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## Assessment of dental implant stability using resonance frequency analysis and quantitative ultrasound methods

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1 **Assessment of dental implant stability using resonance frequency analysis and**  
2 **quantitative ultrasound methods**

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5

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**Abstract**

**Purpose:** Quantitative ultrasound (QUS) and resonance frequency analyses (RFA) are promising methods to assess the stability of dental implants. The aim of this *in vivo* preclinical study is to compare the results obtained with these two techniques with the bone-implant contact (BIC) ratio, which is the gold standard to assess dental implant stability.

**Methods:** Twenty-two identical dental implants were inserted in the tibia and femur of 13 rabbits, which were sacrificed after different healing durations (0, 4, 8 and 13 weeks). For each implant, the ultrasonic indicator (*UI*) and the implant stability quotient (*ISQ*) were retrieved just before the animal sacrifice using the QUS and RFA techniques, respectively. Histomorphometric analyses were carried out to estimate the bone-implant contact ratio.

**Results:** *UI* values were found to be better correlated to BIC values ( $R^2=0.47$ ) compared to *ISQ* values ( $R^2=0.39$  for measurements in one direction and  $R^2=0.18$  for the other direction), which were shown to be dependent on the direction of measurements. Errors realized on the *UI* were around 3.3 times lower to the ones realized on the *ISQ*.

**Conclusions:** QUS provide a better estimation of dental implant stability compared to RFA. This study paves the way for the future clinical development of a medical device aiming at assessing dental implant stability in a patient-specific manner. Clinical studies should confirm these results in the future.

**Keywords:** Implant Stability, Bone-Implant Contact, Quantitative Ultrasound, Resonance Frequency Analysis, Dental Implants.

## 1        **1. Introduction**

2  
3        The clinical assessment of dental implant stability is a difficult problem (1) because it depends on many  
4 parameters such as the implant properties, the surgical protocol and the patient behavior and bone quality  
5 (2). Moreover, there is a lack of standardization of the surgical procedures, in particular concerning the  
6 choice of the duration between implant insertion and loading, which may vary from 0 up to 6 months (3).  
7 An early implant loading may stimulate osseointegration phenomena (4), but may also degrade the  
8 consolidating bone-implant interface (BII) (5) in the case of unstable implants (6). Meanwhile, shortening  
9 the implant loading time is important to (i) avoid tissue losses and to (ii) limit the social impact of facial  
10 disfigurement. Therefore, an accurate evaluation of dental implant stability could help the surgeon to adapt  
11 his/her strategy and more specifically the choice of the healing period in a patient specific manner.

12  
13        Different methods have been suggested to assess the implant stability. Most surgeons still rely on their  
14 proprioception (6) and accurate quantitative methods are required. Magnetic Resonance Imaging (7) and X-  
15 ray based techniques (8) are not adapted due to artifacts generated by the presence of titanium. Impact  
16 methods like the Periotest (*Bensheim, Germany*) (9) present a poor reproducibility (10).

17  
18        Resonance frequency analysis (RFA) is the most commonly used technique to measure implant stability,  
19 and consists in measuring the first bending resonance frequency of a rod screwed into the implant (11). The  
20 Osstell© (*Gothenburg, Sweden*) is based on the RFA technique to measure the harmonic response of an  
21 implant through the implant stability quotient (ISQ), which can provide an assessment of the stiffness of the  
22 bone-implant structure (12), of the cortical bone thickness (13, 14), of the implant anchorage depth into  
23 bone (15) and of the marginal bone level (16). However, the properties of the BII (17) cannot be directly  
24 identified through RFA, and the orientation of the device was found to significantly affect the ISQ score  
25 (18). The correlation between the ISQ and bone implant contact (BIC) is relatively weak and remains a  
26 subject of debate (19-23). Moreover, sensitivity issues of ISQ to changes of periprosthetic bone tissue have  
27 been raised, due to the fact that only the first bending mode is considered (24).

1 Quantitative ultrasound (QUS) (25) represents a promising alternative to RFA in order to investigate  
2 the properties of the BII and therefore to assess dental implant stability. The set-up developed by our group  
3 consists of an ultrasonic echographic transducer screwed inside the implant that can measure the amplitude  
4 of the signal reflected by the bone-implant system. Different works have been carried out *in silico*, *in vitro*  
5 and *in vivo* in order to validate the approach. The interaction between an ultrasonic wave and a cylindrical  
6 implant was modeled numerically (26, 27) at the scale of the implant. Then, a realistic 3-D geometry was  
7 considered (28) and two studies carried out at the microscopic scale and taking into account the implant  
8 surface roughness and the implant threading allowed to quantify the effect of osseointegration phenomena  
9 on the ultrasonic response of the BII (29, 30).

10  
11 Based on this concept, an *in vitro* preliminary study showed that the reflection coefficient of an  
12 ultrasonic wave interacting with the BII significantly decreases as a function of healing time (31). A QUS  
13 device was developed to assess dental implant stability and was validated first *ex vivo* using cylindrical  
14 implants (32), and then *in vitro* using dental implants in a biomaterial (33) and in bovine bone tissue (34).  
15 The performance of RFA and QUS techniques were compared *in vitro* with implants inserted in bone  
16 mimicking phantoms (35). The QUS technique led to a significantly better estimation of different parameters  
17 related to the implant stability compared to the RFA technique (35).

18  
19 An *in vivo* study (36) showed that QUS measurements were significantly sensitive to healing time, but  
20 the positioning of the ultrasonic probe on the implant abutment screw was performed manually, leading to  
21 reproducibility issues. Another *in vivo* study (37) considered a new version of the QUS probe. The results  
22 showed that the QUS technique led to more important variations of the indicator as a function of healing  
23 time compared to the RFA technique. However, the results obtained with the QUS and RFA devices were  
24 not compared to the bone-implant contact (BIC) ratio, which is the gold standard to assess dental implant  
25 stability.

1 The aim of this study is to evaluate the performance of the RFA and QUS techniques to assess dental  
2 implant stability by comparing the results obtained with both methods to those obtained via  
3 histomorphometric analysis, which leads to an estimation of the BIC ratio. Our strategy consists in using  
4 dental implants in rabbits and to consider stability measurements with both techniques (RFA and QUS) at  
5 different healing times.

## 6 7 **2. Materials and Methods**

### 8 ***2.1 Animals***

9 Thirteen New Zealand White 5-months-old male rabbits (Charles River, L'Arbresle, France) with  
10 an average weight of 4.360kg were used in this study. Animals were housed in a metal hutch in an  
11 environment in agreement with the *European guidelines for care and use of laboratory animals*. The study  
12 was carried out according to the EU Directive 2010/63/EU and has been approved by the ethical committee  
13 of the Alfort National Veterinary School (ENVA, project #20287). Temperature was maintained at 19°C  
14 and humidity at 55%. Artificial cyclic lightening and air conditioning system were used in the animal  
15 housing facility. Commercial food and water were provided *ad libitum*.

### 16 17 ***2.2 Surgical procedure***

18 Twenty-two identical conical dental implants manufactured by Zimmer Biomet® (Warshaw, IN,  
19 USA) under the reference TSVT4B10 were used in this study. The implants were made of titanium alloy  
20 (Ti6Al4V), were 10 mm long and had a diameter of 4 mm.

