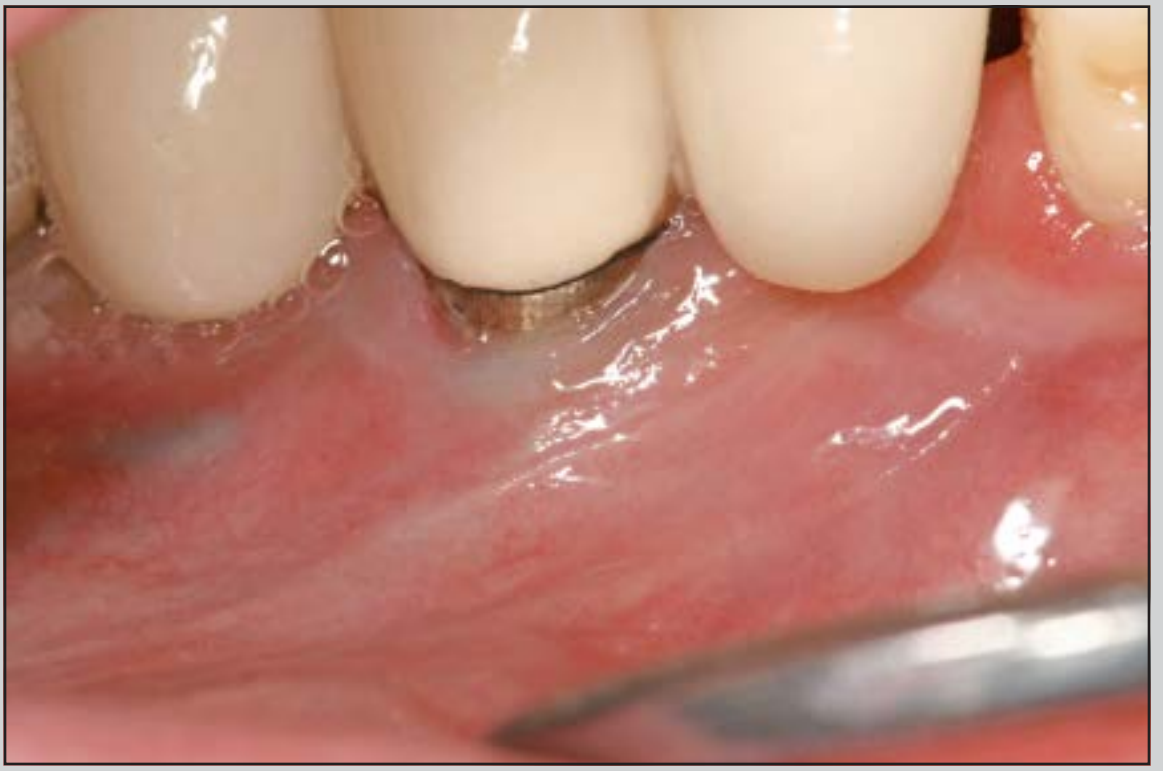
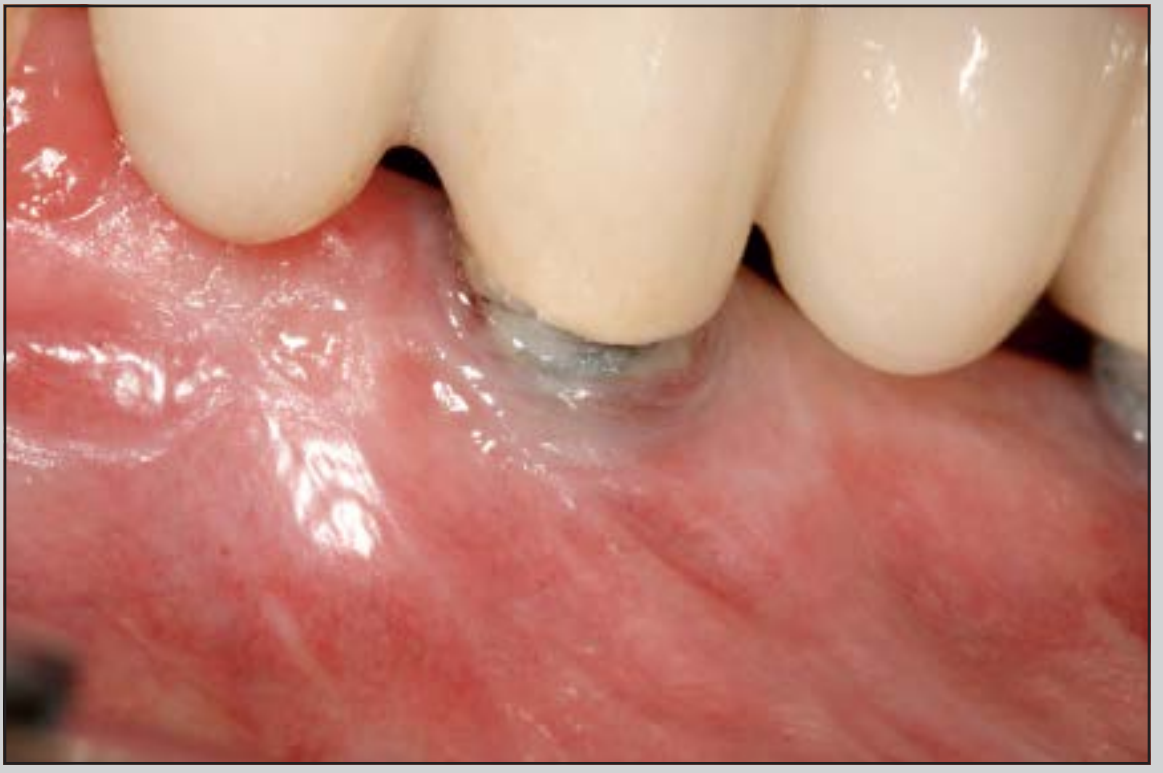
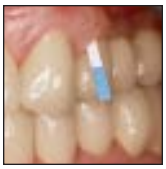




