The European Journal of Orthodontics Advance Access published January 4, 2016

European Journal of Orthodontics, 2016, 1–8
doi:10.1093/ejo/cjv095

Randomized Controlled Trial

Immediate versus delayed loading: comparison of primary stability loss after miniscrew placement in orthodontic patients—a single-centre blinded randomized clinical trial

Marco Migliorati*, Sara Drago*, Fabio Gallo, Leonardo Amorfini***, Domenico Dalessandri****, Stefano Benedicenti***** and Armando Silvestrini-Biavati***

*Orthodontics Department, School of Dentistry, University of Genova, Italy, **Section of Biostatistics, Department of Health Sciences, University of Genova, Italy, ***Private Practice, Gallarate, Italy, ****Department of Orthodontics, School of Dentistry, University of Brescia, Italy, and *****School of Dentistry, University of Genova, Italy

Correspondence to: Marco Migliorati, Department of Orthodontics, School of Dentistry, University of Genova, Largo Rosanna Benzi 10, 16100 Genova, Italy. E-mail: marco.migliorati@unige.it

Abstract

Introduction: The aim of this randomized clinical trial was to compare torque recordings at insertion time and 1 week post-placement between immediately loaded orthodontic miniscrews and an unloaded control group.
Trial design: This RCT was designed as parallel with an allocation ratio of 1:1.
Methods: Eligibility criteria to enroll patients were: needs of fixed orthodontic treatment, no systemic disease, absence of using drugs altering bone metabolism. All patients were consecutively treated in a private practice and the miniscrews were placed by the same author. Patients received ORTHOImplant (3M Unitek) miniscrews and they were blindly divided in two groups: group 1 screws were unloaded between T0 and T1, group 2 received immediately loaded screws with NiTi coil. For each patient, maximum insertion torque (MIT) was evaluated at T0. After 1 week, without loading, the screw torque was measured again (T1) and at the end of the treatment maximal removal torque was evaluated (T2). Torque variation in the first week was considered as the primary outcome.
Randomization: A randomization list was created for the group assignment, with an allocation ratio of 1:1.
Blinding: The study was single blinded in regard of the statistical analysis.
Results: Patients enrolled in the clinical trial were 51 for a total of 81 miniscrews. The recruitment started in November 2012 and the observation period ended in August 2014. Twenty-six and twenty-five patients were analysed in group 1 and 2, respectively. The MIT mean in each placement time was 18.25 Ncm (SD = 3.00), 11.41 Ncm (SD = 3.51) and 10.52 Ncm (SD = 5.14) at T0, T1, and T2 time, respectively. In group 1, the torque decrease between T1 and T0 was statistically higher compared to group 2 (*P* value = 0.003). Statistically significant effects of the placement times on MIT were found (*P* value <0.0001). No serious harm was observed.
Limitations: This study was performed using only direct force on the miniscrew and not using the miniscrew as an indirect anchorage. It was not possible to obtain quantitative data on bone quality or root proximity to miniscrews.

Conclusions: A significant stability loss was observed in the first week in both groups; Group 1 showed a statistically higher torque loss in the first week when compared to the immediately loaded group. There were statistically significant effects of the measurement times on MIT and of the miniscrew location on MIT. The overall failure rate was 7.4%.

Trial registration: This trial was not registered.

Protocol: The protocol was not published before trial commencement.

Introduction

Orthodontic miniscrews are intraoral anchorage devices designed to support biomechanics during orthodontic tooth movement (1, 2). Also known as miniscrews, mini-implants, microscrews, or temporary anchorage devices (3, 4), they are made of a head, a neck, and a threaded shank. The head may show different designs (bracket-like, rounded with slot, etc.) the threaded shank is generally cylindrical, tapered or a combination of the two, and may be self-tapping (i.e. requiring a pre-drilled pilot hole) and/or self-drilling (not requiring a pilot hole). Because of their small diameter, they may be implanted in a wide variety of anatomic sites, such as the alveolar interradicular spaces (5) or the palatal cortical bone (6, 7), in order to attend to treatment anchorage needs (8). The loading protocol for miniscrews loading can be as immediate (9, 10) as delayed (11); in the beginning Kanomi (1) indicated a non-specific period of healing and osseointegration before a screw inserted in the mandible could be loaded; the importance of a healing period was derived by several studies on Branemark protocol on implants (12, 13). Further experimental studies on orthodontic load were not able to demonstrate loaded implant loosening, even when loads were applied immediately (14, 15), so that an immediate loading protocol for orthodontic miniscrews appeared as reasonable. Costa and Melsen studied the tissue reaction around the immediately loaded screws in an animal model and suggested the use of immediately loaded screws as an intra-oral extra-dental anchorage (16). Histomorphometric analyses have shown that the immediate loading of miniscrew implants may help to activate bone remodeling and increase the mineral contents at the loaded region (17–20). Compared to traditional endosseous implants, orthodontic miniscrews have relatively high failure rates, varying from 16.4% (21) to 39% (22); according to recent reviews, the average failure rate is believed to be less than 20% (23–25). Many factors have been proposed to be associated to success rate; among these age, gender, jaw (maxilla or mandible), placement site, tissue mobility (firm or movable tissue), inflammation, distance to the root, insertion torque, loading time, type, length, and diameter of the miniscrew (23, 24, 26–28). Recently, an experimental study on primary stability found that bone properties are more important than the screw geometry in establishing primary mechanical retention (29).

