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Title- A comparison of mandibular incisor proclination when using clear aligners and fixed labial orthodontic brackets

Submitted in accordance with the requirements for the degree of Clinical Doctorate in Dental Surgery (Orthodontics)

Trinity College Dublin, Dublin Dental University Hospital

2015

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- Dr Ebrahim Al-Awadhi

Declaration

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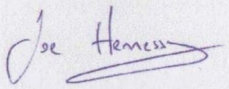

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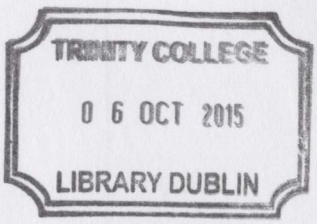

Summary

Title- A randomised clinical trial comparing mandibular incisor proclination produced by fixed labial appliances and clear aligners.

Introduction- The objective of this '2-arm parallel' clinical trial was to compare the mandibular incisor proclination produced by fixed labial appliances and 3rd generation clear aligners.

Methods- Patients underwent a course of orthodontic treatment using fixed labial appliances or clear aligners (Invisalign®). Mandibular incisor proclination was measured by comparing pre-treatment and near end treatment lateral cephalograms. Eligibility criteria included adult patients with mild mandibular incisor crowding (<4 mm) and Class I skeletal bases (ANB 1-4°). The main outcome was the cephalometric change in mandibular incisor inclination to the mandibular plane at the end of treatment. Eligible patients picking a sealed opaque envelope, which indicated their group allocation, was used to achieve randomization. Data were analysed using a Welch two sample t-test.

Results- Forty-four patients (mean age 26.4 ± 7.7 years) were randomised in a 1:1 ratio to either the fixed labial appliance or the clear aligner group. Baseline characteristics were similar for both groups, fixed appliance mean crowding- 2.1 ± 1.3 mm vs clear aligner mean crowding 2.5 ± 1.3 mm, pre-treatment mean mandibular incisor inclination for the fixed appliance group 90.8 ± 5.4° vs 91.6 ± 6.4° for the clear aligner group. Seven patients (5 clear aligner and 2 fixed

appliance) were excluded from the study due to compliance issues. Fixed appliances produced 5.3 ± 4.3° of mandibular incisor proclination. Clear aligners proclined the mandibular incisors by 3.4 ± 3.2°. The difference between the two groups was not statistically significant (p >0.05).

Conclusion- There was no significant difference in the amount of mandibular incisor proclination produced by clear aligners and fixed labial appliances in mild crowding cases.

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1 Introduction

Clear aligners have been introduced as an aesthetic alternative to fixed labial appliances. Over the years these appliances have evolved in an attempt to achieve improved tooth alignment and occlusion. There have been three generations of aligners. The first generation aligners were solely reliant on the removable appliance to move teeth. Following this, a second generation of aligner depended more on attachments being bonded to teeth. The most recent, third generation, has been modified to place different shaped attachments automatically where difficult tooth movements are required. Although fixed appliances have been the backbone of orthodontics for years, patient demands have been the driving force for the development of clear aligners. In addition to improved aesthetics it has been reported that clear aligners are less painful, allow for improved oral hygiene and cause less root resorption than conventional fixed appliances(Miethke and Brauner, 2007; Miller *et al.*, 2007; Barbagallo *et al.*, 2008; Jeremiah *et al.*, 2011).

Despite over 15 years of commercial availability and many millions of cases treated worldwide, very little research has assessed how clear aligners achieve their results. From the available studies, clear aligners would appear to have poorer clinical results when compared to fixed appliances. The aligners ability to extrude, derotate and torque teeth has been questioned (Djeu *et al.*, 2005; Kravitz *et al.*, 2009; Krieger *et al.*, 2011; Krieger *et al.*, 2012). It has, however, been suggested that they can accurately retrocline teeth (Kravitz *et al.*, 2009).

Mandibular incisor proclination is often an unwanted side effect of orthodontic treatment. Excessive proclination can cause poor aesthetics, gingival recession and unstable results. Many studies have compared the amount of lower incisor proclination produced by different orthodontic appliances (Toth and McNamara, 1999; Gill and Lee, 2005; Pandis *et al.*, 2007; Scott *et al.*, 2008). The effect of clear aligners on incisor proclination, however, has yet to be determined. Case reports account for the majority of the literature available with regards to clear aligner treatment. A limited number of poorly designed clinical trials have appraised the ability of aligners to move teeth (Djeu *et al.*, 2005; Kravitz *et al.*, 2009; Krieger *et al.*, 2011; Krieger *et al.*, 2012). This research compares the mandibular incisor proclination produced by fixed labial brackets and 3rd generation clear aligners (Invisalign®, Align Technology Inc, Santa Clara, CA, USA) when treating patients with mild mandibular crowding.

2 Literature Review

2.1 Fixed appliances and tooth movement

Fixed orthodontic appliances have evolved since Angle described the edgewise bracket in 1928 (Angle, 1928). Initially the slot was placed vertically in the bracket, until he realised more control of tooth movements could be obtained by placing the slots horizontally. Three-dimensional control of a tooth was achieved by using a rectangular wire within a rectangular slot. The standard edgewise system had a number of disadvantages, not least the fact that a passive bracket resulted in a requirement for complex wire bending during finishing procedures. These bends also ensured space closure needed to be undertaken using closing loops.

Begg was the next to develop a bracket system, basing it on the concept of differential force (Begg, 1956). His appliance worked by using elastics to tip crowns to their correct positions and then uprighting their roots with auxiliary springs. It relied on round archwires which made finishing procedures complex and time consuming. Kesling, in the 1980s, attempted to resolve some of these problems by creating the Tip-Edge appliance® (TP Orthodontics, Inc, 100 Center Plaza, La Porte, Indiana 46350-9672, USA)(Kesling, 1988). Although this system again tips teeth in the early stages of treatment it allows for the use of rectangular archwires, which are essential when three-dimensional control is required.

Lawrence Andrews was the next to produce a new fixed orthodontic appliance (Andrews, 1979). His system was based on the idea of having prescribed brackets, for each tooth, that moved the teeth into their respective ideal positions. This removed the need for the majority of the wire bends that were required when using the original edgewise appliance. A number of different prescriptions are available for these brackets and this is now the most widely used system in modern orthodontics.

More recently, the use of self-ligating brackets has become popular. Stolzenberg created the original self-ligating bracket in the 1930s (Stolzenberg, 1946). A number of proposed advantages, such as quicker treatment times and more secure ligation of the archwire, have been suggested with the use of these appliances but very few have been scientifically verified (Chen *et al.*, 2010). There are two types of self-ligating brackets, active and passive. Active brackets have a spring-loaded ligation mechanism which presses against the wire when closed. The passive clip does not encroach on the bracket slot lumen and therefore the clip doesn't place a force on the wire.

The theory of how fixed appliances move teeth has created a degree of controversy over the years. There are two types of tooth movements that can be achieved with a fixed appliance. Tipping movements, where the crown moves while the tip of the root stays stationary, and bodily movement where the crown and root move in unison (Profit *et al.*, 2013). It was assumed that the type of movement produced depended on the relation of the applied force to the centre of resistance and the

location of the centre of rotation of the tooth (Isaacson *et al.*, 1993). The centre of resistance is defined as that point on the tooth where, if a single force passed through, pure translation would result (Burstone and Pryputniewicz, 1980). It has been determined for a single rooted tooth the centre of resistance is one third the root length apical to the alveolar crest along the long axis of the root (Burstone and Pryputniewicz, 1980). The centre of rotation is the point about which a body appears to have rotated, as determined from its initial and final positions (Smith and Burstone, 1984). This point will change depending on the force being applied. To achieve pure bodily movement, the applied force must pass directly through the centre of resistance, however forces are usually applied to attachments on the buccal surfaces of teeth making the force coronal and peripheral to the centre of resistance (Iwasaki *et al.*, 2000).

Smith and Burstone described two possible ways force can be applied to a tooth (Smith and Burstone, 1984). A single force can be applied, acting away from the centre of resistance, which is called the 'moment of force' (Isaacson *et al.*, 1993). This force can cause the tooth to tip around the centre of rotation. The second method by which force can be applied is by a pair of equal forces which are parallel and in opposite directions, termed a 'force couple' (Isaacson *et al.*, 1993). With this force application the centre of rotation equals the centre of resistance (Isaacson *et al.*, 1993). As fixed appliances are not able to apply a force directly through the centre of resistance, bodily movement could only be achieved by applying a force at the attachment in the direction of the required movement while at the same time having a counter movement

to prevent tipping (Isaacson *et al.*, 1993). It was Isaacson *et al* who first suggested that pure bodily movement was impossible to achieve and that bodily movements actually occur through a series of tipping and uprighting movements, where crown movement (moment of force) exceeds root movement (moment of couple) and then root movement exceeds crown movement (Isaacson *et al.*, 1993).

2.2 History of Clear Aligners

The theory of using an aligner to straighten teeth was first postulated in the 1940s. In 1945, Kesling produced a tooth positioning appliance to refine the final stages of orthodontic treatment (Kesling, 1946). This positioner was a piece of pliable rubber manufactured from a laboratory wax up of the teeth in class I occlusion (Phan and Ling, 2007). This appliance allowed for minor tooth movements to be achieved while maintaining the alignment of the remaining teeth in the arch. Kesling foresaw that more ambitious tooth movements could be realised with a series of aligners while recognising the limitations of the technology available to him at the time:

" Major tooth movements could be accomplished with a series of positioners by changing the teeth on the setup slightly as the treatment progresses. At present this type of treatment does not seem to be practical. It remains a possibility, however, and the technique for its practical application might be developed in the future" (Kesling, 1946)

Thirty years later, Ponitz introduced an "Invisible Retainer" which used Kesling's idea of prepositioning teeth on a master study model (Ponitz, 1971). Again this appliance could only produce minor tooth movements.

In the early nineties Sheridan described a technique of using clear aligners in conjunction with interproximal tooth reduction (Sheridan *et al.*, 1993). The principle of producing minor tooth movements with individual aligners had not changed. A new 'Kesling set up' was required for every tooth movement and therefore a new impression was taken at almost every visit. This process demanded a large amount of clinical and laboratory time.

In 1999, Align technology released their Invisalign® system. It was the first orthodontic appliance to use computer-aided design (CAD) and computer-aided manufacturing (CAM). Instead of requiring a new impression for each tooth movement, this technology allows for multiple tooth set-ups to be created from a single impression (Hajeer *et al.*, 2004). The advent of this digital process removed the impracticality of previous aligner systems and made Kesling's concept a reality. Other aligner systems use similar principles to achieve their results (Jones *et al.*, 2009) (Table 1). These systems have evolved over time.

Table 1- Clear aligner manufacture

Name of appliance	Country of origin	3D technology used	Website	Attachments	How many aligners	Generation	Average Price
Clear aligner™	UK	Laser	www.clearaligner.co.uk/	No	Unlimited	1st	£114
Clear path ™	USA	Laser	www.clearpathdental.com	No	Unlimited	1st	£890
Clearstep™ now Smilelign	UK	Laser	www.smilelign.com/	Yes	Unlimited	2nd	£750
Simplifive ™ -Red, White and Blue Aligner	USA	Manual	www.ormco.com	No	Seven aligners	1st	£500
MTM Clear-Aligner™	USA	Laser	www.mtmclearaligner.com/	No	Unlimited	1st	£450
Nimrodental Clear aligner™	UK	Laser	www.nimrodental.com/	No	Unlimited	1st	£400
Clear Image Aligners™	USA	Manual	www.specialtyappliances.com	No	Unlimited	1st	£35
ClearAligner™	USA	Manual	www.clear-aligner.com	No	Unlimited	1st	£125
ClearCorrect™	USA	Laser	www.clearcorrect.com	Yes	Unlimited	2nd	£760
Invisalign™	USA	Laser	www.invisalign.com	Yes	Unlimited	3rd	£1690

2.2.1 Classification of Clear Aligners

1st Generation Aligners

The earliest forms of these systems were solely reliant on the aligners to achieve their results. No auxiliary elements were incorporated. These aligners can be fabricated using CAD/CAM technology or manually following Kesling's method.

2nd Generation Aligners

As the aligner systems developed, manufacturers encouraged the use of attachments to improve tooth movements. Clinicians could request composite buttons to be placed on teeth and also could attach inter-maxillary elastics.

3rd Generation Aligners

In an attempt to improve the results, manufacturers again attempted to alter the way aligners delivered force. Attachments were automatically placed by the manufacturer's software where

- Extrusion of Incisors and/or canines are required
- Derotations are required
- Root movements are required

Indentations in the aligners were automatically placed where root torque is needed. The operator could also request non-precision attachments to be placed on teeth where he/she feels they would improve the movements achieved. There are 3 common types of attachments; ellipsoid, bevelled and rectangular. Ellipsoid attachments are used singly for derotations, or in pairs where root movements are

attempted. They are 3mm high, 2mm wide and 0.75-1mm thick and are available for incisors, canines and premolars. When they are used singly, similar to the development of wider brackets in fixed appliances, ellipsoid attachments should allow for greater rotational control. Using them in pairs should allow for production of moments of couple to upright roots. They may also allow the appliance to achieve bodily movement, like labial brackets, through the use of moments of couple and moments of force. Bevelled attachments are used most often when trying to extrude a tooth. They can be 3,4 or 5 mm wide, 2 mm high and from 0.25 to 1.25 mm thick. They have an active border, just like fixed brackets, that should limit the slipping (or loss of tracking) that can occur between the aligner and the tooth. Rectangular attachments are used when large mesiodistal movements are requested. These are 3,4 or 5 mm high, 2 mm wide and 0.5 to 1 mm thick. It is proposed that these attachments will allow teeth to be moved bodily by allowing for a longer span for force application. All three types of attachments are not fully engaged initially when they are bonded to the tooth. As the patient graduates through the different aligners, the attachments become more active until they finally fill the aligner slot. This principle is again similar to working through archwires when using the preadjusted edgewise appliance. Indentations are placed in the aligners where lingual root torque is required for maxillary or mandibular incisors. These indentations in the polyurethane attempt to place increased pressure on specified points on the crown to produce moments of couple and torque the root. These suggested tooth movements have yet

to be verified scientifically. No research has accurately measured the tooth movements produced by clear aligners.

2.3 The Clear Aligner Process

The first step in clear aligner treatment is the production of clinical records (Joffe, 2003). These include maxillary and mandibular impressions, a silicone record of maximum intercuspation, intraoral and extraoral photographs, a panoramic and cephalometric radiograph. Digital or paper copies of these records are sent to the manufacturers. An accurate set of impressions is very important. Materials that can be used include polyvinyl silicone or polyether.

The majority of clear aligner manufacturers use CAD/CAM technology to produce their clear aligners (Table 1). Some companies manufacture the aligners manually which can be more time consuming and limit the amount of appliances that can be requested. Each company has a slightly different manufacturing process with the Invisalign® aligner fabrication the most widely described digital manufacturing procedure. This will now be discussed in greater detail.

After receiving the clinical records Align scan the impressions with a FlashCT® (HYTEC Inc, Los Alamos, New Mexico) to produce a 3 dimensional digital model (Vardimon *et al.*, 2010). This initial scan does not capture all the dental anatomy accurately, particularly in the interproximal region (Beers *et al.*, 2003). Align uses ClinCheck® software to approximate these missing surfaces. Krieger *et al* compared

pretreatment study models and virtual scans produced by ClinCheck® for 35 Invisalign® patients (Krieger *et al.*, 2011). They used Toothmeasure®, a software application developed by Align, to measure the virtual models. This application has not been independently verified but was reported as being accurate by an internal Align study of 10 cases (Miller *et al.*, 2003). Krieger *et al* found a minimal mean difference in measurements of overjet, overbite and dental midline shift (Krieger *et al.*, 2011). They concluded that ClinCheck® provides an accurate virtual pretreatment model. An internal review of 2000 Invisalign® cases found similar results (Beers *et al.*, 2003).

