

<p><b>Institution: Queen Mary University of London</b></p>
<p><b>Unit of Assessment: A1 (Clinical Medicine)</b></p>
<p><b>Title of case study: Radiotherapy for ductal carcinoma in situ reduces recurrence</b></p>
<p><b>1. Summary of the impact</b></p> <p>The primary treatment for ductal carcinoma in situ (DCIS, cancer confined to the milk ducts of the breast) is surgery, and breast-conserving surgery is increasingly preferred over mastectomy. The UK/ANZ DCIS trial, co-led by Queen Mary researchers, showed that following surgery, women with DCIS are significantly less likely to develop invasive disease if given radiotherapy, and that this protection persists long term. NICE recommends that, following adequate breast conserving surgery, adjuvant radiotherapy should be offered to patients with DCIS. This recommendation is also current in the United States, Canada, Australia, and many European countries. Based on current figures, we estimate that in UK alone, around 260 women each year are spared a recurrence of breast cancer as a result of this research.</p>
<p><b>2. Underpinning research</b></p> <p>Ductal Carcinoma In Situ (DCIS), cancer in the milk ducts of the breast, is the commonest type of non-invasive breast cancer in the UK with around 4,650 women diagnosed annually. Following the introduction of the UK National Health Service Breast Screening Programme in 1988, there emerged a substantial increase in the diagnosis of DCIS, which represents 20–25 per cent of screen-detected breast cancers in the UK. The primary treatment is surgery, with breast conserving surgery preferred over mastectomy (which is perceived by many as an over-treatment and is unpopular with patients). Survival following treatment is about 98 per cent, but the risk of local recurrence and a new cancer in the opposite breast is high.</p> <p>In the early 1990s the question of which standard treatments should follow after breast-conserving surgery for DCIS was uncertain. The UK/ANZ DCIS trial was designed to establish whether adjuvant treatment with radiotherapy, tamoxifen, or both tamoxifen and radiotherapy could reduce the likelihood of cancer returning after surgery aimed at completely removing DCIS. Between 1990 and 1998, 1701 women from the UK, Australia, and New Zealand were enrolled in the study. Participants had had complete surgical excision of the lesion.</p> <p>Professor Jack Cuzick, (Head of Centre 1998 - present) was co-designer of the trial, and conducted the data analysis of both the original 2003 report and the 2010 update. He was lead author of the 2010 long-term trial report. The trial was funded in the UK through the UK Coordinating Committee on Cancer Research and the Imperial Cancer Research Fund, and by grants from the Cancer Research Campaign (C569-A10404), and the Medical Research Council.</p> <p>In 2003, initial results (median follow-up 4.4 years) published in the Lancet suggested that radiotherapy reduced new invasive and local recurrences by about half, but no significant effects were noted with tamoxifen treatment [1]. The report on the long-term follow up (median 12.7 years) was published in 2010 [2]. Results showed that radiotherapy after surgery reduced the relative risk of developing invasive cancer in the same breast by almost 70 per cent and decreased recurrent DCIS in the same breast by over 60 per cent, corresponding to an absolute 10-year reduction in local cancer recurrences of 12.3 per cent. Treatment with radiotherapy had no observed effect on cancer risk in the other breast. The trial reported a benefit for tamoxifen in reducing contralateral new breast events.</p> <p>The UK/ANZ DCIS trial results confirmed the long-term beneficial effect of radiotherapy for women with DCIS treated by complete local excision. Women with DCIS are significantly less likely to develop invasive disease if they are given radiotherapy after surgery, and the effect is long lasting. The results, which have been further analyzed in relation to grade of DCIS [3,4], emphasized the importance of radiotherapy for women who have had surgery for high-grade (ie more quickly growing and more likely to spread) DCIS.</p>

