STUDY PROTOCOL

Official title

Evaluation of bone level changes using clear aligners compared to fixed appliances in non-extraction treatment of adult patients: A Randomized clinical trial

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Principal investigator: Ahmed Mohamed Hesham elzoghary

Sponsor: Faculty of Oral and Dental Medicine, Future University in Egypt

Evaluation of bone level changes using clear aligners compared to fixed appliances in non-extraction treatment of adult patients: A Randomized Clinical Trial

Protocol submitted for the partial fulfillment of master's degree in Orthodontics
Faculty of Oral and dental medicine, Future University in Egypt

Submitted by
Name: **ahmed Mohamed hesham elzoghary**
B.D.S., Future University,(2019)

I. Administrative Information

1. Title:

Evaluation of bone level changes using clear aligners compared to fixed appliances in non-extraction treatment of adult patients: A Randomized clinical trial.

2. Trial registration:

The trial will be registered on www.clinicaltrials.gov

3. Protocol version:

2024, First version.

4. Funding:

This research is self-funded.

5. Roles and responsibilities:

Main supervisor: -

- **Prof. Hala Mounir,** BDS, MSc, PhD, Professor – Department of Orthodontics, Faculty of oral and dental medicine, Future University in Egypt: helped develop the research idea and will assist in the interpretation of results and drawing of conclusions.

Co-supervisor: -

- **Prof. Essam Nassef,** BDS, MSc, PhD, Professor — Department of Orthodontics, Faculty of oral and dental medicine, Future University in Egypt: calculated the sample size and will help with patient follow-up, analysis and interpretation of results.
- **Dr. Mostafa Mohamed El-Dawlatly,** BDS, MSc, MOrth (RCSEd), FRCSEd, PhD, Associate Professor of Orthodontics, Faculty of oral and dental medicine, Future University in Egypt: initiated the idea of the project and will supervise the clinical part of the study, outcome interpretation and the writing phase.

Principal investigator:

- **Ahmed Mohamed hesham elzoghary,** BDS: responsible for the clinical part of the study, sample recruitment, follow-up of patients, writing of the thesis and interpretation of results.

Committees:

- Department of Orthodontics and Dentofacial Orthopedics Council
- College Board Committee
- Ethics Committee

II. Introduction

Because malocclusion can undermine self-esteem and physical, social and psychological well-being, many adults pursue orthodontic care to enhance their smile, bite, confidence and quality of

life[1]. Yet a number of patients hesitate, deterred by the long treatment time, the discomfort, the cost and the conspicuous look of conventional buccal fixed appliances[2].

Progress in orthodontic technique has produced discreet alternatives to address these concerns. Lingual appliances are more aesthetic than buccal ones, but practical difficulties limit their use[3]. In 1997 Invisalign® (Align Technology, San Jose, California) turned Kesling's concept into a workable treatment option[4]. Clear aligners — a sequence of removable plastic trays — have grown popular as digital three-dimensional technology and dental materials have advanced; being more comfortable, more aesthetic and less prone to emergencies than fixed appliances[5], they have attracted rising patient demand.

For aligner therapy to count as effective it must correct the original malocclusion and keep the planned and achieved movements closely matched. Many movements nonetheless remain hard to predict[6], so it is important to establish which are performed efficiently and which prove limiting[7]. Several systematic reviews have contrasted the movement accuracy of clear aligners and fixed appliances[8,9], while only a few have looked at the predictability of tooth movement[10,11] or at oral-hygiene outcomes[12].

Orthodontic tooth movement depends on osteoclast- and osteoblast-driven bone remodelling, with bone resorbed on one side of the tooth and deposited on the other. The extent of this remodelling is shaped by several factors:

1. The magnitude and intensity of the force applied, which must be kept within limits that spare the periodontal tissues.
2. The type of movement (controlled or uncontrolled tipping, or bodily movement), each of which remodels bone differently.
3. The morphology of the alveolar bone, since its shape and density govern how it responds.
4. Systemic conditions and medications that alter bone metabolism.

Grasping these changes matters for avoiding iatrogenic harm such as dehiscence (alveolar bone loss that exposes the root surface) and fenestration (window-like defects in the bone). Beyond the bony housing itself, how far and in which direction the incisors tip, and how quickly crowding resolves, are equally central to the safety and efficiency of treatment.

Statement of the problem:

Both Fixed appliances and clear aligners have a negative effect on alveolar bone level[13,14] ,Therefore this study was made to compare the bone level change between clear aligners and fixed appliances in non-extraction treatment of adult patients.

Rationale for carrying out the trial:

To compare, under identical conditions, the change in alveolar bone level and thickness, the mandibular incisor inclination (torque) and the rate of alignment produced by clear aligners versus fixed appliances during non-extraction treatment of adult patients.

Literature Review:

A) Changes in the alveolar bone after levelling and alignment using fixed appliances:

Marcio de Almeida et al. (2015)[15] investigated dentoalveolar changes produced by self-ligating and conventional brackets. Buccal bone thickness and the transversal width of buccal bone were recorded on cone-beam computed tomography (CBCT) with a three-dimensional program (Dolphin) at baseline and again seven months into treatment. In both groups the mandibular buccal bone thickness and the transversal buccal bone width decreased significantly, and buccal bone thickness showed no meaningful relationship with arch expansion. The two bracket systems did not differ significantly in either parameter.

