

## Bölüm 7

# VERTEBRA METASTAZLARI VE TEDAVİDE STEREOTAKTİK RADYOCERRAHİNİN YERİ

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### GİRİŞ

Vertebra metastazı (VM) kanser hastalarında en sık görülen metastaz şekli olup otopsi çalışmalarında kanser hastalarının %70'e yakınında tespit edildiği bildirilmektedir [1-3]. Tedavi edilmemesi durumunda aksiyel ağrıya, mekanik stabilitenin bozulmasına, vertebrada yükseklik kaybı ve kırıklara, ilerleyen süreçte ise omurilik basısı ve hasarına bağlı nörolojik şikâyetlere sebep olabilir. Sistemik kemoterapi ilaçlarındaki gelişmeler, immünoterapi ve hedefe yönelik yeni ajanların metastatik kanserli hastaların sağ kalım sürelerini uzatmasına bağlı olarak lokal hastalık ve ağrı kontrolü daha önemli hale gelmiştir [4-6].

Konvansiyonel radyoterapi (KRT) teknikleri, VM'lerin palyatif amaçlı tedavisinde en sık kullanılan radyoterapi tekniği olmasına karşılık omuriliğin tolerans sınırları altında kalırken hedef vertebrada yüksek radyoterapi dozlarına çıkılmasını mümkün kılmamakta ve yeterince uzun süren ağrı ve hastalık kontrolü sağlanamamaktadır. Son 20 yılda radyoterapi cihazlarında ve tedavi planlama yazılımlarındaki yenilikler, görüntü kılavuzluğunda radyoterapinin uygulanabilmesi, radyoterapi cihazlarına monte edilebilen robotik cihazların geliştirilmesi ve tama yakın hasta hareketsizliği sağlayan ekipmanların kullanılmasıyla VM tedavisinde stereotaktik radyocerrahi (SRC) uygun hastalarda güncel tedavi yaklaşımlarından biri haline gelmiştir [3, 7, 8].

### VERTEBRA METASTAZLARININ PATOFİZYOLOJİSİ

Vertebra metastazı kanser hücresinin kan, direkt invazyon veya lenfatik yayılım yollarından biriyle vertebraya ulaşması sonrasında gerçekleşebilse de en sık vertebra çevresindeki Batson venöz pleksusu aracılığıyla olduğu bilinmektedir [9]. Kan dolaşımına karışan kanserli hücrelerin yalnızca %0,02'sinin klinik olarak anlamlı olabilecek metastaz oluşturabildikleri tahmin edilmektedir [10].

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Sonuç olarak, SRC VM tedavisinde etkin ve uygun hastalar seçildiğinde yan etki profili düşük bir tedavi yöntemidir. En sık yan etkisi vertebrada kompresyon fraktürü gelişimi olup başlangıçta vertebrada yükseklik kaybı olan hastalarda öncelikli tedavi yöntemi olarak tercih edilmemeli, en azından bu tip hastalarda fraksiyone SRC ya da öncesinde lüzumu halinde stabilizasyon cerrahisi uygulanmalıdır. Konvansiyonel radyoterapi tekniklerinin aksine 1-5 günde tamamlanan ve sadece ilgili metastatik vertebrayı hedefleyen SRC ile hem gereksiz kemik iliği toksisitesinin önüne geçilmiş hem de sistemik tedavilerin ara verilmeden devam edilmesi sağlanmış olur.

