Corrosion and Nickel Ion Release of Nickel Titanium Archwires with Ion Implantation Technology in Deflected and Nondeflected States

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ABSTRACT

The purpose of our research was to test the corrosion capabilities and nickel ion release of nickel titanium archwires with and without nitrogen ion implantation technology in deflected and nondeflected states. To achieve this, NeoSentalloy wires with and without IonGuard technology were studied. Potentiodynamic anodic polarization was applied to wire either straight or undergoing deflection with a three point bending force. The corrosion of each sample was determined by the zero current potential, area integration, and pitting potential point from the anodic polarization charts. The nickel ion release was determined by inductively coupled plasma mass spectroscopy analysis (ICP-MS). Scanning electron microscopy images of the wires before and after anodic polarization were also collected. Our study did not detect a significant effect of ion implantation or deflection. Our data does not support the claims that IonGuard protects against corrosion or reduces nickel ion release and in fact, when IonGuard wire is deflected, corrosion occurs more robustly, as seen by the significant interaction effect for area integration.

INTRODUCTION

Nickel sensitivity is a concern in the dental profession as nickel has been shown to have dermatological, toxicological and possibly mutagenic effects and causes more allergic reactions than all other metals combined (Agaoglu et al. 2001, Staffolani et al. 1999). It is estimated that 10-30% of the general population is sensitive to nickel (Kerosuo and Dahl 2007), and adverse reactions can occur in patients undergoing orthodontic treatment (Noble et al. 2008). A recent study found 0.1% to 0.2% incidence

of adverse patient reactions in orthodontic practices due to nickel sensitivity (Kusy 2004). The allergic reactions to nickel are usually Type IV mediated delayed hypersensitivity and can lead to a variety of symptoms including mild skin or mucosal irritation, allergic reactions, generalized dermatoses, and even asthmatic reactions (Kerosuo 2007). Oral signs and symptoms of nickel allergy may be subtle and include a burning sensation, gingival hyperplasia, labial desquamation, angular chelitis, erythema multiforme, severe gingivitis, periodontitis, stomatitis with erythema, peri-oral rash, loss of taste or metallic taste, numbness, and soreness at the sides of the tongue (Noble 2008, Park and Shearer 1983).

Typically, nickel-titanium (NiTi) is the archwire material of choice during the early phases of orthodontic treatment, due to its exceptional shape memory, superelasticity, and delivery of lighter, consistent forces with a greater working range when compared to stainless steel (Widu et al. 1999). These properties allow for more constant stress in the periodontal ligament which leads to optimal tooth movement, minimization of tissue destruction, less patient discomfort and increased intervals between appointments. Nickel titanium archwires contain approximately 50% nickel and release small amounts of nickel into the oral cavity as they corrode. The general mechanism for corrosion and metal ion release occurs when oxygen comes in contact with the metal surface, causing a loss of the passivated layer (Park 1983). Park (1983) reported a release of 40 micrograms of nickel per day from a simulated full- mouth fixed appliance. Increased levels of nickel have been detected in saliva, serum, oral mucosal cells and urine after the placement of orthodontic appliances (Menezes et al. 2007, Agaoglu 2001, Amini et al. 2008). Galvanic corrosion of dissimilar metals and appliance

surface irregularities have been shown to affect the amount of metal released from orthodontic appliances (Amini 2008). Deflection of an archwire could create mechanical deformation of the passivation layer (Peitsch et al. 2007) and could increase the atomic energy level at the surface (Jai et al. 1999) which would tend to allow corrosion to propagate. However, there is conflicting evidence on whether or not stress and loading of archwires causes increased corrosion with Kerosuo et al. (1995), Liu et al. (2007), Segal et al. (2009), Peitsch (2007) and Jai (1999) showing an increase in corrosion with loading and Huang (2003) and Rondelli and Vicentini (2000) showing no effect. Although nickel release has been detected in many studies, it is generally below the daily dietary intake of nickel, which is estimated to be between 300-500 micrograms (Park 1983). Huang et al. (2003) described the critical value necessary to induce allergy between 600-2500 micrograms. Nickel ion release is still a concern in orthodontics, especially in patient that have already been sensitized to nickel, as Fay et al. (2005) revealed that oral exposure of more than 60 ug/L often result in a hypersensitivity response in these nickel-sensitized individuals.

Corrosion is presumed to be detrimental to biocompatibility and esthetics and even to treatment progress, because of its influence on friction (Widu 1999). Manufacturers are aware of the potential for corrosion and try to minimize it by allowing substitutions or additions, coatings, or modifications to the production process. Coatings currently in use include titanium nitride to improve hardness and reduce friction and epoxy resin to improve corrosion resistance and esthetics (House et al. 2008). IonGuard technology (Spire Biomedical, Bedford, MA, USA) uses a nitrogen ion implantation process to modify the surface properties of a material and claims to improve hardness,

reduce friction, and improve corrosion resistance. This process involves bombarding highly energetic beams of nitrogen ions at the bulk material at low temperature and low pressure (Burstone and Farzin-Nia 1995). Ion implantation typically affects the substrate ions a fraction of a micron beneath the surface, so the process does not affect the properties of the bulk material. A 60-120 nm film of titanium nitride is formed and acts as a potential obstacle to degradation of the NiTi archwire because of its more tightly bound structure which allows ions less ability to migrate and diffuse into solution (Yeung et al 2007). Jai (1999) speculated that nitrogen takes the place of nickel atoms, which may lower the relative amount of nickel available to be released. Yeung et al. (2005) reported that the surface nickel concentration is reduced with the nitrogen ion implantion process. Yeung (2007), Gil et al. (1998), Endo et al. (1994), Neumann et al. (2002), and Jai (1999) found a protective effect of ion implantation. Conversely, Peitsch (2007) and Kim and Johnson (1999) showed no effect of surface nitridation on corrosion.

The purpose of this research was to test the corrosion capabilities of NiTi archwires treated with IonGuard technology. We tested wire with and without IonGuard technology and in both static and deflected conditions. We hypothesized that the nitrogen implantation process would improve corrosion resistance and inhibit ion leakage from the archwire to the surrounding solution both in static and deflected testing conditions. We also hypothesized that deflection of the archwire would lead to increased corrosion and nickel ion release. In terms of an interaction effect, we hypothesized that the ion implantation effects would supersede the effects of deflection and therefore corrosion and nickel ion release would be least in the IonGuard nondeflected wire, then IonGuard deflected, then NiTi nondeflected and most in NiTi deflected wires. Anodic

polarization was applied to the archwires because it duplicates the electrochemistry of natural corrosion (Kim 1999) and is able to speed up the corrosion process (Neumann 2002, Widu 1999). The oxidation potential of the oral cavity ranges from -58 to +212 mV (SCE) (Ewers and Greener 1985) and our potentiodynamic tests ranged from -800mV to +250mV for the nickel release data.

MATERIALS AND METHODS

To measure the corrosion of NiTi archwires with and without IonGuard technology in both deflected and nondeflected states, we performed anodic polarization tests. Two types of commercially available 0.016"x 0.022" NiTi archwires, (GAC International, Bohemia, NY, USA) were used: a standard NiTi archwire, NeoSentalloy, (lot # H3Z8) and an IonGuard treated wire, NeoSentalloy IonGuard, (lot #08091213). The archwires were both of equiatomic composition of nickel and titanium.

A 4 cm straight segment of the distal portion of the archwire was cut with a distal end cutter. The mesial 2 cm portion was heated to red hot, looped and attached to an electrical contact wire (Figure 1 in Appendix). The sample was ultrasonically cleaned for 2 minutes in ethanol and the loop and connection to the electrical wire were covered with nail polish as a block out material. For the nondeflected samples, a testing apparatus held an exposed straight segment 13.3 mm in length. For the deflected samples, our testing apparatus applied a three point bending force by deflecting the same length of wire by 1 mm (Figure 2 in Appendix). The deflected testing apparatus had an archwire held with an elastomeric module (AlastiK, 3M Unitek, St. Paul, MN, USA) into an upper right central incisor bracket (Inspire Ice, Ormco, Orange, CA, USA) that was bonded to

acrylic with adhesive (Transbond XT, 3M Unitek, St. Paul, MN, USA). For both test conditions, the surface of the wire beyond the 13.3 mm test length was covered with polyvinylsiloxane and the entire testing apparatus was ultrasonically cleaned for 2 minutes in ethanol.

The testing apparatus was inserted into an electrochemical corrosion cell and submerged in 450 mL of 0.9% sodium chloride titrated to pH 7.4 +/- 0.1 using $C_3H_6O_3$ or NaOH (Figure 3 in Appendix). During anodic polarization, the potential was regulated with a potentiostat and the polarization current and potential were recorded with a plotter. The NiTi wire constituted the working electrode and had an exposed area of 0.261 cm^2. A standard calomel electrode was used as a reference, while a platinum wire served as the counter electrode. We bubbled oxygen-free nitrogen through the electrolyte to deaerate the solution prior to testing as well as during the test. The entire system was equilibrated to 37 degrees.

The open circuit potential was recorded after 15 minutes. The first set of five samples for each group started at a potential of -0.8 V and increased 20 mV/minute in the noble direction after a 999 second delay to an endpoint of 0.25V. This endpoint occurred before the pitting potential for the wire was reached (Figure 4A in Appendix). The second set of five samples for each group began at a potential of -1.0 V and ended at 1.0 V, after the pitting potential was reached (Figure 4B in Appendix). The zero current potential value, integrated area under the corrosion curve from -0.1 V to 0.2 V during passivation, and the pitting potential point were used to determine the corrosion of each sample (Figure 4 in Appendix). The zero current potential point was recorded as the midpoint where the corrosion curve crossed the x axis, while the pitting potential point

was recorded as the point where passivation breaks down and pitting corrosion leads to a sharp increase in the corrosion curve. Both the voltage and current values of the pitting potential point were recorded and analyzed. The solutions from the short runs before pitting potential was reached were collected, buffered to pH <2 using dilute nitric acid and diluted to 500ml with deionized water. Fifty milliliters of the solutions were stored at 4 degrees for inductively coupled plasma mass spectroscopy analysis (ICP-MS; HP 4500 Series, Hewlett Packard, Palo Alto, CA, USA). Each sample was measured in triplicate and the instrument detection limit for nickel 60 was 0.40 ug/L and the method detection limit was 1.2 ug/L. The wire was rinsed with deionized water and analyzed by scanning electron microscopy (Quanta 200, Fei Corp, Hillsboro, OR, USA). Images were captured at high vacuum, 20 kV, and approximately 500x, 2000x and 7000x magnifications. Energy dispersive X-Ray microanalysis (INCA, Oxford Instruments, Concord, MA, USA) was used to identify the composition of the wire and elements in wire inclusions.

Data Analysis

Data was compared using 2X2 factorial ANOVA using SPSS with Tukey post hoc tests. The wire type (NiTi or IonGuard) and deflection state (nondeflected or deflected) were the independent variables and the zero current potential value, integration of the area under the corrosion curve during passivation, nickel ion concentration in solution and pitting potential point (both voltage and current) were the dependent variables.

RESULTS

The means and standard deviations for each of the four groups for all five dependent variables are listed in Table 1. The raw data is shown in Table 2-6 in the Appendix. Table 7 in the Appendix shows the mean, standard deviation, kurtosis and Pearson's correlations for the dependent variables. If the data was not normally distributed it was either winsorized (nickel release data) or normalized by taking the log of the data (area integration and pitting potential point Amps/cm^2 data). Table 8 and 9 in the Appendix show the transformed and backtransformed data for the area integration and pitting potential point current (Amps/cm^2) data. The ANOVA tables for each dependent variable are shown in Tables 10-14 in the Appendix. Figures 5-8 show the estimated marginal means and 95% confidence intervals for the wire type effects, deflection state effects, and interaction effects.

There was not a significant effect of wire type on corrosion or nickel release (Figure 5). Our findings do not support the manufacturer's claims that IonGuard acts as a protective mechanism against corrosion. The trends showed IonGuard had a more positive zero current potential (p=.114), which would be protective, but more nickel release (p=.452) and a lower pitting potential point voltage (p=.231), indicating pitting corrosion occurred earlier. There was not a significant effect of deflection state on corrosion or nickel release (Figure 6). Four out of five of the dependent variables had non-significant results for the interaction effect (Figure 7). The data show trends for deflected IonGuard wires to have initial protective effects (more positive zero current potential values p=.458) but to exhibit more intense pitting corrosion (higher pitting potential point current p=.400) and more nickel release (p=.294). There was a

statistically significant interaction effect between wire type and deflection state for area integration (p=.021), with deflected IonGuard wires showing the greatest area for corrosion during passivation (Figure 8).

Table 1. Mean and standard deviation for each Dependent Variable

Group	Zero Current Potential (V)	Area Integration (V*Amps/cm2)	Nickel Release (ug/L)	Pitting Potential Point (V)	Pitting Potential Point (Amps/cm2)
NiTi Nondeflected	-0.30 (0.08)	8.86E-08 (2.92E-08)	7.63 (10.11)	0.50 (0.20)	5.78E-07 (2.79E-07)
IonGuard Nondeflected	-0.25 (0.08)	5.66E-08 (3.44E-08)	6.32 (8.66)	0.44 (0.08)	5.60E-07 (6.45E-07)
NiTi Deflected	-0.28 (0.07)	1.59E-07 (2.07E-07)	3.34 (4.67)	0.54 (0.15)	8.90E-07 (1.35E-06)
IonGuard Deflected	-0.26 (0.04)	3.90E-07 (4.18E-07)	36.02 (57.92)	0.42 (0.17)	9.62E-07 (1.11E-06)

