Can gamma irradiation during radiotherapy influence the metal release process for biomedical CoCrMo and 316L alloys?

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Abstract: The extent of metal release from implant materials that are irradiated during radiotherapy may be influenced by irradiation-formed radicals. The influence of gamma irradiation, with a total dose of relevance for radiotherapy (e.g., for cancer treatments) on the extent of metal release from biomedical stainless steel AISI 316L and a cobalt-chromium alloy (CoCrMo) was investigated in physiological relevant solutions (phosphate buffered saline with and without 10 g/L bovine serum albumin) at pH 7.3. Directly after irradiation, the released amounts of metals were significantly higher for irradiated CoCrMo as compared to nonirradiated CoCrMo, resulting in an increased surface passivation (enhanced passive conditions) that hindered further release. A similar effect was observed for 316L showing lower nickel release after 1 h of initially irradiated samples as compared to nonirradiated samples. However, the effect of irradiation (total dose of 16.5 Gy) on metal release and surface oxide composition and thickness was generally small. Most metals were released initially (within seconds) upon immersion from CoCrMo but not from 316L. Albumin induced an increased amount of released metals from AISI 316L but not from CoCrMo. Albumin was not found to aggregate to any greater extent either upon gamma irradiation or in the presence of trace metal ions, as determined using different light scattering techniques. Further studies should elucidate the effect of repeated friction and fractionated low irradiation doses on the short- and long term metal release process of biomedical materials.

Key Words: passivation, radicals, radiotherapy, BSA, implant

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INTRODUCTION

CoCrMo alloys and stainless steel grade AISI 316L are biomedical alloys widely used for different dental implants, orthodontic appliances and devices, artificial joint prostheses or orthopedic temporary devices.1–4 They are therefore often present in patients that undergo a radiation cancer treatment (radiotherapy), and might be in the irradiated zone. A common example is radiotherapy of prostate cancer in the presence of artificial hip joints, which make radiotherapy and imaging by computed tomography more complicated due to shielding and perturbation effects.5,6 Reports and reviews on failed implants or insufficient osseointegration after/during radiotherapy for both hip joints7–9 and dental implants10–17 indicate risks of implant failure or loss of the implant upon irradiation, most probably due to tissue damage. These risks increase with increasing irradiation dose.10,11,15,18 This has been questioned in some recent reviews and studies,19,20 and patients that undergo radiotherapy have been recommended dental implant therapy if following some guidelines (e.g., strict monitoring).16,20–23 Pelvic irradiation of patients with gynecological cancer without implants did not result in a higher risk of hip replacement afterward.24 The reviews and studies that suggest an increased risk for failed implants or osseointegration caused by irradiation explained this risk to be related to damage of the bone or soft tissue, altered mechanical properties of the bone, and increased risks of infections. The metallic implant itself may also be affected by gamma irradiation radiotherapy. During radiotherapy, ionizing radiation, in particular gamma-radiation, will be absorbed and result in excitation and ionization of water and aqueous organic systems. These processes cause formation of oxidative and reductive...
radicals and species,25,26 for example, OH−, O2, H2O2, HO2−, H2O2, HO2−, and H2O−. These species may affect the metal release process, the surface oxide characteristics, and/or the corrosion behavior of the implant material. The amount of produced radicals depends on solution pH and is proportional to the total irradiation dose.26 Most studies that investigate metal release and corrosion of stainless steels or other metals and alloys have been performed at higher temperatures and irradiation doses as compared to what would be relevant for the human body and radiotherapy (37°C and 10–145 Gy14 total irradiation dose). An early study on stainless steel AISI 304 in the temperature range from 65 to 250°C in water of different pH and dissolved oxygen content observed a thicker surface oxide and transformation of released metals to insoluble corrosion products, but not an increased total amount of released metals upon exposure to gamma irradiation with a total dose of 120,000–225,000 Gy.27 An evident surface oxidation effect was also observed for a Ni-Cr-Fe Inconel 600 alloy in water (pH 6–10.6) at 150°C, exposed to gamma-irradiation with a total dose of 295,200 Gy.28 The study reported increased release of metals upon irradiation for solutions of the lower pH levels.28 A study on stainless steel AISI 316L at relatively harsh conditions (320°C, 3 weight parts per million H2, neutral pH, a total proton irradiation dose up to 1.04 × 108 Gy) revealed accelerated corrosion and depletion of chromium from the surface oxide upon irradiation.29

To the best of our knowledge, no studies exist that investigate metal release from biomedical materials at conditions of relevance for radiotherapy. This is of interest, since elevated levels, possibly toxic, of released metals upon radiotherapy could detrimentally affect the clinical outcome of the cancer treatment and/or the implant biocompatibility. This might furthermore be of particular interest in high risk groups for implant complications30–34 and/or for the rare cases of metal-induced sarcoma.35–37

The aim of this study was to investigate the extent of metal release from the biomedical materials stainless steel AISI 316L and cobalt-chromium-molybdenum alloy at simulated physiological conditions induced by gamma irradiation with a total dose of relevance for radiotherapy.

