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# Should the galvanic combination of titanium and stainless steel surgical implants be avoided?

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## KEYWORDS

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Bone plates;  
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Titanium;  
Materials testing;  
Principal component analysis

**Summary** It is recommended that one should not combine different metals in orthopaedic devices. The least noble metal in such a galvanic coupling is more likely to corrode. However, some studies have failed to show increased corrosion when titanium and stainless steel are combined. The aim of this study was to determine the fretting corrosion of the contact areas between screws and plates made of these dissimilar metals used for internal fixation of bone fractures. The plates were fixed to a bone-simulating material and subjected to tensile and compressive forces in both human serum and Hank's solution. The outcome variables included in the analyses were weight loss, and release of Ti, Cr, Ni and Mo to the different media. Results from the multiple combinations were subjected to multivariate statistics. Principal component analysis visualised our findings and allowed classification of similar samples and separation of discrepant groups of samples. We found a significant effect of the test medium, but no dramatic effect due to mixing of metals. The titanium screws and plates corroded more in serum than in saline, while the opposite was true for stainless steel. Combination of dissimilar screws and plates did not cause higher weight loss or metal release than the single-material constructions, indicating comparable clinical safety.

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## Introduction

All metal implants corrode in vivo, releasing varying amounts and forms of corrosion products into the surrounding tissues. It is frequently stated that one should not combine devices consisting of different metals in orthopaedic devices.<sup>18,25</sup> The

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recommendation from the AO Foundation is that: "Mixing of stainless steel implants with unalloyed titanium, titanium alloy, and cobalt alloy implants should be avoided for implants that are in contact with each other".<sup>8</sup>

Galvanic corrosion may occur as a consequence of existing electrochemical potential difference between dissimilar biomaterials. The least noble metal in a galvanic coupling is more likely to corrode. Laboratory experiments such as current flow measurements or *in vitro* accelerated corrosion tests can be used to rank materials in terms of corrosion resistance and to decide whether it is safe or unsafe to use dissimilar couples. Some of these laboratory experiments predict that most materials coupled with implant quality stainless steel can be regarded as clinically unsafe.<sup>2,9</sup> However, some studies have failed to show increased corrosion when titanium and stainless steel are combined.<sup>4,24,31</sup>

Both stainless steel and titanium are corrosion resistant due to a passivating protective oxide layer which forms very quickly on the surface. However, fretting corrosion can occasionally be observed when bone plates and screws are clinically retrieved.<sup>21</sup> Typically, the contact of the underside of the screw head with the bearing surface surrounding the plate holes creates fretting corrosion condition due to localised passive film disruption.<sup>5</sup> Titanium is regarded as the more corrosion resistant metal of the two, as stainless steel is more susceptible to surface corrosion phenomena, such as pitting and crevice corrosion. However, grey discoloration in the soft tissue adjacent to titanium implants due to wear products is commonly found in clinical settings.<sup>1,3,16,17,26,30,34</sup>

The aim of this study was to determine the fretting corrosion of the contact areas between surgical screws and plates used for internal fixation of bone fractures. The galvanic combination of titanium and stainless steel versus pure combinations were studied. Principal component analysis (PCA) was used to evaluate the results from the multiple combinations. The outcome variables included in the analyses were weight loss, and release of Ti, Cr, Ni and Mo to the test media Hank's solution and human serum.

## Material and methods

The plates and screws used were commercially available implants for internal fixation of fractures. Four-hole 51 mm Limited Contact-Dynamic Compression Plates (LC-DCP) (Synthes, Stratec Medical, Oberdorf, and Synthes, Matthey Medical Ltd., Bettlach Switzerland) consisting of commercially pure titanium

(cp Ti) (article number: 423.540) and stainless steel (316 L) (article number: 223.540) with matching 3.5 mm × 20 mm screws (Synthes, Stratec Medical, Oberdorf, Switzerland) of the same materials were studied (article number: 404.020 for cp Ti and 204.020 for stainless steel).

