1.0 Complete Research Protocol (HRP-503)

PROTOCOL TITLE:

Include the full protocol title.

Response: A comparison between TiNbTaZr (GUMMETAL) and stainless-steel alloy for space closure with sliding mechanics A pilot randomized clinical trial

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response:

Lubomyr Ravlyk

Orthodontic Department at University at Buffalo School of Dental Medicine

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VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response: Version 1.5 Date: 09-25-2021

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
1	1.5	Change of 0.018” Prescription Bracket only used on the maxillary canines. The remaining dentition in the maxillary arch can have either 0.018” or 0.022” Prescription Brackets.	No changes in any of the consents

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*

2.0 Study Summary

Study Title	**A comparison between TiNbTaZr (GUMMETAL) and stainless-steel alloy for space closure with sliding mechanics *A pilot randomized clinical trial***
Study Design	Pilot randomized clinical trial
Primary Objective	1. Evaluate the total amount of canine retraction (mm) using GUMMETAL and Stainless-steel archwires 2. Evaluate the rate of canine retraction (mm/month) from T_0-T_4.
Secondary Objective(s)	3. Assess the 3-Dimensional control of canines during retraction from T_0-T_4.
Research Intervention(s)/ Investigational Agent(s)	Orthodontic archwires: GUMMETAL vs. Stainless-Steel
IND/IDE #	N/A
Study Population	12-17Y11M male and female patients
Sample Size	16
Study Duration for individual participants	4 months

Study Specific Abbreviations/ Definitions	TiNbTaZr = GUMMETAL SS = Stainless Steel NiTi = Nickel Titanium

3.0 Objectives*

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

Response: To investigate the maxillary canine retraction rate using GUMMETAL and Stainless steel archwires for sliding mechanics. Given GUMMETAL's relatively short presence in the orthodontic field with limited research on its various material properties and clinical applications, its potential in space closure by sliding mechanics warrants investigation.

3.2 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: We hypothesize that GUMMETAL total retraction distance and rate will be lower than the Stainless-steel group. We expect a significant difference between the groups regarding 3-Dimensional control during retraction.

4.0 Scientific Endpoints*

2.1 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: A decrease in the retraction rate (mm/month) / total retraction distance (mm) for the GUMMETAL group versus Stainless-steel group.

5.0 Background*

5.1 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>Space closure mechanics</u>

Space closure mechanics during the course of orthodontic treatment is necessary in cases with generalized spacing, congenitally missing teeth and when teeth are extracted. Space closure during treatment has shown a

correlation to longer treatment times.[1] Orthodontist and patients prefer the shortest duration of treatment possible and this often requires reliable space closure mechanics and minimizing anchorage loss. Lack of knowledge and experience in appropriate space closure mechanics can compromise the patient's occlusion. Thus clinician should understand that space closure is determined by a combination of factors including the biomechanical forces applied, force variation, moment-magnitude, moment-force ratio, force-deflection rate and anchorage unit.[2] Orthodontic armamentarium is vast with mechanical options to achieve adequate space closure; thus, it is important that biomechanical selection be made on an individual basis. Ribeiro et al. identify six key goals which need to be considered for space closure: 1) differential space closure-anchorage control; 2) minimum patient cooperation; 3) axial inclination control; 4) control of rotations and arch width; 5) optimum biological response; and 6) operator convenience.[2]

Biomechanical systems traditionally used to close spaces have been friction (sliding mechanics) and frictionless (closing loop mechanics). Each method presents with its own advantages and disadvantages when it comes to space closure.

Orthodontic Arch wires

Stainless Steel and Cobalt Chromium wires

The ability to move teeth orthodontically via conventional fixed appliances is possible due to the orthodontic archwires. In the earliest parts of the 20th century during Edward Angle's time, gold-alloy use was ubiquitous, because gold itself was too soft for most dental applications. With the introduction of stainless-steel wires, gold-alloys became obsolete due to their prohibitive expense and inferior material qualities.[18] Stainless steel wires were superior in their higher resistance to corrosion, excellent work-hardening properties and low coefficient of friction, making them the orthodontic standard for decades. The most commonly used type is the austenitic 18-8 stainless steel, with chromium and nickel content of 18% and 8%, respectively.[19] Their bracket-wire frictional properties are relatively low making them a gold standard wire for sliding mechanics. The coefficient of friction can be further reduced by application of nanotechnology, such as coating the wire with nickel-phosphorus electroless film impregnated with organic fullerene-like nanoparticles of tungsten disulfide.[20] Stainless steel's high resistance to corrosion can be attributed to the formation of a passivating oxide layer that forms on its surface and blocks oxygen diffusion to the underlying material. Contemporary commercially available stainless steel wires come in wide variety of elastic and yield strength related properties dependent on the different parameters utilized during production, such as freezing and incandescence during cold working.[19] These wires are able to produce

higher forces during a shorter period of time due to their lesser spring back properties, thus storing less energy than nickel-titanium and beta-titanium wires.[19] Biomechanical attachments are able to be soldered using a fastening agent to stainless steel via LASER or tungsten inert gas welding techniques.[19]

