

Guidelines on radiation therapy for breast cancer during the COVID-19 pandemic

The following suggested guidance is based on contributions from international breast cancer experts who have worked together to produce a rapid publication in *Clinical Oncology* (in press): breast cancer clinical oncology consultants contributing on the RCR Clinical Oncology COVID forum webpage using a member log in; and advice from NHS England.

The following guidelines suggest that the risks and benefits are considered and discussed with patients to facilitate shared decision-making. Centres may need/choose to delay RT depending on local circumstances with reference to expert consensus following previous natural disasters¹ and also amend current systemic therapy pathways, but this is outside the remit of these guidelines.

- 1. Omit RT for patients 65 years and over (or younger with relevant co-morbidities) with invasive breast cancer that are up to 30mm with clear margins, grade 1-2, oestrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative and node negative who are planned for treatment with endocrine therapy².**

Trials investigating safe omission of RT can be considered if they do not impact on patients visits and resources are available. Centres may also consider omitting RT for ductal carcinoma in-situ (DCIS) depending on individual risk and benefit.

- 2. Deliver RT in 5 fractions only for all patients requiring RT with node negative tumours that do not require a boost. Options include 28-30Gy in once weekly fractions over 5 weeks or 26Gy in 5 daily fractions over 1 week as per the FAST and FAST Forward trials respectively³⁻⁵.**

N.B. 5-year local relapse data are not yet available for FAST Forward but imminent publication is anticipated. In the meantime, 26Gy in 5 fractions has already been demonstrated to be equivalent with 40 Gy in 15 fractions with respect to 3-year normal tissue outcome. Furthermore, local control is likely to be within acceptable limits given the low local relapse rates in this patient group generally⁶. The FAST Forward protocol and RT planning packs (including nodal subgroup) are available at:

https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/clinical-trials/fast_forward_page/

Partial breast RT using 28.5-6Gy in 5 fractions over 1-2 weeks⁷⁻⁸ can also be considered for selected patients if resources are available for increased complexity and/or to avoid deep inspiration breath hold (DIBH) for left-sided tumours in the upper half of the breast (if DIBH impacts on treatment time). N.B. IMPORT Low⁶ has the same fractionation schedule in the control group as FAST Forward so 26Gy in 5 fractions over 1 week could also be proposed in the partial breast irradiation setting.

If RT is required for DCIS then 5 fractions can be considered as above. DCIS was not included in the FAST Forward study, however it would be reasonable to consider 5 fractions of RT as a pragmatic solution during the COVID-19 pandemic in much the same way that 40Gy in 15 fractions was adopted as standard of care for DCIS despite not being included within the START trial.

3. **Boost RT should be omitted to reduce fractions and/or complexity in the vast majority of patients unless they 40 years old and under, or over 40 years with significant risk factors for local relapse⁹.**

Boost RT has no proven survival advantage so risks and benefits during the COVID-19 pandemic need to be re-evaluated. An example of a significant risk factor is the presence of involved resection margins where further surgery is not possible. Any boost should be either simultaneous and integrated to minimise fractions if resource permits or hypofractionated sequential, e.g. 12Gy in 4 fraction over 4 days.

4. **Nodal RT can be omitted in post-menopausal women requiring whole breast RT following sentinel lymph node biopsy and primary surgery for T1, ER positive, HER2 negative G1-2 tumours with 1-2 macrometastases¹⁰.**

This approach gives this group of patients the option of 5 fractions of RT and may also reduce complexity of planning/treatment.

5. **Consider delivering RT in 26Gy 5 fractions for patients requiring nodal radiotherapy who would have fulfilled the eligibility for the FAST Forward nodal subgroup study (not IMC irradiation) and where nodal RT is still considered necessary during the COVID-19 pandemic**

Some UK Radiotherapy centres have taken the view to extend the use of 26Gy in 5F for patients who require nodal RT. This is based on the FAST Forward nodal subgroup study, which has completed recruitment, but is yet to report. It can be considered when the risk of attending hospital for 15 fractions of radiotherapy currently outweighs the risk of receiving the same treatment as an ethically approved but unreported UK trial during the COVID-19 pandemic for some patients.

