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Impact of a Hydrophilic Dental Implant Surface on Osseointegration: Biomechanical Results in Rabbit

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This study aimed to evaluate the effect of surface hydrophilicity on the biomechanical aspects of osseointegration of dental implants in the tibia and femur of rabbits. Forty-eight mature female New Zealand White rabbits were included, and 96 commercially pure, Grade 4, titanium dental implants (control group), and 96 implants of same macro geometry with the hydrophilic surface (test group) were used in this study. One osteotomy was performed in each tibia and femur on both sides of the rabbit, and four implants were placed in each rabbit. Control and test groups were randomly allocated on the left and right sides. During surgery, insertion torque (ITQ) value of the complete implant placement was recorded. After healing periods of 0, 2, 4, and 8 weeks after surgery, implant stability quotient (ISQ) value, and removal torque (RTQ) values were measured. No statistical difference was observed for ITQ, for ISQ and for RTQ between the control group and test group in tibia/femur for all time periods. The effect of hydrophilic properties on moderately roughened surfaces has no impact in terms of biomechanical outcomes (ISQ values and RTQ values) after a healing period of 2 to 8 weeks in rabbit tibias / femurs.

Introduction

Implant stability is considered as one of the most important factors for a successful osseointegration and it should be maintained from the time of insertion and throughout the healing period.[1] Implant stability is commonly subjected to modifications with time[2] according to the type of contact between the implant and the surrounding bone.[3]

When an implant is inserted into living bone, a mechanical engagement is formed. However, it's only during the healing phases that bone modeling/remodeling process modulates the bone formation to the implant surface and a firm anchorage between living cells and dental implant is developed. Implant stability reflects this scenario, so that from an initial purely mechanical anchorage (primary stability) there is a shift toward a biologic stability (secondary stability). For this reason, the evaluation of implant stability is frequently used as an indirect measure of osseointegration.[4]

The establishment of osseointegration is predictable only if certain prerequisites are fulfilled. Albrektsson et al[5] advocated an exquisite balance of 6 factors consisting of implant material, implant design, implant finish, the status of the bone, surgical technique, and implant loading conditions. From the viewpoint of implant finish, moderately rough surfaces (Sa between 1.0 and 2.0 μm) have some clinical advantages over smooth (Sa between 0.0 and 0.4 μm), minimally rough (Sa between 0.5 and 1.0 μm), and rough surfaces (Sa > 2.0 μm).[6,7] As a consequence, most of the commercially available dental implants today possess a moderately rough surface.

One of the major topics of interest in recent implant research is the modification of implant surface properties, such as surface wettability. Some in vitro and in vivo studies showed the potential of a hydrophilic surface on the biologic aspects of the osseointegration process. The theory is that hydrophilic surfaces

improve the differentiation of bone marrow-derived mesenchymal stromal cells[8] and osteoblasts,[9] promoting early mineralization. Specifically, when such surfaces are in contact with whole blood, the higher binding of platelets will occur with a significant increase of contact activation of the coagulation cascade.[10] Down-regulation of the expression of pro-inflammatory cytokine genes are also reported; in such a manner, hydrophilic surfaces may modulate the inflammatory response, and they would facilitate the enhancement of bone wound healing.[11] In a human study, hydrophilic surfaces exerted a pro-osteogenic and pro-angiogenic influence on gene expression that may be responsible for the superior osseointegrative properties of those surfaces.[12] Previous animal studies showed an increase of bone-to-implant contact in early stages of healing.[13,14] Moreover, the histological findings in humans showed that the degree of osseointegration after 2 and 4 weeks is superior to the hydrophilic implants compared with hydrophobic implants.[15] The effect of hydrophilic surfaces on the biomechanical aspects of osseointegration, that is, implant primary and secondary stability, however, was seldom reported. This in vivo pilot study aimed to evaluate the effect of hydrophilic implant surface on implant primary and secondary stability. We hypothesized that an implant with hydrophilic surface expresses higher degree of secondary stability than an implant with conventional hydrophobic surface.

Materials and Methods

All methodologies were reviewed by an independent statistician out of our research facility.