Matrix Metalloproteinase-8 Levels in Peri-implant Sulcus Fluid Adjacent to Titanium and Zirconium Nitride Surfaces



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During host interaction against oral biofilm, matrix metalloproteinase-8 (MMP-8) is activated, leading to collagenolytic destruction of host tissues. In peri-implantitis patients, the active form of MMP-8 is elevated in peri-implant sulcus fluid (PISF). In this study, MMP-8 in PISF from titanium abutments and those coated with zirconium nitride (ZrN) was compared in vivo in a split-mouth design in 60 patients at 6 weeks, 6 months, and 12 months after prosthetic restoration. At each time point, MMP-8 values in PISF differed significantly between titanium and ZrN abutment surfaces. For example, mean MMP-8 values reached 10 to 12 ng/mL in titanium and only 6.6 to 7.5 ng/mL with ZrN. Similarly, the 75th percentile MMP-8 concentrations were 12 to 15 ng/mL and 8 to 9 ng/mL for titanium and ZrN, respectively. Based on this finding, ZrN-coated abutments seem to exert a beneficial effect regarding collagenolytic tissue destruction driven by MMP-8 in situ. (Int J Periodontics Restorative Dent 2014;34:91–95. doi: 10.11607/prd.1504)

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By provoking an inflammatory host interaction, oral bacterial biofilm is the main cause of periodontitis and peri-implantitis. It triggers an immunologic reaction of the host.[1] Therefore, multiple host factors including matrix metalloproteinase-8 (MMP-8) are activated, leading to collagenolytic destruction of host tissue.[2,3] The active form of MMP-8 (aMMP-8) is highly elevated in gingival crevicular fluid (GCF) and peri-implant sulcus fluid (PISF) in periodontitis[4,5] and peri-implantitis patients,[6,7] respectively. According to the literature, MMP-8 is acknowledged as one of the crucial tissue destructive enzymes in periodontitis and peri-implantitis patients.[3]

According to Teughels et al,[8] surface characteristics of any kind of (hard) material implemented in the oral cavity, including implants, have a significant influence on the amount and quality of biofilm formation. The chemical composition and the type of coating of the respective material(s) and their surface roughness and surface free energy influence biofilm build up. As an example, transmucosal implant surfaces with a higher surface roughness facilitate greater biofilm

formation.[8] However, evidence for the impact of implant surface characteristics on the initiation and development of peri-implantitis is still very limited.[9,10]

Zirconium nitride (ZrN) is a new biomaterial coating that can be used to coat titanium implant surfaces. With this coating, reduced biofilm formation and a changed biofilm quality were registered in in vitro studies[11,12] as well as in investigations in vivo.[13,14] Thus, it appears to exert less plaque retention. However, it is unclear whether this positive effect is reflected by a positive change in the host reaction in situ (ie, less inflammation or less collagenolytic action of MMPs).