Cobalt-chromium alloys were introduced in the 1960s originally for use as watch spring by ELGIU national company, but were quickly manufactured into orthodontic wires (Elgiloy) by the United States based company in Denver, CO; Rocky Mountain Co.[19, 21] These wires shared similar properties with stainless-steel in their high stiffness, however they had the advantage of being heat treatable and available in different tempers. These tempers came in four varieties (usually color-coded) depending on how much cold work had been done during manufacturing.[19] Yellow for the soft or ductile tempers, green for semi-spring temper and red for high spring tempers.[19] These tempers permitted high bendability which allowed for the introduction of various loops, V-bends and offsets in the archwire.[19, 21] Heat hardening at 482°C for seven minutes, allowed for increasing its hardness (strength) after its been shaped into the desired application.[19] Wires which are not heat treated have a smaller spring-back than stainless steel wires.[22] The popularity of these wires in clinical practice is due to their exceptional resistance to corrosion and tarnish, ability to be soldered/welded and inexpensive.[19]

Beta-Titanium wires

Further research and development with titanium alloys eventually yielded β-Titanium archwires with molybdenum. TMA (titanium-molybdenum alloy; Ormco CA, USA) was introduced in the 1980s for orthodontic purposes. Its material characteristics consist of high springiness, strength, good formability, welding capabilities, and ability to hold a bend, making them a brilliant choice for finishing archwires in later stages of edgewise orthodontic treatment.[19, 21, 23] Krishnan et al[28], investigated the welding joinability properties between stainless steel wires and beta-titanium wires, concluding that the latter had better joinability due to their higher resilience and surface / structural characteristics. Beta-titanium wires have corrosion resistance similar to cobalt-chromium and stainless steel wires, along with high biocompatibility due to lack of nickel.[19] This surface resistance can be attributed to the formation of surface passivating oxidation layer.[19] However, this wire also has limitations and is poorly suited for applications that require flexibility and high surface roughness produces excessive friction within the bracket contact hindering sliding mechanics.[21]

Titanium-niobium (TiNb) alloy came into the market with the designation of being a new “finishing wire” from Sybron Dental Specialties Inc., Orange, CA, USA.[29] This material is cryogenic in nature, with superconductivity properties that have been utilized in magnets and magnetic nuclear resonance imaging applications.[30] The alloy’s elemental

composition consists of two out of five (Ti, Nb, Ta, Zr, and Pt) non-hypersensitive elements Ti and Nb, yielding high biocompatibility. Furthermore, the material has excellent resistance to corrosion. Both of these qualities of corrosion resistance and biocompatibility attribute Ti-Nb's wide use in medicine, substituting as a reconstructive material in implant and orthopedic surgeries.[30] Additional, this material has a low modulus of elasticity, making it ideal for distributing stresses between implants and bones.[31] With the incorporation of niobium, the modulus of elasticity is further decreased and corrosion resistance is improved.[30] This corrosion resistance can be attributed to Nb_2O_5 lining the surface layer, inhibiting the fluoride ion action responsible for immediate corrosion in the oral environment.[30] Dalstra et al[29], investigated the load-deflection behavior of TiNb wires compared to stainless steel both in torsional and bending applications. Their results demonstrated that TiNb stiffness in bending is ½ of SS, and torsional properties are 1/3rd of SS. Such results indicate that TiNb could be used for creative bends without generating excessive force levels present in stainless steel wires.[29] Additionally, they showed that TiNb spring-back was 14% lower than that of SS, whereas in torsion it was the same if not higher in some situations. Furthermore, this wire is able to be welded, thus various wire dimensions can be joined together to produced different force systems.[29]

Introduction of GUMMETAL

In 2003 a new β-Titanium alloy was developed at the Metallurgy Research Section of Toyota Central R & D Labs., Inc., Japan, named GUMMETAL. Its composition consists of a body-centered cubic crystal structure with titanium (Ti), niobium (Nb), tantalum (Ta), and zirconium (Zr).[21] GUMMETAL's elemental composition (Ti-36%Nb-2Ta-3Zr+O) produces properties with extensive applications, especially in orthodontic therapy. These elements are contained within the IVa and Va groups on the periodic table of elements. "The remarkable characteristics of this material arise due to the juxtaposition of three electronic magic numbers: 1) a compositional average valance number of 4.24 valance electrons per atom, 2) a bond order (Bo value) of 2.87 based on the DV-x alpha cluster method, and 3) "d" electronic-orbital energy level (Md value) of 2.45 eV".[32]This alloy merges superelasticity with superplasticity at room temperature without work hardening side effects.[33] Additionally, its Young's modulus is extremely low (40 GPa), combined with exceptionally high tensile strength (1100 MPa) producing a material with characteristics previously thought impossible.[23, 34] In comparison, SS has a young modulus of 200 GPa, CoCr at 170 GPa, NiTi at 105 GPa, and Beta-Titanium alloys at 85 GPa.[23] When looking at tensile strength in MPa, stainless steel is at 860 MPa, CoCr at 1000 MPa, NiTi at 700 MPa and Beta-titanium alloy at 860 MPa.[23]