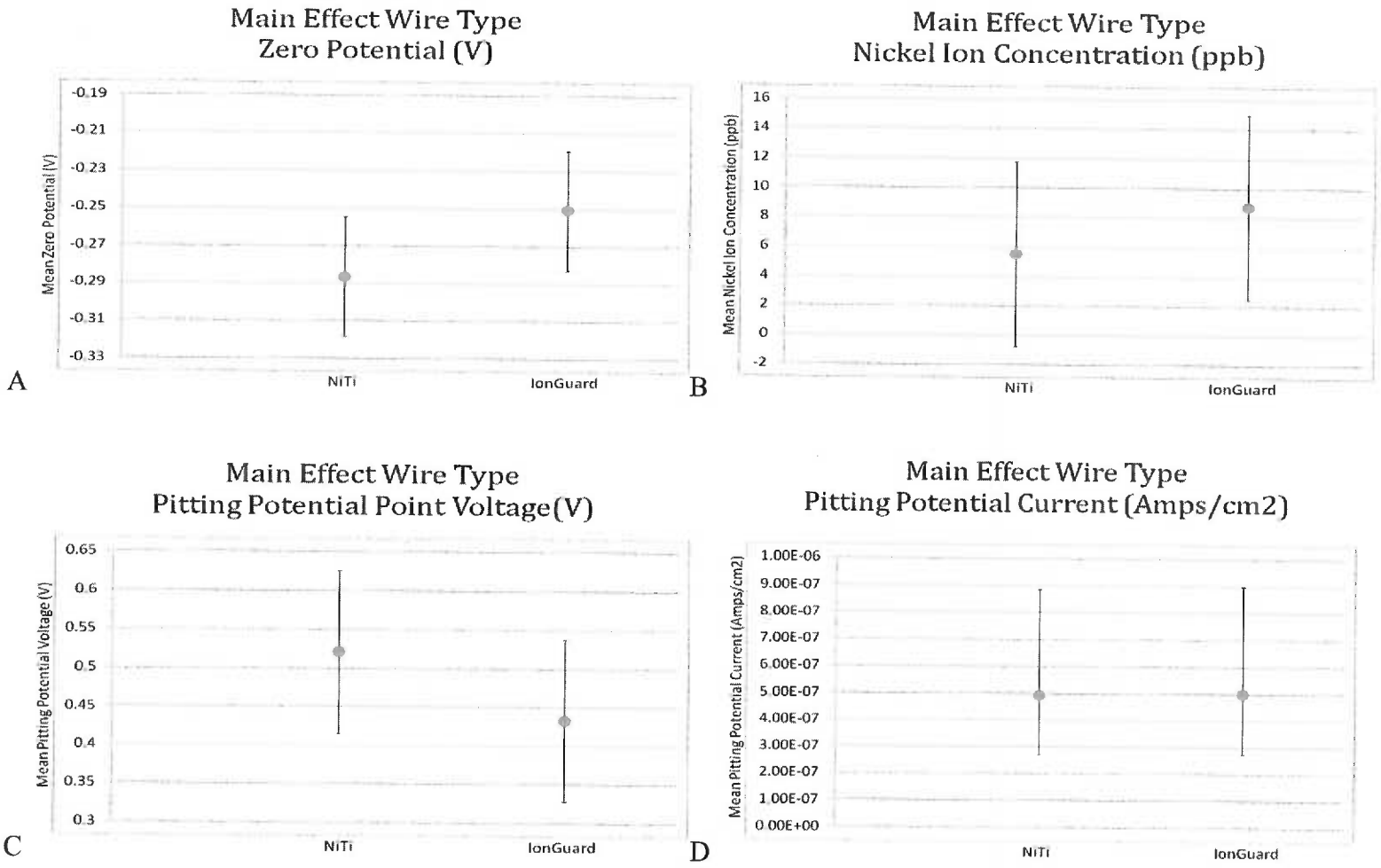

Figure 5. Non-significant effects for wire type were seen for A) zero current potential (p=.114), B) nickel release (p=.452), C) pitting potential point voltage (V) (p=.231), or D) pitting potential point current (Amps/cm^2) (p=.969).

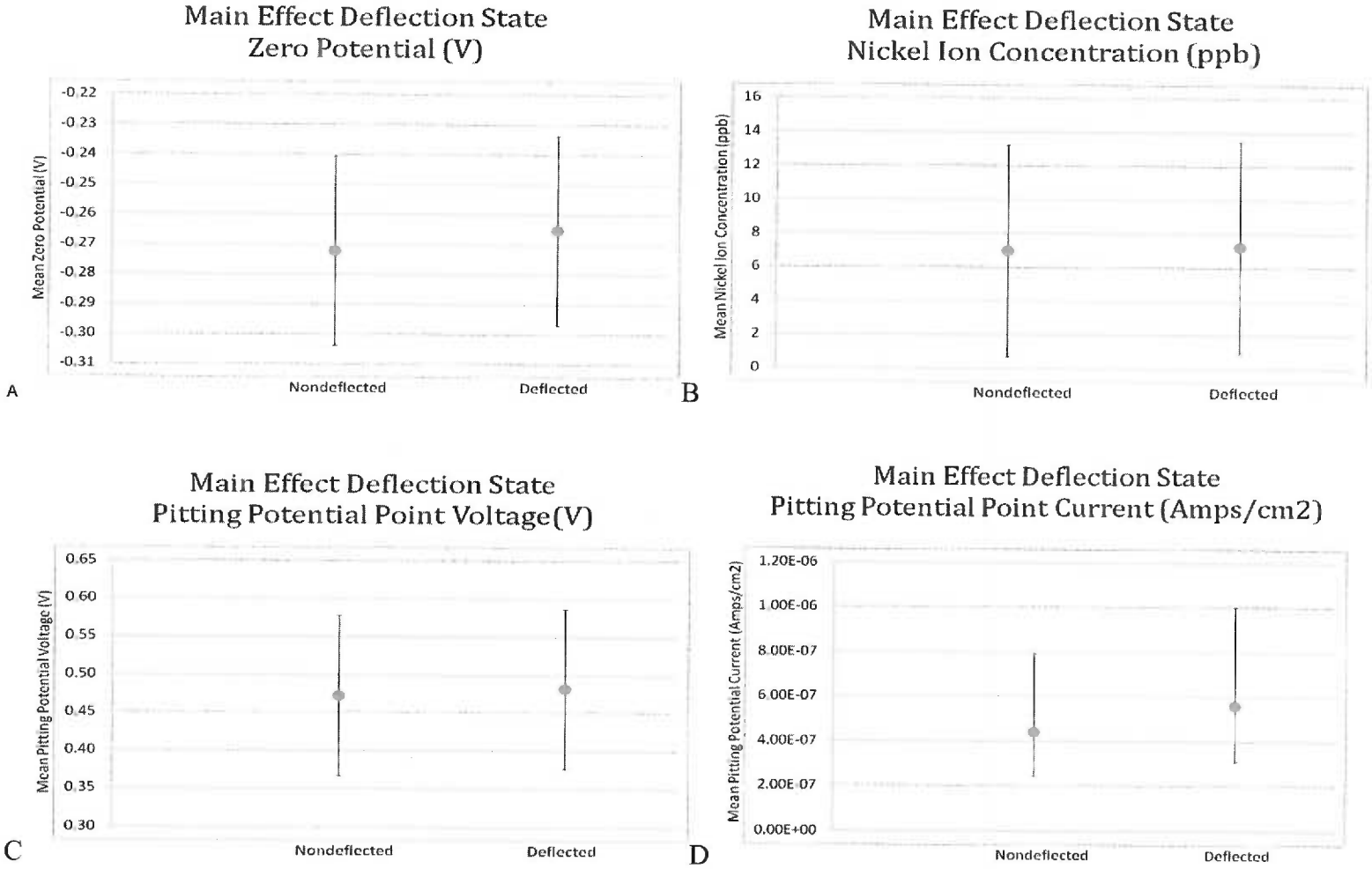

Figure 6. Non- significant effects for deflection state were seen for A) zero current potential (p=.753), B) nickel release (p=.954), C) pitting potential point voltage (V) (p=.897), or D) pitting potential point current (Amps/cm^2) (p=.561).

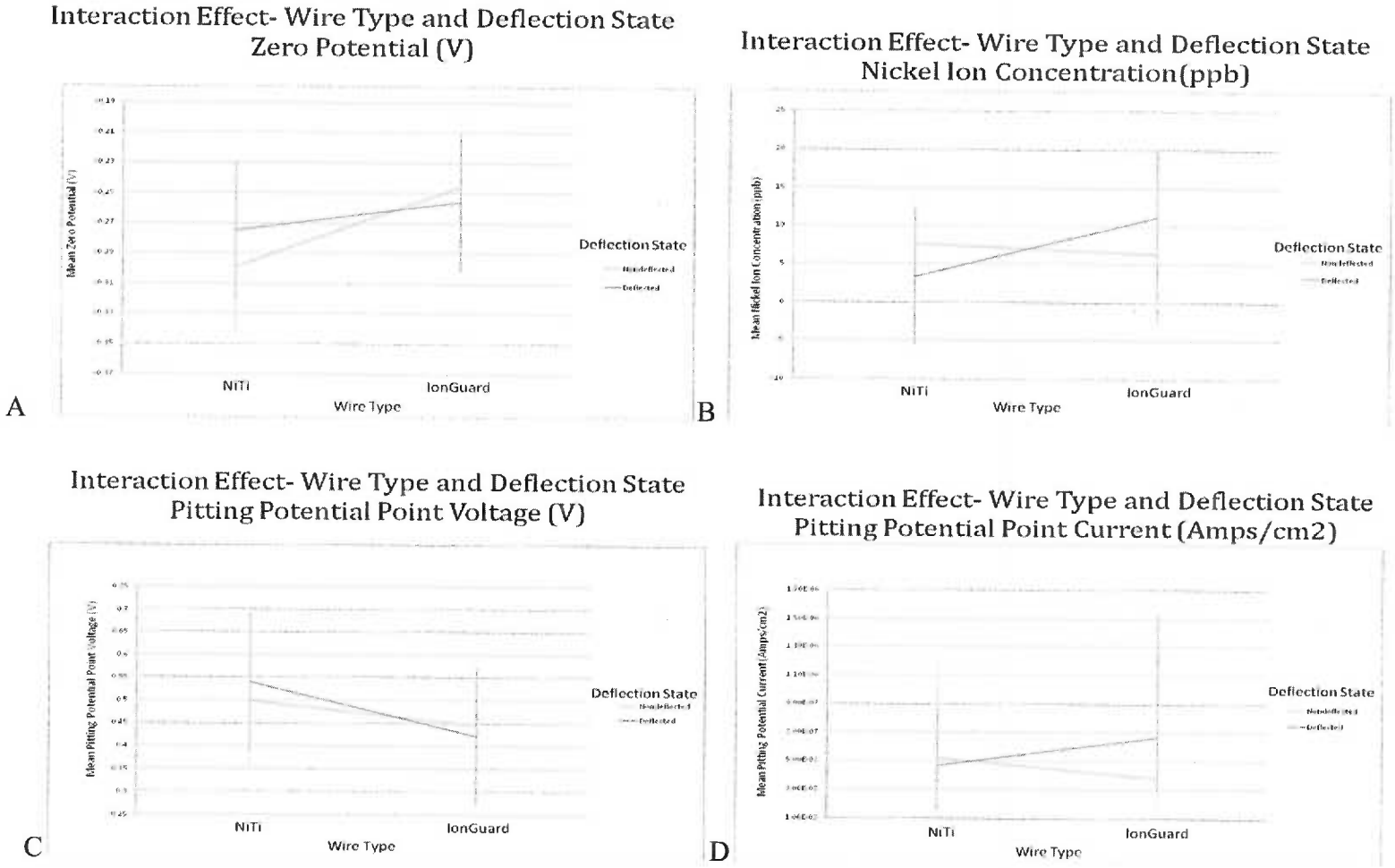

Figure 7. Non- significant interaction effects were seen for A) zero current potential (p=.458), B) nickel release (p=.294), C) pitting potential point voltage (V) (p=.659), or D) pitting potential point current (Amps/cm^2) (p=.400).

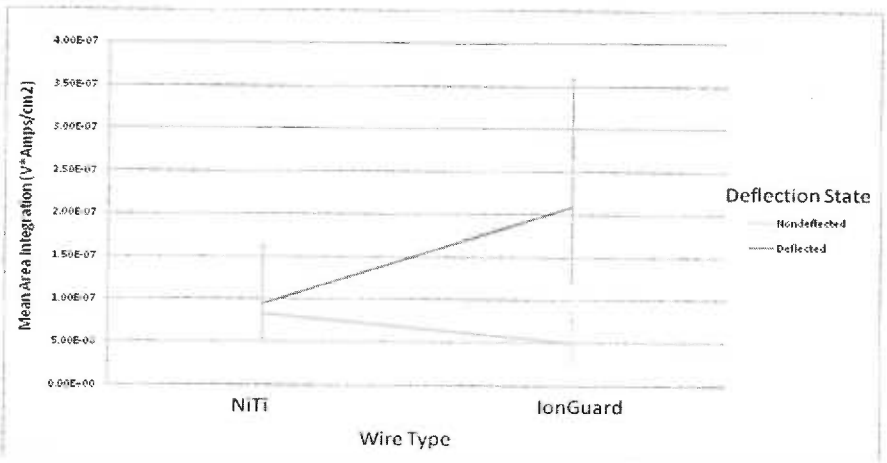

Figure 8. A significant interaction effect was seen for area integration (p=.021). Deflected IonGuard wire showed significantly more corrosion during passivation, as evidenced by more area integration, than nondeflected IonGuard.

SEM

The scanning electron microscopy and energy dispersive x-ray analysis showed significant variability in the composition of wires, with large titanium-rich inclusions visible in both NiTi and IonGuard wires (Figure 9A and B). The wires before corrosion testing had a range of 48.78-75.62% titanium and 24.38-51.22% nickel. Chromium, sodium chloride, iron, carbon and silicates were also detected. Signs of corrosion were visible after anodic polarization testing (Figure 9C).

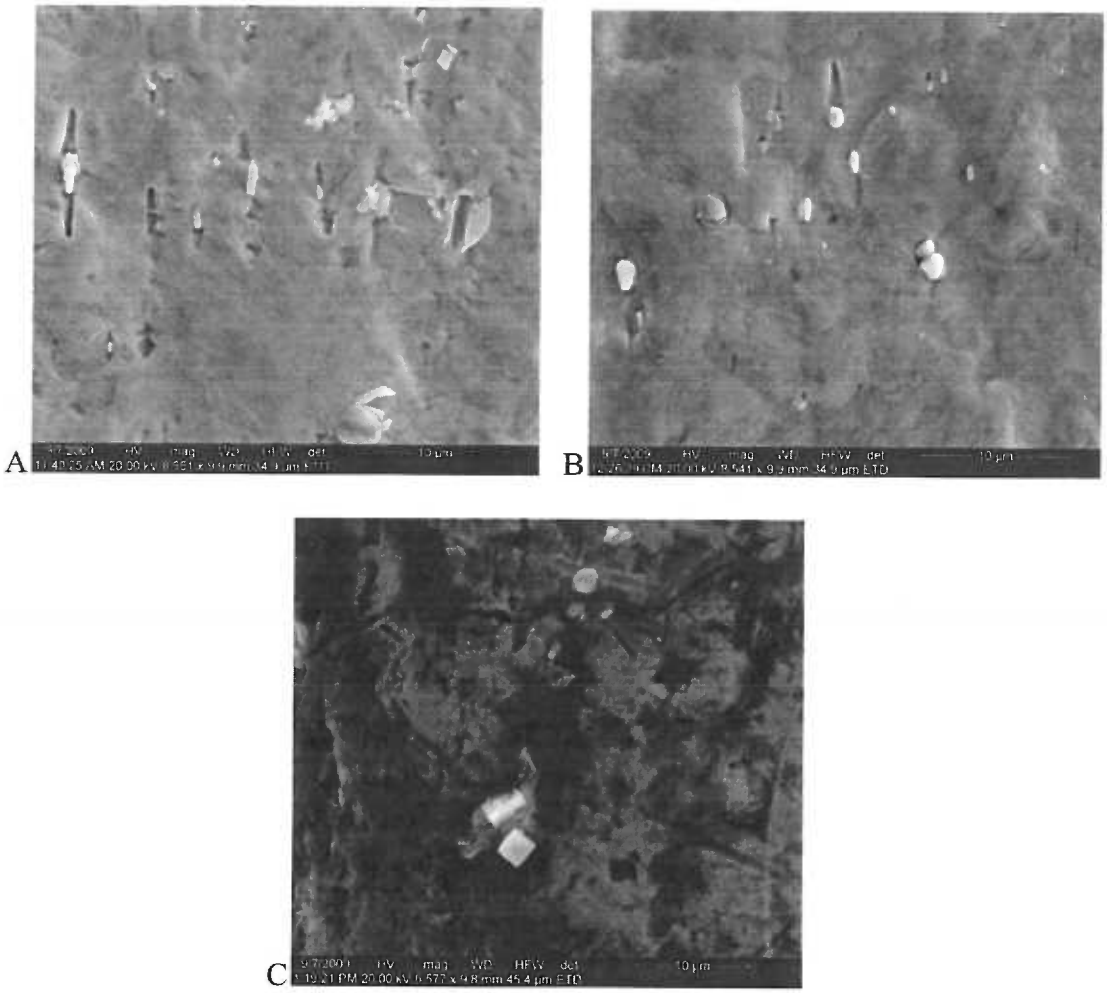

Figure 9. A) NiTi wire pre-corrosion testing. B) IonGuard wire pre-corrosion testing. Titanium-rich inclusions can be seen in both A and B as well as generalized surface irregularity, crevices and silicate dust particles. C) IonGuard Deflected #5 wire after corrosion testing. The sodium chloride crystal has formed in a pit after localized corrosion.

