Complete Research Protocol (HRP-503)

Table of Contents

Template Instructions

Sections that do not apply:

- *In several sections, the addition of checkboxes for **Not Applicable** have been added to the template as responses.*

  - *If an N/A checkbox is present, select the appropriate justification from the list.*

  - *If an N/A checkbox is not present, or if none of the existing checkboxes apply to your study, you must write in your own justification.*

- *In addition:*

  - *For research where the only study procedures are records/chart review: Sections 6, 21, 22, 24, 25, 26 and 27 do not apply.*

  - *For exempt research: Section 6 may not apply. Section 6.1 will still apply if there is a study intervention.*

Studies with multiple participant groups:

- *If this study involves multiple participant groups (e.g. parents and children), provide information in applicable sections for each participant group. Clearly label responses when they differ. For example:*

Response Example
Intervention Group:
Control Group:

Formatting:

- *Do not remove template instructions or section headings when they do not apply to your study.*

If you are pasting information from other documents using the "Merge Formatting" Paste option will maintain the formatting of the response boxes.

Amendments:

- *When making modifications or revisions to this and other documents, use the **Track Changes** function in Microsoft Word.*
- *Update the version date or number **on Page 3.***

PROTOCOL TITLE:

Include the full protocol title.

Response: A Comparison of Class II correction using the Carriere Motion Appliance versus an In-Office Sectional Appliance: Treatment Effects and Efficiency

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response:

Alexandria Newton

Orthodontic Department at University at Buffalo School of Dental Medicine

315-794-9159

amnewton@buffalo.edu

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response: Version 1.0 Date: 07/05/2021

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?

FUNDING:

Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.

Response: Currently no funding is present

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response: No Grant currently funding this study

RESEARCH REPOSITORY:

Indicate where the research files will be kept, including when the study has been closed. The repository should include, at minimum, copies of IRB correspondence (approval, determination letters) as well as signed consent documents. This documentation should be maintained for 3 years after the study has been closed.

Response:

Location: University at Buffalo School of Dental Medicine

*Address:*140 Squire Hall, Buffalo, NY 14214

Department: Department of Orthodontics

1.0 Study Summary

Study Title	A Comparison of Class II correction using the Carriere Motion Appliance versus an In-Office Sectional Appliance: Treatment Effects and Efficiency
Study Design	Pilot randomized clinical trial
Primary Objective	1. To evaluate total treatment time, in months, from the initial bonding appointment until a Class I molar relationship has been achieved and the appliance has been removed (T1) using either the Carriere Motion Appliance (CMA) or an in-office fabricated sectional appliance
Secondary Objective(s)	To evaluate secondary tooth movements (mm, degrees) and changes in skeletal measurements after Class II molar correction using the either the CMA or an in-office sectional appliance, by comparing lateral cephalometric radiograph measurements and digital study model measurements taken at the Initial Records appointment prior to treatment(T0) and immediately after removal of appliance – when a Class I molar relationship has been achieved (T1)
Research	Class II Correction Appliances: CMA vs. a sectional, in

Intervention(s)/ Investigational Agent(s)	office fabricated appliance
IND/IDE #	N/A
Study Population	12-17Y11M male and female patients
Sample Size	16 per treatment group (N = 32)
Study Duration for individual participants	5 months +/- 1 month
Study Specific Abbreviations/ Definitions	CMA= Carriere Motion Appliance ss = Stainless-steel Sagittal first approach = correcting the antero-posterior occlusal relationship prior to the leveling and aligning phase of orthodontic treatment Class I molar relationship = The position of the mesiobuccal cusp of the maxillary first permanent molar occludes distally to the buccal groove of the mandibular first molar, and its distal buccal cusp is positioned in the embrasure between the mandibular first and second molars, when in centric occlusion Class II molar relationship = An occlusal relationship where the buccal groove of the mandibular first molar is positioned distal to the mesiobuccal cusp of the maxillary first molar, when in centric occlusion LFH = lower facial height

2.0 Objectives*

2.1 Describe the purpose, specific aims, or objectives of this research.

Response:

The aim in this study is to explore the efficacy and efficiency of Class II molar correction with the sagittal first approach using either a sectional, in-office fabricated appliance or the CMA by measuring total treatment duration (in months) as well as comparing dental and skeletal measurements taken from lateral cephalometric radiographs obtained prior to Class II correction (T0) and immediately after removal of the appliance (T1). We will also be comparing secondary molar and canine rotational movements after Class II correction by comparing digital dental casts obtained at T0 and T1.

2.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

1. There is no difference in mean duration (in months) of Class II molar correction when using a CMA or an in-office Class II correction appliance.

2. There is no difference in mean skeletal changes (in millimeters, degrees) after Class II correction using CMA or an in-office Class II correction appliance.

3. There is no difference in mean dental changes (in millimeters, degrees) after Class II correction using CMA or an in-office Class II correction appliance.

3.0 Scientific Endpoints*

3.1 Describe the scientific endpoint(s), the main result or occurrence under study.

NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should ***not*** *be a date.*

Response:

We hope to investigate whether the built-in features of the CMA will minimize total treatment time (in months) to achieve Class II correction to a Class I molar relationship when compared to an in-office sectional fabricated Class II correction appliance.

We also hope to investigate whether the CMA's built-in features will cause similar secondary effects after the Sagittal First approach of Class II correction when compared to an in-office sectional fabricated Class II correction appliance. These secondary effects include any additional dental or skeletal changes measured after Class II correction using the appliance aside from distalization of the maxillary buccal segments (canine to first molar).

4.0 Background*

4.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:

<u>The Class I Molar Relationship</u>

Maxillary first molar position is a prominent clinical factor in orthodontic diagnoses and treatment.[1] In Class I normal occlusion, the position of the mesiobuccal cusp of the maxillary first permanent molar occludes distally to the buccal groove of the mandibular first molar. The maxillary first molar is inclined mesially, and its distal buccal cusp is positioned in the embrasure between the mandibular first and second molars. [2] Three

positional factors play a role in maxillary first molar relationship with the opposing dentition. This includes the position of the maxillary first molar in the maxilla, the axial inclination of the maxillary first molar, and the rotation of the maxillary first molar along its long axis.[1] If the maxillary first molar is not positioned in normal occlusion, it can result in an unbalanced occlusion that may be misdiagnosed as a tooth size discrepancy of the opposing dental arch. [2] 83% of patients presenting with malocclusions present with a mesially rotated maxillary first molar.[3] If the maxillary molar is rotated mesially, this allows for more space in the arch, which can affect the remaining occlusal relationships, including canine relationship on the affected side.[2,4]

The Class II Molar Relationship

A Class II molar relationship is indicated when the buccal groove of the mandibular first molar is positioned distal to the mesiobuccal cusp of the maxillary first molar, when in centric occlusion. According to the NHANES III survey, around twenty-two percent of children between the ages of 8 and 11 present with a Class II molar relationship.[5] These individuals can have a variety of different skeletal maxillary and mandibular relationships as well as variations in other identifying features of malocclusion including spacing, overbite and overjet. These differences can lead to variation in the presentation of the soft tissue profile of individuals with a Class II molar relationship.[6]

Skeletally, a retruded mandible is typically present in Class II individuals, however, the maxilla can be protrusive as well. Class II individuals can also present with a range of lower facial heights (LFH) from decreased, to normal, to increased. An orthodontist must take these variations into account when treating Class II patients.[6] In order to address any anteroposterior and vertical discrepancies in Class II individuals, the most ideal time to treat Class II patients is during adolescence, when a patient is still growing.[6]

In a clinical setting, Class II malocclusion is typically divided into 2 subdivisions. Class II Division 1 and Class II Division 2 patients differ in many anteroposterior and vertical aspects, according to cephalometric measurements.[7] Common features of Class II Division 1 patients include at least one of the following characteristics: a Class II skeletal relationship with the maxilla and the maxillary teeth being anteriorly placed in relation to the cranium, the maxillary teeth being anteriorly placed only, underdevelopment of the mandible, posterior placement of a normal-sized mandible, the mandibular dentition being placed posteriorly in a normal sized mandible, or a combination of any of the above findings. Class II Division 1 patients will also have a reduced interincisal angle. [7, 8] The palate of Class II Division 1 patients is typically narrower with a greater distance between the molar and canine due to proclined anterior teeth. [3]