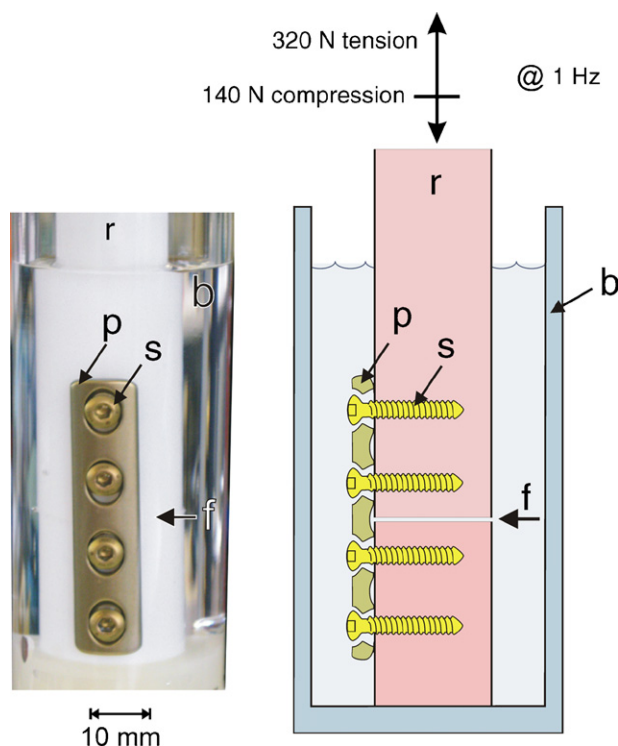
Serum proteins have a significant effect on the corrosion rates of surgical metals, and their presence can either inhibit or accelerate the corrosion phenomena.<sup>4</sup> We therefore chose two different test media, one with proteins, and one without: human serum (Octaplas, Octapharma AG, Vienna, Austria) and Hank's solution (Biochrom AG, Berlin, Germany), respectively.

A total of eight combinations of screws and plates were tested. The cp Ti and stainless steel constructs with similar screws and plates were tested in both serum and Hank's solution. Then the combinations of stainless steel screws in cp Ti plates and vice versa were tested in both solutions.

## Experimental device

A fretting corrosion simulator was constructed to study the fretting corrosion of the contact areas between screw heads and plate-hole countersinks of surgical implants. The LC-DCP plates were fixed by the bone screws with a torque screwdriver at 1.5 Nm between two rods of a bone-simulating material, polyethylene terephthalate (Ertalyte-PETP, Quadrant Engineering Plastic Products, Zürich, Switzerland) (Fig. 1). The material has a tensile modulus of elasticity of 3700 MPa at 23 °C. The rods were 50 and 180 mm long and had a diameter of 20 mm. The samples were kept in separate tubes at 37 °C containing the test solution (40 ml) and mounted in pneumatic actuators.

To simulate forces generated by body load and muscle work, the plates were subjected to alternating forces via the rods varying between 320 N in tension and 140 N in compression. The loading frequency was 60 cycles/min. Experiments were run for 5 days (432,000 cycles). At the completion of an experiment, the screws and plates were removed from the plastic rods and ultrasonically treated in the test solution to remove any loose corrosion products, then dried and weighed. The amount of fretting corrosion was assessed as the weight loss of each plate, the weight loss of the four screws and the concentration of corrosion products in the test solution. The solutions were not centrifuged or filtered before analysis, but the corrosion products were allowed to sink down and the sample was pipetted from the uppermost part of the liquid. The devices were examined by light microscopy after the end of the experiment.



**Figure 1** The Limited Contact-Dynamic Compression Plate mounted in the fretting corrosion simulator. Picture (left) and transversal drawing (right), (p) plate, (s) screw, (r) PETP rod, (f) gap, simulating fracture, (b) container with medium.

## Analyses

The solutions were analysed by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) for Ti, Cr, Ni and Mo. The instrument (Element 2, Thermo Finnigan, Bremen, Germany) was equipped with a high resolution, magnetic sector field. The instrument was operated at medium resolution of approximately 4000 for all isotopes (Ti47, Ti49, Cr52, Ni60 and Mo95), in order to resolve polyatomic interferences present at those mass-to-charge ratios.