DISCUSSION

With nickel hypersensitivity prevalence increasing (Noble 2008) and lower levels of intraoral nickel needed to elicit a reaction in previously sensitized people (Fay 2005), there is a need for orthodontic treatment modalities that limit nickel ion release. Jai (1999) reported that human peripheral blood mononuclear cells were more sensitive to nickel during their proliferative stage, which would be seen with inflammation. During orthodontic treatment patients frequently present with inflammation from poor oral hygiene and repeated trauma from brackets or archwires.

Our study found a nickel release range of 0-135.9 ug/L after potentiodynamic testing NeoSentalloy wires with and without ion implantation from -0.8-0.25 V (SCE). Widu (1999) reported 3.1 mg/L (3,100 ug/L) nickel release at 0.72 V and 17.7 mg/L (17,700 ug/L) nickel release at 1.22 V after potentiostatic testing NeoSentalloy wires for 10 minutes. Widu's significantly higher nickel release values can be explained by the higher voltage tested, above the pitting potential point. Also they did not build up the passivation layer with a potentiodynamic protocol like we did, which would occur intraorally and better simulated the clinical environment.

Passive nickel release has been reported with ranges similar to that seen in our study. Staffolani (1999) reported initial nickel release after 1 day to range from 0.41 to 6.74 ug/L arch of appliances (which would convert to 0.82-13.48 ug/L for a full mouth appliance) depending on the organic content of solution and pH. Kerosuo (1995) reported 22 ug/day of nickel release with full fixed ortho appliances under functional stress, while Park (1983) found 40 ug/day nickel release from a full mouth appliance. Huang (2003) reported RMO NiTi wire released 4.7 ug/cm^2 /day and Wever et al. (1998)

detected initial nickel release of 14.5x10-7 ug/cm^{2}s from NiTi wire (which would convert to 0.12528ug/cm^2 /day). Gil (1998) reported nickel release from NiTi wires with and without surface nitridation ranged from 0-200 ug/L after 2000 hours of passive soaking. Yeung (2007) reported nickel release ranged from 57.9-320 ug/L from NiTi alloys with and without ion implantation after 5 weeks of passive soaking. In all the studies observed, except Widu (1999) and Yeung (2007), the nickel release values were less than the average daily dietary intake of 300-500 ug of nickel (Park 1983, House 2008), below the critical value necessary to induce allergy, which is 600-2500 ug (Huang 2003), and below the cytotoxic threshold concentration of 15-30 ppm (Jai 1999). However, several studies (Our study, Gil 1998, Yeung 2007, and Widu 1999) had nickel release values that were higher than the 60 ug/L which often causes a hypersensitivity response in nickel-sensitized individuals (Fay 2005) and so nickel ion release is still a concern in this patient population. Our results were similar to the passive nickel release values, showing that our potentiodynamic protocol built up the oxide layer similar to passive soaking conditions.

Variation in detected nickel release among studies could be due to a variety of factors. Different materials were tested, which ranged from bands, brackets, stainless steel archwires, NiTi archwires, ion implanted NiTi wires and several combinations of the above. Also the authors used different detection methods. Our study, Gil (1998) and Yeung (2007) used ICP-MS, while the other studies used atomic absorption spectrophotometry (Park 1983, Staffolani 1999, Huang 2003, Wever 1998, Kerosuo1995, Widu 1999). We used ICP-MS because of the increased sensitivity and ability to detect variations in nickel ion concentration down to parts per billion. Within studies that tested

the same material, differences in manufacturer production, finishing and surface roughness could have affected nickel release (Figure 9). Also protocol differences such as pH, temperature, solution, length of test and other parameters could have affected nickel release as has been shown in previous studies (Huang 2003, Staffolani 1999). Another factor is that we heated part of the wire to red hot to bend it to attach it to the electrical wire and previous studies have found an effect on nickel release with heat treatment of the wire (House 2008). We assumed that the portion of the archwire tested was far enough from the heated portion that it was not affected, but this was not confirmed. Also, half of our samples had values less than the method detection limit for nickel 60 of 1.2 ug/L. Nevertheless, our study had nickel release ranges that were comparable to other studies reviewed.

With in vivo studies, nickel has been detected in saliva at increased concentrations after orthodontic appliance placement. Petoumenou et al. (2009) reported an increase in nickel concentration in saliva after bracket placement, median 78 ug/L and after NiTi wire placement, median 56 ug/L, compared to 34 ug/L pretreatment. Souza and Menezes (2008) detected increased nickel immediately after appliance placement (1.72 ug/L as compared to 0.64 ug/L before placement) and large variation in ion concentration among individuals. Agaolu (2001) found nickel release in saliva between 4.12-11.53 ug/L. Our nickel release range of 0-135.9 ug/L was slightly higher than the range seen in bioaccumulation studies, but within an acceptable deviation, which supported our potentiodynamic protocol and the voltages tested as being clinically appropriate. The lower range seen with in vivo studies could be due to calcium

phosphate formation on top of the oxide layer that served as a second barrier against ion diffusion (Wever 1998).

The manufacturers of IonGuard wire suggest that corrosion and nickel release will be reduced from NiTi wires by the application of ion implantation technology. Ion implantation forms a titanium nitride surface layer on NiTi wire that changes the surface structure of the wire. This titanium nitride surface has been shown to alter the formation of the protective oxide layer TiO_2 (Oshida and Hashem 1993). The surface hardness of the wire is increased (Peitsch 2007) which causes a more tightly bound surface structure that allows ions less ability to migrate and diffuse into or out of solution. Jai (1999) speculated that "implantation of ions into near surface regions enhances a metal's surface corrosion resistance by forming amorphous surface layers, thereby eliminating rapid corrosion at grain boundaries, shifting the open- circuit potential into a passive range, where corrosion current densities are low, and inhibiting kinetics of cathodic reactions on the surface." It has further been speculated that ion implantation with nitrogen forces nitrogen ions to take the place of nickel atoms on the wire surface. This lowers the relative amount of nickel available to be released (Jai 1999).

Our study did not find a statistically significant effect of ion implantation on nickel ion release, but there were trends toward IonGuard wire releasing more nickel. The nonsignificant finding could be due to large variation in nickel release and small sample size (n=5 for each group) or manufacturing variation in the ion implantation process. Also, it is possible that the titanium oxide formation that occurs during passivation, occurs as readily and robustly on NiTi surface as on the nitridated surface (Peitsch 2007). Jai (1999) found that passive nickel release ranged from 0.4-4.1 ug/L

from Bioforce sentalloy wires and the nitrogen implanted wires released significantly less nickel than the NiTi wire. Yeung (2007) reported reduced passive nickel release from nitrogen implantated alloys, 57.9 ug/L compared to 320 ug/L from NiTi wires after 5 weeks. Conversely, Peitsch (2007) did not find any protective effect of the surface nitridation on passive nickel release from NeoSentalloy archwires.

Our study found no statistically significant effect of ion implantation of the wire on corrosion, as measured by zero current potential, pitting potential or integrated area. Gil (1998), Endo (1994), Neumann (2002) Yeung (2007) and Jai (1999) reported a protective effect of ion implantation, whereas Peitsch (2007) and Kim (1999) reported no effect. Endo (1994) concluded that the titanium nitride coating improved corrosion resistance when the potential was less than 500 mV and reduced corrosion rates of NiTi alloys by more than one order of magnitude in that range. The trends we found were for IonGuard to have a more noble zero current potential which would support it being protective. However, the pitting potential occured at a lower voltage (247 mV was the lowest detected value for deflected IonGuard). Endo (1994) also found pitting potential occurred at lower voltage but using Ewers (1985) clinically relevant anodic polarization range of -58 to +212 mV (SCE), neither pitting potential would tend not to occur intraorally. Conversely, Neumann (2002) found higher rupture potential for IonGuard 600 mV, compared to 460 mV for NeoSentalloy. Yeung (2007) reported a similar trend with ion implanted alloys displaying a breakdown potential of 1080 mV and NiTi 461 mV.

We hypothesized that deflection would cause an increase in corrosion and nickel release. This hypothesis was based on the assumption that stressing the wire would place

more energy in the archwire, increasing the atomic energy level at the surface thereby reducing the activation energy required for metal ions to be released (Jai 1999). Also deflection could create mechanical deformation of the passivation layer (TiO_2) which would serve as initiation points for corrosion to propagate (Peitsch 2007).

A significant effect of deflection on corrosion and nickel release was not detected in our study with the curvature we tested. Liu (2007), Peitsch (2007), Jai (1999), Segal (2009) and Kerosuo (1995) had reported an effect of deflection on corrosion, whereas Huang (2003) and Rondelli (2000) found no effect. The differences reported in the literature could be due to differences in static (Huang 2003, Rondelli 2000, Liu 2007 and Segal 2009) vs. dynamic deflection (Peitsch 2007, Jai 1999, Kerosuo 1995), wire size studied (ranged from .014" to .018"x.025"), amount of deflection per wire length, and testing conditions (passive soaking versus anodic polarization). Even within the studies that used anodic polarization (Segal 2009, Liu 2007, Huang 2003, Rondelli 2000) there were different protocols in terms of potentiostatic versus potentiodynamic, voltage range tested, rate of voltage increase, end point and extrapolation of the data. Segal (2009) reported that Sentalloy wire is austenite at 37 degrees and predominantly martensite at 5 degrees and that at 1 mm of deflection, the Sentalloy archwire showed signs of phase transformation from austenite to martensite. They found a significant effect of deflection on corrosion rates but without a consistent pattern for all wire types tested and no effect of deflection on pitting potential. This findings were for 14mm of wire deflected 0.75, 1.5 and 3.0 mm. They stated that alterations in stress associated with phase transformation in superelastic NiTi wires may alter corrosion rate differently than wires not concurrently undergoing phase transformation. This could be due to phase

transformation during deflection changing the surface morphology of the wire and exposing microscopic cracks and increased surface area of the wire. Segal (2009) hypothesized that pitting potential may result more from surface defects inherent in the manufacturing process of NiTi wires than directly from the effects of deflection. The amount of deflection or stress on the wire could also effect corrosion and it is possible that the 1 mm deflection over 13.3 mm length tested in this study was not sufficient for alteration of the corrosion properties of the wire. These deflection parameters were tested because they were within the range of clinical activation used with a 16x22 NiTi archwire, but future studies should test varying deflection activations.

We detected a statistically significant interaction effect between wire type and deflection state for area integration and similar but nonsignificant trends for pitting potential and nickel release. IonGuard in a deflected state caused more corrosion during passivation and tended to exhibit more intense pitting corrosion and more nickel release. This could be explained by more surface cracking when the IonGuard wire was bent, exposing sub-microscopic cracks, more surface area and increased corrosion potential. The significant interaction effect for IonGuard but not NiTi could also be due to the nitrogen content in the archwire changing the tranformation temperature and stress (Gil 1998). Interestingly, the trend for deflected IonGuard was protective when it came to zero current potential. This is possible because the atomically tighter surface of titanium nitride is initially less penetrable than the NiTi surface, but as the voltage is increased and corrosion is forced, it breaks down more easily. With a larger sample size it would be clearer if these trends are true findings or simply a side effect of the small sample size and large variablity of the wires tested.

The SEM results of our study showed variability in the composition of wires, large titanium-rich inclusions and trace levels of chromium, sodium chloride, iron, carbon and silicates. The titanium-rich inclusions are formed because of titanium's higher melting point and cooling temperature causing it to cool more quickly during processing. Chromium was detected and is explained by its paragenic relationship with nickel. Nickel and chromium are mined together and not fully separated before manufacturing of archwires. Sodium chloride crystals were detected after forming in corrosion pits. Iron was detected, presumably as an artifact from the manufacturing process of the NiTi wires. Carbon and silicates were detected from dust, dirt and the tape used to hold the wires during SEM testing.

CONCLUSIONS

A significant effect of wire type or deflection state on corrosion and nickel release was not seen in our study. We cannot support the claims that IonGuard protects against corrosion or reduces nickel ion release. In fact, when IonGuard is deflected, we found corrosion occurs more rapidly and more robustly, as seen by the increased area integration during passivation. The data show trends for deflected IonGuard wires to have initial protective effects (more positive zero current potential values) but to exhibit corrosion at a greater intensity (higher pitting potential point current) and more nickel ion release. The large standard deviations kept many of the trends in the data from being statistically significant and therefore more research needs to be done. Variability in the NiTi manufacturing and ion implantation processes may explain the large standard deviations seen.

The amount of nickel release detected in this study ranged from 0-135.9 ug/L, which is similar to the range seen in passive soaking studies and clinical bioaccumulation studies. This supports our potentiodynamic anodic polarization methodology as being more clinically applicable than other testing methods. This nickel release range is less than the average daily dietary intake of 300-500 ug of nickel (Park 1983, House 2008), critical value necessary to induce allergy of 600-2500 ug (Huang 2003), and cytotoxic threshold concentration of 15-30 mg/L (Jai 1999). However, the range from our study included values greater than the 60 ug/L reported to often result in a hypersensitivity response in nickel-sensitized individuals (Fay 2005). As nickel hypersensitivity appears to be increasing due to more frequent use of nickel containing jewelry and increasing prevalence of piercings (Noble 2008), this remains an important area of research where we need better techniques and materials to limit nickel ion release.

FUTURE STUDIES

This study should be replicated with a larger sample size to statistically confirm our findings. The amount of deflection should be varied to test deflection over a clinically useful range. We should also repeat this experiment with alterations in the testing medium to look at the effects of pH, temperature, diet, fluoride, intraoral flora and other intraoral characteristics that have been shown to effect nickel release (Eliades and Athanasiou 2002). Newer methods of coatings and alterations of NiTi wires to prevent nickel release should be tested using similar methodologies to see how they compare to each other.

