

# BÖLÜM 47

## ORTOPEDİK CERRAHİDE DENEYSSEL HAYVAN MODELLERİ

*Op. Dr. İbrahim KAYA<sup>1</sup>  
Araş. Gör. Dr. Furkan ARAL<sup>2</sup>  
Prof. Dr. Hamza ÖZER<sup>3</sup>*

### Giriş

Ortopedi ve Travmatolojide klinik çalışmaların hasta sayısının yetersiz kalabilmesi, uygun kontrol grubunun olmaması, etik problemler, hasta popülasyonun çok değişikene sahip olması gibi bazı sorunları vardır ve bu sorunların üstesinden gelmek için araştırmacılar hayvan deneylerine yönelmektedir (1). Hayvan modelleri, kas-iskelet biyolojisinin çeşitli yönlerini incelemek ve yeni tedaviler geliştirmek ve test etmek için ortopedik araştırmalarda yaygın olarak kullanılmaktadır. Bu modeller fareleri, ratları, tavşanları, domuzları, köpekleri, koyunları ve insan olmayan primatları içerebilir. Hayvan deneylerinin de bazı sorunları vardır: Etik problemler, kemik iyileşmesinin evrimde gelişmişlik ve yaş ile ters orantılı olması, ilaç dozu ayarlanmasında problem yaşanması gibi sorunlar bulunmaktadır (1). Hayvan çalışmasında da uyulması gereken temel ilkeler vardır. Üç R ilkesi 1960'ların başında iki İngiliz biyolog Russel ve Burch tarafından “ The Principle of Humane Experimental Technique “ adlı kitaplarında ortaya atılmıştır. 3R: Replacement (Yerine koyma), Reduction (Azaltma), Refinement (İyileştirme) anlamına gelmektedir (2). Yerine koyma, hayvanların kullanılmasını

<sup>1</sup> Op.Dr., Dr.Abdurrahman Yurtaslan Onkoloji Eğitim ve Araştırma Hastanesi ortopedi ve travmatoloji anabilimdalı eposta:drkayaibrahim@gmail.com  
ORCID iD: 0000-0001-8205-6515

<sup>2</sup> Araş. Gör., Gazi Üniversitesi Tıp Fakültesi, Ortopedi ve Travmatoloji AD. E-posta: drfurkanaral@gmail.com,  
ORCID iD: 0000-0003-4879-6530

<sup>3</sup> Prof. Dr., Gazi Üniversitesi Tıp Fakültesi, Ortopedi ve Travmatoloji AD. E-posta: hamzaozer@gazi.edu.tr,  
ORCID iD: 0000-0001-5107-637X