In fact, miniscrews do not acquire stability *via* osteointegration, but their clinical success is strictly related to the strength of the connection between native bone and the device, also called primary stability (30, 31). As regards bone, implant placement is identical to normal wound healing and produces a sequence of biological events, including peri-implant osteoid formation after 6 days (32). Until new woven trabeculae do appear, mechanical effects must be considered predominant on biological remodeling effects and a certain degree of contact loosening is expected in reply to implant insertion, as a mechanical response due to bone viscoelastic properties (33). To understand how bone adapts to immediate force applied to orthodontic miniscrews in humans and whether loading enhances primary stability in the short period, the present study addressed a clinical trial on insertion and removal torque of immediately loaded and delayed miniscrews.

Specific objectives or hypotheses

The aim of this randomized controlled trial was to compare torque recordings at insertion time and 1 week post-placement between immediately loaded orthodontic miniscrews and an unloaded control group.

Materials and methods

Trial design and any changes after trial commencement

This randomized clinical trial (RCT) was designed as parallel with an allocation ratio of 1:1.

Participants, eligibility criteria, and settings

Eligibility criteria to enroll patients were: needs of fix orthodontic treatment to both arches, needs of skeletal anchorage using miniscrew, absence of systemic diseases, absence of using drugs altering bone metabolism. All patients were consecutively treated in a private practice and the miniscrews were placed by the same author (L.A.), while all data collected in this study were analysed at Genoa University. The clinical study was approved by the university department council with the approval number 724.

Interventions

Intervention in both groups consisted in an orthodontic treatment with multibrackets appliance, during which one or more miniscrews were used to fulfill the objectives of the treatment. The devices used in this trial were the ORTHOImplant (3M Unitek, Monrovia, Calif), 1.8-mm diameter and 10 or 8 mm length. Miniscrew maximum insertion torque (MIT) was measured in Ncm in all patients by a modified torque wrench (model TT50 SD, MHH Engineering, Bramley, UK). Considering that MIT value could be observed in the early phase as well as at the end of insertion (29), MIT was not considered the final torque value, but the peak of torque observed during placement. Patients enrolled in the study were blindly assigned in two groups. In the first group miniscrews were loaded a week after (T1) insertion, while in the second group they were loaded immediately after the insertion. Allocation of patients to the two groups was determined by a computer-generated randomization list using Rv.0.1. (34) software. All screws were loaded by NiTi coil; the applied forces were measured by an analogical force gauge dynamometer (Smart Europe SRL, Torino, Italy) for each patient, with a mean force of 82 g (SD = 24). Biomechanics applied were for retraction, extrusion, and intrusion. MIT was evaluated at T0, after 1 week (T1) torque was measured again by applying a quarter of turn, and at the end of the treatment maximal removal torque (MRT) was evaluated (T2). All data were measured and registered by the same clinician who placed the screws (L.A.). Miniscrews which lost primary stability and had to be removed were defined as a failure.

Outcomes (primary and secondary) and any changes after trial commencement

Torque variation in the first week was considered the primary outcome. As a secondary outcome was considered: 1. the association among the insertion site (mandibular or maxillary) and the MIT values and 2. the assessment of adverse effects of these interventions.

Sample size calculation, power of the study

The sample size estimation calculated that 23 patients achieves 91% power to detect a miniscrew MIT mean of paired differences of −2.20, with an estimated standard deviation of differences of 2.80 and with a significance level (alpha) of 0.05 using a paired *t*-test.

The sample size calculation was performed on the basis of results from a similar recent preliminary ad hoc pilot study (data not published). The baseline mean of miniscrew MIT was set to 20.20, assuming a standard deviation of paired differences of 2.80.

Interim analyses and stopping guidelines

Not applicable.

Randomization

Patients were enrolled in two groups using a computer-generated randomization list with an allocation ratio of 1:1 and by a block size of 2. The randomization list was obtained by R v3.0.1 software environment (34).

Blinding

The study was blinded in regard of the statistical analysis. Data were recorded and blinded for the statistician: blinding was obtained by eliminating from the elaboration file every reference to patient group assignment.

Statistical analysis

Data were analysed by a statistician. Continuous variables are given as means ± standard deviations (SD) and range, whereas categorical variables as number and/or percentage of subjects. Age was categorized using quartiles of the age distribution of our study population (13 to ≤20, >20 to ≤25, >25 to ≤30, >30 to 46). The MIT baseline differences among age, gender, purpose of miniscrews, treatment groups, and miniscrew location were tested by the linear mixed effects (LME) model. In order to investigate the associations of the miniscrew MIT with treatment groups, miniscrew location, and placement times the LME model was performed. In addition, considering that two treatment groups and miniscrew locations were evaluated and three different placement times were taken into account, an exploratory interaction analysis was also carried out to test whether, the miniscrew MITs in treatment groups and miniscrew locations were different according to the placement times, once again, using the LME Model. The likelihood ratio (LR) test was used as a test of statistical significance and in each LME model, the sampling units were considered to be random factor. The failure rates difference among groups was evaluated by the Fisher's Exact test. The analysis of the MIT relative differences (RD) was performed to test whether the MIT RD means in treatment groups were different comparing Time T1 versus Time T0 and Time T2 versus Time T0, respectively.