Implants

Ninety-six commercially available pure Grade 4 titanium (ASTM-F67) dental implants (TRI-NEX Southern Implants S-IPH-2.0) manufactured by Southern Implants (Irene, Centurion, South

Africa) with a hydrophobic surface (water contact angle > 90°) (control group) and 96 not commercially available implants of the same macro geometry with the hydrophilic surface (water contact angle < 1°) (test group) were used in this study. The size of the implant was 3.5 mm in diameter and 8 mm in length. All implant surfaces were treated with alumina particle-blasting (110 µm in diameter) and the surface micro topography was the same in both groups with Sa = 1.55 µm. In the test group, hydrophilicity was achieved by applying a coating with a non-conductive, organic, non-ionic substance having at least one polar covalently bonded group.

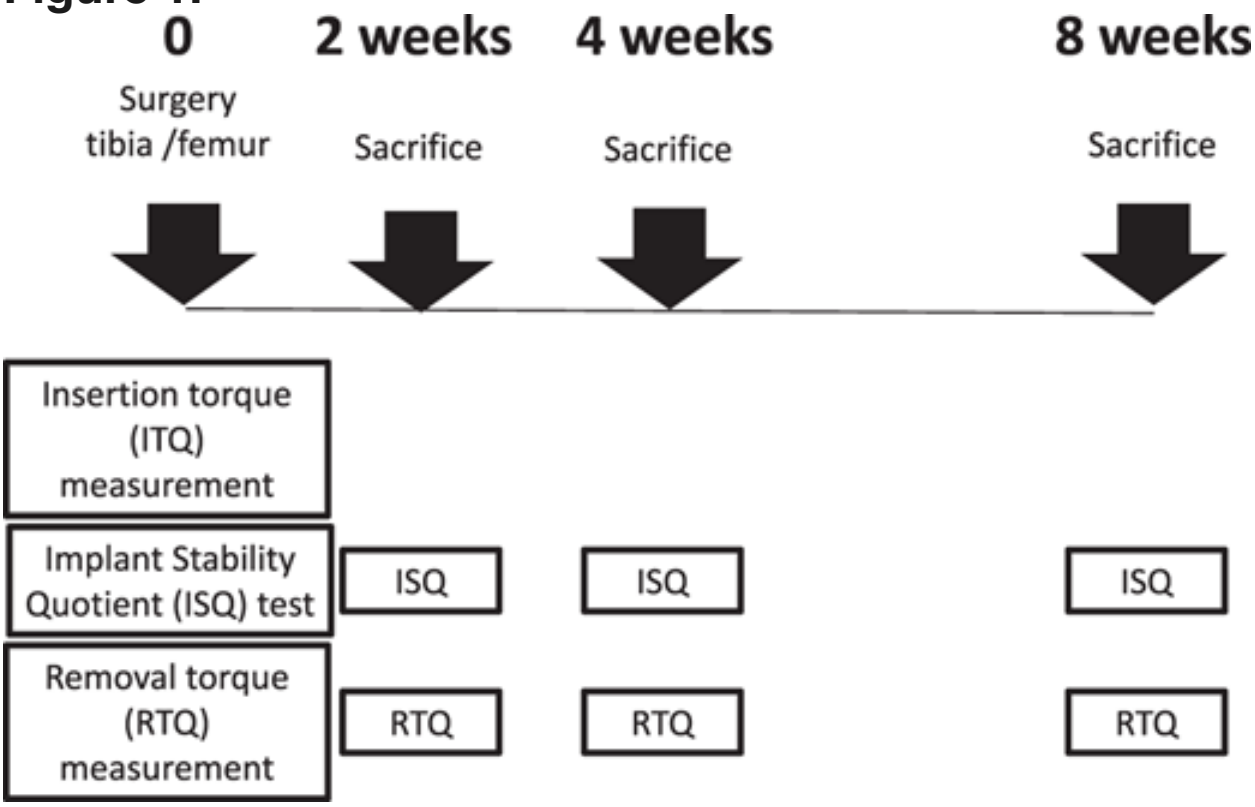
Surgical procedures

This animal study was approved by the ethical committee in the École Nationale Vétérinaire d'Alfort (Maisons-Alfort, Val-de-Marne, France) (reference number: B940462) and it is reported under ARRIVE (Animal Research: Reporting of In Vivo Experiments guidelines,[16] and all animal experimental parts were performed with the veterinarians of the animal facility in École Nationale Vétérinaire d'Alfort.

