Titanium Periimplant Tissue Alterations: A Prospective Cohort Plate Retrieval Study

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Abstract: Commercially pure titanium and titanium alloys have been extensively used in materials to reconstruct the facial skeleton in different forms and sizes. There is yet to be a consensus on removing (or not) the plates and screws after osteosynthesis. Our study tries to investigate the adjacent tissues of the titanium plates used in jaw surgery using inductively coupled plasma optical emission spectrometry. Twenty samples of soft tissue surrounding the titanium plates were retrieved 1 year after placement (fracture sites or orthognathic surgery) and were investigated using inductively coupled plasma optical emission spectrometry. The study found 1.06 ppm titanium in the adjacent soft tissues. Even if there are no clinical signs of the presence of titanium in the soft tissues, our findings suggest that a plate removal is a feasible option for patients to avoid local complications due to titanium migration.

Keywords: titanium; osteosynthesis; soft tissue; titanium alloys; titanium plate; titanium screws

1. Introduction

Commercially pure titanium (CpTi) and titanium alloys are considered to be the best biomaterials due to their characteristics such as biocompatibility, high corrosion resistance, suitable mechanical proprieties, high wear resistance and osseointegration capabilities [1]. It is widely used in the maxillofacial region for fracture stabilization, orthognathic surgery, dental implants, personalized implants and maxillofacial oncology [2,3].

The most frequent causes of implant failure are due to wear, corrosion, debris generation, and metal ions release which can cause hypersensitivity, damage of cell tissue, toxicity and carcinogenicity [4]. Ti is released in tissues in special circumstances, such as plate exposure and contact with certain biological fluids such as saliva [5]. The oxide layer formed on the surface of titanium can be degraded over time by spontaneous mechanical or electromechanical corrosion and will release active metallic compounds into the bloodstream [6]. These particles affect normal tissue physiology [6]. Surface modification processes such as anodization improve the anchoring of bone tissue adjacent to the implants [7]. Traces of CpTi can be found not just in the surrounding tissues [8–10] but even in regional lymph nodes [11], plasma [12], hair or nails [13]. There are even traces of titanium in the adjacent tissues of the titanium dental implants [14]. Exposure, infection, pain or recurrent sinusitis leads to plate removal, but there is not yet a consensus regarding plate removal after surgery [15]. Titanium implant retrieval is recommended in eventful healing; otherwise, removal is still a debate [16].
Current research has investigated the reported negative outcomes [17,18]. Chronic inflammation around titanium implants can induce reactive nitrogen and oxygen free-radicals [19,20]. CpTi is well-documented for its osseointegration capabilities and how it stimulates new bone formation, but the exact effect concerning the adjacent soft tissues is yet unclear [21]. The purpose of this paper is to analyze the surrounding tissues of the CpTi plates using spectrometry, a standardized method of assessing traces of metals that has yet to be validated in soft tissue traces for titanium.

2. Materials and Methods

Periosteum and soft tissue sample samples surrounding titanium plates were taken from 10 patients after jaw surgery (fracture site or orthognathic surgery), two samples from each patient after a period of at least 1 year after plate insertion from the Maxillo-facial department, Cluj-Napoca Emergency County Hospital, Romania. Informed consent from each patient and Ethical Committee approval was received prior to conducting the study.

The SPECTRO CIROS\textsuperscript{CCD} spectrometer (Spectro, Kleve, Germany) was used for Ti determination (n = 20 measurements) by inductively coupled plasma optical emission spectrometry (ICP-OES). Operating conditions are summarized in Table 1. Quantitative measurements were performed based on an 8-point linear calibration curve over the range 0–10 mg L\textsuperscript{-1} in 2\% (v/v) HCl. The calibration solutions were prepared from an ICP multi-element standard solution XVII from Merck (Darmstadt, Germany).

