FULL/ LONG TITLE OF THE TRIAL Orthodontic Patient Experience of Intraoral Scanners Versus Alginate Impressions in the UK: a Single-Centre Randomised Controlled Crossover Trial	
SHORT TITLE/ ACRONYM OPESI Trial	
Version and Date of Protocol:	V2.0 20/02/2022
Sponsor:	University Hospitals of Derby and Burton NHS Foundation Trust
Chief Investigator:	Alison Murray
Local Study Reference:	UHDB/2021/022
IRAS Number:	307434
ISRCTN/ ClinicalTrials.gov number:	ClinicalTrials.gov – NCT05194956
Funder(s):	British Orthodontic Society Foundation Derby Pump Priming Charitable Funds
This protocol has regard for the HRA guidance	

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust, regulatory authorities, and members of the Research Ethics Committee.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.
I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.
I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Protocol 2.0 20/02/2022 authorisation signatures:

Chief Investigator:

Signature: Alison Murray Digitally signed by Alison Murray Date: 2022.03.29 17:14:01 +01'00' ..... Date: 29 / 03 / 2022

Name (please print): Alison Murray .....

For and on behalf of the Study Sponsor (if required):

Signature: Dr Teresa M. Grieve Digitally signed by Dr Teresa M. Grieve Date: 2022.03.30 08:26:08 +01'00' ..... Date: 30/03/2022

Name (please print): Teresa M Grieve .....

Position: Asst. Director R&D .....

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STUDY SUMMARY

Study Title:	Orthodontic Patient Experience of Intraoral Scanners Versus Alginate Impressions in the UK: a Single-Centre Randomised Controlled Crossover Trial
Local Study Reference:	UHDB/2021/022
Study Design:	Single-centre prospective randomised two-period crossover study
Study Participants:	New patients (aged 10 years and older), attending the Royal Derby Hospital orthodontic department, requiring study model impressions taken prior to commencing orthodontic treatment – identified by those patients undergoing Dental Health Education (DHE) appointments on NHS Attend Anywhere, as these patients will be due to start treatment. Those who have previous experience of impressions/intraoral scans in the last 2 years or who have cleft lip and/or palate will be excluded.
Planner Number of Sites:	1
Planned Sample Size:	84
Treatment Duration:	8 weeks (total)
Follow Up Duration:	No follow-up following initial 8 weeks
Planned Start Date:	As per IRAS form start date
Planned Recruitment End Date:	Estimated Last Participant First Visit (LPFV) – October 2022
Planned Study End Date:	Estimated Last Participant Last Visit (LPLV) – as per IRAS form study end date – December 2022
Research Question/ Aims:	Primary Aim: • To investigate patient experience of comfort during intraoral scanning versus alginate impression taking in the orthodontic setting. Secondary Aims: • To investigate patient experience of pain, relative speed of impression, nausea and/or coughing and whether the impression method could be recommended. • To investigate operator experience of ease, confidence, relative speed, and preference for intraoral scanning versus alginate impression taking in the orthodontic setting. • To investigate time taken to undertake an intraoral scan versus an alginate impression

FUNDING AND SUPPORT IN KIND

Funder(s)	**Financial and Non-Financial Support Given**
British Orthodontic Society Foundation	£11,081.08
Derby Pump Priming Charitable Funds	£9,785.00

ROLES & RESPONSIBILITIES

Sponsor

The Sponsor, University Hospitals of Derby & Burton NHS Foundation Trust, take on overall responsibility for appropriate arrangements being in place to set up, run and report the research project. The sponsor is not providing funds for this study, but has taken on responsibility for ensuring finances are in place to support the research.

Funder

The study is funded by British Orthodontic Society Foundation (BOSF) and Derby Pump Priming Charitable Funds

Study Management Committees

Trial Management Group

The trial management group will meet regularly to oversee the day-to-day management of the trial, including all aspects of the conduct of the trial. Any problems with study conduct and participating centers will be raised and addressed during TMG meetings. The trial management group will include all research team members, clinicians involved in screening patients and a dental nurse representative. The study Trial Management Group will meet within the first month of trial commencement and every 2 months thereafter.

Protocol Contributors

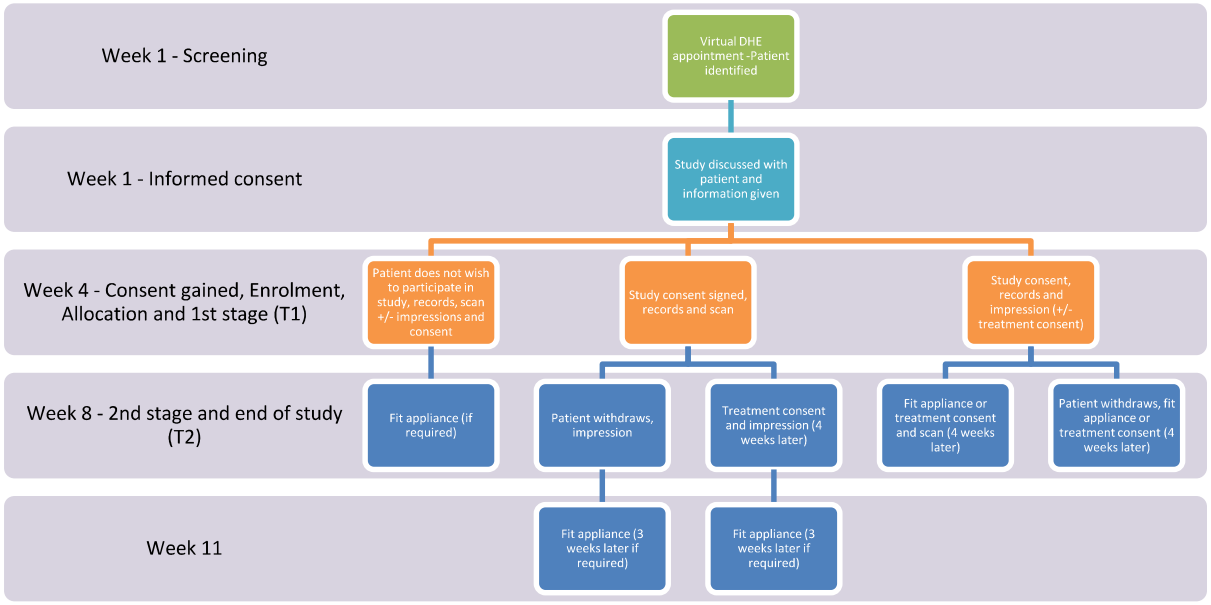
A number of protocol contributors have been involved in the development of this protocol, these include; the Chief Investigator, Co-investigators, Statistician, Data Manager and Trial Manager. Protocol contributors are responsible for inputting into the design of the study, ensuring that it is designed transparently and efficiently.

