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

Roberto Orecchia1,5, Barbara A Jereczek-Fossa1,5, Elena Rondi2, Isa Bossi-Zanetti1,5, Ilaria Meaglia1, Rosa Luraschi2, Maria Cristina Leonardi1, Nicole Rotmensz2, Edoardo Botteri3, Cristiana Fodor1, Agnese Cecconi1, Anna Morra1, Roberta Lazzari1, Annamaria Ferrari1, Federica Cattani2, Viviana Galimberti4, Alberto Luini4, Paolo Veronesi4,5, Stefano Zurrida4,5, Stefano Magrini6, Wolfgang Doerr7,8, Nicole Humble8, Klaus R Trott10-11, Andrea Ottolenghi11, Vere Smyth11, and Umberto Veronesi4

1 Departments of Radiation Oncology, 2 Medical Physics, 3 Epidemiology and Biostatistics, and 4 Senology, European Institute of Oncology, Milan; 5 University of Milan, Milan; 6 University of Brescia, Brescia, Italy; 7 Technische Universität Dresden, Medizinische Fakultät Carl Gustav Carus, Klinik für Strahlentherapie und Radioonkologie, Dresden, Germany; 8 Dept of Radiation Oncology & Christian Doppler Laboratory for Medical Radiation Research in Radiooncology, Medical University, Vienna, Austria; 9 Department of Radiation Oncology, University Hospital, Ulm, Germany; 10 University College of London, Cancer Institute, London, UK; 11 Physics Dept, University of Pavia, Pavia, Italy

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 radiotherapy (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.

Acknowledgments: The research leading to these results has received funding from the European Atomic Energy Community’s Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 231965 (ALLEGRO). The project was coordinated by Prof. Andrea Ottolenghi and included 13 European research centers involved in 7 work packages and 43 tasks. The present study was one of 43 ALLEGRO tasks.

Conflict of interest: none.

Correspondence to: Barbara Alicja Jereczek-Fossa, MD, PhD, Dept of Radiation Oncology, European Institute of Oncology, via Ripamonti 435, 20141 Milan, Italy. Tel +39-02-57489037; fax +39-02-94379227; email barbara.jereczek@ieo.it

Received May 5, 2012; accepted August 6, 2012.