

## Bölüm 1

# PERİODONTOLOJİDE DENEYSEL HAYVAN MODELLERİ

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### GİRİŞ

Periodontitis, dünyadaki en yaygın kronik inflamatuar hastalıklardan biridir ve insanlarda baskın bir kemik patolojisi formudur (Demmer & Papapanou, 2010). Periodontitis ayrıca dişetinde kanama, periodontal cep formasıonyu ve diş çevresini saran bağ dokusunda yıkım ile karakterizedir. Mikrobiyal biyofilm içerisindeki mikroorganizmalar immün sistemi stimüle ederek, diş çevre dokularında yıkım ve sonuç olarak diş kaybına neden olmaktadır (Kara & ark., 2013).

Oral bakteriyel biyofilm varlığı gingival ve periodontal dokularda immün-inflamatuar yanıt provoke ederek periodonsiyumu oluşturan yapılarda ilerleyici yıkımlara sebep olmaktadır. Periodontojide, bu yıkımının ilerlemesini durdurmak için diştaşı temizliği ve kök yüzeyi düzleştirmesi işlemleri uygulanmaktadır. Bununla birlikte iyi oral hijyenin sağlanmasına özen gösterilmektedir. Periodontal tedavinin amacı; etiyolojik faktörleri ortadan kaldırarak periodontal hastlığın gelişiminin durdurulması, oral fonksiyonların rehabilite edilmesi, cerrahi-cerrahi olmayan teknikler ve yönlendirilmiş doku rejenerasyonunda kullanılan biyomaterialyaller yardımıyla kaybedilen dokuların rejenerere edilmesidir (Tobita & ark., 2008; Tomina & ark. 2017).

Buna ek olarak son yıllarda implant çevresi hastalıklar ve tedavi yöntemlerine dair araştırmalar da periodontojide önemli yer tutmaktadır. Peri-implant mukozitis, mukozada bulunan ve peri-implant yumuşak dokuların bakteriyel ataklara karşı konak tepkisini temsil eden inflamatuar bir lezyonu tarif etmektedir. Peri-implantitiste ise buna ek olarak destek kemik dokusu da etkilenmiştir (Lang & Berglundh, 2011). Hayvan deneylerinin sonuçları, mikrobiyal plak kolonizasyonu ve peri-implant hastlığın patogenezi arasında sebep-sonuç ilişkisi olduğunu ortaya koymaktadır (Lindhe & ark., 1992; Lang & ark., 1993; Lang & ark., 1994).

Son yıllarda periodontal hastalıkların tedavi protokollerini değişim göstermektedir. Yeni tedaviler, yeni biyomateryaller ve karmaşık doku mühendisliği yaklaşımları periodontal hastlığın sebep olduğu yıkımı azaltmak için kullanılmak-