More in vivo studies on corrosion and nickel release need to be done because the in vitro studies do not directly correspond to the clinical situation. These in vivo studies need to be done over clinically useful time periods. NiTi wires could be in place for several months to a year depending on rotations present and time needed for initial leveling and alignment. Bonded lingual retainers, generally made out of stainless steel, could remain intraorally for the duration of a patient's lifetime and therefore even longer time periods need to be studied as well. Updated studies that define oxidation potential intraorally should be done and they should study patients in orthodontic appliances to confirm their accuracy in this specific patient population.

Future areas of ion implantation research may branch out into uses of selectively enhancing anchorage by application on brackets and wires, making more esthetic tooth colored wires, or to implant fluoride into archwires to reduce demineralization and white spot lesions (Ryan et al. 1997).

LITERATURE REVIEW

Nickel Hypersensitivity

The nickel hypersensitivity prevalence based on skin patch tests ranges from 0.9-30% (Kolokitha 2008) with a strong female predilection (Saglam 2004). Adverse reactions to orthodontic treatment has been estimated at 0.3-0.4% (Jacobsen 2003) with a harmful response to nickel estimated to occur in 0.1-0.2% of the orthodontic population or 1 out of every 500 to 1000 clinical patients (Kusy 2004). Five to twelve times higher concentrations of contact allergens are needed to cause hypersensitivity reactions on the oral mucosa than to elicit a reaction on skin (Magnusson 1982). The symptoms of local hypersensitivity reactions to dental alloys are metallic taste, changes in salivation, mucous irritations and burning sensation in or around the mouth (Magnusson 1982). Nickel has been shown to impair human polymorphonuclear leukocyte ability to phagocytose bacteria (at 0.05 mol/L nickel), inhibit leukocyte chemotaxis (at 2.5-50 ppm nickel), slow neutrophils and inhibit calcium ion-dependent contractile activity by depolarizing the neutrophil cell membrane. Nickel has also been shown to induce DNA damage by base damage and site specific DNA strand scission. (Eliades 2002). Nickel hypersensitivity appears to be increasing due to more frequent use of nickel containing jewelry and increasing prevalence of piercings (Noble 2008).

Kusy recommends all patients be asked for known allergies in the new patient questionnaire and those with potential nickel allergy should be tested with a skin patch test (Kusy 2004). The use of alternative treatment modalities should be considered in nickel hypersensitive patients. (Noble 2008, Kolokitha 2008, Eliades 2002). If a nickel sensitivity reaction occurs the practitioner should remove the appliances containing

nickel and treat with antihistamines, anesthetics or topical corticosteroids (Noble 2008). Noble described two cases of female patients with intraoral and perioral swelling, itching, burning, and discomfort that resolved fairly quickly after the removal of NiTi wires (Noble 2008). Several studies found that orthodontic treatment does not sensitize a patient to nickel allergy (Saglam 2004, Menezes 2004, Janson 1998, Kerosuo 1996), whereas Bass found an 8.7% conversion rate when they tested the patients 3 months after placement of orthodontic appliances (Bass 1993). A meta analysis in 2008 revealed that orthodontic treatment is not associated with increased nickel hypersensitivity, unless the patient had prior nickel exposure from cutaneous piercings (Kolokitha 2008). A survey of orthodontists and dentists revealed 46% had at least 1 adverse reaction in the past 5 years, a third of which occurred in patients with a history of nickel allergy (Kerosuo 2007). Noble concluded that "though an allergic response to nickel in the oral mucosa from nickel containing orthodontic appliances is more infrequent than from nickel contact on the epidermis, it can occur, particularly in females"(Noble 2008).

Kolokitha et al. (2008) performed a meta analysis to study the prevalence of nickel hypersensitivity in orthodontic patients. The literature review revealed 8 studies eligible for inclusion signifying a lack of high-validity longitudinal studies. The meta analysis found orthodontic treatment is not associated with increased nickel hypersensitivity, unless the patient had prior nickel exposure from cutaneous piercings. The nickel hypersensitivity prevalence ranged from 0.9-30% in the studies reviewed. Some studies showed that orthodontic exposure before cutaneous piercing may lower incidence of nickel hypersensitivity. The authors state that the possibility of orthodontic

appliances to elicit nickel hypersensitivity reactions is not negligible and that alternative treatment modalities can be used for patients that report nickel hypersensitivity.

Saglam et al. (2004) reported on the prevalence of nickel hypersensitivity reactions before and after orthodontic treatment. 82 patients were given a questionnaire and patch test to evaluate hypersensitivity and gingival tissue responses to nickel before, during and after orthodontic treatment. 14.5% of females examined and 0% of males reported a positive skin patch test for nickel. The authors hypothesized that nickel allergy is higher in females because women have more contact with nickel from jewelry, so they are sensitized at an early age. None of the patients displayed an allergic reaction in the gingiva. There was also no association between the before and after treatment hypersensitivity reaction to nickel.

Jacobsen and Hensten-Pettersen (1989) surveyed the Norwegian dental society about adverse reactions in orthodontics. 137 orthodontists responded and reported 425 patients with dermal reactions and 67 patients with intraoral/systemic reactions during the past two years. The authors estimate 1% of the orthodontic patient population exhibits some sort of adverse reactions. Adverse patient reactions were mostly irritant and hypersensitivity reactions, involving dermatoses of the face and neck and occasionally the mucosa and gingiva or systemic reactions. Intraoral reactions involved swelling, redness, soreness, or itching of the gingiva, palate, oral mucosa or lips. "Leaching of material components from these appliances is an essential first step in the development of hypersensitivity reactions. The metal parts of the orthodontic apparatus are often of the stainless steel or nickel containing types, which release known allergens such as nickel, chromium and cobalt."

Jacobsen and Hensten-Pettersen (2003) resurveyed Norwegian orthodontists to assess changes in adverse patient reactions. Symptoms reported ranged from localized inflammation, general allergic symptoms, and headache/general malaise. Adverse patient reactions decreased from 0.8-0.9% as measured in 1987 to 0.3-0.4% as measured in 2000. The new estimates correspond with adverse reactions expected in 1 out of every 300 patients. The decrease was seen mainly in extraoral reactions and was estimated to be due to new coating metallic devices for extraoral appliances. Intraoral reactions showed a small increase from 0.13% in 1987 to 0.18% in 2003, highlighting the need for more intraoral alterations to potential material-derived allergens. Metal appliances and the associated nickel release are considered the most frequent cause of intraoral reactions.

Kusy (2004) stated that 20% of women between ages 16 and 35 and 11% of all women and 2% of men of all age groups are sensitive to nickel. Kusy believed that "these frequencies are growing as wearing costume jewelry, body piercing, trace-element intake from foods, and environmental pollution continue to increase." Patients should be asked for known allergies in a questionnaire. If they indicate potential nickel allergy they should be evaluated for allergenic responses by a qualified professional using a skin patch test, as outlined by the 1984 recommendations of the Council of Dental Materials, Instruments, and Equipment and the Council on Dental Therapeutics. The skin test is more discriminating than the mucosal membrane test because the mucosal membrane is sloughed off, purging potential allergens more readily.

Magnusson et al. (1982) studied nickel allergy and reactions to nickel-containing dental alloys using patch tests because all dental alloys corrode to some extent. Test pieces of dental cobalt-chromium alloys with 1-7% nickel by weight were attached as

patch tests on the backs of 10 women with known contact nickel allergy. Test pieces were also placed in physiologic NaCl solution and the release of nickel and cobalt was determined by atomic absorption spectrophotometry. All ten subjects showed positive reactions to the patch test. In the alloys containing 7% nickel by weight 130 ug nickel release was detected after 5 days and in alloys with 34% nickel by weight, 365 ug nickel release was detected. Higher concentrations of contact allergens are needed to cause reactions on the oral mucosa, with some studies showing between 5-12 times higher concentrations needed than to elicit a reaction on skin. Magnusson also discussed oral administration of nickel aggravating eczema on the hands and other symptoms of local hypersensitivity reactions to dental alloys, such as metallic taste, increased or decreased salivation, mucous irritations and burning sensation in or around the mouth.

Eliades et al. (2002) reviewed aging of orthodontic appliances and the implications for corrosion, nickel release and biocompatibility. Nickel has been shown to impair human polymorphonuclear leukocyte ability to phagocytose bacteria (at 0.05 mol/L nickel), inhibit leukocyte chemotaxis (at 2.5-50 ppm nickel), slow neutrophils and inhibit calcium ion-dependent contractile activity by depolarizing the neutrophil cell membrane. Nickel has also been shown to induce DNA damage by base damage and site specific DNA strand scission. Many of the previous studies on this topic are flawed. In vitro testing does not accurately mimic intraoral environments because they lack the extreme variations in pH, temperature, stress, intraoral flora and their byproducts, plaque, and agitated electrolytes that occur intraorally. Enamel may also adsorb corrosive products which would alter the environment. A proteinaceous film has been observed on NiTi wires after intraoral use and may have a protective effect on corrosion. Serum

studies are flawed because nickel could have been accumulated in an organ and therefore nickel release could be underestimated. Retrieval analysis of used samples is flawed because they do not have any direct evidence of the intraoral process and must rely on inferences. Most in vivo studies are flawed because the observation period is substantially shorter than would occur clinically and collection methods occur at discrete time points rather than continuously. Manufacturing defects and surface irregularity accelerates the corrosion process intraorally. Orthodontic treatment with nickel containing appliances before the patient is sensitized to nickel (usually through ear piercing) may lead to a lower incidence of nickel hypersensitivity. The current thought is that the risk of nickel from orthodontic appliances acting as a sensitizing agent is extremely low in patients who are not hypersensitive to nickel at the start of treatment. The authors suggest using nickel alternatives in patients who have a history of hypersensitivity. The titanium nitride process is mentioned as a nickel alternative that provides poor protection against nickel release.

Noble et al. (2008) performed a review of nickel allergy and orthodontics and reported two cases. The authors hypothesize that nickel sensitivity is increasing due to more frequent use of nickel containing jewelry and intraoral piercings. Nickel leaching from orthodontic appliances has been shown in vitro to maximally occur within the first week and increase significantly when combined with fluoride. Nickel sensitivity has been found to be higher in asthmatic patients. If an adverse reaction occurs the practitioner should remove the NiTi wire and use a stainless steel wire or titanium molybdenum alloy (TMA), which does not contain nickel. If the reaction continues all stainless steel archwires and brackets should be removed. With a severe allergic reaction,

the patient should be treated by a physician with antihistamines, anesthetics or topical corticosteroids. Nickel free brackets include ceramic brackets, polycarbonate brackets or plastic aligners. Two cases of nickel sensitivity were reported. The first patient was a 31 year old female who presented with an "anesthetic-like" feeling in her lips and swelling of the lips. The symptoms resolved five hours after the removal of NiTi wires. The second case was a 15 year old female with intermittent oro-pharyngeal "itching, sandpaper-like roughness, bumps, burning and strong discomfort" which persisted for 6 months. Orthodontic treatment had begun just prior to these symptoms. The NiTi wires were replaced with stainless steel and her symptoms resolved within two weeks. The authors conclude that "though an allergic response to nickel in the oral mucosa from nickel containing orthodontic appliances is more infrequent than from nickel contact on the epidermis, it can occur, particularly in females."

Menezes et al. (2004) studied the incidence of hypersensitivity of metals in orthodontics by using patch tests before and 2 months after placement of orthodontic appliances. Thirty-eight patients were tested for cobalt chloride, copper sulfate, potassium dichromate, iron sulfate, manganese chloride, molybdenum salt, nickel sulfate, and titanium oxide with patch tests on their backs. Positive reactions were elicited from 21.1 % of patients for nickel sulfate and potassium dichromate and 7.9% for manganese chloride. Nickel sulfate caused the reaction with the greatest intensity. No difference was observed before or after the placement of orthodontic appliances, indicating that patients are not sensitized to or made tolerant of metals because of orthodontic appliances.

Janson et al. (1998) studied nickel hypersensitivity before, during and after orthodontic treatment. Nickel patch tests and questionnaire's were given to 170 total patients divided into three groups, one before, one during and one after orthodontic treatment. 28.3% of the subjects showed an allergic reaction to the nickel patch test. A gender difference was observed with 23% female and 5.3% male displaying hypersensitivity reactions. A positive association was found between nickel hypersensitivity and previous allergic history to metals and daily use of metal objects. No difference was found between the three groups, suggesting that orthodontic treatment does not initiate or aggravate a nickel hypersensitivity reaction.

Kerosuo et al. (1996) reported on nickel allergy in adolescents in relation to orthodontic treatment and piercing of the ears. Seven hundred Finnish adolescents were patch tested for nickel allergy and given a questionnaire to find out about age of ear piercing. Nineteen percent of the whole group displayed a nickel allergy. The 68% who had been treated orthodontically showed the same incidence of nickel hypersensitivity. Orthodontic treatment did not seem to affect the prevalence of nickel sensitization. None of the girls treated orthodontically before having their ears pierced showed nickel sensitivity but 35% of girls who had their ears pierced first displayed nickel hypersensitivity. These results suggest that orthodontic treatment before sensitization to nickel, generally through ear-piercing, may reduce the frequency of nickel hypersensitivity. Van der Berg et al found that junior nurses who had had orthodontic treatment at an early age had a lower frequency of nickel allergy than nurses who had no history of treatment. Also reduced frequency of nickel allergy was observed in patients who had had orthodontic treatment at least 6 months before piercing their ears. Nickel

sensitivity was more prevalent in females 30% than males 3%. Olumide found equal rates of nickel sensitization for men and women in Nigeria where similar traditions exist for wearing jewelry for both sexes.

Kerosuo and Dahl (2007) assessed adverse patient reactions during orthodontic treatment with nickel-containing appliances and evaluated the need for and use of nickel-free appliances. They mailed a questionnaire to orthodontists and dentists in Finland and Norway which asked them to retrospectively assess the number of patients with adverse reactions, appliances used, implications on treatment, history of nickel allergy in patients with adverse reactions, and use of and need for nickel-free appliances. Of the 298 responses, 46% had at least 1 adverse reaction in the past 5 years. Headgear was the appliance most commonly attributed to adverse reactions. One third of respondents reported an adverse reaction in patients with a history of nickel allergy. In 58% of patients with adverse reactions, the practitioner changed appliances or discontinue treatment. Most respondents use nickel-containing fixed appliances in nickel-allergic patients. More than half of those surveyed had used nickel-free alternatives due to risk of allergy for at least 1 patient, but only 7% had used nickel-free appliances in more than 10 patients during the last 5 years. Twenty-five percent of respondents expressed no need for nickel-free appliances, 57% expressed occasional need and 18% expressed a slight, but constant need. This study concluded that adverse patient reactions are infrequently associated with orthodontic appliances, even with the high prevalence of nickel allergy in women.