21 Similarly to what was done in previous studies (38-40), each dental implant was placed in the femur  
22 or in the tibia of the rabbits, as shown in Figure 1. The surgical procedure described in more details by  
23 Pearce *et al.* (41) was reproduced. Briefly, a single skin incision was performed on each rabbit leg around  
24 the knee joint. The lateral condyle of each bone was drilled in a stepwise fashion in order to create 10-mm  
25 deep and 4.0-mm wide conical cavities, using surgical drills manufactured by Zimmer Biomet® (2.3, 2.8,  
26 3.4 mm diameter). Before inserting the implants, an isotonic saline solution was used to rinse the cavities in



1 order to remove bone fragments. Three rabbits were sacrificed at 0, 4 and 8 weeks after initial implant  
2 surgery, and four rabbits were sacrificed at 13 weeks after the surgery. The QUS and RFA measurements  
3 were realized just before the animal sacrifice. A total number of implant comprised between 1 and 2 was  
4 inserted in each rabbit.

5

### 6 **2.3 Resonance frequency analysis**

7 The Osstell device (*Ostell, Göteborg, Sweden*) was used to measure the RFA response of each implant in  
8 ISQ units (on a scale from 1 to 100). As recommended by the manufacturer, measurements were realized  
9 using a smart peg screwed into the implant. Moreover, as indicated in Figure 2, each measurement was  
10 performed in two perpendicular directions denoted  $0^\circ$  and  $90^\circ$ , and was repeated three times in order to  
11 assess the reproducibility of the measurements. The values obtained when positioning the axis of the device  
12 parallel (respectively perpendicular) to the bone axis were considered to be in the  $0^\circ$  direction (respectively  
13 in the  $90^\circ$  direction) and were denoted  $ISQ0$  (respectively  $ISQ90$ ). For each sample  $\#i$ , the average and  
14 standard deviation of the three values of  $ISQ0$  (respectively  $ISQ90$ ) were denoted  $ISQ0_i^m$  and  $ISQ0_i^{std}$   
15 (respectively  $ISQ90_i^m$  and  $ISQ90_i^{std}$ ).

16

### 17 **2.4 Quantitative ultrasound device**

18 The QUS device used in the present study is composed of a planar ultrasonic monoelement  
19 transducer (*Sonaxis, Besançon, France*) that generates a broadband ultrasonic pulse with a central frequency  
20 of 10 MHz, which propagates perpendicularly to its active surface. Similarly to what was done in Vayron  
21 *et al.* (37), the ultrasonic probe was fixed onto a healing abutment made of titanium alloy, which was then  
22 screwed into the dental implant. This procedure was followed to avoid positioning problems between the  
23 transducer and the implant axis. A pulser-receiver was connected to the probe with a coaxial cable, and the  
24 radiofrequency (rf) signal was recorded using a transient recorder with a sampling frequency of 100 MHz.  
25 An ultrasonic measurement was performed for each implant, as shown in Figure 3, and the measurements  
26 were made instantaneously.

1 For all measurements, a controlled torque of 3.5 N.cm was applied when screwing the transducer  
2 into the implant, which is approximately 10 times lower than torque values recommended by implant  
3 manufacturers for the implant insertion (42). The reproducibility of the measurements was assessed by  
4 unscrewing the transducer and carrying again the measurement three times for each implant.

5  
6 The method described in Vayron *et al.* (37) was used to derive an ultrasonic indicator  $UI$ , which  
7 was shown to be correlated with the implant stability. The envelop  $S(t)$  of the radiofrequency signal  $s(t)$  was  
8 first determined. Then, an indicator  $I$  that estimates the average amplitude of the signal between 20 and 120  
9  $\mu\text{s}$  was defined following:

$$I = \sum_{i=2000}^{12,000} S(iT_0),$$

10  
11  
12  
13 where  $T_0 = 0.01 \mu\text{s}$  corresponds to the sampling period. In order to obtain values that (i) increase when bone  
14 quantity and quality increase around the implant and (ii) are comprised between 1 and 100, similarly to the  
15 ISQ, the ultrasonic indicator  $UI$  was defined by:

$$UI = 100 - 10 \times I$$

16  
17 For each sample  $\#i$ , the average and standard deviation of the three values of  $UI$  were denoted  $UI_i^m$  and  
18  $UI_i^{std}$ .

## 20 **2.5 Histomorphometric analyses**

21 After the RFA and QUS measurements were realized, the animals were sacrificed and histomorphometric  
22 analyses were performed. The samples were prepared following a procedure for non-decalcified histology  
23 described more extensively by Soffer *et al.* (43) and Chevallier *et al.* (44). The ratio of the implant surface  
24 in intimate contact with mineralized bone tissue was assessed manually by analyzing histomorphometrical  
25 images by classical microscopy. Two histological sections were studied for each sample, so that two

1 histomorphometrical measurements of the BIC could be realized. For each sample #i, the average and  
2 standard deviation of the two BIC ratio was denoted  $BIC_i^m$  and  $BIC_i^{std}$ .

3

## 4 **2.6 Statistical analyses**

5 Analyses of variance (ANOVA) were performed to evaluate the difference between the values of the BIC  
6 ratio, of *ISQ0*, of *ISQ90* and of *UI* obtained with different healing times (0, 4, 8 and 13 weeks). Moreover,  
7 linear regression analyses were carried out in order to determine the correlation between *ISQ*, *UI* and the  
8 *BIC* ratio. All statistical analyses were carried out using the Microsoft Excel software (Redmont, WA, USA).

9 All the procedures detailed in the present work comply with the ARRIVE guidelines.

10

## 11 **3. Results**

### 12 **3.1 Sample analysis and BIC estimation**

13 Figure 4 shows two images corresponding to 2 histological sections together with the corresponding value  
14 of the BIC ratio.

15 Table 1 shows the average value of  $BIC_i^m$  and of  $BIC_i^{std}$  obtained for all samples corresponding to the same  
16 healing duration and to all data pooled. The mean value of  $BIC_i^{std}$  corresponds to an estimation of the  
17 average reproducibility of the BIC measurements. Table 1 also shows the standard deviation of  $BIC_i^m$   
18 obtained for all samples corresponding to the same healing duration and to all data pooled, which  
19 corresponds to the interspecimen variability. ANOVA test of the results obtained with all 22 implants  
20 showed a significant effect of healing time on the BIC ratio (p-value =  $5.8 \times 10^{-5}$  and F-statistic = 14.0),  
21 with BIC values first increasing as a function of healing time and then decreasing for healing times between  
22 8 and 13 weeks. However, an important interindividual variability was also observed for samples with a  
23 healing time of 13 weeks. Moreover, the mean measurement error was comprised between 2.62 and 5.84  
24 for the various values of healing durations.

25

### 3.2 Resonance frequency analysis

Table 1 shows the same parameters corresponding to *ISQ0* and *ISQ90* as the ones shown for the BIC in the last subsection. An ANOVA test of the 22 implants demonstrated a significant effect of healing time on *ISQ0* (p-value =  $6 \cdot 10^{-3}$  and F-statistic = 5.8), but no significant effect of healing time on *ISQ90* (p-value = 0.11 and F-statistic = 3.2). Both *ISQ0* and *ISQ90* first increase as a function of healing time, but then decrease for healing times superior to 4 weeks. The interindividual reproducibility of *ISQ0* decreases as a function of healing time. However, no global trend was observed in the evolution of this same parameter for *ISQ90*.