Forty-eight female New Zealand White Rabbits were conveniently sampled for this pre-clinical pilot study. Such convenience sample size was selected to have a sample number of 12 per each group (Figure 1). After anesthesia by a dose of 250 µl/kg of medetomidine (Domitor, Zoetis, France), 20 mg/kg of ketamine (Imalgene 1000, Merial, Sanofi, France) and 1 mg/kg of diazepam (Valium, Roche, France), both sides of hind limbs of the rabbits were shaved and disinfected by iodine solution. A full-thickness incision was made on the skin, muscle, and periosteum to correspond with the proximal tibia plate and distal femur plate. One implant was placed in each tibia, and one implant was placed in each femur. The control and test groups were randomly allocated on the left and right side. The osteotomy was prepared at the speed of 1200 rpm under constant irrigation of sterile saline

solution. The osteotomy was performed following the manufacturer's drilling protocol, including a tap drill. The implants were positioned using SA-310 W&H Elcomed implant unit (W&H, Bürmoos, Austria), and insertion torque (ITQ) values of the complete implant installation were recorded and stored (Figure 2). The implant stability quotient (ISQ) was also measured after implant placement.

Figure 1.



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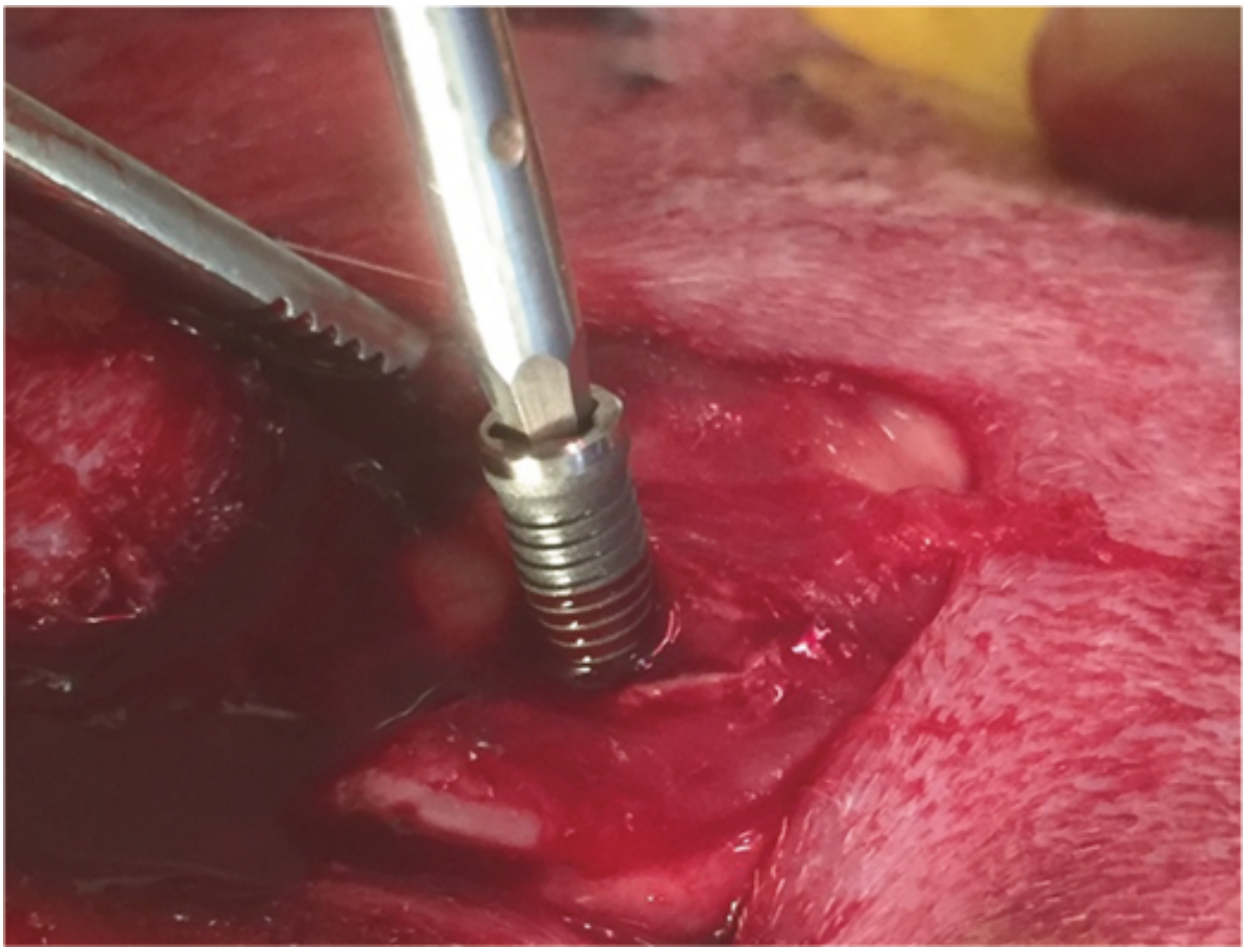
The design flow of the study.