### 3. References to the research

1. UK Coordinating Committee on Cancer Research (UKCCCR) Ductal carcinoma in situ (DCIS) Working Party. Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breast in the UK, Australia, and New Zealand: randomised controlled trial. *Lancet* 2003; 362: 95-102.
2. **Cuzick J**, Sestak I, Pinder SE, Ellis IO, Forsyth S, Bundred NJ, Forbes JF, Bishop H, Fentiman IS, George WO. Effect of tamoxifen and radiotherapy in women with locally excised ductal carcinoma in situ: long-term results from the UK/ANZ DCIS trial. *Lancet Oncology* 2011; 12: 21-29.
3. **Cuzick J**. Treatment of DCIS – results from clinical trials. *Surgical Oncology* 2003; 12: 213-219.
4. Pinder SE, Duggan C, Ellis IO, **Cuzick J**, Forbes JF, Bishop H, Fentiman IS and George WD on behalf of the UK Coordinating Committee on Cancer Research (UKCCCR) Ductal Carcinoma in Situ (DCIS) Working Party. A new pathological system for grading DCIS with improved prediction of local recurrence: results from the UKCCCR/ANZ DCIS trial. *British Journal of Cancer* 2010; 103: 94-100.

### 4. Details of the impact

#### 4a: Change in policy / guidelines

The results of the DCIS trial have had a direct and major impact on health policy and guidelines around the world. Examples include:

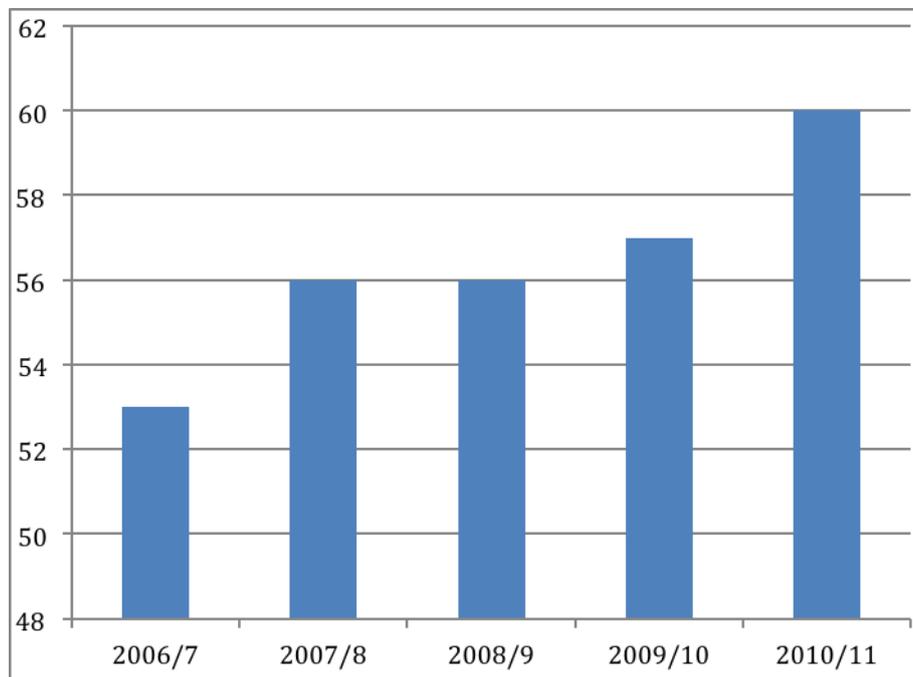
- **UK:** The current UK National Institute for Health and Clinical Excellence Clinical Guideline on treatment for early and locally advanced breast cancer recommends: “*Offer adjuvant radiotherapy to patients with DCIS following adequate breast conserving surgery*” (paragraph 1.11.2) [5].
- **USA:** Following the publication of long-term follow-up findings from the UK/ANZ trial, the US Agency for Healthcare Research and Quality Appropriateness Criteria were amended to include the following recommendation: “*Breast conservation therapy (consists of breast-conserving surgery to achieve negative margins followed by adjuvant radiation therapy to the whole breast) is an acceptable treatment alternative to mastectomy for women with localized DCIS wishing to conserve their breast.*” [6]
- **USA:** A review by US authors in the *International Journal of Surgical Oncology* in late 2012 stated that for DCIS, “*Postoperative radiation therapy in combination with breast-conserving surgery is considered the standard of care, with demonstrated decrease in local recurrence with the addition of radiation therapy.*” [7]
- **CANADA:** According to the Canadian Cancer Society, “*External beam radiation therapy is given after breast conserving surgery, unless there is a medical condition that prevents a woman from receiving radiation*” [8]. Using data from our trial, Canadian clinical practice guidelines developed in 2008 and revised in 2012 state that for patients with DCIS, following breast conserving surgery, adjuvant whole breast radiotherapy is recommended [9].