Following production of the virtual pretreatment models the maxilla and mandible are placed in centric occlusion using ToothShaper® Autobite software (Ali and Miethke, 2012). Another software package, Treat®, aligns individual teeth according to the orthodontist's prescription (Ali and Miethke, 2012). The paths the teeth take to move from the initial to final positions are then specified. The treatment plan is then returned to the clinician for verification. At this stage the clinician can assess the tooth movements that are being proposed and alter the treatment plan where it is necessary.

When the clinician has approved the treatment plan the computer software converts computer images to physical models using a process known as sterolithography (Wong, 2002).

"Sterolithography technology is a solid imaging process that uses a laser beam to expose and solidify successive layers of a photosensitive

liquid until the desired mold is formed in acrylic resin" (Vardimon *et al.*, 2010).

In the case of Invisalign, these models are used to manufacture polyurethane aligners (polyurethane from methylene diphenyl diisocyanate and 1,6-hexanedial, additivies) by using a pressure molding machine (Great lakes Orthodontic Products, Tonawanda, NY) (Vardimon *et al.*, 2010). Each aligner is 0.75mm thick and is designed to move teeth in small increments of no more than 0.2mm (Ali and Miethke, 2012).

The complete series of aligners is sent to the clinician for delivery to the patient. The patient is asked to wear the appliance full time apart from eating, drinking and during oral hygiene procedures. Each aligner should be replaced every 2 weeks (Boyd, 2007). In the more recent generations of aligners small composite buttons, or attachments, can be placed onto specific teeth to aid retention and allow auxiliaries to be used.

2.4 Advantages of Clear Aligners

2.4.1 Aesthetics

Although fixed appliances have been the backbone of orthodontics for years, patients' reluctance to wear labial brackets has been the driving force for the development of alternatives. Clear aligners have a number of reported advantages when compared to conventional fixed orthodontics. They remove the appearance of fixed labial braces and are therefore more aesthetic. Jeremiah *et al.* compared people's perception towards a young female wearing 5 different orthodontic appliances (Jeremiah *et al.*, 2011). A participant was shown a coloured photograph of the patient with either no appliance, a stainless steel fixed orthodontic appliance, a ceramic fixed orthodontic appliance, a gold fixed orthodontic appliance or a clear colourless aligner. The participant was then asked a series of questions related to the patient's social competence, intellectual ability, psychological adjustment and attractiveness. The no appliance patient was perceived as being more intelligent followed by the gold and clear appliance. A trend was noted with regards to the no appliance and clear appliance patient being perceived as more attractive. No other differences were found. This highlights patients' preconceived ideas about conventional orthodontics and the aligner's major aesthetic advantage.

2.4.2 Pain

Most orthodontic procedures result in some degree of discomfort for the patient (Scheurer *et al.*, 1996). A number of studies have investigated the pain produced by different orthodontic appliances

(Nedwed and Miethke, 2005; Miller *et al.*, 2007; Shalish *et al.*, 2012; Cooper-Kazaz *et al.*, 2013). Nedwed and Miethke asked 54 consecutive Invisalign® patients to complete a pain related questionnaire between 3 and 6 months after the start of Invisalign® treatment (Nedwed and Miethke, 2005). Thirty five percent of patients reported never having any pain during appliance wear. Miller *et al.* compared the pain experienced by Invisalign® and fixed appliance patients during the first week of treatment (Miller *et al.*, 2007). Using a visual analogue scale the fixed appliance patients reported that their pain started after 4 hrs of appliance wear, it peaked at 24 hrs and had not returned to baseline measurements by the end of the 7th day. The Invisalign® patient's pain levels had returned to baseline levels by the 5th day of treatment. The overall pain experience of both groups was similar (Miller *et al.*, 2007). Shalish *et al.* compared labial, lingual and Invisalign® treatments (Shalish *et al.*, 2012). Patients were asked to complete a Health-Related Quality of Life Questionnaire for the first 7 days of treatment and then again on the 14th day of treatment. Lingual appliances caused the most discomfort and resulted in the most analgesic use. Invisalign® patients reported the highest pain scores in the first 3 days after insertion but had similar levels of general activity disturbances when compared to the labial appliances. A study of the psychological traits of patients receiving orthodontic treatment concluded that anxious patients preferentially chose to be treated with lingual or clear aligner appliances (Cooper-Kazaz *et al.*, 2013). Overall clear aligner therapy may cause increased pain at the start of treatment when compared to fixed appliances but the symptoms may resolve quicker.

2.4.3 Oral Hygiene

A significant risk of fixed orthodontic treatment is enamel decalcification (Lucchese and Gherlone, 2013). This can lead to unaesthetic white spot lesions and an increased risk of cavitation of enamel. Difficulty in maintaining a high standard of oral hygiene can predispose fixed appliance patients to enamel decalcification. Clear aligner treatment has less impact on the patient's oral hygiene procedures than other forms of orthodontic therapy. Miethke's two papers compared Invisalign® treatment with labial fixed appliance therapy in 2005 and with lingual fixed appliance therapy in 2007 (Miethke and Vogt, 2005; Miethke and Brauner, 2007). Patients receiving lingual fixed appliance treatment had plaque scores that were twice as high as Invisalign® patients. Gingival inflammation was also higher in lingual appliance patients. Plaque scores were significantly lower in Invisalign® patients when compared to labial fixed appliance patients. However the authors do mention thoroughly cleaning some patient's teeth, during the research, when time permitted. This may make the results questionable. Many authors have suggested clear aligners could be used preferentially in patients who had previous periodontal disease due to the aligners limited effect on oral hygiene (Ali and Miethke, 2012). No clinical trials are available to verify this but Turatti *et al* described a case report of a periodontally compromised patient with extruded, protrusive and labially inclined upper incisors with generalised anterior spacing, which was treated successfully with Invisalign® (Turatti *et al.*, 2006). More research is required to

conclusively show whether clear aligners can reduce the risks that coincide with poor oral hygiene procedures during orthodontics.

2.4.4 Speech

Most removable orthodontic appliances can have a temporary effect on the patient's enunciation of certain words. This can be a particular concern to adult patients. Conflicting reports exist as to whether clear aligner treatment affects patients' speech. During Nedwed and Miethke's questionnaire based study, 50% of patients said they had no change to their speech (Nedwed and Miethke, 2005). Schaefer and Braumann described a cohort of 31 patients undergoing Invisalign® therapy (Schaefer and Braumann, 2010). The majority of patients reported some effect on their speech for the first three months of treatment. It seems likely that patients will notice some alteration in their pronunciation but that this should only be temporary.

2.4.5 Root Resorption

Another important risk of orthodontic treatment is external root resorption (Levander and Malmgren, 1988). Lund *et al.*, using cone beam computer tomography (CBCT), concluded that 94 % of patients that had received fixed appliance therapy had at least one tooth with 1mm of root resorption, with 6.6% having a tooth with >4 mm root resorption (Lund *et al.*, 2012). Some authors have postulated that clear aligners would have a reduced rate of root resorption when compared to fixed appliance therapy due to the discontinuous force applied (Boyd, 2008; Ali and Miethke, 2012). In a single case report Brezniak and Wasserstein showed Invisalign® treatment can produce severe root

resorption (Brezniak and Wasserstein, 2008). The value of this observation is limited as certain individuals can be more susceptible to orthodontic induced inflammatory root resorption regardless of what appliance is used (Ngan *et al.*, 2004). Barbagallo *et al.* did investigate the incidence of root resorption in patients receiving ClearSmile® appliances (ClearSmile, Woollongong, Australia) (Barbagallo *et al.*, 2008). Barbagallo *et al.*, again using CBCT, found teeth receiving no orthodontic therapy had limited resorption lesions. Teeth receiving fixed appliance treatment, with light forces being applied, had approximately 5 times more resorption lesions than the no treatment group, while ClearSmile® patients had six times more lesions when compared to patients who received no treatment. However patients who underwent fixed appliance therapy, where heavy forces were applied, resulted in nine times more resorption lesions. These results were statistically significant. They concluded clear aligners have a similar incidence of root resorption as fixed appliance therapy when light forces are applied (Barbagallo *et al.*, 2008).

2.4.6 Other suggested advantages

Multiple case reports have described clear aligners being used to treat many different malocclusions including premolar extraction cases (Honn and Goz, 2006), lower incisor extraction cases (Miller *et al.*, 2002), class II molar correction cases (Fischer, 2010; Schupp *et al.*, 2010a), openbite correction (Schupp *et al.*, 2010c), deep bite cases (Giancotti *et al.*, 2008), joint orthognathtic (Boyd, 2005; Womack and Day, 2008; Marcuzzi *et al.*, 2010) and joint restorative cases (Giancotti

and Ronchin, 2006) and in conjunction with temporomandibular joint treatments (Miller, 2009; Schupp *et al.*, 2010b). In addition Invisalign® treatment reportedly requires fewer routine/emergency appointments and less orthodontic equipment when compared to fixed appliance therapy (Ali and Miethke, 2012). Clear aligners may also be easier to use in patients with multiple heavily restored teeth because they do not require extensive bonding (Boyd, 2008). These treatment claims have yet to be scientifically verified.

2.4.7 Summary

Clear aligners would appear to provide the patient with improved aesthetics and oral hygiene advantages. These appliances appear to have a transient effect on speech although the impact on the patient seems to be minor. Whether clear aligners cause less discomfort to the patient or induce less root resorption requires further investigation.

2.5 Limitations of Clear Aligner Treatment

As with any orthodontic appliance clear aligners have a number of limitations. Many authors have suggested that clear aligners are most successful at treating mildly malaligned occlusions (Joffe, 2003; Crosby and Lee, 2009). Some conditions such as crowding greater than 5mm,

skeletal discrepancies greater than 2mm, centric-relation and centric occlusion discrepancies, severely rotated teeth, severe openbites, teeth requiring extrusion, severely tipped teeth and teeth with short clinical crowns can be difficult to treat with aligner therapy (Phan and Ling, 2007). This may be as result of the clear aligners poorer control of tooth movements when compared to fixed appliances.

2.5.1 Treatment time

Orthodontists are particularly concerned with the time taken to achieve alignment and the quality of the alignment following treatment. This process is dependent on a number of factors including many biological factors beyond the practitioner's control (Sandy *et al.*, 1993). The orthodontist has a direct influence over the appliance used during treatment. When comparing treatment times, Pavoni *et al.* found no difference between Invisalign® and self-ligating brackets in patients with Class I occlusion and mild crowding (mean 4.4 +/- 0.8mm) at the start of treatment (Pavoni *et al.*, 2011). The average length of treatment was 1.8 years for both groups. The authors suggest that if the roots of teeth are well aligned prior to the commencement of treatment, Invisalign® and fixed appliances will have similar treatment times (Pavoni *et al.*, 2011).

2.5.2 Accuracy of tooth movement

There is limited research available assessing the tooth movements produced by clear aligners (Table 2).

Table 2 Comparing accuracy of tooth movements produced by Clear aligners and Fixed appliances

Authors	*Comparison*	*Generation*	*Evaluating system*	*Results*
Djeu et al. 2005	48 Invisalign cases vs 48 fixed appliance cases	1st	American Board of orthodontics objective grading	Similar results for marginal ridge/root alignment Fixed better for buccolingual occlusal relationship and overjet reduction
Kravitz et al. 2008	Alignment with and without attachments	2nd	Assess derotation of 51 canines	No difference
Kravitz et al. 2009	Predicted movements vs actual movements	2nd	Post treatment study models vs Virtual prediction software	41% of predicted movements were achieved
Drake et al. 2012	New aligners Weekly (15 pts) vs Biweekly (37 pts)	2nd	Cone beam CT scans pre and post treatment	No difference in amount of tooth movement achieved

1st Generation Aligners

From its infancy, it was presumed that clear aligners achieved their tooth movements by tipping teeth. The earliest forms of these systems were solely reliant on the aligners to achieve their results. No auxiliary elements were incorporated.

There is limited research available assessing the tooth movements produced by 1st generation aligners. Clements *et al.* found poor post treatment peer assessment ratings (PAR) when they used hard or soft polyurethane clear aligners (Clements *et al.*, 2003). Neither of these aligners became commercially available

In 2005, Djeu *et al.* compared their first 48 Invisalign® patients with a cohort of fixed appliance patients (Djeu *et al.*, 2005). Using the American Board of Orthodontics objective grading system they evaluated the results produced by the different treatment systems. In two categories, marginal ridge alignment and root angulation, Invisalign® and fixed appliances had similar results. However with regards to buccolingual inclination, occlusal contacts, occlusal relationship and overjet reduction, fixed appliances had significantly better scores. These inexperienced authors were using an early version of the Invisalign® system and unsurprisingly found fixed appliance therapy to be superior when treating patients with moderate to severe malocclusions.

Using the same patient cohort as Djeu *et al.*, Kuncio *et al.* assessed the postretention dental changes after Invisalign® and fixed appliance therapy (Kuncio *et al.*, 2007). They found Invisalign® patients had more

relapse, particularly in the maxillary anterior region. The authors postulated that, because Invisalign® is reactivated every 2 weeks, it leads to poorer bone formation and therefore makes it more prone to relapse. This has yet to be researched.

2nd Generation Aligners

In two separate studies, Kravitz *et al.* assessed the accuracy of tooth movements produced by these newer systems (Kravitz *et al.*, 2008; Kravitz *et al.*, 2009). In a prospective clinical study, they compared the virtual tooth movements predicted by ClinCheck® software with the clinical results achieved by aligners alone, aligners with attachments or aligners with interproximal reduction (Kravitz *et al.*, 2008). Fifty-one rotated canines were treated with anterior Invisalign®. The mean accuracy of derotation achieved when compared to the predicted results was 35.8% (Kravitz *et al.*, 2008). The group that received interproximal reduction achieved slightly more accurate movements (43.1%) than the attachment only (33.3%) and independent aligner groups (30.8%), although the differences between the three groups were not significant (Kravitz *et al.*, 2008). Kravitz *et al.* then investigated the accuracy of multiple different tooth movements predicted in a cohort of 37 patients (Kravitz *et al.*, 2009). The overall accuracy of the tooth movements was 41%. Only 29.6% of extrusive movements were achieved. The authors found lower incisor retroclination to be the most predictable tooth movement (Kravitz *et al.*, 2009). Both these clinical trials suggest there is a large difference

between the proposed virtual results and the actual clinical movements. In conclusion, the attachments introduced in the second generation did not improve the overall accuracy.

Drake *et al.* investigated whether placing a new aligner with the same prescription after one week improved the accuracy of the tooth movements (Drake *et al.*, 2012). Only minor crowding in the maxillary incisor region was assessed. Their results were similar, with 55% of predicted tooth movements occurring. By taking a polyvinyl silicone impression, every week for the 8-week period of the trial, the researchers showed that the majority of the tooth movement occurs in the first week of aligner wear. They also suggest that each aligner does not fully express its prescribed tooth movements (Drake *et al.*, 2012).

Krieger *et al.* found that most tooth movements that were predicted were achieved in their study of 50 clear aligner patients (Krieger *et al.*, 2012). However, they found that the predicted overbite reduction was not accomplished in the majority of cases when using Invisalign® (Krieger *et al.*, 2012).

Although these studies highlighted the inability of aligners to achieve the tooth movements predicted, sparse explanation was given for the discrepancies that were found. It can be hypothesised that earlier versions of aligners showed poor control of crown and root movements and that it was necessary to produce a system with more accurate management of the movement of teeth.

3rd generation

As mentioned previously the third generation of aligners is more heavily reliant on composite fixtures being placed on the teeth. These composite buttons are called 'Precision Attachments' and are automatically placed by the computer software where bodily tooth movements are required. It is proposed that these attachments will allow moments of couple to be created as the aligner pushes against the tooth surface. No research is available to verify this suggestion. It remains to be seen whether more accurate tooth movements can be expected with this new system.