Distilled de-ionised water (Millipore Milli-Q, Bedford, MA, USA) was used for dilution of samples and reagents. Analytical grade concentrated nitric acid (Merck, Darmstadt, Germany) was used after additional purification by sub-boiling distillation in a quartz still. The sample aliquots (0.5 ml) were diluted by a factor of 20 with ultra-clean 1% nitric acid before measurements. An internal standard of indium (1 µg/l) was added to all the samples to monitor and to correct for any instrumental fluctuations. Calibration was performed by standard addition using 0.1, 0.2, 0.5, and 2 µg/l calibrating solutions made from a 100 µg/l multielement stock standard solution (Certipur IV, Merck, Darmstadt, Germany).

The composition and sizes of the corrosion products were determined by energy-dispersive X-ray spectroscopy (EDS) on a field-emission scanning electron microscope (ZEISS Supra 55 VP). The accel-

eration voltage was 20 kV. A reference material of stainless steel (Analysen-kontrollprobe 232-1, Dortmund, Germany) was used to ensure the accuracy of these measurements.

## Quality control of elemental analyses

The method detection limit (MDL) for the element analysis was defined as three times the standard deviation in 10 blank solutions measured at different times, taking the dilution into account (20×). The MDL was 0.56 µg/l for Ti, 0.32 µg/l for Ni, 0.10 µg/l for Cr and 0.17 µg/l for Mo. The accuracy of the analytical method was monitored by a reference material (Serorm Trace Elements Serum level 1, lot MI0181, Sero AS, Billingstad, Norway) with a recommended Ti-, Ni-, Cr- and Mo-value of 2.6, 5.5, 1.02, 1.08 µg/l, respectively. We found a median value of 2.55 for Ti ( $n = 10$ ), 5.6 µg/l for Ni ( $n = 22$ ), 1.06 for Cr ( $n = 29$ ) and 1.08 for Mo ( $n = 26$ ). The median recovery was 102.6% for Ni ( $n = 4$ ), 108.6 for Cr ( $n = 5$ ), and 104.8 for Mo ( $n = 5$ ).

## Statistical analysis

Univariate statistical analyses were performed with the SPSS 12.0 software (SPSS Inc., Chicago, IL, USA). The group results were presented as medians, quartiles, minimum and maximum values. The four

groups from the mixed metal experiments had only two parallels each. Therefore we pooled groups with Ti screws and stainless steel plates with stainless steel screws and Ti plates tested in the same type of solution. Statistical comparisons of all combinations were performed by Mann–Whitney test, with  $p < 0.05$  considered statistically significant.

Multivariate statistical analyses were performed with Sirius Version 6.5 software (Pattern Recognition System as, Bergen, Norway). Principal component analysis is a powerful tool for graphical representation of the data and a good starting point for classification of samples and detection of interactions between large numbers of variables and parameters.<sup>15</sup> The principal components (PC) are orthogonal, linear combinations of the original variables. The transformation is chosen such that the first PC expresses the maximum variance or dispersion in the experimental data, the next PC expresses the second largest variance and so on. Later PCs progressively cover the “noise” in the data. In our study we had in total six variables (weight loss of screws and plates, concentration of Ni, Cr, Mo and Ti). This would make a six-dimensional space, which is mathematically possible but impossible to display. In this six-dimensional space a two-dimensional subspace can be determined. A “biplot” of both the objects and variables then display the projection of the multidimensional space that expresses the major features of the data. The projected points will be clustered for samples with similar characteristics and separated for discrepant samples. Samples located near the origin in the PC-projection have average score on the measured variables. The further the elements are located from the origin in the plot, the larger variance they have. The cosine (cos) of the angle between a pair of variable vectors shows the degree of correlation. The highest positive correlation is obtained when the angle between the variable vectors is  $0^\circ$  ( $\cos(0^\circ) = 1$ ). When the angle is  $90^\circ$ , there is no correlation, while the highest negative correlation is obtained when the angle is  $180^\circ$  ( $\cos(180^\circ) = -1$ ). The distance between the objects and the cosine of the angle between the object vectors show the degree of similarity. To reduce and homogenise the variances, the raw data were square rooted, centred and variables standardised to equal variance.

The measured variables representing fretting corrosion were subjected to Soft Independent Modelling of Class Analogy modelling (SIMCA) to develop a multivariate model of all metal combinations to test the influence of serum versus Hank’s solution and if galvanic combinations gave more fretting than the equal metals in screws and plate. We used a method of visualising the SIMCA approach, the

Cooman’s plot,<sup>7</sup> which plots class distances against each other. The criterial distance from the model used, corresponded to the  $p < 0.05$  tolerance level. The class modelling was carried out using the cross-validation method, and a zero principal component model was chosen for all classes.

