

Modifying NiTi shape memory alloys to reduce nickel ions release through ethylenediamine plasma polymerization for biomedical applications

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ABSTRACT

Shape memory alloys (SMAs)—a type of smart materials—offer unique benefits for constructing unique medical implants, especially for heart stents, vertebral nails, and braces. One of the widespread SMAs is nitinol (NiTi) which exhibits extraordinary shape memory ability to recover its initial form. However, due to the result of nickel (Ni²⁺) ions release, long-term usage of NiTi alloys would pose allergic and carcinogenic risks in orthopedics and clinical applications. To tackle these hurdles, we here demonstrate a surface modification technique via plasma polymerization in order to minimize Ni²⁺ ions release. NiTi substrates were initially exploited by plasma polymerization of ethylenediamine (EDA) with varying power values (25–50–75–100 W) and time rates (5–10–15 min) in order to assess the most efficient parameters for minimal toxic metal release. The samples were then tested for 14 days in a biomimicked media. As a result, 75 W–10 min plasma polymerized sample reduced Ni²⁺ ions release by 57.18 % compared to the base specimen. These results offer a significant outcome in deploying NiTi alloys into the biomedical field more safely through surface modifications using the plasma polymerization technique.

1. Introduction

Human beings have sought innovations in materials science and engineering for centuries, especially, for metallic biomedical implants [1]. In particular, smart materials (SMs) would be the key components for the applications of biomedical implants in drug delivery [2,3], tissue engineering [3], biosensing [4–8], medical and cardiovascular stents [9] since SMs are able to respond to the alterations of stress, electric and magnetic field, light, pressure, and temperature [10–12]. Among all of the countless SMs, shape memory alloys (SMAs) are considered to be superior materials because they can revisit their initial shape even after drastic external distortions [13]. SMAs are found to have a parent phase which is mostly austenite, and a martensite phase [14]. When stress or strain is induced to SMAs, a spontaneous transformation starts from the parent phase (austenite) to the softer product phase (martensite). Not only strain/stress initiation, but also inducing temperature drop, changes in the crystal structure, and after relief of stress/strain/

temperature factors, so-called “shape memory” effect occurs via boomeranging to the pre-deformed shape of the material [14,15].

Two key phenomena, shape memory effect (SME) and super-elastic (pseudo-elastic) behavior can elucidate the reorientation of martensite variants as a consequence of the reversible feature. Thanks to their SME and pseudo-elastic capabilities, SMAs have been deployed into many areas [16,17]; for instance, they have been used in electronics, vehicle industry, construction, communication, and military [16,18]. Apart from that, SMAs are also employed in a vast spectrum in the realms of medicine and biomedical engineering. As an example, SMA archwires are operated in the orthodontic area [19]; SMA rods are employed in the orthopedic field for correcting scoliosis [20]; and SMA stents are utilized in the vascular field [20,21]. Metallic materials such as Ti and Ti-based alloys, Co–Cr alloys, stainless steel, and Mg are widely used and commercially available implants [22]. For instance, Ti and Co-based materials mostly provide biointerface and advantageous mechanical properties such as high tensile strength and resilience making them

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perfect candidates for bone tissue-related biomedical applications [23].

NiTi alloys, on the other hand, can exhibit typical paradigms of SMAs including SME and superelasticity properties. NiTi alloys are also considered to have favorable mechanical properties in terms of the response of the biological tissue [20]. Under loading and unloading cycles, the stress/strain curve of the NiTi material holds a highly elastic structure similar to the bone tissue [24]. Therefore, NiTi implants have a considerable amount of interest both in biomedical researchers and surgeons because of their tunable virtuous mechanical properties. However, the biocompatibility of NiTi is still a critical issue [25]. Considering the basics of a biocompatible biomedical material, NiTi should satisfy several requirements such as corrosion resistance [25], low protein accumulation to the surface of the implant [26], and minimal cytotoxicity [25]. The implant's surface serves as the initial point of contact with biological systems. The surface properties, such as area, roughness, binding energy, and wettability play a pivotal role in controlling the performance of the implant, which needs to be biocompatible with the surrounding tissue for protecting the biological system from hazardous elements in the bulk material [27–29].

During the implantation period, biological system will have an abrasive effect and contact shear stress on the implant. For instance, high acidity of specific body fluids [30], serum proteins [31], aggressive ions such as chlorides, hydrocarbonates, and sulfates [32] corrode the surface of the NiTi implant. Abundantly, two mechanisms are employed during corrosion; pitting corrosion [24,30] and crevice corrosion [33]. Pitting corrosion is identified by the local shape of the pits on the surface of the material, and it is caused by halogen materials such as chloride, bromide, and iodide ions [34]. The destructive effect of this corrosion can be portrayed by the TiO_2 content on the surface, chloride amount, and metal alloy composition [35]. On the other hand, crevice corrosion is associated with a high pH level [36]. NiTi implants are both sensitive to pitting—because of the fact that body fluids have high concentrations of Cl^- ions—and crevice corrosion—with the time of the implantation, the material faces with pH 7.35 [31]. As aforementioned, the corrosion product of the NiTi material is the TiO_2 layer on the surface [30–32,34]. This layer however is associated with pitting corrosion, it is advantageous for the NiTi-made SMA implant because TiO_2 layer accumulates in the pitting pores and closes them to ameliorate the corrosion resistivity [37].

In addition to these challenges, the major drawback of NiTi implants is the release of nickel (Ni^{2+}) ions into the biological environment [25,26,33,38,39]. Nearly 10–15 % of the world population suffers from nickel allergy, and when Ni^{2+} ions are released into a biological system; cytotoxicity, hypersensitivity, and DNA damage occur afterward [33,40]. These issues mainly stem from the surface interactions of the NiTi implants which can be decremental for biocompatibility due to potential cytotoxic electrochemical reactions and biofilm formation on the surface of the alloy. Here, in the case of the release of Ni^{2+} ions, the most critical concern is the corrosive effect of the hydrodynamic environment [25,34]. For instance, a case study was conducted with a nickel-containing stent on 20 patients and, 6 of these patients had stent restenosis due to Ni^{+2} ions based metal allergy [41]. In addition, the released amount of Ni^{+2} ions are higher initially than following days or weeks [42]. It is essential to decrease the initial burst corrosive effect in order to limit the amount of released metal ions in the physiological environment.