Contents

LIST OF ABBREVIATIONS

AE	Adverse Event
AGP	Aerosol Generating Procedure
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
EEA	European Economic Area
GCP	Good Clinical Practice
GDP	General Dental Practitioner
HRA	Health Research Authority
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials
PI	Principal Investigator
PIS	Participant Information Sheet
REC	Research Ethics Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
TMG	Trial Management Group
TSF	Trial Site File
UHDB	University Hospitals of Derby and Burton NHS Foundation Trust
VAS	Visual Analogue Scale

STUDY FLOW CHART



STUDY PROTOCOL

1. BACKGROUND

Digital scanning systems are becoming more and more popular and with the advent of the COVID-19 pandemic and the risks surrounding aerosol-generating procedures (AGP) has resulted in practitioners changing their normal practice and finding alternative methods to continue managing their patients. The British Orthodontic Society (2020) suggest that an "intra oral scan may be preferable" to impressions, but both still have the potential to become an AGP if the patient gags or coughs. There have been several studies suggesting that intraoral scanning is superior to conventional impression techniques, with regards to patient preference (Burhardt et al. 2016; Mangano et al. 2018; Yilmaz and Aydin 2019; Luqmani et al. 2020). The perceived benefits of intraoral scanning over conventional impressions are that the scan can be reviewed in real-time, capture can be limited to required areas, it can easily be recaptured and disinfection processes are reduced in time and expense. It also facilitates easy transfer of information to the laboratory, with the reduced likelihood of introducing errors (Sivaramakrishnan et al. 2020; Zimmermann et al. 2015).

A literature search revealed some evidence in the orthodontic setting. Burhardt et al., (2016) concluded that young orthodontic patients preferred the digital impression methods over the conventional alginate method, despite alginate impressions having a reduced chairside time. This cross-over study was limited to patients aged 10-17 years old and had a relatively small sample size of 38, but considered effects such as the carryover effect and the limitations of the use of Likert scale. A similar sized study (n=30), also showed that digital impressions were the most accepted and comfortable in young orthodontic patients compared to conventional alginate impressions (Mangano et al. 2018). Despite showing no significant difference, this study also considered measuring stress induced through the procedure using the State anxiety scale. Grünheid et al. (2014), found that patients preferred conventional impressions due to the scanner tip dimension, although it has been argued that this has now been overcome with the development of narrower tips (Mangano et al. 2018).

Yilmaz and Aydin (2019), in an orthodontic based study, found no significant differences in total time taken to take a scan/impression but did conclude, like others that the digital impression was considered to be more comfortable and also the preferred method for impression taking. A slightly larger study showed no significant differences in the chairside time for both alginate impressions and intraoral scans, but children preferred intraoral scans. This study also gave consideration to costs, stating that both procedures were equal in cost at 3.6 years (Glisic et al. 2019).

In terms of comparisons with polyether materials, as opposed to alginate impression materials, Yuzbasioglu et al. (2014) showed significant differences in their comparative-controlled trial, in favour of digital impressions, among the groups in terms of total working time and processing steps, except for tray selection/patient information. In this trial, all participants experienced both impression methods, 2 weeks apart to aid in erasing memory. The order of which method was utilised first (Impregum) was done based on psychological reasons and contrasted to that of Yilmaz and Aydin (2019) who carried out the conventional impression second.

With the aim to develop a reliable and valid survey, Burzynski et al. (2017) successfully carried out a pilot study prior to concluding that intraoral scanning methods have comparable efficiency to conventional methods of impression taking, dependent on the scanner type. Their survey, like that of Mangano et al (2018), utilised the visual analogue scale (VAS) to reduce the limitations that come with the Likert scale for example. The literature review by Kihara et al. (2020), echoed the same findings in terms of comfort, but focused primarily on the accuracy and practicality of intraoral scanners. A modification of the VAS method is one that is tailored towards children, using emoticons to depict feelings (Cao et al. 2017). This was utilised successfully by Yilmaz and Aydin (2019), who also looked at clinical observations by the operator which could suggest discomfort.

More generally within dentistry, the systematic review carried out by Gallardo et al. (2018) suggested that patients were more likely to prefer digital techniques over conventional techniques. Only 5 studies were analysed due to the limited evidence base in this area. The use of patient reported outcome measures was highlighted in this paper and despite being primarily about use in implant cases, it is still of relevance when considering patient comfort. However, implant impressions may vary in the length of time they take compared to perhaps a full arch impression that is required within orthodontics. A meta-analysis, pooling data from 11 studies (471 patients) suggested a statistically significant number of patients preferring digital impressions, yet also demonstrated a statistically significant increase in the time taken to create a digital impression, depending on the scanner manufacturer (Sivaramakrishnan et al. 2020). Contrary to this, Sfondrini et al. (2018) demonstrated chairside and processing times significantly shorter for the scan method ($p<0.0001$). Prior to these published studies, the review by Goracci et al. (2016) found only studies with participants in the complete permanent dentition, which meant no studies met the standard for sample collection. Since then, a number of studies have included participants of 10-17 years of age and those within the mixed dentition specifically, but these are limited (Mangano et al. 2018; Burhardt et al. 2016; Liczmanski et al. 2020). A narrative review of the literature, involving a larger number of studies (n=132), looked at a number of relevant questions including the advantages/disadvantages, accuracy and applications of digital impressions, but concluded the need for further systematic reviews in the area as well as randomised controlled trials to facilitate meaningful additions to the existing literature base (Mangano et al. 2017).

In addition to the process of taking the impression or scan, the ability to use the subsequent casts is also important in considering whether digital impressions are favoured by the clinical and non-clinical (lab technicians). The above study also showed there was no significant difference between intraoral scanning, gypsum models and digitised gypsum models with regards to measurements used to assess accuracy (Sfondrini et al. 2018). Other studies published also look specifically at the accuracy and reproducibility of different intraoral scanning systems and conventional methods (Lim et al. 2018; Kamimura et al. 2017; Jiménez-Gayosso et al. 2018).

Specifically, the use of intraoral scanning in specialist care has been discussed with regards to cleft patients, in which scanning comfort was significantly higher than in alginate impressions. Importantly, this study considered the reading age of the questionnaire to be delivered to the child, in addition to the parent's perceptions, following the interventions (Chalmers et al. 2016). The use of

digital scanning has also been discussed with regards to orthognathic surgery and its ability to aid in surgical planning (Hernández-Alfaro and Guijarro-Martínez 2013). The consideration to use scanning for fabrication of retainers has been investigated, with conclusions suggesting that digital scanning technology may not be cost-effective and some patients felt the preparation (titanium oxide powder coating) was uncomfortable compared to a conventional impression (Vasudavan et al. 2010).