This clinical study was conducted to compare the levels of the collagenolytic biomarker aMMP-8 in PISF from titanium abutments and those coated with ZrN in vivo in a split-mouth situation.

Method and materials

Sixty patients (mean age, 45 ± 8 years) with a minimum of two missing teeth each were recruited for the study. All participants had excellent systemic health and were selected on the basis of good periodontal condition. Due to a stringent anamnestic protocol, none of the patients were smokers. Moreover, they were not taking any medication, including nonsteroidal anti-inflammatory drugs or endocarditis prophylaxis, and had not received any periodontal treatment for the preceding 2 years.

One week prior to the beginning of the study, supragingival plaque was professionally removed, oral hygiene procedures were established, and ideal gingival health conditions were obtained in all volunteers. All patients were informed and gave their consent.

In a split-mouth design, 262 titanium implants (Nobel Biocare) with titanium abutments as well as ZrN-coated abutments (Nobel-Procera Abutment Titan, Nobel Biocare) were inserted according to standard procedures in each patient in the posterior maxilla and mandible. According to the surgical procedure, all implants where placed 3 months or later after tooth extraction (late implantation). The bone volume was sufficient at the surgical site for standard implant placement assessed by clinical and radiologic examinations. All implants were longer than 10 mm and had a diameter larger than 3.5 mm.

The implants were inserted according to a two-stage surgical protocol. All implants were restored with single crowns or partial dentures without connecting implants to natural teeth. Stage-one surgery was performed for implant placement. After 3 months, implant exposure was implemented in aseptic conditions.

Two weeks after stage-one surgery, the sutures were removed and the patients were instructed to gently brush the area with an ultrasoft bristle toothbrush. Similar to stage-one surgery, routine postsurgical instructions were given to patients after stage-two surgery. Two weeks after stage-two surgery, individually produced computer-aided design/computer-assisted manufacture abutments (Nobel-Procera Abutment Titan, Nobel Biocare) were screwed on to the implant body in place of the former gingiva and the permanent prosthetic restoration (Degudent U, Duceram Kiss, Degudent) was placed. Patients were then recalled for PISF sample collection.

Six weeks (t1), 6 months (t2), and 12 months (t3) after prosthetic restoration, PISF samples were gathered from each of the implants, and aMMP-8 values (aMMP-8 ng/mL of eluate from PISF) were quantified in a specific enzyme-linked immunosorbent assay test.[4,5,15]

Results

The Plaque Index (PI), Gingival Index (GI), and mean probing pocket depth (PPD) scores were within the range of 0 to 1, 0 to 1, and 2 to 3 mm, respectively, throughout the study period for both abutment types. Thus, no analytic comparison was performed for PI, GI, and PPD between abutment types because all scores were near normal. No difference in oral hygiene measures or scores could be found concerning sites with single restorations compared to partial dentures.

Mobility of the implants was assessed after the stage-two surgery and at 6 weeks, 6 months, and 12 months after prosthetic restoration when the patients returned for the PISF sample collection. For all patients of both groups, none of the

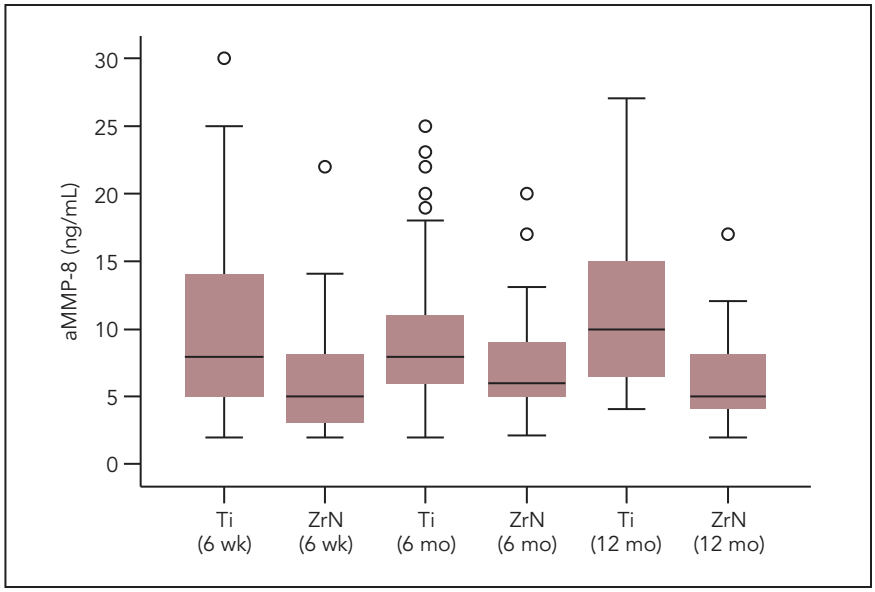

Fig 1 *aMMP-8 values from PISF of titanium abutments (Ti) and zirconium-nitride–coated abutments (ZrN) at different time points after prosthetic restoration.*