To mitigate the effects of corrosion and improve the biocompatibility of the NiTi material, three different approaches have been conducted: (i) third element addition into NiTi, adding Ta or Cu elements increases the corrosion resistance of NiTi [38]; yet, introducing another element to NiTi differs its phase transition temperatures, shape memory effect, and super-elasticity [43]; (ii) nickel-free titanium-based shape memory alloys [38], nickel-free titanium-based TiNb shape memory alloy has a higher corrosion resistance than NiTi [43]; however, NiTi is a much more stronger mechanical structure than that of TiNb [43]; and (iii) thin-film formation on the surface of the NiTi. Thin-film modification

can preserve the overall aspects of the NiTi, such as the chemical composition of the bulk structure, shape memory effect, and super-elasticity. For example, diamond-like carbon thin films are coated onto the surface of the NiTi, and the coated material decreased the release of Ni^{2+} ions [44]. In another example, NiTi is bombarded with N_2 or O_2 gas, and then, annealed at a certain temperature in the post-implantation by plasma immersion ion implantation which is an advantageous method compared to diamond-like carbon thin films due to mitigation of delamination effect [45,46]. Other coating techniques such as electrochemical treatment, etching, and beam irradiation provide favorable surface solutions [47]. However, in these techniques, thick surface coatings on the surfaces result in tensile cracking and delamination because of the lower critical strain stemming from the cohesive properties of brittle layers and low interfacial adhesion disabling to act as Ni^{2+} ion barrier [48]. On the other hand, in plasma polymerization, a chemical surface activation can be obtained through sub-nano thickness coatings without affecting bulk structure [49]. In addition, plasma polymerization has a straightforward procedure where there is no requirement for post-treatment procedures that may affect the bulk property of NiTi.

In this study, we have specifically focused on reducing the release of Ni^{2+} ions and the corrosion via two-stepwise fortification. Initially, the effects of alterations in NiTi surface area were evaluated by grinding reference surface (base) specimens with two different (80 and 120) grinding papers. Afterward, the surfaces of grinded samples were enriched with amine ($-\text{NH}_2$) groups via ethylenediamine (EDA) plasma polymerization due to a high affinity of Ni^{2+} ions towards $-\text{NH}_2$ groups [44] so that the ions can be entrapped inside amine-rich plasma deposited coatings, and accordingly, decreasing the burst effect from corrosion and also reducing the long term release of Ni^{2+} ions. In order to discover the optimized plasma polymerization procedure, a variety of power (25–50–75–100 W) and time (5–10–15 min) parameters were separately tested for both 80 and 120 grit size paper grinded specimens (for 80 grit size 12 plasma polymerized +1 base samples, for 120 grit size 12 plasma polymerized +1 base samples). These plasma films were tested for 14 days in a biomimicked media to monitor both plasma film stability and nickel ion release via contact angle measurements and inductively coupled plasma emission-mass spectroscopy (ICP-MS), respectively. By addressing hazardous metal release from implanted materials, this technique would extend the lifespan and compatibility of biomedical implants with a higher success rate and duration.

2. Materials & methods

2.1. Materials

EDA (Mw: 60.0, p.a. absolute >99.5 %), Dulbecco's modified Eagle's medium (DMEM), nitric acid (HNO_3), Penicillin-Streptomycin-Amphotericin (PSA), and hydrogen peroxide (H_2O_2) were supplied from Sigma Aldrich. Epoxy resin and epoxy resin cure were supplied from Ankara, OSTIM Industrial Zone. Grinding papers with different grit sizes (80 and 120 Atlas) were supplied from Bauhaus. Equiatomic NiTi alloy specimens were supplied from Hacettepe University.

2.2. Methods

2.2.1. Preparation of NiTi specimens

$\text{Ni}_{50.6}\text{Ti}_{49.4}$ (at.%) specimens (1,1, w,w) were cut into the dimensions of 1 cm × 1 cm × 1 mm (width × length × thickness) square plates via wire electric discharge machine (WEDM). Epoxy mold was prepared with a mass ratio of 2:1 (Epoxy resin cure: epoxy resin). Later on, 2 mg of cure and 1 mg of epoxy resin were homogenized by hand mixing for 15 min. After homogenization, the mold was applied to the NiTi specimens in the petri dish, and only one surface were left open for further modifications. Molds were left for curing at room temperature (25 °C) for 24 h. Epoxy merged specimens were then grinded with different grit sizes

(80 and 120 Atlas) to create a surface with distinct topographic structures. Each specimen was grinded with the presence of water in order to avoid heating and remove the grinding residues. Samples in water were applied to sonication in a bath sonicator (Bandelin SONOREX™ SUPER) to dispose of residues. The samples were then washed with ultra-pure water (UPW) and dried prior to the plasma polymerization.

2.2.2. Surface modifications of NiTi via plasma polymerization

The NiTi specimens were placed inside the middle of the plasma chamber. Subsequently, the pump was activated and waited for the chamber pressure to drop to 0.20 mbar in order to evacuate the impurities inside the plasma chamber that may potentially affect the process of the plasma polymerization. After reaching 0.20 mbar inside the plasma chamber, EDA was introduced to the chamber for 5 and 10 min at 3.00 mbar. When the introduction of the monomer was over, we again waited for the chamber pressure to drop at 0.20 mbar. After reaching 0.20 mbar, the plasma treatment was initiated with the parameters given in the Table 1. Following the initiation of the plasma polymerization, to reduce the energetic levels of the monomers inside the chamber, the chamber was again filled with EDA for 5–10 min. Afterwards, plasma polymerization was initiated by applying 25–50–75–100 W and 5–10–15 min parameters for the 80-grinded and 120-grinded specimens (Fig. 1). In the literature, higher powers are found to be ineffective in terms of plasma deposition; hence, optimization power in this study was selected between 25 and 100 W [50]. In addition, the prolonged times (>20 min) did not change the surface atomic concentration; therefore, the optimization of plasma polymerization time in

Table 1

Plasma polymerization parameters for the NiTi specimens prepared with 80 grit size and 120 grit size of grinding papers.

Plasma Polymerization Parameters			
Monomer	Applied Plasma Power (W)	Application Time (min)	Pressure (mbar)
Ethylenediamine (EDA)	25	5-10-15	0.20
	50	5-10-15	
	75	5-10-15	
	100	5-10-15	

this study was kept between 5 and 15 min [51].

2.2.3. Characterization of surface and crystallographic planes of NiTi

Before the plasma polymerization, a diverse of characterizations were performed to evaluate the surface characteristics and crystal structure of the NiTi specimen. To quantitatively measure the dimensions, topography, and surface roughness of the 80 and 120 grinded substrates, Atomic Force Microscope (AFM) (Asylum, Oxford Instrument, U.K.) was employed to analyze NiTi surfaces using Nanosensors PPP-NCHR tip with 42 N m^{-1} force constant on AC Air Topography mode. The imaging was performed with a scan rate of 0.6 Hz ($2 \times 2 \mu\text{m}^2$) and 1.0 Hz ($10 \times 10 \mu\text{m}^2$), and they were then examined using Gwyddion without any data manipulations including filters or smoothing.