Class II Division 2 patients generally show a Class II skeletal relationship and an increased interincisal angle with a skeletal deep bite.[7, 8] Some Class II Division 2 patients may also present with a more narrow arch.[3]

Carriere Motion Appliance

The Carriere Motion Appliance (CMA) is a relatively new appliance that was introduced by Luis Carrière in 2003. The CMA is used to correct Class II (Division 1 and 2) or Class III dentoalveolar malocclusions and achieve a Class I occlusal relationship prior to the leveling and aligning phase of treatment (this method is referred to as the Sagittal First approach). Correcting occlusal relationships in a separate and initial phase eliminates the additional vectors of force that are elicited on the teeth when distalization is performed alongside archwire progression.[4,9] The CMA can be used to correct anteroposterior occlusal relationships in growing patients as well as adults.[4,10,9]

The CMA is made of a Nickle free stainless steel bar with a ball and socket joint, and it is bonded to the labial surface of the maxillary canine and maxillary first molar.[10,9] The device comes in 22 sizes to accommodate for the variation in distance between the buccal surface of the midpoint of the maxillary first molar and the buccal surface of the midpoint of the maxillary canine (or maxillary first premolar if the canine has not erupted).[10] Since the CMA is achieving Class II correction by applying force exclusively along the buccal segment in comparison to Class II correction after the leveling and aligning phase, when a patient is in a non-segmented fixed orthodontic archwire that spans the entire maxillary arch, the inventors believe that the dentition will be less resistant to distalization forces.[4] The canine pad is designed to allow for distalization of the canine without any tipping.[4,10,9] The distal portion of the canine pad is continuous with an arm that has a slight curve over the buccal surfaces of the two premolars and ends in a ball-and-socket joint with the molar pad. The ball has raised surfaces that correspond with depressions in the molar pad socket, which is designed to limit distal rotation of the maxillary first molar to -15-degrees along the longitudinal axis of the molar. The joint also designed to apply torque control of both the maxillary canine and maxillary first molar. [4,10,9]

The molar pad is intended to induce 3 types of movement to correct maxillary first molar position. The first is to upright the maxillary first molar crown if it is mesially inclined. Next is distal rotation around the palatal root when the maxillary first molar is mesially rotated. When the maxillary first molar has been de-rotated, the shoulder of the posterior base of the molar pad is designed to contact the mesial arm of the appliance to prevent over rotation. The last built-in molar movement is distal displacement of the maxillary first molar without distal tipping of the crown. [10,9]

In order to minimize protrusion and proclination of the mandibular incisors during elastic wear, mandibular anchorage in combination with the CMA is necessary.[10,9] The type of mandibular anchorage used depends on the patient's skeletal and muscular characteristics.[9,11] This may include: a passive lingual arch from mandibular first molar to first molar, a Hamula lingual arch (a modified lingual arch designed with Hamula First Fit molar bands that contain occlusal stops on the mesial and distal portions of the bands with two segments of 0.021x 0.025" wire soldered to the stops and bonded to the occlusal surfaces of the mandibular premolars and second molars), a full mandibular fixed appliance (if the patient has a severe curve of Spee or mild mandibular crowding), a mandibular Essix retainer with small composite wedges bonded to the buccal surfaces of molars and premolars, or Miniscrews between the first and second molars. [4,10,9,11]

Class II correction using the CMA requires elastic wear. For elastic wear, during the first month of treatment, 6 oz, 1/4" Class II elastics (elastics extending from a hook located on the canine pad to a button or bracket bonded to the mandibular first molar) should be worn, and should be changed daily. Following the first month of elastic wear, the 6 oz, ¼" Class II elastics will be exchanged for 8 oz, 3/16" elastics. The 8 oz, 3/16" elastics should be worn using the same protocol as the first month of treatment, until Class II correction is achieved.[10] The elastic should be changed daily, and the duration of elastic wear during the day can vary depending on skeletal growth pattern.[10] A low mandibular plane angle case (measured on a lateral cephalometric radiograph) with good perioral muscular strength should be instructed to wear Class II elastics 24 h a day. In high mandibular plane angle cases (also measured on a lateral cephalometric radiograph) who have lighter perioral musculature, elastic wear can be limited to only 14 h per day and should include mostly nighttime wear. [9,11] Patient compliance is generally greater in the beginning of orthodontic treatment when the patient is still motivated versus later on in treatment when a patient may be fatigued, and thus compliance with Class II elastic wear with CMA has been shown to be greater than elastic wear at later stages in orthodontic treatment.[10] The goal before removal of the appliance is to surpass an ideal Class I canine relationship into a superclass I relationship (distal incline of the maxillary canine is in contact with the mesial incline plane of the mandibular cuspid), because some relapse is expected during the leveling and aligning phase treatment. Once the CMA is removed, the canine to first molars should be coligated under the archwire using a 0.012" stainless steel ligature wire in a figure-8 fashion. [4,10]

CMA induces distal rotational movement of the maxillary first molars around their palatal roots and produces a uniform distal force on the posterior segment (from canine to first molar) as a unit. Distalization occurs while simultaneously minimizing maxillary molar tipping and maxillary bicuspid anchorage loss. With proper anchorage control in the mandibular arch, treatment using the CMA claims to minimize mandibular

incisor proclination. The appliance also claims to minimize periodontal reaction, although reasoning for this has not been described. [9,10]

CMA Treatment effects and Treatment Duration

Few studies have investigated the overall treatment effects of Class II correction using the CMA. Research available indicates that the CMA successfully treats a mild to moderate Class II molar and canine relationship prior to the leveling and aligning phase of treatment through molar distalization and changes in overbite and overjet. [4,10-12] Average reported duration of Class II correction using the CMA is 4-6 months. [13,14,15,16,17] No significant skeletal effects were reported in most studies after Class II correction with the CMA in growing patients.[13,14,17] However, one study reported a clinically significant increase in lower facial height (LFH), and a statistically significant restriction of maxillary growth at point A after treatment using the CMA.[15]

Dental effects of the CMA include distal movement of the maxillary canine[10-12] with distal tipping, distal rotation, and extrusion.[16] Reported movements of the maxillary first molar include distal movement with distal tipping and rotation. When comparing treatment effects of skeletal Class I and Class II patients with Class II malocclusion, an increase in mesial movement of the mandibular first molar and mandibular incisor proclination were the only measured differences observed after Class II molar and canine correction in skeletal Class II versus Class I patients. [16]

Short-term side effects reported after CMA use include additional space distal to the maxillary lateral incisors, extrusion of maxillary canines, and exacerbation of arch length discrepancy in the mandibular arch. Protrusion and proclination of mandibular incisors was reported in studies using a lingual arch, fixed appliances, and an Essix retainer for anchorage.[12,13,14, 16,17] Mandibular incisor proclination was more pronounced when treating skeletal Class II patients versus skeletal Class I patients.[16] Mandibular molar mesialization and extrusion was also reported in some studies as a side effect.[16,17] Side effects involving the maxillary first molars after distalization include only minimal distal tipping, which suggests that the appliance aids in maintaining upright position of the maxillary first molars.[14]

There are a limited number of studies reporting treatment duration of Class II correction phase using the CMA. The appliance is more efficient for growing patients, but it is also effective for adults.[10] The CMA workbook states that Class II correction for adults takes an average of 5 months to complete, while children should achieve Class II correction in an average of 3 months.[10] All studies reporting duration of Class II correction were performed on adolescent patients or growing patients. One study reported 4.9 months for patients with skeletal Class I and 4.2 months for patients with skeletal Class II, with a combined average of 4.6 months.