Pantuzo et al. (2007) used a cutaneous sensitivity patch test in 58 patients to test the allergenic potential of conventional metallic orthodontic brackets and "nickel-free"

brackets. Nickel is added to many orthodontic appliances to increase the corrosion resistance and reduce oxidation at high temperatures. Unfortunately when these alloys are present in the oral cavity they corrode and release nickel ions. Because ion release from orthodontic appliances can cause an allergic reaction in the oral cavity, the metallurgical industry has supported research to find hypoallergenic orthodontic accessories. The authors found a significant positive association between patients that were sensitive to nickel and those with a history of contact allergy, highlighting the importance of asking about metal allergies in the patient questionnaire. Twenty-seven percent of the 58 patients evaluated were sensitive to nickel. Of the 16 patients that showed sensitivity to the initial sensitivity patch test, 20.7% showed sensitivity to the test specimen containing nickel while 8.6% were also allergic to the nickel-free test specimen. Therefore, nickel-free test specimen caused a smaller allergic reaction in 31% of patients sensitive to nickel.

In a letter to the editor in the AJODO (2004), David Tidy expressed his concern that we are making too big a deal out of nickel-sensitivity and that "intra-oral reactions are exceedingly rare and even when encountered, are not a major threat to health. These occasional reactions are hardly sufficient ground for denying the benefit of nickel-titanium archwires to all nickel-sensitive patients." Dr. Rahilly and Dr. Price responded that "patients with known nickel sensitivity should be informed that they are at a higher risk of an allergic response from high content nickel titanium archwires. It would therefore be sensible to consider the use of nickel-free alternatives in these patients."

Bass et al. (1993) reported on nickel hypersensitivity in the orthodontic patient. They used a nickel patch test before and after orthodontic treatment to see if treatment

can sensitize a patient. They also measured gingival index, plaque index, and took photographs. They detected an initial nickel sensitivity prevalence of 17.2% with patch tests. There was an 8.7% conversion rate when they tested the patients 3 months after placement of orthodontic appliances. None of the patients that originally had nickel sensitive patch tests showed any signs of nickel hypersensitivity during treatment. The authors speculate that higher concentrations (5-12 times higher have been reported by Nielsen and Klaschka 1971) of allergen are needed to produce a response on the oral mucosa than the skin. Spiechowicz et al. (1984) speculated this could be due to salivary glycoprotein films acting as diffusion barriers, permeability differences between skin and mucosa, different cellular hypersensitivity mechanisms between skin and mucosa and differences in the distribution and function of Langerhans cells.

Nickel Ion Release

Passive nickel release of a quadrant of bands, brackets and stainless steel archwire in sodium chloride solution for 12 days was measured and lead to an estimate that 40 ug of nickel would be released from full-mouth appliances per day (Park 1983). Staffolani (1999) studied a complete arch of appliances with a NiTi wire in varied pH organic and inorganic solutions for 1-28 days and found ion release increased as pH decreased. Nickel ion release was highest the first day and then levels dropped considerably afterwards. pH and organic vs. inorganic solution affected the nickel release. 2.75 ug/L nickel release was detected the first day and a cumulative 8.73 ug/L nickel release was detected after 28 days in inorganic solutions at pH 3.5 compared to 6.7 ug/L initially to 10.49 ug/L cumulative detection in organic acid solution for an arch

of appliances. Huang (2003) studied nickel release from NiTi wires in artificial saliva for 1-28 days at varying pH. RMO wire exhibited the greatest release of nickel ions, with a release of 4.7 ug/cm^2 when immersed for 1 day in pH 2.5 solution. Wever (1998) looked at passive nickel release from NiTi wires in Hank's solution after 1, 2, 3, 7, 10, 17 and 31 days. Initial nickel release was detected at 14.5x10-7 ug/ cm^2 s but could not be detected anymore after 10 days. The authors also found a TiO_2- based passivation layer on the surface of NiTi wire and an outer calcium phosphate layer after soaking, which may serve as a second barrier against ion diffusion. The anodic polarization showed better resistance to chemical breakdown of passivity for NiTi alloy compared to SS, based on a larger difference between the corrosion and breakdown potential. Kerosuo (1995) studied half arch fixed appliances with NiTi wire immersed in sodium chloride for 2 hours, 24 hours and 7 days either statically or mounted to an "oral functioning simulator." The static condition showed an average of 17.1 ug of cumulative nickel release after 8 days while the dynamic condition showed a significantly higher nickel release of 44.2 ug. These values lead to estimates of 22 ug of nickel release per day with full fixed ortho appliances under functional stress. Gil (1998) passively soaked NiTi archwires with and without ion implantation treatment in artificial saliva and the NiTi with nitride showed less nickel release (plateaued after 250 hours around 50 ug/L compared to 200 ug/L for NiTi). Widu (1999) used potentiostatic test to determine rupture potentials and subsequent nickel release of several types of archwires. NeoSentalloy wire had a rupture potential of 370-420 mV and a nickel concentration after 10 minutes of 3.1-17.7 mg/l. The Neo Sentalloy and Titanium Memory wire showed a high tendency toward corrosion, while the Ni-Ti wire and Nitinol displayed low

corrosion tendency which was similar to the control TMA and SS wires. In all the studies observed, except Widu 1999, the nickel release values were small compared to the average daily dietary intake of 300-500 ug of nickel (Park 1983, House 2008) and below the critical value necessary to induce allergy, which is 600-2500 ug (Huang 2003).

House et al. (2008) reviewed corrosion of orthodontic appliances and the potential mechanical, clinical and health implications. Corrosion occurs from simultaneous oxidation and reduction reactions. Orthodontic appliances form a passive surface oxide film to resist corrosion, but this is susceptible to mechanical and chemical disruption. There are many types of corrosion that can occur intraorally: uniform attack, pitting and crevice corrosion, galvanic corrosion, intergranular corrosion, fretting corrosion, stress corrosion, and microbiologically influenced corrosion. Uniform attack is the most common type of corrosion and it affects all metals at varying rates. Pitting and crevice corrosion occurs on orthodontic wires and brackets because they do not have a smooth uniform finish. Hunt et al has demonstrated that polishing NiTi wires reduces the corrosion rate. Galvanic corrosion occurs when two dissimilar metals are joined. In a study assessing potential cytotoxicity of orthodontic appliances, only used stainless steel bands with soldered buccal tubes showed potential fibroblast cytotoxicity. Intergranular corrosion occurs especially with stainless steel during brazing and welding. Fretting corrosion occurs where metal is subjected to sustained loads, such as a bracket-archwire interface. Stress corrosion occurs when an archwire is ligated to a bracket and the reactivity of the metal increases due to loading at stress sites. Microbiologically influenced corrosion occurs as microbes absorb and metabolize metals and their by-products alter the environmental conditions making them more conducive to corrosion.

Many in vitro studies have shown that corrosion susceptibility is increased when in a fluoridated, acidic environment. In vivo studies have not demonstrated a corrosive influence of fluoride-containing toothpastes and teas on titanium or stainless steel brackets. This suggests that fluoride may not play as large a role in corrosion of orthodontic appliances clinically. Manufacturing techniques, such as alloying, heat treatment, cold working and finishing and polishing affect the corrosion of an alloy. Corrosion has also been implicated as a potential cause of wire fracture. General conclusions about wire fracture show that the cause is multifactorial, with corrosion, surface finish, and work hardening during treatment all potential contributors. The incidence of adverse reactions in orthodontics has been estimated at 1:100, with contact dermatitis being responsible for 85% of them, mostly due to headgear. Several studies have shown nickel is released into saliva from orthodontic appliances, but levels are far lower than normal dietary intake. Higher levels of nickel are released from headgear facebows because they contain silver solder which is capable of forming galvanic couples. A study that collected serum and saliva samples found that nickel levels are increased in saliva during the first month but they remained far below the average daily dietary intake. Serum levels of nickel did not differ throughout the study showing that although nickel was detected in saliva it is not absorbed into the bloodstream. Ryhanen et al found a lack of cytotoxic effect of NiTi wires on human fibroblasts. Higher concentrations of contact allergens are required to cause a hypersensitivity reaction on the oral mucosa than on the skin. The conclusions from this review are that "although corrosion of orthodontic devices occurs, it does not appear to result in significant destruction of the metallic components or have significant detrimental effects on

mechanical properties." Nickel ions are released during orthodontic treatment, but the level is far lower than that ingested in an average daily diet. Previous nickel sensitivity and patient's age are the best indicators of nickel hypersensitivity. The relation is not entirely clear and there are some studies that show orthodontic treatment can improve the immune systems tolerance of nickel. "The impact of corrosion on orthodontic treatment and the health of our patients is not well understood. Based on the best current evidence, it does not appear to be a process that should cause concern."

Park and Shearer (1983) reported on the in vitro release of nickel and chromium from simulated orthodontic appliances. Ten simulated orthodontic appliances were fabricated for half of the mandibular arch with bands on the molars and premolars, bonded brackets for the incisors and canines and a stainless steel archwire. The appliances were placed in 0.5% sodium chloride solution for 12 days and elutes were tested by atomic absorption spectrophotometry. Significant amounts of nickel and chromium were released into solution with a total cumulative release of 121 ug of nickel and 40 ug of chromium after 12 days. Based on four quadrants, this study found 40 ug nickel and 36 ug chromium would be released per day from a simulated full-mouth appliance. These findings are below the average daily dietary intake of 300-500 ug of nickel. Despite this, the authors warn that "the clinician should be aware that the release of the metal ions may cause a local hypersensitivity reaction at oral soft-tissue sites."

Staffolani et al. (1999) reported on ion release from orthodontic appliances. This study evaluated the corrosion rate of a complete arch of orthodontic appliances- bands, brackets and a NiTi archwire. Ion release of appliances soaked in organic and inorganic solutions with varying pH for 1-28 days was measured with an atomic absorption

spectrophotometer. Ion release increased as pH decreased. Ion release was highest the first day and then levels dropped considerably afterwards. Lower pH and organic solutions caused more nickel release. 2.75 ug/L nickel release was detected the first day and a cumulative 8.73 ug/L nickel release was detected after 28 days in inorganic solutions at pH 3.5 compared to 6.74 ug/L initially to 10.49 ug/L cumulative detection in organic acid solution for an arch of appliances. Even if values of nickel release were doubled to simulate upper and lower appliances, they would still be extremely small compared to the amount of nickel consumed in the diet. The authors speculate that in vivo, oral hygiene could be an important factor in reducing corrosion because organic acids facilitate the release of metal ions. They also hypothesize that the movement of archwires and friction could cause further corrosion and might increase the release of metal ions from orthodontic appliances in vivo situations. This study concludes "it appears the quantities of metals released in our experiments are low to be cause for concern in utilizing the appliance."

Huang et al. (2003) studied ion release from NiTi wires in artificial saliva with various acidities. Four types of NiTi wires were immersed in artificial saliva at pH varying 2.5-6.25 for varying periods of 1-28 days. Atomic adsorption spectrophotometer determined the amount of nickel and titanium ions released. The morphology of the wire was studied using a SEM. Manufacturer, pH value and immersion period had an effect on ion release. The amount of nickel ions released was below the daily dietary intake level of 300-500 ug and below the critical value necessary to induce allergy 600-2500 ug. Surface defects may be the preferred locations for corrosion due to higher residual stress

and/or non-uniform passive film on the defects. RMO wire exhibited the greatest release of nickel ions, with a release of 4.7 ug/cm^2 when immersed for 1 day in pH 2.5 solution.

Wever et al. (1998) used anodic polarization and x-ray photoelectron spectroscopy (XPS) to study the electrochemical and surface characterization of NiTi wire. XPS was conducted on samples after immersion in Hank's solution for 1, 3, and 17 days. Atomic absorption spectrophotometer was used to determine passive nickel release from Hank's solutions after 1, 2, 3, 7, 10, 17 and 31 days. The authors detected the outermost surface layer of NiTi to be a TiO_2- based passivation layer with minimal amounts of nickel. A calcium phosphate layer was detected on the passive oxide film after soaking in Hank's solution and may serve as a second barrier against ion diffusion. Initial nickel release was detected at 14.5x10-7 ug/cm^{2}s but could not detected anymore after 10 days. The anodic polarization showed better resistance to chemical breakdown of passivity for NiTi alloy compared to SS, based on a larger difference between the corrosion and breakdown potential. The authors conclude that NiTi is a biologically safe material.

Kerosuo et al. (1995) reported on in vitro release of nickel and chromium from simulated orthodontic appliances. Five identical fixed appliances, headgear and quad helixes were constructed for half a simulated dental arch and immersed in sodium chloride for 2 hours, 24 hours and 7 days. A fixed appliance was mounted to an "oral functioning simulator" to see the effects of movement on nickel release. The dynamic conditions were also immersed in sodium chloride and elutes were collected at the same time intervals. The amount of nickel and chromium released were analyzed by flameless atomic absorption spectrophotometry. This study found a detectable release of nickel

from simulated stainless steel fixed appliances. The static condition showed an average of 17.1 ug of cumulative nickel release after 8 days while the dynamic condition showed a significantly higher nickel release of 44.2 ug. Orthodontic appliances in the mouth are exposed to rubbing, stress and friction due to masticatory function and this affects ion release. Dietary intake of nickel is reported between 130- 165 ug/ day and this study found 22 ug of nickel release per day with full fixed ortho appliances under functional stress. "According to most recent studies, nickel-containing prosthetic and orthodontic appliances are generally quite well tolerated, even by nickel-sensitive individuals, and oral administration of nickel has been reported to induce immunological tolerance to nickel in guinea pigs." Kerosuo states that "the quantities released may be negligible from a toxicological standpoint, but might conceivably be of importance in individuals with a high degree of hypersensitivity to nickel."

Widu et al. (1999) studied the corrosion and biocompatibility of orthodontic wires using anodic polarization. They state that "patients who are already sensitized to nickel can show allergic reactions caused by nickel loss from orthodontic devices." They also comment that "growing numbers of orthodontic treatments and the increasing prevalence of nickel allergy in the population require a minimization of the nickel loss from NiTi wires in the oral cavity." The corrosion of a wire could lead to negative consequences on esthetics, biocompatibility and treatment progress due to increased friction. They exposed four nickel-titanium, a titanium-molybdenum and a stainless steel arch wire to pure potentiostatic, pure mechanical and combined potentiostatic and mechanical stresses. Anodic polarization was used to accelerate the corrosion process, which occurs naturally very slowly. The wires were then analyzed for surface changes using atomic

force microscopy (AFM) and nickel loss using atomic absorption spectrophotometer. The NeoSentalloy wires from GAC appeared to be the roughest from AFM analysis. The different brands of NiTi wire showed variability in their corrosion behavior, partly due to differences in production and finishing processes. The Titanium Memory wire and Neo Sentalloy had a high tendency toward corrosion, while the Ni-Ti wire and Nitinol displayed low corrosion tendency which was similar to the control TMA and SS wires. High tendency towards corrosion was defined by low rupture potential (less than 600 mV/NHE) and nickel release between 3.1 and 39.4 mg/L, whereas low tendency toward corrosion was defined by high rupture potential (greater than 600 mV/NHE) and less than 1 mg/L nickel release. NeoSentalloy wire had a rupture potential of 370-420 mV and a nickel concentration after 10 minutes of 3.1 mg/L at 0.72 V/NHE and 17.7 mg/L at 1.22 V/NHE. The authors state that "transfer of laboratory results to the intra-oral situation is impossible as potentiostatic loads in the mouth are much smaller than under laboratory conditions."