As with any evolving technology within the dental profession, the lack of familiarity with the equipment can play a key role in the use of such equipment and deviation away from conventional methods. There are substantial costs involved, both long and short term and consideration then needs to also be given to the manufacturing of study models using the digital scans. Yet, digital scans can reduce the need for storage, disinfection and the 'mess' associated with conventional impression techniques (Christensen 2008). With regards to operator preference, Zitzmann et al. (2017) considered inexperienced dental students' perceptions towards both techniques. The students' preferences favoured digital impressions and they appeared to learn the skill of digital impression taking quicker than conventional impressions. Schott et al. (2019) also explored the student perspective on both techniques and demonstrated the lack of significant difference between the methods from both the clinician and patient perspective, although there was a preference by the students for the digital technique (58.1%). Although based on prosthetic treatment, a study suggested that digital impression techniques were "less time consuming and more convenient" for the clinician and showed statistically significant advantages in terms of recording occlusal contacts, which can be applicable for orthodontic cases (Gjelvold et al. 2016). In terms of which intraoral scanner is preferred, Park et al. (2015) investigated this. The results showed the participants preferred the Trios scanner over the iTero scanner on a number of parameters. Additionally, it demonstrated that training in the use of the scanner changed the views of the participants (dental hygienists) in a positive way.

A 2019 systematic review concluded that there are enough in vivo randomised controlled trials regarding sound teeth but a large part of the current literature is based on in vitro studies. They found that many articles concern patient preferences, comparing different impression methods as well as the accuracy of scanners. No study was found to provide information on the learning process and the time required to develop a high quality of intraoral digital impressions. Only 6 of the 24 studies meeting the criteria were orthodontic in nature, but there had been none carried out here in the United Kingdom (UK) (Biagioni et al. 2019). Since then, in the UK, Luqmani et al. (2020) have looked into patient preference and comfort with intraoral scanning versus alginate impressions, yet patient centred outcomes were secondary to that of Peer Assessment Rating (PAR) differences. Patient focused research has been found to be limited, with many child research studies conducted without children engaging and getting involved with the research process (Marshman et al. 2015; Fleming et al. 2016).

2. RATIONALE

Intraoral scanners are becoming more popular within orthodontic settings, both primary care and secondary care. There are benefits of digital scanning systems such as a reduced environmental impact and reduced storage need but there is limited evidence regarding patient centred outcomes such as comfort in the UK population. Patient-centred care is vital and having a sound evidence-base

is imperative in a clinician's decision towards investing in the equipment and training required. In addition, patient outcomes can feed into future development of the scanners to ensure that patient comfort remains at the forefront. The research will also consider operator preferences which is also highly critical in terms of acceptance of new equipment and it's use within a team. The proposed study will aim to add to the limited evidence base, providing information to the orthodontic community regarding the use of intraoral scanners compared to alginate impressions from both the patient and operator perspectives.

3. OBJECTIVES AND OUTCOME MEASURES/ ENDPOINTS

3.1. Objectives

Primary objective

To compare two methods of impression taking (intraoral scanning and alginate impressions) in a UK orthodontic patient population, aged over 10 years old, with regards to patient comfort.

Secondary objective

To compare two methods of impression taking (intraoral scanning and alginate impressions) in a UK orthodontic patient population, aged over 10 years old, with regards to:

- Pain
- Relative speed
- Nausea and/or coughing
- Perceived time
- Operator experience
- Operator confidence
- Operator preference

3.2. Outcome

Primary outcome

- A 100mm modified Visual Analogue Scale (VA scale) measuring patient comfort during intraoral scanning taking versus alginate impressions taken in the orthodontic setting.

Secondary outcomes

- Four modified 100mm VA scales to measure:
    - Pain;
    - Relative speed of impression;
    - Nausea and/or coughing;
    - Whether the impression method could be recommended; and
- Four 100mm VA scales to measure the orthodontic operator's experience of:
    - Ease of impression;
    - Confidence taking the impression;
    - Relative speed of impression; and
    - Whether the patient felt sick or coughed during the procedure.
- A quantitative time measure will be recorded for:

    - The time (mins and secs) taken to make the impression will also be recorded
- A simple question to determine operator preference for intraoral scanning versus alginate impressions.

4. STUDY DESIGN

Single-centre prospective randomised controlled two-period crossover study to investigate whether intraoral scans are more comfortable for patients than alginate impressions

5. STUDY SETTING

This will be a single centre study based in a secondary care hospital (Royal Derby Hospital – University Hospitals of Derby and Burton NHS Trust). The patients eligible for the study are often referred into the secondary care orthodontic department by primary care dental practitioners or specialist orthodontic practitioners and they will be recruited from this referred population. The patients will be identified for meeting the inclusion criteria during a NHS attend virtual consultation for dental health education (DHE) that occurs prior to orthodontic treatment commencing.

6. ELIGIBILITY CRITERIA

6.1. Inclusion Criteria

All new patients (aged 10 years and older), attending the Royal Derby Hospital orthodontic department, requiring study model impressions taken prior to commencing orthodontic treatment where participants are capable of giving informed consent, or have an acceptable individual capable of giving consent on the patient's behalf (e.g. parent or guardian of a child under 16 years of age).

6.2. Exclusion Criteria

Patients who have:

- Had previous experience of impressions/intraoral scans in the last 2 years
- Cleft lip and/or palate patients
- Been involved in a study in the last 6 months or are currently part of a study

7. STUDY PROCEDURES

7.1. Recruitment

7.1.1. Patient Identification

The patients eligible for the study will be identified by an appropriately trained clinician from the patients attending a virtual NHS Attend Anywhere dental health education appointment with themselves.

7.1.2. Screening

At the virtual NHS Attend Anywhere appointment, the clinician will introduce the trial to the eligible patients and following consent, will utilise a checklist to verbally check if the patient meets the inclusion criteria and those with any exclusion characteristics will not be provided any further information on the trial. They will confirm this by asking the patient and if appropriate, their parent or guardian the necessary questions.

7.2. Consent

Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study (including the collection of identifiable participant data, unless the study has prior approval from the Confidentiality Advisory Group (CAG) and the REC).

The Principal Investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent according to the REC approved protocol and applicable guidelines and regulations.