[16] Another study reported an average of 4.28 months, a third reported 4.4 months, and a fourth study reported an average of 5.2 months. [12,14,15] A fourth study reported 6.3 months for total Class II correction time when using a CMA.[13] When measuring combined total treatment time (CMA followed by fixed appliances) one study reported an average combined total treatment time be 32.3 months with a conclusion that the CMA is not an efficient way to treat Class II malocclusions.[13] However, a second study reported a total treatment time of 18.2 months (5.2 months for CMA and 13.0 months for the rest of the treatment duration), and a third reported an average combined treatment time of 17.6 months.[12,15]

One study measured long-term effects of patients treated with a CMA followed by functional fixed appliance. Results indicated minor changes in molar movement when comparing CBCT measurements taken after removal of the fixed appliance and at a 4-year follow up. However, the inclusion criteria for this study were subjects with a Class I skeletal relationship, and an Angle Class II relationship of at least ½ cusp. The significant changes measured were mesial crown tipping of the maxillary first molars and lingual crown torquing of the mandibular incisors.[18]

CMA From the Patient's Perspective

A number of studies investigated patients' perceptions of CMA treatment. The CMA is an ideal treatment option from a patient perspective, because it is more esthetic and comfortable than edgewise appliances.[4,9] The appliance also shows the progress of distalization through the formation of diastemas between the maxillary anterior teeth.[4,9] Adolescent patient's experience has been reported to be more comfortable and positive when treated with a CMA in comparison to FFRD. Additionally, the debonding or breakage of the CMA was less frequent when compared to the FFRD. [19]

Study Aims

There are a limited number of studies investigating the efficiency of the CMA's built-in features, and whether or not they allow for Class II correction with minimal secondary effects as compared to other Class II correction appliances. This study aims to compare both the secondary dental and skeletal effects and treatment duration when using the CMA for Class II correction prior to comprehensive orthodontic treatment in comparison to an in-office fabricated Class II correction appliance. Benefits of using an in-office fabricated Class II correction appliance may include that the materials needed are already present in-office. Since the CMA comes in 22 sizes to accommodate for the anatomical variation seen in the maxillary arch, utilization of materials in-office may be more beneficial than maintaining an armamentarium of different size CMAs for the right and left sides of the arch.

4.2 Include complete citations or references.

Response:

Literature Cited

1. Frank F. Lamons CWHI. The problem of the rotated maxillary first permanent molar. American Journal of Orthodontics 1961;47:246-272.
2. Stoller AE. The normal position of the maxillary first permanent molar. American Journal of Orthodontics 1954;40:259-271.
3. Henry RG. Relationship of the maxillary first permanent molar in normal occlusion and malocclusion. AMerican Journal of Orthodontics 1956;42:288-306.
4. McFarlane B. Class II correction prior to orthodontics with the carriere distalizer. International Journal of Orthodontics 2013;24:35-36.
5. Proffit WR, Fields HW, Jr., Moray LJ. Prevalence of malocclusion and orthodontic treatment need in the United States: estimates from the NHANES III survey. Int J Adult Orthodon Orthognath Surg 1998;13:97-106.
6. Bishara SE. Class II Malocclusions: Diagnostic and Clinical Considerations With and Without Treatment. Seminars in orthodontics 2006;12:11-24.
7. Al-Khateeb EA, Al-Khateeb SN. Anteroposterior and vertical components of class II division 1 and division 2 malocclusion. Angle Orthod 2009;79:859-866.
8. G. V. Fisk MRC, R.M. Grainger. The morphology and physiology of distoclusion. American Journal of Orthodontics 1953;39:3-12.
9. Carriere L. A new Class II distalizer. J Clin Orthod 2004;38:224-231.
10. Carriere L. The Carriere Motion Workbook: Turn Class II Into Simple Class I Patients. Ortho Organizers, Inc; 2014.
11. Fouda AS, Aboulfotouh MH, Attia KH, Aboulezezz AM. Carriere Motion Appliance with Miniscrew Anchorage for Treatment of Class II, Division 1 Malocclusion. J Clin Orthod 2020;54:633-641.
12. Wilson B, Konstantoni N, Kim KB, Foley P, Ueno H. Three-dimensional cone-beam computed tomography comparison of shorty and standard Class II Carriere Motion appliance. Angle Orthod 2021.
13. Yin K, Han E, Guo J, Yasumura T, Grauer D, Sameshima G. Evaluating the treatment effectiveness and efficiency of Carriere Distalizer: a cephalometric and study model comparison of Class II appliances. Prog Orthod 2019;20:24.
14. Camille L. Sandifer JDE, Clark D. Colville, Ron L. Gallerano, Sercan Akyalcin. Treatment effects of the Carrière distalizer using lingual arch and full fixed appliances. Journal of the World Federation of Orthodontists 2014;3:e49-e54.
15. Franchi HK-BJAMJJPLCML. Treatment effects of the Carriere® Motion 3D™ appliance for the correction of Class II malocclusion in adolescents. The Angle Orthodontist 2019;89:839-846.
16. Areepong D, Kim KB, Oliver DR, Ueno H. The Class II Carriere Motion appliance. Angle Orthod 2020;90:491-499.
17. Amira E. Ahmed SAI, and Maha M. Mohamed. Evaluation of Electromyographic Activity Concomitant to Class II Correction Using Carrier Distalizer Appliance. Al-Azhar Dental Journal for Girls 2020;7:295-303.

18. Hashem AS. Three dimensional assessment of the long-term treatment stability after maxillary first molar distalization with Carriere distalizer appliance. Life Science Journal 2020;17:83-90.
19. Hamilton CF, Saltaji H, Preston CB, Flores-Mir C, Tabbaa S. Adolescent patients' experience with the Carriere distalizer appliance. Eur J Paediatr Dent 2013;14:219-224.
20. Thorsten Grünheid CL, Brent E. Larson. How accurate is Invisalign in nonextraction cases? Are predicted tooth positions achieved? Angle Orthod 2017;87:809- 815.
21. Bethesda MNCoRPaM. NCRP Report 160: Ionizing Radiation Exposure of the Population of the United States; 2009.

5.0 Study Design*

5.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

This will be a pilot randomized clinical controlled trial including males and females with a unilateral or bilateral ½ cusp to full cusp Class II molar and canine relationship and mild to moderate crowding. The sample consists of adolescent patients who are receiving comprehensive full fixed appliance orthodontic treatment at the Postgraduate orthodontic clinic at the UBSDM. Subjects will be randomized into one of two treatment groups. Subjects will receive Class II correction prior to orthodontic treatment using either the CMA or an in-office fabricated Class II correction appliance. Lateral cephalometric radiographs and digital models will be taken at: T0 (initial records appointment) and T1(the appointment where the appliance is removed once Class II molar correction has been achieved). Patients in both treatment groups will use the same mandibular anchorage protocol (essix with 2 mm thickness and a button bonded to the buccal surface of the mandibular first molars). Elastic progression for both treatment groups will follow the protocol recommended by the CMA manufacturer (Force 1 Class II elastics (1/4, 6 oz) will be worn for 1 month, and Force 2 Class II elastics (3/16, 8 oz) will be worn for the remainder of Class II correction). Dental and skeletal changes will be measured using lateral cephalometric radiographs taken at T0 and T1, and rotational movements of the maxillary first molar and canine will be assessed using superimposition of the maxillary models taken at T0 and T1 using the e- model Compare 8.1 software by Geodigm. Treatment duration will be calculated (in months) starting on the date the appliance was bonded and ending on the date of appliance removal. Treatment duration and dental and skeletal movements will be compared between the two treatment groups.