Figure 5 shows the relation between i) *ISQ0* and *ISQ90* and ii) the BIC measured with histomorphometric analyses. A significant correlation was obtained between *ISQ0* and the BIC, while no correlation was obtained between *ISQ90* and the BIC. The vertical error bars correspond to the standard deviation obtained for the three measurements of the ISQ ( $ISQ0_i^{std}$  and  $ISQ90_i^{std}$ ) and indicate the reproducibility of each measurements. The horizontal error bars correspond to the standard deviation obtained for the two measurements of the BIC ( $BIC_i^{std}$ ).

### 3.3 Ultrasonic measurements

Table 1 shows the same parameters corresponding to *UI* as the one shown for the BIC in subsection 3.1. An ANOVA test of the 22 implants demonstrated a significant effect of healing time on *UI* (p-value =  $1.65 \times 10^{-3}$  and F-statistic = 3.16), *UI* increasing as a function of healing time for all data. However, this increase becomes relatively weak between 8 and 13 weeks. Moreover, the interindividual variability of *UI* significantly decreases as a function of healing time, suggesting that a similar value of *UI* is reached for all samples once healing is achieved.

Figure 6 shows the relation between the *UI* and the BIC measured via histomorphometric analysis. The vertical error bars correspond to the standard deviation obtained for the three measurements of the *UI* ( $UI_i^{std}$ ) and indicate the reproducibility of each measurements. The horizontal error bars correspond to the

1 standard deviation obtained for the two measurements of the BIC ( $BIC_i^{std}$ ). A significant correlation was  
2 obtained between *UI* and the BIC.

3 Figure 7 shows the relationship between i) *ISQ0* and *ISQ90* and ii) the *UI*. A significant correlation was  
4 obtained between *ISQ0* and *UI*, whereas no correlation was obtained between *ISQ90* and *UI*.

5

6

## 7 **4. Discussion**

### 8 ***4.1 Originality of the study***

9 The originality of the present study is to compare *ISQ*, *UI* and BIC values obtained for the same samples,  
10 which provides further insight regarding the development of the QUS device dedicated to dental implant  
11 stability measurement. Previously, the relationship between the *UI* and BIC values was investigated for a  
12 lower number of samples compared to the present study (13 in Vayron *et al.* (36); 22 herein). However, the  
13 QUS device was different since the ultrasonic probe was manually positioned on the implant abutment  
14 screw, leading to reproducibility issues, whereas a controlled insertion torque is introduced in the present  
15 study. Moreover, the relationship between the *ISQ* and BIC values have also been previously investigated  
16 (19-23, 45-47) (see subsection 4.3) but none of these studies considered QUS measurements. The present  
17 study shows that QUS measurements (i) are better correlated to BIC values and (ii) have lower errors  
18 compared to RFA measurements.

19

20

### 21 ***4.2 Evolution of ISQ, UI and BIC values with healing time***

22 While a consistent increase of BIC values was obtained for lower values of healing time (0-8 weeks),  
23 BIC values obtained for higher healing duration (8-13 weeks) tend to decrease (see Table 1) and have an  
24 important variability depending on the implant considered. A similar behavior was obtained in previous  
25 studies realized with Labrador dogs (20) and on sheep (37). It may be explained as follows. During implant  
26 surgery, cavity drilling triggers wound healing events and thus promotes remodeling around the implant.

1 However, the lack of mechanical stimulation applied to the implant is likely to lead to bone resorption at  
2 the BII (48, 49), which explains possible bone loss for healing times higher than 8 weeks. This variation of  
3 the BIC as a function of healing time may explain the variation of *UI* values. *UI* first increases significantly  
4 (0-8 weeks), and then tends to reach a constant value (8-13 weeks) with a relatively low values of  
5 interindividual variability (see Table 1), which is in agreement with results obtained in Vayron *et al.* (37).  
6 However, the variation of *ISQ* values as a function of healing time is more difficult to relate to BIC variations  
7 since *ISQ0* decreases for healing times over 4 weeks, and ANOVA tests indicated that similarly as in Vayron  
8 *et al.* (37), no correlation with healing time could be established for *ISQ90*.

9 The maximal measurement errors for BIC values were obtained after 4 weeks of healing (see Table I),  
10 which may be explained as follows. In the early period after implant insertion, bone resorption primarily  
11 occurs around the implant. However, after around 3 to 4 weeks of healing, bone formation increases and  
12 becomes predominant over bone resorption (50, 51). Therefore, after 4 weeks of healing, there is a high  
13 heterogeneity in the amount of bone in contact with the implant, which leads to the high value of  
14  $BIC_i^{std}$  obtained in Table I.

15

### 16 **4.3 Correlation between *ISQ* and BIC values**

17 Figures 5 and 6 show that *ISQ0* and *UI* are correlated to BIC values, whereas no correlation between  
18 *ISQ90* and BIC was obtained. The results shown in Fig. 6 are in agreement with those shown in Fig. 5 since  
19 *ISQ0* and *UI* are significantly correlated, whereas no correlation was obtained between *ISQ90* and *UI*. These  
20 results highlight that *ISQ* values highly depend on the direction of the measurements, which is in agreement  
21 with results from Pattijn *et al.* (18). Moreover, the correlation obtained between *ISQ* and BIC measurements  
22 in the present study was relatively weak. Note that there is also controversy in the literature regarding the  
23 dependence of BIC and *ISQ*, since some studies conclude with a significant correlation between *ISQ* and  
24 BIC (45-47) with P-values varying between 0.016 and 0.024, while other studies showed there was no  
25 correlation between the two aforementioned parameters (19-23).

26

#### 1           **4.4 Correlation between *UI* and *BIC* values**

2           The correlation found between *UI* and *BIC* values is in good agreement with results obtained in our  
3 previous *in vivo* study (36), where a determination coefficient of  $R^2 = 0.45$  was found for the correlation  
4 between *BIC* and the *UI*. Vayron *et al.* (36, 37) showed that the indicator *UI* increased during healing, which  
5 is consistent with the present results since the *BIC* also increases during healing time (13, 52). Moreover, *in*  
6 *silico* (27-29) and *in vitro* (34, 35) studies also showed that *UI* increased when bone quantity around the  
7 implant increases, which may be explained as follows. When the *BIC* is low, the implant surface is mostly  
8 in contact with fibrous tissues, which leads to a stronger gap of mechanical properties at the implant surface  
9 than for higher *BIC*, which corresponds to a situation where the implant is mostly in contact with bone  
10 tissue. Consequently, the transmission coefficient at the *BII* is lower for lower values of the *BIC* (29, 31)  
11 and acoustic energy leakage out of the implant is therefore lower. As a result, the acoustic energy recorded  
12 at the upper surface of the implant is lower when there is more bone in contact with the implant, and the *UI*  
13 thus increases. However, the correlation between the *BIC* and the *UI* found herein is only moderate ( $R^2 =$   
14  $0.47$ ), which may be explained by experimental errors on the *BIC* estimation (see Table I). Furthermore, the  
15 *BIC* is an indicator of bone quantity and not of bone quality, which also influences *QUS* measurements  
16 since the *UI* was shown to increase while (i) trabecular density increases and (ii) cortical thickness increases  
17 (28, 35). Note that the dependence of the *UI* on bone quality was also shown *in silico* (28).