Figure 2.



Dental implant placement (test group) into the rabbit tibia.

Cover screws were connected to the implants, and the flap was repositioned and sutured with resorbable sutures (4-0 Vicryl, Ethicon, Auneau, France).

Analgesic therapy was supplied to the animals with the injection of buprenorphine (Buprecare, Animalcare, York, UK), and meloxicam (Metacam, Boehringer Ingelheim Vetmedica, Inc, Duluth, Ga) for 5 days after surgery. A patch of fentanyl (Duragesic, Janssen Pharmaceutica, Beerse, Belgium) was applied to the animals' skin for 3 days. The animals also received oral antibiotics (enrofloxacin [Baytril]; Bayer Animal Health, Leverkusen, Germany) for 5 days. The animals were kept in separate cages and fed ad libitum.

After euthanasia by a lethal dose of sodium pentobarbital (Euthasol, Vibac, Fort Worth, TX, USA), the tibias and femurs of the animals were dissected and soft tissues were removed from around implants.

Biomechanical tests

In this study, implant stability was evaluated using the following parameters: ITQ values, ISQ values, and removal torque (RTQ) values were recorded.

Primary stability was evaluated by means of ITQ values and ISQ values at the time of implant installation.

Secondary stability was evaluated by means of ISQ values and RTQ values after 2, 4, and 8 weeks from implant installation.

The ISQ value was measured using the Osstell ISQ instrument (Osstell AB, Gothenburg, Sweden), after the connection of the appropriate SmartPeg (Osstell) to the fixture at implant placement and at the animal sacrifice. The measurement was taken 3 times in different directions. The average ISQ value was, therefore, obtained for each implant.

The RTQ test was performed immediately after the animals were euthanized. RTQ value was considered as the value of breaking the interface between the implants and the surrounding bone. The original fixture insertion tool was connected to the implant, and the RTQ value was measured using a calibrated digital torque wrench (P22, Malmö University, Sweden).

Statistical analysis

Data management and statistical analysis were performed using a statistical software package (IBM SPSS Statistics for Mac, v. 22). After checking whether the data could be assumed to fit a normal distribution, non-parametric tests were used. Wilcoxon signed-rank test was used to compare the outcome of the ITQ, RTQ, and ISQ values. The differences were considered statistically significant for $P < .05$. All procedures for statistical analysis were

reviewed by an independent statistician out of our research facility.

Results

During the healing period after surgery, all the rabbits could walk normally and did not show signs of infection or pain in the treated area. The 2 implants in the control group were not osseointegrated at the time of euthanasia. (One was in the tibia for a 4-week healing period, and another was in the femur for an 8-week healing period.) All the implants in the test group were osseointegrated. Therefore, the values of the test group in the same animal with non-osseointegrated implant were excluded from the statistical analysis.

