

BÖLÜM 25

MEME KANSERİ UYGULAMALARINDA FARKLI RADYOTERAPİ TEKNİKLERİ

Hüriye Şenay KIZILTAN¹
Züleyha ÖNGÖREN KADEHÇİ²

GİRİŞ

Meme kanseri hastalarında primer tedavi cerrahi ve gereken hastalarda neoadjuvant veya adjuvant kemoterapi (KT) ve postoperatif radyoterapidir (RT). Yapılan çalışmalarda postoperatif RT ile normalde beklenenden daha düşük bir yaşam avantajı elde edilmesi nedeni ile bu düşüklüğün sebepleri araştırılmıştır. En önemli sebebin özellikle kalp ve akciğerdeki yan etkilere bağlı olduğu tesbit edildiğinden yan etkileri azaltabilmek için farklı radyoterapi (RT) teknikleri geliştirilmiştir. 1980'li yıllarda meme kanserinde postopertaif RT gerekli olan hastalarda iki boyutlu (2D) RT uygulanıyordu. 2D RT ile yan etkiler günümüzdeki RT tekniklerine göre çok daha yüksekti. Normal dokular ancak tanjansiyel meme alanları, wedge kullanarak bir ölçüde azaltılabiliyordu. 1990'lı yıllarda üç boyutlu (3D) konformal tedavilere (3DCRT) geçildikten sonra yan etkilerde büyük oranda düşme görüldü. Kalp ve akciğer toksisitesini daha da düşürmek için yoğunluk ayarlı RT (IMRT) metodu geliştirildi. Ark tedavileri ile RT yan etkileri daha da düşürüldü. Ark tedavilerinin getirdiği bazı sorunlar vardı ve en önemli dezavantajı ise normal organlardaki düşük doz oranlarını artırmasıydı. Hacim ayarlı RT volümetrik modülasyonlu ark tedavisi (VMAT) ve proton tedavileri, yoğunluk ayarlı proton RT (IMPT) ile, meme RT yan etkileri daha da düşürülebilmiştir (1,2).

1970'li yıllarda erken ve geç meme kanserinde lokal nüksleri azaltmak yaşam oranlarını artırmak amacı ile mastektomi tercih edilirdi. Radikal mastektomi son-

¹ Doç. Dr., SBÜ Başakşehir Çam ve Sakura Şehir Hastanesi Radyasyon Onkolojisi Bölümü
hskiziltan@gmail.com

