

Assessment of changes in the oral tactile function of the soft tissues by implant placement in the anterior maxilla: a prospective study

P. Habre-Hallage · N. Bou Abboud-Naman ·
H. Reyhler · D. van Steenberghe · R. Jacobs

Received: 5 August 2008 / Revised: 9 March 2009 / Accepted: 19 March 2009 / Published online: 16 April 2009
© Springer-Verlag 2009

Abstract The aim of the present study was to assess the somatosensory function in the peri-implant soft tissues in the anterior jaw bone by means of two psychophysical tests. Light-touch sensation (LTS) and two-point discrimination (2PD) were performed before, and at planned intervals until 18 months after the placement of one or two implants in the anterior maxilla. The same tests were used on the contralateral control sites. The psychophysical threshold

was determined by performing the staircase method. The mean values and standard deviation of LTS and 2PD, pooled over the four sessions at each test area, were calculated. Despite a large intersubject variation in both the LTS and 2PD, significantly high intra-individual correlations were found ($P < 0.005$). For LTS, the thresholds were not significantly affected over time ($P > 0.05$) on both implant and control sites. The 2PD increased significantly after surgery and maintained the higher discriminatory sense for 1 year (P -value 0.005). The control sites remained stable over time. However, no correlation was revealed between LTS and 2PD perception (Pearson correlation test). In this prospective study, no major differences between the different sites and testing sessions were reported; except for the 2PD thresholds which were lowered after implant surgery. These findings suggest that the regenerated nerves may be responsible for the increased 2PD sensitivity in the peri-implant soft tissue. The unchanged LTS thresholds did not allow confirming this hypothesis.

P. Habre-Hallage
Department of Prosthodontics, Faculty of Dentistry,
Saint-Joseph University, Campus of Medical Sciences,
Damascus Road,
Beirut, Lebanon

N. Bou Abboud-Naman
Department of Periodontology, Faculty of Dentistry,
Saint-Joseph University, Campus of Medical Sciences,
Damascus Road,
Beirut, Lebanon

H. Reyhler
Department of Stomatology and Maxillo-Facial Surgery,
Catholic University of Louvain,
Hippocrate 10,
Brussels 1200, Belgium

D. van Steenberghe
Professor emeritus of the Faculty of Medicine,
Catholic University of Leuven,
Leuven, Belgium

P. Habre-Hallage (✉) · R. Jacobs
Laboratory of Oral Physiology, Department of Periodontology,
Faculty of Medicine, Catholic University of Leuven,
Kapucijnenvoer 7,
Leuven 3000, Belgium
e-mail: pascale.habrehallage@usj.edu.lb

R. Jacobs
e-mail: reinhilde.jacobs@med.kuleuven.be

Keywords Oral implants · Tactile threshold · Perception ·
Psychophysical tests · Oral sensory function

Introduction

The control of oral motor behavior relies on a variety of receptors such as the periodontal mechanoreceptors and the intradental nociceptors [15]. Tooth loss will remove these receptors and reduce the inputs to the brain. The feedback pathway is considerably damaged [22]. After tooth loss, the socket becomes filled by bone. Nerve endings and mechanoreceptors are damaged and remaining nervous tissue may no longer be stimulated and thus lead to nerve degeneration [12] or nervous branches may start sprouting

and simply provide innervation to some more distant structures, like the overlying healed soft tissues [5]. The remaining receptors in the gingiva, alveolar mucosa, and periosteum may partly take over the exteroceptive function [13]. Different types of mechanoreceptors were identified in the oral mucosa. They include Meissner's corpuscles, glomerular endings, Merkel cells, Ruffini-like endings, and free nerve endings. The mechanoreceptors in the denture-bearing gingiva play a predominant role in trigeminal motor control [11, 32]; however, dentures may only partially restore jaw function [17]. When Tübingen implants were used, teeth were more sensitive than implants at low forces application but were equally sensitive at higher forces up to 1,400 cN [33, 34]. With oral implants, the sensory and motor functions seem to improve but fail to reach the same level of sensitivity as dentate subjects [7, 14, 18, 27, 28]. Hence, it remains uncertain whether this improvement can be ascribed to 'osseoreceptors' located in the periosteum or within the bone marrow itself [39].

Oral implants are fixed into the jaw bone, but emerge through the keratinized or alveolar mucosa. The peri-implant junctional epithelium, including its neural components, is similar to that of natural teeth [31].

