braces could also be highly valuable. Previous studies have shown that LIPUS is effective when used with Clear

Aligners. Comparing the outcomes of LIPUS with these two different orthodontic appliances could help determine whether the advantages observed with clear aligners are also applicable to traditional braces. This comparison could further broaden the application of LIPUS in orthodontic treatment.

Future studies are also suggested to evaluate the comparative efficiency of LIPUS across different orthodontic treatment acceleration methods and to explore its relative advantages.

Although standardized measurement procedures and a trained researcher were employed to ensure data accuracy, reliability analysis was not within the scope of this study due to its preliminary nature. Future research should incorporate detailed reliability assessments to further validate the findings.

Finally, while this retrospective study has laid a foundation for understanding the impact of the LIPUS on treatment efficiency and bone radio density, future studies should also explore its effects on orthodontic treatment relapse. Designing studies to evaluate the Aevo System's impact on reducing root resorption could provide critical insights into this technology's safety and long-term benefits. These investigations could significantly advance orthodontic treatment practices, optimizing outcomes and enhancing patient care.

4.13 Conclusion

Within the limitations of this study, the potential impact of LIPUS in enhancing efficiency and patient experience using clear aligners was high. The application of LIPUS could reduce treatment duration. This possible decrease in treatment time can potentially lower the risks of complications such as root resorption and decay, exacerbated by longer treatment durations.

It can be concluded that LIPUS-treated patients required fewer refinements and experienced fewer non-tracking discarded trays, suggesting that it is highly possible that LIPUS promotes a more efficient and stable tooth movement. This efficiency could diminish the number of patient visits and adjustments required, enhancing patient adherence and satisfaction. Additionally, the normalized bone radio density observed in the LIPUS group aligns with other studies, suggesting that LIPUS may facilitate bone remodeling, which is essential for stabilizing teeth in their new positions post-treatment.

While LIPUS has shown promising preliminary results in this study, future research should aim to expand these findings across larger and more diverse populations to confirm its efficacy and utility. Further investigations should also explore the molecular mechanisms by which LIPUS influences bone density and movement at the cellular level to better understand and optimize its clinical applications.

Conducting RCTs and using DEXA to evaluate bone density more accurately when investigating bone quality is suggested.

In conclusion, LIPUS has the potential to be a complementary technology for orthodontics. Its benefits could extend beyond shorter treatment times and normalize bone radio density outcomes. Its integration into orthodontic practice could enhance patient experiences by reducing treatment duration and contribute to orthodontic treatments' overall success and sustainability.

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