² Uzm. Dr., Radyasyon Onkolojisi Bölümü zuleyhakadehci@yahoo.com

KAYNAKLAR

1. Boyages J, Baker L. Evolution of radiotherapy techniques in breast conservation treatment. *Glandular Surgery*. 2018;7(6):576–595.
2. Early Breast Cancer Trialists' Collaborative G, Darby S, McGale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: Meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet* 2011;378:1707–1716. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
3. Ares C, Khan S, Macartain AM, et al. Postoperative proton radiotherapy for localized and loco-regional breast cancer: Potential for clinically relevant improvements? *Int J Radiat Oncol Biol Phys* 2010;76:685–97. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
4. Darby SC, Ewertz M, McGale P, Bennet AM, Blom- Goldman U, Bronnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *New Engl J Med* 2013;368:987–98. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
5. McGale P, Darby SC, Hall P, et al. Incidence of heart disease in 35,000 women treated with radiotherapy for breast cancer in Denmark and Sweden. *Radiotherapy and Oncology*. 2011;100:167–175. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
6. Chan EK, Woods R, McBride ML, et al. Adjuvant hypofractionated versus conventional whole breast radiation therapy for early-stage breast cancer: Long-term hospital-related morbidity from cardiac causes. *International Journal of Radiation Biology Physics*. 2014;88:786–92. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
7. Nilsson G, Holmberg L, Garmo H, et al. Distribution of coronary artery stenosis after radiation for breast cancer. *Journal of Clinical Oncology*. 2012;30: 380–386. [Crossref], [PubMed], [Web of Science [®]], [Google Scholar]
8. Ginzton EL, Nunan CS. History of microwave electron linear accelerators for radiotherapy. *International Journal of Radiation Oncology Biology Physics*. 1985;11:205–16. 10.1016/0360-3016(85)90141-5
9. Abdulkarim BS, Cuartero J, Hanson J, et al. Increased risk of locoregional recurrence for women with T1-2N0 triple-negative breast cancer treated with modified radical mastectomy without adjuvant radiation therapy compared with breast-conserving therapy. *Journal of Clinical Oncology*. 2011;29:2852-2858. 10.1200/JCO.2010.33.4714
10. Horton JK, Jaggi R, Woodward WA, et al. Breast Cancer Biology: Clinical Implications for Breast Radiation Therapy. *International Journal of Radiation Biology Physics*. 2018;100:23-37. 10.1016/j.ijrobp.2017.08.025 [PubMed] [CrossRef] [Google Scholar]
11. Gupta S, King WD, Korzeniowski M, et al. The Effect of Waiting Times for Postoperative Radiotherapy on Outcomes for Women Receiving Partial Mastectomy for Breast Cancer: a Systematic Review and Meta-Analysis. *International Journal of Radiation Biology Physics*. 2016;28:739-749. 10.1016/j.clon.2016.07.010 [PubMed] [CrossRef] [Google Scholar]
12. Boyages J, Bosch C, Langlands AO, et al. Breast conservation: long-term Australian data. *International Journal of Radiation Biology Physics*. 1992;24:253-260. 10.1016/0360-3016(92)90680-G [PubMed] [CrossRef] [Google Scholar]
13. Vrieling C, van Werkhoven E, Maingon P, et al. Prognostic Factors For Local Control in Breast Cancer After Long-term Follow-up in the EORTC Boost vs. No Boost Trial: A Randomized Clinical Trial. *JAMA Oncology*. 2017;3:42-8. 10.1001/jamaoncol.2016.3031 [PubMed] [CrossRef] [Google Scholar]
14. Darby S, McGale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;378:1707-16. 10.1016/S0140-6736(11)61629-2 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
15. Skowronek J, Wawrzyniak-Hojczyk M, Ambrochowicz K. Brachytherapy in accelerated partial breast irradiation (APBI) – review of treatment methods. *Journal of Contemporary Brachytherapy*