Table 1. Operating conditions for the SPECTRO CIROS\textsuperscript{CCD} spectrometer.

| Component | Characteristics |
|-----------|----------------|
| Generator | Free-running 27.12 MHz operated at 1400 W  
             Axial viewing, (X = −3.9 mm, Y = +3.6 mm, Z = +2.6 mm.  
              torch position) |
| Plasma torch | Argon (5.0 quality) flow rates:  
                      Outer gas 12 L min\textsuperscript{-1}  
                      Intermediate gas 0.6 L min\textsuperscript{-1}  
                      Nebulizer gas 1 L min\textsuperscript{-1} |
| Sample introduction system | Four channels peristaltic pump, K2 cross-flow nebulizer,  
                              double-pass Scott-type spray chamber, 2 mL min\textsuperscript{-1} sample uptake rate |
| Polychromator | 160–600 nm double-grating Paschen–Runge mounting,  
              chamber filled with nitrogen |
| Detector | 22 charge-coupled devices (CCDs)  
            Background correction: linear two-point models, best  
            signal-to-background (SNR) strategy, integration time 48 s  
            and three successive measurements for each element. |
| Analytical wavelengths | Ti 334.941 nm. |

Before Ti determination, the biological sample was demineralized for 24 h into concentrated acids (HNO\textsubscript{3} and HCl) at room temperature.

3. Results

All patients included in this study had no clinical signs of inflammation, granulation tissue, fistulae, screw or plate loosening.

Using inductively coupled plasma optical emission spectrometry, after the analysis of the 20 soft tissue samples, 1.06 ppm titanium particles were found in the soft tissue surrounding the titanium plates. The results have been summarized in Table 2.
Table 2. Summarized results of the soft tissue samples retrieved adjacent to titanium plates.

| Patient/Surgical Site    | Tissue Sample Number | Titanium Particles (ppm) | Complications |
|--------------------------|----------------------|--------------------------|---------------|
| 1—Orthognathic           | 1                    | 1.16 ppm                 | None          |
|                          | 2                    | 1.18 ppm                 | None          |
| 2—Orthognathic           | 3                    | 0.95 ppm                 | None          |
|                          | 4                    | 0.82 ppm                 | None          |
| 3—Orthognathic           | 5                    | 0.68 ppm                 | None          |
|                          | 6                    | 1.23 ppm                 | None          |
| 4—Orthognathic           | 7                    | 1.19 ppm                 | None          |
|                          | 8                    | 1.09 ppm                 | None          |
| 5—Fracture site          | 9                    | 1.2 ppm                  | None          |
|                          | 10                   | 0.99 ppm                 | None          |
| 6—Fracture site          | 11                   | 1.27 ppm                 | None          |
|                          | 12                   | 1.3 ppm                  | None          |
| 7—Orthognathic           | 13                   | 1.21 ppm                 | None          |
|                          | 14                   | 0.87 ppm                 | None          |
| 8—Fracture site          | 15                   | 1.17 ppm                 | None          |
|                          | 16                   | 1.26 ppm                 | None          |
| 9—Fracture site          | 17                   | 0.67 ppm                 | None          |
|                          | 18                   | 0.92 ppm                 | None          |
| 10—Orthognathic          | 19                   | 0.76 ppm                 | None          |
|                          | 20                   | 1.28 ppm                 | None          |

The summarized results (Table 3) have been divided into two groups depending on the surgical site, and have been statistically analyzed.

Table 3. Statistical analysis of the results of the soft tissue surrounding the titanium plates.

|            | Average   | Standard Deviation | Min   | Max   |
|------------|-----------|--------------------|-------|-------|
| All sites  | 1.06 ppm  | 0.209 ppm          | 0.67 ppm | 1.30 ppm |
| Orthognathic | 1.03 ppm | 0.207 ppm          | 0.68 ppm | 1.28 ppm |
| Fracture site | 1.09 ppm | 0.219 ppm          | 0.67 ppm | 1.30 ppm |

4. Discussion

This is the first study that uses ICP-OES to analyze soft tissue surrounding titanium plates retrieved from orthognathic and trauma patients. Our study has demonstrated with another investigation method that titanium traces can be found adjacent to the titanium plates.