### MATERIALS AND METHODS

#### Materials

Samples of a biomedical grade cobalt-chromium-molybdenum (CoCrMo) alloy with nitrogen addition in disk shape of 22 mm in diameter and 2 mm in thickness (a total surface area of 9.0 cm²) were supplied by Ionbond, Switzerland, and produced by Aubert & Duval, France, by means of vacuum induction melting followed by electroslag remelting and warm working. The material conforms to the ASTM F1537 Alloy 1 standard. Coupons from sheets of AISI 316L stainless steel (cold-rolled), sized approximately 1.5 × 1.5 cm² (with a total surface area of 4.6–4.8 cm²), were supplied by Thyssen Krupp, Germany. Nominal bulk compositions are given in Table I.

#### Metal release exposure and irradiation

All samples were ground by 1200 grit SiC, ultrasonically cleaned in acetone and isopropyl alcohol for 5 min, dried with cold nitrogen gas, and aged (desiccator; room temperature) for 24 h to enable a defined surface oxide. The samples were then entirely immersed into the solution of interest in acid-cleaned glass vessels. The solution volume was 20 or 30 mL to completely immerse the coupons or disks and enable solution sampling after different exposure times (in the case of CoCrMo disks). The sample area to solution volume ratio was approximately 0.3 cm²/mL and accounted for in the metal release results presented in the unit of µg/cm². In all cases, triplicate samples and one blank sample (without metal samples) were exposed in parallel into phosphate buffered saline (PBS), pH 7.3 ± 0.1, and also in PBS with bovine serum albumin (BSA), 10 g/L (A7906, Sigma Aldrich), denoted PBS + BSA, pH 7.3 ± 0.1. PBS was composed of 8.77 g/L NaCl, 1.28 g/L Na2HPO4, 1.36 g/L KH2PO4, adjusted to pH 7.2–7.4 (at all analytical grade, from VWR or Sigma Aldrich, Sweden), and ultrapure water (18.2 MΩ cm, Millipore, Solna, Sweden). The albumin concentration was lower than present in human blood (about 40 g/L),38 though higher than approximately 0.5–1 g/L that is necessary to adsorb a monolayer of BSA on stainless steel and to significantly enhance the metal release from 316L.39 The 10 g/L BSA concentration was hence chosen as it requires less sample preparation prior to trace metal analysis, as compared with higher concentrations. All samples were irradiated (a Gammacell 1000 Elite, MDS Nordion) for 2 min and 13 s at a gamma irradiation rate of 0.124 Gy/s, resulting in a total irradiation dose of 16.49 Gy. Four milliliter of the 20 mL (316L) or 30 mL (CoCrMo) solution was directly sampled at 0 min (a few seconds) prior to irradiation and another 4 mL directly after irradiation (denoted 2 min and 13 s, or 0.035 h). The exposure was thereafter continued without irradiation for another 58 min (total exposure time of 1 h), after which the metal coupon/disk was separated from the solution. Since no agitation or temperature control was possible inside the gamma cell, all exposures were performed at room temperature and without agitation. Parallel nonirradiated reference samples were treated in the same way outside of the irradiation cell. This resulted in 12 independent CoCrMo samples.

### Table I. Nominal Bulk Alloy Composition of AISI 316L and the CoCrMo Alloy (wt %)

|     | Co  | Cr  | Mn | Ni | Mo | C  | P  | Si | S   | N   | W  |
|-----|-----|-----|----|----|----|----|----|----|-----|-----|----|
| CoCrMo | Ba* | 27.9 | 0.22 | 0.59 | 0.11 | 5.9 | 0.074 | <0.005 | 0.57 | 0.00018 | 0.18 | <0.5 |
| AISI 316L | N/A | 16.6 | 1.0 | 10.6 | 2.1 | 0.03 | 0.02 | 0.4 | 0.001 | N/A | N/A |

* N/A, no data available; bal., balance.
12 independent 316L samples and eight blank solution samples, all sampled at three time points (resulting in 96 solution samples). After the 60 min exposure time, the coupons/disks were rinsed with ultrapure water, dried with nitrogen gas, and stored in a desiccator for postsurface analysis. The solution was acidified to a pH < 2, and analyzed with graphite furnace atomic absorption spectroscopy (GF-AAS) on iron (Fe), chromium (Cr), and nickel (Ni) for the 316L samples, and on cobalt (Co), Cr, and molybdenum (Mo) for the CoCrMo samples. All chemicals were of at least analytical grade, and all equipment and vessels were acid-cleaned by 10% nitric acid for 24 h, and rinsed four times with ultrapure water.