### **KAYNAKÇA**

1. Cole JS, Patchell RA. Metastatic epidural spinal cord compression. *Lancet Neurol* 2008; 7: 459-466.
2. Galasko CS. Skeletal metastases. *Clin Orthop Relat Res* 1986; 18-30.
3. Faruqi S, Tseng CL, Whyne C et al. Vertebral Compression Fracture After Spine Stereotactic Body Radiation Therapy: A Review of the Pathophysiology and Risk Factors. *Neurosurgery* 2018; 83: 314-322.
4. De Angelis R, Sant M, Coleman MP et al. Cancer survival in Europe 1999-2007 by country and age: results of EURO CARE--5-a population-based study. *Lancet Oncol* 2014; 15: 23-34.
5. Chen W, Zheng R, Baade PD et al. Cancer statistics in China, 2015. *CA Cancer J Clin* 2016; 66: 115-132.
6. Marshall DC, Webb TE, Hall RA et al. Trends in UK regional cancer mortality 1991-2007. *Br J Cancer* 2016; 114: 340-347.
7. Foote M, Letourneau D, Hyde D et al. Technique for stereotactic body radiotherapy for spinal metastases. *J Clin Neurosci* 2011; 18: 276-279.
8. Hyde D, Lochray F, Korol R et al. Spine stereotactic body radiotherapy utilizing cone-beam CT image-guidance with a robotic couch: intrafraction motion analysis accounting for all six degrees of freedom. *Int J Radiat Oncol Biol Phys* 2012; 82: e555-562.
9. Nathoo N, Caris EC, Wiener JA, Mendel E. History of the vertebral venous plexus and the significant contributions of Breschet and Batson. *Neurosurgery* 2011; 69: 1007-1014; discussion 1014.
10. Luzzi KJ, MacDonald IC, Schmidt EE et al. Multistep nature of metastatic inefficiency: dormancy of solitary cells after successful extravasation and limited survival of early micrometastases. *Am J Pathol* 1998; 153: 865-873.
11. Vlassov AV, Magdaleno S, Setterquist R, Conrad R. Exosomes: current knowledge of their composition, biological functions, and diagnostic and therapeutic potentials. *Biochim Biophys Acta* 2012; 1820: 940-948.
12. Hoshino A, Costa-Silva B, Shen TL et al. Tumour exosome integrins determine organotropic metastasis. *Nature* 2015; 527: 329-335.
13. Clezardin P. Pathophysiology of bone metastases from solid malignancies. *Joint Bone Spine* 2017; 84: 677-684.
14. Sun YX, Schneider A, Jung Y et al. Skeletal localization and neutralization of the SDF-1(CXCL12)/CXCR4 axis blocks prostate cancer metastasis and growth in osseous sites in vivo. *J Bone Miner Res* 2005; 20: 318-329.

15. Weillbaecher KN, Guise TA, McCauley LK. Cancer to bone: a fatal attraction. *Nat Rev Cancer* 2011; 11: 411-425.
16. Lacey DL, Boyle WJ, Simonet WS et al. Bench to bedside: elucidation of the OPG-RANK-RANKL pathway and the development of denosumab. *Nat Rev Drug Discov* 2012; 11: 401-419.
17. Logothetis CJ, Lin SH. Osteoblasts in prostate cancer metastasis to bone. *Nat Rev Cancer* 2005; 5: 21-28.
18. Cox BW, Spratt DE, Lovelock M et al. International Spine Radiosurgery Consortium consensus guidelines for target volume definition in spinal stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys* 2012; 83: e597-605.
19. Brown JM, Carlson DJ, Brenner DJ. The tumor radiobiology of SRS and SBRT: are more than the 5 Rs involved? *Int J Radiat Oncol Biol Phys* 2014; 88: 254-262.
20. Dewan MZ, Galloway AE, Kawashima N et al. Fractionated but not single-dose radiotherapy induces an immune-mediated abscopal effect when combined with anti-CTLA-4 antibody. *Clin Cancer Res* 2009; 15: 5379-5388.
21. Park HJ, Griffin RJ, Hui S et al. Radiation-induced vascular damage in tumors: implications of vascular damage in ablative hypofractionated radiotherapy (SBRT and SRS). *Radiat Res* 2012; 177: 311-327.
22. Tseng CL, Eppinga W, Charest-Morin R et al. Spine Stereotactic Body Radiotherapy: Indications, Outcomes, and Points of Caution. *Global Spine J* 2017; 7: 179-197.
23. Huo M, Sahgal A, Pryor D et al. Stereotactic spine radiosurgery: Review of safety and efficacy with respect to dose and fractionation. *Surg Neurol Int* 2017; 8: 30.
24. Jabbari S, Gerszten PC, Ruschin M et al. Stereotactic Body Radiotherapy for Spinal Metastases: Practice Guidelines, Outcomes, and Risks. *Cancer J* 2016; 22: 280-289.
25. Amdur RJ, Bennett J, Olivier K et al. A prospective, phase II study demonstrating the potential value and limitation of radiosurgery for spine metastases. *Am J Clin Oncol* 2009; 32: 515-520.
26. Garg AK, Shiu AS, Yang J et al. Phase 1/2 trial of single-session stereotactic body radiotherapy for previously unirradiated spinal metastases. *Cancer* 2012; 118: 5069-5077.
27. Wang L, Xing L, Le Q. SU-E-T-492: The Dosimetric and Clinical Impact of the Metallic Dental Implants on Radiation Dose Distributions in IMRT Head and Neck Cancer Patients. *Med Phys* 2012; 39: 3818.
28. Campos S, Presutti R, Zhang L et al. Elderly patients with painful bone metastases should be offered palliative radiotherapy. *Int J Radiat Oncol Biol Phys* 2010; 76: 1500-1506.
29. Chow E, Harris K, Fan G et al. Palliative radiotherapy trials for bone metastases: a systematic review. *J Clin Oncol* 2007; 25: 1423-1436.
30. Chow E, Zeng L, Salvo N et al. Update on the systematic review of palliative radiotherapy trials for bone metastases. *Clin Oncol (R Coll Radiol)* 2012; 24: 112-124.
31. Gerszten PC, Burton SA, Ozhasoglu C, Welch WC. Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine (Phila Pa 1976)* 2007; 32: 193-199.
32. Ryu S, Jin R, Jin JY et al. Pain control by image-guided radiosurgery for solitary spinal metastasis. *J Pain Symptom Manage* 2008; 35: 292-298.
33. Nguyen QN, Shiu AS, Rhines LD et al. Management of spinal metastases from renal cell carcinoma using stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys* 2010; 76: 1185-1192.