The main feature of this material is the ease to do plastic deformation without disrupting the crystalline structure along with lack of stress-

induced transformations such as NiTi alloys, meaning it possesses true elastic deformation without hysteresis. Such material characteristics result in a metal that does not follow Hooke's law, with behaviors curving to and from the yield point.[23] Unlike SS, Co-Cr, and NiTi which all possess either Chromium or Nickel and have been known to have biocompatibility and toxicity issues, GUMMETAL's elemental constituents are biocompatible.[23] The frictional properties between wire and bracket interface is approximately half that of other titanium wires with appropriate surface treatment according to Toyota R&D department and Takada et al.[32, 35]

Orthodontic archwire manufactured out of GUMMETAL appeared on the market in 2010 by Rocky Mountain Morita Corporation.[33] The manufacturing process avoids high temperatures and alternatively utilizes cold-working for diluting and wire-drawing, which produces a marble-like microstructure that allows the wire to be plastically deformed without dislocating the crystals.[21, 23] Orthodontic application for this new wire is appears promising when considering the properties of the inherent material and its possibilities in tooth movement. These wires are extremely flexible, and super-elastic, they are able to bend with ease and hold that bend, there is an equal loading and unloading force without hysteresis (allowing for controlled orthodontic force), not susceptible to work hardening (intraoral breakage is rare), free of any toxic elements (nickel and heavy metals), generates half the friction of other titanium alloys and possess exceptional tensile strength.[21] Until GUMMETAL, there was no ideal orthodontic wire with all of these characteristics, various wire sizes and types were used for different purposes during treatment (NiTi for leveling and aligning and SS/TMA for finishing and detailing).

Given the low Young's modulus, high deformation intraorally to a round or even a rectangular wire would produce a small force. Such small forces would be appropriate in early stages of treating crowded teeth. Shorter duration of treatment could be possible if rectangular GUMMETAL wires are able to be used earlier in treatment due to the high elasticity, since torque control could be initiated much earlier.[21] Thus, the ability to control teeth in 3-Dimensions is very possible with GUMMETAL, since it can be used in all stages of active treatment, reducing treatment duration and office visits.[21]

Current research has investigated GUMMETAL wires compared to NiTi wires in their effectiveness as an initial archwire in aligning teeth, concluding that GUMMETAL is an adequate alternative to NiTi for the initial orthodontic treatment.[27] No research studies have been published regarding space closure utilizing GUMMETAL for canine retraction. Likewise, there is no published studies on the use of preformed GUMMETAL loop archwires or sliding mechanics for space closure. When considering loop space closure mechanics, it is important that the

archwire have high tensile strength, be able to deflect and produce light continuous forces during the retraction phase of treatment. Given GUMMETAL's high tensile strength (1000-1100MPa), ease of formability and low load/deflection ratio, makes them an ideal candidate for complex loop configurations.[12]

Properties of GUMMETAL and statement of the problem

GUMMETAL's non-linear superelastic properties allow for equal loading and unloading force delivery without any energy loss. Its ductility is 10 times greater than conventional metals making it super-plastic and ideal for forming and bending. Additionally, it doesn't experience work hardening during processing making it strong and durable, with little risk of intraoral breakage.[21] Regarding friction based sliding mechanics, GUMMETAL's friction properties have only been scarcely investigated. Some researchers[21, 32] have claimed that its friction coefficient is low and it is therefore adequate for sliding mechanics. However, they compared GUMMETAL to other titanium wires, stating that the frictional coefficient is half for GUMMETAL depending on the surface treatment.[21, 32] The potential for this wire to become a transitional archwire for final leveling and aligning and then utilized for space closure is high. Thus, it could have benefit to clinicians in areas of cost effectiveness with reduced need for multiple types of wires and potentially efficiency of treatment. Both, In-vitro and clinical studies are needed to understand the effects of GUMMETAL wires for space closure using both friction sliding mechanics and frictionless closing loops mechanics.

2) PURPOSE OF THE RESEARCH

Orthodontic biomaterials are continuously going through research and development, in hopes of producing an archwire that marries the properties of NiTi and SS.