Trace metal analysis
Solution metal analysis was performed using AAS (AAAnalyst 800 instrument, Perkin Elmer), with graphite furnace mode. Calibration curves were based on at least four calibration standards and quality control samples of known concentration were analyzed regularly. The limits of detection, as determined by three times the highest standard deviation of the blank samples, were approximately 1 µg/L for all elements. Some sample concentrations were lower than the corresponding blank concentrations, or lower than the limit of detection denoted “<LOD.” In all cases, the released and nonprecipitated amount of measured metals in solution in the unit µg/cm² is based on the average concentration of three independent replicate samples with the corresponding blank concentration subtracted, multiplied by the initial exposure volume (e.g., 0.03, 0.026, and 0.022 L for CoCrMo disks after 0 min, 2 min and 13 s, and 1 h), and divided by the exposed coupon/disk surface area. The error bars in the figures show the standard deviation of three independent samples.

Analysis of albumin size by dynamic light scattering
In order to investigate whether albumin aggregates or changes its size upon irradiation or due to released metal ions, independent duplicate solution samples of PBS + BSA were prepared with or without the addition of 150 µg/L Co (from CoCl₂) and 5 µg/L Cr (from chromium(III) oxalate trihydrate), concentrations that approximately correspond to 1 mmol/L, and analyzed on two independent disks/coupons for each condition. Wide spectra and detailed spectra (20 eV pass energy) were performed. The intensity and particle concentration of all samples (6.9 ± 2.1 particles/frame) were significantly exceeding the background value for NTA, for which 0.25 particles per frame were observed. The NTA 3.2 software was employed to analyze the data.

Analysis of surface composition by means of X-ray photoelectron spectroscopy
X-ray photoelectron spectroscopy (XPS) was used for surface compositional analysis of the CoCrMo disks and 316L coupons, and a nonexposed (ground, cleaned, and aged) disk/coupon for comparison. Two different locations were analyzed on two independent disks/coupons for each condition. Wide spectra and detailed spectra (20 eV pass energy) on Co 2p, Cr 2p, Mo 3d, for CoCrMo disks, and on Fe 2p, Ni 2p, Mn 2p, and Cr 2p for 316L coupons, as well as O 1 s of each test item including carbon (C 1s) and N 1s were run using a Kratos AXIS UltraDLD X-ray photoelectron spectrometer (Kratos Analytical) with a monochromatic Al X-ray source (150 W) on areas approximately sized 700 × 300 µm². The information depth is about 5–10 nm. Compositional findings of the outermost surface oxide are in the following presented as the relative mass ratio of oxidized metals only. For 2p metals (Co, Fe, Ni, Mn, and Cr), the 2p 3/2 peaks were resolved into their metallic and oxidic peaks (Table II). For Mo 3d, the distinct metallic 3d 5/2 peak (228.2 ± 0.2 eV) as well as the metallic 3d 3/2 (231.3 ± 0.2 eV) peak were subtracted from the 3d peaks in order to obtain the oxidic fraction. C 1s at 285.0 eV (denoted C1) was used as internal standard. For the disks/coupons exposed in PBS + BSA, also the atomic fraction of the nitrogen peak (399.5 ± 0.9 eV) to the sum of the oxidized carbon peaks (denoted C2, at 286.7 ± 0.2 eV, and C3, at 288.5 ± 0.3 eV) was calculated.

Statistics
To identify the significance of differences, a Student’s t test of unpaired data with unequal variance (KaleidaGraph v. 4.0) was employed between two different data sets of independent samples. In the case of different time points for the same disks/coupons, a t test of paired data was used. Differences are counted as significant when p < 0.05, with higher significance for a smaller p value.

RESULTS
Metal release
For CoCrMo, the released and nonprecipitated amount of Co and Cr in solution increased 1.6–3-fold with exposure time.
Statistical differences in solution concentrations of Co and Cr were observed between nonirradiated and irradiated disks after the irradiation period (2 min and 13 s), Figure 1(a), but not after 1 h of exposure. No significant difference was observed between PBS without and with BSA.

Differences could not be calculated for Mo, since the concentrations were below the limits of detection after 0 and 0.03 h, however, the trends were similar as for Co and Cr. In the case of 316L, one of the three coupons showed in several cases higher release compared to the other two coupons. This resulted in large error bars and disabled any

\[\text{FIGURE 1} \] Released and nonprecipitated amounts of Co, Cr, and Mo in solution (aq—aqueous) from the CoCrMo alloy (a), and of Fe, Cr, and Ni from the 316L alloy (b) after 0 (few seconds), 0.035 (2 min 13 s), and 1 h of exposure at room temperature with or without irradiation (during the time period 0–0.035 h) in PBS (pH 7.3) or PBS and 10 g/L BSA (pH 7.3). Statistical differences: *p < 0.05, **p < 0.01, ***p < 0.001. non, nonirradiated; irr, irradiated; <LOD, below limit of detection.