## KAYNAKLAR

1. Roach HI, Shearer JR, Archer C. The choice of an experimental model. A guide for research workers. *J Bone Joint Surg Br.* 1989;71(4):549–53.
2. Schuppli CA, Fraser D. The interpretation and application of the three Rs by animal ethics committee members. *Altern Lab Anim* [Internet]. 2005 [cited 2023 Jan 15];33(5):487–500. Available from: <https://pubmed.ncbi.nlm.nih.gov/16268760/>
3. DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 22 September 2010 on the protection of animals used for scientific purposes (Text with EEA relevance).
4. Andersen ML, Winter LMF. Animal models in biological and biomedical research - experimental and ethical concerns. *An Acad Bras Cienc* [Internet]. 2019 [cited 2023 Jan 15];91(suppl 1). Available from: <https://pubmed.ncbi.nlm.nih.gov/28876358/>
5. Yusuf ERGÜN D. Hayvan Deneylerinde Etik. *Arşiv Kaynak Tarama Derg* [Internet]. 2010 Dec 1 [cited 2023 Jan 15];19(4):220–35. Available from: <https://dergipark.org.tr/tr/pub/aktd/issue/2218/29422>
6. Sommer NG, Hahn D, Okutan B, Marek R, Weinberg A-M, Sommer NG, et al. Animal Models in Orthopedic Research: The Proper Animal Model to Answer Fundamental Questions on Bone Healing Depending on Pathology and Implant Material. *Anim Model Med Biol* [Internet]. 2019 Sep 16 [cited 2023 Jan 15]; Available from: <https://www.intechopen.com/state.item.id>
7. Turner RT, Turner RT, Spelsberg TC, Riggs BL. Skeletal effects of estrogen. *Endocr Rev* [Internet]. 1994 [cited 2023 Jan 15];15(3):275–300. Available from: <https://pubmed.ncbi.nlm.nih.gov/8076582/>
8. Gallagher A, Chambers TJ, Tobias JH. The estrogen antagonist ICI 182,780 reduces cancellous bone volume in female rats. *Endocrinology* [Internet]. 1993 [cited 2023 Jan 15];133(6):2787–91. Available from: <https://pubmed.ncbi.nlm.nih.gov/8243306/>
9. Li XJ, Jee WSS, Chow S -Y, Woodbury DM. Adaptation of cancellous bone to aging and immobilization in the rat: a single photon absorptiometry and histomorphometry study. *Anat Rec* [Internet]. 1990 [cited 2023 Jan 15];227(1):12–24. Available from: <https://pubmed.ncbi.nlm.nih.gov/2195916/>
10. Nunamaker DM. Experimental models of fracture repair. *Clin Orthop Relat Res* [Internet]. 1998 [cited 2023 Jan 15];355(355 Suppl). Available from: <https://pubmed.ncbi.nlm.nih.gov/9917626/>
11. Oheim R, Beil FT, Köhne T, Wehner T, Barvencik F, Ignatius A, et al. Sheep model for osteoporosis: sustainability and biomechanical relevance of low turnover osteoporosis induced by hypothalamic-pituitary disconnection. *J Orthop Res* [Internet]. 2013 Jul [cited 2023 Jan 15];31(7):1067–74. Available from: <https://pubmed.ncbi.nlm.nih.gov/23440966/>
12. Lampropoulou-Adamidou K, Lelovas P, Eleftherios •, Karadimas V, Liakou C, Triantafillopoulos IK, et al. Useful animal models for the research of osteoarthritis.
13. Hunter CB. | 485 Post-traumatic osteoarthritis: from mouse models to clinical trials. *Nat Rev | Rheumatol* [Internet]. 2013 [cited 2023 Jan 15];9:485–97. Available from: [www.nature.com/nrrheum](http://www.nature.com/nrrheum)
14. Kyostio-Moore S, Nambiar B, Hutto E, Ewing PJ, Piraino S, Berthelette P, et al. STR/ort Mice, a Model for Spontaneous Osteoarthritis, Exhibit Elevated Levels of Both Local and Systemic Inflammatory Markers. *Comp Med* [Internet]. 2011 Aug [cited 2023 Jan 15];61(4):346. Available from: [/pmc/articles/PMC3155401/](https://pubmed.ncbi.nlm.nih.gov/2195916/)