GUMMETAL's introduction to the orthodontic field is relatively short. Limited research has been published regarding this wire and its application. Literature has shown that it is comparable to NiTi in the initial early stages of leveling and aligning and relieving crowding, in addition to having advantages over NiTi with its formability and lack of immunogenicity.[27] No current publications have investigated the effects of GUMMETAL wires on maxillary canine retraction with sliding mechanics.

The purpose of this study is to investigate the effects of GUMMETAL wire on space closure using sliding mechanics. Furthermore, no studies have compared GUMMETAL sliding mechanics to that of Stainless Steel, which has remained a gold standard. Evaluation of 3D tooth control by GUMMETAL remains to be investigated.

5.2 Include complete citations or references.

Response:

1. Schneider PP, Kim KB, da Costa Monini A, Dos Santos-Pinto A, Gandini LGJ. Which one closes extraction spaces faster: en masse retraction or two-step retraction? A randomized prospective clinical trial. Angle Orthod 2019;89(6):855-61.

2. Ribeiro GL, Jacob HB. Understanding the basis of space closure in Orthodontics for a more efficient orthodontic treatment. Dental Press J Orthod 2016;21(2):115-25.

3. Redlich M, Mayer Y, Harari D, Lewinstein I. In vitro study of frictional forces during sliding mechanics of "reduced-friction" brackets. American Journal of Orthodontics and Dentofacial Orthopedics 2003;124(1):69-73.

4. Besançon RM, Willis J. Encyclopedia of Physics, 3rd Edition. The Physics Teacher 1985;23(6):386-86.

5. Sekhar JA. Tunable coefficient of friction with surface texturing in materials engineering and biological systems. Current Opinion in Chemical Engineering 2018;19:94-106.

6. Shames IH, Fung YC. Engineering Mechanics. Journal of Biomechanical Engineering 1981;103(1):58-58.

7. Kojima Y, Fukui H. Numeric simulations of en-masse space closure with sliding mechanics. Am J Orthod Dentofacial Orthop 2010;138(6):702 e1-6; discussion 02-4.

8. Southard TE, Marshall SD, Grosland NM. Friction does not increase anchorage loading. Am J Orthod Dentofacial Orthop 2007;131(3):412-4.

9. Kapila S, Angolkar PV, Duncanson MG, Nanda RS. Evaluation of friction between edgewise stainless steel brackets and orthodontic wires of four alloys. American Journal of Orthodontics and Dentofacial Orthopedics 1990;98(2):117-26.

10. Charles J. Burstone RJS. Mechanics of tooth movement. American Journal of Orthodontics 1984;85(4):294-307.

11. Kuhlberg AJ, Priebe DN. Space closure and anchorage control. Seminars in Orthodontics 2001;7(1):42-49.

12. Miceli Beck Guimaraes Blaya GHW, Magali Beck Guimaraes, Luciana Mayumi Hirakata. Evaluation of tensile strength of different configurations of orthodontic retraction loops for obtaining optimized forces. Stomatologija, Baltic Dental and Maxillofacial Journal 2009;11(2):66-69.

13. Techalertpaisarn P, Versluis A. How do mechanical responses at closing loop ends vary when loop position changes? A systematic analysis of vertical, T-, and L-loops. Oral Science International 2013;10(2):58-64.

14. Frederik A. Booth J. Optimum Forces with Orthodontic Loops [Houston, Texas: The University of Texas Dental Branch at Houson; 1971.

15. William R. Proffit HWF, JR., Brent E. Larson, David M. Sarver. Contemporary Orthodontics 6th ed. Philadelphia, PA: Elsevier 2019.

16. Saitowski RE. Continuous arch wire closing loop design, optimization, and verification. Part II. American Journal of Orthodontic and Dentofacial Orthopedics 1997;112(5):487-95.

17. Andrew J. Kuhlberg CJB. T-loop position and anchorage control. American Journal of Orthodontic and Dentofacial Orthopedics 1997;112(1):12-18.

18. Keng FY, Quick AN, Swain MV, Herbison P. A comparison of space closure rates between preactivated nickel-titanium and titanium-molybdenum alloy T-loops: a randomized controlled clinical trial. Eur J Orthod 2012;34(1):33-8.

19. Kotha RS, Alla RK, Shammas M, Ravi RK. An overview of orthodontic wires. Trends in Biomaterials and Artificial Organs 2014;28(1):32.

20. Redlich M, Katz A, Rapoport L, et al. Improved orthodontic stainless steel wires coated with inorganic fullerene-like nanoparticles of WS(2) impregnated in electroless nickel-phosphorous film. Dent Mater 2008;24(12):1640-6.