Regenerative nerve fibers, invaded the superficial layer of the peri-implant epithelium. These nerve fibers contain substance P and possess free nerve endings. Their functions might be a sensory system for pain, touch, and pressure [43, 44].

Merkel cells are important in tactile function and they are normally found in the oral mucosa and in the gingiva. They seem to be absent in the hamster's peri-implant epithelium mucosa [43] but were found in the peri-implant mucosa in humans [31]. Indeed, histological findings report an increased innervation in the peri-implant epithelium after implant placement [44]. Their presence in the periosteum has not been described in the literature [30].

From the current evidence, it remains unclear whether an altered innervation (from periodontal to peri-implant) may have changed the tactile function of implant-rehabilitated sites. To elucidate this question, psychophysical methods can be used. These are non-invasive and well-defined techniques. They allow to relate the physiological functions of the receptors to the subjective experience of the subject [17].

The objectives of this prospective study were to assess the sensory tactile function in peri-implant soft tissue and to investigate if changes in the sensory tactile function occurred over time.

To reach this goal, tactile thresholds of the keratinized and/or alveolar mucosa surrounding oral implants in patients were determined and compared to the contralateral dentate site: (a) before implant placement ; (b) after implant placement but before implant loading; (c) after prosthetic rehabilitation to detect if any change occurs over time.

Materials and methods

Subjects

Nine dentate adults (ages 19–32 years), three males (five implants) and six females (seven implants) were selected based on their dental status. Subjects included had a complete natural dentition with the exception of one or two teeth missing in the anterior region of the maxilla (incisor teeth). These patients had to be rehabilitated with osseointegrated implants (Table 1). The implant insertion was made by the same operator at modum Brånemark. The implants healed under the closed mucosa during a period of 3 to 5 months. The abutments were mounted on the implants 1 month after the second surgery time.

None of the subjects had a history of any neurologic disorder or periodontitis or dysesthesia in the oral cavity. Informed consent was obtained from each participant prior to investigation. Two sensory tests, including light-touch sensation and two-point discrimination were used to determine the passive threshold (without any physical action of the subject). The subjects were asked to report the presence of the object, as soon as it was perceived.

The four consecutive measurements were performed over a period of 18 months: in each subject, one implant was stimulated while the tissues surrounding the contralateral natural tooth served as a control.

The patients were tested in a quiet room with stable illumination while seated comfortably in a dental chair. A protocol form of all testing procedures was presented and explained to the subject before the actual test, the probes were shown to the subject to alleviate his or her apprehension regarding the testing procedure. All the tests were performed at the buccal site of the keratinized or alveolar mucosa in the anterior maxilla for both right and left sides. The subjects were instructed to close their eyes during the whole testing procedure.

Tactile detection threshold or light-touch sensation

The tests were performed by using von Frey filaments (Bioseb™, Chaville, France). This device consists of 20 monofilaments, all of constant length but having a stepwise progression of diameters. Each monofilament is labeled with a number that represents the log₁₀ of the force (mg) required to cause the filament to bend (Fig. 1). The number of the filaments (1.65–6.65) corresponds to a logarithmic function of the equivalent forces of 0.008–300 g, according to the manufacturer.

When the tip of a fiber of given length and diameter was pressed against the tested area at right angles, the force of application increased as long as the researcher continued to advance the probe, until the fiber bent. After bending,

Table 1 Threshold changes for LTS from initial to follow-up examination at the implant and control sites for all subjects

Test type		Implant site				Control site					
		Before implant	Abutment placement	6months	12months	Before implant	Abutment placement	6months	12months		
Light-touch sensation	Filament number	4.18	4.48	4.07	4.22	4.47	4.35	4.45	4.30		
		4.27	4.14	4.30	4.13	4.18	4.15	4.17	4.16		
		3.70	4.10	4.31	4.09	3.65	4.48	4.41	4.17		
		3.76	3.36	3.31	3.28	3.40	3.41	3.45	3.09		
		3.87	3.80	3.89	3.79	3.52	3.50	3.68	3.73		
		4.26	4.44	4.31	4.02	3.52	3.50	3.68	3.73		
		3.47	3.48	3.75	3.45	3.20	3.17	3.32	3.35		
		3.32	3.12	3.72	3.76	3.69	3.60	3.71	3.72		
		4.09	4.06	4.05	3.87	3.86	3.85	3.71	3.80		
		3.72	3.81	3.80	3.69	3.21	3.56	3.29	3.53		
		Mean		3.86	3.88	3.95	3.83	3.67	3.76	3.79	3.76
		Std		0.33	0.45	0.32	0.30	0.41	0.44	0.42	0.38
	Min		3.32	3.12	3.31	3.28	3.20	3.17	3.29	3.09	
Max		4.27	4.48	4.31	4.22	4.47	4.48	4.45	4.30		

LTS light-touch sensation, *mean* mean value of von Frey hair, *std* standard deviation value, *min* minimum value of von Frey hair, *max* maximum value of von Frey hair

continuous probe advancing may induce more bending, but not more force of application which made it possible to apply a reproducible force, within a wide tolerance, to the tested surface.