6.0 Study Intervention/Investigational Agent

6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

Response:

The CMA is made of a rigid, Nickle free stainless-steel bar that extends from a canine pad to form a ball and socket joint with a molar pad. It is bonded to the labial surfaces of the maxillary canine and maxillary first molar, using composite resin in the same fashion that a bracket would be bonded to a tooth for orthodontic treatment. The goal of the CMA is to allow for a sagittal first approach to achieve Class II molar correction prior to comprehensive orthodontic treatment through distalization of the maxillary buccal segments (maxillary canine and beyond) without the additional vectors of force created when completing Class II correction using continuous orthodontic archwire and brackets, and Class II elastics.[4]

The in-office appliance utilized in our treatment will be fabricated by one operator (AN), and it will consist of a 0.022" slot MBT maxillary second molar mini tube that will be modified to have a tube length of 2 mm, and a 0.018" slot MBT maxillary canine bracket. The appliance will be fabricated using a 3d-printed model of the subject's maxillary arch. The maxillary second molar tube will be cemented on the center of the buccal surface of the maxillary first molar of the 3D-printed model. A 0.016x0.022" stainless steel wire with a bayonet bend positioned mesial to the maxillary first molar and a curve extending from the maxillary first molar to the maxillary canine will be placed, and it will guide the placement of the maxillary canine bracket, so that the stainless-steel wire can sit passively in both the molar tube and canine bracket slot. Once the maxillary canine bracket has been bonded, a pre-cut, closed-coil stainless-steel spring that spans from the mesial opening of the first molar tube to the distal wing of the canine bracket will be placed, and the wire will then be steel tied to the maxillary canine bracket, and then it will be cut and cinched mesial to the maxillary canine bracket. The wire will also be cinched 2-3 mm distal to the maxillary molar tube, to ensure that once the wire is placed, the molar still will maintain the ability to rotate, if needed. The operator will then remove the appliance in one piece from the model and will sand blast any excess resin off the bracket and molar tube. The same operator (AN) will instruct the treating resident on how to place the appliance: the molar tube will be placed in the center of the buccal surface of the maxillary first molar and will be light cured. The canine bracket will then be placed so that the bayonet bend is in contact with the mesial surface of the maxillary first molar tube and the wire is passive. The same anchorage protocol and elastic regimen will be utilized in the in-office Class II corrector group.

Both the CMA and the in office fabricated appliance will be utilized for Class II correction prior to comprehensive orthodontic treatment, and mandibular anchorage is necessary for both appliances. In our study we will be utilizing one of the CMA manufacturer's recommended mandibular anchorage protocols: a fabricated 2 mm essix retainer. An orthodontic button will be bonded to the buccal surface of the mandibular first molar on the affected side to provide mandibular anchorage for elastic use during Class II correction. Elastic

progression will follow the protocol recommended by the CMA manufacturer (Force 1 Class II elastics (1/4, 6 oz) will be worn for 1 month, and Force 2 Class II elastics (3/16, 8 oz) will be worn for the remainder of Class II correction) until a Class I molar relationship has been achieved.

1.1 Drug/Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

N/A

6.2 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

Response:

N/A

7.0 Local Number of Subjects

7.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response: 16 subjects per treatment group, (N = 32)

7.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

Approximately 720 to 840 subjects

7.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

Our study will be screening the entire prospective patient pool in the University at Buffalo School of Dental Medicine's orthodontic clinic for the first- and second-year residents. One operator (AN) will instruct all residents completing patient screenings and acceptance of patients on criteria necessary to become a subject in the current study. The same operator will also evaluate all eligible subjects and see if they meet all inclusion criteria and proceed to inform the subjects of their eligibility and purpose of the study. Each resident can screen approximately 60-70 patients over 6 months. If we utilize the patient pools of twelve residents, we can approximate 720 to 840 patients total. Not all patients will meet the inclusion criteria required for the study, and other treatment modalities of Class II correction are available as a part of comprehensive orthodontic treatment. Therefore, not all Class II patients who meet the criteria will be using the CMA or in-office appliance for Class II correction as a part of their comprehensive orthodontic treatment.

8.0 Inclusion and Exclusion Criteria*

*8.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Males and Females

Presenting for comprehensive orthodontic treatment at the Postgraduate orthodontic clinic at the UBSDM

Unilateral or bilateral ½-cusp to full-cusp Class II molar and canine relationship

Growing Patients (~12-17y 11m)

Subjects who do not require extractions as part of treatment mechanics

Mild to moderate crowding

*8.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Patients in mixed dentition

Any missing teeth up to and including permanent first molars

Bilateral molar relationship of less than ½ cusp Class II prior to appliance cementation

8.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response:

☐ Adults unable to consent

☒ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

8.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may ***not*** *be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response: We will include non-English speaking individuals in our study

9.0 Vulnerable Populations*

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

*9.1 For research that involves **pregnant women,** safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

☒ **N/A**: This research does not involve pregnant women.

*9.2 For research that involves **neonates of uncertain viability or non-viable neonates,** safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*9.3 For research that involves **prisoners**, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

*9.4 For research that involves **persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")**, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☐ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*9.5 For research that involves **cognitively impaired adults**, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

Adequate provisions will be made for soliciting the permission of parents or guardians.

Adequate provisions will be made for soliciting the assent of the children.

No greater than minimal risk to children will be present.

The research presents the prospect of direct benefit to the individual subject.

Permission is to be obtained from one parent or guardian

☒ **N/A:** This research does not involve cognitively impaired adults.

9.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. ***Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response: We are not specifically targeting a vulnerable group.

10.0 Eligibility Screening*

10.1 Describe ***screening procedures*** *for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).

Response:

Patients will be screened by their assigned residents according to the protocols set up in the UB Orthodontic Clinic. Each new patient is screened using a specific form supplied by the UB Orthodontic clinic regardless of whether they participate in research or not (I have included a copy of this form with my submission). One research examiner (AN) will review all patient screening forms to determine if the patient meets all necessary inclusion criteria. Once orthodontic records have been taken on the patient by the treating resident, the examiner (AN) will review the records taken (photos, x-rays, digital casts) to confirm that the patient meets all the inclusion criteria in order to participate.

☐ **N/A:** There is no screening as part of this protocol.

11.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

11.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

Subject requirement for the study will be utilizing the current advertising methods in place at the University at Buffalo School of Dental Medicine's Orthodontic Clinic. Nothing new will be mentioned regarding the study in the current advertising methods. New patient screenings will be utilized for study screening purposes and recruitment. If patients meet the necessary inclusion criteria, they

will be contacted by the research examiner and recruited for the study. All necessary information, consent forms and waivers will be provided to the subject and appropriate guardian.

11.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

Prospective subjects will be invited to participate in the current study in a separate room away from other patients/subjects. All subject records, which include health and personal information, will be kept strictly confidential abiding by privacy laws and our own clinic regulations. These records will be encrypted and kept on a password protected computer in the Orthodontic clinic at the University at Buffalo School of Dental Medicine. The subject will have full access to their records. There is restricted access to all patients/subjects utilizing the AXIUM patient management software in place in our clinics. Only treating residents are allowed to view patient records as well as faculty in the Orthodontics department at the University at Buffalo School of Dental Medicine. Subject records and data will not be shared or viewed by anyone other than the examiner and supervising faculty.

11.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

N/A

12.0 Procedures Involved*

*12.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

Subjects will be recruited patients from the Orthodontics Clinic at the University at Buffalo School of Dental medicine who are undergoing comprehensive orthodontic treatment. Patients a unilateral or bilateral ½ cusp to full-cusp Class II molar relationship with mild-moderate crowding will qualify for participation. At the orthodontic consult appointment, eligible patients will receive information on the study and will be asked to participate. A randomization protocol will be followed in order to assign subjects to 1 of 2 study groups for Class II correction (CMA v. In-office fabricated Class II correction appliance) once the subject and parents have agreed to participate in the study and have filled out consent forms. Initial records will be taken at T0 (intraoral photographs, 3D scan, radiographs) before starting orthodontic treatment.

