



GÖTEBORGS UNIVERSITET  
SAHLGRENSKA AKADEMIN

# LONG-TERM SYMPTOMS AFTER BREAST CANCER RADIOTHERAPY

AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Sahlgrenska  
Akademien vid Göteborgs Universitet offentligen försvaras i  
Arvid Carlsson salen, Academicum, Medicinaregatan 3

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av

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Avhandlingen baseras på följande delarbeten:

- I. Lundstedt D, Gustafsson M, Malmström P, Johansson K-A, Alsadius D, Sundberg A, Wilderäng U, Holmberg E, Anderson H, Steineck G, Karlsson P. Symptoms 10-17 years after breast cancer radiotherapy data from the randomised SWEBORG91-RT trial. *Radiotherapy & Oncology* 2010; 97(2):281-7.
- II. Lundstedt D, Gustafsson M, Steineck G, Malmström P, Alsadius D, Sundberg A, Wilderäng U, Holmberg E, Johansson K-A, Karlsson P. Risk factors of developing long-lasting breast pain after breast cancer radiotherapy. *Int J Radiat Oncol Biol Phys*. Epub 2011 Nov 11.
- III. Lundstedt D, Gustafsson M, Steineck G, Johansson K-A, Alsadius D, Sundberg A, Wilderäng U, Holmberg E, Karlsson P. Long-term symptoms after radiotherapy of supraclavicular lymph nodes in breast cancer patients. *Radiotherapy & Oncology* Epub 2012 Feb 7.
- IV. Lundstedt D, Gustafsson M, Steineck G, Johansson K-A, Alsadius D, Sundberg A, Wilderäng U, Holmberg E, Karlsson P. Dose-volume analysis of radiotherapy to the plexus brachialis in breast cancer patients. *Manuscript*

## ABSTRACT

Since breast cancer is the most common cancer among women worldwide and the relative 10-years overall survival is 80% there is an increasing number of women living with a history of breast cancer treatment. This results in a great number of women in the society having received breast cancer radiotherapy. The purpose of this study was to identify and quantify self-reported long-term symptoms/side-effects caused by irradiation and correlate these to patient and treatment related risk factors. Furthermore, we wanted to investigate how the dose-volume distribution of ionizing radiation delivered to a certain anatomical volume contributed to the occurrence of certain symptoms, i.e. a dose-volume response analysis.

We interviewed women that were treated with breast cancer surgery and postoperative radiotherapy up to 20 years earlier; based on these interviews we made a questionnaire. The questionnaire was sent to two different cohorts of women having had breast cancer treatment three to 17 years earlier. Cohort 1: 422 women who were randomised between 1991 and 1997 to receive adjuvant tangential breast irradiation or not after breast conserving surgery with axillary dissection. Cohort 2: 1091 women who had adjuvant breast cancer radiotherapy based on a 3D-dose plan between 1999 and 2004 at Sahlgrenska University Hospital, Gothenburg.

Paper I: Based on cohort 1 we found that 8.8% of the women having undergone radiotherapy and surgery reported weekly breast pain versus 0.6% of the women with surgery alone (RR 15.1 95% CI 2.03-112). Significantly increased occurrence after radiotherapy was also observed for disturbances of skin sensation. Daily life and analgesic use did not differ between the groups. Paper II: Our next step was to identify risk factors that contributed to breast pain after breast cancer radiotherapy (cohort 1 and 2). Higher age at treatment (RR 0.96; 95% CI 0.94-0.98, annual decrease) and longer time since treatment (RR 0.93; 95% CI 0.88-0.98, annual decrease) were related to a lower occurrence of breast pain. For example among women up to 39 years of age at treatment, 23.1% had breast pain, compared with 8.7% among women older than 60 years (RR 2.66; 95% CI 1.33-5.36). In paper III and IV we reported long-term symptoms after radiotherapy including the regional lymph nodes, i.e. irradiation of the plexus brachialis, or not (cohort 2). We found that paraesthesia in the hand was reported by 20% after regional radiotherapy compared to 13% without regional radiotherapy (RR 1.47; 95% CI 1.02-2.11). RR adjusted for oedema in the hand (RR 1.28; 95% CI 0.93-1.76). Among the women who received irradiation  $\geq 40$  Gy to a volume of  $>13.5$  cm<sup>3</sup> of the brachial plexus 25% reported paraesthesia, RR 1.83 (95% CI 1.13-2.95). The risk was still significant after adjustment for oedema (RR 1.64; 95% CI 1.12-2.41).

Conclusions: Radiotherapy after breast-conserving surgery among women treated for breast cancer increases the occurrence of breast pain, especially among younger women. Furthermore, regional radiotherapy increases the occurrence of paraesthesia in the hand and our results indicate that there seems to be a correlation between larger irradiated brachial nerve volumes and an increased risk of reporting paraesthesia.

**Keywords:** Radiotherapy, breast cancer, long-term symptoms, breast pain, supra clavicular, plexus brachialis.

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