- rapy. 2012;4:152-164. 10.5114/jcb.2012.30682 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. Akhtari M, Teh BS. Accelerated partial breast irradiation: advances and controversies. *Chinese Journal of Cancer*. 2016;35:31. 10.1186/s40880-016-0095-1 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 17. Polgar C, Ott OJ, Hildebrandt G, et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. *Lancet Oncology*. 2017;18:259-68. 10.1016/S1470-2045(17)30011-6 [PubMed] [CrossRef] [Google Scholar]
 18. Correa C, Harris EE, Leonardi MC, et al. Accelerated Partial Breast Irradiation: Executive summary for the update of the ASTRO Evidence-Based Consensus Statement. *Practical Radiation Oncology*. 2017;7:73-9. 10.1016/j.prro.2016.09.007 [PubMed] [CrossRef] [Google Scholar]
 19. Tortorelli G, Di Murro L, Barbarino R, et al. Standard or hypofractionated radiotherapy in the postoperative treatment of breast cancer: a retrospective analysis of acute skin toxicity and dose inhomogeneities. *BMC Cancer*. 2013;13:230. doi: 10.1186/1471-2407-13-230. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 20. Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncology*. 2013;14:1086-94. 10.1016/S1470-2045(13)70386-3 [PubMed] [CrossRef] [Google Scholar]
 21. Whelan TJ, Pignol JB, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *The New England Journal of Medicine*. 2010;362:513-20. 10.1056/NEJMoa0906260 [PubMed] [CrossRef] [Google Scholar]
 22. Valle LF, Agarwal S, Bickel KE, et al. Hypofractionated whole breast radiotherapy in breast conservation for early-stage breast cancer: a systematic review and meta-analysis of randomized trials. *Breast Cancer Research and Treatment*. 2017;162:409-417. 10.1007/s10549-017-4118-7 [PubMed] [CrossRef] [Google Scholar]
 23. Dellas K, Vonthein R, Zimmer J, et al. Hypofractionation with simultaneous integrated boost for early breast cancer: results of the German multicenter phase II trial (ARO-2010-01). *Strahlenther Onkologie*. 2014;190:646-53. 10.1007/s00066-014-0658-5 [PubMed] [CrossRef] [Google Scholar]
 24. Virén T, Heikkilä J, Myllyoja K, et al. Tangential volumetric modulated arc therapy technique for left-sided breast cancer radiotherapy. *Radiation Oncology*. 2015;10:79.
 25. Mast ME, Van Kempen-Harteveld L, Heijenbrok MW, et al. Left-sided breast cancer radiotherapy with and without breath-hold: Does IMRT reduce the cardiac dose even further? *Radiotherapy and Oncology*. 2013;108:248-253. doi: 10.1016/j.radonc.2013.07.017. [PubMed] [CrossRef] [Google Scholar]
 26. Hannan R, Thompson RF, Chen Y, et al. Hypofractionated whole-breast radiation therapy: does breast size matter? *International Journal of Radiation Biology Physics*. 2012;84:894-901. 10.1016/j.ijrobp.2012.01.093 [PubMed] [CrossRef] [Google Scholar]
 27. Cunningham L, Penfold S, Giles E, et al. Impact of Breast Size on Dosimetric Indices in Proton Versus X-ray Radiotherapy for Breast Cancer. *Journal of Personalized Medicine*. 2021;11(4):282.
 28. Johansen J, Overgaard J, Rose C, et al. Cosmetic Outcome and Breast Morbidity in Breast-Conserving Treatment. *Acta Oncologica*. 2002;41:369-380. doi: 10.1080/028418602760169433. [PubMed] [CrossRef] [Google Scholar]
 29. Moody A, Mayles W, Bliss J, et al. The influence of breast size on late radiation effects and association with radiotherapy dose inhomogeneity. *Radiotherapy and Oncology*. 1994;33:106-112. doi: 10.1016/0167-8140(94)90063-9. [PubMed] [CrossRef] [Google Scholar]
 30. De Langhe S, Mulliez T, Veldeman L, et al. Factors modifying the risk for developing acute skin toxicity after whole-breast intensity modulated radiotherapy. *BMC Cancer*. 2014;14:1-9. doi:

- 10.1186/1471-2407-14-711. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
31. Dundas K, Atyeo J, Cox J, et al. What is a large breast? Measuring and categorizing breast size for tangential breast radiation therapy. *Australasian Radiology*. 2007;51:589–593. doi: 10.1111/j.1440-1673.2007.01898.x. [PubMed] [CrossRef] [Google Scholar]
 32. Lilie LL, Sabina V, Andreea D, et al. Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer. *Breast Cancer*. 2015;1032-1039
 33. Mulliez T, Speleers B, Madani I, et al. Whole breast radiotherapy in prone and supine position: is there a place for multi-beam IMRT? *Radiation Oncology*. 2013;8:151. doi: 10.1186/1748-717X-8-151. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 34. Krenqli M, Masini L, Caltavuturo T, et al. Prone versus supine position for adjuvant breast radiotherapy: a prospective study in patients with pendulous breasts. *Radiation Oncology*. 2013;8:232. doi: 10.1186/1748-717X-8-232. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 35. Sun T, Lin X, Tong Y, et al. Heart and Cardiac Substructure Dose Sparing in Synchronous Bilateral Breast Radiotherapy: A Dosimetric Study of Proton and Photon Radiation Therapy. *Frontier Oncology*. 2019;9:1456.
 36. Nicolini G, Clivio A, Fogliata A, et al. Simultaneous integrated boost radiotherapy for bilateral breast: a treatment planning and dosimetric comparison for volumetric modulated arc and fixed field intensity modulated therapy. *Radiation Oncology*. 2009;4:27. 10.1186/1748-717X-4-27 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 37. Seppälä J, Heikkilä J, Myllyoja K, et al. Volumetric modulated arc therapy for synchronous bilateral whole breast irradiation—a case study. *Reports of Practical Oncology and Radiotherapy*. 2015;20:398–402. 10.1016/j.rpor.2015.05.011 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 38. Kaidar-Person O, Kostich M, Zagar TM, et al. Helical tomotherapy for bilateral breast cancer: clinical experience. *Breast*. 2016;28:79–83. 10.1016/j.breast.2016.05.004 [PubMed] [CrossRef] [Google Scholar]
 39. Kim SJ, Lee MJ, Youn SM. Radiation therapy of synchronous bilateral breast carcinoma (SBBC) using multiple techniques. *Medical Dosimetry*. 2018;43:55–68. 10.1016/j.meddos.2017.08.003 [PubMed] [CrossRef] [Google Scholar]
 40. RTOG Breast Cancer Atlas for Radiation Therapy Planning: Consensus Definitions. 2017. [Google Scholar]
 41. Viren T, Heikkiä J, Myllyoja K, et al. Tangential volumetric modulated arc therapy technique for left-sided breast cancer radiotherapy. *Radiation Oncology*. 2015;10:79. 10.1186/s13014-015-0392-x [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 42. Mazon R, Etienne-Mastroianni B, Perol D, et al. . Predictive factors of late radiation fibrosis: a prospective study in non-small cell lung cancer. *International Journal of Radiation Biology Physics*. 2010;77:38–43. 10.1016/j.ijrobp.2009.04.019 [PubMed] [CrossRef] [Google Scholar]
 43. Liang X, Bradley JA, Zheng D, et al. Prognostic factors of radiation dermatitis following passive-scattering proton therapy for breast cancer. *Radiation Oncology*. 2018;13:72. 10.1186/s13014-018-1004-3 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 44. Tommasino F, Durante M, D'Avino V, et al. . Modelbased approach for quantitative estimates of skin, heart, and lung toxicity risk for left-side photon and proton irradiation after breast-conserving surgery. *Acta Oncologica*. 2017;56:730–6. 10.1080/0284186X.2017.1299218 [PubMed] [CrossRef] [Google Scholar]
 45. Cuzick J, Stewart H, Rutqvist L, et al. Cause-specific mortality in long-term survivors of breast cancer who participated in trials of radiotherapy. *Journal of Clinical Oncology*. 1994;12:447–53. [Crossref], [PubMed], [Web of Science ®], [Google Scholar]
 46. Early Breast Cancer Trialists' Collaborative G, Darby S, McGale P, Correa C, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: Meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lan-*

