

# HISTOLOGIC ANALYSIS OF HUMAN PERI-IMPLANT BONE IN TYPE 1 OSTEOPOROSIS

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Osteoporosis is a disease that influences the quality of bone tissue. At present, osteoporosis represents a contraindication or a risk factor for osseointegration. The aim of this report was to evaluate the bone-to-implant contact of 2 loaded implants retrieved after prosthetic failure in a woman with type 1 osteoporosis. Histologically, only one implant was osseointegrated, and it appeared surrounded by healthy bone tissue. The bone-to-implant contact presented a mean of 51.25%. No foreign body reaction was found at the bone-to-implant contact, although epithelial downgrowth was observed at the interface. Data from this case report demonstrate that the peri-implant bone histology of the dental implant retrieved from an osteoporotic patient presented no alteration. However, the role of osteoporosis in the long-term success of dental implants needs further investigation.

**Key Words:** dental implants, human histology, osteoporosis, osseointegration, risk factor

## INTRODUCTION

The use of dental implants in oral rehabilitation has gained importance in daily clinical practice. This successful outcome is influenced by several confounding factors such as the bone remodeling response, implant design, implant surface topography, clinical protocols, and physical activity level of the subject.<sup>1,2</sup> In addition, the bone quality is an important factor that can influence the outcome of

dental implant treatments; a higher failure rate has been found in implants placed in grafted areas and type IV bone.<sup>3,4</sup>

Osteoporosis is a metabolic disease that influences the quality of bone tissue. Although osteoporosis may have an influence on periodontal attachment loss,<sup>5</sup> there are no clinical studies that prove a clear association between dental implant failures and osteoporosis.<sup>6,7</sup>

Previous animal studies<sup>8,9</sup> have described the deleterious effect of osteoporosis on the osseointegration process, mainly in trabecular bone volume. Animal studies have also demonstrated that bone resorption and the healing process of the alveolar bone after tooth extraction and dental implant placement were accelerated after ovariectomy.<sup>9,10</sup>

The mechanism by which osteoporosis acts on peri-implant bone is based on the decreased cancellous bone volume and consequently on the rate of bone-to-implant contact. This process reduces the bone tissue support next to dental implants.<sup>11-14</sup>

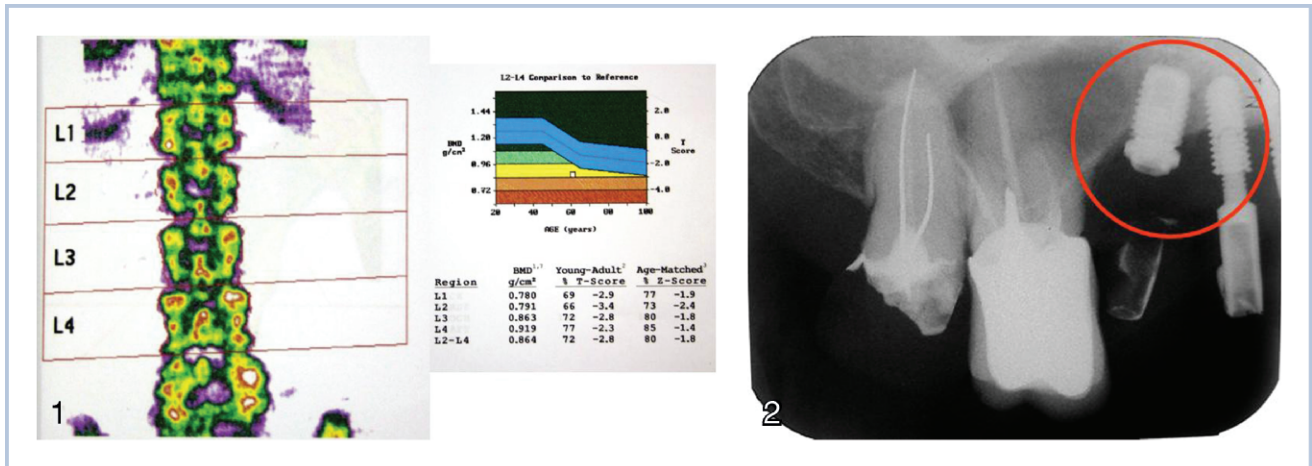
At present, osteoporosis may represent a contraindication or a risk factor for osseointegration; however, several controversial issues may be found in the literature.<sup>1,7,15,16</sup> Therefore, the objective of this report was to evaluate the bone-to-implant contact in

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FIGURES 1 AND 2. FIGURE 1. Primary osteoporosis (type 1, postmenopausal osteoporosis) determined by DPX-IQ AP in the lumbar spine based on the World Health Organization T-scores: T-score <2.5 standard deviation. FIGURE 2. Radiographic view of the retrieved implants (labeled with red circle).

loaded implants retrieved from a woman with osteoporosis.