### TABLE II. X-Ray Photoelectron Spectroscopy (XPS) Binding Energies and Assignments

| Sample Binding Energy (eV) | Assignment | References |
|---------------------------|------------|------------|
| Co 2p\textsubscript{3/2}   | 778.8 ± 0.16 | Co metal 51 |
|                           | 782.3 ± 2.3 | Oxidized Co |
| Fe 2p\textsubscript{3/2}   | 707.1 ± 0.13 | Fe metal 51 |
|                           | 712.3 ± 1.2 | Oxidized Fe |
| Cr 2p\textsubscript{3/2}   | 574.6 ± 0.16 | Cr metal 51 |
|                           | 577.7 ± 0.8 | Cr(III) |
| Mo 3d         | 228.2 ± 0.2, 231.3 ± 0.2 | Mo metal 52 |
|               | 232.6 ± 0.3, 235.8 ± 0.1 | MoO\textsubscript{3} |
| Ni 2p\textsubscript{3/2}  | 853.0 ± 0.14 | Ni metal 51 |
| Mn 2p\textsubscript{3/2}  | 641.3      | Oxidized Mn |
| N 1s          | 394.4 ± 0.07 (if no BSA) | Metal nitride 53 |
|               | 399.5 ± 0.9 | Amine/amide species |
| C 1s          | 285.0      | C–C, C–H bonds |
|               | 286.7 ± 0.2 | C–N, C–O bonds |
|               | 288.5 ± 0.3 | C=C–O, O=C– bonds |
| O 1s          | 530.7 ± 0.3 | Lattice oxide 51 |
|               | 531.8 ± 0.3 | Hydroxide, hydrated, or defective oxide |
|               | 533.2 ± 0.3 | Water, organic oxide |

All binding energies are normalized to C 1 s at 285.0 eV.
statistical comparison. However, the time dependence (increased release with time) was stronger as compared to CoCrMo, due to a very low release during the first seconds of immersion (0 h), Figure 1(a,b). For Ni, significantly lower amounts of Ni in solution were observed after 1 h of exposure for the irradiated coupons in PBS as compared to the nonirradiated coupons, despite similar amounts after 2 min and 13 s for the same coupons, Figure 1(b). After 1 h of exposure, released amounts in PBS + BSA were 3–32-fold larger as compared to PBS, however, these differences were not statistically significant. Co was the main released element quantified in solution for 316L disks and Fe the dominant element released from 316L, even when normalized to their corresponding bulk content in Table I. Cr was the least released element quantified in solution for 316L, and Mo the least released element for CoCrMo, Figure 1. Cr was detected to a smaller extent for AISI 316L as compared to CoCrMo, Figure 1.

### Surface characterization

XPS revealed a surface oxide composition of oxidized cobalt (Co 2p3/2 line at 782.3 ± 2.3 eV), chromium (at 577.7 ± 0.8 eV, corresponding to trivalent chromium), and molybdenum (with two main peaks at 232.6 ± 0.3 and 235.8 ± 0.1 eV corresponding to MoO₂) for CoCrMo, and of oxidized iron (712.3 ± 1.2 eV), chromium (at 577.3 ± 0.8 eV, corresponding to trivalent chromium), and manganese (641.3 eV, only for the abraded reference coupon) for 316L, Table II. The binding energy positions were independent of irradiation or exposure to PBS. The ratio of Co, Cr, and Mo in the surface oxide of the abraded reference disk corresponded nearly to their corresponding bulk content in Table I. Cr was the least released element quantified in solution for 316L, and Mo the least released element for CoCrMo, Figure 1. Cr was detected to a smaller extent for AISI 316L as compared to CoCrMo, Figure 1(a). This is also in agreement with previous observations. Mo was statistically significant enriched in PBS + BSA as compared to PBS (for irradiated disks), Figure 2(a). No difference in the ratio of metal peaks to oxidized metal peaks (0.4 by mass) was observed between the differently exposed CoCrMo disks. The ratio was though higher as compared to the abraded reference disks (0.3 by mass), which indicates a thinner oxide after exposure. Due to individual differences among the coupons, no statistical differences between the reference coupon and the exposed coupons, the irradiation conditions, or the solutions, were observed for 316L, Figure 2(b). However, calculated ratios of metal peaks to oxidized peaks indicated a statistically significant (p < 0.05) thicker oxide for 316L coupons exposed to PBS as compared to the abraded reference coupons (0.24 and 0.29 by mass as compared to 0.35 of the reference), while the oxide of coupons exposed to PBS + BSA seemed to be thinner (though not statistically different, 0.43 and 0.47 by mass). Small, but statistically significant (p < 0.05), differences were also observed for the irradiated coupons as compared to nonirradiated 316L coupons in both PBS and PBS + BSA. This indicates in both cases a thinner oxide in the case of irradiation.