## KAYNAKLAR

1. Aaboe, M., Pinholt, E.M. & Hjorting-Hansen, E. (1994). Unicortical critical size defect of rabbit tibia is larger than 8 mm. *J Craniofac Surg*, 5(3), 201-203. Doi: 10.1097/00001665-199407000-00013
2. Albouy, J.P., Abrahamsson, I., Persson, L.G. & Berglundh T. (2008). Spontaneous progression of peri-implantitis at different types of implants. An experimental study in dogs. I: clinical and radiographic observations. *Clin Oral Implants Res*, 19, 997–1002. Doi:10.1111/j.1600-0501.2008.01589.x
3. Albouy, J.P., Abrahamsson, I., Persson, L.G. & Berglundh T. (2009). Spontaneous progression of ligatured induced peri-implantitis at implants with different surface characteristics. An experimental study in dogs II: histological observations. *Clin Oral Implants Res*, 20, 366–371. Doi:10.1111/j.1600-0501.2008.01645.x
4. Anthony, J., Waldner, C., Grier, C. & Laycock, A. R. (2010). A survey of equine oral pathology. *J Vet Dent*, 27(1), 12–15. Doi:10.1177/089875641002700102
5. Badr, N.A. & El Hadary, A.A. (2007). Hydroxyapatite-electroplated cp- titanium implant and its bone integration potentiality: an in vivo study. *Implant Dent*, 16: 297–308. Doi:10.1097/ID.0b013e31805d7dc4
6. Blomlof, L., Friskopp, J., Appelgren, R., Lindskog, S. & Hammarstrom, L. (1989). Influence of granulation tissue, dental calculus and contaminated root cementum on periodontal wound healing. An experimental study in monkeys. *J Clin Periodontol*, 16(1), 27-32. Doi:10.1111/j.1600-051X.1989.tb01608.x
7. Breivik, T., Opstad, P.K., Gjermo, P. & Thrane, P.S. (2000). Effects of hypothalamic-pituitary-adrenal axis reactivity on periodontal tissue destruction in rats. *Eur J Oral Sci*, 108(2), 115–122. Doi:10.1034/j.1600-0722.2000.00774.x
8. Burgos, P.M., Rasmusson, L., Meirelles, L. & Sennerby, L. (2008). Early bone tissue responses to turned and oxidized implants in the rabbit tibia. *Clin Implant Dent Relat Res*, 10: 181– 190. Doi:10.1111/j.1708-8208.2007.00074.x
9. Carcuac, O., Abrahamsson, I., Charalampakis, G. & Berglundh, T. (2015). The effect of the local use of chlorhexidine in surgical treatment of experimental peri-implantitis in dogs. *J Clin Periodontol*, 42(2), 196-203. Doi:10.1111/jcpe.12332
10. Carmagnola, D., Abati, S., Celestino, S., Chiapasco, M., Bosshardt, D. & Lang N.P. (2008). Oral implants placed in bone defects treated with Bio-Oss, Ostim-Paste or PerioGlas: an experimental study in the rabbit tibiae. *Clin Oral Implants Res*, 19: 1246–1253. Doi:10.1111/j.1600-0501.2008.01584.x
11. Carvalho, C.M., Carvalho, L.F., Costa, L.J., Sa, M.J., Figueiredo, C.R. & Azevedo, A.S. (2010). Titanium implants: a removal torque study in osteopenic rabbits. *Indian J Dent Res*, 21: 349–352. Doi:10.4103/0970-9290.70798
12. Chacon, G.E., Stine, E.A., Larsen, P.E., Beck, F.M. & McGlumphy EA. (2006). Effect of alendronate on endosseous implant integration: an in vivo study in rabbits. *J Oral Maxillofac Surg*, 64, 1005–1009. Doi:10.1016/j.joms.2006.01.007
13. Chen, Y.K. & Lin, L.M. (2010) DMBA-induced hamster buccal pouch carcinoma and VX2-induced rabbit cancer as a model for human oral carcinogenesis. *Expert Review of Anticancer Therapy*, 10(9), 1485–1496. Doi:10.1586/era.10.108
14. Craig, R.G., Kamer, A.R., Kallur, S.P., Inoue, M. & Tarnow, D.P. (2006). Effects of periodontal cell grafts and enamel matrix proteins on the implant- connective tissue interface: a pilot study in the minipig. *J Oral Implantol*, 32(5), 228-236. Doi: 10.1563/820.1