The estimated *P* values were adjusted for multiple comparisons by the Bonferroni correction method and when the adjusted *P* value less than 0.05, the differences were selected as significant. Data were acquired and analysed in R v3.2.3 software environment (34).

Results

Participants flow

In this trial, where 52 patients were randomly assigned to the interventions, one drop-out was observed in the first group. The final sample that received the intended treatment and analysis was 51 patients and 81 miniscrews (Figure 1). The mean miniscrew duration was 201 days (184 and 219 days for group 1 and 2, respectively).

The miniscrews used for analysis were 41 for group 1 and 40 for group 2, respectively. The recruitment started in November 2012 and the observation period ended in August 2014.

Baseline data

The baseline MIT distribution in the levels of the age, gender, purpose of miniscrews, treatment groups, and miniscrew location, with a summary of tests used, were reported in Table 1. The baseline age mean was 25.29 years (SD = 7.83) and the mean MIT at the T0 was 18.25 Ncm (SD = 3.00). Regarding miniscrew location, the MIT mean values at T0 were 16.95 Ncm (SD = 2.85) and 19.58 Ncm (SD = 2.56) for the maxillary and mandibular arch, respectively. The group 1 showed a MIT mean of 18.37 Ncm (SD = 2.63) while a mean of 18.14 Ncm (SD = 3.32) was observed in group 2 (Table 1). No significant MIT baseline differences among age, gender, purpose of miniscrews, and treatment groups were detected (Table 1, LR adjusted *P* values: 0.3475, 1.000, 0.0865, and 0.9157). Comparing the MIT baseline mean in the mandibular arch with that in the baseline maxillary arch a 2.65 Ncm significant difference was observed (Table 1, LR adjusted *P* value = 0.0007).

Demographic and clinical characteristics of the treatment groups at the baseline were reported in Tables 2. Twenty-one 8 mm devices out of 42 and twenty-two 10 mm devices out of 39 were implanted in group 1 and 2, respectively. The overall failure rate was 7.4%. In particular, 5.3% was observed for group 1 while a failure rate of 9.3% was estimated for group 2. No statistically significant difference was found (*P* value = 0.6792) between the two groups.

Numbers analysed for each outcome, estimation, and precision, subgroup analyses

The MIT mean at T1 and T2 was 11.41 Ncm (SD = 3.51) and 10.52 Ncm (SD = 5.14), respectively. The LME model (Table 3), using the complete set of data, demonstrated that no association existed between MIT and the treatment group (LR adjusted *P* value = 0.5391), but there were statistically significant effects of the miniscrew location and the placement times on the MIT (LR adjusted *P* values: 0.0413 and <0.0001). In particular, comparing MIT mean at T1 with that at T0 (Table 3) about a −6.84 Ncm significant decrease (95% CI: −7.81; −5.87) was observed. In addition, a −7.65 Ncm significant decrease (95% CI: −8.67; −6.63) was seen in the mean of MIT at T2 in relation to that at T0. In regards to the miniscrew location, a 1.73 Ncm significant increase (95% CI: 0.17; 3.29) was observed comparing the MIT mean in the mandibular arch with that in the maxillary arch (Table 3, supplementary Figure 1).

The exploratory interaction analysis demonstrated that significant miniscrew MIT differences existed in treatment groups and miniscrew locations (LR adjusted *P* values for interaction: 0.0148 and 0.0338, respectively) according to the placement times. In particular, a −0.43 MIT RD mean and a −0.33 MIT RD mean were estimated according to T1 versus T0 in group 1 and 2, respectively (Table 4). Regarding T2 versus T0, the MIT RD mean of −0.41 and −0.44 were estimated in group 1 and 2, respectively. Comparing MIT RD means in treatment groups according to T1 versus T0 a significant difference (Table 4, Adjusted *P* value = 0.0032) was observed (Figure 2).

Harms

No serious harm was observed but some peri-miniscrew inflammation which therapy was application of clorexidina gel or spray twice a day (Corsodyl, GlaxoSmithKline, Brentford, UK).

Discussion

Limitations and generalizability

This study was performed using only direct force on the miniscrew and not using the miniscrew as an indirect anchorage, thus the results should be considered only for this methodology. Moreover, it was not possible to obtain quantitative data on bone quality or root proximity to miniscrew (no CBCT on patients).

Different loading requests based on treatment needs might have an impact on torque loss.