## MATERIALS AND METHODS

### Subject report

The patient, a 61-year-old white woman had primary osteoporosis (type 1, postmenopausal osteoporosis) determined by DPX-IQ AP (Osteoporosis Bone Densitometry, Minister, Ohio) in the lumbar spine and femoral neck (Figure 1). In another oral surgery, 4 years earlier, the patient had 5 threaded, sandblasted and acid-etched, titanium, screw-shaped implants placed (4 in the posterior maxilla and 1 in the anterior mandible). The patient's anamnesis shows that the diagnosis of osteoporosis was made after implant placement. In addition, the patient follows a calcium-enriched diet and takes some medications with calcium. Glucocorticosteroids or other immunosuppressive drugs were not prescribed.

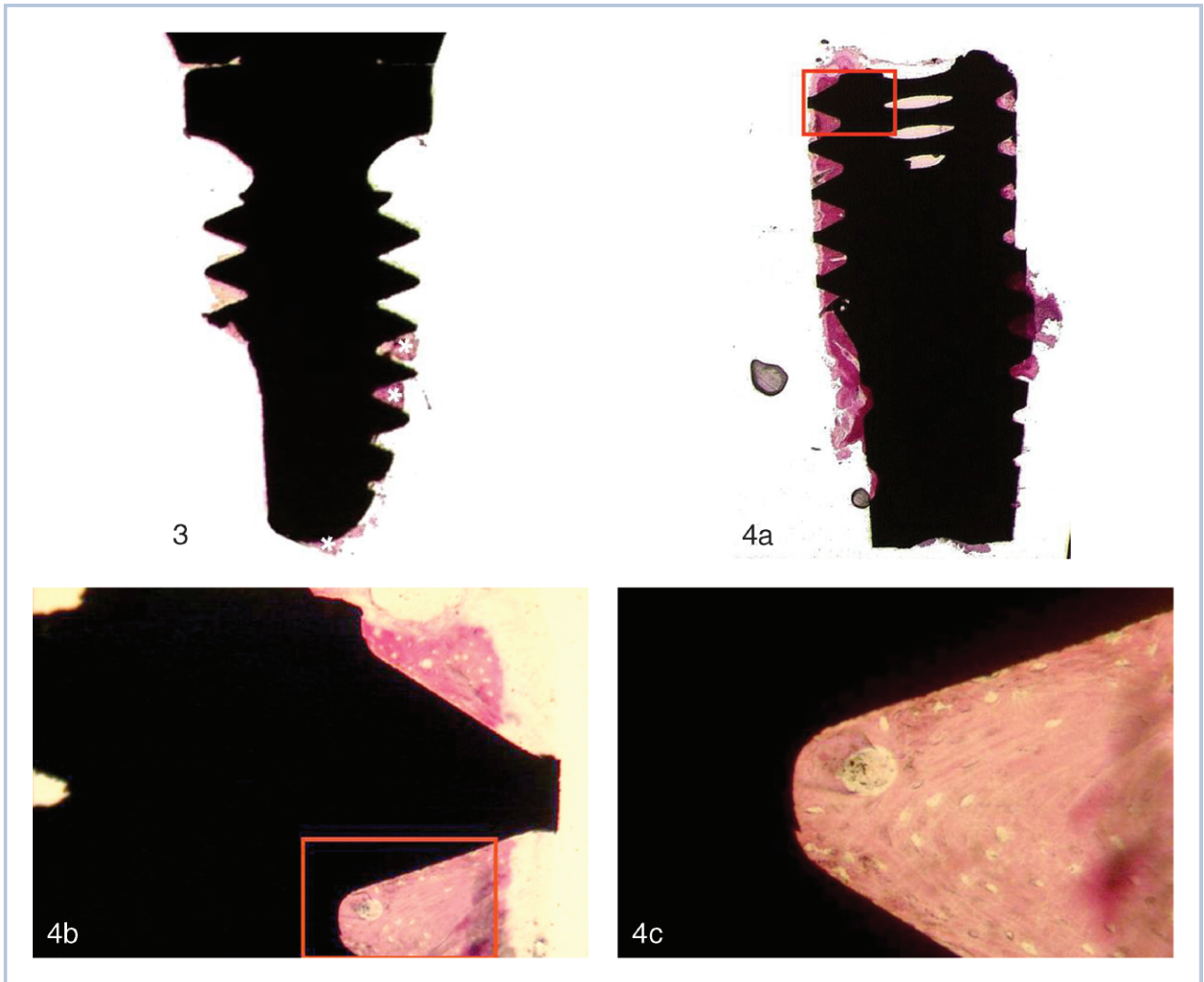
After the failure of fixed prostheses supported by 4 implants in the posterior maxilla, the patient was referred to one of the authors (J.A.S). A periapical x-ray showed that one of the implants was broken and the other showed peri-implant bone loss (Figure 2). The patient complained of increasing dissatisfaction with the restorative treatment, and after carefully planned treatment, the implants were removed for posterior bone grafting and implant placement.