The measured atomic ratio of N/(C2 + C3) was slightly lower compared with the theoretical ratio of 0.48 of BSA (0.41 ± 0.1 in nonirradiated and in irradiated PBS + BSA for rinsed CoCrMo disks, and 0.35 ± 0.04 in nonirradiated and in irradiated PBS + BSA for rinsed 316L coupons).

### Effects of gamma irradiation on the size of albumin

PCCS and NTA measurements were conducted of filtered (0.2 μm) irradiated and nonirradiated PBS + BSA solutions in order to investigate whether the applied gamma irradiation induced albumin aggregation, which could influence the measured amount of released metals in solution or the metal release process. Since previous studies showed the ability of released metal ions in solution to cause albumin aggregation, the same conditions were investigated for
albumin solutions containing 150 µg/L Co and 5 µg/L Cr. These concentrations are similar to their corresponding released levels in solution after 1 h for the CoCrMo alloy. Figure 3 shows the hydrodynamic size distribution of albumin, measured by PCCS (a) and NTA (b). As seen in the figure, no significant difference in albumin size was observed either upon irradiation or in the absence or presence of these trace metal concentrations. A slight change in size, visible by an additional peak at 13 nm, was detected by both PCCS and NTA measurements for irradiated samples as compared to nonirradiated solution samples. However, this difference was not statistically significant. Albumin self-aggregates at all sizes below the cut-off value of the membrane filter (200 nm), Figure 3(b), and is mostly present as a monomer (theoretical triangular structure of 8 x 8 x 3 nm³). Figure 3(a).

DISCUSSION
Radiotherapy for cancer treatments is usually given at daily fractions up to 2 Gy, 3–5 times per week, with a total irradiation dose of 10–145 Gy. For high risk patients, radiotherapy at a total dose of 10–20 Gy may also be given to prevent heterotopic bone formation, a complication for hip arthroplasty, which treats the condition equally effective and operative, or an on-going infection or inflammation, might be at risk to release elevated amounts of metals upon irradiation treatments. This might be particularly important for patients with on-going or known hypersensitivity reactions to metals, and requires further investigations.

That albumin was able to increase the extent of metal release from AISI 316L and change the surface oxide composition (however, not statistically significant in this study), while no such effect was observed for CoCrMo, is in agreement with previous studies. It has been speculated

FIGURE 3. Hydrodynamic size distributions of BSA by intensity (by means of PCCS, a) and by number (by means of NTA, b) of 0.2 µm filtered irradiated and nonirradiated PBS + BSA solutions, and with and without trace amounts of metal ions. non-irr., nonirradiated; irr., irradiated; w ions, with 150 µg/L Co and 5 µg/L Cr.
whether the lack of increased metal release from CoCrMo in the presence of albumin is related to a different protein-surface interaction, as compared to AISI 316L, or due to an increased metal-induced protein aggregation that may result in an underestimation of the amount of released metals in solution from CoCrMo. However, for the low concentrations of released metals in this study and the short time period of exposure to gamma irradiation, no protein aggregation effect was discerned. This observation further suggests that the lower effect of irradiation on the metal release in albumin-containing solution as compared to PBS without albumin for AISI 316L most probably was not due to albumin aggregation.

The metal release rate from CoCrMo was highest during the first few seconds of immersion. A similar trend has for instance been shown for AISI 316L powder in physiological solutions. However, released amounts of metals after a few seconds from the 316L coupons of this study were not measurable. Decreased metal release rates with time furthermore show the importance of a rapidly passivating surface oxide that adjusts to the new environment and results in lower extent of released metals. However, it could also mean that repeated destruction of the surface oxide (e.g., by friction due to joint movements or chewing) would result in relatively high amounts of released metals during the first seconds following the friction event.