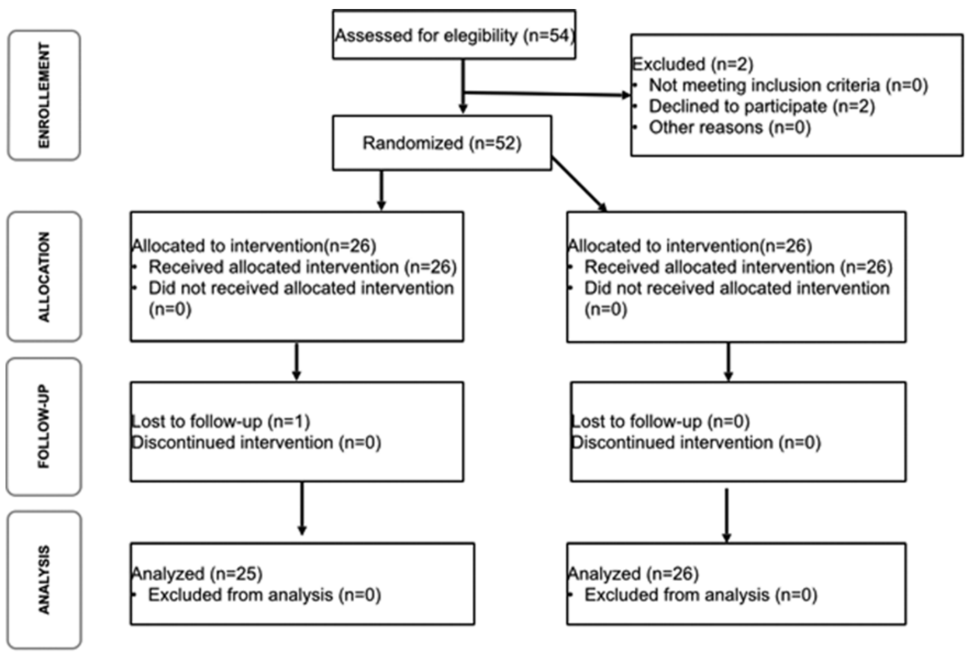

Figure 1. Study flow chart.

Table 1. Demographic and clinical MIT values at the baseline; OMI, orthodontic mini-implants.

	N	Mean ± SD	Range	Beta	Lower CI	Upper CI	LR adjusted *P* value
Age							0.3475
13 to ≤20	21	17.52 ± 2.93	13–24	0	—	—	
>20 to ≤25	20	18.00 ± 2.83	12–24	0.53	−1.70	2.77	
>25 to ≤30	21	18.57 ± 2.99	13–25	1.15	−1.11	3.41	
>30 to 46	19	18.95 ± 3.99	14–25	1.19	−1.10	3.46	
Gender							1.0000
Female	48	18.27 ± 3.18	12–25	0	—	—	
Male	33	18.21 ± 2.77	13–24	−0.11	−1.74	1.53	
Purpose of OMIs							0.0865
Distalization	29	18.14 ± 3.30	12–25	0	—	—	
Intrusion	8	17.25 ± 3.77	13–24	−0.89	−3.63	1.90	
Indirect anchorage	13	19.15 ± 2.51	15–23	1.53	−0.58	3.73	
Extrusion	7	18.71 ± 2.63	16–22	0.97	−1.95	3.97	
Mesialization	24	18.08 ± 2.78	15–25	0.54	−1.40	2.60	
Treatment group							0.9157
1	38	18.37 ± 2.63	13–24	0	—	—	
2	43	18.14 ± 3.32	12–25	−0.50	−2.10	1.11	
Miniscrew location							0.0007
Maxillary arch	41	16.95 ± 2.85	12–25	0	—	—	
Mandibular arch	40	19.58 ± 2.56	16–25	2.65	1.24	4.08	

N, number of observations; Mean ± SD, mean and standard deviation; range, range of values; beta, regression coefficient of the linear mixed-effects models; lower CI, 95% lower confidence interval; upper CI, 95% upper confidence interval; LR adjusted *P* value, likelihood ratio *P* value adjusted by using Bonferroni method.

Two differently long devices were used (8 and 10 mm), but it is known that miniscrews length does not affect their stability (9, 35); on the other hand, since diameter was pointed out as relevant for primary stability (29, 36), in this trial only screws having the same diameter were used, thus the results of this study could be associated to other screws with the same diameter.

Main findings and interpretation

The primary stability of miniscrews is believed to result from mechanical interlock with alveolar cortical bone. Since miniscrews do not achieve their primary stability through osseointegration, their anchorage potential is likely to be influenced by the quality and quantity of bone into which they are placed. Moreover, it is known that loading affects bone mechanical properties in the peri-screw region (37). The purpose of this clinical study was to further explore the relationship between maximum placement torque during miniscrew placement and miniscrew resistance to movement under load in the early stages, up to the appearance of new woven trabeculae, according to what is reported by the literature (32).