## Results

In most of the test specimens we observed wear in the screw–plate interface, with surface degradation and deposits of corrosion products. Metal particles and corrosion products of different sizes were observed by scanning electron microscopy from the test solutions. The stainless steel corrosion product consisted mainly of chromium- and iron oxide particles from  $<1$  to  $5\ \mu\text{m}$ , while the titanium screws and plates released particles of approximately  $1\ \mu\text{m}$  to larger metal fragments of  $450\ \mu\text{m}$ .

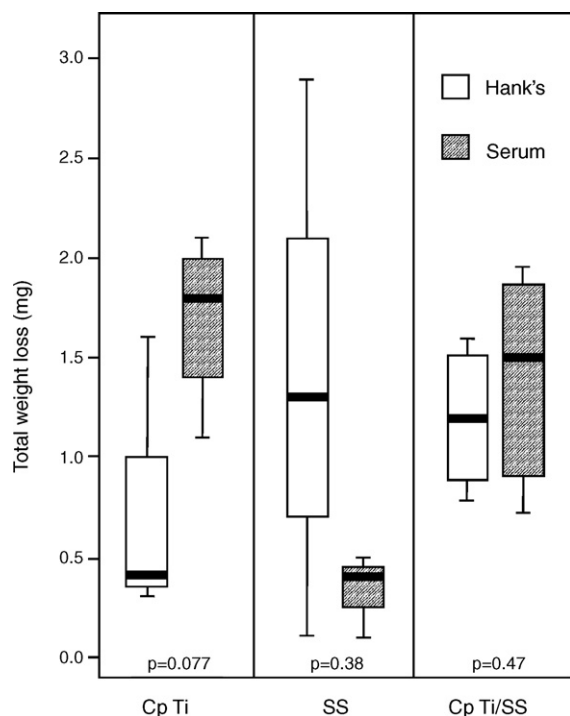
### Univariate analysis

The plates and screws made of cp Ti tested in human serum had higher weight loss than those tested in Hank’s solution (Fig. 2). The concentration of titanium was statistically significantly higher in serum than in Hank’s (Table 1). For stainless steel the weight loss was highest in Hank’s solution, but not statistically significant from serum (Fig. 2). The concentrations of the stainless steel elements nickel and molybdenum were also higher in Hank’s than in serum (Table 1).

The galvanic couples did not show higher weight loss or ionic release than the pure combinations, but the release of Ni and Mo was statistically significantly higher in Hank’s than in serum (Fig. 2 and Table 1).

### Multivariate analysis—principal component analysis

In the discrimination between stainless steel, titanium and the combination of these metals in two different media, 6 variables were used (weight loss of the screw and plate and concentrations of Cr, Ni, Mo and Ti in the media). The two first principal components represented 71.4% of the total variability. The Ni and Mo concentrations and the weight loss of screws were the dominating variables along these principal components. The results from the PCA-plot (Fig. 3) show that similar samples form clusters. The titanium LC-DCP samples in serum and Hank’s are located together in the plot, but are partly separated, with the samples in serum closer to the weight loss-variable. The stainless steel



**Figure 2** Box-plot (medians, quartiles, min and max) of total weight loss (mg) from unmixed (Cp Ti, commercially pure titanium and SS, stainless steel) and galvanic experiments (Cp Ti/SS), tested in both Hank's solution and human serum. The level of significance of the differences between samples tested in Hank's and in human serum was done by Mann–Whitney test.

objects are more scattered, with those in Hank's correlating more with Cr, Ni and Mo concentrations. The galvanic samples in serum were located close to the Ti-samples and shows correlation with the weight loss variables, while the galvanic samples in Hank's were lying in the same direction as the stainless steel samples in Hank's.

SIMCA analysis using the Cooman's plot demonstrated that the test media had high impact on the corrosion rate for all tested metal combinations. Samples of stainless steel tested in Hank's did not share multivariate space with samples tested in serum (Fig. 4a), providing validation for the class separation according to the test-media. The same was true for titanium (Fig. 4b) and the galvanic combinations (Fig. 4c). SIMCA analysis using the Cooman's plot demonstrated also that samples of galvanic combinations were not separated from the models of stainless steel and titanium samples (Fig. 5).