The composition of the aligners being used has also changed with each new generation, in an effort to improve the tooth movements produced. A number of studies have investigated the material used to fabricate the Invisalign® aligners (Bollen *et al.*, 2003; Clements *et al.*, 2003; Schuster *et al.*, 2004; Eliades *et al.*, 2009; Vardimon *et al.*, 2010; Low *et al.*, 2011). Schuster *et al.* investigated the structural changes that can occur in the material during aligner wear (Schuster *et al.*, 2004). After retrieving 10 aligners that had been worn for two weeks, they found that no by-products were released by the polyurethane. However they did show an increase in the Vickers hardness test, which may be caused by the masticatory action on the appliance. The authors suggest this may affect the force being delivered by the aligner (Schuster *et al.*, 2004). An *in-vitro* study agreed that the polyurethane does not leach by-products and shows no cytotoxicity (Eliades *et al.*, 2009).

2.5.3 Compliance

With every removable orthodontic appliance, there is a risk that the patient will not wear the appliance. Lindauer and Shoff found that 1 in 6 patients wearing a removable retainer lost their appliance within the first week of use (Lindauer and Shoff, 1998). A major limitation of clear aligner treatment is its dependence on patient compliance. Boyd has suggested no moderate/severe malocclusions can be treated without full time wear of the appliance (Boyd, 2008). Using the same cohort of patients as Clements *et al.*, Bollen *et al.* evaluated how many patients completed treatment when they used hard polyurethane or soft polyurethane (Bollen *et al.*, 2003). There was little difference between the very low completion rates, 32% for hard versus 27% for soft respectively. Attempts have been made to improve patient compliance. Align have manufactured a compliance indicator for use in young patients in particular. A food dye, Erioglaucine disodium salt, is placed in the vestibular part of the molar segment of the clear aligner (Schott and Goz, 2011). When the dye is exposed to oral fluids it begins to fade. An allowance is made for different saliva compositions with fast and slow indicators being present. The clinician evaluates the wear time by comparing the colour change to 5 potential colours ranging from dark blue/dark blue to clear/clear (Schott and Goz, 2011). An *in vitro* study of these compliance indicators showed the colour change to be very unreliable and easily manipulated (Schott and Goz, 2011). Ensuring patients wear their appliances remains a difficult hurdle for practitioners to overcome and highlights the importance of treating extremely motivated patients.

2.5.4 Practical Limitations

Clear aligners have some practical limitations also. When a series of aligners is fabricated it can be difficult to make changes to the original treatment plan. Even though some manufacturers offer a mid-treatment and an end of treatment correction, this can still be cumbersome and annoying to the patient (Phan and Ling, 2007). Some clinicians find the additional digital paperwork to be time consuming (Phan and Ling, 2007).

2.5.5 Summary

A number of studies have compared the effects produced by clear aligners and fixed appliances (Table 3). An important treatment result that has not been investigated is the difference between the amount of lower incisor proclination produced by each appliance.

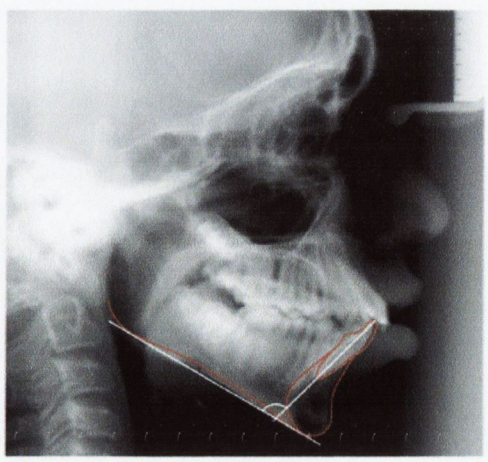
Table 3 Comparing Clear aligner and Fixed appliance results

Effect	*Comparison Study*	*Result*
Aesthetics	Jeremiah et al., 2011	Clear aligners more aesthetic
Pain	Shalish et al., 2012 Miller et al., 2007 Nedwed and Miethke, 2005 Cooper-Kazaz et al., 2013	Clear aligners increased pain at start. Overall similar pain levels
Improved oral hygiene	Miethke and Vogt, 2005 Miethke and Brauner, 2007	Results are inconclusive
Speech	Nedwed and Miethke, 2005 Schaefer and Braumann, 2010	Similar effects
Root Resorption	Barbagallo et al., 2008	Clear aligners and light fixed appliance forces have similar rates of root resorption
Treatment Time	Pavoni et. al., 2011	Similar treatment time
Accuracy of tooth movement	Djeu et. al., 2005	Poorer results from clear aligners

2.6 Cephalometric measurements

Cephalometry has been used to aid diagnosis and monitor treatment and growth since Broadbent introduced the technique in 1931 (Broadbent, 1931). Traditionally, cephalometric analysis was completed by tracing radiographic landmarks on acetate overlays and using these landmarks to measure linear and angular values (Chen *et al.*, 2004). A common method of cephalometrically comparing lower incisor proclination is measuring the angle the mandibular central incisor makes with the mandibular plane. Downs first described this technique in 1956 (Downs, 1956). Since then many authors have used this measurement to assess the lower incisor proclination produced by different orthodontic appliances (Toth and McNamara, 1999; Gill and Lee, 2005; Pandis *et al.*, 2007; Pandis *et al.*, 2010a; Pandis *et al.*, 2010b; Aziz *et al.*, 2012; Upadhyay *et al.*, 2012) (Figure 1).

Figure 1 Downs' method to measure lower incisor inclination, Lateral cephalogram of patient 12 Invisalign group



Another method of comparing the labiolingual position of the mandibular incisors was described Pancherz (Pancherz, 1984). A line tangent is drawn on a lateral cephalogram, between the distobuccal cusp of the maxillary first molar and the incisal vertical overlap. A perpendicular line is then drawn from this line to the sella turcica. A change in lower incisor position can then be detected by measuring the horizontal distance from this perpendicular line to the lower incisor edge (Pancherz, 1984) . More recently, lower incisor to occlusal plane angulation has been used for comparison(Cattaneo *et al.*, 2013).

When comparing mandibular incisor proclination in a non-growing subject, it would appear Down's method is more satisfactory. The other two measurements depend on dental structures which can be unstable and can bring the accuracy of results into question. No study has compared the accuracy of these three methods.

Baumrind and Frantz suggested that two types of errors are associated with headfilm measurements (Baumrind and Frantz, 1971a)

1) Errors of projection- as a result of a three dimensional image being displayed in two dimensions
2) Errors of identification- as a result of inaccurate identification of landmarks (Baumrind and Frantz, 1971a)

The authors found that certain landmarks, such as the lower incisor apex, were more difficult to identify accurately (Baumrind and Frantz, 1971a). The authors also found a higher percentage of errors occurred

when measuring angular values (Baumrind and Frantz, 1971b). They suggested computer-assisted digital cephalometric analysis could limit the errors in identification, as it would allow measurements to be replicated quickly (Baumrind and Frantz, 1971a).

Computer-assisted cephalometry has a number of other advantages over conventional film-based analysis including speed, easier storage, transmission and processing (Chen *et al.*, 2004). A number of authors have compared both forms of cephalometric analysis (Chen *et al.*, 2004; Santoro *et al.*, 2006; Roden-Johnson *et al.*, 2008). Santoro *et al.* used the 'sandwich technique' to expose the phosphor plate and conventional radiographic film simultaneously (Santoro *et al.*, 2006). This ensured radiographs were identically matched. The same operator then traced 47 cephalograms digitally and manually. No statistically significant differences were found with respect to measurement of angles (Santoro *et al.*, 2006). Roden-Johnson *et al.* compared Quick Ceph (Quick Ceph Systems Inc, San Diego, USA) digital tracings with the manual tracings of 30 cephalograms (Roden-Johnson *et al.*, 2008). For landmark identification and angular measurements, both methods obtained the same results (Roden-Johnson *et al.*, 2008). Chen *et al.* found digital analysis to be significantly quicker when used by relatively inexperienced operators (Chen *et al.*, 2004).

2.7 Mandibular incisor proclination

Lower incisor position is paramount during orthodontic treatment planning because of the narrow zone of equilibrium around these teeth. Any unplanned movement of the lower incisors can result in loss of

stability and relapse of the result. Furthermore, because a thin gingival tissue covers these teeth, excessive movements can result in damage to periodontal tissues. This has lead to extensive research on the position of lower incisors during orthodontic treatment. Several reports on the stability of incisor movements and the effect of different appliances on incisor proclination have been published.

To increase the stability of the result, the lower incisors should be maintained in their pretreatment position where they are in equilibrium with the surrounding soft tissues (Mills, 1966). In certain circumstances, mandibular incisor proclination can be beneficial, for example when treating patients who have retroclined incisors as a result of a digit sucking habit or where the lower incisors have become trapped by the lower lip or by the palate in deep overbite cases (Mills, 1966). However, more often it is an unwanted side effect of orthodontic therapy. Excessive mandibular incisor proclination can have a detrimental effect on the result of orthodontic treatment. It can predispose the lower labial segment to instability, gingival recession and poor aesthetics. A recent systematic review has suggested a reduced thickness of free gingival margin, a narrow mandibular symphysis, inadequate plaque control as well as excessive tooth brushing may be more pertinent factors with regards to gingival recession (Aziz and Flores-Mir, 2011).

Many orthodontic appliances can produce labial movement of mandibular incisors. Numerous investigators have compared the incisor proclination produced by different appliances (Table 4)

Table 4 Studies comparing lower incisor proclination produced by different orthodontic appliances

Study	*Type of Appliances*	*Proclination (Mean ± SD)*	*Result*
Gill and Lee 2005	Twin Block (TB)vs Mini block (MB) Functional appliances	TB= 1.3° +/- (not given) MB= 2.4° +/- (not given)	NS
Toth and McNamara 1999	Twin Block (TB) vs Frankel II (FRII) functional appliances	TB = 2.8 +/- 5.4° FrII= 1.1 +/- 3°	NS
Pandis et al. 2010	Self ligating (SL) vs Conventional (C)	SL= 3.1 +/- 8.0° C= 5.5 +/- 6.7°	NS
Scott et al. 2008	Self ligating (SL) vs Conventional (C)	SL= 1.73 +/- 4.06° C= 2.34 +/- 3.72°	NS

NS=Not statistically significant

Functional appliances achieve mainly dentoalveolar changes, with lower incisors proclined up to 7 degrees (Lund and Sandler, 1998). A number of studies have compared the effects of different functional appliances on the lower labial segment. Gill and Lee compared the effects of a conventional modified Clark's Twin-block with a mini-block appliance (Gill and Lee, 2005). The authors assessed whether incremental advancement with the mini-block affected the dentoalveolar changes that were produced. Thirty-five age and sex matched patients were placed in each group. No crowding measurements were described. Cephalometric tracing revealed a

similar amount of lower incisor proclination for both groups. Intra-operator error was assessed by repeating cephalometric measurements for 20 randomly selected radiographs, however interoperator error was not calculated. Toth and McNamara retrospectively compared the Frankel II appliance to a modified Clark's Twin-block appliance and a control group (Toth and McNamara, 1999). Forty patients were treated in each group. The lower incisor to mandibular plane cephalometric angulation changed by 0.2° in the control group, 1.1° in the Frankel II group and 2.8° in the Twin Block group with all groups displaying some proclination. The authors did not describe the pre-treatment crowding or error of the method. Fixed functional appliances achieve overjet correction through similar proclination of the lower labial segment. Hansen *et al.* described a mean 10.8° of lower incisor proclination when using a Herbst appliance during a follow up study of 24 patients with mild lower incisor crowding (Hansen *et al.*, 1997).

Fixed appliance therapy can also result in mandibular incisor proclination. Minimal differences exist between the amount produced by different bracket prescriptions or between conventionally ligated and self ligated brackets (Fleming and Johal, 2010). Pandis *et al.*, in a prospective study, compared mandibular incisor proclination when using a Roth prescription conventional bracket with a Damon self ligating bracket (Pandis *et al.*, 2010b). Twenty-seven patients were treated in each group. All patients had greater than 2mm lower incisor crowding using Little's irregularity index with similar amounts of crowding in each group. Lower incisor proclination was measured using conventional lateral cephalograms taken before and after

treatment. No significant difference was found between the groups. Scott *et al.* reported on a similar study, again using Damon self-ligating brackets (32 patients) to compare to Roth prescription conventional brackets (28 patients) (Scott *et al.*, 2008). Participants had crowding of 5-12mm in the lower arch and were treated with bilateral lower first premolar extractions. Lateral cephalograms were taken pretreatment and when a 0.019x0.025" stainless steel archwire was placed. These radiographs were then traced to compare lower incisor proclination. Again no significant difference was found between the groups. Chen *et al.* pooled the available research and carried out a systematic review comparing self-ligating and conventional brackets under a number of different headings (Chen *et al.*, 2010). They performed a meta-analysis with regards to lower incisor proclination and found conventional brackets produce slightly more proclination (1.5°)(Chen *et al.*, 2010). Recently Cattaneo *et al.* compared the proclination produced by active and passive self-ligating brackets (Cattaneo *et al.*, 2013). They used cone beam computer tomography before and after treatment to assess the lower incisor inclination. They found no difference with regards to lower incisor proclination. The use of the occlusal plane as a stable referencing point, however, may question the accuracy of these results.

In the majority of these comparison studies the appliances produced similar amounts of lower incisor proclination, however no study has compared the mandibular incisor proclination produced by clear aligners and fixed appliances.

2.8 Interproximal Enamel Reduction

Many approaches have been used in orthodontics to try and prevent lower incisor proclination including extraction of teeth, lingual crown torque, delay in bonding the mandibular incisors and interproximal reduction. Interproximal reduction decreases the mesiodistal width of teeth and has become common practice in orthodontic therapy (Chudasama and Sheridan, 2007). Many authors have described the benefits of this treatment modality where space is required (Peck and Peck, 1972; Tuverson, 1980; Sheridan, 1985; Sheridan, 1987; Zachrisson, 2004). The general consensus is that stripping of mandibular incisors should not exceed 0.75mm at each contact point with slightly larger amounts possible on posterior teeth (Chudasama and Sheridan, 2007). Enamel reduction can be performed manually or mechanically and all surfaces should be polished after completion of the procedure (Livas *et al.*, 2013). The available research suggests it does not increase the risk of dental caries, sensitivity or periodontal disease (Zachrisson *et al.*, 2007; Zachrisson *et al.*, 2011). Clear aligner manufactures have encouraged the use of interproximal reduction due to the concerns with closing extraction spaces (Phan and Ling, 2007). Kravitz *et al.* found that interproximal reduction slightly improved the accuracy of the tooth movements achieved during aligner therapy (43.1% of predicted tooth movements achieved) when compared to aligners with attachments only (33.3% of predicted tooth movements achieved) and aligners on their own (30.8% of predicted tooth movements achieved), however the results were not statistically significant (Kravitz *et al.*, 2008). Interproximal reduction may reduce

the amount of lower incisor proclination required to resolve crowding but no research has been completed to confirm this.

3 Materials and Methods

3.1 Study Outline

The study was designed as a prospective, randomized clinical trial. Participants were recruited from patients commencing treatment in the postgraduate clinics at the Dublin Dental University Hospital during October and November 2013.

The Joint Research Ethics Committee at St James' Hospital, Dublin, Ireland, granted ethical approval for this research (Ref. 2013/11/Chairman). The participants were fully informed about the study and written consent was obtained.

3.2 Sample Size

A minimum sample size of 17 participants in each group was proposed for 80% power with a significance level of 0.05%. The sample size was calculated using a two-sample *t-test* power calculation. Means and standard deviations were ascertained from previous research (Pandis *et al.*, 2007). A mandibular incisor inclination change of 6 degrees was considered clinically significant. The power calculation was carried out using the R software version 2.11.1 (Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org).