15. Demmer,R.T. & Papapanou,P.N. (2010) Epidemiologic patterns of chronic and aggressive periodontitis. *Periodontol 2000*, 53,28–44. Doi: 10.1111/j.1600-0757.2009.00326.x
16. Drury, G.I. & Yukna, R.A. (1991). Histologic evaluation of combining tetracycline and allogeneic freeze-dried bone on bone regeneration in experimental defects in baboons. *J Periodontol*, 62(11), 652-658. doi: 10.1902/jop.1991.62.11.652
17. Egelberg, J. (1965). Local effect of diet on plaque formation and development of gingivitis in dogs. I. effect of hard and soft diets. *Odontol Revy*, 16, 31–41.
18. England D. C., Winters, L. M. & Carpenter, L. E. (1954). The development of a breed of miniature swine; a preliminary report. *Growth*, 18(4), 207–214.
19. Evans, R. T., Klausen, B., Ramamurthy, N. S., Golub, L. M., Sfintescu, C. & Genco, R. J. (1992). Periodontopathic potential of two strains of Porphyromonas gingivalis in gnotobiotic rats. *Arch Oral Bio*, 37(10), 813–819. Doi:10.1016/0003-9969(92)90115-O
20. Gilmore, N.D. & Glickman, I. (1959). Some age changes in the periodontium of the albino mouse. *J Dent Res*, 38: 1195-1206. Doi:10.1177/00220345590380062001
21. Guessous, F., Huynh, C., N'Guyen, H., Godeau, G., Giroud, J.P., Meyer, J., Hornebeck, W. & Roch-Arveiller, M. (1994). An animal model for the assessment of gingival lesions. *J Pharmacol Toxicol Methods*, 32(3), 161-167.
22. Doi:10.1016/1056-8719(94)90070-1
23. Harper, D.S., Mann, P.H. & Regnier, S. (1990). Measurement of dietary and dentifrice effects upon calculus accumulation rates in the domestic ferret. *J Dent Res*, 69(2), 447-450. Doi:10.1177/00220345900690020501.
24. Johnson, M.W., Sullivan, S.M., Rohrer, M. & Collier, M. (1997). Regeneration of peri-implant infrabony defects using PerioGlas: a pilot study in rabbits. *Int J Oral Maxillofac Implants*, 12(6), 835-839.
25. Kantarcı, A., Hasturk, H. & Van Dyke, T.E. (2015). Animal models for periodontal regeneration and peri-implant responses. *Periodontology 2000*, 68(1), 66–82. Doi:10.1111/prd.12052
26. Kara, A., Akman, S., Ozkanlar, S., Tozoglu, U., Kalkan, Y., Canakci, C.F. & Tozoglu, S. (2013). Immunomodulatory and antioxidant effects of melatonin in experimental periodontitis in rats. *FreeRadic Biol Med*, 55, 21–26. Doi:10.1016/j.freeradbiomed.2012.11.002.
27. Karatzas, S., Zavras, A., Greenspan, D. & Amar, S. (1999). Histologic observations of periodontal wound healing after treatment with perioglas in nonhuman primates. *Int J Periodontics Rest Dent*, 19(5): 489- 499. Doi: 10.11607/prd.00.0340
28. Kostopoulos, L. & Karring, T. (2004). Susceptibility of GTR-regenerated periodontal attachment to ligature-induced periodontitis. *J Clin Periodontol*, 31(5), 336-340. Doi:10.1111/j.1600-051X.2004.00487.x
29. Kozlovsky, A., Tal, H., Laufer, B.Z., Leshem, R., Rohrer, M.D., Weinreb, M. & Artzi Z. (2007). Impact of implant overloading on the peri-implant bone in inflamed and non-inflamed peri- implant mucosa. *Clin Oral Implants Res*, 18, 601–610. Doi:10.1111/j.1600-0501.2007.01374.x
30. Lallam-Laroye, C., Escartin, Q., Zlowodzki, A.S., Barritault, D., Caruelle, J.P., Barroukh, B., Saffar, J.L. & Colombier M.L. (2006). Periodontitis Destructions Are Restored by Synthetic Glycosaminoglycan Mimetic. *J Biomed Mater Res A*, 79(3), 675–683. Doi:10.1002/jbm.a.30880