Following identification of eligible participants through the screening process, the trial will be discussed in greater detail with the patient and if appropriate, their parent or guardian. This will be done by a trial clinician who is trained in the REC approved research protocol. The discussion will involve:

- An introduction into the trial and why it is being done:
    - "A trial looking at what type of tooth mould (impression) is more comfortable to help improve patient experience of having tooth moulds taken."
- The involvement required by themselves or their child
    - "You or your child would be required to have a digital scan of your teeth and a mould of your or your child's teeth using an alginate material, approximately 4-6 weeks apart. Following each you or your child will be asked to complete a short questionnaire regarding your experience which should take no longer than 2 minutes to complete. The digital scan and impression would be combined with appointments that are required for your or your child's orthodontic treatment"
- The risks of participation including the effect (if any) on their treatment plan.
    - "Both methods of taking a mould could cause you or your child to cough or very rarely, be sick. There are many methods to managing this and our clinicians will talk you or your child through this if this occurs. There have also been rare reports of allergic reactions to the mould material (alginate). The clinician will check for any allergies as part of your orthodontic treatment. Although the length of appointment may be slightly longer, we will aim to minimise any extra time to reduce any school or work time missed by you or your child."
- The ability to withdraw from the study at any point should they wish to themselves or wish for their child to, emphasising that this will have no impact on the care they receive from the department.

- "If at any point during the trial, you or your child wishes to withdraw from the trial, your orthodontic treatment will not be affected and no further data will be collected. Your child is still likely to require a digital scan and, in some cases, an additional dental mould (alginate) as part of their treatment"
- A contact point should they wish to ask further questions regarding the trial.

The information will be verbally discussed and following this, the patient and if appropriate, their parent or guardian, with parental responsibility, will be provided with an information leaflet and an age-appropriate video showing the potential participant the outline of the study and their involvement. The patient and if appropriate, their parent or guardian will then be given time to consider the information and ask any questions. Their consent will be confirmed when they attend for their next visit, in which they will either be enrolled in the study and allocated appropriately, or if they decline their consent, will continue with their normal orthodontic care, without any further information on the trial. For children under the age of 16 unable to consent for themselves, their assent will be sought before enrolment into the study and the appropriate assent form signed.

The PI will take responsibility for ensuring that all vulnerable subjects are protected and participate voluntarily in an environment free from coercion or undue influence. Adults unable to consent for themselves will not be included in the study. Any patient who wishes to withdraw at any point during the trial can do so without reason and without this affecting or prejudicing the delivery of their orthodontic care. Any further information requested by a patient or their parent or guardian will be provided in a timely manner, ideally within 5-7 working days.

7.3. The Randomisation Scheme

The allocation to each group will be confirmed following enrolment into the trial. The participants will be randomised by the research team using an online randomisation tool. They will be assigned to having the alginate impression before or after the scan, using 1:1 randomisation with mixed block sizes to ensure equal allocation to groups. Treatment order will remain concealed until the patient has been enrolled in the study, when the allocation will be revealed on a patient-by-patient basis.

7.3.1. Method of Implementing the Allocation Sequence

The randomisation tool to be used is an online randomisation system, which will be accessed by the research team within the trial. The allocation sequence will be concealed until the patient is enrolled in the study at which point, the research team will request the next treatment allocation from the online tool. The patient will be provided with a participant number which will then be used throughout the trial to report any collected trial data anonymously. Allocation to a group will only occur during working hours (Monday to Friday 9am-5pm).

7.4. Blinding

It would be impossible to blind the clinicians and the participants from the order of scan and impression they will receive as the process for each type of record is different. Blinding will however

occur when the VAS scores are measured, with the completed questionnaires being quantified without knowledge of whether the results relate to an intraoral scan or an impression with the use of a concealment method such as a scratch sticker. These can be measured and confirmed and then the information placed in a case report form (CRF) following revealing of the mould type performed.

7.5. Unblinding

The participants and clinicians will not be blinded, so unblinding will not be required. The assessors will be blinded to the type of mould whilst measuring the VA scales and the revealing of this will be completed once the measurements are all completed to allow for entry into the CRF.

7.6. Study Assessments

Following confirmation of eligibility and a discussion regarding the study the patients will attend an appointment 3 weeks later where a clinician will gain the necessary consent and assent as per **7.2**. Children will have been given an age-appropriate explanation of what they are helping the research team achieve through information sheets and what the study involves in order to gain appropriate assent. Those who do not wish to participate can continue their orthodontic care. All enrolled participants will be treated as per the agreed protocols and will be allocated to a treatment sequence as per **7.3**. With consent, a letter will be provided to the patient and/or their parent/guardian to be given to their general dental practitioner (GDP) to inform them that they will be participating in this study. During the appointments, they will also see a therapist/clinician to undertake any other necessary records or treatment e.g., photographs required for their orthodontic treatment (outside of the study).

The clinicians and nurses involved in the study will be appropriately trained in the study protocol and calibrated to ensure the correct process is followed.

Once the participant has provided appropriate consent/assent, the following procedure will be followed:

- One unit will be set up with an operator and a nurse
- Participants in the alginate impression group:
    1. The unit the participant will be treated in, will be set up appropriately with relevant materials ready.
        - The alginate to be used will be: Zhermack orthoprint® orthodontic alginate material
    2. A timer will be started when the participant is seated in the chair
    3. The operator will carry out the impression as normal
        - Tray selection
        - Alginate mixing
        - Tray seating
        - Alginate setting
        - Tray removal
        - Wax bite
        - Clean up of the participant's face

4. The timer will be stopped
5. Questionnaires
    - Participant will be asked to complete a questionnaire (modified VAS using pictorial anchors)
    - Operator will be asked to complete a questionnaire
6. These will be collected for analysis
7. The participant will then have records taken as part of their normal orthodontic care, if not done already +/- a discussion to consent for orthodontic treatment
8. The participants will return a minimum 4 weeks later for a second appointment (if they have not had an intraoral scan already) in which they will undertake the process for 'Participants in the intraoral scanner group'

- Participants in the intraoral scanner group
    1. The unit the participant will be treated in, will be set up appropriately with relevant materials ready. The interchangeable covering will be placed over the scanner ready for use.
        - The intraoral scanning device to be used will be: Trios® 3 intraoral scanner (3Shape)
        - The staff will be appropriately trained and will be requested to carry out a minimum of 10 scans prior to the study beginning
    2. A timer will be started when the participant is seated in the chair
    3. The scan will be carried out as per the manufacturer's directions to include a full mouth scan and bite registration and saved on the scanner system.
    4. The timer will be stopped
    5. Questionnaires
        - Participant will be asked to complete a questionnaire (modified VAS using pictorial anchors)
        - Operator will be asked to complete a questionnaire
    6. These will be collected for analysis
    7. The participant will then have records taken as part of their normal orthodontic care, if not done already +/- a discussion to consent for orthodontic treatment +/- fit of any orthodontic appliance required.
    8. The participants will return a minimum 4 weeks later for a second appointment (if they have not had an alginate impression already) in which they will undertake the process for 'Participants in the alginate impression group'