#### 4b: Change in clinical practice

Changes in policy and guidelines have been followed by changes in practice. For example:

- **UK:** British Association of Surgical Oncology audit figures show that in 2001-02 only 46% of UK patients with non-invasive breast cancer who had undergone breast-conserving surgery received radiotherapy, but by 2010-11 this had increased to 60% and the trend was rising (see Figure 1 overleaf) [10,11].
- **USA:** An audit of a large US Health Maintenance Organization, Kaiser Permanente, in

2010 showed that 57% of 3,000 women treated for DCIS in this organisation in the previous 10 years were given adjuvant radiotherapy after breast-conserving surgery, and that the odds of a woman receiving radiotherapy rose significantly over the time period of the study [12].



**Figure 1:** Percentage of non-invasive breast cancers in the NHS Breast Screening Programme treated by breast conserving surgery receiving radiotherapy

#### 4c: Change in morbidity

The greatest impact of adjuvant radiotherapy treatment for the affected women is decreased morbidity resulting from reduced recurrence rates. In the UK each year, around 3,115 of the 4,650 women diagnosed with DCIS opt for breast conserving surgery [13]. Without adjuvant radiotherapy 623 of these women would face recurrence within ten years, but with adjuvant radiotherapy, recurrence risk is reduced by almost 70%. Based on current figures, 60% of women who undergo breast-conserving surgery now receive adjuvant radiotherapy (1869 women) each year, among whom 261 recurrences are prevented.

#### 5. Sources to corroborate the impact

5. NICE Guideline 2009 'Breast cancer (early and locally advanced): diagnosis and treatment' [www.nice.org.uk/CG80](http://www.nice.org.uk/CG80) (reviewed 2012 and confirmed still current).
6. American College of Radiography Appropriateness Criteria for Ductal Carcinoma in Situ. [www.guidelines.gov/content.aspx?id=35163#Section424](http://www.guidelines.gov/content.aspx?id=35163#Section424)
7. Lee RJ, Vallow LA, McLaughlin SA, Tzou KS, Hines SL, and Peterson JL. Ductal Carcinoma In Situ of the Breast. *International Journal of Surgical Oncology* 2012; doi:10.1155/2012/123549
8. Canadian Cancer Society recommendations for treating early breast cancer. [www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/stage-0/?region=en](http://www.cancer.ca/en/cancer-information/cancer-type/breast/treatment/stage-0/?region=en)
9. Alberta Health Services. Clinical Practice Guideline BR-006: Adjuvant Radiation Therapy for Ductal Carcinoma In Situ (reviewed April 2012). [www.albertahealthservices.ca/hp/if-hp-cancer-](http://www.albertahealthservices.ca/hp/if-hp-cancer-)

## Section 1.01 Impact case study (REF3b)

[guide-br006-adjuvant-rt-dcis.pdf](#)

10. NHS Breast Screening Programme and Association of Breast Surgery. An Audit of Screen Detected Breast Cancers for the Year of Screening April 2010 to March 2011. NHS Cancer Screening Programmes 2012.  
[www.cancerscreening.nhs.uk/breastscreen/publications/baso2010-2011.pdf](http://www.cancerscreening.nhs.uk/breastscreen/publications/baso2010-2011.pdf)
11. NHS Breast Screening Programme and British Association of Surgical Oncology Breast Group. *An audit of screen detected breast cancers*. NHS Cancer Screening Programmes 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012. See previous reference and similar data for past years from [www.cancerscreening.nhs.uk](http://www.cancerscreening.nhs.uk)
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13. McGuire KP, Santillan AA, Kaur P *et al.* Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. *Annals of Surgical Oncology* 2009; 16: 2682-90.