21. Chang HP, Tseng YC. A novel beta-titanium alloy orthodontic wire. Kaohsiung J Med Sci 2018;34(4):202-06.

22. Ingram SB, Jr., Gipe DP, Smith RJ. Comparative range of orthodontic wires. American Journal of Orthodontics and Dentofacial Orthopedics 1986;90(4):296-307.

23. Hasegawa S. A new super elasto-plastic Ti alloy GUMMETAL-simplyfing treatment procedure, Clinical use of GUMMETAL. Tokyo, Japan: Hannah Orthodontics p. 8.

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25. Meling TR, Odegaard J. The effect of short-term temperature changes on superelastic nickel-titanium archwires activated in orthodontic bending. Am J Orthod Dentofacial Orthop 2001;119(3):263-73.

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titanium-tantalum-zirconium archwires during initial orthodontic alignment in adolescents: A double-blind randomized clinical trial. Angle Orthod 2018;88(3):348-54.

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29. Dalstra M, Denes G, Melsen B. Titanium-niobium, a new finishing wire alloy. Clinical Orthodontics and Research 2000;3(1):6-14.

30. Ilievska I, Karashanova D, Petrunov V, et al. Characterization of titanium–niobium orthodontic archwires used in orthodontic treatment. Bulgarian Chemical Communications 2016;48:183-87.

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32. Hasegawa S. A Concept of En Bloc Movement of Teeth Using Gummetal Wire: Quintessence Publishing Company; 2014.

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34. Gordin DM, Ion R, Vasilescu C, et al. Potentiality of the "Gum Metal" titanium-based alloy for biomedical applications. Mater Sci Eng C Mater Biol Appl 2014;44:362-70.

35. Takada M, Nakajima A, Kuroda S, et al. In vitro evaluation of frictional force of a novel elastic bendable orthodontic wire. Angle Orthod 2018;88(5):602-10.

36. El-Timamy A, El Sharaby F, Eid F, et al. Effect of platelet-rich plasma on the rate of orthodontic tooth movement: A split-mouth randomized trial. Angle Orthod 2020.

6.0 Study Design*

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

Response: This will be a randomized pilot split-mouth clinical trial of patients with spaces ≥ 3mm distal to the maxillary canines in need of closure through sliding mechanics. The sample consists of adolescent patients regardless of Angle's molar malocclusion who are receiving comprehensive full fixed appliance orthodontic treatment. Preformed conjoint archwires half being GUMMETAL and the other half SS, will be utilized. Each patient will have one side of the maxilla randomly allocated into the SS or GUMMETAL treatment group. The study will follow a split-mouth design to reduce the confounding variables from patient to patient on space closure mechanics. The maxillary arch in each subject will be randomized into a SS side or GM side using a random number

generator. Spaces will be measured at; T0 is initial records, T1 is initiation of space closure, T2 will be 4 weeks after the initiation of space closure, T3 is another 4 weeks of space closure evaluation and T4 will be the final evaluation of space closure after 4 weeks from T3, via 3D intraoral scans of maxillary arches. Space measurement and calculations will utilize 3Shape software to measure the distance of canine movement based off the distal surface. Sliding mechanics will be activated through NiTi coil springs from the maxillary canines to the maxillary molars. The force will be standardized to 150 gms and will be measured each visit. The same provider will activate the NiTi coil spring for retraction, along with data collection. Superimposition of scans will be utilized to assess outcome measures.

7.0 Study Intervention/Investigational Agent

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

Response: Orthodontic archwire of rectangular shape with dimensions of 0.016 x 0.022" and the following composition TiNbTaZr (GUMMETAL). Its reported properties include: non-linear superelasticity, ductility of 10x that of conventional metals, lack of work-hardening, extremely low modulus of elasticity (40 GPa), high tensile strength (1100 MPa), low friction, high springback without hysteresis and biocompatibility.

7.1 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

8.0 Local Number of Subjects

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

Response: 16 patients

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

Response: 60-70 patients

8.3 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: We will be collaborating with the entire patient pool in our orthodontic residency clinic for the first- and second-year residents. Research examiner will instruct residents doing patient screenings and acceptance of patients on criteria necessary to become a subject in the current study. Research examiner will then 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 20-30 patients in the course of 2-3 months. If we utilize the patient pools of twelve residents, we can approximate 240 patients total of which the study needs only 6.67% of to get 16 subjects.

9.0 Inclusion and Exclusion Criteria*

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

NOTE: This may be done in bullet point fashion.

Response:

- Adolescents of both gender (12-17Y11M),
- undergoing orthodontics treatment with full fixed appliances,
- good oral hygiene / health,
- with bilateral spaces 3 ≥ mm distal to the maxillary permanent canines,
- normal and hypodivergent growth patterns.

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

NOTE: This may be done in bullet point fashion.