2.2.4. Contact angle measurements of NiTi surfaces submerged in DMEM

The film durability and stabilization tests were carried out for the NiTi surfaces submerged in DMEM in order to assess the effect of body simulation on the plasma polymerized thin film. In this circumstance, the surface wettability of NiTi surfaces submerged in DMEM was characterized by a sessile drop method. Before the characterization, submerged specimens were rinsed with UPW, and then, dried with an air compressor. Later, $10 \mu\text{l}$ of UPW was dropped onto the NiTi surfaces by micropipette, and the droplets on the surfaces were visualized via a camera system. Measurements were conducted by using a tangent curve from the triple angle point for the 1st, 7th, 10th, and 14th days of DMEM submerged specimens.

2.2.5. Inductively coupled plasma – mass spectrometer (ICP-MS) analysis

In the preparation of the NiTi specimens, a commercial Epoxy Resin (A base 2 g/B curing agent 1 g) was used to enable only one surface for Ni^{2+} ion release study and surface modification. After that, untreated (base) and plasma-treated specimens (80-grinded and 120-grinded) were submerged into 2 ml of Dulbecco's modified Eagle's medium (DMEM) supplemented with %1 Penicillin-Streptomycin-Amphotericin (PSA) at (37°C) incubator shaker in order to mimic a biological environment. The media was drawn after 1 day from the day in which the plasma polymerization procedure was conducted. After refreshing the media, the other samples were taken on the 7th and 14th days with the same protocol. To carry out an ion release study, the collected media

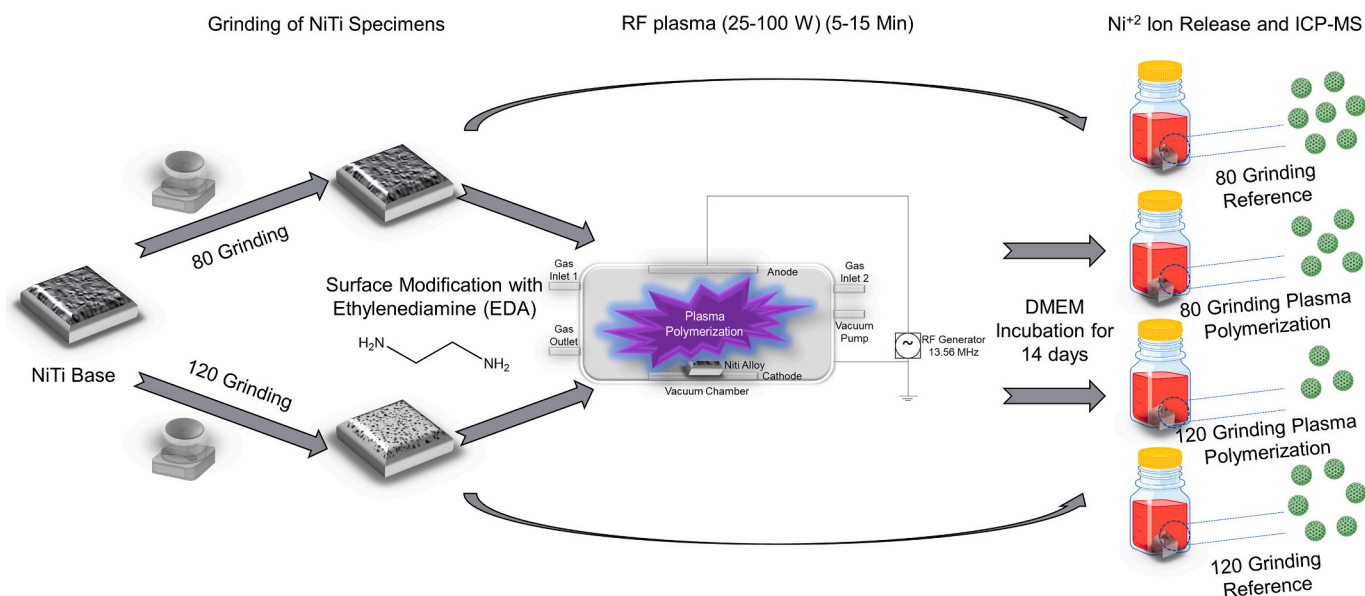


Fig. 1. The illustration depicts multiple steps covering the plasma film coating of NiTi shape memory alloy surfaces via power/time-dependent EDA polymerization after grinding them with different (80–120 grit) papers. Here, the NiTi-base and plasma film-coated specimens were incubated for 14 days in order to quantify Ni^{2+} ions release through ICP-MS.

Table 2

Parameters for heating-cooling procedure to minimize the contents in DMEM media (except Ni^{2+} ions) for the extraction of Ni^{2+} ions.

Step	Power (W)	Time (Min)	Temperature Program	Applied Energy (kJ)
1	120 W	16	Heating	117 kJ
2	0 W	16	Cooling	0 kJ
3	120 W	16	Heating	117 kJ
4	0 W	16	Cooling	0 kJ
5	120 W	16	Heating	117 kJ

from the samples and a control DMEM sample were used. In the course of the inductively coupled plasma emission mass spectroscopy (ICP-MS) (Thermo iCAP RQ ICP-MS) analysis, the digestion of biomolecules procedure was carried out in order to extract Ni^{2+} ions from the drawn media. The digestion was performed with HNO_3 (1:2, v:v) and H_2O_2 (3:1, v:v) inside the domestic microwave with the steps depicted in the Table 2. After the heating procedure, further dilution had been carried out by using ultra-pure water (1:9). The released Ni^{2+} ions from NiTi specimens were detected by using these samples via ICP-MS.

3. Results & discussion

The grit size of the grinding paper had a considerable effect on the surface roughness, as well as affecting the surface wettability. Briefly, grit size and surface roughness are inversely proportional to each other, where the lowest grit size will result in the highest surface roughness [52,53]. Hence, the increased surface roughness will also enhance the surface wettability according to Wenzel's Eq. [54]. As depicted in the AFM images ($10\ \mu\text{m} \times 10\ \mu\text{m}$ and $2\ \mu\text{m} \times 2\ \mu\text{m}$) (Fig. 2), the roughness values of NiTi specimens prepared with 80 and 120 grit sizes of the grinding paper, were evaluated in Table 3. According to the AFM results, the NiTi specimen grinded with 80 grit size paper had a rougher surface than that of the one grinded with 120 grit size paper. On the z-axis, there

Table 3

Roughness average (Ra) value, root mean square (Rms), and maximum depth height (Mdh) of NiTi morphologies.