Further studies should therefore investigate repeated friction in combination with fractionated irradiation treatments at conditions of relevance for radiotherapy. The following main conclusions were drawn:

1. Generally, the effect of irradiation (total dose of 16.5 Gy) was small, but detectable in some cases. It is therefore expected to be only clinically relevant in cases where other factors such as friction and corrosion, possibly synergistically, exist.
2. Irradiated CoCrMo disks released higher amounts of metals directly after irradiation (during the first 2 min and 13 s) as compared to nonirradiated CoCrMo disks. No differences in released metals were observed during the concomitant nonirradiated exposure up to 60 min for the same disks. This was most probably related to an irradiation-accelerated surface passivation effect.
3. No significant differences in metal release among the different investigated conditions were observed for 316L due to individual differences among replicate coupons, except that nickel release was lower after 1 h of exposure in irradiated coupons in PBS as compared to nonirradiated coupons (despite similar or higher levels directly after irradiation, 2 min and 13 s, of the same coupons). This indicates an irradiation-accelerated surface passivation effect.
4. The presence of albumin in solution resulted in a reduced surface oxide thickness for 316L, coupled to nonsignificant increased amounts of released metals and a nonsignificant enrichment of chromium in the surface oxide. No such effects were observed for CoCrMo except for a slight enrichment of chromium in the surface oxide in the presence of albumin.
5. Most metals were released into solution from CoCrMo during the first seconds of immersion, independent of whether they were exposed to radiation or not.
6. No albumin aggregation in solution was observed at the conditions of this study either in the presence or absence of metal ions or irradiation.

CONCLUSION

The amount of released metals from biomedical stainless steel AISI 316L and CoCrMo in physiologically relevant fluids (PBS with and without 10 g/L BSA at pH 7.3) was investigated as a function of gamma irradiation with a total dose of relevance for radiotherapy. The following main conclusions were drawn:

1. Generally, the effect of irradiation (total dose of 16.5 Gy) was small, but detectable in some cases. It is therefore expected to be only clinically relevant in cases where other factors such as friction and corrosion, possibly synergistically, exist.
2. Irradiated CoCrMo disks released higher amounts of metals directly after irradiation (during the first 2 min and 13 s) as compared to nonirradiated CoCrMo disks. No differences in released metals were observed during the concomitant nonirradiated exposure up to 60 min for the same disks. This was most probably related to an irradiation-accelerated surface passivation effect.
3. No significant differences in metal release among the different investigated conditions were observed for 316L due to individual differences among replicate coupons, except that nickel release was lower after 1 h of exposure in irradiated coupons in PBS as compared to nonirradiated coupons (despite similar or higher levels directly after irradiation, 2 min and 13 s, of the same coupons). This indicates an irradiation-accelerated surface passivation effect.
4. The presence of albumin in solution resulted in a reduced surface oxide thickness for 316L, coupled to nonsignificant increased amounts of released metals and a nonsignificant enrichment of chromium in the surface oxide. No such effects were observed for CoCrMo except for a slight enrichment of chromium in the surface oxide in the presence of albumin.
5. Most metals were released into solution from CoCrMo during the first seconds of immersion, independent of whether they were exposed to radiation or not.
6. No albumin aggregation in solution was observed at the conditions of this study either in the presence or absence of metal ions or irradiation.

