## Second malignancies following breast cancer treatment: a case-control study based on the Peridose methodology. ALLEGRO project (task 5.4)

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## ABSTRACT

Aims and background. To calculate peripheral radiation dose to the second primary site in patients who have developed a second malignancy after breast cancer radio-therapy (index cases) and to compare it with dose in the analogous anatomical site in radiotherapy-treated breast cancer patients who did not experience a second malignancy (controls). To evaluate the feasibility of Peridose-software peripheral dose calculation in retrospective case-control studies.

**Material and study design.** A case-control study on 12,630 patients who underwent adjuvant breast radiotherapy was performed. Minimum 5-year follow-up was required. Each index case was matched with 5 controls by 1) year of birth, 2) year of radiotherapy and 3) follow-up duration. Peridose-software was used to calculate peripheral dose.

**Results.** 195 second cancers were registered (0.019% of all patients treated with adjuvant irradiation). Several methodological limitations of the Peridose calculation were encountered including impossibility to calculate the peripheral dose in the patients treated with intraoperative or external electron beam radiotherapy, in case of second tumors located at <15 cm from the radiotherapy field etc. Moreover, Peridose requires full radiotherapy data and the distance between radiotherapy field and second primary site. Due to these intrinsic limitations, only 6 index cases were eligible for dose calculation. Calculated doses at the second cancer site in index cases and in an analogous site in controls ranged between 7.5 and 145 cGy. The mean index-control dose difference was -3.15 cGy (range, -15.8 cGy and +2.7 cGy).

**Conclusions.** The calculated peripheral doses were low and the index-control differences were small. However, the small number of eligible patients precludes a reliable analysis of a potential dose-response relationship. Large patient series followed for a long period and further improvement in the methodology of the peripheral dose calculation are necessary in order to overcome the methodological challenges of the study. *Key words:* breast cancer radiotherapy, Peridose, peripheral dose, second primary tumors.

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