Methods

Chest Radiation therapy

Chest RT was defined according to the COG Long-Term Follow-up (LTFU) Guidelines; it included any exposure with potential impact to the lung parenchyma: total body irradiation, mini-mantle, mantle, whole lung, extended mantle, subtotal lymphoid irradiation, total lymphoid irradiation, chest (thorax), and mediastinal. Patients who received only spinal radiation were not considered as having received chest RT. Specific definitions are detailed in the table below:

Field	Definition
Total body irradiation	Entire body; encompassing all radiation fields
Mini-mantle	Bilateral cervical (neck), supraclavicular and axillary fields
Mantle	Bilateral cervical (neck), supraclavicular, mediastinal, hilar, and axillary fields
Extended mantle	Mantle and para-aortic fields
Subtotal lymphoid (STLI)	Mantle + para-aortic + splenic
Total lymphoid (TLI)	Mantle + inverted Y (para-aortic/pelvic) + splenic
Chest (thorax)	May include any of the following: Mediastinal, hilar, whole lung, chest wall
Mediastinal	Mediastinum and bilateral hilar fields

Chest RT dose was calculated according to minimum dose delivered to a field. Radiation dose calculations followed the COG LTFU Guidelines which state:

"Some sections of the COG LTFU Guidelines relevant to radiation exposure include dose specifications. These specifications indicate the minimum dose of radiation that is believed (based on available evidence and the recommendations of the expert panel) to place patients sufficiently at risk of the referenced late effect to recommend screening....If a patient received radiation to more than one field relevant to a particular guideline section during a single planned course of radiation treatment, the field that received the largest radiation dose should be used in making the determination as to the applicability of the indicated guideline sections. Exception: if patient received radiation to the same field at different times (e.g., at time of diagnosis and at relapse), these doses should be added together when considering the applicability of the indicated guideline section."

For example, if a patient with Hodgkin lymphoma received 12 Gy of RT to the axillary field combined with 18 Gy of RT to the mediastinum as part of frontline therapy, and then received 12 Gy of TBI as part of conditioning therapy during relapse, their total RT dose would be 30 Gy (18 Gy [max dose during initial therapy] + 12 Gy [relapse]).

Methodology for Selection of Healthy Controls

Healthy controls were recruited from two groups: friends and family members of cancer survivors enrolled in the study (recruitment method A), and members of the community (recruitment method B). Controls were recruited sequentially, representing a stratified sample based on the distribution of demographic characteristics of cancer survivors enrolled on the study (current age [≤30 years old/ >30 years old], sex [male/female]).

Recruitment method A: We asked each study participant to identify up to 5 friends or family members that could serve as controls in the study. Information packets (describing the study) were provided to these individuals either by mail or by the cancer survivors. Individuals meeting the eligibility criteria and interested in participating were asked to contact the study staff by email or phone using a toll-free number.

Recruitment Method B: Healthy controls were also recruited using flyers placed throughout the City of Hope campus. The advertisements briefly introduced the study and directed individuals interested in participating to contact study staff.

Once contacted, study staff confirmed eligibility. Informed consent was obtained via mail, and a comprehensive PFT and blood draw were scheduled upon receipt of informed consent.

Modified Medical Research Council (MRC) Dyspnea Questionnaire

	Yes	No
Are you troubled by shortness of breath when hurrying on ground level or walking up a slight hill?	O	O
Do you notice shortness of breath walking with other people of your own age on level ground?	O	O
Do you have to stop for breath when walking at your own pace on level ground?	O	O
Are you short of breath when washing or dressing?	O	O
Are you short of breath at rest?	O	O