Specimen (Specimen Dimension-Preparation Method)	Roughness Average (Ra)	Root Mean Square (Rms)	Maximum Depth Height (Mdh)
10–10 μm , NiTi grinded with 80-grit size of paper	115.1 nm	19.1 nm	284.9 nm
10–10 μm , NiTi grinded with 120-grit size of paper	80.4 nm	18.1 nm	184.2 nm
2–2 μm , NiTi grinded with 80-grit size of paper	21.81 nm	6.7 nm	53.5 nm
2–2 μm , NiTi grinded with 120-grit size of paper	19.05 nm	4.9 nm	44.9 nm

are some jut-outs with a maximum height of 53.5 nm for the specimens prepared with 80 grit size of grinding paper. Furthermore, there was an evenly distributed island-like structure with a height of 44.9 nm for the specimens obtained by 120 grit size of grinding paper.

Once plasma polymerization has been performed to 80 and 120 grit size paper grinded specimens with a variety of power (25–50–75–100 W) and time (5–10–15 min) parameters (24 plasma polymer film applied and 2 base specimens (reference, plasma film unmodified), totally 26 samples), the contact angle measurements were conducted to monitor the film stability under DMEM conditions. To further evaluate the effects of hydrostatic forces in body circulation, NiTi specimens were placed inside a shaker incubator ($37\ ^\circ\text{C}$) for 14 days. To assess the effects of power and time on plasma polymerization, the contact angle between plasma film-coated/uncoated NiTi surfaces and liquid droplets was executed. According to the contact angle results from base (reference) and plasma film-coated NiTi specimens, the wettability and surface energy values were presented in Fig. 3. Accordingly, the wetting

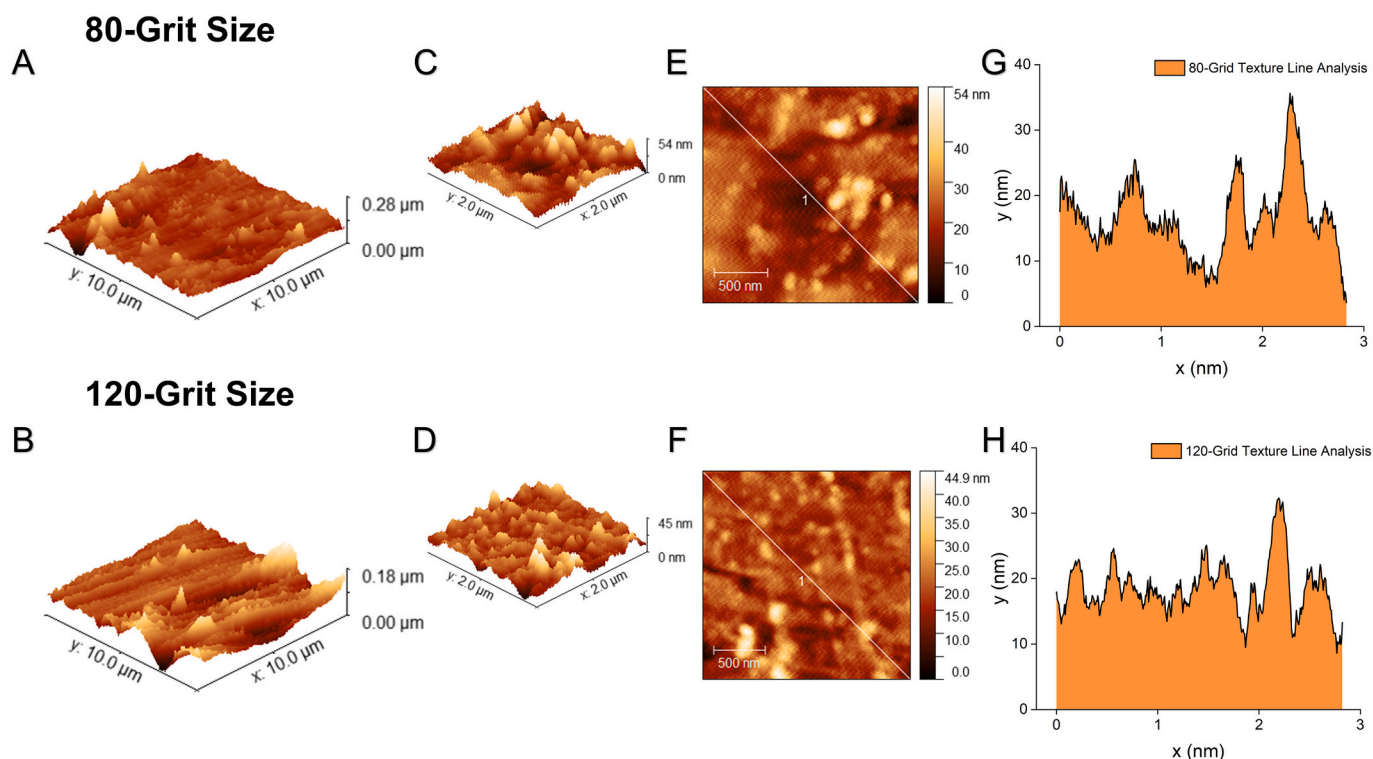


Fig. 2. AFM images show the grinded NiTi alloys surfaces prepared with 80-grit size and 120-grit size of papers. Samples from a surface of (A–B) $10\ \mu\text{m} \times 10\ \mu\text{m}$, (C–D) $2\ \mu\text{m} \times 2\ \mu\text{m}$ of surfaces are demonstrated. (E–F) The top-view and (G–H) cross-section analyses of the surfaces are depicted at the aforementioned surface dimensions.