Models of subjects assigned to the in the in-office fabricated appliance group will be 3D printed, and one operator (AN) will fabricate custom devices for each subject. The buccal surface of the maxillary first molar will be etched for 12s using 35% phosphoric acid, rinsed, dried, and Assure Plus bonding agent will then be applied to the buccal surface of the maxillary first molar, and light cured for 10 s using an LED curing light. A pre-pasted 0.022 Slot MBT second molar minitube that has been modified to have a 2 mm tube length will be placed in the center of the buccal surface of the maxillary first molar and light cured for 40 s. A 0.016x0.022 stainless-steel wire will be roughly sectioned to be longer than the distance from the maxillary first molar to the maxillary canine for ease of placement. Once the wire has been placed through the buccal tube of the molar bracket, it will be marked and a bayonet bend will be placed mesial to the molar tube. A slight curve will be bent into the wire to span the premolars, so that the wire is able to passively rest on the buccal surface of the maxillary canine. The wire will then be used to position the canine bracket, so that the wire rests passively in both the canine and molar brackets. The maxillary canine will be prepared using phosphoric acid etch and assure plus in the same fashion as the molar bracket. A 0.018 MBT maxillary canine bracket will be placed and cured using the stainless-steel wire as a template to ensure passive placement. Once both brackets are placed, the wire will be cut so that a small section of wire remains mesial to the maxillary canine and distal to the maxillary first molar. The wire will then be cinched mesial to the maxillary canine tie-wing. The wire will also be cinched distal to the maxillary first molar, with 2-3 mm of excess wire distal to the maxillary first molar to ensure that the molar can rotate during treatment, if needed. The distance from the mesial opening in the buccal tube of the maxillary first molar to the most distal portion of the canine bracket will be measured, and an closed-coil stainless-steel spring will be sectioned to measure the span from the distal tie-wing of the maxillary canine to the mesial portion of the maxillary molar tube. The wire will be placed into the brackets with the closed-coil spring spanning the molar and canine, and a stainless-steel tie will be used to secure the wire into the canine bracket. The fabricated device will then be removed from the model and the excess cement on the molar and canine pad will be carefully removed prior to cementation in the patient's mouth.

For the CMA group Orthocad software will be used by one operator (AN) in order to measure the distance from the center of the buccal surface of the first molar to

the center of the facial surface of the canine (in mm). This measurement will be used to determine the proper size CMA device needed for the study.

Prior to the bonding appointment, digital cases of the mandibular arches of all subjects will be 3D printed, and essix retainers with 2 mm thickness will be fabricated to include an opening on the buccal surfaces of the mandibular first molars for placement of a button to anchor the Class II elastics during treatment.

At the bonding appointment, for both study groups, proper isolation methods will be placed according to the treating resident's preference. Maxillary first molars and canines will be etched using 35% phosphoric acid for 12 s, rinsed, and air thinned using an air water syringe. Assure plus bonding agent will be placed on the molar and canine buccal surfaces, air thinned, and light cured for 10 s. Packable composite will be placed on the molar and canine pads (CMA group) or the maxillary first molar tube and canine bracket (in-office appliance group). The molar pad (for the CMA group) and the first molar bracket (for in-office appliance group) will be positioned onto the center of the buccal surface of the maxillary first molar, and once it has been properly positioned, the canine pad (CMA group) or canine bracket (in-office appliance group) will be placed passively. Excess cement will be removed, and each pad/tube/bracket will be light cured using an LED curing light for 40 s. The mandibular essix retainer will then be placed and adjusted according to patient comfort level. Once the patient is comfortable with the essix retainer, it will be used as a template to mark the buccal surfaces of the mandibular first molars for placement of the buttons. The mandibular first molars will be etched using 35% phosphoric acid for 12 s, rinsed, and air thinned using an air water syringe. Assure plus bonding agent will be placed on the molar and canine buccal surfaces, air thinned and light cured for 10 s. Packable composite will be placed on the pad of the orthodontic buttons, and the buttons will be placed and excess cement will be removed. The buttons will be light cured for 20 s each.

Isolation will then be removed and the patient will be instructed to wear the essix retainer 24 hours a day and to only take it out to eat and when completing hygiene methods. The patient will be given Force 1 Class II elastics (1/4, 6 oz) and will be instructed on how to place them from either the hook on the canine pad (CMA group) or the hook on the canine bracket (in-office appliance group) to the button on the mandibular first molars. The patient will be instructed to wear the elastics 24 hours a day and to only remove them when eating and completing hygiene methods, and to change elastics daily.

The patient will be seen 1 month later and will be given Force 2 Class II elastics (3/16, 8 oz) and will be instructed to wear them using the same protocol for the remainder of their class II correction. The patient will be evaluated each month until a Class I molar and canine relationship has been obtained.

Once a Class I molar and canine relationship has been obtained, The CMA or in office appliance will be removed, and an intraoral scan and lateral cephalometric radiograph will be taken immediately after removal of the appliance(s) (T1). The

total duration (in months) of Class II correction, starting at the bonding appointment and ending at the T1 appointment will be recorded for each subject.

Superimposition & Data Analysis

Once T0 and T1 records are obtained, lateral cephalometric tracing and measurements will be completed and recorded by one operator (AN). Superimpositions will be constructed using T0 and T1 lateral cephalometric tracings. Initial cephalometric measurement (T0) will be subtracted from final cephalometric measurements (T1) for each value (Please see table in section 12.2 for a complete list of lateral cephalometric measurements and their descriptions).

Intraoral scan data will be collected with an iTero Element 3D Scanner. Digital models will be superimposed using the Best fit method described in a study conducted by Grünheid and Larson.[20] Maxillary model superimpositions will be used to address the difference in maxillary first molar and canine rotational positions before versus after Class II correction (˚). Mean values for all measurements (lateral cephalometric and digital model superimposition) will be calculated for each treatment group and statistical analyses will be ran using he Statistical Package for the Social Sciences (SPSS) to compare means.

Intra-examiner reliability will be addressed by randomly selecting 5 lateral cephalograms 2 weeks after initial measurements were performed and having the same operator (AN) repeat the landmarking, superimpositions and measurements. The same operator will also repeat measurements on 5 casts 2 weeks after measurements are conducted for the maxillary first molar and canine rotational measurements. Intra-class correlation coefficients will be calculated in order to determine intra-examiner reliability based on the first and second measurements ($P < 0.05$).

12.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

Patient Age

Total treatment time (in months) starting from the initial bonding appointment to T1 appointment

3D position of the maxillary molar and maxillary canine (using digital models) at T0 and T1

Lateral cephalometric values (listed below) at T0 and T1

Cephalometric Dentoalveolar Measurements

X-Axis	SN minus 7 degrees
Y-Axis	Perpendicular line to the X-axis drawn through the S point
U6-Y (mm)	Linear distance of the maxillary first molar to the Y plane
L6-Y (mm)	Linear distance of the mandibular first molar to the Y plane
IMPA (˚)	Incisor mandibular plane angle
L1-Y (mm)	Linear distance of the mandibular central incisor to the Y plane
L1-NB (mm)	Linear distance of the mandibular incisor to a vertical line drawn through Nasion and Point B
L1-NB (˚)	Angle between the mandibular incisor and a vertical line drawn through Nasion and Point B
L1-APo (mm)	Linear distance of the mandibular incisor to a vertical line drawn through Point A and Pogonion
U6-PP (˚)	Inclination of maxillary first molar
L1–MP (˚)	Angle of mandibular incisor relative to mandibular plane
Molar Relationship (mm)	Distal of U6 and L6 in relation to occlusal plane
Overjet (mm)	Anteroposterior distance from U1 tip to L1 tip
Overbite (mm)	Vertical distance from U1 tip to L1 tip

Cephalometric Maxillary Sagittal Skeletal Measurements

SNA Angle (˚)	Sella-Nasion to A point
Point A to nasion perp (mm)	A point in relation to Nasion perpendicular
Co-A (mm)	Maxillary length, Condylion to A point

Cephalometric Mandibular Sagittal Skeletal Measurements

SNB Angle (˚)	Sella-Nasion to B point
Pg to nasion perp, mm	Pogonion in relation to Nasion perpendicular
Co-Gn, mm	Mandibular length, Condylion to Gonion

Cephalometric Maxillomandibular Measurements

ANB (˚)	Skeletal relationship, Angle from A point to Nasion to B point
Wits, mm	Jaw disharmony using A point and B point relative to occlusal plane
Max-Mand differential (mm)	Difference between Co–Gn and Co–A

Cephalometric Vertical Skeletal Measurements

ANS-Me (mm)	Lower facial height, Anterior nasal spine to Menton
FH to mand plane (°)	Mandibular plane angle in relation to Frankfort horizontal
FH to occlusal plane (°)	Occlusal plane in relation to Frankfort horizontal
FH to mand plane (°)	Mandibular plane angle in relation to Sella-Nasion
SN to occlusal plane (°)	Occlusal plane in relation to Sella-Nasion
Ar-Go-Me (°)	Gonial angle

12.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response:

All de-identified measurements will be placed in a microsoft excel document (a sample of this document will be submitted with this form).