The filament should not be allowed to slip but must remain pinned to the gingiva at the point of initial contact. The force is continuously applied for 1 s and then removed (Fig. 2). The subjects were instructed to respond “yes” (i.e., contact was felt during the stimulation) or “no” (i.e., contact was not felt during the stimulation).

The threshold calculation was determined by performing the psychophysical staircase method [9]. A first filament is applied. If the subject reports a negative answer (does not detect a pressure) a filament with a larger diameter is used

and applied with increasing intensity until the subject reacts then the pressure is immediately increased by using a larger filament. This procedure continued until eight minimum values were recorded and the threshold was calculated as the average of these values. Fake stimuli—which means approaching the subject with a probe but turning the probe slightly so that no contact with the tissue was achieved—were applied after peaks 5 and 11 as false positives. These may have occurred when the subject detected the movement of the examiner’s hand as it approached with the probe. If the subject did not report a sensation during the blank

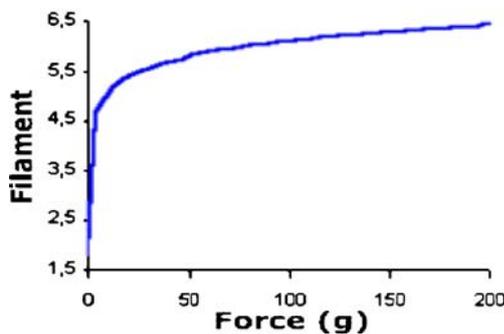


Fig. 1 The relation between the filament number and the force (g) developed by the filament bending is reported in this graph provided by the manufacturer (Bioseb™, Chaville, France): the filament number represents log10 of the force (mg) required to cause the filament to bend

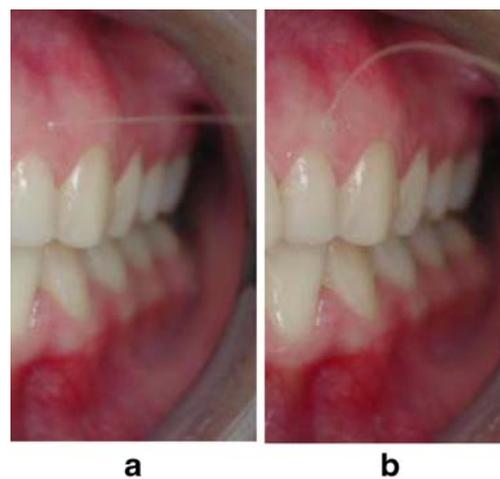


Fig. 2 The use of the light-touch sensation instrument (Von Frey Filament, Bioseb™, Chaville, France): **a** the filament was applied on the tested area at right angles, **b** the filament was pressed until the fiber bent

stimuli, the test was continued. If he did, the test was discontinued and the subject was questioned about what kind of stimulus he had perceived. The whole procedure was explained again and the test was restarted later. The stimulation sessions were interleaved with periods of rest of 5 min to avoid fatigue.

The tactile spatial acuity thresholds or two-point discrimination thresholds

Two-point discrimination thresholds can be done with ordinary dividers. When the closed dividers touched the skin, the perception is of being touched with only a single point. As the dividers are opened more and more on successive applications to the skin, at a certain distance, the perception is of being touched at two points. This test was performed using a dedicated custom-made device [19]. A tip made by a 1.5-mm diameter wire was connected to a hinge handle of a constant force periodontal probe (Brodontic™, Prima, Byfleet, UK), which can apply a constant 25 N force to oral tissue surfaces. Fifteen plastic disks were made by self-curing acrylic resin in which two wires were embedded at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, 20 mm). Each wire was sphere-shaped at the end. This test was performed very carefully to make sure that these two points simultaneously contacted the tissue surface about 2 s, although one of these two points might touch prior to another (Fig. 3). In order to convince the subjects that the sensation of one or two points was possible they were demonstrated that either one or two points would be in contact with the alveolar mucosa. In fact, only the blank stimuli were tested with one probe. All other stimuli involved two simultaneous contacts. The staircase method was also used to evaluate the two-point discrimination. When the subjects answered ‘two points’, it was marked as ‘+’. The next application was a disk with a narrower interprobe distance. This procedure was repeated until subjects answered ‘one point’, which was marked as ‘-’.