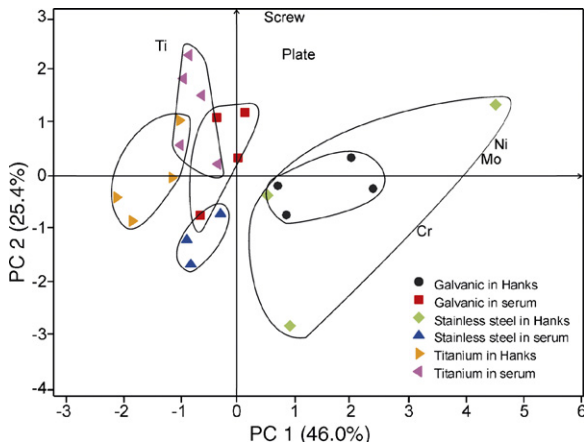
## Discussion

The purpose with this study was to determine the corrosion of the contact areas between screw heads

**Table 1** Metal concentrations ( $\mu\text{g/l}$ ) from unmixed and galvanic metal experiments expressed as medians (quartiles, or min–max, when only 3 samples), and level of significance of the differences between samples tested in Hank's solution and in human serum, using Mann–Whitney test

Metal combinations	Solution (N)	Ti	Ni	Cr	Mo
Ti plate/Ti screw	Hank's (4)	9.3 (5.5–9.2)	4.8 (4.3–6.1)	0.25 (0.2–0.34)	0.3 (0.1–0.7)
	Serum (3)	21.2 (15.1–75.8) $p = 0.027$	1.7 (<DL–14.3) $p = 0.62$	2.7 (0.5–7.3) $p = 0.25$	0.4 (0.1–1.2) $p = 0.89$
SS plate/SS screw	Hank's (3)	<DL	229.8 (205.4–4801.0)	14.9 (10.4–40.3)	15.3 (10.6–102.8)
	Serum (3)	<DL	33.9 (30.7–91.8) $p = 0.05$	13.1 (6.7–18.1) $p = 0.51$	3.4 (3.4–12.4) $p = 0.12$
Ti plate/SS screw + SS plate/Ti screw	Hank's (4)	3.0 (0.6–5.5)	851.6 (241.3–1600.6)	28.7 (14.4–44.9)	23.4 (12.0–43.3)
	Serum (4)	9.6 (2.1–25.8) $p = 0.25$	30.9 (14.2–55.7) $p = 0.021$	10.9 (4.8–16.6) $p = 0.08$	4.3 (2.7–9.1) $p = 0.021$

Ti: Titanium. SS: Stainless steel.