The median / mean ITQ values for the control group and test group in tibias and femurs are shown in Table 1. The sample number of each group, respectively, was 48. The difference between the groups for both tibias and femurs was not statistically significant.

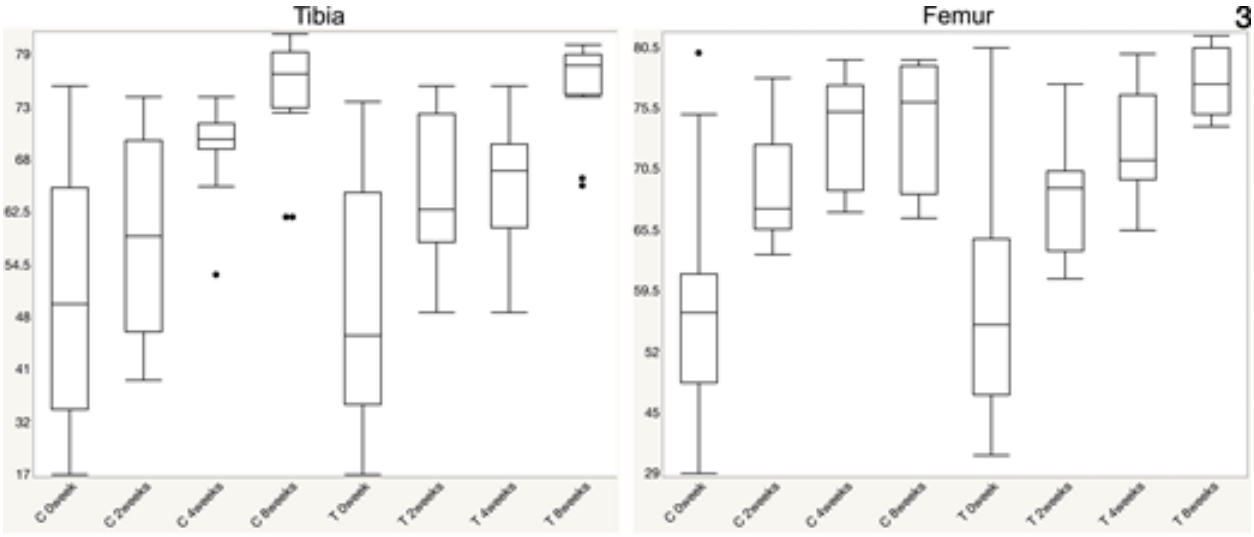
Table 1

Insertion torque values

	Tibia				Femur			
Group	Median	Mean (SD)	Sample number (df)	*P* Value	Median	Mean (SD)	Sample Number (df)	*P* Value
Control	13.6	14.6 (7.58)	48 (47)		19.8	19.6 (7.51)	48 (47)	
Test	14.2	16.0 (8.45)	48 (47)	0.541	20.5	20.4 (8.21)	48 (47)	0.761