David T. Garlock et al. (2016)[47] set out to measure how the marginal alveolar bone height of the anterior mandible changes after treatment and whether these changes relate to morphological or treatment factors. Fifty-seven matched CBCT scans taken before and after treatment were examined for cortical bone thickness, ridge width, the apex-to-labial-cortex distance and the CEJ-to-crest distance. Vertical bone loss averaged 1.16 ± 2.26 mm facially and 1.33 ± 2.50 mm lingually, varying widely between individuals; baseline cortical thickness, ridge width and particular movements affected the outcome, yet incisor-inclination change showed no significant link to alveolar bone height. Treatment therefore alters the bone around the lower incisors, but these alterations cannot be attributed to inclination alone.

Ibiapina DJ et al. (2016)[16] looked at how the upper arch's transverse dimensions and the buccal bone-plate thickness change during the levelling phase with self-ligating and conventional brackets in sixteen patients. Both groups showed only a small decrease in buccal bone-plate thickness, with no notable difference between the two bracket types.

Shaza Hammad et al. (2018)[17] used CBCT to compare labial alveolar bone thickness in the incisor region during the first treatment phase with self-ligating versus conventional brackets. The labial bone thickness of the upper incisors did not differ significantly between the two groups.

Juliana F. Morais et al. (2018)[18] recorded bone thickness and CEJ-to-crest bone height at the maxillary central incisors, second premolars and buccal roots of the first molars before and after non-extraction alignment. At the incisors and the mesiobuccal root of the first molars, bone thickness fell and bone height rose significantly; arch dimensions widened alongside tipping, bone loss tracked with the amount of crowding and premolar-region expansion, and thinner starting bone was linked to greater apical migration at the incisors. The authors concluded that self-ligating alignment expanded the arch through tipping and produced both horizontal and vertical bone loss at the incisors and first-molar mesiobuccal roots.

Michelle Sendyk et al. (2019)[48] reviewed how alveolar bone thickness changes after non-surgical treatment in adults, searching MEDLINE, EMBASE and LILACS up to July 2018 for prospective clinical studies. Of the twelve eligible studies, most reported thinner alveolar bone after treatment, chiefly on the palatal aspect of the incisors, implying that tooth movement frequently produces a significant loss of bone thickness, especially palatally.

Chung-Chen Jane Yao et al. (2020)[49] studied the alveolar bone surrounding the lower anterior teeth during pre-surgical decompensation in skeletal Class III patients of differing vertical patterns. Twenty-nine patients awaiting two-jaw surgery were grouped by mandibular-plane angle (low, average and high), and pre- and post-treatment CBCT and digital-model data were assessed for bone thickness and height at the apical level. Bone height fell in every group, and facial divergence, incisor irregularity, tooth position, treatment time and inclination change all significantly affected the loss. The authors cautioned that decompensating the lower anterior teeth carries a risk to bone support across all facial types.

Kensuke Matsumoto et al. (2020)[50] used CBCT to examine dehiscence and pre- to post-treatment changes in alveolar bone height and width at the mandibular central incisors of 60 skeletal Class II patients. Greater L1-NB and IMPA values (reflecting proclination) went together with marked vertical bone loss, narrower alveolar bone and a raised dehiscence risk, especially beyond certain limits (L1-NB > 0.71 mm, IMPA > 3.02°); a 2.00 mm L1-NB change or an 8.02° IMPA change carried a 50% probability of vertical bone loss. The authors stressed thorough three-dimensional planning and warned that pronounced incisor movement may call for additional measures to safeguard the periodontium.

B) Changes in the alveolar bone level and thickness after levelling and alignment using clear aligners:

Ibtehal Almagrami et al. (2023)[13] used CBCT to compare, between clear aligners and conventional fixed appliances, both the alveolar bone changes and the frequency and severity of orthodontically induced inflammatory root resorption (OIIRR) at the maxillary incisors. Each approach significantly thinned the alveolar bone and significantly increased OIIRR in the incisor region — more so with fixed appliances — though the OIIRR increase was clinically negligible in most patients. Both also significantly lowered alveolar bone height, the largest reduction occurring labially at the lateral incisors in the aligner group.

Mohamed Abdelaziz Gaafar et al. (2023)[14] used CBCT to assess how clear aligners affect the buccal bone after treatment. Bone thickness was affected only negligibly by either aligners or braces; bone height, however, differed significantly between the groups, decreasing less in the aligner group than in the fixed-appliance group.

Marcio Antonio de Figueiredo et al. (2023)[27] used CBCT to explore how maxillary orthodontic expansion affects the alveolar bone in adults treated with aligners, concluding that, within the study's limits, the mild upper-arch expansion achieved with Invisalign in adults produced no clinically meaningful loss of alveolar bone thickness.

Alasqah et al. (2024)[28] examined the link between clear aligner treatment and alveolar bone height, finding that bone defects increased significantly after treatment. Particular teeth differed markedly before and after treatment, patients who had interproximal stripping also showed significant changes, and the mean differences reached significance for nearly every variable

studied. Participant age correlated positively and significantly with the extent of bone defects both before and after treatment, and pretreatment and posttreatment defects were strongly correlated.