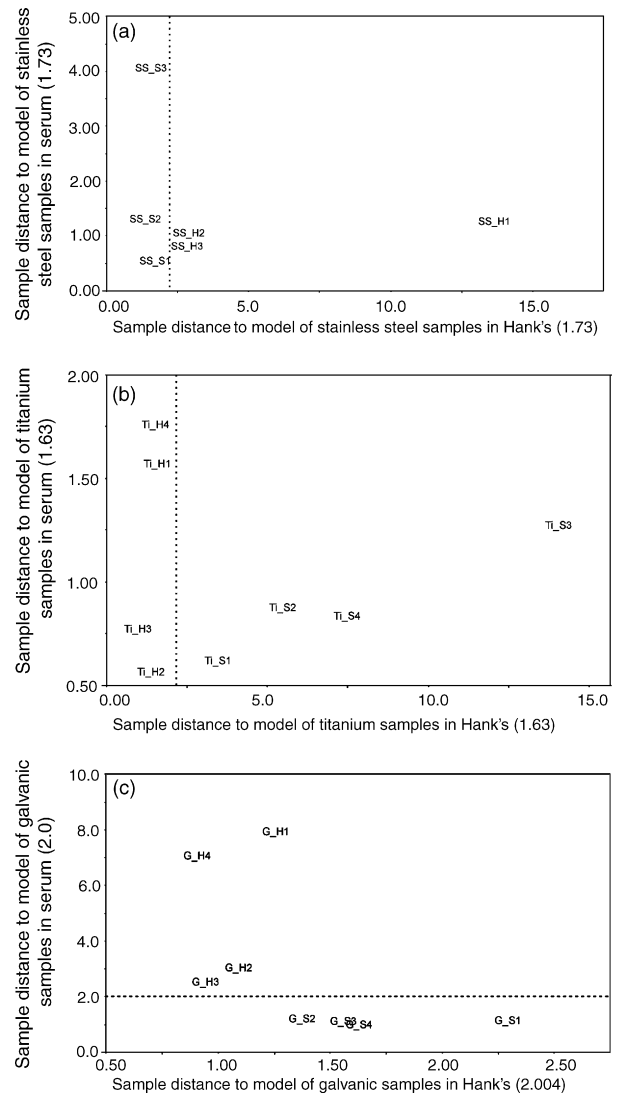


**Figure 3** Principal component analysis plot (biplot) of all LC-DCP samples tested in both serum and Hank's solution. The original (23 samples  $\times$  6 variables) data matrix is projected onto a two-dimensional coordinate system defined by principal components 1 and 2 (PC1 and PC2), which describe the largest and second largest variance among the variables. In this example the first two PCs explain (46.0 + 25.4)% of the total variance. Points close together indicate similar corrosion characteristics with respect to the measured variables. Samples belonging to the same test-category are encircled.

and plate countersinks of osteosynthesis plates. The galvanic combination of titanium and stainless steel versus pure combinations were studied. We simulated the clinical conditions regarding the mechanical and chemical environment.

The use of a standardised screw torque ensured that the plates exerted uniform contact pressure on the bone substitute. The torque used to insert the screws was 1.5 Nm, a value that is somewhat higher than the mean torque used by surgeons in a clinical setting, which has been shown to be around 0.6–0.7 Nm for stainless steel and titanium constructs.<sup>19</sup> The torque value is 65% of the overall torsional strength of the screws as required by the relevant standard of 2.3 Nm (ISO 6475:1989).<sup>12</sup> Thus, it is assumed that the fixation of the plates corresponds to a well fixed osteosynthesis. At a greater torque value than we used in our study, it is reasonable to assume that the screw–plate motion had been reduced and thereby the fretting corrosion and particle release, and a smaller torque could have given more abrasion and more corrosion.<sup>4</sup>

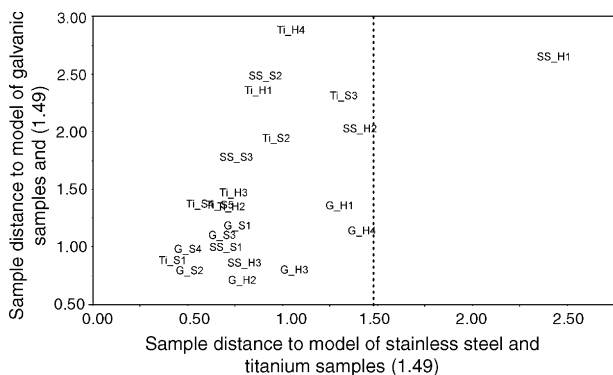
The loading pattern of the plate/screw constructs bridging fractures is complex, and also alters as the fracture heals. To simulate forces generated by body load and muscle work, the plates were subjected to alternating forces with higher magnitude in tension than in compression. The axial tensile and compressive forces used in this study did not cause gross permanent deforma-



**Figure 4** Cooman's plot of SIMCA demonstrating that LC-DCP samples of stainless steel (SS) (a), titanium (Ti) (b) and galvanic combinations (G) (c), were separated in the multivariate space according to the test media, Hank's solution (H) and serum (S). The axis shows the samples residual distance to the class models. Dotted line indicates the critical sample distance from the model used, which corresponds to the  $p < 0.05$  tolerance level.

tion of the construct and were comparable to what can be assumed in, e.g. the unloaded forearm.<sup>28</sup> The loading frequency and duration for 432,000 cycles is more intense than in a clinical situation, but mimics the number of load-cycles one could experience on, e.g. the forearm for the fracture healing time of 3–6 months. In principle, the fracture devices should be removed after they have fulfilled their function.

