In Reply to Struikmans et al

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Published in:
International Journal of Radiation Oncology Biology Physics

DOI:

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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Download date: 17-09-2023


In Reply to Struikmans et al.

To the Editor: We thank Struikmans et al for their interest in our consensus statement.1 We are in agreement, as highlighted in multiple locations of our manuscript, that “advances have been made in photon cardiac sparing with techniques such as deep-inspiratory breath hold,” which may reduce the absolute risk of breast cancer radiation therapy in the modern era.2 In addition, improvements in cardiologyc medicine are likely to lower the risk of cardiovascular events, including death, in those burdened with radiation-associated coronary disease in the years ahead.3 Nevertheless, patients with chronic coronary disease are still at high risk of acute cardiovascular events.3,5 Thus, preventing radiation therapy-associated cardiac disease remains of paramount importance, particularly given the advances in multidisciplinary breast cancer care, which have prolonged life expectancies of patients diagnosed with the disease.

The authors call into question the linear, no-threshold relationship between cardiac dose and major coronary events proposed by Darby et al and validated by others in large population-based studies.6–8 To do so, they highlight 15-year results from the European Organization for Research and Treatment of Cancer (EORTC) 22922-10925 trial, which randomized patients to regional node irradiation (RNI) versus no RNI in patients with early-stage breast cancer. However, in this study the incidence of cardiac disease was significantly higher in those who received RNI, which increases cardiac dose. The cumulative incidence rate at 15 years for any cardiac disease was 9.4% (95% confidence interval, 8.0%-10.8%) versus 11.1% (95% confidence interval, 9.6%-12.7%) for those treated without or with RNI (P = .04), translating into a relative increase of approximately 18% with RNI. The increased cardiac morbidity partially off-set the small breast cancer mortality benefit of RNI observed in that study.9

The authors have previously acknowledged limitations in their ability to accurately estimate cardiac dose of individual patients who participated in the trial owing to a lack of computed tomography–based treatment planning.9 According to the Darby model, the 18% relative increase in cardiac disease, as observed in the RNI arm of EORTC 22922-10925, would be predicted following approximately 2.5 Gy mean heart dose.5 Such an increase in cardiac exposure might have been expected in the RNI arm. Interestingly, the absolute difference in cardiac disease between the 2 arms continues to diverge past 15 years (Fig. 2C from Poortmans et al9). We look forward to further follow-up for cardiac events, which are concentrated later in life, and applaud the authors for carrying out these detailed toxicity analyses. Nevertheless, the sum of the currently available data, including EORTC 22922-10925, support a causal relationship between cardiac dose and cardiac adverse events. In our consensus statement, we advocate for “additional work...to better delineate the relationship among...dose volume parameters, systemic therapy, and host factors with various cardiac endpoints.” However, the linear, no-threshold relationship between cardiac dose and radiation-associated cardiac events originally put forward by Darby et al remains the most evidence-based and patient-centered model to guide breast cancer radiation therapy. Moreover, the available data supports the use of cardiac sparing strategies, including proton therapy, to mitigate the risk of radiation-associated cardiac morbidity.

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This work was supported in part by K12 HD065987 (R.W.M.).
Disclosures: R.B.M.V. reports travel funds from Varian (2017) and IBA (2018). J.A.B. reports travel funds from IBA (2018). Unrelated to this manuscript, A.Y.H. has received research funding from Merck and GSK and received consulting fees from La Roche Posay. M.F. reports being a consultant for Augmenix and Boston Scientific related to lecturing and training of new users of rectal spacers. Unrelated to this manuscript, R.A.A. reports being on the scientific advisory board and receiving honoraria from TAE Life Sciences. X.D. has a patent related to spot-scanning proton arc therapy and this patent has been licensed to IBA.
In Regard to Steenbakkers et al.

To the Editor: We read the article titled “Parotid Gland Stem Cell Sparing Radiotherapy for Head and Neck Cancer Patients: A Double-Blind Randomized Controlled Trial” by Steenbakkers et al with great interest.1 We recently published a cross-sectional study on the same issue and were looking forward to a prospective randomized trial.2 Ipsilateral parotid gland function affected by the dose to both the contralateral parotid gland and stem cells is an important

Disclosures: none.