A minimum of 4 weeks between the two appointments is intended as a washout period to prevent bias. This period fits with the timelines that we currently work towards when managing orthodontic laboratory work. If a participant does not attend the second follow-up, an attempt will be made to rearrange the appointment to fall within the protocol timeline (minimum 4 weeks apart). If this is not possible, the participant will be considered lost-to-follow-up and the enrolment list updated. As per the clinicians' clinical obligations any children or vulnerable adults not brought or attending appointments will be managed as per the local safeguarding guidelines.

Appliances require an appointment 3-4 weeks following an alginate impression being created to allow the lab to produce the appliance and for it to then be fitted. In those participants whom have alginate impression carried out after the intraoral scan, a third appointment to fit the appliance may

be required, although this is unlikely to extend the overall orthodontic treatment which could be 24-30 months on average.

Once the participants have left the unit/surgery, the necessary infection control procedures will be in place to allow for processing of the conventional impressions and storage of the digital intraoral scans.

Once all data is obtained, operators will be asked a single question to indicate their preference – either conventional alginate impression or intraoral scanner.

All data obtained will then be gathered and entered into a study database to be analysed statistically as described in **10.3.** The participants will be able to withdraw at any point and no further data will be collected.

7.7. Withdrawal Criteria

Any participant and/or their parent or guardian, if appropriate who wishes to withdraw at any point during the trial can do so without reason and without this affecting or prejudicing the delivery of their orthodontic care. Any participant who has an adverse event during the course of the trial, will be considered on a case-by-case basis by the research team for withdrawal.

On withdrawal, the participant and/or their parent or guardian will be asked the reason for withdrawal, but have a right to provide no specific reason. This will be recorded to analyse for biases and to consider the effect this may have on the final results. Once withdrawn, the participants will not be followed up as part of the study and their normal orthodontic treatment will continue.

A participant and/or their parent/guardian losing the capacity to consent would be withdrawn from the study. The data collected within the study would be non-identifiable and therefore would be retained for analysis.

Participants that have withdrawn from the study will not be replaced, as the sample size calculation in **10.1** accounts for dropouts.

7.8. Storage and Analysis of Samples

No samples are to be collected and therefore this is not applicable.

7.9. End of Study

The end of study will be defined as when all data has been received and queries resolved. The CI will notify the Sponsor, participating sites and REC within 90 days of the end of study. The clinical study report will be written within 12 months of the end of study.

8. SAFETY REPORTING

8.1. Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant, including occurrences which are not necessarily caused by or related to study procedures.
Related AE	An untoward and unintended response in a participant to a study procedure. This means that a causal relationship between the study procedure and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Related SAE	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the study procedures.
Related & Unexpected SAE	A serious adverse event that; • is believed with reasonable probability to be due to one of the study procedures. • the nature and severity of which is not consistent with the information provided in the protocol i.e. it is not listed as an expected occurrence.

8.2. Operational Definitions for (S)AEs

The following circumstances are not considered SAEs:

- Routine treatment or monitoring of the studied indication not associated with any deterioration in condition.
- Treatment which was elective or pre-planned, for a pre-existing condition not associated with any deterioration in condition.
- Any admission to hospital or other institution for general care where there was no deterioration in condition.

- Treatment on an emergency, outpatient basis for an event **not** fulfilling any of the definitions of serious as given above and not resulting in hospital admission.

As a low-risk study, any AE occuring will be recorded within the CRF and participant's medical records. The study is comparing two approaches to impression taking which are used routinely within the orthodontic department, therefore the perceived study risks are no greater than that normally faced by orthodontic patients. The study is unlikely to encounter any significant adverse events and therefore will not be reporting these.

8.3. Recording and Reporting SAEs

All AEs and SAEs must be recorded from the time of randomisation until 4 weeks after the last visit.

All SAEs occurring during the duration of the study must be recorded by the investigator within the CRF. The PI is responsible for checking for SAEs when participants attend for treatment and follow-up.

All related and unexpected SAEs must be reported by the investigator using the 'non-CTIMP safety report to REC form' from the HRA website. The completed form should be submitted to the Sponsor and REC within 15 days of the CI becoming aware of the event. Safety information will be reviewed during trial management group meetings.

UHDB contact information:
Email: uhdb.randdsae@nhs.net

8.3.1. Assessment of AEs and SAEs

8.3.1.1 Severity

The investigator should determine the severity of the AE;

- Mild: no interference with daily activities.
- Moderate: moderate interference with daily activities.
- Severe: considerable interference with daily activities (e.g. inability to work).

NOTE: to avoid confusion or misunderstanding the term "severe" is used to describe the intensity of the event, which may be of relatively minor medical significance, and is NOT the same as "serious" which is described in the safety definitions.

8.3.1.2 Causality

Clinical judgement should be used to determine the relationship between the study procedures and the occurrence of each AE;

- Not-related: There is no evidence of a causal relationship between the event and study procedures.

- Related: There is evidence of a causal relationship between the event and study procedures i.e. a relationship to the study procedures cannot be completely ruled out.

Assessment of causality must be made by a medically qualified doctor (usually the principal investigator).

8.3.1.3 Expectedness

The assessment of expectedness is only required if the event is deemed to be related to study procedures.

- Expected: Event previously identified and described in the protocol.
- Unexpected: Event not previously described in the protocol.

The expectedness assessment is delegated to the CI

8.4. Pregnancy reporting

Pregnancy reporting is not applicable as the method utilises types of tooth mould routinely carried out in the orthodontic clinic. There are no contraindications to their use in pregnancy.

8.5. Reporting Urgent Safety Measures

If any urgent safety measure is taken the research team should inform the Sponsor with 24 hours using the Sponsors safety incident reporting form. The Sponsor will inform the REC and participating sites of the measures taken and the circumstances giving rise to those measures within 3 days on implementation of the urgent safety measure.