3.3 Inclusion Criteria

- Over 18 years old
- mild mandibular crowding (<4mm of crowding)
- required non-extraction orthodontic treatment

- Antero-posterior maxillary and mandibular skeletal pattern within average range (ANB cephalometric measurement 1-4 degrees)

3.4 Exclusion Criteria

- Complex medical histories
- Pregnancy
- Dental/periodontal disease

3.5 Recruitment

Patients were recruited from the orthodontic waiting lists in the order they appeared on the waiting list. A non clinical gatekeeper contacted ten patients at a time, from the waiting lists, until the sample size was achieved. The gatekeeper posted an information letter, a patient information sheet and a consent form to the patient. The patient was asked to contact the gatekeeper if they were interested in participating in the research. The patient was then given an appointment for an initial assessment. If the patient did not wish to participate in the research they were still be offered orthodontic treatment immediately. Consenting to particapation in the research will not enable the patients to 'jump the queue'

3.6 Pre-treatment Records

A total of 44 patients fulfilled the inclusion criteria, 22 in each group. All patients were consented for treatment and inclusion in the clinical

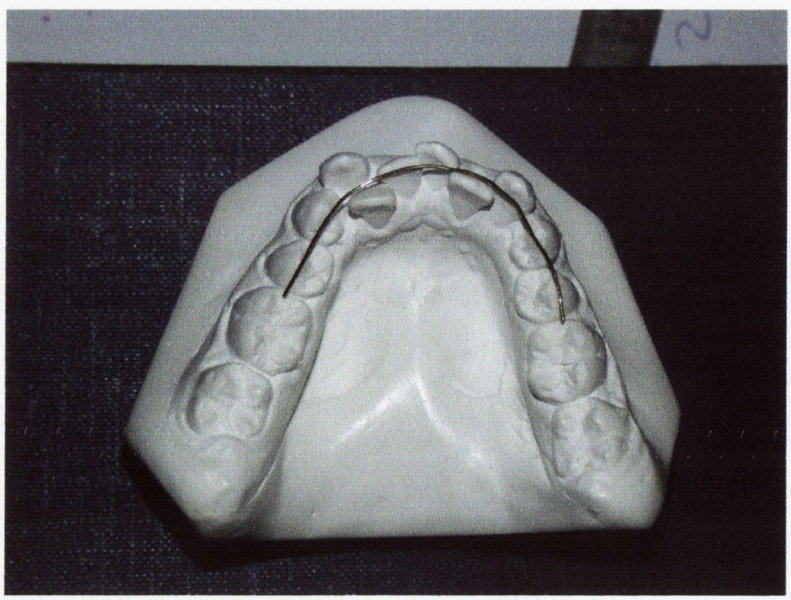
trial. Each participant had maxillary and mandibular alginate (Zhermack fast setting elastic mint flavour hydrogum alginate, Zhermack SpAVia Bovazecchino, 100 45021 Badia Polesine (RO)-Italy) impressions made for study model fabrication. Disposable plastic stock trays (Dentaurum O-Trays, Dentaurum GmbH & Co. KG, Turnstraisse 31, 75228 Ispringen. Germany) were used to make each impression. The impressions were rinsed in water and then disinfected with CIDEX® OPA (ASP, 33 Technology Drive, Irvine, CA 92618 USA) for 5 minutes. The impressions were then washed again with water for 1 minute, as recommended by the manufacturers, before being placed in plastic sealed bags and labelled. The impressions were poured within one hour in Type 3 stone (Super White Orthodontic Stone, Whipmix, 361 Farmington Avenue, P.O. Box 17183, Louisville, KY, 40217 USA). A full series of clinical photographs (Extraoral repose, smiling and profile: Intraoral frontal, right and left buccal, maxillary and mandibular occlusal) were taken of all participating patients using a Canon 1100D digital camera (Canon USA Inc, 1 Canon Park, Melville NY 11747, USA). A digital lateral cephalogram (Proline 2002 PM CC, Planmeca Oy, Asentajankatu 6, FIN-00880 Helsinki, Finland) was taken with the patient in the natural head position (looking into their own eyes in a mirror) immediately prior to the commencement of treatment.

3.7 Crowding Assessment

A single operator calculated crowding using the 44 pre-treatment study models, in a room with natural light. Crowding was assessed

using the Nance brass wire technique, where the combined mesiodistal widths of the teeth from the mesial aspect of the first molar to the mesial aspect of the first molar are subtracted from the arch perimeter length (Figure 2) (Nance, 1947). The contact points between the teeth were marked and the mesiodistal widths were measured using a digital caliper ABSOLUTE (Moore & Wright LTD, Bowers Metrology Ltd, Bradford, West Yorkshie, BD3 8HU, UK). The caliper had a resolution of 0.01 mm. Arch perimeter was calculated using a 0.5 mm diameter brass wire shaped to follow the arch form. This was then measured using a stainless steel clinical ruler (Henry Schein, Melville, New York, USA). Each measurement was repeated three times and the mean recorded.

Figure 2 Nance Brass Wire technique



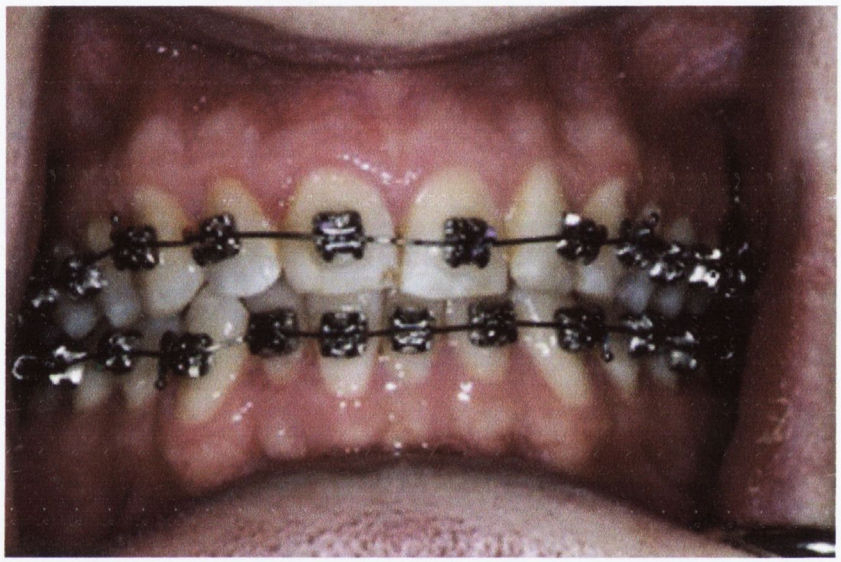
3.8 Group Allocation

Eligible patients picking a sealed opaque envelope, which indicated their group allocation, was used to achieve randomization. Patients who did not wish to have the proposed treatment were removed from the study.

3.9 Fixed Appliance group

A single postgraduate student under the supervision of a consultant orthodontist treated 22 patients using self-ligating pre-adjusted edgewise brackets with an MBT prescription and 0.022"x 0.028" slot (Forestadent, Westliche Karl-Friedrich-Str. 151, 75172 Pforzheim, Germany). Maxillary and mandibular arches were treated (Figure 3). A standard archwire sequence was used (0.014" round, 0.018" round, 0.018x0.025" rectangular martinsitic active nickel-titanium alloys (OrthoCare, 1 Riverside Estate, Saltaire, West Yorkshire, BD17 7DR) and 0.019x0.025" stainless steel (Ormoco 1332 South Lone Hill, Avenue Glendora, CA 91740). Maxillary arch treatment was completed on a non-extraction basis for both groups and therefore had no effect on the lower incisor proclination produced. No auxiliary appliances or elastics were used during the study period. Interproximal reduction, using stainless steel tooth stripping blades (Tooth Stripper Kit, OrthoCare, 1 Riverside Estate, Saltaire, West Yorkshire, BD17 7DR), was completed where required. Each patient was seen on a 6 weekly basis. Patients were treated until lower arch alignment was achieved (crowding measurement =0 mm).

Figure 3 Fixed appliance treatment

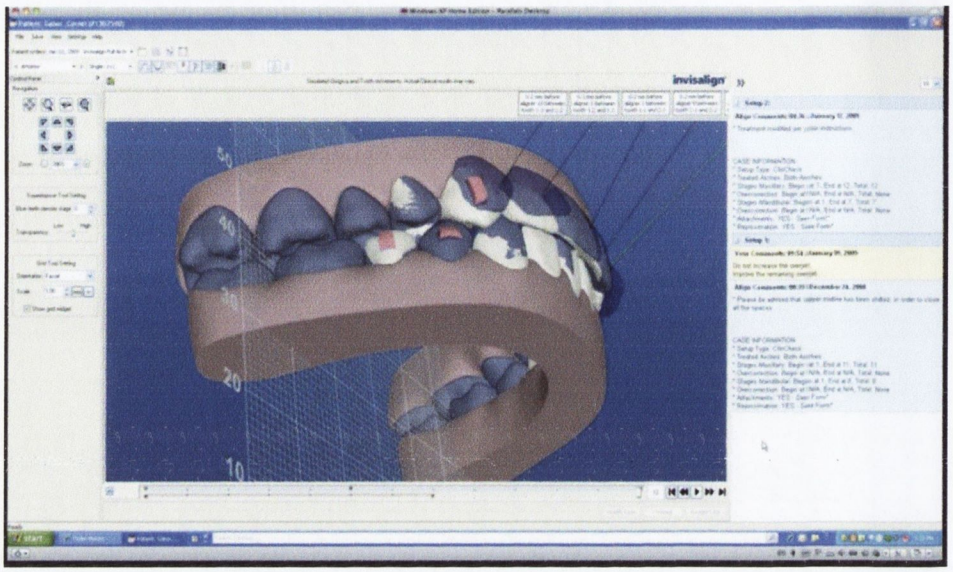


3.10 Invisalign group

The same lead operator treated 22 patients with Invisalign® clear aligners (Align Technology Inc, Santa Clara, CA, USA). Each aligner was 0.75mm thick polyurethane. The appliances were fabricated using the Invisalign® protocol. Maxillary and mandibular impressions were made using a combination of a putty and light body polyvinylsiloxane impression (PRESIDENT, Colene/Whaledent AG, Feldwiesenstrasse 20, 9450 Altstatten/Switzerland). Align supplied disposable plastic trays

for impression fabrication. These impressions were also washed with water, placed in CIDEX® OPA (ASP, 33 Technology Drive, Irvine, CA 92618 USA) for 5 minutes then rinsed again with water prior to being packed for postage to Align technology Inc (Santa Clara, CA, USA). A silicone 'squash bite' (Take 1 Advanced, Kerr Corporation, 1717 West Collins Orange, CA 92867, USA) in centric occlusion was also recorded and sent to Align. A full series of clinical photographs (Extraoral repose, smiling and profile: Intraoral frontal, right and left buccal, maxillary and mandibular occlusal) taken using a Canon 1100D digital camera (Canon USA Inc, 1 Canon Park, Melville NY 11747, USA) were uploaded to the Invisalign® Doctor's site (www.invisalign.com). The pre-treatment lateral cephalogram and orthopantomograph were also uploaded. A treatment plan was formulated using Align's ClinCheck® software (Align Technology Inc, Santa Clara, CA, USA) by the lead operator, a postgraduate in orthodontics, and then authorised by a consultant orthodontist who is an experienced Invisalign® provider (Figure 4). Again patients were treated until lower arch alignment was achieved (crowding measurement =0 mm).

Figure 4 Clincheck software



No restrictions were placed on the amount of interproximal reduction that could be used or on the number of optimised attachments that could be placed. The aligners were then fabricated, delivered to each patient and checked for fit and accuracy. The patient was then reviewed two weeks later for delivery of their second aligner and, if necessary, Smartforce® attachments (Align Technology Inc, Santa Clara, CA, USA) were placed using custom matrices from Align Technology. A conventional etch and bond system was used to place Transbond LR (3M Unitek, 2724 South Peck Road, Monrovia, California 91016, USA) composite attachments. Each patient was subsequently seen on a six weekly basis and asked to change their aligners every two weeks (Figure 5 and 6).

Figure 5 Pre aligners

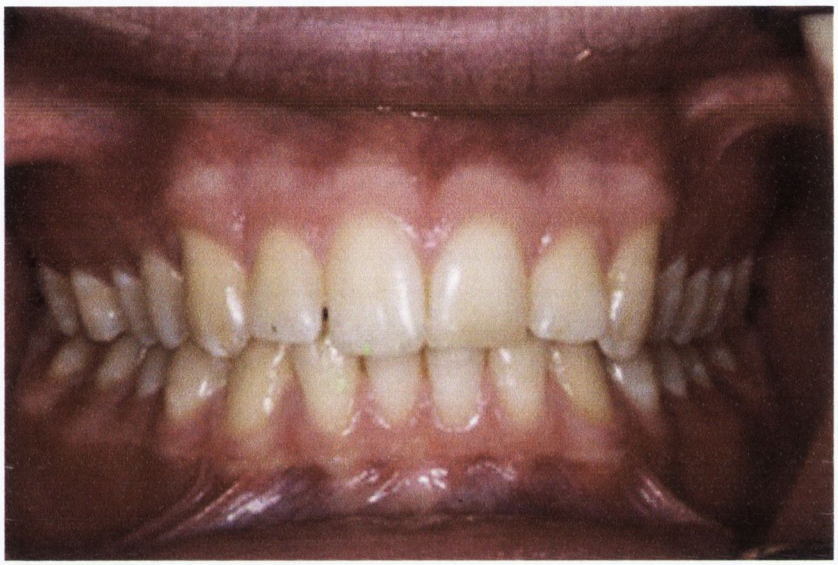
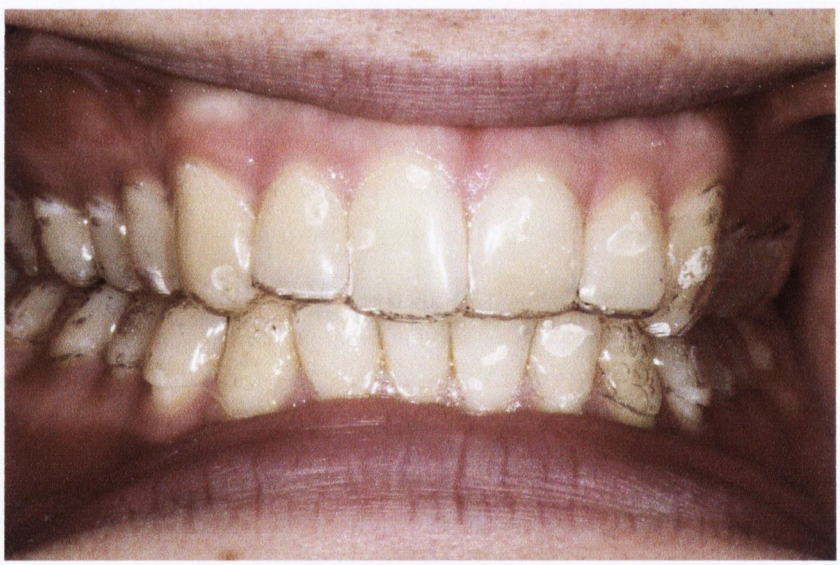


Figure 6 Aligners in situ



3.11 Radiographic Measurements

Each participant had a pre-treatment digital lateral cephalogram (Proline 2002 PM CC, Planmeca Oy, Asentajankatu 6, FIN-00880 Helsinki, Finland) taken with the patient in the natural head position (looking into their own eyes in a mirror) immediately prior to the

commencement of treatment. Lateral cephalograms were repeated near the end of treatment. Pre-treatment and near end treatment lateral cephalograms were digitally traced by the lead operator using the 'Quick Ceph System' (Quick Ceph Systems Inc, San Diego, USA) installed on an iMac computer (Apple, Infinite Loop, Cupertino, CA 95014, USA). The mandibular incisor inclination was assessed using the angular measurement of mandibular incisor to mandibular plane as described by Downs (Figure 1) (Downs, 1956). Each measurement was repeated 3 times and the mean recorded.