- cet 2011;378:1707–16. [Crossref], [PubMed], [Web of Science *], [Google Scholar]
47. Chung E, Corbett JR, Moran JM, et al. Is there a dose-response relationship for heart disease with low-dose radiation therapy? *International Journal of Radiation Biology Physics*. 2013;85:959–64.
 48. Taylor CW, Nisbet A, McGale P, et al. Cardiac doses from Swedish breast cancer radiotherapy since the 1950s. *Radiotherapy Oncology*. 2009;90:127–35. [Crossref], [PubMed], [Web of Science *],
 49. Wang W, Purdie TG, Rahman M, et al. Rapid automated treatment planning process to select breast cancer patients for active breathing control to achieve cardiac dose reduction. *International Journal of Radiation Biology Physics*. 2012;82:386–93. [Crossref], [PubMed], [Web of Science *], [Google Scholar]
 50. Ares C, Khan S, Macartain AM, et al. Postoperative proton radiotherapy for localized and locoregional breast cancer: Potential for clinically relevant improvements? *International Journal of Radiation Biology Physics*. 2010;76:685–97.
 51. Jimenez RB, Goma C, Nyamwanda J, et al. Intensity modulated proton therapy for postmastectomy radiation of bilateral implant reconstructed breasts: A treatment planning study. *Radiotherapy and Oncology*. 2013;107:213–7. [Crossref], [PubMed], [Web of Science *], [Google Scholar]
 52. Duma MN, Brauman R, Budach W, et al. Heart-sparing radiotherapy techniques in breast cancer patients: a recommendation of the breast cancer expert panel of the German society of radiation oncology (DEGRO). *Strahlenther Onkologie*. 2019;195(10):861–871.
 53. Tsuchiya K, Kinoshita R, Shimizu S, et al. Dosimetric comparison between intensity-modulated radiotherapy and standard wedged tangential technique for whole-breast radiotherapy in Asian women with relatively small breast volumes. *Radiology Physics Technology*. 2014;7:67–72. doi: 10.1007/s12194-013-0232-3. [PubMed] [CrossRef] [Google Scholar]
 54. Dogan N, Cuttino L, Lloyd R, et al. Optimized dose coverage of regional lymph nodes in breast cancer: the role of intensity-modulated radiotherapy. *International Journal of Radiation Biology Physics*. 2007;68:1238–50. doi: 10.1016/j.ijrobp.2007.03.059. [PubMed] [CrossRef] [Google Scholar]
 55. Hurkmans CW, Cho BCJ, Damen E, et al. Reduction of cardiac and lung complication probabilities after breast irradiation using conformal radiotherapy with or without intensity modulation. *Radiotherapy and Oncology*. 2002;62:163–71. doi: 10.1016/S0167-8140(01)00473-X. [PubMed] [CrossRef] [Google Scholar]
 56. Hong L, Hunt M, Chui C, et al. Intensity-modulated tangential beam irradiation of the intact breast. *International Journal of Radiation Biology Physics*. 1999;44:1155–64. doi: 10.1016/S0360-3016(99)00132-7. [PubMed] [CrossRef] [Google Scholar]
 57. Jin GH, Chen LX, Deng XW, et al. A comparative dosimetric study for treating left-sided breast cancer for small breast size using five different radiotherapy techniques: conventional tangential field, filed-in-filed, Tangential-IMRT, Multi-beam IMRT and VMAT. *Radiation Oncology*. 2013;8:89. doi: 10.1186/1748-717X-8-89. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
 58. Popescu CC, Olivotto IA, Beckham WA, et al. Volumetric modulated arc therapy improves dosimetry and reduces treatment time compared to conventional intensity-modulated radiotherapy for locoregional radiotherapy of left-sided breast cancer and internal mammary nodes. *International Journal of Radiation Biology Physics*. 2010;76:287–95. doi: 10.1016/j.ijrobp.2009.05.038. [PubMed] [CrossRef] [Google Scholar]
 59. Johansen S, Cozzi L, Olsen DR. A planning comparison of dose patterns in organs at risk and predicted risk for radiation induced malignancy in the contralateral breast following radiation therapy of primary breast using conventional, IMRT and volumetric modulated arc treatment technique. *Acta Oncology*. 2009;48:495–503. doi: 10.1080/02841860802657227. [PubMed] [CrossRef] [Google Scholar]