12.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Axium medical records will be accessed in order to obtain patient age to determine if he or she is eligible for our study and to calculate total treatment duration (in months). Imaging records (Radiographs, Intraoral and Extraoral Photographs, 3D Intraoral Scans) and Clinical evaluation will be used to collect data.

*12.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

If there are any findings relating to the subject's dental health will be shared with the subject and guardian and will also be notified to their primary care provider when necessary. If any anecdotal findings arise, they will be mentioned to the subject and guardians as well.

*12.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

If the subjects wish to know the results of the study, they will be notified in person once all data results have been calculated and analyzed.

13.0 Study Timelines*

13.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

6 months (from screening to recruitment into the study)

13.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

The study will last during a specific portion of the patient's treatment; it will finish before the patient's treatment has been completed. They will have followed up visits to finish their orthodontic treatment. The full duration of the study is expected to be 5 months +/- 1 month depending on patient compliance. Initial records will be collected at T0. Upon removal of the device, T1 will records will be taken (lateral cephalometric radiograph and digital scan; final records for this study).

13.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response:

18 months

14.0 Setting

14.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

The study will be conducted in the Orthodontic Clinic at the University at Buffalo School of Dental Medicine. The facility has 20 individual operatories for orthodontic residents to administer treatment. Each operatory is equipped with all standard of care equipment and necessary instruments to treat patients in full orthodontic capacity. The entire facility and all of the computer systems are equipped with encrypted login devices connected to each operatory computer. Each computer can be accessed by university issued identification badges, once activated each individual is instructed to input their credentials in order to access

the university's patient management software, AXIUM. University at Buffalo School of Dental Medicine Orthodontic clinic patients can only be viewed by SDM faculty, staff and residents/SDM students, all others are restricted from accessing. Patient electronic health records along with schedules are not left open while treating patients to avoid any neighboring patients view of other's personal information. The computers will automatically log out of the individual's username after thirty minutes of idle time. Any input to the patient's electronic health record, notes, diagnostic codes, treatment plans, etc., are required to be reviewed by the supervising faculty for completeness and approved through the faculty's identification card swipe prior to dismissal of the patient. The facility is restricted to faculty, staff and residents of the University at Buffalo School of Dental Medicine's Orthodontic Clinic. No other individuals have access to the facility, and patients are only allowed to enter accompanied by resident or faculty during appropriate clinic operating hours and supervision. The facility is otherwise locked outside of clinic hours and restricted only to the custodian staff overnight and on the weekends. The intraoral 3D scanner located in the university's Orthodontics clinic has its own operatory in a designated corner of the facility, with appropriate barriers and positioning of the iTero scanner to prevent disclosure of private sensitive information to those around. There is a designated computer laboratory for residents and faculty to work on research projects, data analysis, treatment planning, and for educational purposes. There is a limit to the number of occupants in the computer room at any given time, and there is adequate spacing between individual computers to ensure individual privacy. The same security measures are present for the computers in the laboratory as in the operatories.

14.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

15.0 Community-Based Participatory Research

15.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining

knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

15.2 Describe the composition and involvement of a community advisory board.

Response:

☒ **N/A:** This study does not have a community advisory board.

16.0 Resources and Qualifications

*16.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

Principle Investigator: *Alexandria Newton, DMD, MA.* PGY2 Orthodontic Resident at University at Buffalo School of Dental Medicine. She completed her DMD training at Midwestern University College of Dental Medicine-IL in 2020. She obtained her Master of Arts degree in Biomedical Sciences at Midwestern University College of Health Sciences-IL in 2015. She completed her Bachelor's in Science at Utica College in 2014. While at Midwestern University, she worked on a research projects involving landmarking facial scans of subjects to investigate whether there are differences in facial characteristics between individuals related to individuals with cleft palate in comparison to individuals who are not related to individuals with cleft palate. Her previous research experience will be advantageous to this current study along with her dental knowledge and continuing orthodontic training / experience. She has been a resident of the Buffalo area for one year, and she has lived in New York state for most of her life.

Supervising the Investigator: *David A. Covell, Jr., DDS, PhD*. Dr. Covell is Professor and Chair, Department of Orthodontics, University at Buffalo School of Dental Medicine. Over the past three decades he has engaged in collaborative research projects related to the field of orthodontics, aimed at discovering the boundaries of new technologies, investigating the properties and relative

effectiveness of biomaterials, and evaluating the efficacy of a variety of treatment approaches. He has mentored graduate students in over 20 clinically-related research projects, the results of which have been published in a number of highly regarded journals in the field of dentistry.

Describe other resources available to conduct the research.

16.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

The time that will be allotted to research will be equivalent to 8 FTE hours per week. This time will be utilized to:

- Fabricate each in-office appliance and mandibular essix retainer for the subjects included in the study
- Collect, store, and organize all records and data for each subject
- Perform necessary orthodontic adjustments for each patient
- Analyze data collected and work on the statistical analysis

16.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

The design of the study maintains minimal risk given that the orthodontic treatment is routine. The additional radiation received by patients when taking the additional lateral cephalogram for T1 measurements is minimal. In the United States, annual natural background radiation exposure, which does not include medical exposure or exposure through consumer products, is around 3.1 mSv. Average annual medical radiation exposure is around 3.0 mSv, and average total annual exposure including background, medical, and consumer exposure is around 6.1 mSv.[21] A standard lateral cephalogram taken at the University at Buffalo School of Dental Medicine's Orthodontic clinic is around 0.6577 mSv, and therefore the exposure would be minimal in comparison.

All subjects will have access to all orthodontic resources they might need. If questions or concerns arise throughout treatment, all subjects will have access to the University at Buffalo School of Dental Medicine's

Orthodontic Clinic emergency hotline, which will be able to route them to an on-call orthodontics resident, who can contact the PI. There are emergency procedures in place as well which they can access if necessary, during any time in the treatment. If the patient experiences any psychological distress throughout the study, there are resources available which can easily be accessed.

16.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

The research protocol will be available in both hard copy and electronic copy for all who are involved in the study. A streamlined version of the protocol will also be available for those involved. There will be a presentation for orthodontic residents, faculty and staff before patient recruitment commences in order to ensure that everyone who is involved can ask any questions and understands the workflow of the protocol. During this presentation, the duties and responsibilities of those who are involved will be explained and addressed.

17.0 Other Approvals

1.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

☒ **N/A:** This study does not require any other approvals.

18.0 Provisions to Protect the Privacy Interests of Subjects

18.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

During the recruitment phase, the purpose and protocol of the study will be explained to patients in an enclosed, private setting containing the primary investigator, treating resident, subject, and subject guardian only. The participants

at any point are free to refuse treatment and anything during treatment that they do not feel comfortable with. The patients have the authority to leave the study any time throughout the study.

18.2 Indicate how the research team is permitted to access any sources of information about the subjects.

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

Consent forms are provided to all orthodontics patients for completion prior to the initial bonding appointment once they are accepted as patients in our orthodontic clinic. These consent forms include privacy consents and HIPAA waivers. The patients will be informed that their private information will be used only for educational and research purposes within the University at Buffalo School of Dental Medicine's Orthodontic Clinic.