15. Clements KM, Price JS, Chambers MG, Visco DM, Poole AR, Mason RM. Gene Deletion of Either Interleukin-1, Interleukin-1-Converting Enzyme, Inducible Nitric Oxide Synthase, or Stromelysin 1 Accelerates the Development of Knee Osteoarthritis in Mice After Surgical Transection of the Medial Collateral Ligament and Partial Medial Meniscectomy. *ARTHRITIS Rheum* [Internet]. 2003 [cited 2023 Jan 15];48(12):3452–63. Available from: <https://onlinelibrary.wiley.com/doi/10.1002/art.11355>
16. Janusz MJ, Little CB, King LE, Hookfin EB, Brown KK, Heitmeyer SA, et al. Detection of aggrecanase- and MMP-generated catabolic neopeptides in the rat iodoacetate model of cartilage degeneration. *Osteoarthr Cartil*. 2004 Sep;12(9):720–8.
17. Ghosh P, Burkhardt D, Read R, Bellenger C. Recent advances in animal models for evaluating chondroprotective drugs. *J Rheumatol Suppl* [Internet]. 1991 Feb 1 [cited 2023 Jan 15];27(SUPPL. 27):143–6. Available from: <https://europepmc.org/article/med/2027116>
18. Pond MJ, Nuki G. Experimentally-induced osteoarthritis in the dog. *Ann Rheum Dis* [Internet]. 1973 [cited 2023 Jan 15];32(4):387. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1006123/>
19. Bone and Osteoarthritis. *Bone Osteoarthr*. 2007;
20. Hulth A, Lindberg L, Telhag H. Experimental Osteoarthritis in Rabbits: Preliminary report. *Acta Orthop Scand* [Internet]. 1970 [cited 2023 Jan 15];41(5):522–30. Available from: <https://www.tandfonline.com/action/journalInformation?journalCode=iort20>
21. Slätis P, Rokkanen P. *Acta Orthopaedica Scandinavica* Regeneration of the Femoral Head After Subcapital Osteotomy: An Experimental Study on Young Rabbits. 2009 [cited 2023 Jan 15]; Available from: <https://www.tandfonline.com/action/journalInformation?journalCode=iort20>
22. Sabouni K, Ozturk Y, Kacar | Erkan, Hasan |, Mutlu S, Solakoglu S, et al. Assessment of bone healing using (Ti,Mg)N thin film coated plates and screws: Rabbit femur model. 2020 [cited 2023 Jan 15]; Available from: <https://onlinelibrary.wiley.com/doi/10.1002/jbm.b.34694>
23. Effect of autocontrol micromotion intramedullary interlocking nail on fracture healing: an experimental study | *Chinese Journal of Traumatology* [Internet]. [cited 2023 Jan 15]. Available from: <https://mednexus.org/doi/abs/10.5555/cjt.1008-1275.09.03.p152.01>
24. Sigurdson U, Reikeras O, Erik Utvag S. Conversion of External Fixation to Definitive Intramedullary Nailing in Experimental Tibial Fractures. *J Investig Surg* [Internet]. 2010 [cited 2023 Jan 15];23(3):142–8. Available from: <https://www.tandfonline.com/action/journalInformation?journalCode=iivs20>
25. Bonnarens F, Einhorn TA. Production of a standard closed fracture in laboratory animal bone. *J Orthop Res* [Internet]. 1984 [cited 2023 Jan 15];2(1):97–101. Available from: <https://pubmed.ncbi.nlm.nih.gov/6491805/>
26. Doetsch AM, Faber J, Lynnerup N, Waˆtjen IW, Bliddal H, Danneskiold-Samsøe B. Clinical Investigations The Effect of Calcium and Vitamin D 3 Supplementation on the Healing of the Proximal Humerus Fracture: A Randomized Placebo-Controlled Study. *Calcif Tissue Int*. 2004;75:183–8.
27. El-Rashidy AA, Roether JA, Harhaus L, Kneser U, Boccaccini AR. Regenerating bone with bioactive glass scaffolds: A review of in vivo studies in bone defect models. *Acta Biomater*. 2017 Oct 15;62:1–28.