Runzhi Guo et al. (2021)[51] in a systematic review with meta-analysis of alveolar bone change at the maxillary and mandibular anterior teeth during treatment, found that defects such as dehiscence and fenestration generally worsen with incisor retraction and proclination but can partially resolve during retention through favourable long-term remodelling supported by tooth reorientation and natural bone adaptation. The authors underlined the need to control how much and in which direction the anterior teeth are moved so as to protect the alveolar housing.

Claudia Scigliano Valerio et al. (2021)[52] used CBCT to track alveolar bone and interdental bone-septum changes at the mandibular incisors after non-extraction correction of crowding in 32 adults with Class I malocclusion. The CEJ-to-facial-crest distance increased significantly (marginal bone loss), a change tied to the severity of crowding (irregularity index) rather than to the amount of proclination; dehiscence appeared only on the facial side of the incisors, and facial marginal bone changes correlated significantly with changes in the interdental septum. The results imply that crowding severity, not inclination, is the more decisive factor in facial bone loss during alignment.

C) Interproximal enamel reduction:

John J. Sheridan et al.[19] set out guidelines for air-rotor stripping (ARS) to relieve mild-to-moderate crowding, particularly alongside clear plastic appliances such as Essix and Invisalign. He advised removing only a measured amount of enamel (roughly 1 mm) per buccal interproximal site, first opening the contact with a coil spring or separator for access, correcting rotations before stripping, shielding the interdental tissue with an indicator wire, recontouring the proximal surfaces to an acceptable form and smoothing them with phosphoric-acid gel, stripping in sequence while securing anchorage, avoiding pre-emptive stripping and prescribing fluoride to aid remineralisation. He recommended that ARS serve as an adjunct rather than a stand-alone technique.

Jessica Nataly Gómez-Aguirre et al. (2021)[20] examined the consequences of interproximal enamel reduction (IPR) in orthodontics. Following IPR there was no enamel demineralisation, no increase in caries, no periodontal change and no dental sensitivity, and IPR proved quicker than extraction given the length of treatment. The author concluded that IPR can effectively address dental crowding in practice without causing harm.

Zamira Kalemaj et al. (2021)[21] investigated how closely implemented interproximal reduction matches the amount planned in everyday practice, and which factors improve the procedure. Implemented IPR was frequently less than planned, especially at the lower canines and distal surfaces; burs achieved more precise reduction than hand strips, and a measuring gauge improved accuracy. Because several factors influence how IPR is carried out, the author stressed careful execution to keep it accurate.

Giuseppina Laganà et al. (2021)[22] compared the interproximal reduction planned by ClinCheck software with that actually carried out by an orthodontist after aligner treatment. The software

planned an average of 0.62 mm in the upper and 1.92 mm in the lower arch, and the enamel actually removed averaged 0.62 mm maxillary and 1.93 mm mandibular; the mismatch between planned and performed IPR averaged just 0.00 mm upper and 0.01 mm lower. The in-vivo enamel reduction thus matched the ClinCheck plan closely.

Dina Jawhar Butrus et al. (2023)[23] examined enamel surface nanotopography after interproximal reduction, quantified its effect on surface roughness and asked whether polishing with topical fluoride is needed. None of the IPR procedures materially altered enamel nanotopography, whether or not polishing was performed, and polishing meaningfully reduced roughness only in the disc group.

D) Clear aligners:

Neal D. Kravitz et al. (2009)[24] measured how accurately removable polyurethane aligners (Invisalign) move teeth. Overall accuracy averaged 41%; lingual constriction was most accurate (47.1%) and extrusion least accurate (29.6%) — particularly for the maxillary (18.3%) and mandibular (24.5%) central incisors — followed by mesiodistal tipping of the lower canines (26.9%). Canine rotation was far less accurate than other movements and fell off sharply beyond 15°, lingual crown tip outperformed labial crown tip, and same-type maxillary and mandibular teeth did not differ significantly in accuracy.

Gabriele Rossini et al. (2015)[4] reviewed the evidence on how well clear aligners control tooth movement. Aligners levelled and aligned the arches, controlled anterior intrusion but not extrusion, controlled posterior but not anterior buccolingual inclination, achieved upper-molar bodily movement of roughly 1.5 mm, and were notably poor at rotating rounded teeth. Given the number, quality and variability of the studies, the authors urged that these findings be read cautiously.

Alissa F. Borda et al. (2020)[25] contrasted the effectiveness and efficiency of fixed appliances and clear aligners in teenagers with mild malocclusion. Both worked similarly well, but aligners gave significantly better tooth alignment, occlusal relations and overjet, and came out ahead once the number of appointments, emergencies and total treatment time were taken into account.

Alessandra Putrino et al. (2021)[53] reviewed recent developments in clear aligner systems, concentrating on key features such as materials, gingival-margin design, attachments, divots and auxiliaries, selecting 31 relevant studies from a database search. Aligners have diversified and evolved considerably, gaining efficiency and wider clinical use, though topics such as gingival-margin design and auxiliaries remain under-studied. The authors stressed the value of extending research beyond the dominant Invisalign system to confirm the performance of the many competing aligner brands.