Mechanical Loading/ Stress/ Wire Deflection and Corrosion

Segal (2009) studied Sentalloy (at 37 and 5 degrees C) and TMA (at 37 degrees C) wires during electrochemical corrosion tests while deflected 0, 0.75, 1.5 and 3.0 mm. All wires showed their lowest mean corrosion current density when not deflected and increased levels when deflected, often to significant levels, leading to the conclusion that stress increases corrosion rates in orthodontic wires. Because pitting potentials showed no consistent patterns for deflection, stress might not be a factor in susceptibility to localized pitting corrosion, which may result more from surface defects inherent in the

manufacturing process of NiTi wires. The authors stated that alterations in stress associated with phase transformation in superelastic NiTi wires may alter corrosion rates differently than wires not concurrently undergoing phase transformation. Liu (2007) deflected NiTi wire 3 mm during electrochemical testing and found stressed wires showed more corrosion potential, higher corrosion current density, lower polarization resistance and lower passive current. SEM revealed evidence of localized corrosion after electrochemical testing. Jai (1999) found that wires strained either statically or cyclically with an Instrom machine for 24 hours showed significantly more nickel release than those that were passively soaked, with a range of 0.4-4.1 ug/L. Peitsch (2007) found that wires mechanically loaded at a loading frequency of 5 Hz released significantly more nickel (~45ng/ cm^2d) compared to nonloaded wires (<1ng/ cm^2d) after passively soaking them.

Huang (2003) stressed NiTi wires in a tensile test machine with 0, 50, 100 and 150 g and tested them with potentiodynamic tests in artificial saliva at varying pHs. The load had no influence on pitting potential, protection potential, and passive current density. Mean pitting potential of NiTi wire occured at less than 330 mV (SCE), which they stated could occur intraorally as the potentials of implant materials intraorally are between 100- 500 mV(SCE) by Hoar and Mears (1966). Other studies have followed the clinically applicable range of -58 to +212 mV (SCE) established by Ewers (1985), which would make these pitting potential values clinically unlikely. Rondelli (2000) used anodic polarization to study NiTi wire either straight and arched with 4% strain and found no effect of strain or stress induced martensite phase transformation on the corrosion behavior as measured by pitting and corrosion potential.

Segal et al. (2009) studied the influence of stress and phase on corrosion of a superelastic nickel- titanium orthodontic wire. Sentalloy (at 37 and 5 degrees C) and TMA (at 37 degrees C) wires were subjected to electrochemical corrosion tests while deflected 0, 0.75, 1.5 and 3.0 mm. The martensite to austenite transformation begins at -3.8 degrees C and ends at 23.9 degrees C. On cooling, the austenite to martensite transformation begins at 19.7 degree C and ends at 12.2 degrees C. The Sentalloy wire is austenite at 37 degrees and predominantly martensite at 5 degrees. However, at 1 mm of deflection, the Sentalloy archwire showed signs of phase transformation from austenite to martensite. Significant differences were detected in OCP and corrosion current density for the three wires and deflection groups but a consistent trend was not observed. All three wires showed their lowest mean corrosion current density when not deflected and increased levels when deflected, often to significant levels, leading to the conclusion that stress increases corrosion rates in orthodontic wires. Pitting potential for the Sentalloy wires showed no apparent pattern among the different deflection groups but had a mean of 353 +/- 76 mV. These findings indicate that stress might not be a factor in susceptibility to localized corrosion, which may result more from surface defects inherent in the manufacturing process of NiTi wires acting as initiation sites for localized corrosion. The authors summarize that alterations in stress associated with phase transformation in superelastic NiTi wires may alter corrosion rate differently than wires not concurrently undergoing phase transformation.

Liu et al. (2007) looked at the effect of load deflection on corrosion behavior of NiTi wire. A three point bending force that deflected the wire 3 mm was applied to NiTi archwires during electrochemical testing. Stressed wires showed more corrosion

potential, higher corrosion current density, lower polarization resistance and lower passive current. The authors hypothesize that the wire deflection caused areas of cracking and buckling of the oxide layer which left the wire susceptible to corrosion. SEM revealed evidence of localized corrosion after electrochemical testing.

Huang (2003) investigated the corroison resistance of stressed NiTi and stainless steel (SS) orthodontic wires in acid artificial saliva (pH 2 and 5) using potentiodynamic tests. The wires were loaded with a custom-made tensile test machine with 0, 50, 100 and 150 g. SEM of as received wires showed more surface roughness and defects of NiTi wires than SS, presumably caused by the production process. SEM after cyclic potentiodynamic tests showed pits in both NiTi and SS wire. The results showed that pH had a significant influence on corrosion parameters (pitting potential, protection potential, and passive current density) but load had no influence. Lower pH showed decreased pitting potential and passive ranges for stressed NiTi and SS, with a more significant decrease seen for SS. The mean pitting potential and passive ranges were lower for NiTi wires than for SS, regardless of pH or load. Mean pitting potential occured at less than 330 mV (SCE) for NiTi wires tested. The article referenced Hoar and Mears (1966) stating that the potentials of implant materials intraorally are between 100- 500 mV(SCE)- which would make NiTi susceptible to pitting in vivo. NiTi wire was less susceptible to crevice corrosion than SS, as evidenced by the lower passive current density for NiTi.

Rondelli and Vincentini (2000) looked at the passive film stability of NiTi wires when stressed using anodic polarization. The passivating film on NiTi is primarily made of TiO_2. Potentiodynamic tests were performed on various types of NiTi, stainless steel,

cobalt-chromium alloy and titanium wire in NaCl and artificial saliva. The NiTi wire was tested in both straight and arched configurations. Scratch tests were also performed to see how quickly a passivation film could reform. No effect of 4% strain or stress induced martensite phase transformation was observed on the corrosion behavior. No effect of electrolyte solution type -NaCl or artificial saliva was detected. The NiTi alloy displayed a low repassivation capacity, lower than the other wire types tested.

Evidence of Bioaccumulation of Nickel Ion Release

Contact dermatitis from nickel is the most common adverse health effect of nickel and occurs in 10-20% of the general population (Klaassen 2008). In humans, 29-40% of an orally ingested stable nickel isotope was absorbed, compared to 55-77% absorbed from occluded skin, which could explain the decreased likelihood of oral hypersensitivity reaction (Fay 2005). Nickel is absorbed into the gastrointestinal tract as a lipophilic, low molecular weight compound (Fay 2005) through calcium or iron channels or by the divalent metal transport protein-1 and transported in the blood by albumin, histidine and alpha2-microglobulin (Klaassen 2008). Nickel is eliminated from the body in urine, hair, skin, milk, and sweat. The average daily intake of nickel from the diet is 69-162 ug, from drinking water is 8 ug and from air inhalation is 0.04 ug. Foods with high nickel content are oatmeal, spinach, asparagus and peas. Nuts have 3 ug/L nickel and cocoa has 10 ug/L. 2-12 ug of nickel are inhaled for each pack of cigarettes. Nickel levels in drinking water range from 0.55 to 25 ug/L. The average dietary nickel intake for the US population is 0.374 ug/kg body weight/day. One study found that the sensitizing level for nickel was 100-1,000 times higher than the level needed to cause a hypersensitivity

reaction in a previously sensitized individual. Oral exposure of 0.06 mg Ni/kg will often result in a hypersensitivity response in nickel-sensitized individuals (Fay 2005).

Petoumenou (2009) looked at saliva samples before orthodontic treatment, immediately after bonding, after 2 weeks, after placing NiTi archwires, 4 weeks later and 8 weeks later. The nickel concentrations differed up to 100 ug/L between patients with a median 34 ug/L pretreatment. There was an increase in nickel concentration after bracket placement, median 78 ug/L and after NiTi wire placement, median 56 ug/L. Souza (2008) studied patients with removeable appliances with bonded brackets and collected saliva samples before, and 10 minutes, 24 hours, 7 days, 30 days and 60 days after appliance delivery. They detected increased nickel immediately after appliance placement (1.72 ug/L as compared to 0.64 ug/L before placement) and large variation in ion concentration among individuals. In vivo corrosion appears to level off quickly which may result from the formation of a protective biofilm on the brackets. Agaolu (2001) measured saliva and serum nickel levels in 20 patients from each of these five groups: before treatment, 1 week, 1 month, 1 year and 2 year after appliance placement. Nickel salivary levels were highest in the first month and decreased to initial levels in the rest of the groups with a range of 4.12-11.53 ug/L. Serum levels showed significant increases in ion concentration in the second-year group. Serum nickel levels were detected between 7.87-10.27 ug/L compared to normal serum levels of 0.2 ug/L. Amini (2008) found that the nickel content in the oral mucosa of orthodontic patients was significantly higher than controls 21.74 versus 12.26 ng/ml. Menezes (2007) analyzed urine samples before and 2 months after orthodontic appliances were placed and found a significant increase in nickel after appliance placement.

The Toxicological Update for Nickel (Fay 2005) showed that in humans, 29-40% of an orally ingested stable nickel isotope was absorbed, compared to 55-77% absorbed from occluded skin. Nickel is absorbed into the gastrointestinal tract as a lipophilic, low molecular weight compound and is transported in the plasma by binding to albumin. The primary target of nickel toxicity is the respiratory tract after inhalation of nickel, the immune system after inhalation, oral or dermal exposure and possibly the reproductive system and developing organism after oral exposure. Chronic bronchitis, reduced lung function and cancer of the lungs and nasal sinuses, are the most serious harmful effects of nickel and have occurred after inhalation of nickel in nickel refineries or nickel-processing plants. "The U.S. Department of Health and Human Services (DHHS) has determined that nickel metal may reasonably be anticipated to be a carcinogen and nickel compounds are known human carcinogens. The International Agency for Research on Cancer (IARC) has determined that some nickel compounds are carcinogenic to humans and that metallic nickel may possibly be carcinogenic to humans. The EPA has determined that nickel refinery dust and nickel subsulfides are human carcinogens." Animal studies with oral exposure to nickel at levels much greater than those normally found in the diet have produced lung disease in dogs and rats, and affected the stomach, blood, liver, kidneys, immune system and reproduction and development in rats and mice. The summary states that when nickel is administered orally, no tissues accumulate nickel significantly. Nickel is eliminated from the body in urine, hair, skin, milk, and sweat. Nickel is thought to play roles as cofactors in metalloenzymes or as a cofactor that helps with iron absorption from the intestines. The average daily intake of nickel

from the diet is 69-162 ug, from drinking water is 8 ug and from air inhalation is 0.04 ug. Foods with high nickel content are oatmeal, spinach, asparagus and peas. Nuts have 3 ug/L nickel and cocoa has 10 ug/L. 2-12 ug of nickel are inhaled for each pack of cigarettes. Nickel levels in drinking water range from 0.55 to 25 ug/L. The average dietary nickel intake for the US population is 0.374 ug/kg body weight/day. The authors state that "after an individual becomes sensitized to nickel, dermal contact with a small amount of nickel or oral exposure to fairly low doses of nickel can result in dermatitis." One study found that the sensitizing level for nickel was 100-1,000 times higher than the level needed to cause a hypersensitivity reaction in a previously sensitized individual. Oral exposure of 0.06 mg Ni/kg will often result in a hypersensitivity response in nickel-sensitized individuals. Some studies found a genetic susceptibility factor that may predispose some people to develop nickel sensitivity. The report states that the amount of nickel in foods and drinking water are "too low to be of concern."

The textbook Toxicology The Basic Science of Poisons (Klaassen 2008) states that "nickel is ubiquitous in nature, and the general population is exposed to low levels of nickel in air, cigarette smoke, water, and food. These exposures are generally too low to be of toxicological concern." Nickel is absorbed in the intestines through calcium or iron channels or by the divalent metal transport protein-1 and transported in the blood by albumin, histidine and alpha2-microglobulin. The authors state that urinary nickel may serve as a suitable measure of current nickel exposure. Contact dermatitis from nickel is the most common adverse health effect of nickel and occurs in 10-20% of the general population. Nickel can cause "genotoxicity, producing DNA strand breaks, mutations, chromosomal damage, cell transformation, and modulation of DNA repair." "The

carcinogenic properties of metallic nickel are believed to be due to ionic nickel, which can slowly dissolve in the body from nickel compounds."

Petoumenou et al. (2009) looked at nickel concentration in saliva of patients with nickel titanium appliances. The introduction speculates that nickel hypersensitivity may occur by nickel activating monocytes and endothelial cells and changing the concentration of intercellular adhesion molecule-1 (ICAM-1) by endothelial cells. Arsenides and sulphides are nickel complexes that are carcinogenic, allergenic and mutating substances. Nickel has also been shown to induce DNA alterations by base damage and site-specific DNA strand scission as it inhibits enzymes that restore DNA breaks. Dietary ingestion and inhalation of nickel is estimated to be 74 ug per day. Patients supplied saliva samples before ortho treatment, immediately after bonding, after 2 weeks, after placing archwires, 4 weeks later and 8 weeks later. The nickel concentrations differed up to 100 ug/L between patients before treatment with a median 34 ug/L pretreatment. There was an increase in nickel concentration after bracket placement (median 78 ug/L) and after NiTi wire placement (median 56 ug/L).

Souza et al. (2008) studied nickel levels in saliva in patients with simulated fixed orthodontic appliances. Removeable appliances with bonded brackets were worn for 60 days and saliva was collected before and 10 minutes, 24 hours, 7 days, 30 days and 60 days after appliance delivery. They detected increased nickel immediately after appliance placement (1.72 ug/L as compared to 0.64 ug/L before placement) and large variation in ion concentration among individuals. In vivo corrosion appears to level off quickly which may result from the formation of a protective biofilm on the brackets.

Agaoglu et al. (2001) studied the nickel and chromium levels in saliva and serum of patients with fixed orthodontic appliances. Blood and saliva were collected from 100 patients total in five different groups- before treatment, 1 week, 1 month, 1 year and 2 years after appliance insertion. Electrothermal atomic absorption spectrophotometry was used to determine the nickel and chromium levels. Serum levels showed significant increases in ion concentration in the second-year group. Saliva levels for nickel and chromium were highest in the first month and decreased to initial levels in the rest of the groups. Mean concentration of salivary nickel is between 1-55 ug/L. This study found release of nickel in saliva between 4.12-11.53 ug/L, which are within the normal ranges and far below the average daily dietary intake of 300 ug. Normal serum levels of nickel were reported in the literature as 0.2 ug/L. In this study, serum nickel levels were between 7.87-10.27 ug/L. The authors attribute the higher values to the venipuncture with a stainless steel needle. It was concluded that "fixed orthodontic appliances release measurable amount of nickel and chromium when placed in the mouth, but this increase doesn't reach toxic levels for nickel and chromium in the saliva and serum."