Firstly, it was found that there were statistically significant effects of placement time on MIT. Particularly, a torque relative difference mean of −37.5% between T0 and T1 was estimated. There are many factors that may lead to this phenomenon; in particular data should be interpreted under the mechanical consideration that like screws, miniscrews were conceived to transform a torsional couple into a compression force (38), and when the screw encounters a specific tightening torque, a composite tensile/torsional deformation state exists. The torsion moment is necessary to guarantee stability, and can be seen as the imposition of a deformation on an elastic material (bone), with the aim of generating a pre-stressed state in the screw. Once the miniscrew is inserted into the bone trabeculae, a so-called relaxation phenomenon occurs; this happens every time the bone remains in a deformed position, and over time leads to a reduction in the initially induced tensile state (39). The relaxation phenomenon can be understood by imagining the bone as a spring whose rigidity decreases over time in two discrete periods of evolution. As described by Sasaki (40), the two periods should be considered separately:

Period I: the relaxation evolves very quickly but with progressively decreasing rapidity. In compact bone, the duration of this phase is 10^4 s, while in spongy bone, 95 per cent of the reduction in the tensile state occurs over a period of 100 s.

Period II: the relaxation evolves very slowly (and for certain periods is almost unchanging) in compact bone, taking times of the order of 10^6 s to complete. In spongy bone, the times are considerably less, but an exact quantification is difficult to determine due to the paucity of relaxation which occurs in the second period.

Sasaki observed that periods I and II can be explained by the composition of the bone (composite biphasic material), which is

Table 2. Demographic and clinical characteristics of the treatment groups.

	Treatment group		
	1	2	Row Total
Age			
13 to ≤ 20	9	5	14
>20 to ≤25	9	4	13
>25 to ≤30	4	8	12
>30 to 46	3	9	12
Gender			
Female	14	16	30
Male	11	10	21
Purpose of OMIs			
Distalization	9	7	16
Intrusion	1	5	6
Indirect anchorage	6	5	11
Extrusion	2	3	5
Mesialization	7	6	13
Miniscrew location			
Maxillary arch	9	16	25
Mandibular arch	16	10	26

Table 3. Descriptive statistics and output of linear mixed-effects model.

Variable	*N*	Mean ± SD	Beta	Lower CI	Upper CI	LR adjusted *P* value
Placement time						<0.0001
T0	81	18.25 ± 3.00	0	-	-	
T1	81	11.41 ± 3.51	-6.84	-7.81	-5.87	
T2	81	10.52 ± 5.14	-7.65	-8.67	-6.63	
Treatment group						0.5391
1	114	13.34 ± 5.11	0	-	-	
2	129	13.73 ± 5.36	-0.49	-1.16	2.14	
Miniscrew location						0.0413
Maxillary arch	123	12.90 ± 4.65	0	-	-	
Mandibular arch	120	14.16 ± 5.69	1.73	0.17	3.29	

N, number of observations; Mean ± SD, mean and standard deviation; beta, regression coefficient of the linear mixed-effects models; lower CI, 95% lower confidence interval; upper CI, 95% upper confidence interval; LR adjusted *P* value, likelihood ratio *P* value adjusted by using Bonferroni method.

Table 4. Analysis of the maximum insertion torque relative differences.

			Student's *t*-test			
Contrast	Mean in group 1	Mean in group 2	*t*	df	*P*-value	Adjusted *P* value
Time T1 versus Time T0	−0.43	−0.33	−3.30	64	0.0016	0.0032
Time T2 versus Time T0	−0.41	−0.44	0.53	67	0.5979	1.0000

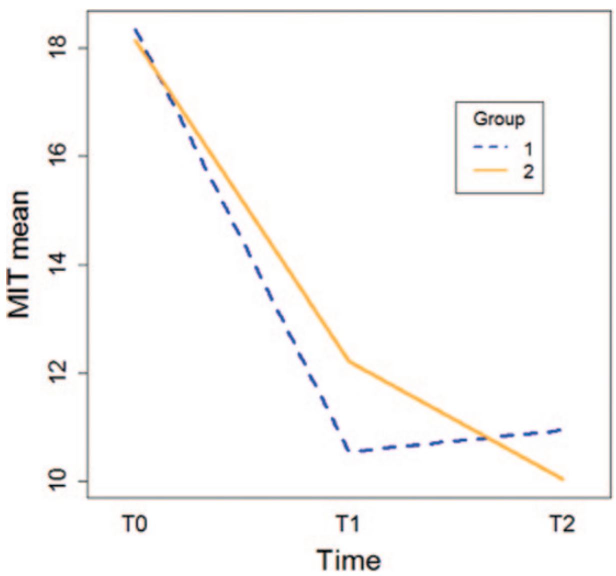

Figure 2. Maximum insertion torque mean values at different observation timepoints, with respect to groups.

made up of a hydroxyapatite mineral component fixed onto a collagen matrix attributed with viscous behaviour. Elastic modulus of the bone is a resultant of a compression and damper effect. The mineral part has an anisotropic behaviour, while the organic phase has the main viscoelastic properties. In fact, an increase in temperature and hydration, and the occurrence of demineralization phenomena characterize period I, which is dominated by relaxation of the fibrous structure of collagen. Upon completion of period I, the relaxation of the mineral phase, present from the beginning, is perceptible, characterizing period II with very moderate reductions that develop over a long period of time (40). However, one big problem in understanding biomechanical effects of relaxation is that period II of relaxation (11.6 days) is roughly comparable with the remodeling cycle in bone and the study of the two overlapping effects is very difficult. For this reason in the present study we preferred to conduct the observation 1 week post-placement, before biological effects of peri-implant osteoid formation become important.