31. Lang, N.P., Bragger, U., Walther, D., Beamer, B. & Kornman, K.S. (1993). Ligature-induced peri-implant infection in cynomolgus monkeys. I. Clinical and radiographic findings. *Clin Oral Implants Res*, 4, 2–11. Doi:10.1034/j.1600-0501.1993.040101.x
32. Lang, N.P., Wetzel, A.C., Stich, H. & Caffesse RG. (1994). Histologic probe penetration in healthy and inflamed peri-implant tissues. *Clin Oral Implants Res*, 5, 191–201.
33. Doi:10.1034/j.1600-0501.1994.050401.x
34. Lang, N.P. & Berglundh, T. (2011). Periimplant diseases: where are we now?—Consensus of the Seventh European Workshop on Periodontology. *J Clin Periodontol*, 38(11), 178–181. Doi:10.1111/j.1600-051X.2010.01674.x
35. Lindhe, J., Hamp, S. & Löe, H. (1973) Experimental Periodontitis in the Beagle Dog. *J Periodontal Res*, 8(1):1–10. Doi:10.1111/j.1600-0765.1973.tb00735.x
36. Lindhe, J., Berglundh, T., Ericsson, I., Liljenberg, B. & Marinello C. (1992). Experimental breakdown of peri-implant and periodontal tissues. A study in the beagle dog. *Clin Oral Implants Res*, 1992, 3, 9–16. Doi:10.1034/j.1600-0501.1992.030102.x
37. Ling, L.J., Lai, Y.H., Hwang, H. & Chen, H. (1994). Response of regenerative tissues to plaque: a histological study in monkeys. *J Periodontol*, 65(8), 781-787. Doi:10.1902/jop.1994.65.8.781
38. Listgarten, M.A., Johnson, D., Nowotny, A., Tanner, A.C. & Socransky, S.S. (1978). Histopathology of Periodontal Disease in Gnotobiotic Rats Monoinfected with Eikenella Corrodens. *J Periodontal Res*, 13(2), 134–148. Doi:10.1111/j.1600-0765.1978.tb00162.x
39. Madden, T.E. & Caton, J.G. (1994). Animal models for periodontal disease. *Methods Enzymol*, 235, 106-119.
40. Mann, P.H., Harper, D.S. & Regnier, S. (1990). Reduction of calculus accumulation in domestic ferrets with two dentifrices containing pyrophosphate. *J Dent Res*, 69(2), 451-453. Doi: 10.1177/00220345900690020601
41. Martines, R.T., Sendyk, W.R., Gromatzky, A. & Cury PR. (2008). Sand- blasted/acid-etched vs smooth-surface implants: implant clinical reaction to experimentally induced peri-implantitis in Beagle dogs. *J Oral Implantol*, 34, 185–189. Doi:10.1563/0.880.1
42. Monje, A., Insua, A., Monje, F., Munoz, F., Salvi, G.E., Buser, D. & Chappuis V. (2018). Diagnostic accuracy of the implant stability quotient in monitoring progressive peri-implant bone loss: An experimental study in dogs. *Clin Oral Implant Res*, 29 (10), 1016-1024. Doi:10.1111/clr.13368.
43. Nakajima, K., Hamada, N., Takahashi, Y., Sasaguri, K., Tsukinoki, K., Umemoto, T. & Sato S. (2006). Restraint stress enhances alveolar bone loss in an experimental rat model. *J Per Res*, 41(6), 527–534. Doi:10.1111/j.1600-0765.2006.00901.x
44. Oskarsson, M., Otsuki, M., Welander, M. & Abrahamsson, I. (2018). Peri-implant tissue healing at implants with different designs and placement protocols: An experimental study in dogs. *Clin Oral Implant Res*, 29(8), 873-880. Doi:10.1111/clr.13339
45. Oz, H.S. & Puleo, D.A. (2011). Animal Models for Periodontal Disease. *J Biomed Biotechnol*, 2011, 754857. Doi: 10.1155/2011/754857.
46. Page, R.C. & Schroeder, H.E. (1982). *Periodontitis in Man and Other Animals. A Comparative Review*. S Karger Ag. University of Michigan. ISBN: 380552479X, 9783805524797.
47. Pimental, S.P., Barrella, G.E., Casarin, R.C., Cirano, F.R., Casati, M.Z., Foglio, M.A., Figueira, G.M. & Ribeiro, F.V. (2012) Protective effect of topical Cordia verbenacea in a rat periodontitis model: immune-inflammatory, antibacterial and morphometric assays. *BMC Complement Altern Med*, 12, 224. Doi: 10.1186/1472-6882-12-224.