### Histological processing and evaluation

The implants were removed using an internal 4.25-mm wide trephine. The implants, together with surround-

ing bone tissues, were then immediately stored in 10% buffered formalin and processed to obtain thin ground sections with the Precise 1 Automated System (Assing, Rome, Italy). The specimens were dehydrated in an ascending series of alcohol rinses and embedded in a glycol methacrylate resin (Technovit 7200 VLC, Kulzer, Wehrheim, Germany). After polymerization, the specimens were sectioned longitudinally along the major axis of the implant with a high-precision diamond disk at about 150  $\mu\text{m}$  and ground down to about 30  $\mu\text{m}$ . Two slides were obtained for each implant. The slides were stained with basic fuchsin and toluidine blue. Histomorphometry of bone-to-implant contact percentage was performed using a light microscope (Laborlux S, Leitz, Wetzlar, Germany) connected to a high-resolution video camera (3CCD, JVC KY-F55B, Milan, Italy) and interfaced to a monitor and personal computer (Intel Pentium III 1200 MMX, LG, Manaus, AM, Brazil). This optical system was associated with a digitizing pad (Matrix Vision GmbH, Milan, Italy) and a histometry software package with image-capturing capabilities (Image-Pro Plus 4.5, Media Cybernetics Inc, Immagini & Computer Snc, Milan, Italy). The measurements of the bone-to-implant contacts were performed at a magnification of about 160 $\times$ .

As one of the implants had failed, that is, it presented no osseointegration (Figure 3), only one implant was histometrically evaluated (Figure 4A). The peri-implant bone from the retrieved implant appeared to be healthy. The bone tissue was mostly compact, and some osteocytes were presented in their lacunae (Figures 4B and 4C). In some portions of the interface the bone tissue appeared in close contact with the dental implant surface, whereas narrow spaces could be



FIGURES 3 AND 4. FIGURE 3. Ground section of retrieved dental implant depicting lack of osseointegration and soft tissue (\*) (basic fuchsin and toluidine blue staining, original magnification  $\times 16$ ). FIGURE 4. Histologic ground section of the implant retrieved from the maxilla (basic fuchsin and toluidine blue staining). (a) Broken implant showing pristine bone mostly lamellar and compact (original magnification  $\times 16$ ); (b) detail of the red frame shown in Figure 4a. There is an apposition of bone in close contact with the implant surface (original magnification  $\times 40$ ); (c) detail of the frame shown in Figure 4b. The bone tissue was mostly compact, and some osteocytes were presented in their lacunae (original magnification  $\times 100$ ).

detected in other areas. The bone-to-implant contact presented a mean of 51.25%. No foreign body reaction was found at the bone-to-implant contact, although epithelial downgrowth was observed at the interface.