#### 18 19 20           **4.5 Comparison between *RFA* and *QUS* techniques**

21           Previous studies showed that the *QUS* technique is more sensitive to variations of *in vitro* implant  
22 stability (35) and to healing time (37) compared to the *RFA* techniques, which is in agreement with the  
23 present study. Besides a better correlation of the *UI* with *BIC* values compared to *ISQ*, ultrasonic  
24 measurements were also more reproducible than *ISQ* measurements, with a mean standard deviation on *UI*  
25 values equal to 0.51 while the mean standard deviation on *ISQ* values was equal to 1.69 (see Table 1 and  
26 Fig. 4 and 5). The better sensitivity of *QUS* compared to *RFA* to variations of the *BIC* can be explained

1 physically. The ISQ is related to the resonance frequency of the bone-implant system, which depends on  
2 properties of the entire host bone that vibrates when excited mechanically (24). However, QUS  
3 measurements are only sensitive on bone tissue located at a distance lower than around 30  $\mu\text{m}$  from the  
4 implant surface (28-30), which corresponds to the region of interest where osseointegration phenomena are  
5 known to occur (31, 53). Therefore, QUS are likely to be more sensitive to the properties of the BII and to  
6 osseointegration phenomena.

7

#### 8 ***4.6 Limitations***

9 The present study has several limitations. First, only one type of implant was considered and the  
10 comparison between RFA and QUS should be done with other implant types. The dimensions of the implant  
11 are likely to affect both the RFA results (54) and the QUS results. Therefore, slightly different results might  
12 be obtained for a different implant design. Here, we chose to focus on a single implant design to limit the  
13 number of parameters in our study, especially since the sample number was already small. A future study  
14 could confirm the better correlation between QUS results and the BIC for different implant designs.

15 Second, uncertainties on the estimation of BIC values was high because (i) only two BIC measurements  
16 could be realized for each implant and (ii) BIC measurements were realized on 2D histological sections,  
17 and can therefore only approximate actual BIC values on the entirety of the 3D implant.

18 Third, a relatively low number of rabbits was considered herein, which is justified by ethical reasons and  
19 because it corresponds to the range of sample numbers used in previous studies using the Osstell device (15,  
20 22). Studies with more animals should be performed in the future.

21 Fourth, the only parameter representing the progress of osseointegration considered herein was the BIC,  
22 which is not representative of the evolution of bone quality during healing.

23 Fifth, the exact position of the implant in rabbit bone was not controlled and a bi-cortical fixation may  
24 sometimes be obtained, which is usual for the present animal model, which has been used in (38-40, 55).

25 However, obtaining a bi-cortical fixation does not jeopardize the results obtained herein because the aim of  
26 this paper was not to assess the evolution of the healing process itself (as it was the case in (38) for instance),



1 but to compare the sensitivity of the QUS and RFA methods on these changes. On the contrary, for the  
2 aforementioned objective, it is interesting to consider a wide range of situations in order to obtain an  
3 important variability in terms of implant stability. Note that we considered implants in femoral and tibial  
4 bone, which have different properties with different ratio of cortical layer and trabecular bone, in order to  
5 obtain a wide range of implant stability to be able to compare the QUS and RFA technique for various  
6 healing conditions.

7

## 8 **Conclusion**

9 The present study allows to assess the performances of RFA and QUS techniques to assess dental  
10 implant stability by comparing the results obtained for the same samples with both methods to BIC ratio  
11 measurements. A better correlation between the BIC and the *UI* was found compared to the ISQ, which was  
12 shown to be dependent on the direction of measurements. Moreover, the errors realized on the *UI* were 3.3  
13 times lower to the ones realized on the ISQ. These results may be explained by the reproducibility and by  
14 the principle of measurements of both methods. Future works should now focus on the development of an  
15 ultrasonic device that could be used in clinical practice in the future to estimate dental implant primary and  
16 secondary stability. In particular, clinical studies could help to define a target value for the *UI* above which  
17 an implant is considered to be stable enough to be loaded.

## 18 **Acknowledgements**

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20 Union's Horizon 2020 research and innovation program (grant agreement No 682001, project ERC  
21 Consolidator Grant 2015 BoneImplant).

22

## 23 **Conflict of interest**

24 The authors declare no conflict of interest.

25

## 26 **References**

- 1 1. Haiat G, Wang H-L, Brunski J. Effects of Biomechanical Properties of the Bone-Implant  
2 Interface on Dental Implant Stability: From In Silico Approaches to the Patient's Mouth.  
3 Annual Review of Biomedical Engineering. 2014;16(1):187-213.
- 4 2. Franchi M, Bacchelli B, Giavaresi G, De Pasquale V, Martini D, Fini M, et al. Influence of  
5 Different Implant Surfaces on Peri-Implant Osteogenesis: Histomorphometric Analysis in  
6 Sheep. Journal of Periodontology. 2007;78(5):879-88.
- 7 3. Raghavendra S, Wood MC, Taylor TD. Early wound healing around endosseous  
8 implants: a review of the literature. Int J Oral Maxillofac Implants. 2005;20(3):425-31.
- 9 4. Buser D, Ingimarsson S, Dula K, Lussi A, Hirt HP, Belser UC. Long-term stability of  
10 osseointegrated implants in augmented bone: a 5-year prospective study in partially  
11 edentulous patients. Int J Periodontics Restorative Dent. 2002;22(2):109-17.
- 12 5. Abrahamsson I, Berglundh T, Linder E, Lang NP, Lindhe J. Early bone formation  
13 adjacent to rough and turned endosseous implant surfaces. An experimental study in the dog.  
14 Clin Oral Implants Res. 2004;15(4):381-92.
- 15 6. Serra G, Morais LS, Elias CN, Meyers MA, Andrade L, Muller C, et al. Sequential bone  
16 healing of immediately loaded mini-implants. Am J Orthod Dentofacial Orthop.  
17 2008;134(1):44-52.
- 18 7. Hecht S, Adams WH, Narak J, Thomas WB. Magnetic resonance imaging susceptibility  
19 artifacts due to metallic foreign bodies. Vet Radiol Ultrasound. 2011;52(4):409-14.
- 20 8. Albrektsson T, Dahl E, Enbom L, Engevall S, Engquist B, Eriksson AR, et al.  
21 Osseointegrated oral implants. A Swedish multicenter study of 8139 consecutively inserted  
22 Nobelpharma implants. J Periodontol. 1988;59(5):287-96.
- 23 9. Schulte W, d'Hoedt B, Lukas D, Muhlbradt L, Scholz F, Bretschgi J, et al. [Periotest--a  
24 new measurement process for periodontal function]. Zahnarzt Mitt. 1983;73(11):1229-30,  
25 33-6, 39-40.
- 26 10. Meredith N, Friberg B, Sennerby L, Aparicio C. Relationship between contact time  
27 measurements and PTV values when using the Periotest to measure implant stability. Int J  
28 Prosthodont. 1998;11(3):269-75.
- 29 11. Meredith N, Alleyne D, Cawley P. Quantitative determination of the stability of the  
30 implant-tissue interface using resonance frequency analysis. Clin Oral Implants Res.  
31 1996;7(3):261-7.
- 32 12. Ersanli S, Karabuda C, Beck F, Leblebicioglu B. Resonance frequency analysis of one-  
33 stage dental implant stability during the osseointegration period. J Periodontol.  
34 2005;76(7):1066-71.
- 35 13. Seong WJ, Kim UK, Swift JQ, Hodges JS, Ko CC. Correlations between physical  
36 properties of jawbone and dental implant initial stability. J Prosthet Dent. 2009;101(5):306-  
37 18.
- 38 14. Merheb J, Van Assche N, Coucke W, Jacobs R, Naert I, Quirynen M. Relationship  
39 between cortical bone thickness or computerized tomography-derived bone density values  
40 and implant stability. Clin Oral Implants Res. 2010;21(6):612-7.
- 41 15. Meredith N, Shagaldi F, Alleyne D, Sennerby L, Cawley P. The application of resonance  
42 frequency measurements to study the stability of titanium implants during healing in the  
43 rabbit tibia. Clin Oral Implants Res. 1997;8(3):234-43.
- 44 16. Friberg B, Jisander S, Widmark G, Lundgren A, Ivanoff CJ, Sennerby L, et al. One-year  
45 prospective three-center study comparing the outcome of a "soft bone implant" (prototype  
46 Mk IV) and the standard Branemark implant. Clin Implant Dent Relat Res. 2003;5(2):71-7.