9. DATA HANDLING

9.1. System and Compliance

Research data for each participant will be collated on the paper case report form (CRF) for each participant. This will be completed by clinicians trained in the research protocol. Each CRF form will include:

- Front cover sheet
- Eligibility form
- Demographic information
- Screening information
- Randomisation/registration form
- Confirmation of eligibility
- Primary and secondary end-points
- Treatment form (dates of alginate impression and intraoral scan)
- Participant Completion (documenting the date, reason and circumstances for the cessation of visits or data collection due to withdrawal, death, progression or other)
- Adverse Event
- Serious Adverse Event
- Collated, quantified data from questionnaires

- Participant Withdrawal
- End of Trial/Withdrawal form
- Investigator sign-off

The data for analysis will be transferred by the research team onto a Microsoft® Excel spreadsheet and checked by two different team members to ensure correct transferral.

9.2. Source Data

The CRF will be a source document as data will be entered directly onto this during the participant visits. The outcomes will be measured using a non-standard visual analogue scale (VAS). The VAS created for the participants to complete is modified with pictorial anchors to be easier to understand and interpret, particularly considering the likely age demographic of the participants. The VAS scales will be interpreted by appropriately trained clinicians and the information transferred onto the CRF forms following quantification.

The investigator and UHDB will retain records of all participating patients, all original signed informed consent forms and copies of the CRF pages.

9.3. Data Workflow

Data validation will occur at several stages:

- During and after completion of the CRFs
- When data has been entered onto the electronic data collection tool
    - Using validation drop down options to restrict data entry
- When data entry has been completed and prior to analysis.
    - Lists of missing data will be created and checked against the CRFs
    - Any values outside of predefined values will be highlighted and checked against the CRFs
    - Once validation is completed, the electronic data collection tool will be locked to prevent any further changes

Each CRF will be completed by clinicians trained in the research protocol. As each CRF will have a unique participant number, this will prevent duplicate entries. The data will be pseudonymised from the point of allocation to a treatment sequence using participant number only. The CRF forms will be maintained in a research folder which will be kept in a locked cabinet.

Once completed or withdrawn, information from the CRF will be transferred to an electronic data collection tool by a research team member. The electronic data collection tool with the collated participant data from the CRF forms will be maintained on an NHS trust computer. This will be checked by a second member of the research team members to ensure correct transfer of information (single data entry with second look and source data verification). This will also ensure that data is not duplicated as each participant number will be unique.

The chief investigator will have overall responsibility for the quality of data entry and quality. Once all entries are completed, the data set will be locked to prevent any further changes and released to the statistical team for analysis.

The data will be backed up onto an NHS Microsoft OneDrive and any queries written on a data clarification form for response by the research team with 5 working days. A backup and recovery log will be maintained in the TSF.

9.4. Data Access and Security

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections.

The final pseudonymised data set will be transferred using NHS.net email to the statistical team, in accordance to the UK Data Protection Act 2018.

Data will not be transferred outside of the EEA.

9.5. Archiving

At the end of the study, following completion of the end of study report, UHDB will securely archive all centrally held study related documentation for a minimum of 5 years. At the end of the defined archive period arrangements for confidential destruction will be made. It is the responsibility of each PI to ensure that data and all essential documents relating to the study are retained securely for a minimum of 5 years after the end of study, and in accordance with national legislation. UHDB will notify sites when study documentation held at sites may be archived, and then destroyed. All archived documents must continue to be available for inspection by appropriate authorities upon request.

10. STATISTICS AND DATA ANALYSIS

10.1. Sample Size Calculation

The sample size has been calculated using the following parameters:

- The sample size has been calculated to detect a Minimal Clinically Important Difference (MCID) in the VAS scales of 11mm or more (Yilmaz and Aydin 2019).
- Null hypothesis – Based on the MCID, there is no difference in patient experience of comfort during intraoral scanning versus alginate impression taking in the orthodontic setting.
- Alternate hypothesis – Based on the MCID there is a difference in patient experience of comfort during intraoral scanning versus alginate impression taking in the orthodontic setting.
- The sample size of 39 (per treatment sequence) is based on an alpha of 0.05 and power of 0.9, assuming a standard deviation of 29.85 and a difference of 11mm on the VAS score (Yilmaz and Aydin 2019).

- To account for dropouts, an additional 7% will be recruited, resulting in a total sample size of 42 per treatment sequence (84 in total). This dropout rate was observed in Yilmaz and Aydin (2019).
- In addition, a recruitment rate of 30% of eligible patients is assumed. This is based on discussions with the research team and is the standard recruitment rate assumed by Derby Clinical Trials Support Unit in the absence of recruitment rate data from published studies.
- The sample size calculations were carried out in STATA®, a statistical analysis package.

10.2. Planned Recruitment Rate

The recruitment of 39 patients (per treatment sequence) will be completed in 7 months at 1 centre assuming the minimum recruitment rate of 15 patients / month will be achieved from the first month of recruitment. This recruitment forecast adjusts for expected recruitment fatigue towards the end of the recruitment period.

10.3. Statistical Analysis

10.3.1. Summary of Baseline Data and Flow of Patients

Descriptive statistics will be presented to summarize the distribution of baseline variables across each of the treatment sequences. The continuous baseline variables (age) will be reported with means & 95% confidence intervals (95% CI), if shown to be normally distributed using a combined skewness and kurtosis test, otherwise, will be reported with medians & Interquartile Ranges (IQR). The categorical variables (participant sex) will be reported with frequencies & percentages.

A Consolidated Standards of Reporting Trials (CONSORT) flow diagram will be produced, showing the frequency of patients/participants;

- Assessed for eligibility,
- Frequency of each reason for not being eligible
- Found eligible,
- Excluded before consent (and the frequency of each reason for exclusion),
- Consented,
- Excluded before randomisation (and the frequency of each reason for exclusion),
- Randomised,
- Allocated to each randomisation group,
- That received each allocated intervention,
- That did not receive each allocated intervention,
- Lost to follow-up (and the frequency of each reason for loss to follow-up) for each analysis group,
- Analysed for each analysis group,
- Not analysed (and the frequency of each reason for not being analysed) for each analysis group.

10.3.2. Outcome Analysis

The primary outcome

The primary endpoint is the difference between two (identical) visual analogue scales (VAS) measuring the comfort of each procedure. One VAS will measure the comfort of the impression and the other VAS will measure the comfort of the scan. Each VAS will be measured by two operators and a mean of their measurements will be recorded for each scale. The difference between each participant's mean comfort VAS scores will be calculated. The mean of the differences will be reported for each treatment sequence with 95% confidence intervals.

The difference between the paired VAS will be compared using analysis of variance (ANOVA) that will analyse the period, treatment and sequence effects of the comfort scores. Analysis of the primary endpoint will be assessed using 2-sided 0.05 levels, consistent with the type I alpha level used in the trial design.