3.12 Error of the method

The intra-examiner reproducibility was assessed by repeating the crowding and mandibular incisor inclination measurements, 4-weeks after the original measurements, on 20 randomly selected radiographs and study models. Reliability was calculated using a paired *t-test* comparing the logarithmic of the results. The results were found to be not statistically significant, $p = 0.33$ for cephalometric measurements and $p = 0.35$ for crowding measurements.

Table 5 Paired t-tests to assess intra and inter-examiner errors for cephalometric measurements

	Mean Difference	95% Confidence Level	p-value
Intra-examiner	-0.0005	-0.0016 – 0.0006	0.33
Inter-examiner	-0.0011	-0.0038 – 0.0017	0.43

A consultant orthodontist, repeating measurements on 20 randomly selected radiographs and study models, assessed inter-examiner reproducibility. The logarithmic of these results were compared to the lead operator's measurements using a paired *t-test*. Again the results were not statistically significant, p = 0.43 for cephalometric measurements and p = 0.46 for crowding measurements.

Table 6 Paired t-tests to assess intra and inter-examiner errors for crowding measurements

	Mean Difference	95% Confidence Level	p-value
Intra-examiner	-0.0033	-0.011 – 0.0044	0.35
Inter-examiner	-0.024	-0.046 – 0.094	0.46

Random error was calculated using the Dahlberg equation $D = \sqrt{\sum_{i=1}^{N} \frac{d_i^2}{2N}}$ where d_i is the difference between the first and the second measure, and N is the sample size that was re-measured. Random error was also found to be insignificant with D = 0.7 degrees of random error for cephalometric measurements and D = 0.36 mm of random error for crowding measurements.

3.13 Statistical Analysis

The data were analysed using R software version 2.11.1. The change in mandibular incisor angulation in the Invisalign® and fixed appliance groups were compared using a Welch two sample *t-test*. Non-compliant patients were removed from the study and were not included in the final statistical analysis.

4 Results

Treatment end point was defined as when lower arch alignment was achieved (crowding measurement =0 mm). Two patients in the Invisalign® group would not comply with appliance wear and discontinued treatment. A further three patients in the Invisalign® group were unavailable for final records. One patient was pregnant and could not receive a cephalometric radiograph and the other two patients did not have lower arch alignment by the end of the research period. Two patients in the fixed appliance group were removed from the study due to oral hygiene issues. Figure 7 displays the CONSORT patient flow chart.

Figure 7 CONSORT flow chart

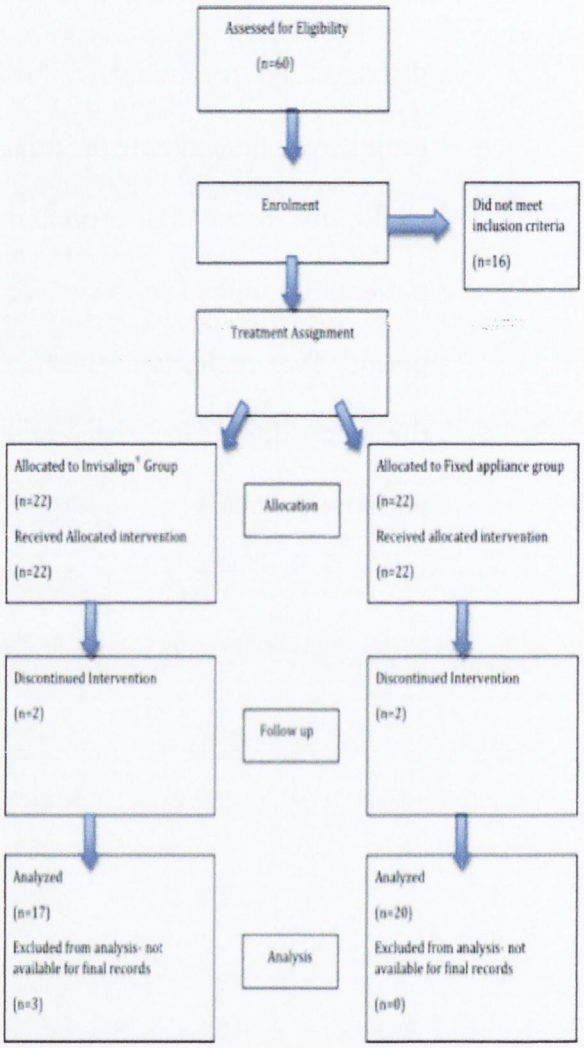


Table 7 shows the distribution of demographic variables between the treatment groups.

Table 7 Descriptive statistics for the demographic and clinical characteristics of pre-treatment study groups (n=44)

	Total	*Mean ± SD Invisalign® group*	*Fixed appliance group*
Age (years)	26.4 ± 7.7	29.1±7.5	23.7± 7.0
Crowding (mm)	2.3±1.3	2.5± 1.3	2.1±1.3
Incisor Inclination (°)		91.6 ±6.4	90.8 ± 5.4

No significant pre-treatment differences were found between the groups. More female patients took part in the research with 14 in the clear aligner group and 13 in the fixed appliance group.

The mandibular incisor inclinations for the Invisalign® (Table 8) and fixed appliance groups (Table 9) are shown below.

Table 8 Invisalign® group mandibular incisor inclination pre-treatment, post-treatment and inclination change

Patient	*Pre Invisalign Degrees*	*Post Invisalign Degrees*	*Inclination Change Degrees*
1	94	94	0
2	99	103	4
3	92	99	7
4	101	101	0
5	94	96	2
6	93	98	5
7	88	90	2
8	82	82	0
9	100	100	0
10	97	102	5
11	84	94	10
12	98	99	1
13	84	86	2
14	90	90	0
15	93	101	8
16	81	88	7
17	87	92	5
Mean +/- SD	91.6 ± 6.4	95.0 ± 6.2	3.4 ± 3.2

Table 9 Fixed labial appliance group mandibular incisor inclination pre-treatment, post-treatment and inclination change

Patient	*Pre Fixed Degrees*	*Post Fixed Degrees*	*Inclination change Degrees*
1	96	101	5
2	94	97	3
3	89	90	1
4	89	101	12
5	91	98	7
6	85	87	2
7	98	99	1
8	82	87	5
9	87	93	6
10	87	87	0
11	83	83	0
12	102	105	3
13	89	100	11
14	97	98	1
15	97	99	2
16	89	96	7
17	89	104	15
18	88	97	9
19	88	98	10
20	96	102	6
Mean +/- SD	90.8 ± 5.4	96.1 ± 6.2	5.3 ±4.3

The variance for both groups was plotted and was found to be similar for both groups. All patients included in the final analysis had aligned arches at the end of the research period. The vast majority of cases (76% Invisalign group, 65% Fixed group) had a change in mandibular incisor inclination that would not be considered to be clinically significant (≤6°).

A Welch two sample *t-test* compared mandibular incisor proclination produced by Invisalign® (3.4° ± 3.2°) and fixed labial appliances (5.3° ± 4.3°). The results were not found to be statistically significant (p= 0.14).

Table 10 Welch two sample t-test comparing mandibular incisor proclination produced by Invisalign® and Fixed labial appliances.

	Mean Difference	95% Confidence Level	p-value
Mandibular Incisor Proclination	-1.89	-4.43 – 0.65	0.14

5 Discussion

Clear aligners have been marketed as an aesthetic alternative to fixed labial brackets, however very little research has been carried out to verify this claim. The proposed advantages of clear aligners include easier oral hygiene procedures, improved aesthetics and less pain when compared to fixed appliance therapy (Ali and Miethke, 2012). Limited research has ascertained that tooth movements with clear aligners appear to be less predictable (Kravitz *et al.*, 2008; Kravitz *et al.*, 2009; Krieger *et al.*, 2011). Clear aligners have evolved over time in an attempt to improve the tooth movements that could be achieved. Prior to this study, mandibular incisor proclination produced by clear aligners had not been assessed. The aim of this prospective clinical trial was to compare the mandibular incisor proclination produced by fixed appliances and 3rd generation clear aligners (Invisalign®) when treating patients with mild mandibular crowding.

Two groups of patients with similar amounts of mild lower crowding were treated with either fixed labial appliances or Invisalign® aligners. Mandibular incisor proclination was calculated using digital radiographs. No statistically significant differences were found between the treatment groups ($p > 0.05$)

Lower incisor proclination has been recognised as a side effect of fixed appliance therapy for a number of years. Mills suggested some cases where moving the mandibular incisors labially was desirable (Mills, 1966). In the vast majority of cases however, the orthodontist

endeavours to maintain the anteroposterior position of the lower labial segment. This philosophy has developed as a result of multiple trials highlighting the negative impact of excessive mandibular incisor proclination (Mills, 1968; Little *et al.*, 1988). Mills maintained that a mandibular incisor movement of greater than 2 mm will produce an unstable result (Mills, 1968). Little *et al.*, following the Seattle studies, commented that lower incisor proclination has a very high relapse rate (Little *et al.*, 1988). As well as stability concerns, lower incisor proclination can predispose a patient to soft tissue loss and gingival recession. This can have a detrimental effect on the patient's oral health by exposing them to an increased risk of hypersensitivity and root caries. Although recently the true extent to which incisor proclination affects gingival health has been questioned, it would seem a reasonable assumption that if a tooth is moved from its zone of support, adverse consequences can be expected (Aziz and Flores-Mir, 2011). Excessive incisor proclination can also produce a poor aesthetic result. Lower lips do not always respond with a 1:1 ratio to mandibular incisor movements, but excessive proclination is likely to cause poor facial aesthetics (Roos, 1977).

Having ascertained the importance of lower incisor inclination, it is reasonable to question what effect an appliance may have on the mandibular labial segment. As mentioned previously, numerous studies have assessed the lower incisor proclination produced by various different fixed and removable orthodontic appliances (Table 1). No study, however, has compared the lower incisor proclination produced by clear aligners to the proclination produced by fixed labial appliances.

With an increase in the use of these aligners a prospective clinical trial to assess this became more urgent.

Forty-four patients were randomly assigned to either the Invisalign® or fixed labial appliance groups. Pre-treatment assessment revealed both groups had similar age profiles (29.1± 7.5yrs vs 23.7±7.0yrs), crowding (2.5 ± 1.3mm vs 2.1± 1.3mm) and mandibular incisor proclination (91.6°±6.4° vs 90.8°± 5.4°). The majority of patients were female (61%), which is in agreement with previous studies that have found women to be the predominant participants in adult orthodontics (Tayer and Burek, 1981; Nattrass and Sandy, 1995; Fritz *et al.*, 2002)

Both treatment modalities resulted in lower incisor proclination. Invisalign® produced a mean proclination of 3.4°±3.2°. The fixed appliances produced a mean lower incisor proclination of 5.3°±4.3°. The differences were statistically and clinically insignificant. Six patients in the Invisalign group and five patients in the fixed appliance group had 1° or less change in their lower incisor inclination. This is an interesting finding and would suggest both treatments maintain the lower labial segment inclination in a high percentage of cases (30%). The vast majority of cases (70%) had a change in mandibular incisor inclination that we would not consider to be clinically significant (≤6°). This may have been expected as a result of the mild crowding at the start of treatment.

This research found fixed appliances proclined the lower labial segment by 5.3°±4.3°. This is in agreement with studies done by Pandis *et al.* and Scott *et al.* who compared different types of bracket systems *(Scott et*

al., 2008; Pandis et al., 2011). Pandis *et al.* used similar inclusion criteria and methodology as this research, although their participants had slightly more crowding (5.43±2.27 mm). Scott *et al.* obtained their results from patients who had undergone four first premolar extractions (Scott *et al.*, 2008; Pandis *et al.*, 2011). As mentioned previously, no research had assessed the mandibular incisor proclination produced by clear aligner treatment.

Djeu *et al.* used the American Board of Orthodontics objective grading system to assess the results achieved with Invisalign®. This assesses tooth alignment, marginal ridge uniformity, buccolingual inclination of posterior teeth, occlusal contacts, occlusal relationship, overjet and interproximal contacts (Djeu *et al.*, 2005). An orthopantomagraph is also used to record root alignment. However, mandibular incisor inclination is not recorded.

Kravitz *et al.* recorded the accuracy of the tooth movements predicted by ClinCheck® software (Kravitz *et al.*, 2009). They digitally superimposed pre and post-treatment study models. While the authors did suggest that Invisalign® could constrict the lower labial segment adequately, no measurements of the actual movements achieved were described. The authors also commented that it was likely that proclination would be difficult with the Invisalign® system (Kravitz *et al.*, 2009). They did include patients with missing posterior teeth and extraction cases which may explain the increased number of participants with retroclined lower incisors.

Krieger *et al.* also used ClinCheck® software to assess the accuracy of tooth movements achieved when using Invisalign® aligners (Krieger *et al.*, 2012). They measured the maxillary and mandibular arch lengths digitally. They suggested that an increase in arch length was an indication of labial segment protrusion (Krieger *et al.*, 2012). They commented that 58% of their patients had some increase in mandibular arch length post Invisalign® treatment (Krieger *et al.*, 2012). Drake *et al.* compared the tooth movements achieved when changing an aligner weekly or biweekly (Drake *et al.*, 2012). They used cone beam computer tomography to measure the movement of the participants' maxillary central incisor over an eight-week period. No other teeth were assessed. The authors concluded that most of the movements achieved by the clear aligners were through tipping of crowns (Drake *et al.*, 2012). These results are broadly in agreement with our findings, with 71% of the Invisalign® patients having lower incisor proclination, however the tipping was not shown to be excessive and was similar to that which occurred when using fixed appliances in mild crowding cases.

It has been stated that fixed labial appliances will align the lower labial segment by not only tipping teeth but also through the use of rectangular archwires, by torquing the roots of teeth (Isaacson *et al.*, 1993). This implies that clear aligners would procline lower incisors more than fixed appliances when treating similarly crowded cases. The fact that this was not a finding from our research may be explained by a number of factors.

Firstly, fixed appliances often apply a protrusive force on teeth during the initial phase of treatment. As mesial canine tip is expressed in the bracket system, the lower incisors are proclined (McLaughlin *et al.*, 2001). This labial movement may be counteracted in the later stages of treatment, however this involves a significant amount of 'round tripping' of teeth. Some authors have advocated the use of auxiliary wires or 'lacebacks' to inhibit this mesial movement but this appears to have limited success (Fleming *et al.*, 2013). Clear aligners can align teeth individually with one aligner potentially only moving one tooth. This gradual segmented movement may minimize the proclination that occurs.

The method by which fixed appliances and clear aligners apply forces to teeth may also have had a bearing on the results that were found. It has been described that fixed appliances place a force coronal and buccal to the centre of resistance of a tooth (Isaacson *et al.*, 1993). This can result in tipping and proclination, particularly in the lower labial segment. Clear aligners will place a force along the complete length of the crown of the tooth. This may create forces closer to the centre of resistance of the tooth and minimise the amount of proclination that occurs

A further reason may be the recent developments in clear aligner treatment i.e. the creation of the third generation of aligners. These newer aligners use accurately placed composite attachments to increase the control of tooth movement and they also have indentations in the polyurethane to place increased pressure on specific points on the crown of the tooth to produce torque in the root of the tooth. It is

difficult to say whether torquing of the lower labial segment roots prevented excessive proclination in the clear aligner group. It is also not possible to confirm whether the recent aligner developments have contributed to these results, as no previous studies accurately measured lower incisor proclination.

If this clinical trial were to be repeated using more moderately crowded archs the results may be different. A clinical trial, using clear aligners to treat patients who require extractions, is needed to conclusively answer whether attachments can torque roots of teeth. It would then be possible to ascertain if space closure was achieved through tipping or bodily movement of teeth.