Fig. 3 The two-point discrimination instrument was applied on the tested area for 2 s then removed

Subsequently, a series with increasing distance was applied. When eight maximum and eight minimum values were recorded, the average threshold was calculated. Two extra blank stimuli were applied after peaks 5 and 11. This means that only one point of the probes made contact with the mucosa. If the subject answered correctly (‘one point’) the test could be continued. Otherwise, the test was stopped and the subject would be thoroughly reformed about the experimental procedure. The average of these values was calculated.

Data and statistical analysis

Descriptive statistics were used to summarize all measurements. Pressure sensitivity thresholds, did not require log transformation, since monofilament numbers already correspond to log-force in milligrams. The mean values and standard deviation of LTS and 2PD pooled over the four sessions, at each test area, were calculated. Since the same subjects were submitted to repeated measures, Friedman’s ANOVA with two independent variables (time and person) was performed. It assessed their independent effect concurrently, and determined whether they interact with respect to their effect on the threshold. After obtaining a significant ANOVA test, the multiple-comparison Scheffe’s test was performed. It was used for all possible paired comparisons (e.g., 2PD before implant placement and 2PD at abutment connection) to determine which time periods were significantly different from each other. The evaluation of threshold as a function of time at implant and control sites, at the four testing sessions, was performed using the Wilcoxon signed-rank test. This test was used to compare thresholds between the implant and control at matching sites, and to test their stability between sites. Its use is limited to the comparison of two groups at a time. Finally, the Pearson’s correlation coefficient was used to evaluate the relationship between the LTS and the 2PD tests among the different sites, for each subject. It measured the tendency of the variables to increase or decrease together. A level of significance of 0.05 was chosen for all the statistical tests.

Results

Characteristics of subjects

Out of the nine enrolled patients, eight were seen at all control visits. One patient (female, two implants) was lost to follow-up because she moved abroad after the prosthetic rehabilitation. All subjects reported perceived sensitivity to tactile stimuli. None of the subjects reported areas in which very light tactile-stimuli-produced pain.

Tactile detection threshold

The measurement of the threshold of the light-touch sensation on both implant and control sites, before implant placement, at abutment connection, 6 and 12 months after prosthetic rehabilitation are shown in Table 1 (Fig. 4).

The results were reported using the logarithmic value of the LTS thresholds; but for the statistical analysis, the LTS threshold values in (g) were used. The thresholds were not significantly affected by time (P -value 0.26) on the implant site and (P -value 0.41) at the control site. But these were significantly affected by subjects at both sites (P -value 0.005)

Tactile detection thresholds were not significantly different (Wilcoxon signed-rank test) between the implant and control sites at the four testing periods. At the individual level, one patient exhibited large variations in LTS thresholds (implant 3)

The tactile spatial acuity thresholds

The measurement of the tactile spatial acuity thresholds on both implant and control sites, before implant placement, at abutment connection, 6 and 12 months after prosthetic rehabilitation are shown in Table 2. At the implant sites, five sites (implants no 3, 4, 6, 7, and 9) showed lowered 2PD thresholds at 12 months while the five remaining sites (implants no 1, 2, 5, 8, and 10), showed no or very small differences. The differences in thresholds values did not exceed 2 to 3 mm. At the control sites, three of the ten sites (1, 5, and 8) showed more important 2PD thresholds values compared to the threshold distance on the homologous area at the implant site (Fig. 5).

The 2PD thresholds, were significantly affected, per subject at both sites (P -value 0.00) for implant and control sites; they were also significantly affected by time (P -value 0.005) on the implant site but not significant (P -value 0.68) at the control site (two-way ANOVA). Since a significant ANOVA test was obtained at the implant side, the multiple

comparison Scheffe's test was performed, for all possible paired comparisons (e.g., 2PD before implant placement and 2PD at abutment connection) to determine which time periods were significantly different from each other. A significant difference was found at two periods, before implantation and 12 months after the prosthetic rehabilitation (0.13; 2.33), and at abutment connection and 12 months after the prosthetic rehabilitation (0.23; 2.48).

The 2PD thresholds were not significantly different (Wilcoxon signed-rank test) between the implant and control sites at the four testing periods.

