RADIOTHERAPY

INTRODUCTION

Radiotherapy is a method for preventing local recurrence not OS! It is useful to break patients into:

1. **Age groups - very young (<40), <50yrs, >50yrs, >65yrs**
2. **Risk factors - low risk disease (T1NO, G1-2, ER+, HER2-) and high risk (LVI, G3, T3/4, N1+)**

This guides whether you give standard 26Gy 5Fr over 5 days, to de-escalate (partial/omit) or to escalate - boost breast dose, give post Mx, and add in supraclavicular irradiation.

GUIDANCE

NICE 2018

- **Whole breast Radiotherapy:**
  - Offer: to all those having BCS for invasive disease and can consider in DCIS after discussion. NB guidance out of date with practice - 3 weeks not FAST.
  - Consider PARTIAL if
    - Age >50, <3cm, and G1-2 and ER+ve/ and HER2- AND endocrine therapy
    - Discuss LR same at 5 years but not clear after 5 years
  - Consider OMISSION (enrol in PRIMETIME 2) if:
    - Age >65 and T1NO and G1-2 and ER+ve and HER2- AND endocrine therapy
  - Consider a boost
    - if “high risk”. RCR suggest age <50 and high risk get boost

No radiotherapy = 50 of 1000 women over 10 years recur, reduced to 10 of 1000 with radiotherapy. But survival unchanged at 10 years. No increase in serious late effects if radiotherapy is given (e.g. cardiac or secondary cancer).

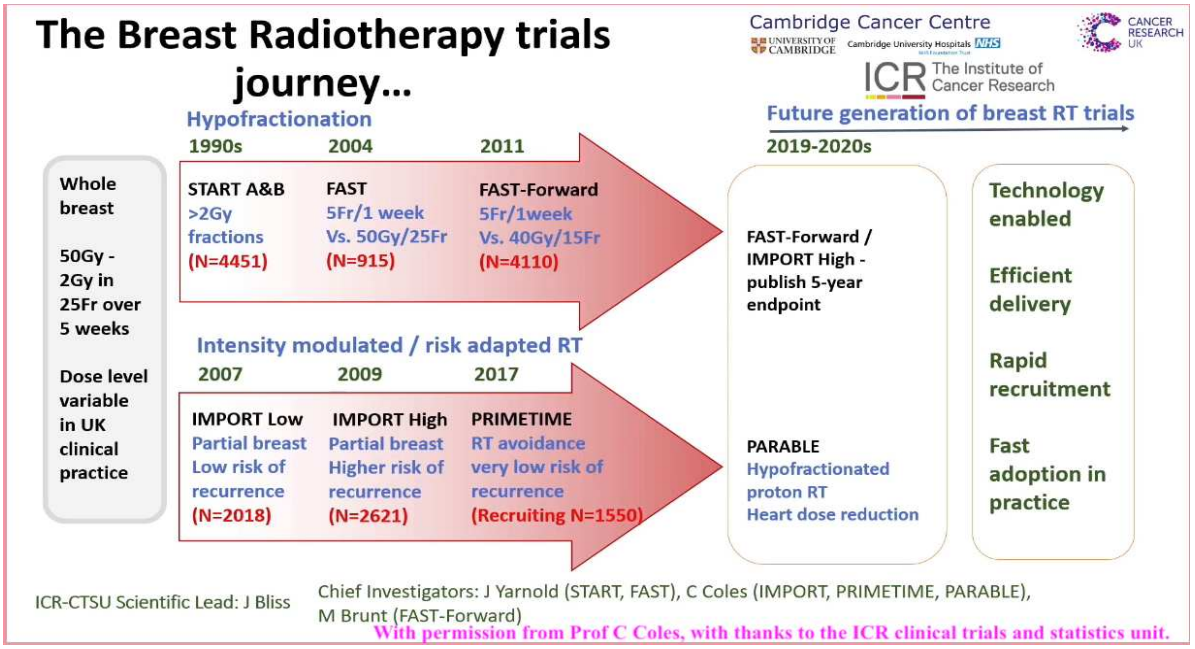
- **Post mastectomy chest wall Radiotherapy**
  - Offer: Margin +, N2+
  - Consider: T3/4, **Can enrol in SUPREMO - see below
- **Supraclavicular Radiotherapy**
  - Offer: N1 AND risk factors (e.g. mentioned T3/4, LVI, G3) or N2 disease