34. Hall WA, Stapleford LJ, Hadjipanayis CG et al. Stereotactic body radiosurgery for spinal metastatic disease: an evidence-based review. *Int J Surg Oncol* 2011; 2011: 979214.
35. Patchell RA, Tibbs PA, Regine WF et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet* 2005; 366: 643-648.
36. Klekamp J, Samii H. Surgical results for spinal metastases. *Acta Neurochir (Wien)* 1998; 140: 957-967.
37. Al-Omair A, Masucci L, Masson-Cote L et al. Surgical resection of epidural disease improves local control following postoperative spine stereotactic body radiotherapy. *Neuro Oncol* 2013; 15: 1413-1419.
38. Hashmi A, Guckenberger M, Kersh R et al. Re-irradiation stereotactic body radiotherapy for spinal metastases: a multi-institutional outcome analysis. *J Neurosurg Spine* 2016; 25: 646-653.
39. Jain AK, Yamada YJ. The role of stereotactic body radiotherapy and stereotactic radiosurgery in the re-irradiation of metastatic spinal tumors. *Expert Rev Anticancer Ther* 2014; 14: 1141-1152.
40. Thibault I, Al-Omair A, Masucci GL et al. Spine stereotactic body radiotherapy for renal cell cancer spinal metastases: analysis of outcomes and risk of vertebral compression fracture. *J Neurosurg Spine* 2014; 21: 711-718.
41. Chiang A, Zeng L, Zhang L et al. Pain flare is a common adverse event in steroid-naïve patients after spine stereotactic body radiation therapy: a prospective clinical trial. *Int J Radiat Oncol Biol Phys* 2013; 86: 638-642.
42. Pan HY, Allen PK, Wang XS et al. Incidence and predictive factors of pain flare after spine stereotactic body radiation therapy: secondary analysis of phase 1/2 trials. *Int J Radiat Oncol Biol Phys* 2014; 90: 870-876.
43. Sahgal A, Weinberg V, Ma L et al. Probabilities of radiation myelopathy specific to stereotactic body radiation therapy to guide safe practice. *Int J Radiat Oncol Biol Phys* 2013; 85: 341-347.
44. Cunha MV, Al-Omair A, Atenafu EG et al. Vertebral compression fracture (VCF) after spine stereotactic body radiation therapy (SBRT): analysis of predictive factors. *Int J Radiat Oncol Biol Phys* 2012; 84: e343-349.
45. Rose PS, Laufer I, Boland PJ et al. Risk of fracture after single fraction image-guided intensity-modulated radiation therapy to spinal metastases. *J Clin Oncol* 2009; 27: 5075-5079.
46. Moussazadeh N, Lis E, Katsoulakis E et al. Five-Year Outcomes of High-Dose Single-Fraction Spinal Stereotactic Radiosurgery. *Int J Radiat Oncol Biol Phys* 2015; 93: 361-367.
47. Guckenberger M, Mantel F, Gerszten PC et al. Safety and efficacy of stereotactic body radiotherapy as primary treatment for vertebral metastases: a multi-institutional analysis. *Radiat Oncol* 2014; 9: 226.