Amini et al. (2008) reported on the metal content of oral mucosa cells in patients with and without fixed orthodontic appliances. 60 subjects, 30 with and 30 without orthodontic appliances had their buccal mucosa swabbed with an interdental brush. The sample was analyzed for nickel, chromium and cobalt ions by atomic absorption spectrophotometry. The nickel content in the oral mucosa of orthodontic patients was significantly higher than controls 21.74 versus 12.26 ng/ml. The authors conclude that more follow-up is needed to determine the long-term effects of nickel release.

Menezes et al. (2007) studied the urinary excretion levels of nickel in orthodontic patients to see the systemic response to corrosion products of orthodontic appliances. Twenty- one patients provided urine samples before orthodontic appliances were placed and two months after. Samples were analyzed by atomic absorption spectrophotometry. A statistically significant increase was found in the nickel content after placement of orthodontic appliances. Nickel is not a cumulative toxin- it is absorbed by the GI tract and excreted primarily by the kidneys. A study by Jensen et al showed a dose-dependent cutaneous reaction to oral exposure of nickel at levels varying from 0.3 mg nickel, which is equivalent to values in the normal daily diet, to 4.0 mg nickel. The biological effect of increases in systemic nickel levels is unknown. This study concluded "although increases in metal ion levels have been detected in most patients after placement of orthodontic appliances, the levels are not sufficient to cause alarm; however, additional in- vitro and in- vivo studies should be done to determine safe levels of nickel."

Ion Implantation Treatment (IonGuard Technology)

The ion implantation process forms a 60-120 nm titanium nitride film (Yeung 2007) that has a significantly reduced surface nickel concentration (Yeung 2005). The titanium nitride alters the formation of the protective oxide layer (Oshida 1993). Yeung (2007) found that ion implanted NiTi alloys displayed better corrosion resistance, as evidenced by a higher breakdown (pitting) potential 1080 mV compared to 461 for NiTi. They also reported reduced nickel release with ion implanted alloys releasing 57.9 ug/L after 5 weeks compared to 320 ug/L for NiTi. Endo (1994) reported that titanium nitride coatings applied by arc ion plating produced a 1-2 um thick titanium nitride film with a

top TiO_2 layer, a middle layer of TiNx and an inner layer of TiN. The titanium nitride coating improved corrosion resistance when the potential was less than 500 mV and reduced corrosion rates of NiTi alloys by more than one order of magnitude in that range. Neumann (2002) looked at the corrosion and fracture resistance of ion implantation surface modifications using anodic polarization and found higher rupture potential for IonGuard (600 mV compared to 460 mV for NeoSentalloy) and a corrosion process that starts at higher potentials and leads to visibly less surface destruction of the wire as evidenced by SEM. Conversely, Kim (1999) found during his investigation of the corrosive potential of nitride-coated nickel titanium using potentiostatic anodic dissolution in 0.9% NaCl solution that the nitride coating had no effect on corrosion.

Husmann (2000) found the mean frictional loss of NeoSentatolly was significantly reduced from 46.2% to 40.8% when ion implantation process was used however there was large variation in response for the wires tested. Burstone and Farzin-Nia (1995) found that the coefficients of friction were significantly reduced for ion imlanted TMA wires (static .13, kinetic .10) compared to untreated wire (static .52, kinetic .51) in both static and kinetic tests. They also saw less variation in wires treated with ion implantation. Gil (1998) tested NiTi superelastic archwires treated with nitrogen diffusion and found an increase in the surface hardness of the alloy and reduction in the coefficient of friction from 0.55 to 0.25. Ryan (1997) found statistically increased in vitro retraction of canines with NiTi and Beta-Titanium wires that were treated with IonGuard. Wichelhaus (2005) studied the effects of surface nitridation on friction in NiTi wires and found initially the IonGuard wire showed significantly less friction (23% less) than the NeoSentalloy wire, but after 4 weeks of clinical use they showed no differences.

Yeung et al. (2007) compared the mechanical properties, corrosion resistance, and cytocompatibility of nitrogen plasma-implanted NiTi alloys to other medical grade materials. 1mm thick discs were formed for NiTi, stainless steel and titanium alloys. Cyclic electrochemical tests were performed in simulated body fluids at pH 7.42 that spanned from -500 mV to +1500 mV at a rate of 600 mV/h. Breakdown (pitting) potential occurred at a higher value, 1080 mV, for ion implanted alloys compared to the untreated NiTi, 461 mV. Passive nickel release was measured after 5 weeks with ICP-MS and the ion implanted alloy released significantly less nickel, 57.9 ug/L compared to 320 ug/L for untreated NiTi. X-ray photoelectron spectroscopy revealed a 60-120 nm titanium nitride layer on the nitrogen implanted alloy, which had an increased surface hardness. The authors did report that roughness is slightly increased after plasma treatment but with a specific pattern that favors cell proliferation. Yeung concluded that nitrogen implantation increased corrosion resistance and reduced nickel ion release.

Yeung et al. (2005) investigated NiTi alloys after plasma immersion ion implantation. They found surface nickel concentrations of the ion implanted alloys to be much lower than the untreated NiTi alloys.

Oshieda and Hashem (1993) studied titanium oxide formation on titanium that had been nitridated with arc ion plating. They found that the nitride surface altered the thickness and formation time of the titanium oxide passivation layer. The nitrided samples took 2.24 times longer oxidation time to form the same degree of oxidation. The TiO_2 layer formed by the un-nitrided samples was 1-2 microns, whereas the nitride samples formed a 0.3-0.5 micron oxide layer.

Endo et al. (1994) reported on the effects of titanium nitride coatings applied by arc ion plating on surface and corrosion characteristics of NiTi alloy using potentiodynamic polarization, scanning electron microscopy and x ray diffraction. A 1-2 um thick titanium nitride film was detected on the alloy and it consisted of three titanium compounds- a top TiO_2 layer, a middle layer of TiNx and an inner layer of TiN. The anodic polarization results showed that the titanium nitride coating had a free corrosion potential (zero current potential) 400 mV more positive (more noble) than the NiTi alloy alone. Passivation for the titanium nitride coating group occured approximately 2 orders of magnitude lower than the value for the NiTi alloy alone, but was much shorter in duration and typically broke down after 500 mV (pitting potential) compared to 1200 mV for the NiTi alone. SEM of the alloys after anodic polarization revealed cracks in the titainum nitride film and corrosion pits forming in those areas. The polarization resistance values for the titanium nitride coating were more than one order of magnitude higher than for the NiTi alloy, showing that the corrosion rate from 50-100 mV was reduced by the titanium nitride coating. The authors conclude that the titanium nitride coating improved corrosion resistance when the potential was less than 500 mV and reduced corrosion rates of NiTi alloys by more than one order of magnitude in that range.

Neumann et al. (2002) looked at the corrosion and fracture resistance of coated and conventional orthodontic archwires. The authors looked at teflon, polyethylene or ion implantation surface modifications on NiTi, beta-titanium and stainless steel wires. Anodic polarization was applied to archwires to speed up the corrosion process. Separate wires were tested for the effects of cyclic mechanical loading by moving a glass rod vertically 1.5 mm with a frequency of 1 Hz 5,000 times in contact with the wire. The

IonGuard wire had a rupture potential of 600 mV compared to 460 mV for NeoSentalloy. The higher rupture potential for IonGuard results in a corrosion process that starts at higher potentials and lead to visibly less surface destruction of the wire as evidenced by SEM. Structural changes were seen in the NeoSentalloy wires with and without IonGuard after mechanical stress.

Kim et al. (1999) investigated if there was a difference in the corrosive potential of stainless steel, nickel titanium, nitride-coated nickel titanium, epoxy-coated nickel titanium, and titanium orthodontic wires. They determined the breakdown potential of each wire using potentiostatic anodic dissolution in 0.9% NaCl solution. They also evaluated the surface changes qualitatively using scanning electron microscopy. Results showed that the epoxy coating decreased corrosion, while the nitride coating had no effect on corrosion. Titanium and epoxy coated NiTi wires showed the least corrosive potential. Stainless steel and some NiTi wires underwent pitting and localized corrosion. These authors recommended using titanium or epoxy-coated wires in patients with nickel allergy due to lower corrosive potential.

Husmann et al. (2000) looked at friction in coated archwires. Ion implantaion involves a negative loading process of high- energy, positively charged radicals penetrating a substrate surface and binding with the substrate. The mean frictional loss of NeoSentatolly was significantly reduced from 46.2% to 40.8% when ion implantation process was used. The Teflon coating process showed the lowest frictional losses (6.1%). There was a large standard deviation for the wires tested which could be due to manufacturing variability or adjustments in the wire in the experimental set-up.

Burstone and Farzin-Nia (1995) studied friction of TMA wires after ion implantation. The ion implantation process involves ionizing nitrogen and oxygen and accelerating them at energies of several hundred to several thousand electron volts towards an archwire. The vapor flux of ions is generated with an electron beam evaporator in a vacuum and when it is accelerated at the archwire it creates a hard layer of TiN and TiO on the surface of the archwire and immediately below it. This layer creates large compressive forces in the archwire at the atomic level, which improves fatigue resistance, ductility and reduces friction. The effects of surface flaws are also decreased because of superficial compressive forces. This process does not alter wire dimensions and leaves no sharp interface between coatings and wire. Frictional forces were measured for TMA wires with and without ion implantation. Coefficients of friction were significantly reduced for ion imlanted TMA wires (static .13, kinetic .10) compared to untreated wire (static .52, kinetic .51) in both static and kinetic tests. Less variation was seen in wires treated with ion implantation. The ion implantation process had no effect on modulus of elasticity or tensile strength and improved the ductility and fracture and fatigue resistance of TMA wire.

Gil et al. (1998) tested NiTi superelastic archwires treated with nitrogen diffusion. They found an increase in the surface hardness of the alloy due to an increase in titanium nitride film formed by a chemical reaction between the substrate and nitrogen gas. The optimum treatment for nitrogen diffusion appears to be 900 degrees Celcius for 20 minutes. The nitrogen diffusion treatment reduced the coefficient of friction from 0.55 in NiTi without the treatment to 0.25 with the surface treatment. Static solutions of artificial saliva with archwires in place were sampled at 1, 3, 5, 10, 24, 120, 168, 360 and 540

hours. NiTi with nitride had concentrations of nickel release that increased quickly initially and then plateaued just above 50 ug/L after 100 hours. The NiTi wire also had a quick increase in nickel release and plateaued around 200 ug/L after 250 hours. The titanium nitride surface layer therefore acted as an obstacle to biodegradation and reduced the nickel and titanium ion release as measured by ICP-MS.

Ryan et al. (1997) studied the effects of ion implantation on rate of tooth movement in vitro with the hypothesis that the wires with the least frictional force would produce the most movement. Stainless steel wire, NiTi with and without IonGuard, and Beta-titanium wire with and without IonGuard were placed in a testing apparautus that simulated canine retration with 150 gm force. They found statistically increased tooth movement with wires that were treated with IonGuard. The average measurements of tooth movement in decreasing order were: stainless streel (3.75 mm), NiTi with Ionguard (2.5 mm), Beta-titanium with Ionguard (1.35 mm), NiTi (1.19 mm) and Beta-titanium (0.92 mm). The authors hypothesize that ion implantation technology could be used inside bracket slots to selectivly enhance anchorage.

Wichelhaus et al. (2005) studied the effects of surface nitridation on friction in NiTi wires. Ion implantation hardens a metallic substrate by implanting high energy ions in a very thin layer on the surface. There is mechanical stress induced by the mismatch of the implanted ions in the crystal structure of the substrate. Neosentalloy archwires with and without IonGuard were tested for friction using a Universal test machine as received and after 4 weeks in a patient's mouth. Titanol with and without gold finish was also tested. Initially the IonGuard wire showed significantly less friction than the NeoSentalloy wire- 23% lower. After 4 weeks intraorally all wires showed increased

coefficients of friction and no difference between the surface nitridated wires and NeoSentalloy wires. The surface roughness of the wires also increased after clinical use. The authors state that the positive effect of surface nitridation was lost after the wires were used intraorally for 4 weeks.

Ion Implantation Treatment and Mechanical Loading

Peitsch (2007) found that the mechanically loaded wires released significantly more nickel (~45ng/cm^{2}d) compared to nonleaded wires (<1ng/cm^{2}d). The authors did not find any protective effect of the surface nitridation. SEM revealed surface irregularities present on the surface nitridated wires compared to a smooth surface on the uncoated wires. Jai (1999) looked at nickel release from Bioforce Sentalloy wires with and without IonGuard in artificial saliva in strained or unstrained conditions. Nickel release ranged from 0.4-4.1 ug/L and the nitrogen implanted wires released significantly less nickel than the NiTi wire. The wires that were strained showed significantly more nickel release than those that were passively soaked. They detected nickel was cytotoxic at levels above 29 ppm, which is similar to 30 ppm (Bour 1994 and Everness 1990) and 15-30 ppm (Messer and Lucas 1996). Less cell proliferation was seen in human peripheral blood mononuclear cells (PBMC) exposed to 2.9 ppm nickel. The authors also found that PBMCs were more sensitive to nickel during their proloferative stage, which would be seen with inflammation. They conclude that the amount of nickel released would be insufficient to cause cellular hypersensitivity or cytotoxicity and that repeated trauma and inflammation may be the source of nickel-induced reactions from orthodontic appliances.

Peitsch et al. (2007) looked at passive nickel release and mechanical loading of NeoSentalloy archwire with and without IonGuard and found that the mechanically loaded wires released significantly more nickel (~45ng/cm^{2}d) compared to nonloaded wires (<1ng/cm^{2}d). The authors postulate that the mechanical deformation could have damaged the passivating TiO_2 layer on the surface leading to the increased nickel release. The 5 Hz loading frequency tested represents approximately 5 times that of chewing. They repeated the tests in both ultrapure water and saline solution and found no difference in the testing solution used. The authors did not find any protective effect of the surface nitridation. The insignificant finding could be due to the large variation seen in nickel release and small sample size (n= 5). Another explanation is that the TiO_2 layer is almost identical in a nitridated and uncoated surface. SEM revealed surface irregularities present on the surface nitridated wires compared to a smooth surface on the uncoated wires.