19.0 Data Management and Analysis*

19.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

Intra-examiner reliability will be addressed by randomly selecting 5 lateral cephalograms 2 weeks after initial measurements were performed and having the same operator (AN) repeat the landmarking, superimpositions and measurements. The same operator will also repeat measurements on 5 casts 2 weeks after measurements are conducted for the maxillary first molar and canine rotational measurements. Intra-class correlation coefficients will be calculated in order to determine intra-examiner reliability based on the first and second measurements ($P < 0.05$).

Statistical analysis will be performed using SPSS. A Shapiro-Wilk test will be run to assess for normality. If the data are normally distributed, independent t-tests will be ran to compare means between the two treatment groups. If normality assumptions are not met, a Wilcoxon Rank-Sum test will be used to compare means between the two treatment groups for all measurements.

19.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

Sample size estimation: Based on a power of 80% and a significance level of 0.05, it was determined that a sample of size of 16 per treatment group, or a total of 32 participants, would be sufficient in order to have a standardized effect size of 1.02366. These calculations were made based on mean values reported for total treatment time (in months) to achieve Class II correction using a CMA in previous studies. [12,14,15,16]

19.3 Describe any procedures that will be used for quality control of collected data.

Response:

One investigator (AN) will be mapping lateral cephalometric radiographs and performing all measurements on patient records, as well as fabricating all in-office appliances and mandibular essix retainers to reduce heterogeneity. The research examiner and supervisors will be ensuring that the data is good quality and is adequate for analysis. All patient records and data will be encrypted, deidentified and properly stored and secured on our computer network. A Code Key file will be stored in a separate protected drive.

20.0 Confidentiality*

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*1.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

The data will be stored within the encrypted and protected network and on the research examiner's University at Buffalo School of Dental Medicine Orthodontic Clinic hard drive. This specific network drive is only accessible by the research examiner using her specific credentials to access the information. The computers which will allow this access will be present in the orthodontic facility where the research will be conducted. There will be password protection to access the computers, as well as physical limitations that are in place to limit access to the facility. In order to access these computers, individuals need physical keys as well as swipe privileges of their ID badges. Subject data will be stored in multiple folders which will also have encryption built in with specific password protection to the data that only the examiner and supervising research faculty will have access to.

1.2 A. How long will the data be stored?

Response: 3 years post-study

20.1 A. Who will have access to the data?

Response: Research Examiner and Supervising Research Faculty

20.2 A. Who is responsible for receipt or transmission of the data?

Response: Research Examiner

20.3 A. How will the data be transported?

Response: Digitally via the encrypted network described above

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☒ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 21.0)*

1.3 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

N/A

1.4 B. How long will the specimens be stored?

Response:

N/A

20.4 B. Who will have access to the specimens?

Response:

N/A

20.5 B. Who is responsible for receipt or transmission of the specimens?

Response:

N/A

20.6 B. How will the specimens be transported?

Response:

N/A

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

21.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response: This study is of minimal risk. Patients' treatment notes will be reviewed after each visit to ensure safety.

21.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Efficacy data:

Duration of treatment required to obtain a Class I molar and canine relationship (months)

Changes in skeletal and tooth position (mm, °) before versus after Class II correction (Lateral Cephalometric radiographs taken at T0, T1, digital models taken at T0 and T1).

Patient age at T0.

21.3 Describe any safety endpoints.

Response: N/A

21.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response: N/A

21.5 Describe the frequency of safety data collection.

Response: N/A

21.6 Describe who will review the safety data.

Response: N/A

21.7 Describe the frequency or periodicity of review of cumulative safety data.

Response: N/A

21.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response: N/A

21.9 Describe any conditions that trigger an immediate suspension of the research.

Response: N/A

22.0 Withdrawal of Subjects*

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*22.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Subjects may be withdrawn from the study without their consent if the following occur:

- Develop any indication of root resorption
- Develop any periodontal issues during the study
- Develop any health-related issues during the study
- Voluntarily want to leave the study or cease treatment
- Do not come regularly as needed for the study
- Patient becomes pregnant

22.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

The subjects may withdraw their consent and discontinue at any time throughout the study. If a patient decides to withdraw from the study, any collected data of the subject will be destroyed and discarded accordingly.

22.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

If subjects withdraw from the research, their data will be kept confidential and abide by all privacy regulations. It will not be used in the research study however as the data will not be complete. It will be maintained for approximately 3 years.

23.0 Risks to Subjects*

23.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

Since our subjects will be receiving orthodontic treatment by orthodontic residents under the supervision of faculty members who are adequately trained orthodontists, we will have inherent minimal risks which are routine in orthodontic treatment. These risks include:

- Tooth discomfort
- Tissue abrasion from the appliances
- White spot lesions on enamel structure of teeth (due to plaque build up and lack of hygiene)
- Root resorption
- Periodontal issues (gingivitis, inflammation, periodontitis, can develop due to plaque and lack of hygiene)
- Discomfort (due to tooth movement and biomechanical forces)
- Halitosis (due to plaque retention and lack of hygiene)
- Reduced esthetics (Orthodontic appliances are bonded to the labial tooth surfaces which can be un-esthetic to patients, development of spacing mesial to the appliances as distalization of the buccal segments occurs)

- TMJ issues
- Broken appliances (bracket, wires, springs)
- Infection (lack of oral hygiene)
- Allergies to the materials used for treatment (Including common allergies to nickel and latex)

23.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

- All biomechanical orthodontic forces will be standardized and delivered within standard of care parameters, keeping forces continuous but light to reduce any potential risk of pain, discomfort, and root resorption.
- Subjects will be given appropriate oral hygiene tools (floss threaders, proxy brushes, toothbrushes, plaque disclosing tablets) and instruction on how to maintain oral health prior to starting orthodontic treatment. This will ensure that each subject is aware of the hygiene required during treatment, which will reduce the risk of white spot lesions, periodontal issues, and halitosis. Reduced inflammation will also provide more comfort to the subject during treatment.
- To reduce risk of discomfort and abrasion, subjects will be given orthodontic wax to place on brackets or wires that give them any discomfort and will be instructed on how to use the wax. Wires and retainers will be trimmed accordingly, and the subject will be asked prior to leaving if there is anything bothering them to reduce discomfort.
- At each adjustment visit, subjects will be assessed clinically extra orally and intraorally to evaluate any changes and look for pathology, inflammation, abrasions, and any tooth damage (white spot lesions, fractures, caries). Tissues will be assessed for inflammation and erythema. Radiography will be taken to assess the root anatomy, alveolar bone level, TMJ anatomy and screen for any pathology)
- Subjects will be able to communicate with the research examiner if there are any issues between adjustment visits (discomfort, broken appliance, pain, difficulty chewing/eating, psychological issues). They will be either seen for an emergency visit to address the concern or guided via tele-dentistry communication to resolve the issue if possible.
- Subjects will have their medical and dental history updated at every visit (including their initial screening visit) to ensure that all appropriate changes in their health are on record. They will be asked about any concerns or issues they are having, which will be recorded and addressed accordingly.

- Regarding subjects who have or develop an allergic reaction to nickel or latex, there will be appropriate changes made to their treatment to prevent the allergy.

*23.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response:

This current study is minimal risk. The general risks are a broken appliance and the minimal risk of additional radiation exposure.

23.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response: If the patient becomes pregnant, their participation will be terminated due to the possible risk of radiographic exposure to the fetus.

23.5 If applicable, describe risks to others who are not subjects.

Response: N/A

24.0 Potential Benefits to Subjects*

24.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

Patients presenting for orthodontic treatment seek to improve their dentition in both function and esthetics. By participating in this study, they will be achieving their goals through the treatment mechanics that will be utilized. Spaces will be closed, appropriate Angle's classification will be achieved, appropriate overjet and overbite will be achieved, all the while maintaining teeth in the healthy boundaries of the alveolar bone.