Discussion

The gingiva contains round and oval lamellar corpuscles [25]. These receptors respond to mechanical stimuli and are involved in the co-ordination of lip and buccal muscles during mastication [19, 21]. The same receptors are found in the gingiva and in the oral mucosa [17]. They are sensitive to mechanical stimuli, requiring displacements of only a few to tens of micrometers to be activated. The sensory receptors are more frequently found in the anterior part of the mouth with a lower sensitivity in the ridge crest compared to the vestibular areas, suggesting that receptor density was more important in the latter [37, 38].

After tooth extraction, the formation of keratinized, scarless tissue occurs [35, 36, 42]. The thickness of the healed mucosa is not related to the original gingival thickness [24, 33] and could affect its mechanical properties, such as elasticity [3]. Loss of teeth should be considered an amputation and could thus result in a neurophysiological deficit comparable to the loss of a limb. Tooth extraction damages a large number of sensory nerve fibers of the inferior alveolar nerves, and alters projection to the sensorimotor cortex [29]. Consequently, the nerve trunks may degenerate in response to the loss of stimulation [12]. Adjacent tissues may also respond, with afferent projections, to presumably reprogrammed sensorimotor representation in an attempt to restore sensory function [18]. Linden and Scott were able to stimulate nerves of periodontal origin in healed extractions sockets, which implies that the nerve endings were still present in the alveolar bone [26]. Various branches originating from the trigeminal ganglion may reinnervate other structures such as the overlying oral mucosa [5]. The reinnervation was less dense toward the superficial mucosa in comparison to the buccal and lingual.

Animal studies have demonstrated that regenerated nerve fibers in the peri-implant gingiva showed the same neural characteristics as those in the junctional epithelium surrounding teeth [10]. Garzino et al. [11] compared the density of mucosal innervation between edentulous and dentate subjects. They reported a decreased number of sensory receptors in the

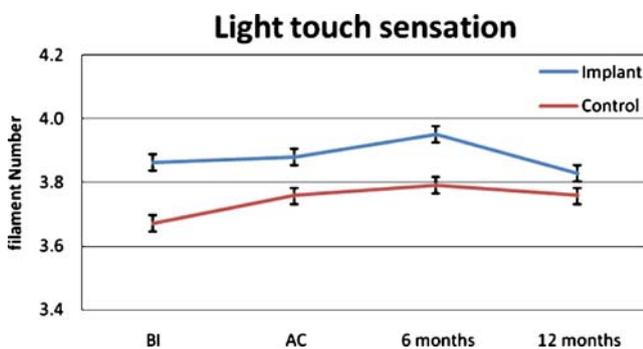


Fig. 4 Graph showing the average thresholds for LTS from initial to follow-up examination for all subjects. *VF bef. I* von Frey test before implant placement. *VF at abutment* von Frey test at abutment placement. *VF 6 months* von Frey test at 6 months. *VF 12 months* von Frey test at 12 months

Table 2 Threshold changes for 2PD, from initial to follow-up examination—implant- and control-side for all subjects

Test type		Implant site				Control site			
		Before implant	At Abutment placement	6 months	12 months	Before implant	At Abutment placement	6 months	12 months
Two-point discrimination	Threshold (mm)	3.25	4.44	3.56	4.31	6.19	4.56	5.00	4.94
		4.50	3.63	6.13	5.06	3.75	4.25	4.63	4.69
		8.88	9.25	6.94	5.69	5.94	6.25	5.31	4.44
		10.00	8.81	8.06	7.31	4.94	8.44	7.69	7.50
		5.25	5.94	5.25	4.50	7.75	6.63	5.63	6.25
		10.06	10.25	10.25	8.38	7.94	7.94	8.88	8.25
		7.25	7.44	5.63	4.69	7.13	6.25	5.88	6.00
		5.81	5.06	5.00	4.50	7.81	7.63	7.69	7.31
		8.38	8.75	8.13	6.31	6.44	6.75	6.50	6.31
		7.38	8.13	6.69	7.38	5.50	5.75	6.13	4.81
	mean	7.08	7.17	6.56	5.81	6.34	6.44	6.33	6.05
	std	2.33	2.26	1.91	1.45	1.37	1.36	1.36	1.33
	min	3.25	3.63	3.56	4.31	3.75	4.25	4.63	4.44
max	10.06	10.25	10.25	8.38	7.94	8.44	8.88	8.25	

2PD two-point discrimination, *mean* mean value, *std* standard deviation value, *min* minimum value, *max* maximum value

edentulous mucosa but a minor increase in the number of nerves in the peri-implant mucosa and a significant increase of innervation in the distal peri-implant mucosa. These changes could partially explain the clinically observed differences in sensory skills before and after implant placement [11].