Despite the early torque decrease, which reflects the relaxation phenomenon, miniscrews stayed stable through all the treatment and overcame orthodontic loading. By testing removal torque in Göttinger minipigs mandibles after a period of loading, Buchter *et al.* (41) suggested that immediate loading of miniscrews can be performed without loss of stability when the load-related biomechanics do not exceed an upper limit of tipping moment at the bone rim (300 cN and 3 mm of distance from the crestal bone. It was also reported that immediate loading is possible if the applied force is less than 2 N (9).

Secondly, there were statistically significant effects of the miniscrew location on MIT; particularly, the MIT mean in the mandibular arch was significantly higher than the MIT mean in the maxillary arch. This is coherent with the anatomy of the alveolar bone, as MIT is related to cortical thickness, cortical density, and medullary bone density (42) and the maxilla and the mandible show significantly different values for these characteristics (27). In a study where CT scans were examined to achieve accurate three-dimensional bone thickness measurements in dental areas, significantly different cortical thickness values were found in different locations (43).

Finally, the exploratory interaction analysis demonstrated that: (I) Significant miniscrew MIT differences existed in treatment groups according to the placement times. The analysis of the MIT relative differences comparing time T0 and T1 showed a significant difference between treatment groups. In particular, the relative difference in group 2 (immediately loaded) was significantly lower than its counterpart in group 1 (delayed). This reflects what an histomorphometric analysis found on adult male monkeys, that is BIC in the unloaded controls was much lower at 1 week and progressively increased, but without reaching the same level as the loaded sample (17). However, in the present study, time seems to level the initial differences in torque decrease, because at T2 groups cannot be anymore distinguished on the basis of a torque analysis. This could depend on the fact that late stability, which refers to the implant's stability after the first complete turnover of immediate peri-implant bone tissue (2–4 months, depending on bone turnover rates), is a result of the balance between accumulated microstrain of peri-implant bone tissue (amount of bone microdamage) and its healing capacity (remodeling rate) (5).

Nakagaki *et al.* (44) observed that the bone mineralization of the compression region of cortical bone surrounding immediately loaded miniscrews was significantly higher than that of the tension region, while the bone-to-implant contact amount was approximately the same, and they concluded that immediate loading does not inhibit osseointegration of miniscrew implants but may stimulate bone mineralization, which would explain why immediate loading could contribute to maintain a higher torque value in the early phases. (II) Significant miniscrew MIT differences existed in miniscrew locations according to the placement times, even though the trend of MIT mean in mandibular and maxillary arch according to placement time seemed like similar in two groups (Supplementary Figure 1). Moreover, this trial was not randomized for miniscrew locations and a significant difference, comparing the mandibular baseline MIT mean with that in the maxillary arch at baseline, was observed.

In this case, the results came from the exploratory interaction analysis and the influence of miniscrew location on MIT should be considered carefully. In addition, a randomization for both treatment group and miniscrew locations should be helpful in further studies to prevent the selection bias and to insure against the accidental bias.

Further studies are needed in order to understand whether placement and early torque recordings can be associated to clinical success, even though it seems unlikely that long term stability can be predicted only on the basis of placement torque absolute values (45). No adverse effects of these interventions were observed.

Conclusions

The present study led to the following conclusions:

1. There were statistically significant effects of the measurement times on MIT;
2. the MIT mean 1 week post-placement was significantly lower than the MIT mean at insertion time;
3. the mean removal torque was significantly lower than the insertion torque values.

Supplementary material

Supplementary material is available at *European Journal of Orthodontics* online.