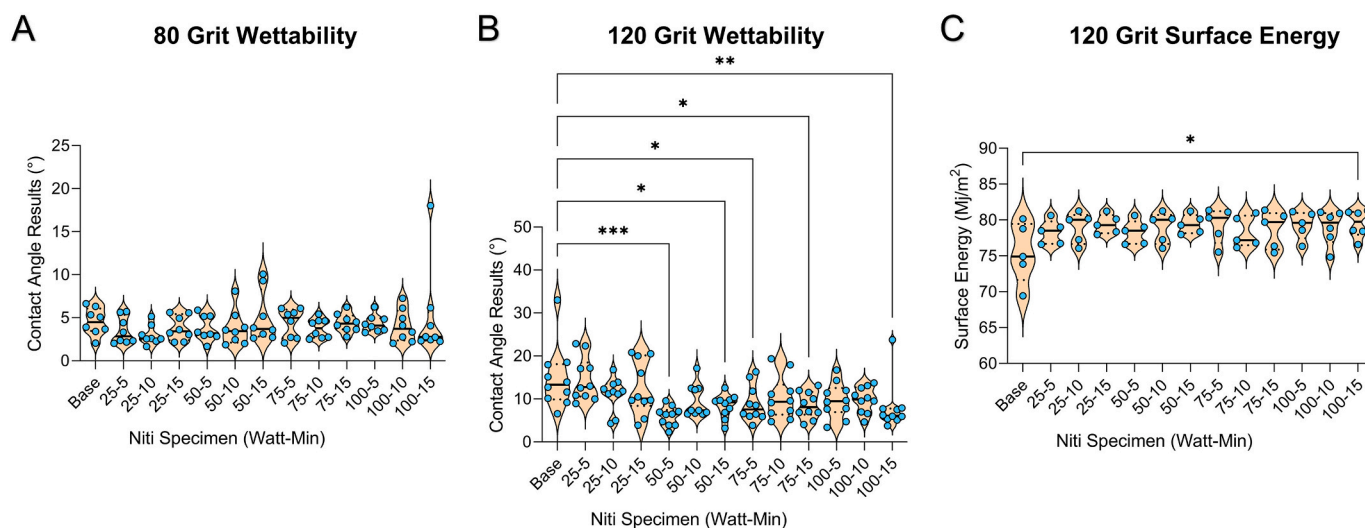


Fig. 3. Contact angle and surface energy results are demonstrated for the modified NiTi alloys under various plasma power and plasma exposure time for 14 days. Wettability characteristics of the surfaces are prepared with (A) 80 grit size and (B) 120 grit size of grinding paper. (C) The surface energy of the one prepared with 120 grit size of grinding paper is demonstrated. Statistical assessments are performed for the data through one-way ANOVA followed by Dunnett analysis. The statistical difference is depicted as * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$. Black color solid lines represent median values and dashed lines stand for mean values of upper and lower data points of medians.

capability of NiTi specimens was found to be inversely proportioned with the grit size which can be directly correlated with the Wenzel's equation. Overall contact angle values of 120 grinded NiTi specimens were higher than 80 grinded NiTi specimens (Fig. 3a-b). Before submerging NiTi specimens into the DMEM solution (T_0), the reference specimen grinded with 80 grit size grinding paper gave $18.03^\circ \pm 1.32^\circ$ wettability value, and the other reference specimen grinded with 120 grit size grinding paper gave $33.02^\circ \pm 3.51^\circ$ wettability value. After finding the T_0 values, all of the base and plasma film-coated NiTi specimens were submerged into the DMEM solution and the plasma film durability and stability test was started under an abrasive environment. After 24 h (1st day), the reference specimen prepared with 80 grit size of grinding paper resulted in $2.31^\circ \pm 4.45^\circ$, and the other reference specimen obtained with 120 grit size of grinding paper led to $12.72^\circ \pm 17.00^\circ$. To further analyze the plasma film endurance, surface energies of the base and plasma film-coated NiTi specimens made with 120 grit size of grinding paper were presented in Fig. 3c. since these specimens acted differently from their own base (reference) result in the aspect of wettability. The reference specimen of 120 grinded NiTi resulted in a 69.43 MJ/m^2 surface energy value at T_0 . After 24 h from submerging NiTi samples into the DMEM solution (1st day), surface energy of the base specimen which was grinded with 120 grit size of grinding paper, drastically increased to 74.90 MJ/m^2 surface energy value. On the other hand, plasma film-coated 120 grinded NiTi surfaces maintained their surface energy values at the end of the first day. The base specimen's surface energy value increased by 5.48 MJ/m^2 , whereas plasma film-coated NiTi surface energies increased by a mean value of 1.61 MJ/m^2 .

EDA is an amine-rich plasma precursor; and hence, when the plasma polymerization of EDA was performed, NiTi surfaces were deposited by $-\text{NH}_2$ groups so that surface energy and hydrophilicity increases. In addition, fluctuation in both surface wettability and energy values was expected in the plasma film-uncoated NiTi due to the abrasive environment of the DMEM. On the other hand, it was also observed that the

plasma film-coated NiTi surfaces were hindered by this abrasive environment relatively lower than that of the plasma film-uncoated NiTi surfaces. With respect to this, the plasma film-coated surfaces maintained their surface wettability and surface energy values.

The aforementioned wettability and surface energy values also can be correlated with the theory and micropits which were produced by the corrosive effect making the surface hydrophilic, thus further lowering the contact angle result of the reference specimens [55]. Most of the plasma film-coated NiTi surfaces revealed better wettability characteristics as compared to the uncoated base NiTi surfaces. In addition, the surfaces grinded with 80 grit size of the paper indicated higher wettability than the surfaces grinded with 120 grit size of the paper. Since grinding with 80 grit size paper provides high surface roughness, it also allows a high probability of $-\text{NH}_2$ deposition via plasma polymerization onto the surface of NiTi specimens. However, this is not an indication for these surfaces to become more capable to entrap Ni^{2+} ions when plasma polymerization of EDA is applied to the NiTi surface. Even though 80 grinded specimens have more surface area than 120 grit size paper specimens, they also have more area to release Ni^{2+} ions which may further indicate that plasma polymerization could be insufficient for 80 grit size surfaces. The surfaces which were obtained with 120 grit size of grinding paper and modified with plasma polymerization revealed relatively low fluctuations in the wettability data throughout 14 days when compared to the base specimen suggesting that the coated surfaces maintained their film structure. On the other hand, wettability data fluctuations in the plasma film-coated specimens which were grinded 80 grit size of the paper displayed comparable results with the base specimen. Accordingly, this could be resulted from either the extreme deteriorations of plasma film composition or the abrasive conditions of the DMEM environment. If the film composition was totally disrupted, plasma film-coated specimens would act as an uncoated specimen. Even though the film composition was maintained, the abrasive conditions of the DMEM might have the potential to corrode the surface of NiTi