Both LTS and 2PD are simple but reliable oral sensory tests [16]. Despite a large intersubject variation in the LTS

and 2PD, the thresholds were significantly affected in the present investigation at the subject level for both sites. The observed session-to-session threshold variability could be either due to variation in psychological factors (i.e., “response bias”) or to individual differences in the tactile sensitivity of the oral mucosa [40].

With regard to tactile detection threshold and in accordance with previous studies, the LTS thresholds were not significantly affected by time both at the implant and dentate control sides [2, 4, 23]. The lack of differences observed at the four testing sessions illustrate the variability of the tested afferents, their density, and/or variations in the processing within the central nervous system of tactile information [20]. A decrease of the light-touch sensation would indicate a deterioration of the large myelinated fiber function [6]. This lack of difference contrasts with other studies reporting an increased sensitivity after tooth extraction, attributed to the regeneration of nerve fibers into the soft tissues [26]. Sometimes a loss of tactile sensitivity was reported after surgery, but this is not always reflected in psychophysical testing [1, 8]. The presence [31] or absence of Merkel cells [43] in the peri-implant soft tissue did not seem to affect the LTS threshold values.

The size of a receptive field varies over the body surface, with those located on the extremities being the smallest, growing in size along the leg or arm, and reaching a maximum size on the trunk [41]. Thus, for the 2PD, one should consider that two sensations need to be evoked and thus the stimuli must activate at least two primary afferent fibers. In the present study, the measurement of the 2PD thresholds was significantly affected over time on the

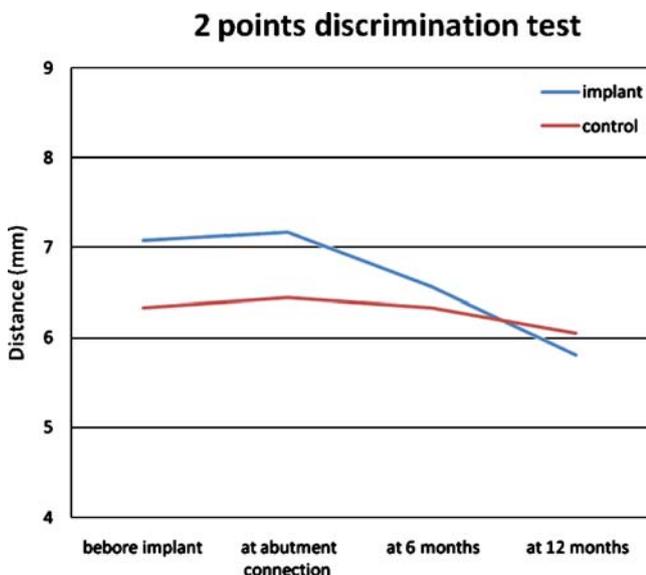


Fig. 5 Graph showing the average thresholds for 2PD from initial to follow-up examination for all subjects. 2PD bef. 1 two-point discrimination test before implant placement. 2PD at abutment two-point discrimination test at abutment placement. 2PD 6 months two-point discrimination test at 6 months. 2PD 12 months two-point discrimination test at 12 months

implant but not at the control site. The increased sensitivity to 2PD at the implant site which may reflect the origin of the regenerating nerves, i.e., the larger myelinated A α afferent nerve fibers. These results are in agreement with the hypothesis proposed by Linden and Scott who attributed the increased sensitivity to nerve fibers regenerating into adjacent soft tissues [26].

The 2PD threshold levels showed an increased sensitivity at 12 months after the prosthetic rehabilitation. These findings suggest that the surgery had no effect on the soft tissues sensitivity but the regenerated nerve fibers may have increased the sensitivity in the peri-implant soft tissues 12 months after implant loading. These findings are in accordance with the results of Essick who assessed the borders of decreased sensitivity to pinprick in patients with mandibular nerve injuries [8]. The magnitudes of loss of light-touch sensitivity were greatest while they were the least in two-point discrimination tests.

Conclusion

The present study revealed no major changes in the tactile sensitivity of the gingiva over time and after surgery except for decreased 2PD thresholds after months at the side of implantation. These findings suggest that the regenerated nerves increased the 2PD sensitivity in the peri-implant soft tissue. The lack of changes in LTS thresholds did not confirm or infirm this hypothesis. Thus, more research on larger patient samples will be needed.