Jai et al. (1999) looked at passive nickel release from orthodontic archwires and cellular immune response to nickel. Bioforce Sentalloy wires with and without IonGuard and stainless steel wires were tested in artificial saliva either statically or cyclically strained with an Instrom machine for 24 hours. They also looked at unstrained samples up to 7 days in solution. Immune response was tested on human peripheral blood mononuclear cells (PBMC) and using the trypan blue exclusion method at varying nickel concentrations 0-29 ppm. Nickel release ranged from 0.4-4.1 ug/L and the nitrogen implanted wires released significantly less nickel than the NiTi wire. The authors speculated that "implantation of ions into near surface regions enhances a metal's surface corrosion resistance by forming amorphous surface layers, thereby eliminating rapid

corrosion at grain boundaries, shifting the open- circuit potential into a passive range, where corrosion current densities are low, and inhibiting kinetics of cathodic reactions on the surface." They also speculate that ion implantation with nitrogen takes the place of nickel atoms on the wire surface, lowering the amount of nickel available to be released. The wires that were strained showed significantly more nickel release than those that were passively soaked. The authors speculate that "straining introduces energy into the arch wire, thereby increasing the energy level of atoms at the surface. This effectively reduces the activation energy required for metal ions to be released into an electrolyte." They detected nickel was cytotoxic at levels above 29 ppm. Less cell proliferation was seen in PBMC exposed to 2.9 ppm nickel. They note two other studies by Bour 1994 and Everness in 1990 that found 30 ppm nickel sufficient to elicit a cytotoxic response and Messer and Lucas 1996 found 15-30 ppm nickel cytotoxic. The authors also found that PBMCs were more sensitive to nickel during their proloferative stage, which would be seen with inflammation. They conclude that the amount of nickel released would be insufficient to cause cellular hypersensitivity or cytotoxicity and that repeated trauma and inflammation may be the source of nickel-induced reactions from orthodontic appliances.

Anodic Polarization

Ewers (1985) determined the electrochemical nature of the oral cavity by measuring the oxidation potential Eh (SCE) of nine patients in vivo using microelectrode techniques. The oxidation potential ranged from -58 to +212 mV (SCE).

Ewers et al. (1985) determined the electrochemical nature of the oral cavity so that the anodic polarization in vitro data could be better applied to in vivo situations. The authors measured the pH and oxidation potential Eh (SCE) of nine patients in vivo using microelectrode techniques. They sampled 5 specific sites and looked at both periodontally compromised patients and patients who had received minimal dental care. The oxidation potentials were collected using an electrometer, a silver-silver chloride reference electrode and a gold counter electrode at 35 degrees. The oxidation potential ranged from -58 to +212 mV (SCE) and pH ranged from 6.1 to 7.9. Previous studies reported unstimulated saliva ranged from -17 to +152.5 mV (SCE) for oxidation reduction potentials of the mouth. The pH and oxidation potentials differed based on site, periodontal health, and nature and quality of restorations present.

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APPENDIX

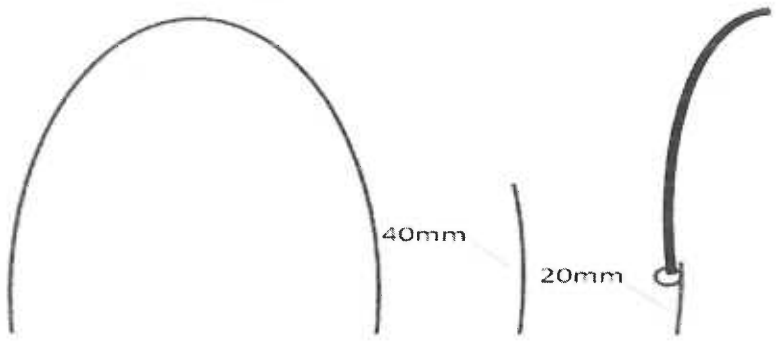
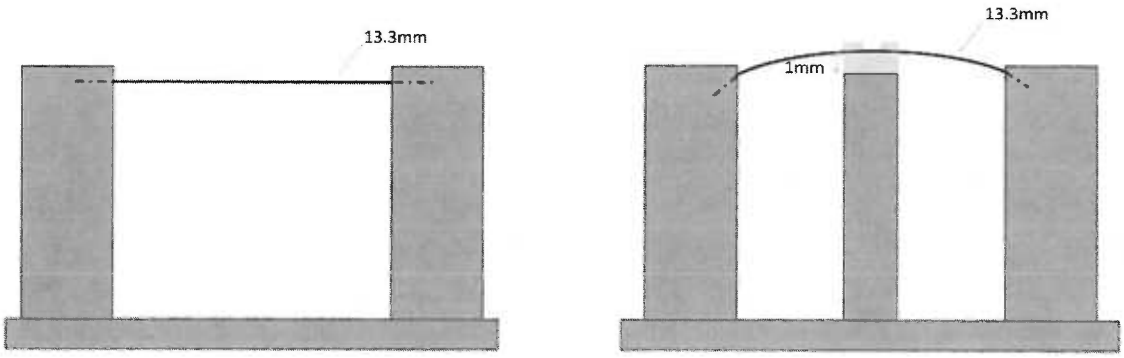


Figure 1. A 4cm straight segment of the distal portion of an .016"x.022" archwire was cut. The mesial 2cm were heated to red hot, looped and attached to electrical wire.



Nondeflected Deflected

Figure 2. 13.3 mm of wire were tested in an acrylic testing apparatus, either in nondeflected or deflected states. The nondeflected samples were held straight. The deflected samples underwent a three point bending force that deflected the wire by 1mm.

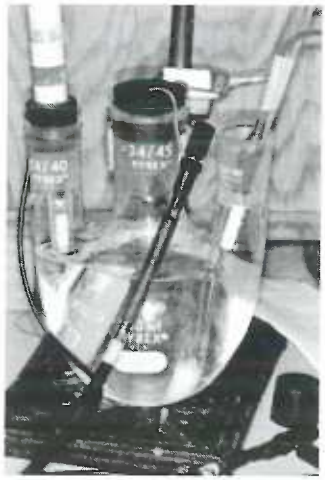
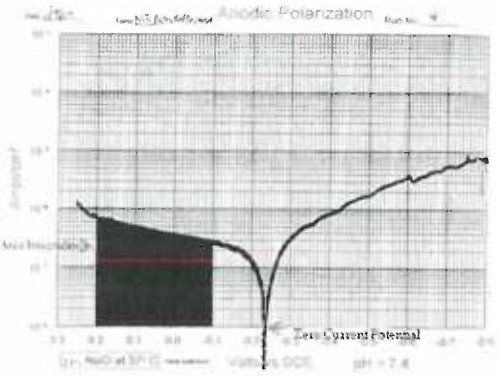
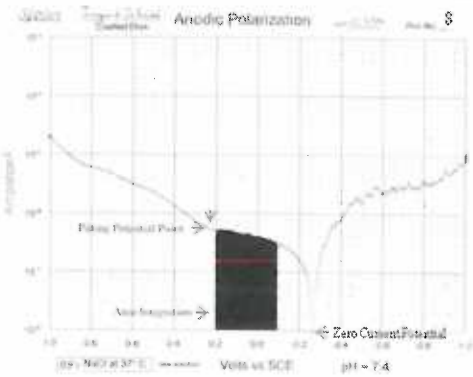


Figure 3. The electrochemical corrosion cell: the NiTi wire was the working electrode, the platinum wire was the counter electrode and the standard calomel electrode was used as a reference. This photograph also shows the bubbler deaerating the system.



A



B

Figure 4. A) Anodic Polarization Chart of NiTi nondeflected #4. This is an example of a short run starting at a potential of -0.8V to an endpoint of 0.25V, before the pitting potential for the wire was reached. These short run samples were used for zero current potential, area integration and nickel release data collection. B) Anodic Polarization Chart of IonGuard Deflected #8. This is an example of a long run starting at a potential of -1.0V to an endpoint of 1.0V, after the pitting potential for the wire was reached. These long run samples were used for zero current potential, area integration and pitting potential point (both voltage and current) data collection.

Raw Data

Table 2. Zero Current Potential (V) from Anodic Polarization on Trials #1-10

Trial	NiTi Nondeflected	IonGuard Nondeflected	NiTi Deflected	IonGuard Deflected
1	-0.259	-0.177	-0.273	-0.252
2	-0.213	-0.137	-0.141	-0.243
3	-0.194	-0.195	-0.214	-0.181
4	-0.236	-0.204	-0.224	-0.217
5	-0.230	-0.180	-0.213	-0.240
6	-0.381	-0.304	-0.365	-0.298
7	-0.331	-0.262	-0.308	-0.271
8	-0.385	-0.283	-0.325	-0.264
9	-0.391	-0.364	-0.326	-0.316
10	-0.365	-0.355	-0.360	-0.275
mean	-0.299	-0.246	-0.275	-0.256
sd	0.079	0.079	0.074	0.039

Table 3. Area Integration (V*Amps/cm2) from Anodic Polarization on Trials #1-10

Trial	NiTi Nondeflected	IonGuard Nondeflected	NiTi Deflected	IonGuard Deflected
1	1.33326E-07	4.44011E-08	6.89587E-07	1.24062E-06
2	8.847E-08	3.394E-08	8.354E-08	9.476E-07
3	7.329E-08	6.341E-08	8.130E-08	5.324E-08
4	1.113E-07	3.291E-08	1.690E-07	6.090E-08
5	1.039E-07	4.449E-08	6.627E-08	5.231E-07
6	1.148E-07	4.398E-08	4.022E-08	4.728E-07
7	3.301E-08	6.443E-08	3.985E-08	5.713E-08
8	9.315E-08	3.282E-08	5.257E-08	1.056E-07
9	7.076E-08	5.685E-08	3.811E-08	7.757E-08
10	6.414E-08	1.484E-07	3.271E-07	3.603E-07
mean	8.862E-08	5.657E-08	1.588E-07	3.899E-07
sd	2.92497E-08	3.43785E-08	2.06685E-07	4.17783E-07

Table 4. Nickel Ion Release (ug/L) Calculated by ICP-MS on Trials #1-5

Trial	NiTi Nondeflected	IonGuard Nondeflected	NiTi Deflected	IonGuard Deflected
1	0.37	0.00	0.54	37.64
2	0.77	0.00	4.59	3.95
3	0.86	0.00	11.02	2.18
4	22.81	15.31	0.00	0.40
5	13.35	16.30	0.54	135.90
mean	7.63	6.32	3.34	36.02
sd	10.1098461	8.663828253	4.674601933	57.92352873

Table 5. Pitting Potential Point Voltage(V) from Anodic Polarization on Trials #6-10

Trial	NiTi Nondeflected	IonGuard Nondeflected	NiTi Deflected	IonGuard Deflected
6	0.256	0.432909091	0.702545455	0.364636364
7	0.483545455	0.450909091	0.359636364	0.372090909
8	0.753636364	0.582545455	0.426545455	0.246545455
9	0.623363636	0.371363636	0.687363636	0.411272727
10	0.383363636	0.382181818	0.528454545	0.713272727
mean	0.499981818	0.443981818	0.540909091	0.421563636
sd	0.195551006	0.084355074	0.153027127	0.174298398

Table 6. Pitting Potential Point Current (Amps/cm2) from Anodic Polarization on Trials #6-10

Trial	NiTi Nondeflected	IonGuard Nondeflected	NiTi Deflected	IonGuard Deflected
6	6.600E-07	2.050E-07	2.800E-07	2.950E-06
7	2.300E-07	4.100E-07	2.550E-07	3.600E-07
8	9.700E-07	1.600E-07	3.400E-07	5.200E-07
9	6.200E-07	3.250E-07	2.750E-07	4.200E-07
10	4.100E-07	1.700E-06	3.300E-06	5.600E-07
mean	5.780E-07	5.600E-07	8.900E-07	9.620E-07
sd	2.79052E-07	6.44855E-07	1.3476E-06	1.11415E-06

TABLE 7. The mean, standard deviation, kurtosis and Pearson's correlation for the five dependent variables.

Dependent Variable	Mean	Std. Deviation	Kurtosis	N	1	2a	3a	4
1. Zero Current Potential Value (V)	-0.269	0.07	-0.94	40				
2. Area Integration (V*Amps/cm2)	1.73E-07	2.61E-07	8.11	40				
2a. Normalized Area Integration log (V*Amps/cm2)	2.26E-08	9.62E-09	0.78	40	-.04			
3. Nickel Release (ug/L)	13.327	30.52	15.31	20				
3a. Normalized Nickel Release winsorized (ug/L)	7.1	9.051	-0.52	20	-.16	-.09		
4. Pitting Potential Point Voltage (V)	0.477	0.152	-0.83	20	-.21	-.06	0	
5. Pitting Potential Point Current (Amps/cm2)	7.48E-07	8.84E-07	4.42	20				
5a. Normalized Pitting Potential Point Current log (Apms/cm2)	3.90E-08	8.33E-09	0.76	20	-.26	.874**	0	-.07

Note: ** Pearson's Correlation is significant at the 0.05 level (2-tailed).
N's range from 20-40

TABLE 8. Natural Log Transformed and Back Transformed Area Integration (Amps/cm2)

		Transformed				Back Transformed (Geometric Means)		
				95% Confidence Interval			95% Confidence Interval	
Time	Type	Mean	Std. Error	Lower Bound	Upper Bound	Mean	Lower Bound	Upper Bound
NiTi	Nondeflected	2.119E-08	2.673E-09	1.577E-08	2.662E-08	8.326E-08	4.842E-08	1.432E-07
	Deflected	2.243E-08	2.673E-09	1.701E-08	2.785E-08	9.421E-08	5.478E-08	1.620E-07
IonGuard	Nondeflected	1.621E-08	2.673E-09	1.079E-08	2.163E-08	5.059E-08	2.942E-08	8.700E-08
	Deflected	3.040E-08	2.673E-09	2.498E-08	3.582E-08	2.090E-07	1.215E-07	3.594E-07

TABLE 9. Natural Log Transformed and Back Transformed Pitting Potential Point Current (Amps/cm2)

		Transformed				Back Transformed (Geometric Means)		
				95% Confidence Interval			95% Confidence Interval	
Time	Type	Mean	Std. Error	Lower Bound	Upper Bound	Mean	Lower Bound	Upper Bound
NiTi	Nondeflected	3.948E-08	3.930E-09	3.116E-08	4.780E-08	5.183E-07	2.256E-07	1.191E-06
	Deflected	3.842E-08	3.930E-09	3.010E-08	4.674E-08	4.662E-07	2.029E-07	1.071E-06
IonGuard	Nondeflected	3.625E-08	3.930E-09	2.792E-08	4.457E-08	3.752E-07	1.631E-07	8.623E-07
	Deflected	4.197E-08	3.930E-09	3.365E-08	5.029E-08	6.649E-07	2.893E-07	1.528E-06

TABLE 10-14. ANOVA tables with main and interaction effects, degrees of freedom, F value and p value for each of the five dependent variables. A p value of <0.05 was considered significant.

Table 10. Analysis of Variance Table for Zero Current Potential (V)

Source	df	F	p
Wire	1	2.620	.114
Deflection	1	.100	.753
Wire * Deflection	1	.563	.458
Error	36		
Total	40		

Note: df = degrees of freedom, F = F ratio, p = Type I error probability of given F ratio

Table 11. Analysis of Variance Table for Area Integration (V*Amps/cm2)

Source	df	F	p
Wire	1	.312	.580
Deflection	1	8.319	.007*
Wire * Deflection	1	5.867	0.021*
Error	36		
Total	40		

Note: df = degrees of freedom, F = F ratio, p = Type I error probability of given F ratio