25.0 Compensation for Research-Related Injury

☐ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

*25.1 **If the research procedures carry a risk of research related injury,** describe the available compensation to subjects in the event that such injury should occur.*

Response:

Research related injury will be compensated appropriately per University at School of Dental Medicine policies.

25.2 Provide a copy of contract language, if any, relevant to compensation for research related injury.

*NOTE: If the contract is not yet approved at the time of this submission, submit the current version here. If the contract is later approved with **different language regarding research related injury**, you must modify your response here and submit an amendment to the IRB for review and approval.*

Response: N/A

26.0 Economic Burden to Subjects

26.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

Patients will be required to cover the following costs by participating:

- Fees associated with comprehensive orthodontic treatment
- No additional costs will be required in order to participate in the study

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

27.0 Compensation for Participation

27.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

☒ **N/A:** There is no compensation for participation. This section does not apply.

28.0 Consent Process

28.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 29.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 29.0)*

28.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

Consent will take place at the University at Buffalo School of Dental Medicine in the Orthodontic Clinic, in the privacy of a closed-in room outside of the orthodontic clinic. Prospective subjects will be able to voice any questions or concerns with absolute privacy, prior to providing their consent to participate in the study.

28.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

Prospective subjects will be allotted appropriate time to discuss amongst themselves and appropriate parent / guardians with or without the research examiner present, if needed. Prospective subjects will have permission to come back later to inform the research examiner of their decision if they need additional time to think and discuss outside of the clinic prior to committing. Prospective subjects can take as long as needed to make their decision and voice their concerns, there will be no time restriction or pressure from the research team.

28.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

Subjects will be asked at every visit if they wish to continue in their current research study. The subject will have full autonomy to withdraw or continue. There will be appropriate documentation that will be signed by the subject to ensure consent was given.

28.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*
- *Steps that will be taken to minimize the possibility of coercion or undue influence*

- *Steps that will be taken to ensure the subjects' understanding*

Response:

☐ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☐ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 28.8)*

28.6 Indicate which language(s) other than English are likely to be spoken/understood by your prospective study population or their legally authorized representatives.

NOTE: The response to this Section should correspond with your response to Section 8.4 of this protocol.

Response: Spanish, Arabic, French, Haitian

28.7 If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language, how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study, and any process to ensure ongoing consent. Indicate the language that will be used by those obtaining consent.

NOTE: Guidance is provided on "SOP: Informed Consent Process for Research (HRP-090)."

Response:

During the orthodontic screening appointment, prospective subjects will be assessed on their proficiency in English. If they find difficulty understanding (reading, writing, and speaking) English, their preferred language of communication will be noted. Appropriate language translators will be made available to subjects that are not English speaking. All documentation will be translated accordingly so that the patient has full comprehension of the documents and consents they are to sign.

During the recruitment phase of the study, the language translator will be present during each of the discussions with the research subjects. Appropriate extra time will be allotted for translation communication between the research examiner and subjects, to ensure that the subjects have adequate time to understand the information. English langue will be used to obtain consent.

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults.
(Skip to Section 28.9)

28.8 Describe the process to determine whether an individual is capable of consent.

Response:

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent.
(*Skip to Section 28.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 28.9 and 28.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 28.11 and 28.12).*

28.9 Describe how you will identify a Legally Authorized Representative (LAR). Indicate that you have reviewed the "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" for research in New York State.

NOTE: Examples of acceptable response includes: verifying the electronic medical record to determine if an LAR is recorded.

Response:

☒ We have reviewed and will be following "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."

28.10 ***For research conducted outside of New York State****, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response: N/A

28.11 Describe the process for ***assent of the adults****:*

- *Indicate whether assent will be obtained from all, some, or none of the subjects.* ***If some, indicate which adults will be required to assent and which will not.***

Response: N/A

- ***If assent will not be obtained from some or all subjects, provide an explanation of why not.***

Response: N/A

*28.12 Describe whether **assent of the adult** subjects will be documented and the process to document assent.*

NOTE: The IRB allows the person obtaining assent to document assent on the consent document using the "Template Consent Document (HRP-502)" Signature Block for Assent of Adults who are Legally Unable to Consent.

Response: N/A

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☐ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 29.0)*

*28.13 Describe the criteria that will be used to determine **whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research** under the applicable law of the jurisdiction in which the research will be conducted **(e.g., individuals under the age of 18 years)**. For research conducted in NYS, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children."*

NOTE: Examples of acceptable responses include: verification via electronic medical record, driver's license or state-issued ID, screening questionnaire.

Response:

Subject's medical record, screening forms and discussion with parent/guardian will be utilized to assess subject's legality to consent to treatment / procedures involved in research.

*28.14 **For research conducted outside of New York State**, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)."*

Response: N/A

28.15 Describe whether parental permission will be obtained from:

Response:

☒ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☐ Parent permission will not be obtained. A waiver of parent permission is being requested.

NOTE: The requirement for parent permission is a protocol-specific determination made by the IRB based on the risk level of the research. For guidance, review the "CHECKLIST: Children (HRP-416)."

*28.16 Describe whether permission will be obtained from individuals **other than parents**, and if so, who will be allowed to provide permission. Describe your procedure for determining an individual's authority to consent to the child's general medical care.*

Response:

If there is no known living parent, then the next individual to give permission / consent for the subject to participate in research would have to be the legal guardian. To assess legitimacy of legal guardianship, appropriate documentation will need to be provided by said individual. Once documentation has been verified, authority to consent will be approved.

*28.17 Indicate whether assent will be obtained from all, some, or none of the **children**. If assent will be obtained from some children, indicate which children will be required to assent.*

Response:

Assent will be obtained from all adolescent subjects in the research study.

28.18 When assent of children is obtained, describe how it will be documented.

Response:

Assent will be document in the same manner as consent from the legal guardian / parent. Appropriate documentation will provide all information for the subject, all questions will be answered, and patient will have freedom to speak for themselves on their participation. Signature will be gathered from the child / adolescent, and paperwork will be scanned into the patient's electronic health record for safe keeping.

29.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

29.1 If the research involves a waiver or alteration of the consent process, please review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure that you have provided sufficient information for the IRB to make the determination that a waiver or alteration can be granted.

NOTE: For records review studies, the first set of criteria on the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" applies.

Response: N/A

29.2 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response: N/A

30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 31.0)

30.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

31.0 Multi-Site Research (Multisite/Multicenter Only)*

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

31.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed across all sites.

Response: N/A

*31.2 If this is a multi-site study **where you are the lead investigator**, describe the processes to ensure communication among sites, such as the following.*

- *All sites have the most current version of the IRB documents, including the protocol, consent document, and HIPAA authorization.*
- *All required approvals have been obtained at each site (including approval by the site's IRB of record).*
- *All modifications have been communicated to sites, and approved (including approval by the site's IRB of record) before the modification is implemented.*
- *All engaged participating sites will safeguard data as required by local information security policies.*
- *All local site investigators conduct the study appropriately in accordance with applicable federal regulations and local laws.*
- *All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.*

Response: N/A

31.3 Describe the method for communicating to engaged participating sites.

- *Problems (inclusive of reportable events)*
- *Interim results*
- *Study closure*

Response: N/A

*31.4 If this is a multicenter study **where you are a participating site/investigator**, describe the local procedures for maintenance of confidentiality.*

- *Where and how data or specimens will be stored locally?*
- *How long the data or specimens will be stored locally?*

- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

Response: N/A

31.5 If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Local recruitment methods are described elsewhere in the protocol.

- *Describe when, where, and how potential subjects will be recruited.*
- *Describe the methods that will be used to identify potential subjects.*
- *Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)*

Response: N/A

32.0 Banking Data or Specimens for Future Use*

☒ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*32.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response: N/A

32.2 List the data to be stored or associated with each specimen.

Response: N/A

32.3 Describe the procedures to release banked data or specimens for future uses, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Response: N/A