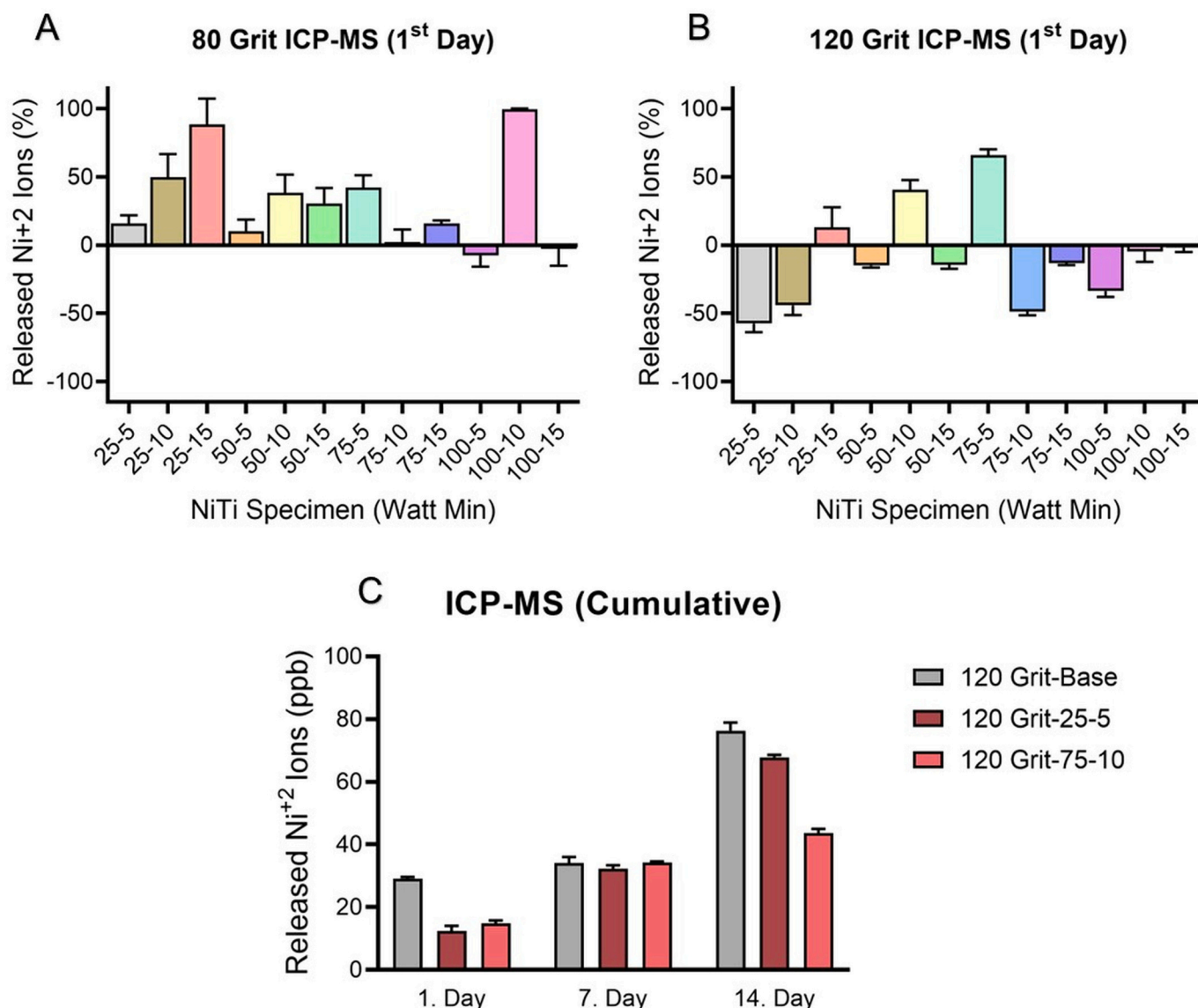


Fig. 4. Inductively coupled plasma emission-mass spectroscopy (ICP-MS) demonstrates the release of nickel (Ni^{2+}) ions from base and plasma film modified NiTi alloys under various plasma power and exposure time. The 1st-day ion release ratio from (A) the samples grinded with 80 grit size of paper and (B) the samples grinded with 120 grit size of paper. (C) The cumulative-ion release examination is demonstrated for the samples prepared with 120 grit size of paper, along with the same specimen treated for base, 25 W-5 min, and 75 W-10 min and their various incubation time (the 1st-7th-14th days). Statistical assessments are performed for the data through one-way ANOVA followed by Dunnnett analysis.

specimens due to rough surface characteristics, so that 80 grinded base and film-coated specimens wettability outcomes appeared similarly in the 1st, 7th, 10th, and 14th days.

In the Ni^{2+} ion release study, NiTi substrates with and without plasma film were tested in terms of film stability by evaluating released nickel ions by ICP-MS. Moreover, depending on several power and time values, optimum parameters of plasma polymerization were investigated for minimum Ni^{2+} ion release in a bio-mimicked media. Since the release of Ni^{2+} ions is much higher initially (1st day), it is essential to decrease the burst (initial) effect of the fluidic environment on substrates. As depicted in wettability and surface energy analysis, specimens grinded with 80 grit size of the paper and treated with plasma

polymerization had a similar and randomized release of Ni^{2+} ions on the 1st day (Fig. 4a). This may suggest that specimens grinded with 80 grit size of the paper were not appropriate for plasma polymerization even if 80 grit size grinding provides a higher surface area to the specimens. In addition, the surface topography of 80 grinded specimens might not be suitable for plasma polymerization since there is a possibility of disruption in the orientation of the functional groups in order to trap the released Ni^{2+} ions. Furthermore, plasma film could be immediately disrupted when NiTi specimens were submerged in an abrasive DMEM environment. Almost all of the 80 grinded specimens were incapable of reducing the Ni^{2+} ion release on the 1st day as shown in the ICP-MS results. On the other hand, specimens grinded with 120 grit size of the

paper and treated with plasma polymerization showed promising results as some of the specimens decreased the released Ni^{2+} ions down to $\sim 50\%$ for the 1st day (Fig. 4b). The reduced Ni^{2+} ion release was obtained in the plasma parameters of 25 W-5 min, 25 W-10 min, 50 W-5 min, 50 W-15 min, 75 W-10 min, 75 W-15 min, 100 W-5 min, 100 W-10 min, and 100 W-15 min. In particular, the reductions in the released ions were calculated as 57.53 %, 48.56 %, and 44.07 % for 25 W-5 min, 75 W-10 min, and 25 W-10 min, respectively; and this shows the achievement for the released ions on the first day. From the literature, for the plasma polymerization of EDA via low-pressure RF plasma, powers between 60 and 80 W are the optimized values in terms of consistent $-\text{NH}_2$ deposition on the surface [56–59]. Consequently, since 75 W-10 min reduced the amount of released Ni^{2+} ion down to 48.56 %, this condition was selected to conduct further long-term release experiments. As stated in the literature, lower plasma power values are not mostly suitable for EDA [59,60]. However, 25 W-5 min plasma parameter significantly dropped the release of Ni^{2+} ions on the first day, and therefore, it was also selected for further long-term release experiments since the main focus is to reduce the released Ni^{2+} ions. Hence, after the 1st day investigations, 25 W-5 min and 75 W-10 min parameters were selected for further ion release experiments since these are the ones that have the minimum Ni^{2+} ion release ratio. After that, 2 weeks of Ni^{2+} ion release study was conducted for the specimens 25 W-5 min and 75 W-10 min in order to evaluate the relationship between surface structure and plasma parameters.