References

1. Kanomi, R. (1997) Mini-implant for orthodontic anchorage. *Journal of Clinical Orthodontics*, 31, 763–767.
2. Ohmae, M., Saito, S., Morohashi, T., Seki, K., Qu, H., Kanomi, R., Yamasaki, K.I., Okano, T., Yamada, S. and Shibasaki, Y. (2001) A clinical and histological evaluation of titanium mini-implants as anchor for orthodontic intrusion in the beagle dog. *American Journal of Orthodontics and Dentofacial Orthopedics*, 119, 489–497.
3. Mah, J. and Bergstrand, F. (2005) Temporary anchorage devices: a status report. *Journal of Clinical Orthodontics*, 39, 132–136.
4. Cornelis, M.A., Scheffler, N.R., De Clerck, H.J., Tulloch, J.F. and Behets, C.N. (2007) Systematic review of experimental use of temporary skeleletal anchorage devices in orthodontics. *American Journal of Orthodontics and Dentofacial Orthopedics*, 131(4 Suppl), S52–S58.
5. Park, J. and Cho, H.J. (2009) Three-dimensional evaluation of interradicular spaces and cortical bone thickness for the placement and initial stability of microimplants in adult. *American Journal of Orthodontics and Dentofacial Orthopedics*, 136, 314.e1–314.e12.
6. Bernhart, T., Vollgruber, A., Gahleitner, A., Dörtbudak, O. and Haas, R. (2000) Alternative to the median region of the palate for placement of an orthodontic implant. *Clinical Oral Implants Research*, 11, 595–601.
7. Gracco, A., Lombardo, L., Cozzani, M. and Siciliani, G. (2008) Quantitative conebeam computed tomography evaluation of palatal bone thickness for orthdontic miniscrew placement. *American Journal of Orthodontics and Dentofacial Orthopedics*, 134, 361–369.
8. Janssen, K.I., Raghoebar, G.M., Vissink, A. and Sandham, A. (2008) Skeletal anchorage in orthodontics—a review of various systems in animal and human studies. *The International Journal of Oral & Maxillofacial Implants*, 23, 75–88.
9. Miyawaki, S., Koyama, I., Inoue, M., Mishima, K., Sugahara, T. and Takano-Yamamoto, T. (2003) Factors associated with the stability of titanium screws placed in the posterior region for orthodontic anchorage. *American Journal of Orthodontics and Dentofacial Orthopedics*, 124, 373–378.
10. Cha, J.Y., Lim, J.K., Song, J.W., Sato, D., Kenmotsu, M., Inoue, T. and Park, Y.C. (2009) Influence of the length of the loading period after placement of orthodontic mini-implants on changes in bone histomorphology: microcomputed tomographic and histologic analysis. *International Journal of Oral and Maxillofacial Implants*, 24, 842–849.
11. Zhang, Q., Zhao, L., Wu, Y., Wang, H., Zhao, Z., Xu, Z., Wei, X. and Tang, T. (2011) The effect of varying healing times on orthodontic mini-implant stability: a microscopic computerized tomographic and biomechanical analysis. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics*, 112, 423–429.
12. Schnitman, P.A., Wöhrle, P.S., Rubenstein, J.E., DaSilva, J.D. and Wang, N.H. (1997) Ten-year results for Brånemark implants immediately loaded with fixed prostheses at implant placement. *The International Journal of Oral & Maxillofacial Implants*, 12, 495–503.
13. Sagara, M., Akagawa, Y., Nikai, H. and Tsuru, H. (1993) The effects of early occlusal loading on one-stage titanium alloy implants in beagle dogs: a pilot study. *The Journal of Prosthetic Dentistry*, 69, 281–288.
14. Wehrbein, H. and Diedrich, P. (1993) Endosseous titanium implants during and after orthodontic load—an experimental study in the dog. *Clinical Oral Implants Research*, 4, 76–82.
15. Akin-Nergiz, N., Nergiz, I., Schulz, A., Arpak, N. and Niedermeier, W. (1998) Reactions of peri-implant tissues to continuous loading of osseointegrated implants. *American Journal of Orthodontics and Dentofacial Orthopedics*, 114, 292–298.
16. Melsen, B. and Costa, A. (2000) Immediate loading of implants used for orthodontic anchorage. *Clinical Orthodontics and Research*, 3, 23–28.
17. Luzi, C., Verna, C. and Melsen, B. (2009) Immediate loading of orthodontic mini-implants: a histomorphometric evaluation of tissue reaction. *European Journal of Orthodontics*, 31, 21–29.
18. Chen, Y., Kang, S.T., Bae, S.M. and Kyung, H.M. (2009) Clinical and histologic analysis of the stability of microimplants with immediate orthodontic loading in dogs. *American Journal of Orthodontics and Dentofacial Orthopedics*, 136, 260–267.
19. Chen, Y., Lee, J.W., Cho, W.H. and Kyung, H.M. (2010) Potential of self-drilling orthodontic microimplants under immediate loading. *American Journal of Orthodontics and Dentofacial Orthopedics*, 137, 496–502.
20. Serra, G., Morais, L.S., Elias, C.N., Meyers, M.A., Andrade, L., Muller, C. and Muller, M. (2010) Sequential bone healing of immediately loaded mini-implants: histomorphometric and fluorescence analysis. *American Journal of Orthodontics and Dentofacial Orthopedics*, 137, 80–90.
21. Schätzle, M., Männchen, R., Zwahlen, M. and Lang, N.P. (2009) Survival and failure rates of orthodontic temporary anchorage devices: a systematic review. *Clinical Oral Implants Research*, 20, 1351–1359.
22. Tsui, W.K., Chua, H.D. and Cheung, L.K. (2012) Bone anchor systems for orthodontic application: a systematic review. *International Journal of Oral and Maxillofacial Surgery*, 41, 1427–1438.
23. Manni, A., Cozzani, M., Tamborrino, F., De Rinaldis, S. and Menini, A. (2011) Factors influencing the stability of miniscrews. A retrospective study on 300 miniscrews. *European Journal of Orthodontics*, 33, 388–395.
24. Papageorgiou, S.N., Zogakis, I.P. and Papadopoulos, M.A. (2012) Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. *American Journal of Orthodontics and Dentofacial Orthopedics*, 142, 577–595.
25. Dalessandri, D., *et al.et al*. (2014) Determinants for success rates of temporary anchorage devices in orthodontics: a meta-analysis (n > 50). *European Journal of Orthodontics*, 36, 303–313.
26. Lim, H.J., Eun, C.S., Cho, J.H., Lee, K.H. and Hwang, H.S. (2009) Factors associated with initial stability of miniscrews for orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*, 136, 236–242.
27. Motoyoshi, M., Yoshida, T., Ono, A. and Shimizu, N. (2007) Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. *The International Journal of Oral & Maxillofacial Implants*, 22, 779–784.
28. Mesa, F., Muñoz, R., Noguerol, B., de Dios Luna, J., Galindo, P. and O'Valle, F. (2008) Multivariate study of factors influencing primary dental implant stability. *Clinical Oral Implants Research*, 19, 196–200.
29. Migliorati, M., Drago, S., Schiavetti, I., Olivero, F., Barberis, F., Lagazzo, A., Capurro, M., Silvestrini-Biavati, A. and Benedicenti, S. (2014) Orthodontic miniscrews: an experimental campaign on primary stability and bone properties. *European Journal of Orthodontics*. First published on December 24, 2014, pii:cju081.
30. Brettin BT, *et al.et al*. (2008) Bicortical vs monocortical orthodontic skeletal anchorage. *American Journal of Orthodontics and Dentofacial Orthopedics*, 134, 625–635.
31. Migliorati, M., Benedicenti, S., Signori, A., Drago, S., Barberis, F., Tournier, H. and Silvestrini-Biavati, A. (2012) Miniscrew design and bone characteristics: an experimental study of primary stability. *American Journal of Orthodontics and Dentofacial Orthopedics*, 142, 228–234.
32. Raghavendra, S., Wood, M.C. and Taylor, T.D. (2005) Early wound healing adjacent to dental implants: a review of the literature. *International Journal of Oral and Maxillofacial Implants*, 20, 425–431.
33. Guedes, R.M., Simões, J.A. and Morais, J.L. (2006) Viscoelastic behaviour and failure of bovine cancellous bone under constant strain rate. *Journal of Biomechanics*, 39, 49–60.
34. R Core Team (2015). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/.
35. Park, H.S., Jeong, S.H. and Kwon, O.W. (2006) Factors affecting the clinical success of screw implants used as orthodontic anchorage. *American Journal of Orthodontics and Dentofacial Orthopedics*, 130, 18–25.
36. Estelita Barros, S., Janson, G., Chiqueto, K., Gamba Garib, D. and Janson, M. (2011) Effect of mini-implant diameter on fracture risk and self-drilling efficacy. *American Journal of Orthodontics and Dentofacial Orthopedics*, 140, e181–e192.
37. Iijima, M., Nakagaki, S., Yasuda, Y., Handa, K., Koike, T., Muguruma, T., Saito, T. and Mizoguchi, I. (2013) Effect of immediate loading on the biomechanical properties of bone surrounding the miniscrew implants. *European Journal of Orthodontics*, 35, 577–582.
38. Manghi, F. (1996) Stabilità dei collegamenti a vite. *Macchine*, 1, 7–14.