#### DISCUSSION

Clinical investigations have suggested that osteoporosis is not always a risk factor for osseointegration; however, osteoporosis is now being regarded as a relative contraindication for oral rehabilitation using dental implants.<sup>7,15-18</sup>

Although several studies relate the role of local and systemic factors in the long-term success of dental implants, less is known concerning factors affecting the stability of oral implants after the abutment placement process and occlusal loading.<sup>19</sup> Furthermore, the role of endogenous factors in cellular turnover and differentiation is less documented.<sup>6</sup>

In subjects with osteoporosis, the decreased net bone volume, as well as the reduced capacity to withstand optimal load, may be affected by a combination of these modulated cellular activities that are influenced by lower levels of estrogen in postmenopausal osteoporosis.<sup>10</sup> In addition, bone-to-

implant integration gradually increases, and once it is established, the accumulated rate of bone-attachment to implants is maintained.<sup>20</sup> Unlike the regular bone remodeling that occurs in the trabecular area, this phenomenon is not accompanied by apparent bone turnover or resorption.<sup>21,22</sup>

In this case report it was possible to evaluate the bone-to-implant contact in a patient classified as type 1 osteoporosis, in accordance with the criteria established by the World Health Organization based on T-scores: T-score <2.5 standard deviation. It is important to note that according to the patient's anamnesis, the osteoporosis was diagnosed after implant placement. The histomorphometric evaluation presented a considerable percentage of bone-to-implant contact and a healthy peri-implant bone. The concern that dental implants are contraindicated in subjects with osteoporosis is based on the assumption that this metabolic disease affects the jaws in the same way as it affects other parts of the skeleton, such as the lumbar spine, femur neck, and forearm.<sup>23</sup> However, osteoporosis in the lumbar spine or femur neck does not imply the presence of the same status in the jaw bones.<sup>15,24</sup>

In some clinical investigations, factors such as the subjects' gender and age were not correlated with long-term failures.<sup>3,15,25</sup> This may suggest that once bone-to-implant integration is established in these subjects, there may not be a significant number of clinical failures.<sup>6,7</sup> In addition, the presence of the dental implant may create a distinct and unique cellular environment and a scaffold for bone marrow osteogenic cells to form new bone tissue,<sup>2</sup> mainly in the earlier stages, depending on the microstructure of the implant surface topography<sup>4</sup> and loading time and force.<sup>26</sup>

Implant-supported prostheses in jawbone are affected not only by systemic factors but also by many local factors, such as the periodontal conditions of the remaining teeth, number and distribution of dental implants in the arch, occlusion, and bite forces. There may be some differences in bone healing and remodeling between the long bones and the jawbones after dental implant placement.<sup>6,11</sup> According to several investigations, in subjects with postmenopausal osteoporosis, the rate of trabecular bone loss is higher than in healthy subjects,<sup>27</sup> despite the fact that the rate of cortical bone loss is only slightly above normal.<sup>28</sup>

In conclusion, the results of the present case report suggest that osteoporosis may not present a contraindication of implant placement, at least after established osseointegration. However, further studies

are needed to elucidate the relationship of the findings in this case report in a sample of a larger size and in subjects with disorders such as postmenopausal and/or senile osteoporosis.

