

First estimate of amount of radiotherapy dose wasted in compensating for tumour growth between treatments

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For the first time, researchers have estimated the daily dose of radiotherapy that could be wasted in compensating for cancer cell growth that occurs overnight and during weekends in patients with early breast cancer.

In research to be presented to the 2013 European Cancer Congress (ECC2013) [1] today (Monday), Professor John Yarnold will say that, until now, there has been contradictory evidence as to whether gaps between radiotherapy treatments, for instance overnight or at weekends, makes any difference to the overall effectiveness of radiotherapy on [breast cancer](#), and, if it does make a difference, why that could be.

"Traditionally, breast cancer has not been regarded as a fast growing cancer, unlike some other cancer types, but our research now suggests that a significant part of the daily radiotherapy curative dose is 'used up' in compensating for tumour growth overnight and over weekends. We have estimated that the amount of radiotherapy dose that is used up in this way corresponds to approximately 0.60 Gray (Gy) [2] per day," says Prof Yarnold, who is Professor of Clinical Oncology at The Institute of Cancer Research, London, and Honorary Consultant at the Royal Marsden NHS Foundation Trust (London, UK).

"This is the first numerical estimate to suggest that the duration of a course of radiotherapy has an effect on local cancer cure for patients

with early breast cancer. The results of our analysis are hypothesis-generating; they offer an explanation as to why prolonged radiotherapy schedules may allow cancer cells to fight back, and suggest that breast cancer cell growth rates after surgery are higher than historically assumed. If confirmed, it means that current trends to deliver shorter radiotherapy schedules are likely to bear fruit in the future. However, I should emphasise that current schedules delivered over five weeks or more remain highly effective, and patients should follow recommendations from their specialists."

Radiotherapy is normally given as a series of treatments over a number of weeks in order to destroy any remaining cancer cells in the breast, chest wall or underarm area after surgery, and to reduce the risk of the cancer recurring in the same breast, while, at the same time, minimising harm to the healthy tissues.

Prof Yarnold and Ms Jo Haviland, a senior statistician at The Institute of Cancer Research (ICR) Clinical Trials and Statistics Unit (CTSU) based their research on the Standardisation of Breast Radiotherapy (START) trials (START Pilot, START A and START B), which have been evaluating the effects of giving shorter radiotherapy schedules after surgery for early breast cancer patients in the UK since 1986. [3]

The researchers used data from 5,861 UK patients who were enrolled between 1986 and 2002 into the three START randomised clinical trials that compared different schedules for delivering radiotherapy. The START Pilot and START A trials compared the international standard of giving a total of 50 Gy in 25 daily doses of 2.0 Gy over five weeks versus two other schedules of slightly higher daily doses of 3.0–3.3 Gy over the same time period. The START B trial compared the international standard (50 Gy in 25 daily doses of 2.0 Gy over five weeks) with a shorter schedule giving a total of 40 Gy in 15 daily doses of 2.67 Gy over three weeks. After a follow-up period of ten years, the

three-week schedule was shown to be as good as the five-week schedule at preventing the cancer from recurring in the same breast and has since been adopted as the standard in the UK. In terms of safety, the three-week schedule was gentler on the normal tissues, with fewer late side-effects.

Using the data from these trials, the researchers then estimated the effect of overall radiotherapy treatment time on the risk of the cancer recurring, comparing the three-week schedule with the five-week schedules. They used a statistical model that took into account the total dose, the size of the daily dose, the length of time over which the radiotherapy was given, and factors known to be associated with the risk of the cancer recurring in the same breast. They found that approximately 0.60 Gy of the daily radiotherapy dose was being wasted during the five-week treatment schedules to compensate for [cancer cells](#) growing.

"This suggests that a shorter one-week radiotherapy schedule, replacing the five to seven-week schedules that were more usual in the past, may be more effective against breast cancer recurrence and reduce the chances of side-effects on the surrounding normal tissues. In addition, shorter treatment schedules would be more convenient for patients, with benefits including fewer trips to the hospital, and also highly cost-effective for health services," says Prof Yarnold.

Future work will investigate whether reducing the overall treatment time further is as safe and as effective as the current three-week schedule which has been standard practice in the UK since 2009, following publication of the five-year results from the START A and START B trials.

"The UK FAST Forward phase III trial is an example of this research, comparing the current UK standard three-week schedule with two

radiotherapy dose levels of a one-week schedule in women with early breast cancer. This trial is well on the way to recruiting 4000 women," he will conclude.

President of ECCO, Professor Cornelis van de Velde, commented: "This is important research that suggests that the overall treatment time with radiotherapy could make a difference to outcomes for women with early breast cancer. If further investigations confirm that a shorter [radiotherapy](#) schedule is as effective as the current standard of care, it will be another step towards making treatments easier and more bearable for patients, and possibly cheaper for healthcare services."

More information: [1] The 2013 European Cancer Congress is the 17th congress of the European Cancer Organisation (ECCO), the 38th congress of the European Society for Medical Oncology (ESMO) and the 32nd congress of European Society for Therapeutic Radiology and Oncology (ESTRO).

[2] One Gray is the absorption of one joule of energy, in the form of ionising radiation, per kilogram of matter.

[3] The START trials were co-ordinated by the Cancer-Research UK-funded Clinical Trials and Statistics Unit at The Institute of Cancer Research (ICR-CTSU), and represent a long-term partnership between Prof Yarnold as the clinical lead and ICR-CTSU as an NCRN accredited/UKCRC Registered Clinical Trials Unit with a strong interest in radiotherapy trials.

[4] This work was funded by Cancer Research UK, UK Medical Research Council and UK Department of Health.

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