Byron Chou et al. (2023)[26] compared the efficacy and efficiency of clear aligners and fixed appliances in adolescents with Class I and II moderate-to-severe malocclusions, analysing 72 cases from one orthodontist (47 aligner, 25 fixed) matched for baseline features, Discrepancy Index and Cast Radiograph Evaluation scores. Outcomes did not differ significantly, but aligner cases finished significantly sooner (24 versus 27 months on average) with fewer scheduled visits (16

versus 24), while emergency visits were comparable. Both modalities were therefore equally effective, aligners being more efficient in time and number of visits.

Mariana Paes Muro et al. (2023)[54] reviewed 33 studies — mostly non-extraction Invisalign cases — to gauge the effectiveness and predictability of clear aligner therapy. Aligners handled mild-to-moderate crowding and improved malocclusion well, but predictability varied by movement: buccolingual tipping was highly accurate whereas rotation, intrusion and extrusion were less dependable and overbite correction was limited. The authors warned that clinical predictability is often overstated, urging realistic expectations, careful case selection and research beyond a single aligner system.

E) Rate of alignment and levelling using Little's Irregularity Index:

Little RM (1975)[35] devised a quantitative way to gauge mandibular anterior irregularity by measuring directly on the lower cast with a calliper graduated to tenths of a millimetre and held parallel to the occlusal plane. The Irregularity Index adds together the linear displacements of the five adjacent anatomic contact points of the lower incisors; tests of its reliability and validity were favourable, and the index has since been applied in many trials to assess the dentition before, during and after treatment.

Canuto et al. (2010)[36] studied, retrospectively in 23 patients (mean starting age 13.36 years), the long-term stability of upper incisor alignment after non-extraction fixed-appliance treatment. Casts were measured before treatment (T1), after treatment (T2) and three years later (T3) for the Little Irregularity Index, the intercanine, interpremolar and intermolar widths and arch length and perimeter, using one-way ANOVA with Tukey tests. Most arch dimensions stayed stable, but upper incisor crowding relapsed substantially (about 1.52 mm) over the long term.

Zafarmand et al. (2014)[37] explored which variables relate to recurring anterior crowding in first-premolar extraction and non-extraction cases. The arch Irregularity Index was measured on study models of 40 patients (21 extraction, 19 non-extraction) before treatment (T1), after treatment (T2) and after retention (T3), with the Wilcoxon test for within-group and the Mann–Whitney test for between-group differences. The mean starting index (7.23 mm extraction, 6.13 mm non-extraction) dropped to 0 mm after treatment and rose again at post-retention to 2.11 mm and 1.65 mm, the changes being significant to the same degree in both groups.

Ghaffar et al. (2022)[38] tested whether low-level laser therapy speeds the resolution of mandibular anterior crowding by timing overall levelling and alignment with Little's Irregularity Index after the first archwire. Thirty-two women aged 18–25 with lower anterior crowding, an Angle Class I molar relationship and an index of 4–10 mm were randomised to laser or control groups, with computational models tracking the index. The laser group showed a markedly higher average improvement in alignment and lower pain scores than the controls.

Jahanbin et al. (2019)[39] compared how efficiently Damon-3 self-ligating and MBT pre-adjusted brackets align teeth in the early stage. Upper dental irregularity improved significantly more over

the four-month alignment period with the self-ligating brackets than with the conventional ones, while bracket type made no difference to the pain reported during alignment.

Alrasheed et al. (2022)[55] tested how reliably Little's Irregularity Index, tooth-size arch-length discrepancy and Bolton ratios can be read from intraoral photographs and photographs of plaster models, using 52 arches from 26 patients with a manual calliper on the casts as reference. Agreement was high for both intraoral photographs (intraclass correlation 0.90–0.99) and plaster-model photographs (0.88–0.99), showing that these parameters can be measured accurately and consistently from photographs of the arches.

Yassir et al. (2019)[56] compared treatment quality between 0.018-inch and 0.022-inch slot MBT appliances in patients aged 12 and over, using block randomisation (77 in the 0.018-inch and 76 in the 0.022-inch group, mean age 19.1 years). Incisor inclination improved on average by 2.9° versus 1.6° for the upper incisors and 2.7° versus 1.4° for the lower, mean ABO CR-EVAL scores were 34.7 and 34.5, and PAR reductions averaged 74.1% and 77.1%. The authors found that occlusal-outcome consistency, incisor inclination and the patient experience were neither statistically nor clinically different between the two slot sizes.

Detterline et al. (2010)[57] used the American Board of Orthodontics Objective Grading System to compare cases finished with 0.018-inch and 0.022-inch slot brackets. The 0.018-inch slot gave significantly shorter treatment times and lower ABO-OGS scores across four categories (alignment/rotations, marginal ridges, overjet and root angulations) and a lower total, remaining lower than the 0.022-inch slot for alignment/rotation and total score after ANCOVA. The authors judged these differences, though statistically favouring the 0.018-inch slot, to be clinically unimportant.