- 1 17. Aparicio C, Lang NP, Rangert B. Validity and clinical significance of biomechanical  
2 testing of implant/bone interface. *Clin Oral Implants Res.* 2006;17 Suppl 2:2-7.
- 3 18. Pattijn V, Jaecques SVN, De Smet E, Muraru L, Van Lierde C, Van der Perre G, et al.  
4 Resonance frequency analysis of implants in the guinea pig model: Influence of boundary  
5 conditions and orientation of the transducer. *Medical Engineering & Physics.*  
6 2007;29(2):182-90.
- 7 19. Ito Y, Sato D, Yoneda S, Ito D, Kondo H, Kasugai S. Relevance of resonance frequency  
8 analysis to evaluate dental implant stability: simulation and histomorphometrical animal  
9 experiments. *Clin Oral Implants Res.* 2008;19(1):9-14.
- 10 20. Abrahamsson I, Linder E, Lang NP. Implant stability in relation to osseointegration: an  
11 experimental study in the Labrador dog. *Clin Oral Implants Res.* 2009;20(3):313-8.
- 12 21. Monje A, Insua A, Monje F, Munoz F, Salvi GE, Buser D, et al. Diagnostic accuracy of the  
13 implant stability quotient in monitoring progressive peri-implant bone loss: An experimental  
14 study in dogs. *Clin Oral Implants Res.* 2018;29(10):1016-24.
- 15 22. Kunnekel AT, Dudani MT, Nair CK, Naidu EM, Sivagami G. Comparison of delayed  
16 implant placement vs immediate implant placement using resonance frequency analysis: a  
17 pilot study on rabbits. *J Oral Implantol.* 2011;37(5):543-8.
- 18 23. Dagher M, Mokbel N, Jabbour G, Bouabboud Naaman N. Resonance Frequency  
19 Analysis, Insertion Torque, and Bone to Implant Contact of 4 Implant Surfaces. *Implant*  
20 *dentistry.* 2014;Publish Ahead of Print.
- 21 24. Rittel D, Dorogoy A, Haiat G, Shemtov-Yona K. Resonant frequency analysis of dental  
22 implants. *Medical Engineering & Physics.* 2019;66:65-74.
- 23 25. de Almeida MS, Maciel CD, Pereira JC. Proposal for an Ultrasonic Tool to Monitor the  
24 Osseointegration of Dental Implants: Sensors (Basel). 2007 Jul;7(7):1224-37.; 2007.
- 25 26. Mathieu V, Anagnostou F, Soffer E, Haiat G. Numerical simulation of ultrasonic wave  
26 propagation for the evaluation of dental implant biomechanical stability. *J Acoust Soc Am.*  
27 2011;129(6):4062-72.
- 28 27. Vayron R, Nguyen VH, Bosc R, Naili S, Haiat G. Finite element simulation of ultrasonic  
29 wave propagation in a dental implant for biomechanical stability assessment. *Biomech Model*  
30 *Mechanobiol.* 2015;14(5):1021-32.
- 31 28. Vayron R, Nguyen VH, Bosc R, Naili S, Haiat G. Assessment of the biomechanical  
32 stability of a dental implant with quantitative ultrasound: A three-dimensional finite element  
33 study. *The Journal of the Acoustical Society of America.* 2016;139(2):773-80.
- 34 29. Heriveaux Y, Nguyen VH, Haiat G. Reflection of an ultrasonic wave on the bone-implant  
35 interface: A numerical study of the effect of the multiscale roughness. *J Acoust Soc Am.*  
36 2018;144(1):488.
- 37 30. Heriveaux Y, Nguyen VH, Brailovski V, Gorny C, Haiat G. Reflection of an ultrasonic  
38 wave on the bone-implant interface: Effect of the roughness parameters. *J Acoust Soc Am.*  
39 2019;145(6):3370.
- 40 31. Mathieu V, Vayron R, Soffer E, Anagnostou F, Haiat G. Influence of healing time on the  
41 ultrasonic response of the bone-implant interface. *Ultrasound Med Biol.* 2012;38(4):611-8.
- 42 32. Mathieu V, Anagnostou F, Soffer E, Haiat G. Ultrasonic Evaluation of Dental Implant  
43 Biomechanical Stability: An In Vitro Study. *Ultrasound in Medicine & Biology.*  
44 2011;37(2):262-70.

- 1 33. Vayron R, Karasinski P, Mathieu V, Michel A, Lorient D, Richard G, et al. Variation of the  
2 ultrasonic response of a dental implant embedded in tricalcium silicate-based cement under  
3 cyclic loading. *Journal of Biomechanics*. 2013;46(6):1162-8.
- 4 34. Vayron R, Mathieu V, Michel A, Haiat G. Assessment of In Vitro Dental Implant Primary  
5 Stability Using an Ultrasonic Method. *Ultrasound in Medicine & Biology*. 2014;40(12):2885-  
6 94.
- 7 35. Vayron R, Nguyen VH, Lecuelle B, Haiat G. Evaluation of dental implant stability in  
8 bone phantoms: Comparison between a quantitative ultrasound technique and resonance  
9 frequency analysis. *Clin Implant Dent Relat Res*. 2018.
- 10 36. Vayron R, Soffer E, Anagnostou F, Haiat G. Ultrasonic evaluation of dental implant  
11 osseointegration. *Journal of Biomechanics*. 2014;47(14):3562-8.
- 12 37. Vayron R, Nguyen V-H, Lecuelle B, Albini Lomami H, Meningaud J-P, Bosc R, et al.  
13 Comparison of Resonance Frequency Analysis and of Quantitative Ultrasound to Assess  
14 Dental Implant Osseointegration. *Sensors (Basel, Switzerland)*. 2018;18(5):1397.
- 15 38. Scarano A, Piattelli A, Quaranta A, Lorusso F. Bone Response to Two Dental Implants  
16 with Different Sandblasted/Acid-Etched Implant Surfaces: A Histological and  
17 Histomorphometrical Study in Rabbits. *BioMed Research International*. 2017;2017:8.
- 18 39. Bodelón OG, Clemente C, Alobera MA, Aguado-Henche S, Escudero ML, Alonso MCG.  
19 Osseointegration of Ti6Al4V dental implants modified by thermal oxidation in osteoporotic  
20 rabbits. *International journal of implant dentistry*. 2016;2(1):18-.
- 21 40. Mori H, Manabe M, Kurachi Y, Nagumo M. Osseointegration of dental implants in rabbit  
22 bone with low mineral density. *Journal of Oral and Maxillofacial Surgery*. 1997;55(4):351-61.
- 23 41. Pearce AI, Richards RG, Milz S, Schneider E, Pearce SG. Animal models for implant  
24 biomaterial research in bone: a review. *Eur Cell Mater*. 2007;13:1-10.
- 25 42. Kanawati A, Richards MW, Becker JJ, Monaco NE. Measurement of clinicians' ability to  
26 hand torque dental implant components. *J Oral Implantol*. 2009;35(4):185-8.
- 27 43. Soffer E, Ouhayoun PJ, Meunier A, Anagnostou F. Effects of autologous platelet lysates  
28 on ceramic particle resorption and new bone formation in critical size defects: The role of  
29 anatomical sites 2006. 86-94 p.
- 30 44. Chevallier N, Anagnostou F, Zilber S, Bodivit G, Maurin S, Barrault A, et al. Osteoblastic  
31 differentiation of human mesenchymal stem cells with platelet lysate. *Biomaterials*.  
32 2010;31(2):270-8.
- 33 45. Nkenke E, Hahn M, Weinzierl K, Radespiel-Troger M, Neukam FW, Engelke K. Implant  
34 stability and histomorphometry: a correlation study in human cadavers using stepped  
35 cylinder implants. *Clin Oral Implants Res*. 2003;14(5):601-9.
- 36 46. Scarano A, Degidi M, Iezzi G, Petrone G, Piattelli A. Correlation between implant  
37 stability quotient and bone-implant contact: a retrospective histological and  
38 histomorphometrical study of seven titanium implants retrieved from humans. *Clin Implant  
39 Dent Relat Res*. 2006;8(4):218-22.
- 40 47. Acil Y, Sievers J, Gulsas A, Ayna M, Wiltfang J, Terheyden H. Correlation between  
41 resonance frequency, insertion torque and bone-implant contact in self-cutting threaded  
42 implants. *Odontology*. 2017;105(3):347-53.
- 43 48. Pietrzak W. *Musculoskeletal Tissue Regeneration: Biological Materials and  
44 Methods* 2008.
- 45 49. Li Z, Muller R, Ruffoni D. Bone remodeling and mechanobiology around implants:  
46 Insights from small animal imaging. *J Orthop Res*. 2018;36(2):584-93.