39. Lakes, R.S. and Katz, J.L. (1979) Viscoelastic properties of wet cortical bone—II. Relaxation mechanisms. *Journal of Biomechanics*, 12, 679–687.
40. An, Y.H. and Draughn, R.A. (eds) (2000) *Mechanical Testing of Bone and the Bone-Implant Interface*. CRC Press, Boca Raton, FL, pp. 334–335.
41. Büchter, A., Wiechmann, D., Koerdt, S., Wiesmann, H.P., Piffko, J. and Meyer, U. (2005) Load-related implant reaction of mini-implants used for orthodontic anchorage. *Clinical Oral Implants Research*, 16, 473–479.
42. Cha, J., *et al.et al*. (2010) Mini-screw stability evaluated with computerized tomography scanning. *American Journal of Orthodontics and Dentofacial Orthopedics*, 137, 73–79.
43. Silvestrini Biavati, A., Tecco, S., Migliorati, M., Festa, F., Marzo, G., Gherlone, E. and Tete`, S. (2011) Three-dimensional tomographic mapping related to primary stability and structural miniscrew characteristics. *Orthodontic and Craniofacial Research*, 14, 88–99.
44. Nakagaki, S., Iijima, M., Handa, K., Koike, T., Yasuda, Y., Saito, T. and Mizoguchi, I. (2014) Micro-CT and histologic analyses of bone surrounding immediately loaded miniscrew implants: comparing compression and tension loading. *Dental Materials Journal*, 33, 196–202.
45. Meursinge Reynders, R.A., Ronchi, L., Ladu, L., Etten-Jamaludin, F. and Bipat, S. (2012) Insertion torque and success of orthodontic mini-implants: a systematic review. *American Journal of Orthodontics and Dentofacial Orthopedics*, 142, 596–614.