The secondary outcomes

- Four modified 100mm VA scales to measure the participant's experiences of:
    - Pain;
    - Relative speed of impression;
    - Nausea and/or coughing;
    - Whether the impression method could be recommended; and
- Four 100mm VA scales to measure the orthodontic operator's experience of:
    - Ease of impression;
    - Confidence taking the impression;
    - Relative speed of impression; and
    - Whether the participant felt sick or coughed during the procedure.
- The time taken to make the impression or complete the scan will be recorded (mins)
- A simple question to determine operator preference for intraoral scanning versus alginate impressions.

The 8 secondary outcomes measured by VAS and the time taken to make the impression or complete the scan will be compared using analyses of variance suitable for a crossover study, that will test the period, treatment and sequence effects on these nine secondary outcomes. The mean differences between the paired VAS scores (e.g., Pain from scan and pain from impression) will be reported with 95% confidence intervals.

The operator's preference will be reported using descriptive statistics. The frequency and percentages will be recorded.

In addition, two secondary analyses of the primary outcome may be undertaken. The first analysis will be conducted and will use a two-period two-treatment mixed effects model: Participant effects will be treated as random and a treatment-by-period interaction (for this analysis, this is the carryover effect) will be included in the model. If some participants have not complied with the protocol, a second analysis of the primary outcome will be conducted just including participants that were compliant (i.e.

a per protocol analysis). For both of these analyses, the mean effects will be reported, with 95% confidence intervals.

Only the primary analysis will be compared against a specific level of significance. The secondary analyses should be considered as hypothesis generating rather than providing firm conclusions.

The analysis will be undertaken by the study statistician. The study statistician will draft the Statistical Analysis Plan (SAP) according to CTU-SOP-019 (Statistical Analysis Plan), which will be reviewed by the CI and approved by the CI and the study statistician. The analysis will be carried out using STATA® and a statistical report produced.

10.4. Subgroup Analyses

There will be no subgroup analyses.

10.5. Adjusted analyses

There will be no adjusted analyses.

10.6. Interim Analysis and Criteria for the Premature Termination of the Study

There will be no interim analyses.

The Sponsor may suspend or prematurely terminate either the entire study, or the study at an individual site, for significant reasons that must be documented (e.g. an unacceptable risk to participants or serious repeated deviations from the protocol/ regulations). If this occurs the Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e. participants, investigators, participating sites, REC, regulatory bodies).

10.7. Analysis Groups

All participants who were randomised and experienced at least one of the study treatments will be included in the primary analysis. Participants will be analysed according the treatment sequence they received, if this differs from the treatment sequence to which they were allocated.

The potential re-analysis of the primary analysis will be carried out on a per protocol basis (i.e. only participants without major protocol deviations who completed the study with the treatment that was originally allocated will be included).

All participants who completed the study will be included in the other secondary analyses. Participants will be analysed according the treatment sequence they received, if this differs from the treatment sequence to which they were allocated.

10.8. Procedure(s) to Account for Missing or Spurious Data

Once identified as eligible, participants will receive two appointments a minimum 4 weeks apart from one another. Having the appointment time and date early, allows for the participant and their parent or guardian, if appropriate, to plan around school and work as much as possible. Prior to their appointments, they receive a text message reminder from the hospital. Any missed appointments will be managed in line with local policy, particularly concerning safeguarding of children and vulnerable adults.

If there are missing data in the primary endpoint, then multiple imputation using chained equations will be applied. The plausibility that outcome data are missing at random (MAR) from the primary endpoint will be examined, and if it doesn't hold, sensitivity analysis will be conducted. A complete case analysis will be performed for secondary trial outcomes.

11. MONITORING, AUDIT & INSPECTION

As a low-risk study, a monitoring plan is not required.

12. ETHICAL AND REGULATORY CONSIDERATIONS

12.1. Assessment and Management of Risk

The benefit of participating on the trial is the ability of the participant to help provide their first-hand experience of a very commonly carried out orthodontic procedure. Better understanding from a patient's perspective can be useful to the clinician as well as to manufacturers of impression materials and intraoral scanning devices in future development. A patient undergoing orthodontic treatment within the department would require an intraoral scan and often an addition alginate impression as part of their normal care, and therefore participation would not significantly deviate away from this.

The exclusion criteria have been selected to prevent bias within the study and to exclude those patients that a scan or impression may be carried out differently within their normal orthodontic care. Those that have previously had scans or impressions in the last 2 years may already have an experience which could influence their questionnaire answers. Those with cleft lip or palate, may require modifications of the normal impression methods and therefore inclusion within the study would put them through extra treatment, which for them may not be as comfortable.

Due to the need to complete questionnaires and gain informed consent and assent, appointments with the participant may be slightly longer. We have, therefore, have tailored the washout period between appointments to a time period that would fit with a patient's normal orthodontic appointments, so as to limit the number of times the patient would have to come into the hospital and reducing the time missed at work or school. The average overall time for orthodontic treatment for a patient is 2-2.5 years and the study itself does not anticipate extending this beyond what would normally be required by the patient.

The visual analogue scale used to collect information from the participants following the intraoral scan or impression will be modified with pictorial anchors to help patient understanding, particularly if the participant is a child. This will be piloted to check health literacy, ease of use and clarity of instructions and amended accordingly.

Low risk is anticipated by participating in the trial.

- There is a risk of participant's coughing or gagging during both procedures, with the potential for aerosol generation.
    - The team treating the participants will follow necessary protocols, including that of personal protective equipment, in line with COVID processes.
    - Any accompanying individuals/parents of the participant will be asked to wait outside the department, limiting footfall within the surgery.
    - If the participant does gag during an impression or intraoral scan, the clinician will implement measures to reduce this as much as possible and to ease any anxiety by the participant.
    - There are only isolated cases of allergic reaction to alginate materials. The incidence of such reactions is unknown due to the lack of published evidence (Syed 2015)
    - To reduce the risk of this occurring, the clinician will check known allergies and medical history with the participant and/or the parent/guardian as part of their normal orthodontic treatment and this information can then be highlighted.

12.2. Peer review

This study has been peer reviewed as part of the British Orthodontic Society Foundation (Funder) application process.

12.3. Public and Patient Involvement

Prior to use, the participant and parent information sheets and questionnaires will be piloted with our orthodontic population to ensure that they are age-appropriate for the patients that may be eligible for the trial. This will include looking at health literacy as well as ease of use and clarity of the instructions given. Feedback from this will be used to make any necessary amendments prior to use in the trial.