28. Mienaltowski MJ, Birk DE, Mienaltowski MJ, Birk DE. 3 Mouse Models in Tendon and Ligament Research. *Adv Exp Med Biol.* 802.
29. Omoto T, Yimiti D, Sanada Y, Toriyama M, Ding C, Hayashi Y, et al. Tendon-Specific Dicer Deficient Mice Exhibit Hypoplastic Tendon Through the Downregulation of Tendon-Related Genes and MicroRNAs. *Front Cell Dev Biol* [Internet]. 2022 Jun 14 [cited 2023 Jan 15];10. Available from: <https://pubmed.ncbi.nlm.nih.gov/35784484/>
30. Chen W, Sun Y, Gu X, Cai J, Liu X, Zhang X, et al. Conditioned medium of human bone marrow-derived stem cells promotes tendon-bone healing of the rotator cuff in a rat model. *Biomaterials.* 2021 Apr 1;271:120714.
31. El-Habta R, Chen J, Pingel J, Backman LJ. Tendinosis-like changes in denervated rat Achilles tendon. *BMC Musculoskelet Disord* [Internet]. 2018 Nov 30 [cited 2023 Jan 15];19(1):1–9. Available from: <https://bmcmusculoskeletdisord.biomedcentral.com/articles/10.1186/s12891-018-2353-7>
32. Iwanaga Y, Morizaki Y, Uehara K, Tanaka S, Sakai T, Saito T. Robust Suture Combination for Rat Flexor Tendon Repair Model. *J Hand Surg Glob Online.* 2020 Nov 1;2(6):354–8.
33. Tansley S, Uttam S, Ureña Guzmán A, Yaqubi M, Pacis A, Parisien M, et al. Single-cell RNA sequencing reveals time- and sex-specific responses of mouse spinal cord microglia to peripheral nerve injury and links ApoE to chronic pain. [cited 2023 Jan 15]; Available from: <https://doi.org/10.1038/s41467-022-28473-8>
34. Roux KM, Cobb LH, Seitz MA, Priddy LB. Innovations in osteomyelitis research: A review of animal models. *Anim Model Exp Med* [Internet]. 2021 Mar 1 [cited 2023 Jan 15];4(1):59–70. Available from: <https://pubmed.ncbi.nlm.nih.gov/33738438/>
35. Farelerde oluşturulan osteomyelit modellerinde yabancı cisim uygulanmasının lokal ve sistemik infeksiyon bulguları üzerine etkileri [Internet]. [cited 2023 Jan 15]. Available from: <https://www.acarindex.com/artroplasti-artroskopik-cerrahi-yeni-adi-eklem-hastaliklari-ve-cerrahisi/farelerde-olusturulan-osteomyelit-modellerinde-yabanci-cisim-uygulanmasinin-lokal-ve-sistemik-infeksiyon-bulgulari-uzerine-etkileri-857821>
36. Jin T, Mohammad M, Hu Z, Fei Y, Moore ERB, Pullerits R, et al. A novel mouse model for septic arthritis induced by *Pseudomonas aeruginosa*. *Sci Reports* 2019 91 [Internet]. 2019 Nov 14 [cited 2023 Jan 15];9(1):1–10. Available from: <https://www.nature.com/articles/s41598-019-53434-5>
37. Bremell T, Lange S, Yacoub A, Ryden C, Tarkowski A. Experimental *Staphylococcus aureus* arthritis in mice. *Infect Immun* [Internet]. 1991 [cited 2023 Jan 15];59(8):2615–23. Available from: <https://pubmed.ncbi.nlm.nih.gov/1855981/>
38. Grün NG, Holweg P, Tangl S, Eichler J, Berger L, van den Beucken JJJP, et al. Comparison of a resorbable magnesium implant in small and large growing-animal models. *Acta Biomater* [Internet]. 2018 Sep 15 [cited 2023 Jan 15];78:378–86. Available from: <https://pubmed.ncbi.nlm.nih.gov/30059798/>
39. Shen XZ, Qu F, Li CB, Qi W, Lu X, Li HL, et al. Comparison between a novel human cortical bone screw and bioabsorbable interference screw for graft fixation of ACL reconstruction. *Eur Rev Med Pharmacol Sci.* 2021;22(1):111–8.
40. Allen MJ, Turner AS, Sairyo K, Ferrara L. Basic Science Symposium III: Animal Models for Orthopaedic Implant Evaluation. *SAS J* [Internet]. 2008 [cited 2023 Jan 15];2(4):195–200. Available from: <https://pubmed.ncbi.nlm.nih.gov/25802622/>