Evidence

Hypofractionation is the main topic currently (as well as de-escalation currently PRIMETIME)

FAST-Forward Lancet, May 2020-changed practice readily in the context of COVID-19

- 4k, multi-centre RCT non-inferiority including T1-T3, N0-1, M0 having BCS
- Excluded RadioTx to axilla
- Allowed for endocrine and anti-her2 but not concurrent chemotherapy
- Three arms - standard 40Gy in 40Fr over 3 weeks, 26Gy and 27gy in 5Fr over 5 days
- Assumed 2% LR at 5yrs for 40 Gy, non-inferiority predefined as ≤1·6% excess for five-fraction schedules (critical hazard ratio [HR] of 1·81).
- Protocol amended to exclude low rx ie those who fit PRIMETIME criteria so that event rate increased
- Patient demographics: ~70% T1, 28% T2, only 1-2%T3, and 80% were N0, 80% ER+ and HER2- i.e. representative of the patients we see.
- **Showed non-inferiority and resulted in the 26Gy 5 Fr over 5 days being adopted**



"Omission in over 65 years with ER+ Stage 1 disease is based on the CALBG 9343 trial (over 70yrs) and the PRIMETIME II (over 65yrs) in which patients must be on endocrine and whereby local/regional relapse was 90% without and 98% with radiotherapy in CALBG and ipsilateral breast tumour recurrence rate of 0.9% with and 9.8% without radiation in PRIMETIME II. There is no survival benefit."

Historically

- B-06 showed that LRR @ 20yrs reduced from 39% to 14% for BCS with RadioTx, so we know we need to give it in majority!

- EBCTG Meta-analysis 2011 was similar 35% to 19.3% LRR. “Halves recurrence”. 1 cancer death presented at 15 yrs.

Tumour bed boosting

- EORTC 10882/22881 “Boost or no Boost” LRRR @10yrs from 10.2% to 6.2%.
- Distinction in age groups: < 40 years was 23.9% to 13.5%, >40 years was 7.8% to 4.9%.

Post mastectomy

- SUPREMO trial finished recruiting 2014
- Post Mx + ANC patients both NAC and non NAC randomized to RadioTx to chest wall or standard treatment
- Need either;
    - pT3 and ANC proven Node negative *ANC must have at least 8 nodes
    - pT2 + 1 of: G3, LVI or both BUT ANC proven node negative
    - PT1-2 and 1-3 of 8+ Nodes positive ie LN1 but no additional rx factors
- In NAC patients it is a little more complicated but mainly based on pre NAC disease

Intraoperative radiotherapy - has not really taken off in UK practice

- ELLIOT - higher LR with intra vs external beam.
- TARGIT- A supports use in age>-45yrs, <-3.5cm, N0-1 disease.

DCIS

- SweDCIS, NSABP-17, EORTC 10853, UK/ANZ - Meta-analysis of all 4 trials show that the HR 0.46 i.e. more than halved the rate of ipsilateral breast events per year. 10 year cumulative risk 28.1% to 12.9% when RadioTx given. No effect on the OS.
- Sloane 2018 showed RadioTx LRR reduced significantly, with a ARR 3.1% BUT does not effect OS. The most benefit is in those with high grade DCIS. Endocrine also has an effect.
- Overall, there is a huge variation in this through the UK but it is very reasonable to give RadioTx in HG DCIS, especially if younger. See DCIS sheet for more details.

Brachytherapy?

- GEC-ESTRO 2016 did show a benefit in terms of reduced early skin toxicity but overall this has not taken off in practice.