F) Mandibular incisor inclination and alignment: clear aligners versus fixed appliances:

Hennessy et al. (2016)[40] compared how much the lower incisors proclined under fixed labial appliances versus third-generation clear aligners (Invisalign) in adults with mild crowding. Patients with a Class I skeletal pattern and under 4 mm of lower crowding were randomised by sealed envelope, and inclination change was read from pre-treatment and near-end lateral cephalograms in 44 evenly split patients (mean age 26.4 years) of comparable baseline. Fixed appliances proclined the incisors by 5.3° on average and aligners by 3.4°, a non-significant difference, indicating that the two approaches procline the incisors similarly in mild crowding.

Papageorgiou et al. (2016)[41] assessed the torque efficacy of square and rectangular archwires in 0.018-inch and 0.022-inch conventionally ligated brackets of a single prescription. Brackets were mounted on identical acrylic-resin maxilla models on the Orthodontic Measurement and Simulation System, several stainless-steel wires were tried in each slot, and moments were logged after 15° of buccal root torque was applied gradually to the right central incisor. Rectangular archwires expressed torque more effectively, particularly in the 0.018-inch slot.

Mittal et al. (2015)[58] conducted a retrospective study of whether final upper and lower anterior inclinations differ between Roth and MBT pre-adjusted edgewise prescriptions, comparing the

torque each achieved. Analysis of 40 post-treatment casts (20 Roth, 20 MBT) from well-finished cases showed that the MBT and Roth prescriptions ended with essentially the same final inclinations of the upper central incisor, lower central incisor and upper canine.

Piva et al. (2020)[59] examined the effective torque of four prescriptions (MBT, Roth, Damon and Edgewise) on plaster models from 30 patients with ideal torque by bonding 0.022 × 0.028-inch tubes and measuring the play between the tubes and 0.019 × 0.025-inch or 0.021 × 0.025-inch stainless-steel wires. Across all prescriptions the 0.019 × 0.025-inch wire held torque better than the 0.021 × 0.025-inch wire, and the Roth prescription gave effective-torque values nearest zero (least average change); expressed torque thus varies with prescription and wire size, directly affecting anterior inclination control.

Gu et al. (2017)[42] compared the effectiveness and efficiency of Invisalign and conventional fixed appliances in mild-to-moderate cases using the Peer Assessment Rating (PAR) index, on matched pretreatment and posttreatment records of 48 Invisalign and 48 fixed-appliance patients. Baseline PAR and the PAR reduction did not differ between groups, but Invisalign finished 5.7 months sooner on average, while logistic regression showed Invisalign patients were significantly less likely to reach "great improvement." The authors concluded that both are effective, with fixed appliances offering better optimal results and Invisalign greater time efficiency.

Ke et al. (2019)[43] asked whether clear aligners match conventional fixed appliances in a systematic review of studies to August 2018, of which eight comparative studies (two RCTs and six cohort studies) qualified. Aligners appeared less able than braces to achieve proper occlusal contacts, control torque, widen the arch and hold retention, yet Objective Grading System scores did not differ significantly and aligners shortened treatment significantly. The authors concluded that both effectively correct malocclusion, with aligners adding the advantages of segmented movement and shorter treatment.

Yassir et al. (2022)[44] appraised the current evidence on clear aligner effectiveness in an overview of systematic reviews, screening 361 reviews and retaining 18 of moderate-to-high quality published to July 2021. Aligners suited mild-to-moderate malocclusion but were less favourable for severe or complex cases; treatment-duration results were mixed (possibly shorter for simpler cases), and aligners offered better periodontal health, lower root-resorption risk and greater comfort but more relapse, with unclear pain findings and less interference with eating. With the evidence rated moderate overall, the authors held that aligners are a viable alternative to fixed appliances for mild-to-moderate cases and called for more high-quality randomised trials.

G) Reliability of CBCT for assessment of dento-skeletal parameters:

Vandana Kumar et al. (2008)[31] compared cephalometric measurements from CBCT-synthesised lateral cephalograms (built with both orthogonal and perspective projections) against conventional lateral cephalograms in 31 patients whose CBCT data were handled in Dolphin 3D. Twelve linear and five angular measurements from each source were compared by repeated-measures ANOVA ($\alpha = 0.01$), with no significant differences except the Frankfort–mandibular plane angle ($P < .0001$)

— evidence that CBCT-derived measurements match conventional radiographs closely and that separate 2D imaging may be unnecessary when a volume already exists.

Baumgaertel et al. (2009)[60] tested the reliability and accuracy of dental measurements taken from CBCT reconstructions of 30 human skulls. Ten parameters (overbite, overjet, intermolar and intercanine widths, arch length and others) were measured both directly on the skulls with a precise digital calliper and digitally on the CBCT images. Both approaches were highly reliable (intraclass correlations above 0.90); CBCT slightly underestimated the true values, but only significantly when several measurements were pooled, so CBCT measurements are reliable apart from minor, correctable systematic error.

Agrawal et al. (2013)[32] reviewed how CBCT is used throughout orthodontics, from diagnosis to planning — locating impacted teeth accurately, readily identifying and classifying root resorption, and placing orthodontic implants precisely relative to nearby structures. The authors noted that CBCT volumes can be turned into a lateral cephalogram with an adjustable head position, permit soft-tissue, airway and TMJ evaluation and yield 3D study models without alginate impressions, and that Invisalign aligners, indirect bonding trays and custom brackets and wires can all be built from CBCT data.