48. Polejaeva I. A., Chen, S. H., Vaught, T. D., Page, R.L., Mullins, J., Ball, S., Dai, Y., Boone, J., Walker, S., Ayares, D.L., Colman, A. & Campbell, K.E. (2000). Cloned pigs produced by nuclear transfer from adult somatic cells. *Nature*, 407(6800), 86–90. Doi:10.1038/35024082
49. Roeterink, C. H., Van Steenbergen, T. J. M., De Jong, W. F. B. & De Graaff, J. (1984). Histopathological effects in the palate of the rat induced by injection with different black-pigmented *Bacteroides* strains. *J Per Res*, 19(3), 292–302.  
50. Doi:10.1111/j.1600-0765.1984.tb00820.x
51. Romanos, G.E., Henze, M., Banihashemi, S., Parsanejad, H.R., Winckler, J. & Nentwig, G.H. (2004). Removal of epithelium in periodontal pockets following diode (980 nm) laser application in the animal model: an in vitro study. *Photomed Laser Surg*, 22(3), 177-183.  
52. Doi:10.1089/1549541041438597
53. Selvig, K.A. (1994). Discussion: animal models in reconstructive therapy. *J Periodontol*, 65(12), 1169-1172. Doi:10.1902/jop.1994.65.12.1169
54. Schliephake, H. & Aleyt, J. (1998). Mandibular onlay grafting using prefabricated bone grafts with primary implant placement: an experimental study in minipigs. *Int J Oral Maxillofac Implants*, 13(3), 384- 393.
55. Schmitt, J.M., Buck, D.C., Joh S.P., Lynch S.E. & Hollinger J.O. (1997). Comparison of porous bone mineral and biologically active glass in critical sized defects. *J Periodontol*, 68(11), 1043-1053. Doi: 10.1902/jop.1997.68.11.1043
56. Schou, S., Holmstrup, P. & Kornman, K.S. (1993). Non-Human Primates Used in Studies of Periodontal Disease Pathogenesis: A Review of the Literature. *J Periodontol*, 64 (6), 497–508. Doi: 10.1902/jop.1993.64.6.497
57. Schou, S., Holmstrup, P., Stoltze, K., Hjorting-Hansen, E., Fiehn, N.E. & Skovgaard, L.T. (2002). Probing around implants and teeth with healthy or inflamed peri-implant mucosa/gingiva. A histologic comparison in cynomolgus monkeys (*Macaca fascicularis*). *Clin Oral Implants Res*, 13, 113–126.
58. Schou, S., Holmstrup, P., Skovgaard, L.T., Stoltze, K., Hjorting-Hansen, E. & Gunderson, H.J. (2003). Autogenous bone graft and ePTFE membrane in the treatment of peri-implantitis. II. stereologic and histologic observations in cynomolgus monkeys. *Clin Oral Implants Res*, 14(4), 404-411.
59. Schwarz, F., Herten, M., Sager, M., Bieling, K., Sculean, A. & Becker J. (2007). Comparison of naturally occurring and ligature- induced peri-implantitis bone defects in humans and dogs. *Clin Oral Implants Res*, 18, 161–170. Doi:10.1111/j.1600-0501.2007.01482.x
60. Schwarz, F., Igglaut, G. & Becker, J. (2012). Quality assessment of reporting of animal studies on pathogenesis and treatment of peri-implant mucositis and peri-implantitis. A systematic review using the ARRIVE guidelines. *J Clin Periodontol*, 39(12): 63–72.
61. Sculean, A., Karring, T., Theilade, J. & Lioubavina, N. (1997). The regenerative potential of oxytalan fibers. an experimental study in the monkey. *J Clin Periodontol*, 24(12): 932-936. Doi:10.1111/j.1600-051X.1997.tb01214.x
62. Sculean, A., Donos, N., Brecx, M., Karring, T. & Reich, E. (2000a). Healing of fenestration-type defects following treatment with guided tissue regeneration or enamel matrix proteins. an experimental study in monkeys. *Clin Oral Investig*, 4(1), 50-56. Doi:10.1007/s007840050113