- 1 50. Soto-Peñaloza D, Caneva M, Viña-Almunia J, Martín-de-Llano JJ, Peñarrocha-Oltra D,  
2 Peñarrocha-Diago M. Bone-Healing Pattern on the Surface of Titanium Implants at Cortical  
3 and Marrow Compartments in Two Topographic Sites: an Experimental Study in Rabbits.  
4 *Materials* (Basel, Switzerland). 2018;12(1):85.
- 5 51. McCullough JJ, Klokkevold PR. The effect of implant macro-thread design on implant  
6 stability in the early post-operative period: a randomized, controlled pilot study. *Clin Oral*  
7 *Implants Res.* 2017;28(10):1218-26.
- 8 52. Matsumoto H, Ochi M, Abiko Y, Hirose Y, Kaku T, Sakaguchi K. Pulsed electromagnetic  
9 fields promote bone formation around dental implants inserted into the femur of rabbits. *Clin*  
10 *Oral Implants Res.* 2000;11(4):354-60.
- 11 53. Huja S, Katona R, Burr D, Garetto P, Roberts W. Microdamage adjacent to endosseous  
12 implants1999. 217-22 p.
- 13 54. Nappo A, Rengo C, Pantaleo G, Spagnuolo G, Ferrari M. Influence of Implant  
14 Dimensions and Position on Implant Stability: A Prospective Clinical Study in Maxilla Using  
15 Resonance Frequency Analysis *Appl Sci.* 2019;9(5):860.
- 16 55. Matsuzaki T, Ayukawa Y, Matsushita Y, Sakai N, Matsuzaki M, Masuzaki T, et al. Effect  
17 of post-osseointegration loading magnitude on the dynamics of peri-implant bone: a finite  
18 element analysis and in vivo study. *J Prosthodont Res.* 2019;63(4):453-9.  
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1 **Tables**

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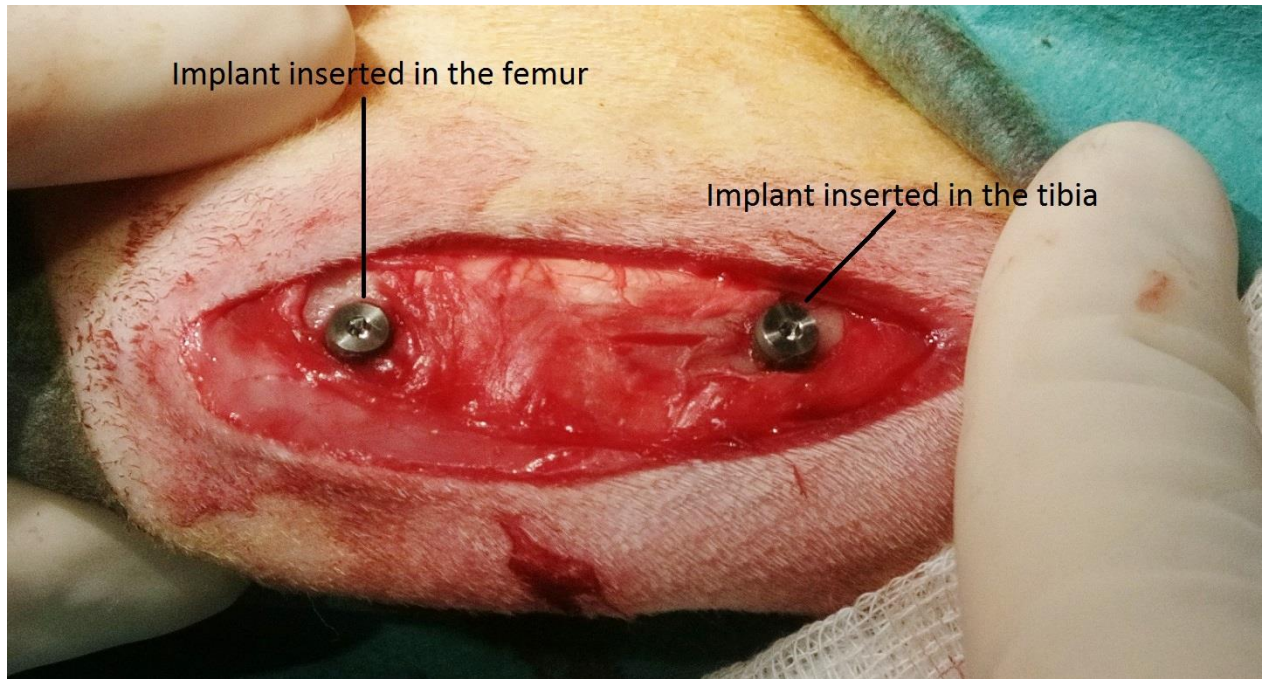
Table 1: Average value, mean measurement error and interindividual variability obtained for the BIC ratio, *ISQ0*, *ISQ90* and *UI* values for each healing duration and for all data pooled.