implants showed signs of mobility. No mechanical complications were observed. The success rate of the implants and restorations was 100%. In general, healing was uneventful.

Figure 1 depicts the median aMMP-8 values from PISF as well as the percentile distributions related to the implants at the different time points.

The mean values of aMMP-8 reached 10.3 to 12.1 ng/mL in titanium abutments during the 12 months of investigation, while values of 6.6 to 7.5 ng/ml were found on ZrN abutments (Figs 2 to 6). Similarly, the median aMMP-8 data were 8.0 to 10.0 ng/mL adjacent to titanium abutments compared with 5.0 to 6.0 ng/mL with ZrN abutments. An analogous distribution existed concerning the 75th percentile data, ranging from 11.5 to 15.0 ng/mL in titanium abutments compared to 8.0 to 9.0 ng/mL in ZrN abutments. Accordingly, a wider spread of the maximum

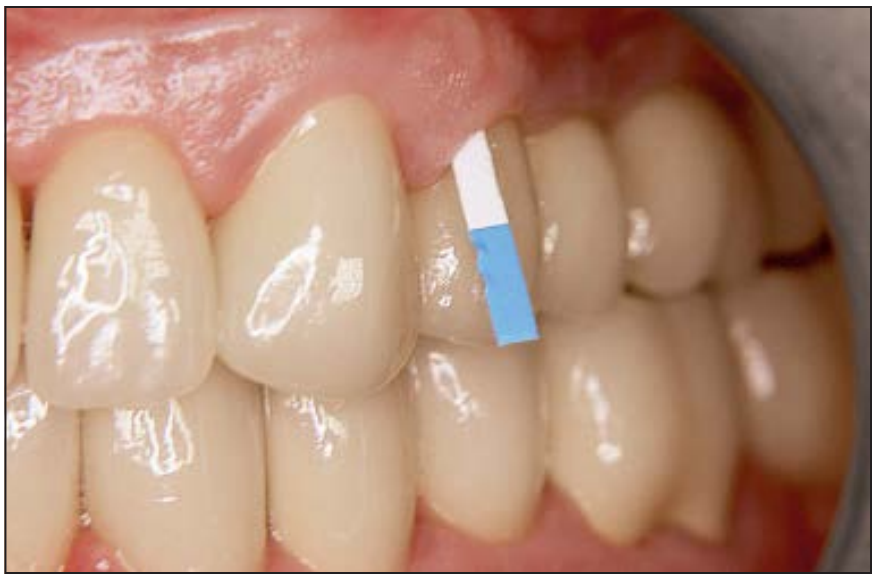

Fig 2 *PISF samples in situ.*

Fig 3 *ZrN-coated abutment.*

Fig 4 *Titanium abutment.*

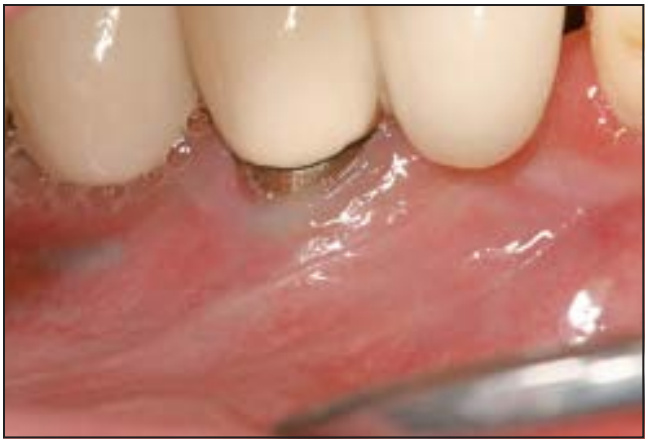

Fig 5 *One year after prosthetic restoration with ZrN-coated abutments.*

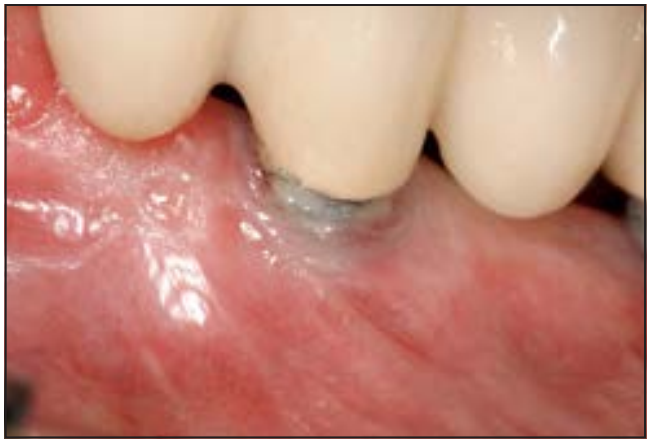

Fig 6 *One year after prosthetic restoration with titanium abutments.*

values of aMMP-8 occurred with titanium abutments (44 to 80 ng/mL) compared with ZrN abutments 25 to 44 ng/mL). At each time point, statistically significant differences were proven to exist between the two abutments surfaces (t1: $P < .0005$; t2: $P = .001$; t3: $P < .0005$).

Discussion

Only a few studies measured aMMP-8 in relation to oral implants.[6,7,16] However, no quantitative data were available that could be used as a benchmark or to allow a comparison between different implant brands and/or surfaces. While these studies referred mainly to peri-implantitis, Salvi et al[17] recently documented a substantial elevation of MMP-8 in the PISF of implants in a 3-week experimental mucositis study, with the MMP-8 increase being higher than in a simultaneous experimental gingivitis study. This latter study shows that implants are prone to collagenolytic tissue breakdown even in a very short time period of only 3 weeks of neglected oral hygiene. These authors used a different MMP-8 antibody in their test, so the magnitude of their MMP-8 findings cannot be compared to the present study. Nevertheless, the findings of Salvi et al are generally in agreement with those of Xu et al,[7] who documented a tenfold higher concentration of MMP-8 at peri-implantitis sites compared with periodontitis sites.