Accordingly, the samples grinded with 120 grit size (NiTi-base sample and the ones were treated for 25 W-5 min, and 75 W-10 min) were cumulatively monitored on the 1st, 7th, and 14th days in terms of the release of Ni^{2+} ions (Fig. 4c). On the 7th day, both plasma parameters provided comparable results with the base specimen. However, on the 14th day, 75 W-10 min plasma parameter successfully trapped most of the released Ni^{2+} ions compared to 25 W-5 min and base specimen. It was observed that Ni^{2+} ion release for 75 W-10 min was 43.643 ± 1.296 ppb; on the other hand, for 25 W-5 min and base specimen the release amount was 67.815 ± 0.814 ppb and 76.314 ± 2.575 ppb, respectively. Approximately, half of the released Ni^{2+} ions were suppressed by the 75 W-10 min plasma parameter. Moreover, the 25 W-5 min plasma parameter have showed promising capability on the 1st day to trap Ni^{2+} ions; however, it was not as consistent as the 75 W-10 min plasma parameter. This suggests that the film composition in the 25 W-5 min plasma parameter may be destroyed after the 7th day and released some of the Ni^{2+} ions to the surrounding DMEM environment.

Table 4 underscores a range of surface modifications and their corresponding success rates, media used, and treatment durations. Among these methods, the Diamond like carbon film (DLC) coating stands out with an impressive success rate of 80 % in PBS, which is one of the most corrosive media; however, the time period of the study is relatively short, and it does not possess value regarding the long-term decrease of Ni^{2+} ions [61]. Conversely, nitrogen plasma immersion ion implantation demonstrated a success rate of 35 % in the same PBS environment for a quite long duration [62]. Anodization treatment by laser and

electropolishing displayed moderate success rates of 51 % and 47 % in simulated body fluid and water over 11 days and 7 days, respectively [63,64]. Zwitterionic hydrogel coating exhibited a 57 % success rate within 5 days in the DMEM environment [65]. Plasma polymerization of EDA (our study) showed the same 57 % success rate, yet in a longer time duration. These findings highlight the importance of plasma polymerization of EDA in terms of both the high success rate and durability of film in biomimicking media. This method would be a remedy for short and long-term toxic metal release from implanted materials therefore enabling longevity and compatibility of biomedical devices.

On the 14th day of the Ni^{2+} ion release study, an XPS survey was conducted on the specimens grinded with 120 grit size of grinding paper and surface modified with 25 W-5 min and 75 W – 10 min plasma parameters because the fact that these parameters were selected and tested by ICP-MS characterization for the 1st-7th-14th days (Fig. 5). All of the specimens provided two Oxygen (O) peaks at 529.8 eV and 531.7 eV corresponding to C–O and C=O functional groups due to the DMEM environment. The peaks at the Carbon (C) element differed from NiTi base to 25 W-5 min, 75 W-10 min, those at 284.3 eV aliphatic carbon (C-C/C-H) and 287.5 eV C-N/C=N were stemmed at all of the specimens, yet the peak around 288.5 eV (O-C-O/N-C=O) was observed in the plasma polymerized samples [66]. The unmodified base specimen had 4 Nitrogen (N) peaks which were at 399.94 eV and 400.24 eV both representing the NH-C=O and N=C/N $\equiv$ C functional groups possibly occurred due to the abrasive environment of DMEM [67]. In addition, 396.88 eV and 407.09 eV peaks were attributed to bond stretching of N-C/N-O. The N1 peak for 25 W-5 min was at 399.79 eV representing the N=C bonds [68]. There were two N1 peaks for 75 W-10 min plasma parameter, 399.47 eV and 399.79 eV representing stretching or straining of NH-C=O and N=C/N $\equiv$ C bonds. Furthermore, the deconvoluted peak for the unmodified base specimen had 3 components where 869.54, 852.26, and 854.52 eV represented Ni⁰ 2p 1/2 intermetallic NiTi position, NiTi (Ti⁰), and NiO (Ni²⁺), respectively. The surface prepared with 25 W-5 min also displayed a deconvoluted peak consisting of 3 components where 869.54 eV represented NiTi (Ti⁰) and both 852.86eV/852.26 eV represents NiO (Ni²⁺). Lastly, the one obtained with 75 W-10 min plasma parameter had a deconvoluted peak consisting of 4 components where 855.34eV/861.13 eV represented NiO (Ni²⁺), 852.19 eV stated NiTi, and 869.43 eV denoted Ni⁰ 2p 1/2 intermetallic NiTi position.

Moreover, the surface elemental compositions of 120 grit size: NiTi base, 25 W-5 min, and 75 W-10 min specimens also were depicted in Fig. 6, after 14 days of shaker-based incubation. The C, N, O, Ni, and Ti are common peaks on the surface of the specimens. In the NiTi base, the surface C atomic ratio was found the highest (61.60 %), whereas Ni (0.89 %), N (2.87 %), and O (29.13 %) atomic ratios were the lowest. On the other hand, in the condition of 75 W-10 min, the Ni (2.87 %) and O (49.47 %) atomic ratios were observed to be the highest confirming that the ability to contain Ni ions inside the coating of EDA plasma film, and enhanced surface oxide (TiO₂), so that 75 W-10 min polymerization parameter was more positive than that of 25 W-5 min in terms of $-\text{NH}_2$

Table 4

The comparison table of coating methods for decreasing Ni^{2+} ion release.

Method	The success rate	Media	Time	Refs
Plasma Polymerization of Ethylenediamine	57 %	Dulbecco's modified Eagle's medium (DMEM)	14 days	Our study
Anodization treatment by laser	51 %	Simulated Body Fluid (SBF)	11 days	[63]
Diamond like carbon-film (DLC) coating	80 %	Phosphate-buffered Saline (PBS)	5 days	[61]
Nitrogen Plasma Immersion Ion Implantation	35 %	Phosphate-buffered Saline (PBS)	7 days	[62]
Electropolishing	47 %	Water	7 days	[64]
Zwitterionic Hydrogel Coating	57 %	Dulbecco's modified Eagle's medium (DMEM)	5 days	[65]