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REFERENCES

1. Virtanen S. Corrosion of biomedical implant materials. Corros Rev 2008;26(2–3):147–171.
2. Virtanen S, Milosevic I, Gomez-Barrena E, Trebse R, Salo J, Konttinen YT. Special modes of corrosion under physiological and simulated physiological conditions. Acta Biomater 2008;4:468–476.
3. Milosevic I. Metallic materials for biomedical applications: Laboratory and clinical studies. Pure Appl Chem 2011;83(2):309–324.
4. Chen Q, Thouas GA. Metallic implant biomaterials. Mater Sci Eng R 2015;87:1–57.
5. Rubin M, Morin O, Chen J, Gillis A, Pickett B, Aubry JF, Akazawa C, Speight M, Roach I, Pouliot J. The use of megavoltage cone-beam CT to complement CT for target definition in pelvic radiotherapy in the presence of hip replacement. Br J Radiol 2006;79(947):918–921.
6. Reft C, Alecu R, Das IJ, Gerbi BJ, Keall P, Lief E, Mijnheer BJ, Papanikolaou N, Sibata C, Van Dyk J. Dosimetric considerations for patients with HIP prostheses undergoing pelvic irradiation. Report of the AAPM Radiation Therapy Committee Task Group 63. Med Phys 2003;30(6):1162–1182.
7. Donati D, Zavatta M, Gozzi E, Giacomini S, Campanacci L, Mercuri M. Modular prosthetic replacement of the proximal femur after resection of a bone tumour. Bone Joint J 2001;83(8):1156–1160.
8. Jacobs JJ, Kull LR, Frey GA, Gitelis S, Sheinkop MB, Kramer TS, Rosenkohl A. Early failure of acetabular components inserted without cement after previous pelvic irradiation. J Bone Joint Surg 1995;77(12):1829–1835.
9. Massin P, Duparc J. Total hip replacement in irradiated hips. A retrospective study of 71 cases. Bone Joint J 1995;77(6):847–852.
10. Esser E, Wagner W. Dental implants following radical oral cancer surgery and adjuvant radiotherapy. Int J Oral Maxillofac Implants 1997;12(4):552–557.
11. Granström G. Osseointegration in irradiated cancer patients: An analysis with respect to implant failures. J Oral Maxillofac Surg 2005;63(5):579–585.
12. Ihe S, Kopp S, Gundlach K, Konstantinovic VS. Effects of radiation therapy on craniofacial and dental implants: A review of the...
13. Sugerman PB, Barber MT. Patient selection for endosseous dental implants: oral and systemic considerations. Int J Oral Maxillofac Implants 2002;17(2):191–201.
14. Smith Nobrega A, Santiago JF, de Faria Almeida DA, dos Santos DM, Pellizer EP, Goiato MC. Irradiated patients and survival rate of dental implants: A systematic review and meta-analysis. J Prosthet Dent 2016;116(8):888–896.
15. Chrzanovski BR, Albrektsson T, Wennemar A. Dental implants in irradiated versus non-irradiated patients: A meta-analysis. Head Neck 2016;38(3):448–481.
16. Mancha de la Plata M, Gias LN, Diez PM, Muñoz-Guerra M, González-García R, Lee G-YC, Castrejón-Castrejón S, Rodriguez-Camargo FJ. Osseointegrated implant rehabilitation of irradiated oral cancer patients. J Oral Maxillofac Surg 2012;70(5):1052–1063.
17. Chen H, Liu N, Xu X, Xu X, U. Smoking, radiotherapy, diabetes and osteoporosis as risk factors for dental implant failure: A meta-analysis. PloS One 2013;8(8):e71955.
18. Noo N. Dental implant survival in irradiated oral cancer patients: a systematic review of the literature. Int J Oral Maxillofac Implants 2012;28(5):1233–1242.
19. Zen Filho EV, de Souza Tolentino E, Santos PSS, Eisele DW. Viability of dental implants in head and neck irradiated patients: A systematic review. Head Neck 2016;38(1):E2229–E2240.
20. Schiegnitz E, Al-Nawas B, Kammerer P, Grötz K. Oral rehabilitation with dental implants in irradiated patients: A meta-analysis on implant survival. Clin Oral Investig 2014;18(3):687–698.
21. Anderson L, Meraw S, Al-Hezaimi K, Wang H-L. The influence of radiation therapy on dental implantology.Implant Dent 2013;22(1):31–38.
22. Harrison JS, Stratemann S, Redding SW. Dental implants for patients who have had radiation treatment for head and neck cancer. Spec Care Dent 2003;23(6):223–229.
23. Wagner W, Esser E, Ostkamp K. Osseointegration of dental implants in patients with and without radiotherapy. Acta Oncol 1998;37(1–8):693–696.
24. Dybkv E, Furnes O, D. Fossa S, T. Trovik C, Lie SA. Pelvic irradiation does not increase the risk of hip replacement in patients with gynecological cancer: A cohort study based on 8,507 patients. Acta Orthop 2014;85(8):852–866.
25. Ershov BG, Gordeev AV. A model for radiolysis of water and aqueous solutions of H₂O, H₂O₂ and O₂. Radiat Phys Chem 2008;77(9):928–935.
26. Cagnoni DS, Grimaldi N, Sabatino MA, Soroka IL, Jonsson M. Radiation-engineered functional nanoparticles in aqueous systems. J Nanosci Nanotechnol 2015;15(5):3445–3467.
27. Ishigure K, Fujita N, Tamura T, Oshima K. Effect of gamma radiation on the release of corrosion products from carbon steel and stainless steel in high temperature water. Nucl Technol 1980;50(2):169–177.
28. Musa A, Wren J. Combined effect of gamma-radiation and pH on corrosion of Ni-Cr-Fe alloy inocel 600. Corros Sci 2016;109:1–12.