Response:

- Systemic diseases or syndromes,
- abnormalities in tooth shape and/or size,
- previous orthodontic treatment,
- medications that can affect the outcome of the study,

- craniofacial anomalies,
- periodontal disease or attachment loss,
- significant root resorption prior to or during the study (more than 1/3rd root length).
- Patients with known allergy to nickel

9.3 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

9.4 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 not be including Non-English-speaking subjects. All of the treatment is available as Standard of Care and no potential benefits would be inequitably withheld from Non-English-speakers.

10.0 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.

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

Response:

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

*10.2 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.

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

Response:

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

*10.4 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:

- 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
- Permission is to be obtained from one of the parents

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

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

Response:

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

10.6 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

11.0 Eligibility Screening*

11.1 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 arrive to the clinic for a standard clinic screening appointment. Patient eligibility will be reviewed in the EMR after the intake appointment. Once the treating resident and supervising faculty have diagnosed and treatment planned the case, the supervising research resident will be notified. The research resident will communicate with the treating resident about the patient's diagnosis and proposed treatment plan prior to the patient's consultation. Eligibility of patients to the research will be decided from the diagnostic data and proposed treatment plan. If the individual has a treatment plan that meets eligibility criteria, they will be considered as eligible subjects.

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

12.0 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.

12.1 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: they

There will not be any recruitment materials utilized in this research study. Once the patient is deemed eligible per the procedures in 11.1, the supervising researcher will be present during the treating resident's standard clinic consultation with the patient. During the consultation the researcher will introduce

the research study and explain all aspects / what to expect if they were to consent to participate. All consent and study paperwork will be present during the consultation for the patient to review, ask questions and sign if they consent.

12.2 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: Patients will be invited to participate in the current study in an separate room away from other patients, during their standard clinic consultation visit.

12.3 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

13.0 Procedures Involved*

*13.1 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**:* Once the subject has been screened and been deemed eligible to participate in the study the following procedures will take place.

Standard of Care:

- Conventional Full Fixed appliances will be bonded to all permanent teeth (either 0.018" or 0.022" MBT prescription brackets), the maxillary canine bracket prescription will be 0.018" MBT (0.018" straight wire brackets MBT; 3M Oral Care, St. Paul, MN, USA)
- Phase of leveling and aligning will proceed through standard archwire progression, until 0.016 x 0.022" sized wire is able to be engaged.

- Sliding mechanics of canine retraction utilizing NiTi Closed Coil Springs to produce 150g of retraction force, utilizing the first molars and premolars as anchoring units.
- Correx Orthodontic Gauge will be utilized to verify 150g of force generation.

Research:

- A split mouth design will be utilized per patient, randomly assigning the upper left and right sides of the maxilla, through a random number generator.
- Split archwire design will utilize a crimpable binding mechanism to allow for joining of the SS and GUMMETAL wires together dividing at the junction of the maxillary central incisors.
- Patient's occlusion will be discluded to prevent interferences prior to retraction mechanics utilizing bite-turbos on the buccal inclines of the palatal cusps of the maxillary first molars.
- Intraoral scan will be taken utilizing an iTero intraoral scanner prior to beginning retracting mechanics on the upper canines (this will be timepoint T_0).
    - Appointment date, patient name, age, sex and position of Canine T_0 will be collected into the data sheet.
- If there is a need for absolute anchorage, miniscrews will be utilized on a per case basis.
- T_1 will begin canine retraction on both side of the maxillary arch.
    - Intraoral scan will be done
    - Data collection will be done: appointment date, patient name, position of Canine T_1
- Each activation of the NiTi Closed Coil spring will be performed by the research examiner.
- After four weeks the patient will return for an adjustment visit:
    - Intraoral scan will be done
    - Data collection will be done: appointment date, patient name, position of Canine T_2
    - Reactivation of retraction coil will be done
- After another four weeks the patient will return for an adjustment visit:
    - Intraoral scan and data collection will be done
    - This will mark T_3 and reactivation of the retraction coil will be done by the research examiner.
- Final four weeks of retraction the patient will return for an adjustment visit:
    - Final intraoral scan, intraoral photographs, radiographs and data collection will be done marking T_4 of data collection.
- There will be no more data collection following the T_4 data collection point. The patient will continue orthodontic treatment per the treating resident's treatment plan agreed upon during the consultation.

- Data analysis will be performed by the researcher and statistician from the data collected from the patient.
    - Four consecutive digital models will be superimposed using 3-Shape analyzer software. Color-coded superimposition will be performed to verify the accuracy and precision of the superimposition.
    - To evaluate rate of canine retraction, total retraction distance and 3D tooth control, will be measured through the superimposition models
- Canine movement rate (mm/month) and total retraction distance (mm) will be assessed for the patient based on the position of the canine starting at T_0 to T_4.