Conflicts of interest None.

References

1. Abarca M, van Steenberghe D, Malevez C, De Ridder J, Jacobs R (2006) Neurosensory disturbances after immediate loading of implants in the anterior mandible: an initial questionnaire approach followed by a psychophysical assessment. *Clin Oral Invest* 10:269–277
2. Aviv JE, Hecht C, Weiberg H, Dalton JF, Urken ML (1992) Surface sensibility of the floor of the mouth and tongue in healthy controls and in radiated patients. *Otolaryngol Head Neck Surg* 107:418–423
3. Bale E, White FH (1982) Quantitative light and electron microscopical studies of the epithelial-connective tissue junction in intraoral mucosae. *J Microsc* 128:69–78
4. Cordeiro PG, Schwartz M, Nevers RI, Tuma R (1997) A comparison of donor and recipient site sensation in free tissue reconstruction of the oral cavity. *Annals of Plastic Surgery* 39:461–468
5. Desjardins RP, Winkelmann RK, Gonzalez JB (1971) Comparison of nerve endings in normal gingiva with those in mucosa covering edentulous alveolar ridges. *J Dent Res* 50:867–879
6. Dyck PJ, Curtis DJ, Bushek W, Offord K (1974) Description of Minnesota thermal disks and normal values of cutaneous thermal discrimination in man. *Neurology* 24:325–330
7. El-Sheikh AM, Hobkirk JA, Howell PGT, Gilthorpe MS (2003) Changes in passive tactile sensibility associated with dental implants following their placement. *Int J Oral Maxillofac Implants* 18:266–272
8. Essick GK, Patel S, Trulsson M (2002) Mechanosensory and thermosensory changes across the border of impaired sensitivity to pinprick after mandibular nerve injury. *J Oral Maxillofac Surg* 60:1250–1266
9. Falmagne JC (1985) Elements of psychophysical theory. In Oxford: Clarendon. 1st edition, pp. 219–220.
10. Fujii N, Ohnishi H, Shirakura M, Nomura S, Ohshima H, Maeda T (2003) Regeneration of nerve fibres in the peri-implant epithelium incident to implantation in the rat maxilla as demonstrated by immunocytochemistry for protein gene product 9.5 (PGP9.5) and calcitonin gene-related peptide (CGRP). *Clin Oral Implants Res* 14:240–247
11. Garzino M, Ramieri G, Panzica G, Preti G (1996) Changes in the density of protein gene product 9.5-immunoreactive nerve fibers in human oral mucosa under implant-retained overdentures. *Archives of Oral Biology* 41:1073–1079
12. Hansen JH (1980) Neurohistological reactions following tooth extractions. *Int J Oral Surg* 9:411–426
13. Jacobs R, van Steenberghe D (1991) Comparative evaluation of the oral tactile function by means of teeth or implant-supported prostheses. *Clin Oral Implants Res* 2:75–80
14. Jacobs R, van Steenberghe D (1993) Comparison between implant-supported prostheses and teeth regarding the passive threshold level. *Int J Oral Maxillofac Implants* 8:549–554
15. Jacobs R, van Steenberghe D (1994) Role of periodontal ligament receptors in the tactile function of teeth: a review. *J Periodontal Res* 29:153–167
16. Jacobs R, Wu C-H, Goossens K, Van Loven K, van Steenberghe D (2001) Perceptual changes in the anterior maxilla after placement of endosseous implants. *Clin Implant Dent Relat Res* 3:148–155
17. Jacobs R, Wu CH, Goossens K, Van Loven K, Van Hees J, van Steenberghe D (2002) Oral versus cutaneous sensory testing: a review of the literature. *J Oral Rehabil* 29:923–950
18. Jacobs R, van Steenberghe D (2006) From osseoperception to implant-mediated sensory-motor interactions and related clinical implications. *J Oral Rehabil* 33:282–292
19. Johansson RS, Vallbo AB (1979) Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol* 286:283–300
20. Johansson RS, Vallbo AB (1980) Spatial properties of the population of mechanoreceptive units in the glabrous skin of the human hand. *Brain Res* 184:353–366
21. Johansson RS, Trulsson M, Olsson KA, Westberg K-G (1988) Mechanoreceptor activity from the human face and oral mucosa. *Exp Brain Res* 72:204–208
22. Klineberg I, Murray G (1999) Osseoperception: sensory function and proprioception. *Adv Dent Res* 13:120–129
23. Komiyama O, De Laat A (2005) Tactile and pain thresholds in the intra- and extra-oral regions of symptom-free subjects. *Pain* 115:308–315
24. Kydd WL, Daly CH, Wheeler JB 3rd (1971) The thickness measurement of masticatory mucosa in vivo. *Int Dent J* 21:430–441
25. Lambrichts I, Creemers J, van Steenberghe D (1992) Morphology of neural endings in the human periodontal ligament: an electron microscopic study. *J Periodontal Res* 27:191–196
26. Linden RW, Scott BJ (1989) The effect of tooth extraction on periodontal ligament mechanoreceptors represented in the mesencephalic nucleus of the cat. *Arch Oral Biol* 34:937–941
27. Lundqvist S, Haraldson T (1992) Oral function in patients wearing fixed prosthesis on osseointegrated implants in the maxilla: 3-year follow-up study. *Scand J Dent Res* 100:279–283