60. Gagliardi G, Constine LS, Moiseenko V, et al. Radiation dose-volume effects in the heart. *International Journal of Radiation Biology Physics*. 2010;76:S77–85. doi: 10.1016/j.ijrobp.2009.04.093. [PubMed] [CrossRef] [Google Scholar]
61. Gagliardi G, Lax I, Söderström S, et al. Prediction of excess risk of long-term cardiac mortality after radiotherapy of stage I breast cancer. *Radiotherapy and Oncology*. 1998;46:63–71. doi: 10.1016/S0167-8140(97)00167-9. [PubMed] [CrossRef] [Google Scholar]
62. Qiu JJ, Chang Z, Wu QJ, et al. Impact of Volumetric Modulated Arc Therapy Technique on Treatment With Partial Breast Irradiation. *International Journal of Radiation Biology Physics*. 2010;78:288–96. doi: 10.1016/j.ijrobp.2009.10.036. [PubMed] [CrossRef] [Google Scholar]
63. Levin WP, Kooy H, Loeffler JS, et al. Proton beam therapy. *British Journal of Cancer*. 2005;93:849–854. doi: 10.1038/sj.bjc.6602754. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
64. Kammerer E, Le Guveleu J, Abdulhamid C, et al. Proton therapy for locally advanced breast cancer: A systematic review of the literature. *Cancer Treatment Reviews*. 2018;63:19–27.
65. Alexandre MCS, Andreas Kotsanis A, Cunningham L, et al. Estimating the second primary cancer risk due to proton therapy compared to hybrid IMRT for left sided breast cancer. *Acta Oncology*. 2021 Mar;60(3):300–304. doi: 10.1080/0284186X.2020.1862421.
66. Paddick IA. Simple scoring ratio to index the conformity of radiosurgical treatment plans, technical note. *Journal of Neurosurgery*. 2000; 93:S219–22. 10.3171/jns.2000.93.supplement_3.0219 [PubMed] [CrossRef] [Google Scholar]
67. Wu Q, Mohan R, Morris M, Lauve A, Schmidt-Ullrich R. Simultaneous integrated boost intensity-modulated radiotherapy for locally advanced head-and-neck squamous cell carcinomas. I: dosimetric results. *International Journal of Radiation Biology Physics*. 2003; 56:573–85. 10.1016/s0360-3016(02)04617-5 [PubMed] [CrossRef] [Google Scholar]
68. Feuvret L, Noel G, Mazon JJ, et al. Conformity index: A review. *International Journal of Radiation Biology Physics*. 2006;64:333–42. [Crossref], [PubMed], [Web of Science *], [Google Scholar]
69. Wang X, Zhang X, Dong L, Liu H, Gillin M, Ahamad A, et al. Effectiveness of noncoplanar IMRT planning using a parallelized multiresolution beam angle optimization method for paranasal sinus carcinoma. *International Journal of Radiation Biology Physics*. 2005;63:594–601. [Crossref], [PubMed], [Web of Science *], [Google Scholar]
70. Maureen LGK, Jeanine EV, Nicola SR. Optimizing MR-Guided Radiotherapy for Breast Cancer Patients. *Frontier Oncology*. 2020; 10: 1107. doi: 10.3389/fonc.2020.01107
71. Lagendijk JJW, Raaymakers BW, Raaijmakers AJE, et al. MRI/linac integration. *Radiotherapy and Oncology*. 2008;86:25–9. 10.1016/j.radonc.2007.10.034 [PubMed] [CrossRef] [Google Scholar]
72. Klüter S. Technical design and concept of a 0.35 T MR-Linac. *Clinical Translational Radiation Oncology*. (2019) 18:98–101. 10.1016/j.ctro.2019.04.007 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
73. Ahn KH, Hargreaves BA, Alley MT, et al. MRI guidance for accelerated partial breast irradiation in prone position: imaging protocol design and evaluation. *International Journal of Radiation Biology Physics*. 2009;75:285–93. 10.1016/j.ijrobp.2009.03.063
74. Schmidt MA, Payne GS. Radiotherapy planning using MRI. *Physics in Medicine and Biology*. 2015;60:R323–61. 10.1088/0031-9155/60/22/R323
75. Acharya S, Fischer-Valuck BW, Mazur TR, et al. Magnetic resonance image guided radiation therapy for external beam accelerated partial-breast irradiation: evaluation of delivered dose and intrafractional cavity motion. *International Journal of Radiation Biology Physics*. 2016;96:785–92. 10.1016/j.ijrobp.2016.08.006
76. Raaijmakers AJE, Raaymakers BW, Lagendijk JJW. Integrating a MRI scanner with a 6 MV radiotherapy accelerator: dose increase at tissue-air interfaces in a lateral magnetic field due to returning electrons. *Physics in Medicine and Biology*. 2005;50:1363–76. 10.1088/0031-