There are a number of limitations of this clinical trial. Firstly the use of lateral cephalometric radiographs to assess mandibular incisor inclination is not 100% accurate. Baumrind and Frantz described the problems with using cephalometrics to assess angulations (Baumrind and Frantz, 1971b). They noted that the lower incisor apex, in particular, can be very difficult to locate. Every effort was made to reduce the chance of measurement error when tracing the pre and near end lateral cephalometrics. Each measurement was repeated three times and the mean taken. The use of digital radiographs made this process more operator friendly. The intra-operator and inter-operator errors were not significant. As mentioned previously, other methods of measuring lower incisor inclination have been shown to be unreliable.

Secondly the use of interproximal reduction (IPR) in each group could not be verified as being equal. While both groups had the exact amount

planned prior to the start of treatment, it was difficult to assess precisely how much interproximal reduction was carried out. However, the risk of intergroup differences was reduced by the fact that the same operator treated all the patients, thus controlling the IPR that was completed. Very small variations between the groups cannot be ruled out but they are unlikely to have affected the overall results.

Five patients in the Invisalign® group could not be included in the final results. Two of these patients had compliance issues, which is obviously a significant limitation of removable appliance therapy. The majority of patients tolerated the appliance well. One Invisalign® patient became pregnant during the research and was not available for the near end lateral cephalogram. A further two patients did not have lower arch alignment by the end of the research period. Nineteen out of twenty treated Invisalign® cases required a refinement period at the end of treatment which can lengthen the treatment time significantly. The treatment time differences between the groups will be discussed in a future document. Two fixed appliance patients were removed from the research as a result of poor oral hygiene. Intention to treat analysis was not performed in this study due to a number of concerns. Firstly it was ascertained that the patients who were removed from the study had received a minimal intervention and therefore indicated very little about the efficiency of either treatment. Secondly the authors were concerned that any treatment effect would be diluted due to non-compliance. Finally there was a possibility that heterogeneity could be introduced if non-compliant patients, dropouts and compliant subjects were mixed together in the final analysis

6 Conclusion

Clear aligner treatment has undoubtedly become more widespread in the last number of years. Very few clinical trials have assessed how this appliance moves teeth. When comparing mandibular incisor proclination produced by Invisalign® and fixed labial appliance treatment, in mild crowding cases, no difference was ascertained. This research opens the door for more complex clinical trials to be completed. These future trials should tell the clinician whether clear aligner therapy is a viable alternative to fixed appliance treatment.

Further research

- Treatment times for both treatment groups
- Changes in mandibular inter-canine width for both treatment groups
- Mandibular incisor proclination for cases with moderate crowding treated with clear aligners
- Compare root alignment in premolar extraction cases treated with clear aligners and fixed appliances

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8 Appendices

i) Ethical approval application form

STANDARD APPLICATION FORM

For the Ethical Review of

Health-Related Research Studies, which are not Clinical Trials of Medicinal Products For Human Use

as defined in S.I. 190/2004

DO NOT COMPLETE THIS APPLICATION FORM

IF YOUR STUDY IS A CLINICAL TRIAL OF A MEDICINAL PRODUCT

Title of Study: A MEASUREMENT OF THE DENTAL PROCLINATION PRODUCED BY INVISALIGN ORTHODONTICS

Principal Investigator:

Dr Joe Hennessy_____

Applicant's Signature:_____ _____

_____

TABLE OF CONTENTS MANDATORY /OPTIONAL

This Application Form is divided into Sections.

Sections A, B, C, D, E, J, K, L are **Mandatory.**

Sections F, G, H, and I are optional. Please delete Sections F, G, H, and I if these sections do not apply to the application being submitted for review.

IMPORTANT NOTE: Please refer to **Section I** within the form before any attempt to complete the Standard Application Form. **Section I** is designed to assist applicants in ascertaining if their research study is in fact a clinical trial of a medicinal product.

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

SECTION A GENERAL INFORMATION

SECTION A IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

A1 TITLE OF THE RESEARCH STUDY:

A MEASUREMENT OF THE DENTAL PROCLINATION PRODUCED BY INVISALIGN ORTHODONTICS

A2 Principal Investigator(s):

Title: Dr **Name:** Joe Hennessy

Qualifications: Ba.BDent.Sc.MFDS

Position: Postgraduate in Orthodontics

Dept: Orthodontic Dept

Organisation: Dublin Dental University Hospital

Address: Lincoln Place, Dublin 2

TEL: 0863577131 E-MAIL: joe.hennessy@dental.tcd.ie

A3 (a) Is this a multi-site study? Yes

A3 (b) Please name each site where this study is proposed to take place and state the lead investigator for each site:

Site:	**Lead Investigator:**
DUBLIN DENTAL UNIVERSITY HOSPITAL	JOE HENNESSY

A3 (C) FOR ANY OF THE SITES LISTED ABOVE, HAVE YOU GOT AN OUTCOME FROM THE RESEARCH ETHICS COMMITTEE (WHERE APPLICABLE)?

I was asked by Trinity's Ethics committee to apply to JREC

A4. CO-INVESTIGATORS:

A5. Lead contact person who is to receive correspondence in relation to this application or be contacted with queries about this application.

Title: Dr. **Name:** Joe Hennessy

Address: **Dublin Dental University Hospital**

Lincoln Place,

Dublin 2

TEL (WORK): 01 6127388 TEL (MOB.): 0863577131

E-MAIL: joe.hennessy@dental.tcd.ie

A6. Please provide a lay description of the study.

This study will compare how much tooth movement is produced by clear orthodontics braces (Invisalign) with the amount of tooth movement produced by conventional orthodontic braces ('train-tracks'). It will use the radiographs that are taken during a standard course of orthodontic treatment to measure these tooth movements. No addition records will be taken. Patients who are undergoing Invisalign treatment and patients who are undergoing conventional orthodontic treatment will participate in the study. How far the braces procline the lower teeth is of particular interest as this has never been accurately measured. The patients will receive the same orthodontic treatment whether or not they are participants in the study

A7 (A) IS THIS STUDY BEING UNDERTAKEN AS PART OF AN ACADEMIC QUALIFICATION? Yes

A7 (b) IF YES, **please complete the following:**

Student Name: **Joe Hennessy** **Course:** **Doctorate in Clinical Dentistry specializing in Orthodonics**

Institution: **Dublin Dental University Hospital**
Academic Supervisor: Dr Ebrahim Al-Awadhi and Dr Therese Garvey

SECTION B STUDY DESCRIPTORS

SECTION B IS MANDATORY

B1. Provide information on the study background.

In 1997 Align Technology Inc (Santa Clara, CA, USA) introduced Invisalign® as an aesthetic alternative to fixed labial braces. Although fixed appliances have been the backbone of orthodontics for years, patients' reluctance to wear fixed appliances has been the driving force for the development of Invisalign®. Invisalign®, a series of 1 mm thermoplastic aligners, offers several advantages over fixed appliances. The main advantage of Invisalign® is its aesthetics making it more attractive to patients. Furthermore, Invisalign® is more comfortable for the patient and

does not impede oral hygiene procedures[1]. It has been suggested that Invisalign® requires less clinical chair time and fewer emergency appointments[1].

There are, however, several drawbacks associated with Invisalign®. A limitation of Invisalign® is the inability to alter a treatment plan once a set of aligners has been fabricated. Patient compliance is necessary because the appliances are removable. There is also a current belief among orthodontists that certain types of movements such as bodily tooth movement, tooth derotation and tooth extrusion are difficult to achieve with Invisalign®. Few studies have assessed the efficiency of Invisalign® in producing different tooth movements. These studies found individual tooth movements difficult to predict with Invisalign®[2, 3, 4].

Ali SA, Miethke HR. Invisalign, an innovative invisible orthodontic appliance to correct malocclusions: Advantages and disadvantages. Dent Update 2012 May;39(4):254-6, 258-60

Phan X, Ling PH. Clinical limitations of Invisalign. J Can Dent Assoc. 2007 Apr;73(3):263-6

Clements KM, Bollen AM, Huang G, King G, Hujoel P, Ma T. Activation time and material stiffness of sequential removable orthodontic appliances. Part 2: dental improvements. Am J Orthod Dentofacial Orthop 2003; 124: 502-8

Kravitz ND, Kusnoto B, BeGole E, Obrez A, Agran B. How well does Invisalign work? A prospective clinical study evaluating the efficacy of tooth movement with Invisalign. Am J Orthod Dentofacial Orthop. 2009 Jan;135(1):27-35.

B2. List the study aims and objectives.

The aim of this study is to measure the amount of mandibular incisor proclination that occurs during Invisalign® therapy. This will be compared to the amount of mandibular incisor proclination produced by self ligating conventional brackets. The study may offer practitioners, who use Invisalign®, guidelines on the amount of mandibular incisor proclination that can be expected. This may allow for better case selection when using aligners and improved success rates.

B3. List the study endpoints (if applicable).

The study end point will be after six months of orthodontic treatment

B4. Provide information on the study design.

This study will be a prospective.

Two groups, of 20 patients each, will be selected from the Invisalign orthodontic waiting list at the Dublin Dental University Hospital and from the conventional orthodontic waiting list at the regional orthodontic unit in St James' Hospital. A non clinical gatekeeper will contact ten patients at a time, from the waiting lists, until the sample size is achieved. The gatekeeper will post an information letter, a patient information sheet and a consent form to the patient. The patient will be asked to contact the gatekeeper if they are interested in participating in the research. The patient will then be given an appointment for an initial assessment. Study casts of these patients will be assessed to ensure they meet the inclusion criteria. Each patient will have pre-treatment records taken including study models, a lateral cephalometric radiograph and an orthopantomograph. A Peer Assessment Rating calibrated Orthodontist, who is not involved in the research, will assess the lower study cast of each patient and provide them with a PAR score.

B5. Provide information on the study methodology.

Those patients who meet the inclusion criteria will be divided into two groups. Twenty will have aligners fabricated following the Invisalign® protocol. Rim lock trays will be customised using the patients study models and heavy body polyvinylsiloxane (PVS) impression material will be used. Light body PVS will be washed over the patient's teeth and a 'putty/wash' impression will be made. A wax bite in centric occlusion will also be recorded. A treatment plan will be formulated by the lead operator (a Specialist Registrar in orthodontics) and then authorised by a Consultant orthodontist who is an experienced Invisalign® provider. The second group of twenty patients will have MBT prescription self ligating brackets placed.

Following fabrication, aligners will be delivered to each patient and checked for fit and accuracy. If necessary, Smartforce attachments will be placed using custom matrices from Align Technology. Each patient will be seen on a weekly basis whether or not an aligner change is required. The end of treatment will be the completion of an entire series of aligners. Proclination for both patient groups will be measured after 6 months of treatment by repeating a lateral cephalogram

Pre-treatment and mid-treatment lateral cephalograms will be digitally traced by the lead operator using the 'Quick Ceph System' (Quick Ceph Systems Inc, San Diego, USA). The mandibular incisor inclination will be assessed using the angular measurement of lower incisor to mandibular plane. This has been shown to be accurate and reproducible[1]. Each measurement will be repeated 3 times and the mean will be recorded.

You QL, Hagg U. A comparison of three superimposition methods. Eur J Orthod 1999; 21: 717-725

B6. What is the anticipated start date of this study?

September 2013

B7. What is the anticipated duration of this study?

Six months

B8 (a) How many research participants are to be recruited in total?

40

B8 (b) Provide information on the statistical approach to be used (if appropriate) / source of any statistical advice.

To evaluate the reliability of the measurements twenty lateral cephalograms will be randomly chosen and mandibular incisor inclination will be remeasured by the same examiner and an independent examiner again. A second set of measurements will be carried out in blinded manner and under the same conditions 4 weeks after the first measurement. The intra-examiner and inter-examiner reliability will be evaluated using the paired *T-test* after log-transformation of incisor inclination measurements in addition to the 95% confidence interval. The significant level will be set at $\alpha = 0.05$. The error of the method will be calculated according to Dahlberg's equation. A Student T test will be used to evaluate the difference between the proclination achieved by Invisalign and the proclination achieved by self ligating brackets.

B8 (c) Please justify the proposed sample size and provide details of its calculation (including minimum clinically important difference).

If a 5.5 degree difference is seen between the different treatment systems, 20 patients are needed in each group to make the results statistically significant. Two-sample t test power calculation

n = 16.68972

delta = 6

sd = 6

sig.level = 0.05

power = 0.8

alternative = two.sided

NOTE: n is number in *each* group

power.t.test(delta=6, sd=6, type="two.sample",alternative="two.sided", power=0.8)

These figures where calculated using a previous studies results. A difference of 6 degrees would be seen as clinically important.

B8 (d) Where sample size calculation is impossible (e.g. It is a pilot study and previous studies cannot be used to provide the required estimates) then please explain why the sample size to be used has been chosen.

N/A

SECTION C study PARTICIPANTS

SECTION C IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

SECTION C1 PARTICIPANTS – SELECTION AND RECRUITMENT

C1. 1 How many research participants are to be recruited? At each site (if applicable)? And in each treatment group of the study (if applicable)?

NAME OF SITE:	NAMES OF TREATMENT GROUP (IF APPLICABLE)		
	INSERT NAME OF GROUP:	INSERT NAME OF GROUP:	INSERT NAME OF GROUP:
DUBLIN DENTAL UNIVERSITY HOSPITAL	**Invisalign group- 22**		
REGIONAL ORTHODONTIC UNIT, ST JAMES' HOSPTIAL	**Bracket group- 22**		

C1.2 How will the participants in the study be selected?

Two groups, of 22 patients each, will be selected from the Invisalign orthodontic waiting list at the Dublin Dental University Hospital

C1.3 How will the participants in the study be recruited?

A non clinical gatekeeper will contact ten patients at a time, from the waiting lists, until the sample size is achieved. The gatekepper will post an information letter, a patient information sheet and a consent form to the patient. The patient will be asked to contact the gatekeeper if they

are interested in participating in the research. The patient will then be given an appointment for an initial assessment. Study casts of these patients will be assessed to ensure they meet the inclusion criteria

C1.4 What are the main inclusion criteria for research participants? (please justify)

Each Group will have the same inclusion criteria

Mild mandibular crowding as defined by the Little Index

A PAR score of <15 (mild crowding)

No requirement for interproximal reduction

A cephalometric ANB of 1-4 degrees (no skeletal discrepancy)

No caries or periodontal disease

No extraction requirement

C1.5 What are the main exclusion criteria for research participants? (please justify)

Each group will have the same exclusion criteria

Participants cannot be pregnant as 3 dental radiographs will need to be taken during the research.

C1.6 Will any participants recruited to this research study be simultaneously involved in any other research project?

Not to my knowledge

SECTION C2 PARTICIPANTS – INFORMED CONSENT

C2.1 (a) Will informed consent be obtained? Yes

C2.1 (c) If yes, how will informed consent be obtained and by whom?

Joe Hennessy (lead researcher) will take consent prior to the beginning of treatment. The patient will be given written and oral information

about the research by the gatekeeper and at their screening appointment (a minimum of 7 days prior to the start of treatment). The research will be explained again on the day of treatment prior to signing the consent form.

The patient will have multiple opertunities to ask questions about the treatment.

C2.1 (d) Will participants be informed of their right to refuse to participate and their right to withdraw from this research study?

Yes. If the patient no longer wants to participate in the research they will continue to be offered orthodontic treatment. As with any elective treatment, the patient can discontinue their orthodontic treatment whenever they wish. Their medical records will be stored on password protected computers in the Dublin Dental Hospital

C2.1 (f) Will there be a time interval between giving information and seeking consent? Yes

C2.1 (g) If yes, please elaborate.

A minimum of 7 days will be allowed between the screening appointment and the signing of the consent

SECTION C3 adult participants - CAPACITY

C3.1 (a) Will all adult research participants have the capacity to give informed consent? YES

SECTION c4 participants under the age of 18

C4.1 (a) Will any research participants be under the age of 18 i.e. Children?

No

SECTION C5 PARTICIPANTS - CHECKLIST

Please confirm if any of the following groups will participate in this study. This is a quick checklist for research ethics committee members and it is recognised that not all groups in this listing will automatically be vulnerable or lacking in capacity.