13.2 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:

- Demographic (patient name, age, sex)
- Canine Retraction Rate (mm/month)
- Position of Canine T0-T4
- Total retraction distance (mm)

13.3 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: Data collection spreadsheet is uploaded in Click. Intraoral 3D scans of the upper arch via iTero scanner

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

Response: Patient data will be pulled from the University at Buffalo School of Dental Medicine EMR database as well as the Orthodontic Department at the SDM record systems. Systems used are:

- Dolphin (used for imaging storage: photographs and radiographs)
- OrthoCad (used for 3D model storage)
- AXIUM – (medical, dental and treatment history database – EMR software)

*13.5 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 clinical 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, as per SOC protocols. If any anecdotal findings arise, they will be mentioned to the subject and guardians as well.

*13.6 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. Aggregated study results can potentially be presented at conferences and / or published in journal articles.

14.0 Study Timelines*

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

Response: 6 months (from screening to recruitment into the study)

14.2 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 will be four months. Initial records will be collected at T0. T1 will be the beginning of study, with adjustment and data collection happening every four weeks. Final records will be collected at T4.

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

Response: 14 months

15.0 Setting

15.1 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 facility where the study will be conducted is the Orthodontics Department at the University at Buffalo School of Dental Medicine. The facility has individual operatories (twenty total) for residents to administer orthodontic treatment. Each operatory is equipped with all standard of care equipment and necessary tools 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 only be accessed via university issued identification badges, once activated each individual has to input their credentials to access our patient management software, AXIUM. Orthodontic department patients can only be viewed by faculty, staff and residents in the department, 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 after thirty minutes of idle will automatically log the individual off for security purposes. Any input to the patient's electronic health record, notes, diagnostic codes, treatment plans, etc., have to fully be reviewed by the supervising faculty prior to dismissal of the patient. The facility is restricted to faculty, staff and residents of the Orthodontic Department. 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. Our intraoral 3D scanner 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. Only a certain amount of people is allowed in the room and there is spacing between individual computers so that there is adequate space between users. The same security measures are present for the computers in the laboratory as in the operatories.

15.2 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.

16.0 Community-Based Participatory Research

16.1 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.

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

Response:

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

17.0 Resources and Qualifications

*17.1 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: *Dr. Lubomyr Ravlyk.* PGY2 Orthodontic Resident at University at Buffalo School of Dental Medicine. Completed his DDS training at University at Buffalo School of Dental Medicine, 2019. Completed his Bachelors in Science from St. John Fisher College, 2015. While at St. John Fisher, worked on two different research projects, one involving Organic Chemistry and various catalysts to increase product yield, and the other working with *C. elegans* nematode and fluorescent microscopy to determine effects of gene mutations that are analogous to cilia mutations in humans. His previous research experience will be advantageous to this current study along with his dental knowledge and

continuing orthodontic training / experience. Has been living in the local area for most of his life and is very familiar with the local culture and society.

Supervising the Investigator: *Dr. Thikriat Al-Jewair*. Dr. Thikriat Al-Jewair is the Associate Professor and Director of the Advanced Education Program in Orthodontics Department of Orthodontics. In addition to her accomplishments in Orthodontics, Dr. Al-Jewair, has several Masters degrees in the fields of Business administrations, Dental Public Health, and Orthodontics. She also has a Certificate in Clinical Research from Harvard Medical School. She is a Diplomate of the American Board of Orthodontics and a Fellow of the Royal College of Dentists of Canada in both Orthodontics and Dental Public Health. Dr. Al-Jewair is the author or co-author of over 50 publications. She mentored over 40 MS and professional students and has completed multiple prospective and retrospective clinical studies prior to this project.

Describe other resources available to conduct the research.

17.2 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:

- Develop the appropriate archwire system to facilitate a split mouth design with the intervention and control group
- 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

17.3 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 and there will not be a substantial increase in risk. All patients will have access to all resources they might need. If there are questions or concerns, they will have the Orthodontic department's emergency hotline, which will be able to route them to the appropriate individual that can help them. 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 issues there are resources available which can easily be accessed.

17.4 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 entire protocol will be available in hard copy and electronic copy for anyone who will be involved in the research study. A streamlined version of the protocol will also be available for all who will be involved. There will be a presentation before patient recruitment commences 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.

18.0 Other Approvals

18.1 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.

19.0 Provisions to Protect the Privacy Interests of Subjects

19.1 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: All participants will be communicated to in a private office enclosed setting where there will be no one else to overhear what is discussed. The participants will only be meeting with research examiner and supervising faculty. The participants at any point are free to refuse treatment and anything during treatment that they do not feel comfortable with and leave the study at their own discretion.