63. Sculean, A., Donos, N., Brecx, M., Reich, E. & Karring, T. (2000b). Treatment of intrabony defects with guided tissue regeneration and enamel-matrix-proteins. an experimental study in monkeys. *J Clin Periodontol*, 27(7), 466-472.  
64. Doi: 10.1034/j.1600-051x.2000.027007466.x
65. Sorensen, W.P., Löe, H. & Ramfjord, S.P. (1980). Periodontal disease in the Beagle dog. A cross sectional clinical study. *J Periodontal Res*, 15(4), 380-389. Doi:10.1111/j.1600-0765.1980.tb00295.x
66. Stenport, V.F. & Johansson, C.B. (2008). Evaluations of bone tissue integration to pure and alloyed titanium implants. *Clin Implant Dent Relat Res*, 10, 191–199. Doi:10.1111/j.1708-8208.2007.00077.x
67. Struillou, X., Boutigny, H., Soueidan, A. & Layrolle, P. (2010). Experimental Animal Models in Periodontology: A Review. *Open Dent J*, 4, 37–47.  
68. Doi:10.2174/1874210601004010037
69. Takahashi, D., Odajima, T., Morita, M., Kawanami, M. & Kato, H. (2005). Formation and Resolution of Ankylosis under Application of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) to Class III Furcation Defects in Cats. *J Periodontal Res*, 40(4), 299–305. Doi:10.1111/j.1600-0765.2005.00794.x
70. Tamaki, N., Orihuela-Campos, R.C., Inagaki, Y., Fukui, M., Nagata, T. & Ito, H. (2014). Resveratrol improves oxidative stress and prevents the progression of periodontitis via the activation of the Sirt1/AMPK and the Nrf2/antioxidant defense pathways in a rat periodontitis model. *Free Radical Biology and Medicine*, 75, 222–229.  
71. Doi:10.1016/j.freeradbiomed.2014.07.034
72. Taubman, M. A., Yoshie, H., Wetherell Jr., J. R., Ebersole, J. L. & Smith, D. J. (1983). Immune response and periodontal bone loss in germfree rats immunized and infected with *Actinobacillus actinomycetemcomitans*. *J Per Res*, 18 (4), 393–401. Doi:10.1111/j.1600-0765.1983.tb00375.x
73. Taubman, M. A., Stoufi, E. D., Seymour, G. J., Smith, D. J. & Ebersole, J. L. (1988). Immunoregulatory aspects of periodontal disease. *Adv Dent Res*, 2(2), 328– 333.  
74. Doi:10.1177/08959374880020022201
75. Tobita, M., Uysal, A.C., Ogawa, R., Hyakusoku, H. & Mizuno, H. (2008). Periodontal tissue regeneration with adipose-derived stem cells. *Tissue Eng Part A*, 14(6), 945–953.  
76. Doi:10.1089/ten.tea.2007.0048
77. Tomina, D., Roman, A., Condor, D., Dinu, C. & Petruțiu, S.A. (2017). Experimental rat model – is it still used? – review article. *HVM Bioflux*, 9(4), 130-136.
78. Tsetsenekou, E., Papadopoulos, T., Kalyvas, D., Papaioannou, N., Tangl, S. & Watzek, G. (2012). The influence of alendronate on osseointegration of nanotreated dental implants in New Zealand rabbits. *Clin Oral Implants Res*, 23, 659– 666. Doi:10.1111/j.1600-0501.2011.02189.x
79. Wang, S., Liu, Y., Fang, D. & Shi, S. (2007). The miniature pig: a useful large animal model for dental and orofacial research. *Oral Dis*, 13(6), 530–537. Doi:10.1111/j.1601-0825.2006.01337.x
80. Weinberg, M.A. & Bral, M. (1999). Laboratory Animal Models in Periodontology. *J Clin Periodontol*, 26(6), 335–340.  
81. Doi:10.1034/j.1600-051X.1999.260601.x
82. Weishan, L., Dechao, L. & Rongrong, Q. (2016). Effects of Porphyromonas gingivalis on interleukin-33 expression in rabbit vascular endothelium tissues. *Hua Xi Kou Qiang Yi Xue Za Zhi*, 34(4), 354-357. Doi:10.7518/hxkq.2016.04.007

83. Yamashita, K., Eastcott, J. W., Taubman, M. A., Smith, D. J. & Cox, D. S. (1991). Effect of adoptive transfer of cloned actinobacillus actinomycetemcomitans-specific T helper cells on periodontal disease. *Infection and Immunity*, 59(4), 1529–1534.
84. Yang, G.L., He, F.M., Yang, X.F., Wang, X.X. & Zhao, S.F. (2008). Bone responses to titanium implants surface-roughened by sandblasted and double etched treatments in a rabbit model. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 106, 516–524. Doi:10.1016/j.tripleo.2008.03.017
85. Zhou, T., Chen, D., Li, Q., Sun, X., Song, Y. & Wang, C. (2013) Curcumin inhibits inflammatory response and bone loss during experimental periodontitis in rats. *Acta Odontol Scand*, 71(2):349-356.
86. Doi:10.3109/00016357.2012.682092
87. Zitzmann, N.U., Abrahamsson, I., Berglundh, T. & Lindhe J. (2002). Soft tissue reactions to plaque formation at implant abutments with different surface topography. An experimental study in dogs. *J Clin Periodontol*, 29, 456–461. Doi:10.1034/j.1600-051X.2002.290511.x
88. Zitzmann, N.U., Berglundh, T., Ericsson, I. & Lindhe J. (2004). Spontaneous progression of experimentally induced periimplantitis. *J Clin Periodontol*, 31, 845–849. Doi:10.1111/j.1600-051X.2004.00567.x