12.4. Research Ethics Committee (REC) & Regulatory Considerations

The study will be conducted in compliance with the approved protocol and the Declaration of Helsinki. The protocol and all related documentation (e.g. informed consent form, PIS, questionnaires) have been reviewed and received approval by a Research Ethics Committee (REC). The investigator will not begin any participant activities until approval from the HRA and REC has been obtained and documented. All documentation and correspondence must be retained in the trial master file/investigator site file. Substantial amendments that require HRA and REC (where applicable) review will not be implemented until the HRA and REC grants a favourable opinion (with the exception of those necessary to reduce immediate risk to participants).

It is the responsibility of the CI to ensure that an annual progress report (APR) is submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, annually until the study is declared ended. The CI is also responsible for notifying the REC of the end of study (see Section 6.9) within 90 days. Within one year of the end of study, the CI will submit a final report with the results, including any publications/abstracts to the REC.

Before any site can enroll a patient into the study confirmation of capacity must be sought from the site's research and development (R&D) department. In addition, for any amendment that will potentially affect the site's permission, the research team must confirm with the site's R&D department that permission is ongoing (Section 11.10).

12.5. Protocol Compliance / Non-compliance Reporting

The investigator is responsible for ensuring that the study is conducted in accordance with the procedures described in this protocol. Prospective, planned deviations and/or waivers to the protocol are not acceptable, however accidental protocol deviations (non-compliances) may happen and as such these must be recorded. Non-compliances should be recorded in the CRF and/or a non-compliance log kept in the ISF. All non-compliances should be reviewed and assessed by the PI (or appropriately delegated individual) to determine if they meet the criteria of a "serious breach" (Section 12.6). Non-compliances which are found to frequently recur are not acceptable, will require immediate action, and could potentially be classified as a serious breach.

12.6. Notification of Serious Breaches to GCP and/or the Protocol

A "serious breach" is a departure from the protocol, Sponsor procedures (i.e. SOPs), or regulatory requirements which is likely to effect to a significant degree –

(a) The safety or physical or mental integrity of the subjects of the study; or
(b) The scientific value of the study.

If the PI (or delegate) is unsure if a non-compliance meets these criteria, they should consult the Sponsor for further guidance.

If a serious breach is identified the investigator should notify the Sponsor immediately (i.e. within 1 working day) using the 'Non-CTIMP Notification of a Serious Breach' form. The report will be reviewed by the Sponsor and CI, and where appropriate, the Sponsor will notify the REC within 7 calendar days of being made aware of the breach.

12.7. Data Protection and Patient Confidentiality

The study will be conducted in accordance with the Data Protection Act 2018. The investigator must ensure that participant's anonymity is maintained throughout the study and following completion of the study. Participants will be identified on all study specific documents (except for the informed consent form and enrolment log) only by the participants study specific identifier (and initials if deemed necessary). This identifier will be recorded on documents, biological samples and the database. The Investigator Site File will hold an enrolment log detailing the study specific identifier alongside the names of all participants enrolled in the study.

All documents will be stored securely with access restricted to study staff and authorised personnel.

The CI (Alison Murray) will act as the custodian of the data generated in the study.

12.8. Financial and Other Competing Interests for the Chief Investigator, Principal Investigators at Each Site and Committee Members for the Overall Study Management

There are no conflicts of interest that could influence study design, conduct or reporting to declare.

12.9. Indemnity

As UHDB is acting as the research Sponsor for this study, NHS indemnity applies. NHS indemnity provides cover for legal liabilities where the NHS has a duty of care. Non-negligent harm is not covered by the NHS indemnity scheme. UHDB, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional circumstances an ex-gratia payment may be offered.

12.10. Amendments

If changes to the study are required these must be discussed with the Sponsor, who is responsible for deciding if an amendment is required and if it should be deemed substantial or non-substantial. Substantial amendments will be submitted to the relevant regulatory bodies (REC, HRA) for review and approval. The amendments will only be implemented after approval and a favourable opinion has been obtained. Non-substantial amendments will be submitted to the HRA for their approval/ acknowledgment. Amendments will not be implemented until all relevant approvals are in place.

12.11. Access to Final Study Dataset

The final dataset will be accessed by the following individuals who are based at the UHDB Trust:

- Trishna Patel
- Esme Warren-Westgate
- Anjli Patel
- Alison Murray
- Sponsor
- CTU – Statisticians

13. DISSEMINATION POLICY

13.1. Dissemination Policy

Intellectual property arising from the study will remain ownership of the University Hospitals of Derby and Burton NHS Foundation Trust. On completion of the study, the data will be analysed and tabulated. This will feed into a Final Study Report. It is anticipated that the results of the study will be published by the research team in an appropriate peer-reviewed journal. The funders request

that the information is placed within the public domain within 6 months. In like with funding terms and conditions, the final report will be submitted to the BOSF and published on their webpages. Additionally, it is expected that the study will be presented at the British Orthodontic Conference and the aim is for publication in the Journal of Orthodontics or the most relevant journal. In all publications and presentations, the BOSF and the Derby Pump Priming Grant Charitable Funds will be appropriately acknowledged.

Participants will be able to request results of the study following publication of the results and contact details have been provided within the participant/parent information leaflet.

13.2. Authorship Eligibility Guidelines and any Intended Use of Professional Writers

It is expected that any first drafts of publications for academic journals and the final study report will first be authored by the TMG as per the named CI and co-applicants. Final authorship shall be in accordance with the International Committee of Journal Medical Editors (ICJME) guidance (International Committee of Medical Journal Editors 2019).

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15. APPENDICES

15.1. Appendix 1 – Schedule of Assessments

Procedures	**Visits**			
	1. Screening	**2. Treatment phase**		**3. Follow up**
Informed consent	X	X		
Demographics		X		
Medical history	X	X	X	
Dental health education	X			
Eligibility assessment	X			
Randomisation		X		
New patient examination (if necessary)		X		
Orthodontic treatment consent		X	X	
Compliance				
Assessment 1 (Alginate impression)		X	X	
Assessment 2 (Intraoral scan)		X	X	
Orthodontic treatment including appliance fit				X
Adverse event assessments		X	X	X
Physician's Withdrawal Checklist	X	X	X	

15.2. Appendix 2 – Amendment History

Amendment No.	**Protocol version no.**	**Date issued**	**Author(s) of changes**	**Details of changes made**
1	2.0	20/02/2022	Trishna Patel	Removal of reference to Gillick competence and individuals with parental consent rights Added reference to the assent form Update version number and dates Added NCT number Minor formatting/spelling amendments