Being the first study of our knowledge using ICP-OES to assess titanium in soft tissue, we cannot compare the results with similar papers. The value of 1.06 ppm cannot be compared to another value and further studies are necessary to validate this method and to cross-check the results.

Histological studies have shown titanium particles in the soft tissue adjacent to plates without any inflammatory response [8]. Another study by Torgersen et al. showed similar results after retrieving the soft tissue around titanium miniplates and analyzing them with histology, Energy-dispersive X-ray spectroscopy (EDXA) and Scanning electron microscope (SEM) [9]. No inflammatory response was also found.

Another paper found dense particles in the tissue surrounding the dental implant at 6 months [22]. It is believed that electrochemical and mechanical processes such as stress corrosion cracking, corrosion fatigue and fretting corrosion may interact and cause structural failure and accelerate the release of metal particles and ions [23,24].

In an in vitro model using New Zealand rabbits, titanium implants were placed in the tibia. Traces of titanium have been found in remote organs, but no toxic levels were detected and the concentration was below the normal intake average [25].
Another study concerning the immuno-inflammatory response adjacent to titanium plates after mandibular fractures by Katou et al. [26] using histology, immunohistochemistry, immunoelectron microscopy and EDX demonstrates the persistence of mild to moderate inflammation and fibrous tissue adjacent to the Ti plates. The design of this research paper did not use consecutive patients, and this may represent a risk of bias regarding patients selection. This may explain the lack of complications in this paper.

An additional paper by Kim et al. [27] studying soft tissue response after titanium plate removal after fractures and bone graft using light microscopy and transmitted electron microscopy (TEM) shows the persistence of titanium in the connective tissue. Their recommendation is to remove the titanium plates due to concern about the progression of local tissue damage.

In a prospective cohort study [6], inductively coupled plasma atomic emission spectroscopy (ICP-AES) was used to measure levels of titanium after miniplates removal, and no correlation was found regarding the Ti level and the duration of the plating. Their findings suggest that the miniplates ought to be removed only in cases of complaints such as infection, hypersensitivity, dehiscence or screw-loosening.

Increased production of pro-inflammatory cytokines and enhanced free radical generation in the soft tissue adjacent to titanium plates were found in a recent study by Borys et al. [28]. Exposure to titanium alloys has been shown to induce apoptosis of the periosteum. Another study by the same team [19] suggests that exposure to titanium plates leads to oxidant/antioxidant imbalances and to oxidative damage of the periosteum surrounding the titanium plates, although no clinical signs were evident.

Recent developments [29] have shown that there is a significant difference in cell tissue reaction to different brands and types of titanium alloys. This implies that there is yet a consensus on the actual tissue reaction and potential local damage due to the lack of standardized titanium plates.

Other studies [30] have revealed a link between the surface roughness with the bacterial adhesion and subsequent complications.

Regarding this presumed inconsistency of the titanium used in plates and screws, Pinto et al. [16] published a comprehensive study and found that there is not a correlation between the physical and chemical composition of removed plates with the need to retrieve them.

5. Conclusions

The inductively coupled plasma optical emission spectrometry revealed traces of titanium surrounding the soft tissue adjacent to titanium plates, although no clinical signs were evident. Removing the plates and screws may be beneficial to avoid possible complications due to local and distance tissue response.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.
Abbreviations

CpTi  Commercially pure titanium
ICP-OES  Inductively coupled plasma optical emission spectrometry
ICP  Inductively coupled plasma
CCDs  Charge-coupled devices
Ti  Titanium
SNR  Signal-to-background
EDXA  Energy-dispersive X-ray spectroscopy
SEM  Scanning electron microscope
EDX  Energy-dispersive X-ray spectroscopy
TEM  Transmitted electron microscopy

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