29. Raiman SS, Was GS. Accelerated corrosion and oxide dissolution in 316L stainless steel irradiated in situ in high temperature water. J Nucl Mater 2017;493:207–218.
30. Mabilleau G, Kwon Y-M, Pandit H, Murray DW, Sabokbar A. Metal-on-metal hip resurfacing arthroplasty: A review of periprosthetic biological reactions. Acta Orthop 2008;79(6):734–747.
31. Soares AM, Leite-Ferreira F, Leite-Ferreira M, Gruen T, Amstutz HC. Risk factors affecting outcome of metal-on-metal surface arthroplasty of the hip. J Orthop Traumatol 2004;18:97–103.
32. Park H-S, Jeong S-H, Kwon O-W. Factors affecting the clinical success of screw implants used as orthodontic anchorages. Am J Orthod Dentofacial Orthop 2006;130(1):18–25.
33. Mccarthy EW, Schrader MA, A. O. R, Henning F, Sauer R. Prevention of heterotopic bone formation with early post operative irradiation in high risk patients undergoing total hip arthroplasty: Comparison of 10.00 Gy VS 20.00 Gy schedules. Int J Radiat Oncol Biol Phys 1987;13(3):365–369.
34. Seegenschmiedt MH, Keilholz L, Martus P, Goldmann A, Wölfl R, Henning F, Sauer R. Prevention of heterotopic ossification about the hip: Final results of two randomized trials in 410 patients using either preoperative or postoperative irradiation therapy. Int J Radiat Oncol Biol Phys 1997;39(1):161–171.
35. Hedberg YS, Odnevall Wallinder I. Metal release from stainless steel in biologically relevant solutions. J Biomed Mater Res B 2010;92B(1):67–72.
36. Mazzucchelli M, Goiato MC. Irradiated patients and survival rate of dental implants: A systematic review and meta-analysis. PloS One 2013;8(8):e71955.
37. Hedberg Y. Odnevall Wallinder I. Metal release and speciation of released chromium from a biomedical CoCrMo alloy into simulated physiologically relevant solutions. J Biomed Mater Res B 2014;102(4):693–699.
38. Hirayama K, Akashi S, Furuya M, Fukushima K-i. Radioprotective effect of folate and vitamin C on dental implants in patients with oral cancer: A randomized controlled clinical trial. J Dent 2016;44(1):141–148.
39. Hedberg Y, Wang X, Hedberg J, Lundin M, Blomberg E, Odnevall Wallinder I. Surface-plate interactions on different stainless steel grades—Effects of metal adsorption, surface changes and metal release. J Mater Sci Med Mater 2013;24(4):1015–1033.
40. Hedberg Y, Odnevall Wallinder I. Metal release and speciation of released chromium from a biomedical CoCrMo alloy into simulated physiologically relevant solutions. J Biomed Mater Res B 2014;102(4):693–699.
41. Anthony P, Keys H, McCollister Evarts C, Rubin P, Lush C. Prevention of heterotopic bone formation with early post operative irradiation in high risk patients undergoing total HIP arthroplasty: Comparison of 10.00 Gy VS 20.00 Gy schedules. Int J Radiat Oncol Biol Phys 1987;13(3):365–369.
42. Seegenschmiedt MH, Keilholz L, Martus P, Goldmann A, Wölfl R, Henning F, Sauer R. Prevention of heterotopic ossification about the hip: Final results of two randomized trials in 410 patients using either preoperative or postoperative irradiation therapy. Int J Radiat Oncol Biol Phys 1997;39(1):161–171.
43. Hedberg YS, Odnevall Wallinder I. Metal release from stainless steel in biologically relevant solutions. J Biomed Mater Res B 2010;92B(1):67–72.
44. Hedberg Y, Odnevall Wallinder I. Metal release and speciation of released chromium from a biomedical CoCrMo alloy into simulated physiologically relevant solutions. J Biomed Mater Res B 2014;102(4):693–699.
45. Anthony P, Keys H, McCollister Evarts C, Rubin P, Lush C. Prevention of heterotopic bone formation with early post operative irradiation in high risk patients undergoing total HIP arthroplasty: Comparison of 10.00 Gy VS 20.00 Gy schedules. Int J Radiat Oncol Biol Phys 1987;13(3):365–369.
46. Seegenschmiedt MH, Keilholz L, Martus P, Goldmann A, Wölfl R, Henning F, Sauer R. Prevention of heterotopic ossification about the hip: Final results of two randomized trials in 410 patients using either preoperative or postoperative irradiation therapy. Int J Radiat Oncol Biol Phys 1997;39(1):161–171.
47. Hedberg YS, Odnevall Wallinder I. Metal release from stainless steel in biologically relevant solutions. J Biomed Mater Res B 2010;92B(1):67–72.
48. Hedberg Y, Odnevall Wallinder I. Metal release and speciation of released chromium from a biomedical CoCrMo alloy into simulated physiologically relevant solutions. J Biomed Mater Res B 2014;102(4):693–699.
49. Hirayama K, Akashi S, Furuya M, Fukushima K-i. Radioprotective effect of folate and vitamin C on dental implants in patients with oral cancer: A randomized controlled clinical trial. J Dent 2016;44(1):141–148.
50. Anthony P, Keys H, McCollister Evarts C, Rubin P, Lush C. Prevention of heterotopic bone formation with early post operative irradiation in high risk patients undergoing total HIP arthroplasty: Comparison of 10.00 Gy VS 20.00 Gy schedules. Int J Radiat Oncol Biol Phys 1987;13(3):365–369.