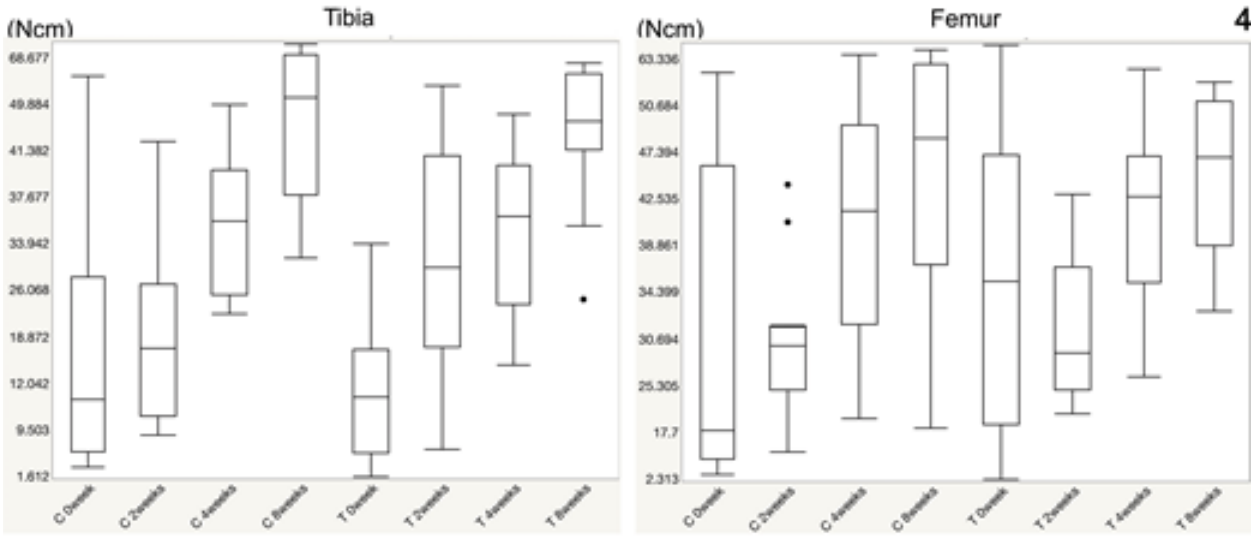
The median / mean ISQ and RTQ values are shown in Figure 3 and 4, respectively. At each time point, from 0 to 8 weeks of healing, the difference between control and test group was not statistically significant in either the tibia or the femur. In both, the tibias and femurs, ISQ and RTQ values showed time-dependent increases during the 8-week healing period in both the control group and the test group.

Figures 3 and 4.



Sample number	48	12	11	12	48	12	11	12
median	50.00	59.25	70.00	76.50	45.75	62.75	67.00	78.00
Mean (SD)	48.28 (16.83)	57.38 (12.08)	68.68 (5.61)	74.96 (6.51)	48.20 (16.69)	63.17 (8.57)	64.95 (7.25)	75.67 (5.18)
P value C VS T	0.954	0.083	0.158	0.593				

48	12	12	11	48	12	12	11
56.50	67.25	75.25	76.00	54.50	69.00	71.25	77.50
55.95 (11.01)	68.79 (4.24)	73.79 (4.35)	74.59 (4.85)	56.64 (11.02)	68.25 (5.02)	72.21 (4.53)	77.77 (3.12)
0.768	0.638	0.636	0.636				



Sample number	12	12	11	12	12	12	11	12
median	10.52	17.91	34.83	50.67	11.00	28.72	34.91	47.37
Mean (SD)	16.97 (15.80)	19.29 (10.34)	33.91 (8.27)	52.20 (16.39)	12.11 (8.69)	28.66 (13.41)	32.43 (10.04)	47.10 (10.58)
P value C VS T	0.638	0.136	0.657	0.530				

12	12	12	11	12	12	12	11
19.49	29.89	42.00	47.75	35.64	29.14	42.49	46.81
24.95 (20.30)	27.97 (9.81)	41.84 (11.09)	47.64 (14.31)	35.27 (22.47)	30.92 (6.64)	41.76 (8.72)	45.06 (8.05)
0.272	0.695	0.754	0.050				

Figure 3. Implant stability quotient values. **Figure 4.** Removal torque values.

Discussion

In the present study, titanium implants provided with a hydrophilic surface were compared with titanium implants provided with a conventional hydrophobic surface in terms of biomechanical stability. Aiming on this, ITQ, RTQ test, and resonance frequency analyses were performed. Such mechanical parameters, which are frequently applied in in vivo research to assess implant stability, are affected by the type of interlocking between the implant and the bone.[17] Different from ITQ value, which solely relies on the initial implant fixation to the bone, RTQ and ISQ values are the results of primary stability and biologic process because of the implant-bone interaction (secondary stability). Therefore, RTQ and ISQ values depend on the contact between the bone and the implant after a healing period, and they are often used to estimate the quality of osseointegration.[18]

The surface properties and chemical composition can modulate the implant osteoconductive characteristics.[7] Undeniably, the moderately rough surface can support the increase of the secondary stability, compared with smoother surfaces.[19,20] However, there is some hint that the microtopography of the surface may alter initial implant stability as well. More specifically, a rough surface can increase the ITQ compared with smooth surfaces.[21]

However, in the present study, the primary stability, in terms of ITQ and the ISQ at the time of surgery, showed no statistical difference between the test and control groups, both in tibias and femurs. It can be said that, from the observation of this study, the initial stability may not be influenced by the hydrophilic properties of the implant surface.