## REFERENCES

1. Okamura A, Ayukawa Y, Iyama S, Koyano K. Effect of the difference of bone turnover on peri-titanium implant osteogenesis in ovariectomized rats. *J Biomed Mater Res A*. 2004;70:497–505.
2. Davies JE. Mechanisms of endosseous integration. *Int J Prosthodont*. 1998;11:391–401.
3. Friberg B, Jemt T, Lekholm U. Early failures in 4641 consecutively placed Bränemark dental implants. A study from stage I surgery to the connection of completed prostheses. *Int J Oral Maxillofac Implants*. 1991;6:142–146.
4. Shibli JA, Grassi S, Cristina de Figueiredo L, et al. Influence of implant surface topography on early osseointegration: a histological study in human jaws. *J Biomed Mater Res B Appl Biomater*. 2007;80:377–385.
5. Wactawski-Wende J, Grossi SG, Trevisan M, et al. The role of osteopenia in oral bone loss and periodontal disease. *J Periodontol*. 1996;67(suppl):1076–1084.
6. van Steenberghe D, Jacobs R, Desnyder M, Maffei G, Quirynen M. The relative impact of local and endogenous patient-related factors on implant failure up to the abutment stage. *Clin Oral Implants Res*. 2002;13:617–622.
7. Amorim MA, Takayama L, Jorgetti V, Pereira RM. Comparative study of axial and femoral bone mineral density and parameters of mandibular bone quality in patients receiving dental implants. *Osteoporos Int*. 2006;17:1494–1500.
8. Duarte PM, Cesar Neto JB, Goncalves PF, Sallum EA, Nociti FH. Estrogen deficiency affects bone healing around titanium implants: a histometric study in rats. *Implant Dent*. 2003;12:340–346.
9. Duarte PM, de Vasconcelos Gurgel BC, Sallum AW, Filho GR, Sallum EA, Nociti FH Jr. Alendronate therapy may be effective in the prevention of bone loss around titanium implants inserted in estrogen-deficient rats. *J Periodontol*. 2005;76:107–114.
10. Ozawa S, Ogawa T, Iida K, et al. Ovariectomy hinders the early stage of bone-implant integration: histomorphometric, biomechanical, and molecular analyses. *Bone*. 2002;30:137–143.
11. Qi MC, Zhou XQ, Hu J, et al. Oestrogen replacement therapy promotes bone healing around dental implants in osteoporotic rats. *Int J Oral Maxillofac Surg*. 2004;33:279–285.
12. August M, Chung K, Chang Y, Glowacki J. Influence of estrogen status on endosseous implant osseointegration. *J Oral Maxillofac Surg*. 2001;59:1285–1289.
13. Keller JC, Stewart M, Roehm M, Schneider GB. Osteoporosis-like bone conditions affect osseointegration of implants. *Int J Oral Maxillofac Implants*. 2004;19:687–694.
14. Roberts WE, Simmons KE, Garetto LP, DeCastro RA. Bone physiology and metabolism in dental implantology: risk factors for osteoporosis and other metabolic bone diseases. *Implant Dent*. 1992;1:11–21.
15. Dao TT, Anderson JD, Zarb GA. Is osteoporosis a risk for osseointegration of dental implants? *Int J Oral Maxillofac Implants*. 1993;8:137–144.
16. Fujimoto T, Niimi A, Nakai H, Ueda M. Osseointegrated implants in a patient with osteoporosis: a case report. *Int J Oral Maxillofac Implants*. 1996;11:539–542.
17. Eder A, Watzek G. Treatment of a patient with severe

osteoporosis and chronic polyarthritis with fixed implant-supported prosthesis: a case report. *Int J Oral Maxillofac Implants.* 1999;14:587–590.

18. Friberg B. Treatment with dental implants in patients with severe osteoporosis: a case report. *Int J Periodont Rest Dent.* 1994;14:349–353.

19. Kronstrom M, Palmqvist S, Soderfeldt B. Prosthodontic decision making among general dentists in Sweden. III: the choice between fixed partial dentures and single implants. *Int J Prosthodont.* 2000;13:34–40.

20. Fujimoto T, Niimi A, Sawai T, Ueda M. Effects of steroid-induced osteoporosis on osseointegration of titanium implants. *Int J Oral Maxillofac Implants.* 1998;13:183–189.

21. Marco F, Milena F, Gianluca G, Vittoria O. Peri-implant osteogenesis in health and osteoporosis. *Micron.* 2005;36:630–644.

22. Drage N, Palmer R, Blake G, Wilson R, Crane F, Fogelman I. A comparison of bone mineral density in the spine, hip and jaws of edentulous subjects. *Clin Oral Implant Res.* 2007;18:496–500.

23. Jeffcoat MK, Chesnut CH. 3rd Systemic osteoporosis and

oral bone loss: evidence shows increased risk factors. *J Am Dent Assoc.* 1993;124:49–56.

24. Klemetti E, Vainio P, Lassila V. Mineral density in the mandibles of partially and totally edentate postmenopausal women. *Scand J Dent Res.* 1994;102:64–67.

25. Lazzara RJ, Porter SS, Testori T, Galante J, Zetterqvist L. A prospective multicenter study evaluating loading of osseointegrated implants two months after placement: one-year results. *J Esthet Dent.* 1998;10:280–289.

26. Degidi M, Piattelli A. 7-year follow-up of 93 immediately loaded titanium dental implants. *J Oral Implantol.* 2005;31:25–31.

27. Ruegsegger P, Dambacher MA, Ruegsegger E, Fischer JA, Anliker M. Bone loss in premenopausal and postmenopausal women. A cross-sectional and longitudinal study using quantitative computed tomography. *J Bone Joint Surg Am.* 1984;66:1015–1023.

28. Gaumet N, Brailon P, Seibel MJ, Pointillart A, Coxam V, Davicco MJ. Influence of aging on cortical and trabecular bone response to estradiol treatment in ovariectomized rats. *Gerontology.* 1998;44:132–139.