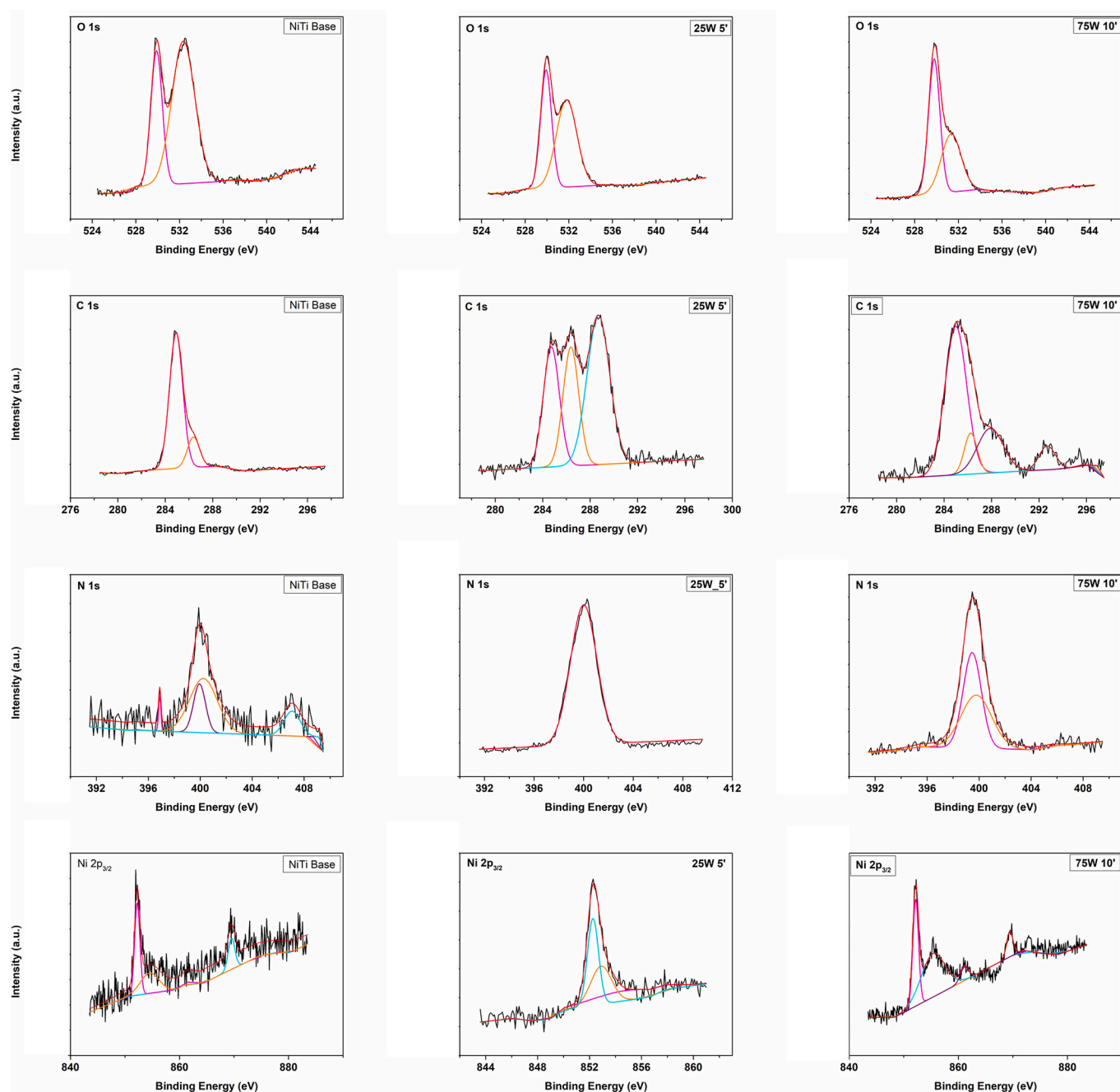


Fig. 5. The XPS spectra exhibits O, C, N, and Ni elements for the NiTi base prepared with 120 grit size of paper, along with various conditions, i.e., 25 W-5 min and 75 W-10 min on the 14th day of the Ni^{2+} ions release.

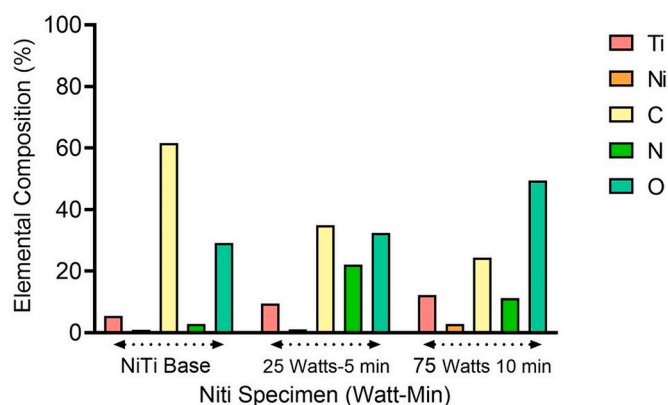


Fig. 6. The XPS-elemental composition analysis provides the elemental ratios of Ti, Ni, C, N, and O for the specimens prepared with 120 grit size of paper, along with the other specimens treated with various parameters (25 W-5 min and 75 W-10 min) after 14 days of DMEM incubation.

functional group deposition. With regards to our main objective, our two-step surface modification method successfully reduced Ni^{2+} ion release and trapped these ions inside the plasma polymerized EDA thin films.

4. Conclusion

The release of cytotoxic Ni^{2+} ions is a severe restriction for the NiTi implants stemming from their surface structures and interactions with immersed media. In order to decrease Ni^{2+} ion release, we first changed the surface roughness of NiTi samples by grinding with 80 and 120 grit size papers and subsequently applied plasma polymerization films through ethylenediamine monomer with varying power levels (25–100 W) and different durations (5–15 min). As per the AFM results, it was observed that 80 grit size of grinding paper formed NiTi surfaces has more roughness than the ones prepared with 120 grit size of grinding paper. It is known that the higher the surface roughness, the lower the ability to entrap Ni^{2+} ions, because high surface roughness and randomized surface topography are two major obstacles to maintaining the structural composition of the surface coating. To step forward this knowledge, we also showed that NiTi samples grinded with a grit size of 120 and treated with plasma polymerization has proven to be more effective in reducing the release of Ni^{2+} ions than samples grinded with 80 grit size and coated with a plasma polymer film. Moreover, after conducting a thorough analysis of contact angle measurements, XPS, and ICP-MS, it was found that the optimal plasma polymerization parameter for surfaces prepared with 120 grit size of grinding paper is 75 W of power and 10 min of treatment time. This sample maintained the film structure for 14 days and decreased the release of Ni^{2+} ions down to ~50 %. Our results provide a significant potential of EDA plasma polymerized coatings on Ni^{2+} ion release when compared to anodization, ion implantation, hydrogel coating, and electropolishing. Still, DLC coatings reduce significant amounts of Ni^{2+} ions; however, the delamination effect of DLC possesses inapplicability. In conclusion, our findings confirmed the significance of the surface topography and relevant effects of roughness on both plasma polymerization and Ni^{2+} ion release from NiTi samples which can be adapted to biomedical stent, implant, prosthesis, and dental brace applications.

CRedit authorship contribution statement

Barkan Kagan Durukan: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Visualization, Writing – original draft, Writing – review & editing. **Kutay Sagdic:** Conceptualization, Data curation, Formal analysis,

Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Benat Kockar:** Conceptualization, Formal analysis, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing. **Fatih Inci:** Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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