Ruellas et al. (2016)[61] showed that CBCT yields accurate, precise measurements without image magnification and is well suited to evaluating growth and treatment outcomes through careful comparison of three-dimensional images. Rather than depending on linear or curved measurements, CBCT registration draws on numerous anatomical points, shapes and volumetric data, so superimposing surface models lets clinicians follow craniofacial growth, gauge treatment change, judge long-term stability and spot early anatomical change; comparing images from different time points also quantifies the size and direction of skeletal or dental displacement.

Verónica García-Sanz et al. (2017)[62] evaluated CBCT's reliability and accuracy for measurements made with soft tissues present, using six embalmed cadaver heads from which the condyles were later removed. Condylar volume was measured by water displacement and three linear dimensions by digital calliper (the reference), while 3D-scanner surface models were superimposed on the CBCT reconstructions to isolate the condyles. CBCT was highly reliable for both volume and linear measurements (coefficients of variation under 3%, intraclass correlations above 0.90) and agreed closely with the reference, confirming its accuracy for linear and volumetric assessment.

Gianluca Gambarini et al. (2018)[33] noted that fenestration is a fairly frequent finding and argued that CBCT should therefore precede any surgical, implant or orthodontic treatment to avoid complications from pre-existing fenestrations, concluding that CBCT is an effective and convenient means of diagnosing fenestration.

Dandan Song et al. (2021)[34] reported that CBCT surpasses intraoral imaging in diagnostic accuracy and reliability for detecting, classifying and measuring peri-implant bone defects,

supplying diagnostic and decision-making information that conventional intraoral imaging cannot provide.

H) Reliability of scanned and digital models:

Nalcaci et al. (2014)[29] checked the reliability of measurements taken after superimposing three-dimensional digital models by comparing them with lateral cephalometric radiographs and photocopied plaster models for assessing upper-molar distalisation. The amount of molar distalisation did not differ significantly among the three methods, so 3D digital models reliably capture upper-molar distalisation and are a valid alternative to conventional measurement.

L. S. Lemos et al. (2015)[30] assessed the reliability of measurements on digital casts scanned with the 3Shape R700 scanner, which reproduces surfaces with a non-destructive laser and leaves the plaster cast intact. Across 26 casts, six linear measurements on the plaster were compared with the same measurements on the digitised models, and the digital models proved reliable and an acceptable alternative to plaster casts for orthodontic measurement and analysis.

Hayashi et al. (2013)[63] examined the accuracy and reliability of new three-dimensional scanners and found the TRIOS (3Shape) scanner highly accurate and dependable; a further comparison put it ahead of the iTero, leading to the conclusion that the TRIOS is a suitable device for capturing a patient's dental structures.

Kim & Lagravère (2016)[64] compared Bolton analysis performed on digital models from Ortho Insight 3D laser scanning against plaster models and CBCT images in 50 patients. CBCT was analysed in AVIZO, the plaster models measured with a digital calliper and the Bolton ratios computed in Ortho Insight 3D; for judging the spatial relationship of the arches, the laser-scanned digital models proved significantly more accurate than either the physical models or CBCT.

Tomita et al. (2018)[65] compared the accuracy of digital models from intraoral scanning with desktop scans of conventional impression/plaster models, using a contact coordinate-measuring machine to fix the reference distances between ceramic spheres on epoxy models. Alginate and silicone impressions were cast and desktop-scanned, digital models were also captured intraorally, and twelve linear-distance combinations were measured on each; overall the three groups differed little, but across five linear distances the intraoral-scan group was more accurate than the impression-based groups, suggesting intraoral scans may exceed scans of conventional impressions in accuracy.

Adel et al. (2022)[66] assessed how accurately three 3D digital-model registration programs measure linear tooth movement relative to a 3D digital virtual setup. Pre-treatment upper and lower scans from twenty aligner patients were turned into digital setups in OrthoAnalyzer, then the setups and pre-treatment scans were imported as STL files into three programs (Geomagic, OrthoAnalyzer and Compare) to detect linear tooth-position changes. None of the three programs agreed poorly with the digital setup on any movement metric, and agreement was best for buccolingual movements.

Database research:

A search was performed on electronic databases (PubMed, Cochrane Library).

III. Aim of the study

The aim of this study is to compare the bone level change between clear aligners and fixed appliances in non-extraction treatment of adult patients.

A- PICO format:

Patient / Population: adult patients having mild-to-moderate mandibular anterior crowding (2–6 mm).

Intervention: clear aligners.

Comparator: fixed orthodontic appliance.

Outcome: change in alveolar bone level and thickness, mandibular incisor inclination (torque) and rate of alignment.

B- Research question:

Do clear aligners and fixed appliances differ in the change in alveolar bone level and thickness, mandibular incisor inclination and rate of alignment during levelling and alignment of non-extraction adult cases?

IV. Objective of the study

Research hypothesis:

The null hypothesis of this research is that there is no difference between clear aligners and fixed appliances in the change in alveolar bone level.

Primary objective:

– To evaluate the change in alveolar bone level.

Secondary objectives:

– To evaluate the change in alveolar bone thickness.

– To evaluate the change in mandibular incisor inclination (torque).

– To evaluate the rate of alignment.

Study design:

Randomized clinical trial (two-arm, parallel-group, 1:1 allocation).