9155/50/7/002

77. Park JM, Shin KH, Kim J, et al. Air–electron stream interactions during magnetic resonance IGRT: skin irradiation outside the treatment field during accelerated partial breast irradiation. *Strahlentherapie und Onkologie*. 2018;194:50–9. 10.1007/s00066-017-1212-z
78. Den Hartogh MD, Philippens MEP, van Dam IE, et al. MRI and CT imaging for preoperative target volume delineation in breast-conserving therapy. *Radiation Oncology*. 2014;9:1–9. 10.1186/1748-717X-9-63
79. Giezen M, Kouwenhoven E, Scholten AN, et al. MRI- versus CT-based volume delineation of lumpectomy cavity in supine position in breast-conserving therapy: an exploratory study. *International Journal of Radiation Biology Physics*. 2012;82:1332–40. 10.1016/j.ijrobp.2011.05.008
80. Kirby AM, Yarnold JR, Evans PM, et al. Tumor bed delineation for partial breast and breast boost radiotherapy planned in the prone position: what does MRI add to X-ray CT localization of titanium clips placed in the excision cavity wall? *International Journal of Radiation Biology Physics*. 2009;74:1276–82. 10.1016/j.ijrobp.2009.02.028
81. Mouawad M, Biernaski H, Brackstone M, et al. Reducing the dose of gadolinium-based contrast agents for DCE-MRI guided SBRT: the effects on inter and intra observer variability for preoperative target volume delineation in early stage breast cancer patients. *Radiotherapy Oncology*. 2019;131:60–5. 10.1016/j.radonc.2018.11.020
82. Horton JK, Blitzblau RC, Yoo S, et al. . Preoperative single-fraction partial breast radiation therapy: a novel phase 1, dose-escalation protocol with radiation response biomarkers. *International Journal of Radiation Biology Physics*. 2015;92:846–55. 10.1016/j.ijrobp.2015.03.007
83. Vasmel JE, Groot Koerkamp ML, Kirby AM, et al. . Consensus on contouring primary breast tumors on MRI in the setting of neoadjuvant partial breast irradiation in trials. *k* (in press:). 10.1016/j.prro.2020.03.011
84. Winkel D, Bol GH, Kiekebosch IH, et al. Evaluation of online plan adaptation strategies for the 1.5T MR-linac based on “First-In-Man” treatments. *Cureus*. 2018;10:1–7. 10.7759/cureus.
85. Acharya S, Fischer-Valuck BW, Kashani R, et al. . Online magnetic resonance image guided adaptive radiation therapy: first clinical applications. *International Journal of Radiation Biology Physics*. 2016;94:394–403. 10.1016/j.ijrobp.2015.10.015
86. Kontaxis C, Bol GH, Stemkens B, et al. Towards fast online intrafraction replanning for free-breathing stereotactic body radiation therapy with the MR-linac. *Physics in Medicine and Biology*. 2017;62:7233–48. 10.1088/1361-6560/aa82ae
87. Desislava KL, Mariela VS, Svilen M, et al. Intraoperative Radiotherapy with Balloon-Based Electronic Brachytherapy System—A Systematic Review and First Bulgarian Experience in Breast Cancer Patients. *Current Oncology*. 2021;28(5): 3932–3944.
88. Herskind C, Ma L, Liu Q, et al. Biology of high single doses of IORT: RBE, 5 R's, and other biological aspects. *Radiation Oncology*. 2017;12:1–14. doi: 10.1186/s13014-016-0750-3. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
89. Pilar A, Gupta M, Ghosh Laskar S, et al. Intraoperative radiotherapy: Review of techniques and results. *Ecanermedicalscience*. 2017;11:750. doi: 10.3332/ecancer.2017.750. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
90. Herskind C., Wenz F. Radiobiological aspects of intraoperative tumour-bed irradiation with low-energy X-rays (LEX-IORT) Translational Cancer Research. 2014;3:3–17. [Google Scholar]
91. Silverstein MJ, Fastner G, Maluta S, et al. Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 1—ELIOT. *Annal of Surgery and Oncology*. 2014;21:3787–3792. doi: 10.1245/s10434-014-3998-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
92. Rivard MJ, Davis SD, DeWerd LA, et al. Calculated and measured brachytherapy dosimetry parameters in water for the Xofig Axxent X-Ray Source: An electronic brachytherapy source. *Medical Physics*. 2006;33:4020–4032. doi: 10.1118/1.2357021. [PubMed] [CrossRef] [Google Scholar]

