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Clinical Investigation: Breast Cancer

Radiation Dose to the Esophagus From Breast Cancer Radiation Therapy, 1943-1996: An International Population-Based Study of 414 Patients

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Summary

The authors reconstructed doses incidentally delivered to the esophagus of breast cancer patients treated with radiation therapy during 1943-1996 in North America and Europe. Fields treating the supraclavicular and/or internal mammary lymph nodes were used for 85% of patients and delivered the highest doses within 3 regions of the esophagus: cervical (population median 38 Gy),

Purpose: To provide dosimetric data for an epidemiologic study on the risk of second primary esophageal cancer among breast cancer survivors, by reconstructing the radiation dose incidentally delivered to the esophagus of 414 women treated with radiation therapy for breast cancer during 1943-1996 in North America and Europe.

Methods and Materials: We abstracted the radiation therapy treatment parameters from each patient's radiation therapy record. Treatment fields included direct chest wall (37% of patients), medial and lateral tangentials (45%), supraclavicular (SCV, 64%), internal mammary (IM, 44%), SCV and IM together (16%), axillary (52%), and breast/chest wall boosts (7%). The beam types used were ^{60}Co (45% of fields), orthovoltage (33%), megavoltage photons (11%), and electrons (10%). The population median prescribed dose to the target volume ranged from 21 Gy to 40 Gy. We reconstructed the doses over the length of the esophagus using abstracted patient data, water phantom measurements, and a computational model of the human body.

Results: Fields that treated the SCV and/or IM lymph nodes were used for 85% of the patients and delivered the highest doses within 3 regions of the esophagus: cervical (population median 38 Gy), upper thoracic (32 Gy), and middle thoracic (25 Gy). Other fields (direct chest wall, tangential, and axillary) contributed substantially lower doses (approximately 2 Gy). The

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cervical to middle thoracic esophagus received the highest dose because of its close proximity to the SCV and IM fields and less overlying tissue in that part of the chest. The location of the SCV field border relative to the midline was one of the most important determinants of the dose to the esophagus.

Conclusions: Breast cancer patients in this study received relatively high incidental radiation therapy doses to the esophagus when the SCV and/or IM lymph nodes were treated, whereas direct chest wall, tangentials, and axillary fields contributed lower doses.

Introduction

Breast cancer is the most common cancer among women worldwide and has among the highest rates of survivorship in Western Europe and North America (1, 2). As survival has improved and use of radiation therapy (RT) has expanded (3, 4), understanding the late effects of breast cancer RT has become increasingly important. Several studies have demonstrated an elevated risk of second primary esophageal cancer by comparing incidence rates in patients who received RT with those who did not (5). However, no previous study has documented the pattern of RT doses along the esophagus from a large number of patients treated with a wide variety of radiation fields.

Recently an international study investigated the risk of second primary esophageal cancer among breast cancer survivors in North America and Western Europe (6). To derive a dose–response relationship, it was necessary to reconstruct the doses incidentally delivered along the esophagus in the breast cancer patients treated with RT (7-9). In this article we describe the dose reconstruction method and summarize doses delivered to the esophagus from breast cancer RT during 1943-1996. An analysis of the doses is presented according to treatment parameters including field location and beam energy.

Methods and Materials

Breast cancer surgery and RT techniques

The patients for this study were selected from a case–control study of esophageal cancer among 289,748 ≥5-year survivors of breast cancer, treated between 1943 and 1996 and who were registered in 1 of 5 European and North American population-based cancer registries (6). The case–control study included 452 patients who received RT. For this analysis, we included the 414 women for whom the RT records contained sufficient information to reconstruct doses. Included in the study were 156 cases of second primary esophageal cancer and 258 controls (2 controls per case) matched on registry, birth date, race (United States only), breast cancer diagnosis date, and survival after breast cancer. This study was approved by each study center's institutional review board and exempted from review by the National Cancer Institute because analyses used only existing deidentified data.

The surgical approach to treat breast cancer patients changed considerably during the study period (Fig. 1a). Before 1975 more than 80% of patients had a mastectomy, and less than 10% of patients had a lumpectomy. By 1995 fewer than 40% of the patients had a mastectomy, and more than 60% had a lumpectomy. With the transition from mastectomy to lumpectomy, there were simultaneous modifications in the RT techniques (Fig. 1b and c). The use of direct anterior chest wall (CW) postmastectomy treatment decreased beginning in the late 1970s, from 44% of patients to 10% by the late 1990s. The tangential fields were parallel-opposed fields tangent to the CW, treating the CW or the entire breast, whereas the boost was a small localized field delivering additional dose to the tumor bed. The use of tangential fields increased from 27% to 87% from 1975 to 1996, and these were more often delivered after lumpectomy. The supraclavicular (SCV) and internal mammary chain (IM) fields were direct anterior fields treating the regional lymph nodes. The SCV treatments also used a posterior field in early years. The medial border of the SCV fields was located along the body midline or a few centimeters either side of midline. The IM fields generally extended to the midline. As an alternative to treating the IM and SCV nodes in 2 separate fields, they were sometimes treated together in a single SCV-IM field, also called "hockey stick" (HS). An axillary field, direct and posterior, often completed the SCV irradiation. The use of SCV, IM, and SCV-IM fields decreased after 1975, with these types of fields generally reserved for advanced node-positive cases in later years.

We abstracted each patient's RT parameters, including treatment location(s), prescribed dose to the target volume or incident dose at d_{max} or in air, number of fields, field configuration(s), field size(s), and beam energies. In addition, dose per fraction was abstracted for a subset of patients with treatment field types of greatest interest to us (SCV, IM, and tangentials). The treatment beam types included ^{60}Co (45% of fields), orthovoltage (33%), megavoltage photons (11%), and electrons (10%). Orthovoltage was most frequently used until the late 1960s, followed by ^{60}Co during the 1970s and 1980s, and electrons and megavoltage photons from the late 1980s onward. The total prescribed dose to the tumor varied widely, from <15 to 65 Gy (Fig. 2), and generally increased with number of fractions. For example, for tangential fields, total prescribed tumor doses of 35 Gy and 50 Gy were typically delivered in 14 fractions and 25 fractions, respectively. We also observed differences in total dose and dose per fraction based on beam type. The total prescribed doses and number of fractions were typically lower (ie, higher dose per fraction) for orthovoltage compared with ^{60}Co or megavoltage photon beams. For example, for orthovoltage treatments of SCV (with IM) fields, a total prescribed dose of 30 Gy was typically delivered in 10 fractions, whereas using ^{60}Co, 40 Gy was delivered in 15 fractions.

Dose reconstruction

Before approximately 1980, computed tomography (CT) examinations were not available for RT treatment planning. Hence we had no information about individual patient size and shape. To reconstruct the doses, we used a computational phantom model of the human body (7) representing a typical adult patient. The median body mass index (BMI) of our cohort was 24 kg/m^2,