Outcomes:

	Outcome	*Method of measurement*	*Unit of measurement*
Primary	Alveolar bone level	Cone-beam CT (OnDemand software)	Millimetres
Secondary	Alveolar bone thickness	Cone-beam CT (OnDemand software)	Millimetres
	Mandibular incisor inclination (torque)	Cone-beam CT (Invivo / Anatomage software)	Degrees
	Rate of alignment	Little's Irregularity Index on superimposed scanned models	Millimetres

V. Methods (participants, interventions and outcomes)

Study settings:

The study will be performed in the outpatient clinic of the Department of Orthodontics and Dentofacial Orthopedics, Faculty of Oral and Dental Medicine, Future University in Egypt. The recruited sample will be drawn from the Egyptian population.

Eligibility criteria:

Inclusion criteria:

(a) Adult patients, 18–25 years of age, of both genders, with mild-to-moderate mandibular anterior crowding (2–6 mm).

(b) Angle Class I molar relationship with normal overjet (1–3 mm) and overbite (1–2 mm).

(c) Full permanent dentition with a healthy periodontium.

(d) Normal anteroposterior and vertical skeletal pattern.

Exclusion criteria:

(a) Any local or systemic problem or trauma that may affect the growth and development of the facial structures.

(b) History of previous orthodontic or interceptive treatment.

(c) Loss of periodontal attachment.

(d) Craniofacial anomalies, facial asymmetry or skeletal discrepancy.

Intervention:

A) **Medical History Questionnaire** will be completed by the patient to exclude any systemic condition.

B) **Clinical Examination:** the oral structures will be examined for caries, fracture or missing teeth, and the gingival tissues for gingivitis, periodontitis, attachment loss, recession, lesions and gingival biotype.

C) Diagnosis: the patient will be checked against the inclusion criteria and a full set of records will be taken as part of the routine treatment procedure.

D) Clinical procedure:

Group I (Fixed appliances) (FA):

In Fixed appliance group. Brackets of the preadjusted edgewise type (0.022-inch slot, MBT prescription; American Orthodontics, Sheboygan, Wis) will be bonded from first molar to first molar in both arches after conventional acid etching. Leveling then will be proceeded through a set archwire progression—0.014-inch NiTi, 0.016-inch NiTi, 0.016 × 0.022-inch NiTi, and 0.017 × 0.025-inch stainless steel—each wire will be kept in place and replaced at the following visit once the heavier wire will be fully engaged.

Group II (Clear aligners) (CA):

Each arch will be scanned intraorally (TRIOS 5; 3Shape, Copenhagen, Denmark), and the case will be set up in dedicated software (Ortho Analyzer; 3Shape) with the tooth movements stagging and attachments will be positioned to suit the intended corrections. Working models will be printed by digital light processing (Photon Mono X; Anycubic, Shenzhen, China); on these, aligners will be thermoformed (CA Clear Aligner sheets; Scheu-Dental, Iserlohn, Germany) using a positive-pressure machine (Ministar; Scheu-Dental) and then trimmed. Attachments will be placed with flowable composite through templates, and every aligner was worn for 14 days. Interproximal reduction will be carried out in either arm with motor-driven double-sided strips and gauge confirmation.

Evaluation of bone level and thickness on CBCT:

The axial, coronal and sagittal planes of the CBCT volume will be reoriented perpendicular to the long axis of each assessed tooth, the long axis being defined as the line connecting the incisal midpoint to the centre of the apical foramen. From the axial view, a reference line is drawn connecting the labial and lingual cemento-enamel junction (CEJ). Labial and lingual alveolar bone thickness (ABT) will be measured at 3, 6 and 9 mm apical to the CEJ (crestal, mid-root and apical thirds). Alveolar bone level (ABH) will be measured from the CEJ to the alveolar crest on the labial and lingual sides of the mandibular central incisors, lateral incisors and canines. Alveolar bone level and thickness are assessed on two CBCT scans only – one taken before bonding and aligner delivery (T0) and one taken after completion of levelling and alignment, within six months (T3) – and the change between the two is calculated; limiting CBCT to these two time points minimises radiation exposure.

Evaluation of mandibular incisor inclination (torque) on CBCT:

The DICOM files will be analysed in Invivo (Anatomage) software. Bony landmarks (right and left antegonial notches and menton, defining the mandibular plane) and dental landmarks (incisal/cusp point, apex and centroid of each mandibular incisor and canine, defining each long axis) will be located on the 3D volume and refined on the axial, sagittal and coronal slices. Incisor inclination

(torque) is measured as the inner angle between each tooth's long axis and the mandibular plane on the sagittal view, before (T0) and after treatment (T3).

Evaluation of the rate of alignment:

The rate of alignment will be measured over the six-month levelling and alignment period from four sets of records taken at four time points – T0 (baseline), T1, T2 and T3 – at eight-week intervals, giving four mandibular impressions (or digital scans) taken every eight weeks (that is, at alternate follow-up visits). For each record, landmarks are identified in 3Shape Ortho Analyzer software and Little's Irregularity Index – the sum of the linear displacements of the five anatomic contact points of the mandibular anterior teeth from canine to canine – is measured. The reduction in the index between successive time points, and the percentage improvement from T0 to T3, describe the rate of alignment.