References

1. Gay HA, Santiago R, Gil B, Remedios C, Montes PJ, López-Araujo J, Chévere CM, Imbert WS, White J, Arthur DW, Horton JK, Jagsi R, Rabinovich R, Beriwal S, Viswanathan A, Erickson BA, Rengan R, Palma D, Loo BW Jr, Kavanaugh JA, Bradley J, Yom SS, Harari PM, Lee Burnett O 3rd. Lessons Learned From Hurricane Maria in Puerto Rico: Practical Measures to Mitigate the Impact of a Catastrophic Natural Disaster on Radiation Oncology Patients. *Pract Radiat Oncol*. 2019 Sep - Oct;9(5):305-321.
2. Kunkler IH, Williams LJ, Jack WJ, Cameron DA, Dixon JM; PRIME II investigators. Breast-conserving surgery with or without irradiation in women aged 65 years or older with early breast cancer (PRIME II): a randomised controlled trial. *Lancet Oncol*. 2015 Mar;16(3):266-73. doi: 10.1016/S1470-2045(14)71221-5.
3. Brunt AM, Haviland J, Sydenham M, Algurafi H, Alhasso A, Bliss P, Bloomfield D, Emson M, Goodman A, Harnett A. FAST Phase III RCT of Radiotherapy Hypofractionation for Treatment of Early Breast Cancer: 10-Year Results (CRUKE/04/015). *IJROBP* (2018) 102 (5): 1603-1604.
4. Brunt AM, Wheatley D, Yarnold J, Somaiah N, Kelly S, Harnett A, Coles C, Goodman A, Bahl A, Churn M, Zotova R, Sydenham M, Griffin CL, Morden JP, Bliss JM; FAST-Forward Trial Management Group. Acute skin toxicity associated with a 1-week schedule of whole breast radiotherapy compared with a standard 3-week regimen delivered in the UK FAST-Forward Trial. *Radiother Oncol*. 2016 (120): 114-118
5. Brunt AM, Haviland JS, Sydenham MA, Alhasso A, Bloomfield D, Chan C, Churn M, Cleator S, Coles CE, Emson M, Goodman A, Griffin C, Harnett A, Hopwood P, Kirby A, Kirwan C, Morris C, Sawyer E, Somaiah N, Syndikus I, Wilcox M, Wheatley D, Zotova R, Bliss JM, Yarnold JR. OC-0595: FAST-

Forward phase 3 RCT of 1-week hypofractionated breast radiotherapy: 3-year normal tissue effects. *Radiotherapy and Oncology* Volume 127, Supplement 1, April 2018, S311-S312.

6. Coles CE, Griffin CL, Kirby AM, Titley J, Agrawal RK, Alhasso A, Bhattacharya IS, Brunt AM, Ciurlionis L, Chan C, Donovan EM, Emson MA, Harnett AN, Haviland JS, Hopwood P, Jefford ML, Kaggwa R, Sawyer EJ, Syndikus I, Tsang YM, Wheatley DA, Wilcox M, Yarnold JR, Bliss JM; IMPORT Trialists. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results from a multicentre, randomised, controlled, phase 3, non-inferiority trial. *Lancet*. 2017 Sep 9;390(10099):1048-1060.
7. Livi L, Meattini I, Marrazzo L, Simontacchi G, Pallotta S, Saieva C, Paiar F, Scotti V, De Luca Cardillo C, Bastiani P, Orzalesi L, Casella D, Sanchez L, Nori J, Fambrini M, Bianchi S. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. *Eur J Cancer*. 2015 Mar;51(4):451-63.
8. First results of the preoperative accelerated partial breast irradiation (PAPBI) trial. van der Leij F, Bosma SC, van de Vijver MJ, Wesseling J, Vreeswijk S, Rivera S, Bourcier C, Garbay JR, Foukakis T, Lekberg T, van den Bongard DH, van Vliet-Vroegindewij C, Bartelink H, Rutgers EJ, Elkhuizen PH. First results of the post-operative accelerated partial breast irradiation (PAPBI) trial. *Radiother Oncol*. 2015 Mar;114(3):322-7.
9. Bartelink H, Maingon P, Poortmans P, Weltens C, Fourquet A, Jager J, Schinagl D, Oei B, Rodenhuis C, Horiot JC, Struikmans H, Van Limbergen E, Kirova Y, Elkhuizen P, Bongartz R, Miralbell R, Morgan D, Dubois JB, Remouchamps V, Mirimanoff RO, Collette S, Collette L; European Organisation for Research and Treatment of Cancer Radiation Oncology and Breast Cancer Groups. Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. *Lancet Oncol*. 2015 Jan;16(1):47-56. doi: 10.1016/S1470-2045(14)71156-8.
10. Bloomfield DJ; Core Group facilitated by The Royal College of Radiologists. Development of postoperative radiotherapy for breast cancer: UK consensus statements – a model of patient, clinical and commissioner engagement? *Clin Oncol (R Coll Radiol)*. 2017 Oct;29(10):639-641.