<b>Healing time (weeks)</b>		<b>0</b>	<b>4</b>	<b>8</b>	<b>13</b>	<b>All data</b>
<b>Number of implants</b>		<b>6</b>	<b>5</b>	<b>5</b>	<b>6</b>	<b>22</b>
<b>Number of animals</b>		<b>3</b>	<b>3</b>	<b>3</b>	<b>3</b>	<b>13</b>
<b>BIC</b>	<b>Mean value of <math>BIC_i^m</math></b>	<b>18.61</b>	<b>45.53</b>	<b>58.50</b>	<b>49.51</b>	<b>42.22</b>
	Mean value of $BIC_i^{std}$ (measurement error)	3.32	5.84	3.87	2.62	3.68
	Standard deviation of $BIC_i^m$ (interindividual variability)	12.56	5.57	4.94	15.14	18.52
<b>ISQ0</b>	<b>Mean value of <math>ISQ0_i^m</math></b>	<b>63.00</b>	<b>75.52</b>	<b>73.88</b>	<b>70.67</b>	<b>70.41</b>
	Mean value of $ISQ0_i^{std}$ (measurement error)	1.18	0.23	1.67	1.95	1.29
	Standard deviation of $ISQ0_i^m$ (interindividual variability)	9.15	3.82	3.55	1.63	7.11
<b>ISQ90</b>	<b>Mean value of <math>ISQ90_i^m</math></b>	<b>71.38</b>	<b>84.08</b>	<b>77.40</b>	<b>74.0</b>	<b>76.35</b>
	Mean value of $ISQ90_i^{std}$ (measurement error)	0.75	1.82	2.73	3.08	2.08
	Standard deviation of $ISQ90_i^m$ (interindividual variability)	12.39	3.86	6.31	7.61	9.16
<b>UI</b>	<b>Mean value of <math>UI_i^m</math></b>	<b>66.01</b>	<b>74.53</b>	<b>80.42</b>	<b>82.47</b>	<b>75.71</b>
	Mean value of $UI_i^{std}$ (measurement error)	0.73	0.54	0.47	0.31	0.51
	Standard deviation of $UI_i^m$ (interindividual variability)	11.18	4.41	2.79	1.63	9.00

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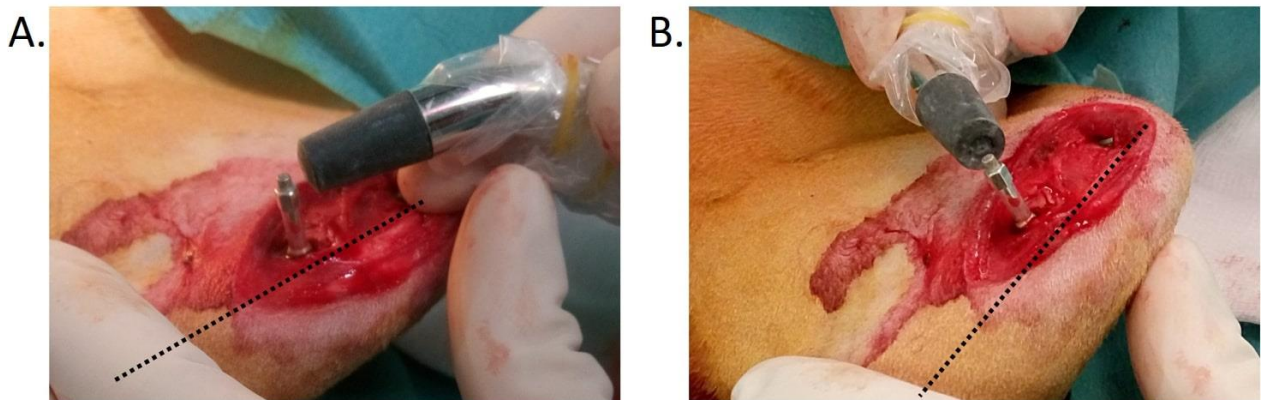
1 **Figure legends**

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4 Figure 1: Photography of two dental implants inserted in a rabbit femur and tibia.



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6 Figure 2: Measurement configuration of the implant stability quotient (ISQ) using the RFA device realized  
7 in two perpendicular directions (A: 0° and B: 90°). Dotted lines represent the tibia axis.

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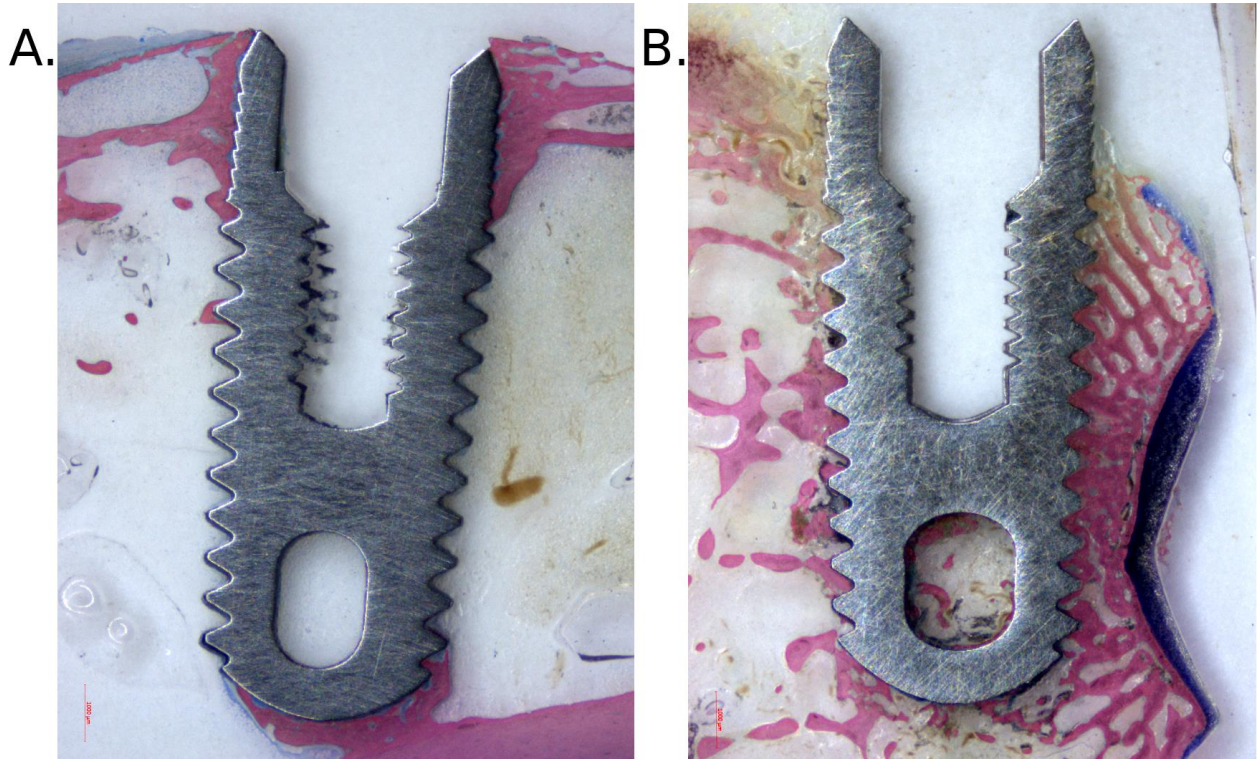


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3 Figure 3: Measurement configuration of the ultrasonic indicator using the ultrasonic transducer screwed into  
4 a dental implant.