19.2 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: Patients will be screened for eligibility for the study, after they have been diagnosed in clinic and treatment planned. We will be utilizing a partial HIPAA Waiver (HRP-611) for the purposes of pre-screening records. Once they have agreed to enroll, children will sign an assent form and their parents will sign an informed consent with HIPAA Authorization.

20.0 Data Management and Analysis*

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

Response: Statistical analysis will be performed using the Statistical Package for the Social Sciences (SPSS). To assess normality of all quantitative variable distributions the Shapiro-Wilk Test will be utilized. To evaluate statistical significance in the difference between experimental and control groups for preoperative and postoperative measurements, a paired t-test will be used[36]. The level of significance will be set to $p \leq 0.05$ and to assess inter- and intraobserver reliability the intraclass correlation coefficients were obtained.

20.2 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 would be sufficient to detect a difference of 0.5mm or greater.

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

Response: 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.

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 per SOC.

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

Response: Efficacy data: canine retraction amount and monthly rate

21.3 Describe any safety endpoints.

Response: NA

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: NA

21.5 Describe the frequency of safety data collection.

Response: NA

21.6 Describe who will review the safety data.

Response: NA

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

Response: NA

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

Response: NA

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

Response: NA

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: If the subjects:

- Develop any indication of root resorption
- Develop any periodontal issues during the course of 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

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 their participation at any time. At which point, all 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 not be used in the research study as the data will not be complete. It will be destroyed and discarded accordingly. The IRB correspondence and signed consent forms from withdrawn subjects will be maintained for 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: Breach of confidentiality is a risk to participating in this study. Since this is a clinical research study, which will be utilizing orthodontic techniques and mechanics to achieve orthodontic treatment, we will have inherent risks which are routine in orthodontic treatment. These risks will be explained to the patient as part of the Standard of Care protocol.

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

Response: Procedures performed to mitigate risk of confidentiality breach are described in the Confidentiality section.

To reduce the probability / magnitude of risks in the standard clinical procedures, safety measures will be implemented per SOC protocol.

- 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.
- Patients will be given appropriate oral hygiene tools (floss threaders, proxy brushes, tooth brushes, plaque disclosing tablets) and instruction prior to starting orthodontic treatment. This will ensure that each patient is aware of the hygiene required during treatment. This will also reduce the risk of white spot lesions, periodontal issues, and halitosis. Reduced inflammation will also provide more comfort to the patient during treatment.
- To reduce risk of discomfort and abrasion, patients will be given orthodontic wax to place on brackets or wires that give them any discomfort. Patient's wires will be trimmed accordingly and patient will be asked prior to leaving if there is anything bothering them to reduce discomfort.
- Each adjustment visit patients 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)
- Patients will be able to communicate 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.
- Patients will have their medical and dental history updated at every 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 patients who have or develop an allergic reaction to nickel, 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 risk is a broken appliance, which is a risk inherent to standard clinical care for these patients.

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

Response: N/A

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

Response: Current risk of COVID-19 infection, otherwise there is risks to others who are not subjects.

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: There are no direct benefits to subjects on this study, they are being randomized to standard treatments that are available to any patient outside of the research context.

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: This study is of minimal risk, and there is no additional anticipated risk for participating in this study

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: NA, this study is not sponsored.

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 as part of their regular care:

- Standard clinical fees associated with comprehensive orthodontic treatment
- There will <u>not</u> be additional cost to receiving the GUMMETAL wire.

☐ **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 27.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 27.0)*

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 Department. Specifically, this will take place in the privacy of a faculty office which will be completely closed and private. Patients will be able to ask their questions and concerns with absolute privacy.

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: Patients will be allotted appropriate time to discuss amongst themselves and appropriate parent / guardians with or without the research examiner present, whichever they prefer. If subjects need more time to think and discuss outside of the clinic and come back at a later time to make their decision to participate this is acceptable. Patients 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: Patients will be asked at every visit if they wish to continue in their current research study. Patient will have full autonomy to withdraw or continue. There will be appropriate documentation that will be signed by the patient 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 26.8)

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 6.4 of this protocol.

Response: N/A

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: N/A

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults.
(Skip to Section 26.9)

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 26.13)*

When a person is not capable of consent due to cognitive impairment, a legally authorized representative should be used to provide consent (Sections 26.9 and 26.10) ***and, where possible, assent of the individual should also be solicited*** *(Sections 26.11 and 26.12).*

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 27.0)*

*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: Patient's medical record, screening forms and discussion with parent/guardian will be utilized to assess patient'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)."

*28.16Describe 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 patient 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 child subjects in the research study.

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

Response: Assent will be documented 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. There will be separate assent paperwork for children ages 12 and younger and for those 13-17 years of age.

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:

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:

30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 29.0)

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.