Regarding periodontitis, it could be established that elevated activities of MMP-8[18] or elevated concentrations of MMP-8[4,19] have a predictive value, thus showing a later occurring periodontal tissue breakdown. Taken together with the elevated MMP-8 concentrations in cases of experimental mucositis[17] and at sites with peri-implantitis,[7] the early diagnosis of tissue breakdown as well as meticulous cleanliness from the beginning of oral implant treatment is of utmost importance.

According to the literature, in periodontitis, aMMP-8 levels ≤ 8 ng/mL are defined as compatible with a healthy state.[5,15] To the best of the authors' knowledge, only these data can be used for comparison. Regarding the ZrN abutments, the aMMP-8 mean values, median values, and 75th percentiles altogether reflect a standard of collagenolytic healthiness, while titanium abutments exert elevated aMMP-8 levels, with the means and median values being borderline or above this cutoff at any time point.

It should be noted that the maximum aMMP-8 values in cases of titanium abutments (80 ng/mL) as well as in cases of ZrN abutments (44 ng/mL) are most elevated at t1, ie, 6 weeks after commencement of the prosthetic restoration. It can therefore be assumed that in both groups, some patients still exhibit an active healing phase 6 weeks after surgery.

As previously mentioned, a surface coated with ZrN reduced biofilm formation and quality.[11–14] In this study, it could not be proven whether the significantly reduced values of the tissue destructive biomarker aMMP-8 were due to less plaque retention or to surface chemistry. Also, the study was not designed to evaluate whether the obstruction of aMMP-8 refers to less plaque biofilm formation, to improved mechanical stress of the supporting tissues, or to both of these factors.

Conclusion

At different time periods after prosthetic restoration (6 weeks, 6 months, and 12 months), ZrN-coated abutments showed significantly lower aMMP-8 values in their PISF compared to titanium abutments, where statistically significantly higher PISF-derived aMMP-8 values were measured. Based on these findings, ZrN-coated abutments exert a beneficial effect not only concerning biofilm formation in vitro, but also regarding collagenolytic tissue destruction driven by MMP-8 in situ.

Acknowledgment

The authors reported no conflicts of interest related to this study.

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