C5.1 Patients Yes

C5.2 Unconscious patients No

C5.3 Current psychiatric in-patients No

C5.4 Patients in an emergency medical setting No

C5.5 Relatives / Carers of patients No

C5.6 Healthy Volunteers No

C5.7 Students No

C5.8 Employees / staff members No

C5.9 Prisoners No

C5.10 Residents of nursing homes No

C5.11 Pregnant women No

C5.12 Women of child bearing potential Yes

C5.13 Breastfeeding mothers No

C5.14 Persons with an acquired brain injury No

C5.15 Intellectually impaired persons No

C5.16 Persons aged > 65 years No

C5.17 If yes to any of the above, what special arrangements have been made to deal with issues of consent and assent (if any)?

Patients will be informed they will still receive orthodontic treatment whether or not they participate in the research.

Women of child bearing potential will be asked if they are pregnant prior to radiographs being taken. No radiographs will be performed on pregnant patients.

SECTION D research PROCEDURES

SECTION D IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

D1. WHAT RESEARCH PROCEDURES OR INTERVENTIONS (OVER AND ABOVE THOSE CLINICALLY INDICATED AND/OR OVER AND ABOVE THOSE WHICH ARE PART OF ROUTINE CARE) WILL RESEARCH PARTICIPANTS UNDERGO WHILST PARTICIPATING IN THIS STUDY?

No additional procedures will be performed on the participants. They will be treated in the same manner as any patient undergoing routine orthodontic therapy. They will have the same clinical records taken before, during and after treatment

D2. If there are any potential harms resulting from any of the above listed procedures, provide details below:

Orthodontic treatment is associated with risks. The risks associated with this type of treatment include:

(i) Failure to wear the appliances for the required number of hours per day, not using the product as directed by your doctor, missing

appointments, and erupting or atypically shaped teeth can lengthen the treatment time and affect the ability to achieve the desired results;

(ii) Dental tenderness may be experienced after switching to the next aligner in the series;

(iii) Gums, cheeks and lips may be scratched or irritated;

(iv) Teeth may shift position after treatment. Consistent wearing of retainers at the end of treatment should reduce this tendency;

(v) Tooth decay, periodontal disease, inflammation of the gums or permanent markings (e.g. decalcification) may occur if patients consume foods or beverages containing sugar, do not brush and floss their teeth properly before wearing the invisalign products, or do not use proper oral hygiene and preventative maintenance;

(vi) The aligners may temporarily affect speech and may result in a lisp, although any speech impediment caused by the invisalign® products should disappear within one or two weeks;

(vii) Aligners may cause a temporary increase in salivation or mouth dryness and certain medications can heighten this effect;

(viii) Attachments may be bonded to one or more teeth during the course of treatment to facilitate tooth movement and/or appliance retention. These will be removed after treatment is completed;

(ix) Teeth may require interproximal recontouring or slenderizing in order to create space needed for dental alignment to occur;

(x) The bite may change throughout the course of treatment and may result in temporary patient discomfort.

(xi) At the end of orthodontic treatment, the bite may require adjustment ("occlusal adjustment").

(xii) Supplemental orthodontic treatment, including the use of bonded buttons, orthodontic elastics, auxiliary appliances/ dental devices (e.g. temporary anchorage devices, sectional fixed appliances), and/or restorative dental procedures may be needed for more complicated treatment plans where aligners alone may not be adequate to achieve the desired outcome.

(xiii) Teeth which have been overlapped for long periods of time may be missing the gingival tissue below the inter-proximal contact once the teeth are aligned, leading to the appearance of a "black triangle" space.

(xiv) Aligners are not effective in the movement of dental implants

(xv) General medical conditions and use of medications can affect orthodontic treatment;

(xvi) Health of the bone and gums which support the teeth may be impaired or aggravated;

(xvii) Oral surgery may be necessary to correct crowding or severe jaw imbalances that are present prior to wearing the Invisalign product. If oral surgery is required, risks associated with anesthesia and proper healing must be taken into account prior to treatment;

(xviii) A tooth that has been previously traumatized, or significantly restored may be aggravated. In rare instances the useful life of the tooth may be reduced, the tooth may require additional dental treatment such as endodontic and/or additional restorative work and the tooth may be lost;

(xix) Existing dental restorations (e.g. crowns) may become dislodged and require re-cementation or in some instances, replacement;

(xx) Short clinical crowns can pose appliance retention issues and inhibit tooth movement;

(xxi) The length of the roots of the teeth may be shortened during orthodontic treatment and may become a threat to the useful life of teeth;

(xxii) Product breakage is more likely in patients with severe crowding and/or multiple missing teeth;

(xxiii) Orthodontic appliances or parts thereof may be accidentally swallowed or aspirated;

(xxiv) In rare instances, problems may also occur in the jaw joint, causing joint pain, headaches or ear problems;

(xxv) Allergic reactions may occur; (Very rare)

(xxvi) Teeth that are not at least partially covered by the aligner may undergo supraeruption;

D3. What is the potential benefit that may occur as a result of this study?

The participants will receive orthodontic treatment to straighten their teeth. The study may offer practitioners, who use Invisalign®, guidelines on the amount of mandibular incisor proclination that can be expected. This may allow for better case selection when using aligners and improved success rates.

D4 (A) WILL THE STUDY INVOLVE THE WITHHOLDING OF TREATMENT?

NO

D5. HOW WILL THE HEALTH OF PARTICIPANTS BE MONITORED DURING AND AFTER THE STUDY?

Monitoring of the health of participants is not necessary.

D6 (A) WILL THE INTERVENTIONS PROVIDED DURING THE STUDY BE AVAILABLE IF NEEDED AFTER THE TERMINATION OF THE STUDY? **YES**

D6 (B) IF YES, PLEASE STATE THE INTERVENTION YOU ARE REFERRING TO AND STATE WHO WILL BEAR THE COST OF PROVISION OF THIS INTERVENTION?

The patients will be provided orthodontic treatment until they are satisfied with the result.

D7. PLEASE COMMENT ON HOW INDIVIDUAL RESULTS WILL BE MANAGED.

The patient's orthodontic needs will be treated during and after the research. If the patient requires dental restorations or any other dental treatment they will be referred to their general dental practitioner (GDP). The patient will be returned to the care of their GDP at the end of their orthodontic treatment

D8. PLEASE COMMENT ON HOW AGGREGATED STUDY RESULTS WILL BE MADE AVAILABLE.

The aggregated results will be submitted as part of a thesis

D9. WILL THE RESEARCH PARTICIPANT'S GENERAL PRACTITIONER BE INFORMED THE RESEARCH PARTICIPANT IS TAKING PART IN THE STUDY (IF APPROPRIATE)? **NON-APPLICABLE**

D10. WILL THE RESEARCH PARTICIPANT'S HOSPITAL CONSULTANT BE INFORMED THE RESEARCH PARTICIPANT IS TAKING PART IN THE STUDY (IF APPROPRIATE)?

NON-APPLICABLE

SECTION E data protection

SECTION E IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

SECTION E1 data processing - consent

E1.1 (A) WILL CONSENT BE SOUGHT FOR THE PROCESSING OF DATA? **YES**

SECTION E2 data processing - GENERAL

E2.1 WHO WILL HAVE ACCESS TO THE DATA WHICH IS COLLECTED?

The Lead researcher and his supervisors will have access to the data

E2.2 WHAT MEDIA OF DATA WILL BE COLLECTED?

Electronic data

E2.3 (A) WOULD YOU CLASS THE DATA COLLECTED IN THIS STUDY AS **anonymous, irrevocably anonymised, pseudonymised, coded or identifiable data?**

The data will be coded, with the information retained on password protected Dublin Dental University Hospital

E2.3 (B) IF 'CODED', PLEASE CONFIRM WHO WILL RETAIN THE 'KEY' TO RE-IDENTIFY THE DATA?

The lead researcher will retain the 'key'

E2.4 WHERE WILL DATA WHICH IS COLLECTED BE STORED?

The electronic data will be stored on password-protected computers at the sites of collection

E2.5 PLEASE COMMENT ON SECURITY MEASURES WHICH HAVE BEEN PUT IN PLACE TO ENSURE THE SECURITY OF COLLECTED DATA.

The electronic data will be stored on password-protected computers at the sites of collection. Each patient will have a unique Dublin Dental University Hospital and will be allocated a unique random research number. The lead researcher will have a spreadsheet that matches the research numbers to the hospital numbers. This will be password protected. Only the research number will be used during thesis formation.

E2.6 (A) WILL DATA COLLECTED BE AT ANY STAGE LEAVING THE SITE OF ORIGIN?

NO

E2.7 WHERE WILL DATA ANALYSIS TAKE PLACE AND WHO WILL PERFORM DATA ANALYSIS (IF KNOWN)?

At the site of collection

e2.8 (A) AFTER DATA ANALYSIS HAS TAKEN PLACE, WILL DATA BE DESTROYED OR RETAINED?

Retained

E2.8 (B) PLEASE ELABORATE.

This data will be part of the patients' clinical records. It therefore will be retained for 8 years after the end of treatment

E2.8 (D) IF RETAINED, FOR HOW LONG, FOR WHAT PURPOSE, AND WHERE WILL IT BE RETAINED?

This data will be part of the patients' clinical records. It therefore will be retained for 8 years after the end of treatment. It will be retained on the electronic clinical record systems at the sites of collection

E2.9 PLEASE COMMENT ON THE CONFIDENTIALITY OF COLLECTED DATA.

The data will not be disclosed to any third parties

E2.10 (A) WILL ANY OF THE INTERVIEW DATA COLLECTED CONSIST OF AUDIO RECORDINGS / VIDEO RECORDINGS?
NO

E2.11 (A) WILL ANY OF THE STUDY DATA COLLECTED CONSIST OF PHOTOGRAPHS/ VIDEO RECORDINGS? **NO**

SECTION e3 ACCESS TO HEALTHCARE RECORDS

E3.1 (A) DOES THE STUDY INVOLVE ACCESS TO HEALTHCARE RECORDS (HARD COPY / ELECTRONIC)? **NO**

E3.2 (A) WHO OR WHAT LEGAL ENTITY IS THE DATA CONTROLLER IN RESPECT OF THE HEALTHCARE RECORDS?

The data controller is the hospital board in the Dublin Dental University Hospital

E3.2 (B) WHAT MEASURES HAVE BEEN PUT IN PLACE BY THE DATA CONTROLLER WHICH MAY MAKE ACCESS TO HEALTHCARE RECORDS PERMISSIBLE WITHOUT CONSENT?

The researcher is involved in the direct care of the patient(s) whose healthcare records he proposes to access

SECTION f HUMAN BIOLOGICAL MATERIAL

f1 Bodily Tissue / Bodily Fluid Samples - general

F1 1 (a) Does this study involve human biological material? NO

section G radioactive material / diagnostic or therapeutic ionising radiation

G1 radioactive material / diagnostic or therapeutic ionising radiation - general

G1.1 (a) Does this study/trial involve exposure to radioactive materials or does this study/trial involve other diagnostic or therapeutic ionising radiation? N

SECTION H MEDICAL DEVICES

H1 (A) IS THE FOCUS OF THIS STUDY/TRIAL TO INVESTIGATE/EVALUATE A MEDICAL DEVICE? **YES**

If the answer to question H1 (a) is No, please delete the following questions in this Section.

H1 (B) IF YES, WHAT IS THE NAME OF THE MEDICAL DEVICE OR DEVICE NOMENCLATURE (SYSTEM OF NAMING THE MEDICAL DEVICE)?

Invisalign Clear braces

H1 (C) IF YES, PLEASE PROVIDE A GENERAL DESCRIPTION OF THE MEDICAL DEVICE.

Invisalign aligners, developed by Align Technology, Inc. ("Align") consist of a series of clear plastic, removable appliances that move your teeth in small increments

H2 (A) DOES THE DEVICE HAVE A CE MARK?

YES

H2 (B) IF THE DEVICE HAS A CE MARK, IS IT PROPOSED TO USE THE DEVICE WITHIN THE TERMS OF ITS CE MARK OR OUTSIDE THE TERMS OF ITS CE MARK? **WITHIN**	
H2 (D) CE MARK NUMBER:	

H3. IF AN APPLICATION TO CONDUCT A CLINICAL INVESTIGATION OF A MEDICAL DEVICE, WILL THE MEDICAL DEVICES SECTION OF THE IRISH MEDICINES BOARD BE REVIEWING THIS CLINICAL INVESTIGATION OF A MEDICAL DEVICE?

NON APPLICABLE

SECTION I MEDICINAL PRODUCTS / COSMETICS / FOOD AND FOODSTUFFS

Section I is designed to assist applicants in ascertaining if their research study is in fact a clinical trial of a medicinal product. Section I is optional. Please delete if this section does not apply.

SECTION I.1 NON-INTERVENTIONAL TRIALS OF MEDICINAL PRODUCTS

I1.1 (a) Does this study involve a medicinal product? No

SECTION I.2 COSMETICS

I2.1 (a) Does this study involve a cosmetic? No

SECTION I.3 FOOD AND FOOD SUPPLEMENTS

I3.1 (a) Does this study involve food or food supplements? No

SECTION j INDEMNITY

SECTION J IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

J1 (A) IS EACH SITE IN WHICH THIS STUDY IS TO TAKE PLACE COVERED BY THE CLINICAL INDEMNITY SCHEME (CIS)? **YES**

J2 (A) IS EACH MEMBER OF THE INVESTIGATIVE TEAM COVERED BY THE CLINICAL INDEMNITY SCHEME (CIS)? **YES**

J3 (A) WHO OR WHAT LEGAL ENTITY IS THE SPONSOR OF THIS RESEARCH STUDY?

J3 (B) WHAT ADDITIONAL INDEMNITY ARRANGEMENTS HAS THE SPONSOR PUT IN PLACE FOR THIS RESEARCH STUDY IN CASE OF HARM BEING CAUSED TO A RESEARCH PARTICIPANT (IF ANY)?

No additional indemnity

SECTION k COST AND RESOURCE IMPLICATIONS and funding

SECTION K IS MANDATORY

IMPORTANT NOTE: This application form permits the applicant to delete individual questions within each section depending on their response to the preceding questions. Please respond to each question carefully and refer to the accompanying *Guidance Manual* for more in-depth advice prior to deleting any question.

K1 (A) ARE THERE ANY COST / RESOURCE IMPLICATIONS RELATED TO THIS STUDY? **NO**

K2 (a) Is funding in place to conduct this study? YES

K2 (c) Please state the source of funding (industry, grant or other) and the amount of funding.

The patients will pay for their orthodontic treatment

K2 (d) Is the study being funded by an external agency? NO

K2 (f) Do any conflicts of interest exist in relation to funding? Please elaborate.

No

K2 (g) Please provide additional details in relation to management of funds.

N/a

K3. Please provide details of any payments (monetary or otherwise) to investigators.

N/a

K4. Please provide details of any payments (monetary or otherwise) to participants.