Follow-up period:

Follow-up for both the fixed-appliance and clear-aligner groups will be every 4 weeks. At each visit, progress is monitored, the fixed appliances are activated or the next set of aligners is delivered, any required interproximal reduction is performed, and oral-hygiene measures are reinforced. For the clear-aligner group, each set of aligners is fabricated in the departmental laboratory ahead of the scheduled visit so that it can be delivered at the four-weekly appointment.

E) Oral Hygiene Measures: scaling and polishing to maintain healthy gingiva and demonstration of oral-hygiene measures for both groups. Retainers will be provided and a one-year post-treatment evaluation advised.

F) Criteria for discontinuing or modifying allocated interventions:

- If the patient does not comply with aligner wear, wear is prolonged until the desired movement is achieved.
- If the patient does not attend for longer than three months and cannot be contacted, the intervention is discontinued.

G) Methods of measuring all outcomes: linear and angular measurements will be made on the pre-, post- and follow-up scanned casts and on the CBCT to assess bone level and thickness, incisor inclination and the rate of alignment.

H) Blinding: owing to the nature of the study, the operator and patients cannot be blinded. The outcome assessors will be blinded by concealing the patient's name on the pre- and post-treatment records used for analysis.

VI. Sample size

Statistical methods:

Categorical data will be represented as frequency (n) and percentage (%) and analysed using the chi-square test. Numerical data will be explored for normality by inspecting the distribution and applying the Kolmogorov–Smirnov and Shapiro–Wilk tests. Normally distributed data will be

presented as mean and standard deviation and analysed with the independent t-test; data violating normality will be presented as median and range and analysed with the Mann–Whitney U test. The significance level will be set at $p \leq 0.05$ for all tests. Statistical analysis will be performed with R statistical analysis software version 4.3.2 for Windows[45].

Sample size calculation:

A power analysis was designed to have adequate power for a two-sided test of the null hypothesis of no difference between groups in bone-level change. Adopting an alpha (α) of 0.05, a beta (β) of 0.2 (power = 80%) and an effect size (d) of 1.55 derived from a previous study[46], the required sample was 16 cases (8 per group). The sample was increased by 20% to compensate for possible dropout during follow-up, giving 20 cases (10 per group). The calculation was performed with R statistical analysis software version 4.3.2 for Windows[45].

VII. Data collection, management and analysis

Patients will be recruited from the clinic of the Department of Orthodontics at Future University in Egypt. Data for the primary and secondary outcomes will be collected from intra oral scans and CBCT taken before and after treatment.

Plans to promote participant retention and complete follow-up:

- Telephone numbers of all included patients will be recorded as part of the written consent.
- All patients will receive reminder telephone calls at the predetermined follow-up dates.
- Punctuality and the number of missed appointments will be monitored regularly.

Data management:

- All data – photographs, models and radiographs – will be entered electronically at the Department of Orthodontics and Dentofacial Orthopedics.
- Data from cast analysis will be organised in spreadsheets and backed up on secure cloud storage for permanent retention.
- Patient data will carry sequential ID numbers, revised at each step to avoid any mixing of data between patients.

Statistical analysis:

The principal investigator will extract the required data from the intra oral scans taken before, during and after treatment and cbcts taken before and after treatment and the data will be sent to a specialised statistician for analysis.

VIII. Monitoring

A) Data monitoring:

Monitoring will be conducted periodically by the supervisors, who will oversee all steps of the protocol and resolve any problems arising during the trial.

B) Harms:

Any harm occurring before entry to the study will be reported as unrelated; harm occurring after entry will be recorded and documented by the principal investigator, and its severity and potential causal relationship to the intervention addressed.

C) Auditing:

The supervisors will review the interventions and resulting data and will periodically follow the trial's progress, including recruitment, adherence to interventions and reporting of harms; meetings with the senior supervisor will be held to monitor progress and any needed adjustments.

Research ethics approval:

This protocol and the template informed-consent form will be reviewed by the Ethics Committee of Scientific Research, Faculty of Oral and Dental Medicine, Future University in Egypt.

Protocol amendments:

Any modification that may affect the conduct of the study, the potential benefit to the patient or patient safety will require a formal amendment agreed by the Department of Orthodontics and Dentofacial Orthopedics and approved by the Ethics Committee before implementation.

Consent:

The principal investigator will provide a detailed explanation of the study interventions to each patient and will obtain a written consent, in Arabic, before treatment begins.

Confidentiality:

Personal information collected during the study will be stored separately from the study records in locked files accessible only to the supervisors responsible for auditing and analysis, and all reports and forms will be identified by a coded ID number. Participant information will not be used outside the study except with the participant's written permission.

Declaration of interests:

No financial interests are declared by the supervisors or the principal operator. This study is part of a Master's degree in Orthodontics, Faculty of Oral and Dental Medicine, Future University in Egypt, and is self-funded by the principal investigator.

Ancillary and post-trial care:

Any complication associated with the intervention will be managed by the principal operator, after which patients will continue their regular orthodontic treatment according to the treatment plan.

Dissemination policy:

The trial results will be made available to participants, healthcare professionals and the public through publication in high-quality national and international journals; a copy of the thesis will be deposited in the Future University library and distributed to the main universities in Egypt.

IX. References

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