The experimental design of this study involving a large number of combinations (eight) would involve a huge number of experiments if standard univariate



**Figure 5** Cooman's plot of SIMCA demonstrating that all the LC-DCP samples of galvanic combinations (G) fall within the model of stainless steel (SS) plus titanium samples (Ti). All objects, except SS\_H1 were gathered to the left of the dotted vertical line. The axis shows the samples residual distance to the class models. Dotted line indicates the criterial sample distance from the model used, which corresponds to the  $p < 0.05$  tolerance level. See also legend to Fig. 4.

statistical procedures were to be applied in order to have sufficient statistical power. By the multivariate statistical method using principal component analysis it was possible to visualise similarities or patterns between samples based on fewer samples and based on linear combinations of the variables. This is especially applicable when the data are highly correlated.

It was evident that fretting contributes to corrosion of both cp Ti and stainless steel in LC-DCP plating systems. The titanium screws and plates corroded more extensively in serum than in saline, while the opposite was true for stainless steel. The experiments with human serum can be regarded as being closest to the clinical setting, which is in favour of stainless steel. The weight loss of titanium is most likely to be due to release of metal debris from abrasion (galling), while for stainless steel electrochemical corrosion is the predominant cause of metal ion release. The weight loss measurements are confounded by the variable transfer of precipitated metal-oxides. However, the concentration measurements in the test solutions give additional information and support the weight loss measurements.

The combination of Ti and steel implants gave approximately the same weight loss and metal release as the combinations with similar materials, which was confirmed by the principal component analysis, which showed that the combinations with dissimilar metals did not deviate from the combinations with similar materials. The findings in the present study are supported by other in vitro studies which have failed to show an excessive galvanic corrosion between titanium and stainless steel.<sup>4,24,31</sup>

Surgeons are generally hesitant to mix components made of different metals due to potential galvanic corrosion. Nevertheless, back in 1975, Ruedi and Perren suggested combining titanium plates with stainless steel screws, making a less stiff plate available without the risk of screw fractures.<sup>22</sup> An additional advantage was that they found less titanium wear debris in surrounding tissues for stainless screws with cp titanium plates when compared with cp titanium plates and screws. The authors were aware of increased stainless steel corrosion compared to pure titanium combinations, but they regarded it as safe and no worse than a combination consisting of stainless steel only.

In the case of stainless steel constructs, serum proteins may exert a lubricating effect that reduce abrasion and fretting. Another effect of serum proteins are metal binding. It is suggested that degradation products from metallic implants do not exist as unbound ionic or colloidal forms in the serum, but mostly bound to proteins.<sup>10</sup> The proteins are known to behave differently with different metals, since their role in a corrosive environment is governed by several factors such as the surface chemistry of the metal, protein absorption characteristics, interaction of protein molecules with other ions present in the electrolyte solution, and pH.<sup>13</sup> Proteins can form protein layers on the metal surface which also protect against corrosion. Our results do indicate such a mechanism, because galvanic coupling of Ti and steel implants caused significantly lower release of Ni, Cr and Mo in serum than in Hank's solution. The body chemistry is different from our in vitro test conditions, there are, for example, more anaerobic conditions, reducing oxide layer formation. The pH in vivo may also vary, potentially affecting corrosion rates. The pH in the body is around 7.4, but because of inflammation it may change in tissues following surgery to as low as 4 or 5.<sup>6</sup>

A larger fraction of the corrosion products from stainless steel had an ionic character compared with titanium, which releases more wear particles. It has been shown that corrosion products from stainless steel can cause pain, inflammation and allergic reactions.<sup>6,11,20,23</sup> Titanium is regarded as more biocompatible than stainless steel due to its strong passivating ability and lower toxicity.<sup>14</sup> However, the release of titanium particles can cause foreign body reaction with activation of macrophages, release of cytokines which can induce osteolysis, and eventually loosening of the implants designed for long-term use, e.g. arthroplasties.<sup>1,17,27,32,33</sup> Both stainless steel and titanium LC-DCP systems are still regarded as having acceptable biocompatibility taking into consideration their intended use as fracture fixation devices.<sup>14,29</sup>



## Conclusion

The main finding was that the galvanic combination of titanium and stainless steel did not accelerate the corrosion in the plating system. Based on metal release in an in vitro test, it appears that combination of stainless steel and titanium plating components does not pose a clinical risk.

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## Conflict of interest

The authors confirm that there is no financial conflict of interest in this study.

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