The implant microgeometry (surface topography) has an important role during the osseointegration processes, especially in the shifting period between the initial mechanical stability and secondary stability.[7] The biological processes begin with proteins

and macromolecule adsorption onto the implant surface, and the moderately rough surface provokes rapid and successful integration.[22] Hydrophilic property also demonstrated enhanced osseointegration at early stages in the in vitro/in vivo experiments and clinical study.[23] In the clinical study by Tallarico et al,[23] hydrophilic implants did not show ISQ decrease between the 2nd and 4th week after implant surgery, showing a more even pattern of ISQ values compared with the sandblasted and acid-etched surface implants with hydrophobic property. However, the surface modifications provided to the test implants in this study did not impact the secondary stability either. Even though the RTQ and the ISQ values showed a time-dependent increase in both groups, no significant difference between groups was noted at each time point. Both groups showed a similar trend of secondary stability during the healing period. This means that the improvement of osseointegration by hydrophilic surfaces does not reach the level that can affect the mechanical fixation of the implants in bone, both immediately after implant placement and during the first healing phases. Our initial hypothesis was therefore rejected.

Similar results were reported by Park et al,[24] in which they compared moderately roughened surfaces with and without hydrophilicity in terms of bone-to-implant contact (BIC) (%) and ISQ values in rabbit femurs, and the results indicated significantly higher BIC (%), but no differences in the ISQ values at the 2-week healing period. Numerous in vivo studies have reported the implant BIC (%) and some studies showed that hydrophilic surfaces lead to increased bone apposition in the moderately roughened surface at early,[25,26] and in longer healing periods.[27] Trisi et al reported hydrophilic implants showed 30% higher BIC (%) concerning non-hydrophilic implant; however, no statistical differences were detected between the 2 groups in ISQ values. Sheep with iliac crests were tested with a healing period of 2 months.[27]

In another study by Ferguson et al, the RTQ values were on average 8%–21% higher for hydrophilic implants than for non-hydrophilic implants in miniature pig's maxilla after teeth extraction.[28] However, during a healing period of 8 weeks, RTQ values were the highest after 4 weeks of healing, then decreased at 8 weeks. Such results seem to differ from the present findings. However, it must be acknowledged that the experimental model used was different from the present one.

To conclude, the present study failed to show any significant difference between implants with hydrophilic surface and implants with conventional hydrophobic surface in terms of stability, both primary and secondary.

However, the present findings have to be interpreted with caution. This study model, though extensively used in implant research, does hardly resemble the clinical condition in a human. Arguably, the advantageous characteristics of a surface with an increased wettability of the surface would enhance the osseointegration in the trabecular compartment, more than in the cortical one.[15] Therefore, the lack of trabecular bone in the animal model used might have prevented the potential benefits of the hydrophilicity of the surface.

Additionally, in our study we did not assess the osseointegration in terms of histomorphometric analysis, such as BIC (%). Therefore, our conclusions should be interpreted only in the limited circumstances of implant stability. Future studies are needed to confirm this preliminary data. Such comparison between implants with hydrophilic and hydrophobic surface should be tested in an animal model with a larger trabecular compartment and then in humans.

Conclusion

Within the limits, the present study demonstrated that dental implants provided with the hydrophilic moderately roughened surface could integrate in an animal model, but they did not show any significant improvement of primary and secondary stability compared with implants provided with a hydrophobic surface. Future research should confirm the present results of biomechanical parameters with histomorphometric parameters.

Abbreviations

BIC:
bone-to-implant contact
ISQ:
implant stability quotient
ITQ:
insertion torque
RTQ:
removal torque

Acknowledgements

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