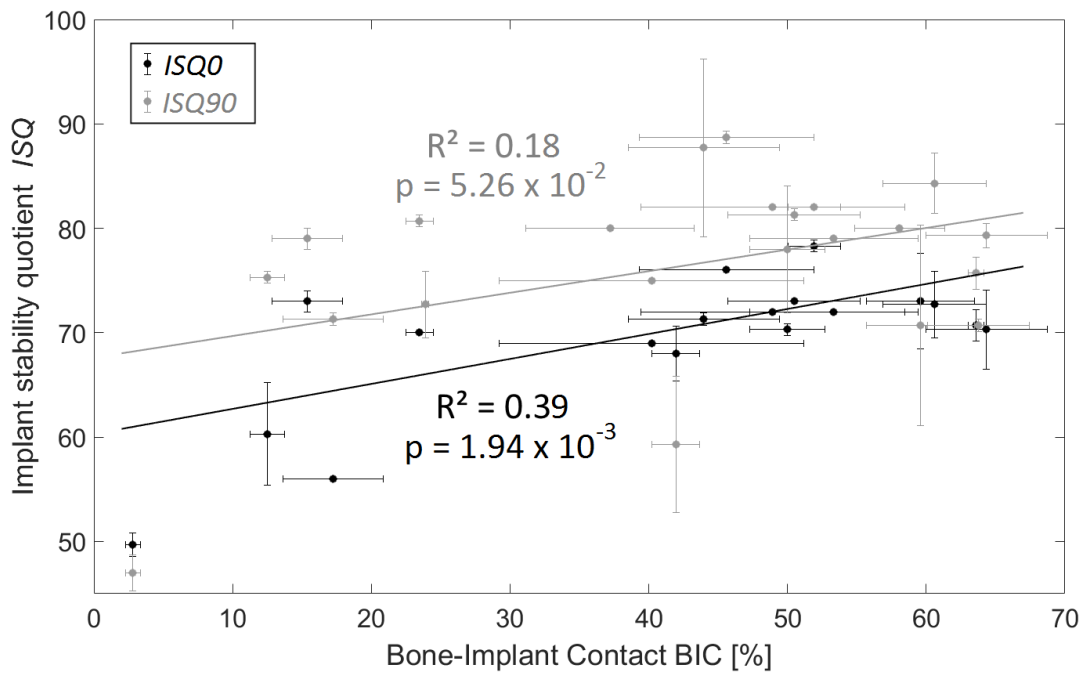
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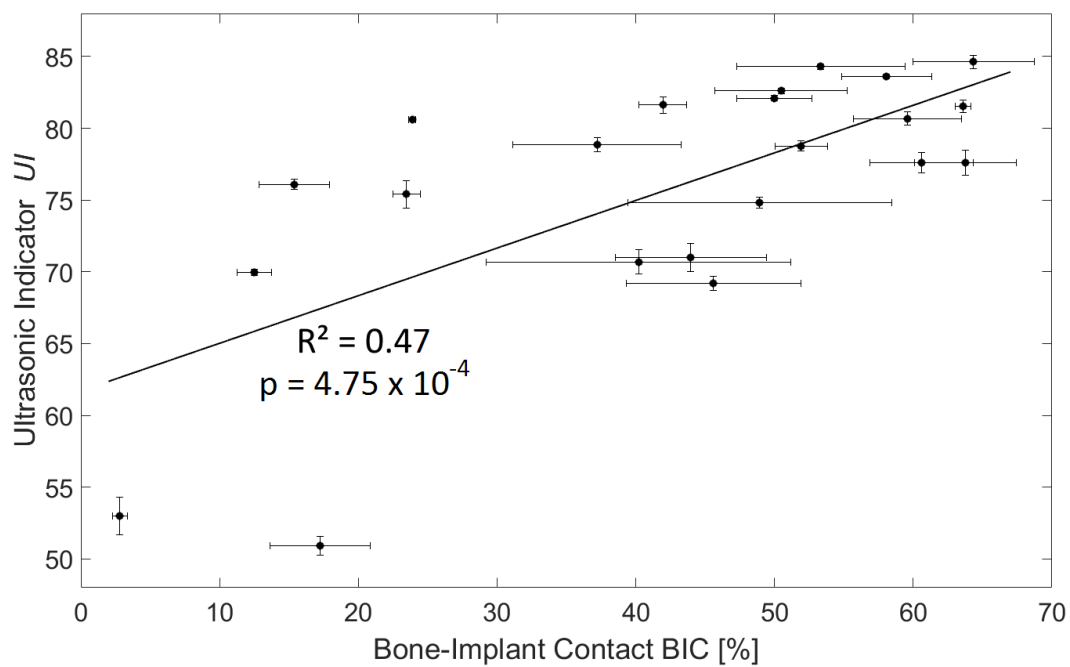


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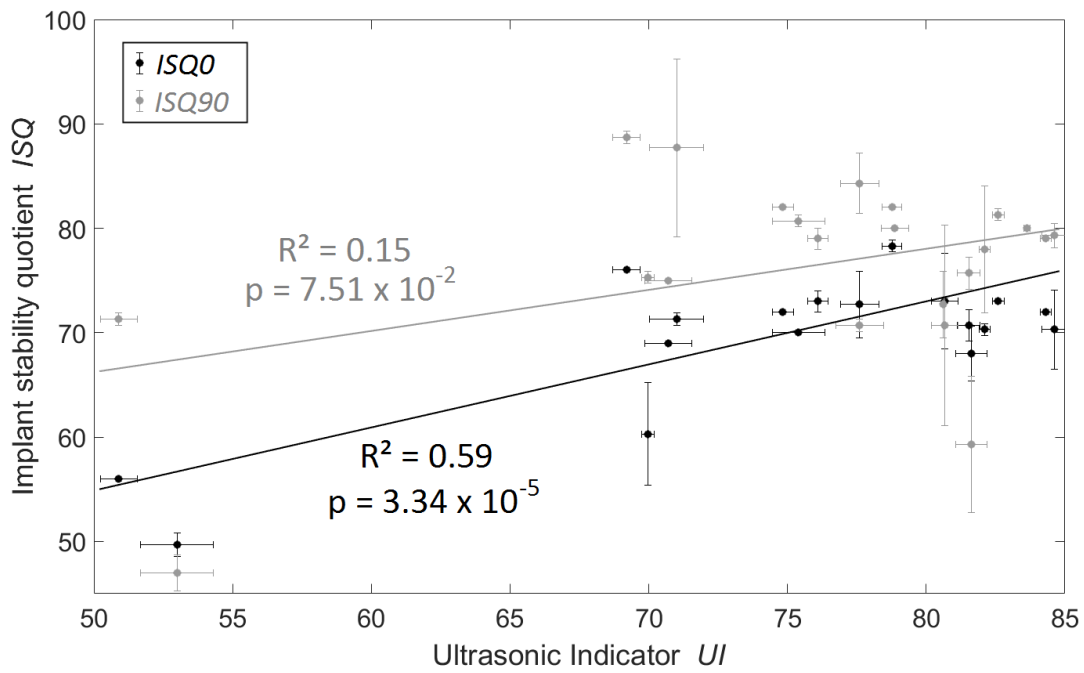
Figure 4: Images of the histologic section of a dental implant (A) directly after implantation in a rabbit tibia and (B) after 8 weeks of healing time. Mineralized bone tissues correspond to the pink regions of interest of the image and were colored with Van Gieson's stain. The BIC was respectively equal to (A) 24.1% and (B) 60.4%.



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 2 Figure 5: Relationship obtained between the ISQ measured in the directions 0° (black points) and 90° (grey  
 3 points) and the BIC. The solid lines correspond to a linear regression analysis. The error bars denote the  
 4 reproducibility of the measurements. The determination coefficients are indicated.  
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1  
 2 Figure 6: Relationship obtained between *UI* and the BIC. The solid lines correspond to a linear regression  
 3 analysis. The error bars denote the reproducibility of the measurements. The determination coefficient is  
 4 indicated.  
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1  
 2 Figure 7: Variation of the i)  $ISQ$  measured in the directions  $0^\circ$  (black points) and  $90^\circ$  (grey points) and ii)  
 3 the  $UI$ . The solid lines correspond to a linear regression analysis. The error bars denote the reproducibility  
 4 of the measurements. The determination coefficients are indicated.