28. Lundqvist S (1993) Speech and other oral functions. Clinical and experimental studies with special reference to maxillary rehabilitation on osseointegrated implants. *Swed Dent J Suppl* 91:1–39
29. Mason AG, Holland GR (1993) The reinnervation of healing extraction sockets in the ferret. *J Dent Res* 72:1215–1221
30. Macefield VG (2005) Physiological characteristics of low-threshold mechanoreceptors in joints, muscle and skin in human subjects. *Clin Exp Pharmacol Physiol* 32:135–144
31. Marchetti C, Farina A, Cornaglia AI (2002) Microscopic, immunocytochemical, and ultrastructural properties of peri-implant mucosa in humans. *J Periodontol* 73:555–563
32. Mericske-Stern R (1994) Oral tactile sensibility recorded in overdenture wearers with implants or natural roots: a comparative study. *Int J Oral Maxillofac Implants* 9:63–70
33. Mühlbradt L, Ulrich R, Möhlmann H, Schmid H (1989) Mechanoperception of natural teeth versus endosseous implants revealed by magnitude estimation. *Int J Oral Maxillofac Implants* 4:125–130
34. Mühlbradt L, Ulrich R, Möhlmann H, Schmid H, Wendler K (1990) Die wahrnehmung von überschwelligem kräften an enossalen implantaten und natürlichen zähnen. *Zahnärztl. Implan- tol* VI:161–165
35. Muller HP, Schaller N, Eger T, Heinecke A (2000) Thickness of masticatory mucosa. *J Clinical Periodontol* 27:431–436
36. Muller W, Schroeder HE (1980) Differentiation of the epithelium of the human hard palate. *Cell Tissue Res* 209:295–313
37. Ogawa T, Ogimoto T, Sumiyoshi K, Koyano K (2003) Pressure-pain threshold of oral mucosa and its region-specific modulation by pre-loading. *J Oral Rehabil* 30:1062–1069
38. Rapp R, Kirstine WD, Avery JK (1957) A study of the multiplicity of nerve endings in the human gingiva and periodontal membrane. *J Canad Dent Assoc* 23:637–645
39. Rowe MJ, Tracey DJ, Mahns DA, Sahai V, Ivanusic JJ (2005) Mechanosensory perception : are there contributions from bone associated receptors? *Clin Exp Pharmacol Physiol* 32:100–108
40. Sessle BJ, Yao D, Nishiura H, Yoshino K, Lee JC, Martin RE, Murray GM (2005) Properties and plasticity of the primate somatosensory and motor cortex related to orofacial sensorimotor function. *Clin Exp Pharmacol Physiol* 32:109–114
41. Sukotjo C, Abanmy AA, Ogawa T, Nishimura I (2002) Molecular cloning of wound inducible transcript (wit 3.0) differentially expressed in edentulous oral mucosa undergoing tooth extraction wound-healing. *J Dental Res* 81:229–235
42. Suzuki Y, Matsuzaka K, Ishizaki K, Tazaki M, Sato T, Inoue T (2005) Characterization of the peri-implant epithelium in hamster palatine mucosa: behavior of Merkel cells and nerve endings. *Biomed Res* 26:257–269
43. Tanaka T, Kido MA, Ibuki T, Yamaza T, Kondo T, Nagata E (1996) Immunocytochemical study of nerve fibers containing substance P in the junctional epithelium of rats. *J Periodontal Res* 31:187–194
44. Weinstein S (1962) Tactile sensitivity of the phalanges. *Percept Mot Skills* 14:351–354

Copyright of Clinical Oral Investigations is the property of Springer Science & Business Media B.V. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.