93. Costa P, Oliveira F, Fonseca G, et al. PD-0482: Early breast cancer treated with an electronic IORT system: Report of the first patients treated in Portugal. *Radiotherapy and Oncology*. 2015;115:S237–S238. doi: 10.1016/S0167-8140(15)40478-5. [CrossRef] [Google Scholar]
94. Dickler A, Ivanov O, Syed AM N, et al. Five Year Results of a Multicenter Trial Utilizing Electronic Brachytherapy to Deliver Intraoperative Radiation Therapy in the Treatment of Early-Stage Breast Cancer. *International Journal of Radiation Biology Physics*. 2015;93:E24–E25. doi: 10.1016/j.ijrobp.2015.07.607. [CrossRef] [Google Scholar]
95. Chowdhry VK, Bushey JA, Kwait RM, et al. Intraoperative radiation therapy as part of planned monotherapy for early-stage breast cancer. *Journal of Radiation Oncology*. 2018;7:167–173. doi: 10.1007/s13566-017-0338-z. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
96. Gandía A, Molina G, Ibañez R, et al. EP-1314: Breast treatments with Axxent equipment. Comparison with Mammosite for skin, lung and heart dose. *Radiotherapy and Oncology*. 2018;127:S721. doi: 10.1016/S0167-8140(18)31624-4. [CrossRef] [Google Scholar]
97. Ding J, Guo Y, Li Q, et al. The incidence of postoperative radiotherapy-induced acute dermatitis in breast cancer and its influencing factors for Chinese women. *Onco Targets and Therapy*. 2018;11:1665–1670. doi: 10.2147/OTT.S156066. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
98. Takenaka T, Yamazaki H, Suzuki G, et al. Correlation Between Dosimetric Parameters and Acute Dermatitis of Post-operative Radiotherapy in Breast Cancer Patients. *In Vivo*. 2018;32:1499–1504. doi: 10.21873/invivo.11406. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
99. Hensley FW. Present state and issues in IORT Physics. *Radiation Oncology*. 2017;12:37. doi: 10.1186/s13014-016-0754-z. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
100. Showalter SL, Petroni G, Trifiletti DM, et al. A Novel Form of Breast Intraoperative Radiation Therapy With CT-Guided High-Dose-Rate Brachytherapy: Results of a Prospective Phase 1 Clinical Trial. *International Journal of Radiation Biology, Physics*. 2016;96:46–54. doi: 10.1016/j.ijrobp.2016.04.035. [PubMed] [CrossRef] [Google Scholar]
101. Vaidya JS, Bulsara M, Baum M, et al. Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGIT-IORT) for early breast cancer: TARGIT-A randomised clinical trial. *BMJ*. 2020;370:m2836. doi: 10.1136/bmj.m2836. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
102. Orecchia R, Veronesi U, Maisonneuve P, et al. Intraoperative irradiation for early breast cancer (ELIOT): Long-term recurrence and survival outcomes from a single-centre, randomised, phase 3 equivalence trial. *Lancet Oncology*. 2021;22:597–608. doi: 10.1016/S1470-2045(21)00080-2. [PubMed] [CrossRef] [Google Scholar]