N/a

SECTION l ETHICAL ISSUES

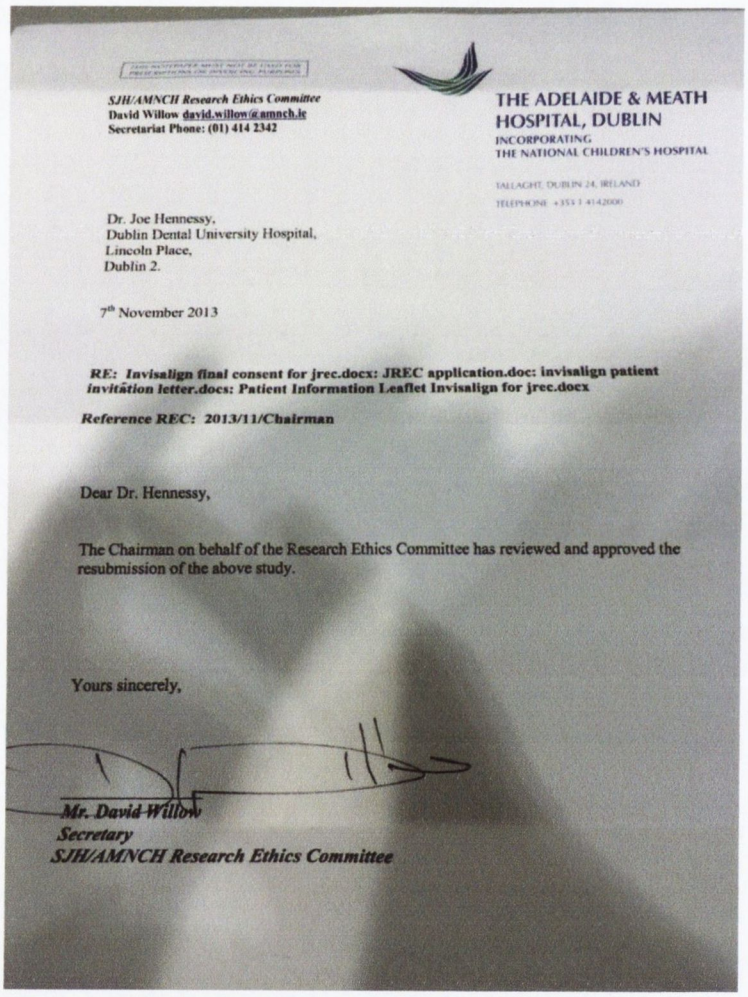
SECTION L IS MANDATORY

L1. Please identify any particular additional ethical issues that this project raises and discuss how you have addressed them.

To the best of my knowledge no other additional ethical issues exist

PLEASE ENSURE THIS APPLICATION FORM IS FULLY COMPLETED AS INCOMPLETE SUBMISSIONS WILL NOT BE REVIEWED.

ii) Ethical Approval



SJH/AMNCH Research Ethics Committee
David Willow david.willow@amnch.ie
Secretariat Phone: (01) 414 2342

THE ADELAIDE & MEATH HOSPITAL, DUBLIN
INCORPORATING
THE NATIONAL CHILDREN'S HOSPITAL

TALLAGHT, DUBLIN 24, IRELAND
TELEPHONE +353 1 414 2000

Dr. Joe Hennessy,
Dublin Dental University Hospital,
Lincoln Place,
Dublin 2.

7th November 2013

RE: Invisalign final consent for jrec.docx: JREC application.doc: invisalign patient invitation letter.docx: Patient Information Leaflet Invisalign for jrec.docx

Reference REC: 2013/11/Chairman

Dear Dr. Hennessy,

The Chairman on behalf of the Research Ethics Committee has reviewed and approved the resubmission of the above study.

Yours sincerely,

Mr. David Willow
Secretary
SJH/AMNCH Research Ethics Committee

iii) Fixed appliance informed consent and agreement for treatment

PATIENT'S INFORMED CONSENT AND AGREEMENT

REGARDING FIXED ORTHODONTIC TREATMENT

Your doctor has recommended Fixed appliances for your orthodontic treatment. Although orthodontic treatment can lead to a healthier and more attractive smile, you should also be aware that any orthodontic treatment has limitations and potential risks that you should consider before undergoing treatment.

Orthodontic treatment is associated with risks. The risks associated with this type of treatment include:

(i) Dental tenderness may be experienced

(ii) Gums, cheeks and lips may be scratched or irritated;

(iii) Teeth may shift position after treatment. Consistent wearing of retainers at the end of treatment should reduce this tendency;

(iv) Tooth decay, periodontal disease, inflammation of the gums or permanent markings (e.g. decalcification) may occur if patients consume foods or beverages containing sugar, do

not brush and floss their teeth properly

(v) The appliances may temporarily affect speech and may result in a lisp, although any speech impediment caused should disappear within one or two weeks;

(vi) Teeth may require interproximal recontouring or slenderizing in order to create space needed for dental alignment to occur;

(vii) The bite may change throughout the course of treatment and may result in temporary patient discomfort.

(viii) At the end of orthodontic treatment, the bite may require adjustment ("occlusal adjustment").

(ix) Teeth which have been overlapped for long periods of time may be missing the gingival tissue below the inter- proximal contact once the teeth are aligned, leading to the appearance of a "black triangle" space.

(x) General medical conditions and use of medications can affect orthodontic treatment;

(xi) Health of the bone and gums which support the teeth may be impaired or aggravated;

(xii) A tooth that has been previously traumatized, or significantly restored may be aggravated. In rare instances the useful life of the tooth may be reduced, the tooth may require additional dental treatment such as endodontic and/or additional restorative work and the tooth may be lost;

(xiii) Existing dental restorations (e.g. crowns) may become dislodged and require re-cementation or in some instances, replacement;

(xiv) The length of the roots of the teeth may be shortened during orthodontic treatment and may become a threat to the useful life of teeth;

(xv) In rare instances, problems may also occur in the jaw joint, causing joint pain, headaches or ear problems;

(xvi) Allergic reactions may occur;

INFORMED CONSENT

I have been given adequate time to read and have read the preceding information describing orthodontic treatment with Fixed appliances. I understand the benefits, risks, alternatives and inconveniences associated with treatment as well as the option of no treatment. I have been sufficiently informed and have had the opportunity to ask questions and discuss concerns about orthodontic treatment. I understand that payment of 1,250 euro is required for each arch treated with Fixed appliances.

Signature

Print Name

Date

Witness

Print Name

iv) Invisalign appliance informed consent and agreement for treatment

PATIENT'S INFORMED CONSENT AND AGREEMENT

REGARDING INVISALIGN® ORTHODONTIC TREATMENT

Your doctor has recommended the Invisalign system for your orthodontic treatment. Although orthodontic treatment can lead to a healthier and more attractive smile, you should also be aware that any orthodontic treatment (including orthodontic treatment with Invisalign aligners) has limitations and potential risks that you should consider before undergoing treatment.

DEVICE DESCRIPTION

Invisalign aligners, developed by Align Technology, Inc. ("Align") consist of a series of clear plastic, removable appliances that move your teeth in small increments. Invisalign`s product line combines your doctor's diagnosis and prescription with sophisticated computer graphics technology

to develop a treatment plan which specifies the desired movements of your teeth during the course of your treatment. Upon approval of a treatment plan developed by your doctor, a series of customized Invisalign aligners is produced specifically for your treatment.

PROCEDURE

You may undergo a routine orthodontic pre-treatment examination including radiographs (x-rays) and photographs. Your doctor will take impressions of your teeth and send them along with a prescription to the Align laboratory. Align technicians will follow your doctor's prescription to create a

ClinCheck® software model of your prescribed treatment. Upon approval of the ClinCheck treatment plan by your doctor, Align will produce and ship a series of customized aligners to your doctor. The total number of aligners will vary depending on the complexity of your malocclusion and the doctor's treatment plan. The aligners will be individually numbered and will be dispensed to you by your doctor with specific instructions for use. Unless otherwise instructed by your doctor, you should wear your aligners for approximately 20 to 22 hours per day, removing them only to eat, brush and floss. As directed by your doctor, you will switch to the next aligner in the series every two weeks or as directed by your doctor. Treatment duration varies depending on the complexity of your doctor's prescription. Unless instructed otherwise, you should follow up with your doctor at a minimum of every 6 to 8 weeks. Some patients may require bonded aesthetic attachments and/or the use of elastics during treatment to facilitate specific orthodontic movements. Patients may require additional impressions and/or refinement aligners after the initial series of aligners.

Orthodontic treatment is associated with risks. The risks associated with this type of treatment include:

(i) Failure to wear the appliances for the required number of hours per day, not using the product as directed by your doctor, missing appointments, and erupting or atypically

shaped teeth can lengthen the treatment time and affect the ability to achieve the desired results;

(ii) Dental tenderness may be experienced after switching to

the next aligner in the series;

(iii) Gums, cheeks and lips may be scratched or irritated;

(iv) Teeth may shift position after treatment. Consistent wearing of retainers at the end of treatment should reduce this tendency;

(v) Tooth decay, periodontal disease, inflammation of the gums or permanent markings (e.g. decalcification) may occur if patients

consume foods or beverages containing sugar, do

not brush and floss their teeth properly before wearing the invisalign products, or do not use proper oral hygiene and preventative maintenance;

(vi) The aligners may temporarily affect speech and may result in a lisp, although any speech impediment caused by the invisalign® products should disappear within one or two weeks;

(vii) Aligners may cause a temporary increase in salivation or mouth dryness and certain medications can heighten this effect;

(viii) Attachments may be bonded to one or more teeth during the course of treatment to facilitate tooth movement and/or appliance retention. These will be removed after treatment is completed;

(ix) Teeth may require interproximal recontouring or slenderizing in order to create space needed for dental alignment to occur;

(x) The bite may change throughout the course of treatment and may result in temporary patient discomfort.

(xi) At the end of orthodontic treatment, the bite may require adjustment ("occlusal adjustment").

(xii) Supplemental orthodontic treatment, including the use of bonded buttons, orthodontic elastics, auxiliary appliances/ dental devices (e.g. temporary anchorage devices, sectional fixed appliances), and/or restorative dental procedures may be needed for more complicated treatment plans where aligners alone may not be adequate to achieve the desired outcome.

(xiii) Teeth which have been overlapped for long periods of time may be missing the gingival tissue below the inter- proximal contact once the teeth are aligned, leading to the appearance of a "black triangle" space.

(xiv) Aligners are not effective in the movement of dental implants.

(xv) General medical conditions and use of medications can affect orthodontic treatment;

(xvi) Health of the bone and gums which support the teeth may be impaired or aggravated;

(xvii) Oral surgery may be necessary to correct crowding or severe jaw imbalances that are present prior to wearing the Invisalign product. If oral surgery is required, risks associated with anesthesia and proper healing must be taken into account prior to treatment;

(xviii) A tooth that has been previously traumatized, or significantly restored may be aggravated. In rare instances the useful life of the tooth may be reduced, the tooth may require additional dental treatment such as endodontic and/or additional restorative work and the tooth may be lost;

(xix) Existing dental restorations (e.g. crowns) may become dislodged and require re-cementation or in some instances, replacement;

(xx) Short clinical crowns can pose appliance retention issues and inhibit tooth movement;

(xxi) The length of the roots of the teeth may be shortened during orthodontic treatment and may become a threat to the useful life of teeth;

(xxii) Product breakage is more likely in patients with severe crowding and/or multiple missing teeth;

(xxiii) Orthodontic appliances or parts thereof may be accidentally swallowed or aspirated;

(xxiv) In rare instances, problems may also occur in the jaw joint, causing joint pain, headaches or ear problems;

(xxv) Allergic reactions may occur;

(xxvi) Teeth that are not at least partially covered by the aligner may undergo supraeruption;

INFORMED CONSENT

I have been given adequate time to read and have read the preceding information describing orthodontic treatment with Invisalign aligners. I understand the benefits, risks, alternatives and inconveniences associated with treatment as well as the option of no treatment. I have been sufficiently informed and have had the opportunity to ask questions and discuss concerns about orthodontic treatment with

Invisalign`s product line with my doctor from whom I intend to receive treatment.

I understand that I should only use the Invisalign product line after consultation and prescription from an Invisalign trained doctor, and I hereby consent to orthodontic treatment with

Invisalign`s product line that have been prescribed by my doctor.

Due to the fact that orthodontics is not an exact science, I acknowledge that my doctor and Align Technology, Inc. ("Align") have not and cannot make any guarantees or assurances concerning the outcome of my treatment.

I understand that payment of 250 euro is required for each arch treated with Invisalign. If I require further orthodontic treatment I understand the cost will be increased to 2500 euro.

.

Signature

Print Name

Date

Witness

Print Name

v) Patient invitation letter

Dear Sir or Madam,

You are currently on the orthodontic waiting list for the Dublin Dental Hospital/ Regional Orthodontic Unit at St James Hospital. I am writing to ask if you would like to take part in some research while having your orthodontic treatment.

The research is interested in measuring the type of tooth movement that a clear plastic brace can achieve.

If you are interested in participating in this research please read the attached patient information sheet and consent form. If you still would like to be considered for this particular treatment please contact 01 6127391. The treatment is not suitable for every patient so you will be asked to attend an initial assessment visit prior to entering the research. If you do not fit the inclusion criteria you will still receive conventional orthodontic treatment at the Dublin Dental Hospital/ Regional Orthodontic Unit at St James Hospital. Please do not hesitate to contact the number above if you have any questions about any of the information provided

vi) Patient information leaflet

Title: A Measurement of the Dental Proclination produced by Invisalign Orthodontics

You are being asked to take part in a research study. It is important that you read the following information carefully before consenting to treatment. We would be happy to answer any questions you may have.

What is the aim of this study?

The aim of this study is to measure the amount of tooth movement Invisalign can achieve. The objective is to offer practitioners, who use Invisalign, guidelines on the amount of tooth movement that can be expected. This may allow for better case selection when using aligners and improved success rates. The average length of treatment is 14 months.

What is Invisalign?

Invisalign aligners, developed by Align Technology, Inc. ("Align") consist of a series of clear plastic, removable appliances that move your teeth in small increments. Invisalign`s product line combines your doctor's diagnosis and prescription with sophisticated computer graphics technology to develop a treatment plan which specifies the desired movements of your teeth during the course of your treatment. Upon approval of a treatment plan developed by your doctor, a series of customized Invisalign aligners is produced specifically

for your treatment. .

Eligibility

It must be highlighted that Invisalign is not suitable for everyone. It is specifically designed to fix minor alignment issues. The inclusion criteria for this study are

1) Require tooth movements in upper teeth only
2) Require minor tooth movements
3) No caries or periodontal disease

4) No extraction requirement
5) At least 18 years old
6) An ability to attend multiple appointments over a 14 month period
7) An ability to undergo radiographic examination. For example, cannot be pregnant

If you do not meet the inclusion criteria at the initial assessment you will not receive Invisalign treatment. You will continue to be on the orthodontic waiting list at the Dublin Dental Hospital and will be offered regular fixed orthodontic treatment.

Procedure

If you are included in this study you will have two radiographs (an orthopantomagraph and lateral cephalogram) and impressions of your teeth taken during the treatment. You will be consulted if any other radiographs are required. You may be required to attend the Dublin Dental Hospital on a weekly basis. It is essential that you attend all these appointments. Failure to attend will result in you being removed from the study. The average length of treatment is 14 months. Your treatment may be longer or shorter. If at the end of treatment you are not happy with the results you will be offered further orthodontic treatment at the Dublin Dental Hospital. Only

orthodontic treatment will be carried out by the Dublin Dental Hospital. It will be your responsibility if you require restorations or any other dental procedures.

Benefits

At the end of the course of orthodontic treatment you will have straight teeth with reduced crowding

The types of dental treatments provided in this study are an alternative to:

1) No treatment
2) Fixed orthodontic treatment

Confidentiality

Your identity will remain confidential. Your name will not be published and will not be disclosed to anyone outside the hospital

Compensation

Your doctors are covered by standard medical malpractice insurance. Nothing in this document restricts or curtails your right

Voluntary Participation

You have volunteered to participate in this study. You may quit at any time. If you decide not to participate, or if you quit, you will not be penalized and will not give up any benefits which you had before entering the study.

Stopping the study

You understand that your doctor may stop your participation in the study at any time without your consent.

Permission

This study has ethical approval from the Joint Ethics Research Committee at St James' Hospital, Dublin.

Other Relevant Information

You will have to pay for the Invisalign treatment that is provided. The cost of this treatment is 500 euro. If further fixed orthodontic treatment is required there will be no addition payment required. *You can get more information or answers to your questions about the study, your participation in the study, and your rights, from Dr Joe Hennessy who can be telephoned at 01 6127388. If your doctor learns of important new information that might affect your desire to remain in the study, he or she will tell you.*