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Breast Imaging in Women Previously Irradiated for Hodgkin Lymphoma

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Abstract

Background—Women treated with mantle irradiation for Hodgkin Lymphoma (HL) are at an increased risk of developing breast cancer (BC). Current guidelines recommend screening breast magnetic resonance imaging (MRI) as an adjunct to mammography (M) in these patients. There are limited data, however, as to the impact of breast MRI on cancer detection rates. The aim of the current study is to evaluate the use of breast MRI in in survivors of HL treated and followed at a single institution.

Methods—We retrospectively reviewed 980 female patients treated with mantle irradiation for HL between 1961 and 2008. Records were reviewed to determine age at radiotherapy treatment, radiotherapy dose, breast imaging (including M and breast MRI), biopsy results if applicable, and incidence of BC.

Results—118 patients had breast imaging performed at our institution. Median age at HL diagnosis was 28 years (range 10–69). Median radiotherapy dose was 36 Gy (range 20–45 Gy). Seventy-nine patients (67%) underwent M screening only, 1 (1%) breast MRI only, and 38 (32%) both M and breast MRI. Of these 38, 19 (50%) underwent 54 screening MRI studies (range per patient = 1–8), 13 (34%) underwent preoperative MRI for workup of BC, and 6 (16%) initiated screening MRI of the contralateral breast only after diagnosed with BC. Fifty-nine biopsies were performed: 47 were prompted by suspicious M findings only, 10 by palpable findings on physical examination, and 2 by suspicious breast MRI findings. Of the 47 biopsies performed by M, 24 revealed malignant disease while 23 proved to be benign. All 10 biopsies performed by palpation were malignant. Both biopsies prompted by MRI findings were benign. With M, there were 34 true positive (TP) findings in 32 patients, 23 false positive (FP) findings, and 1 false negative (FN) finding. With screening MRI, there were 2 FP findings, one FN finding, and no TP findings.

Conclusions—The role of screening breast MRI in women previously irradiated for HL is evolving. Further education of patients and physicians is important to increase awareness of more

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sensitive breast cancer screening modalities in this high-risk population. Future studies are necessary to determine the appropriate integration of screening breast MRI into the ongoing follow up of these women.

Keywords

Hodgkin Lymphoma (HL); Breast Imaging; Breast Magnetic Resonance Imaging (MRI)

INTRODUCTION

Long-term survivors of Hodgkin Lymphoma (HL) are at an increased risk of developing a treatment-related secondary malignancy (1). In particular, girls and young women under the age of 30 treated with chest radiotherapy have a significantly increased lifetime risk of developing breast cancer compared to the general population (2–4). Based on this increased risk, the American Cancer Society, the American College of Radiology, and the Society of Breast Imaging recommend annual screening breast magnetic resonance imaging (MRI) as an adjunct to annual screening mammography for these patients (5, 6). These recommendations, based on expert consensus opinion, have evolved from the experience of screening breast MRI in women with a strong family history of breast cancer or those with a BRCA 1 or 2 mutation (7, 8).

For survivors of HL, however, there are limited data and experience as to how to optimally incorporate breast MRI into their long-term follow up and health maintenance. Although breast MRI has a high sensitivity for detecting breast cancer, it has a modest specificity compared to mammography (9). Furthermore, overall costs raise important questions, including timing of initiation of screening MRI, frequency of its use, and whether there are clinical and/or HL treatment-related factors that might predict which patients would benefit most from additional breast imaging.

The goal of the current study is to evaluate breast imaging in a group of women previously treated with chest irradiation for HL. In this report, we review and characterize the mammographic and breast MRI findings as well as breast biopsies in a cohort of women previously irradiated for HL to determine features that may help guide the optimal use of screening breast MRI in this patient population.

MATERIALS AND METHODS

With institutional review board approval, a retrospective review of all patients treated with chest irradiation for HL at Stanford University Medical Center was performed. Between 1961 and 2008, 980 females were identified. Only those patients who had breast imaging performed at our institution, including mammography and/or breast MRI, were included, as outside breast imaging studies were not available for review. Records were reviewed to determine the age at radiotherapy treatment, radiotherapy dose received, mammographic and breast MRI findings, breast biopsy results if applicable, and the incidence of breast carcinomas detected.

Screening mammography consisted of standard cranial-caudal and medial lateral oblique images. When abnormal findings were identified, diagnostic mammography was performed to include lateral medial images as well as spot or magnification views as indicated. Since 2002, mammography was performed using a GE 2000D Senographe or Essential digital mammography unit (GE Milwaukee, Wisconsin) equipped with R2 Computer Assisted Detection (CAD) systems (Sunnyvale, CA). Since 2004, all diagnostic mammography was performed using digital technology. All mammographic and MR images were reviewed by dedicated, fellowship trained breast diagnostic radiologists. Imaging characteristics were reported according to the ACR BI-RADS Reporting System (10). Patients with suspicious or indeterminate mammographic findings underwent focused ultrasound (US) and US-guided or stereotactic biopsy if indicated. Pathology was recorded and correlated retrospectively with the mammographic findings.

Breast MR imaging was performed in a 1.5-T scanner (Echospeed; GE Medical Systems, Milwaukee, WI). All images were obtained in the prone position with a dedicated phased array breast coil (MRI Devices, Waukesha, WI). Whole breast rapid dynamic MR images and high-spatial-resolution fat-nulled MR images were contemporaneously acquired by using a combination of dynamic 3-dimensional (3D) spiral MRI to obtain initial kinetic enhancement curves during the wash-in phase of gadolinium (GD) contrast by methods previously described (11-13). Intravenous GD (Gadoteridol, Bracco Diagnostics, Princeton, NJ or Magnevist, Berlex, Berlin, Germany) at a dose of 0.1 mmol/kg was infused as a rapid bolus at a rate of 2 to 3 mL/s using a power injector (Spectris, Medrad). Immediately following this injection, high-spatial-resolution transfer (3DSSMT) imaging was done to collect information regarding morphology followed by additional dynamic 3D spiral MRI to obtain delayed kinetic enhancement curves. The raw data were then post processed on the GE Advantage Windows workstation (Advantage Windows, GE, Milwaukee, WI) (12, 13). These curves were classified as highly suspicious (rapid initial uptake with washout or plateau), indeterminate suspicion (rapid initial uptake with sustained late phase), or low suspicion (slow uptake with a persistent late phase) (12). The MRI was timed in relation to the menstrual cycle in cases where it was feasible with respect to the patient's availability, regularity of her cycle, and if it did not significantly delay any workup and treatment of a previously diagnosed cancer. Menstrual cycle information was recorded on a breast history form that was available for evaluation by the diagnostic radiologist at the time of interpretation. Screening MRI studies, defined as MRI studies performed as a screening technique without a prior diagnosis of breast cancer, were obtained annually, alternating every 6 months with screening mammography. Diagnostic MRI studies, defined as preoperative breast MRI studies performed for workup of a breast cancer that was diagnosed by another modality, were obtained after completion of diagnostic mammography and/or ultrasound.

MR imaging characteristics reported included size and morphology of any mass, the location in the breast, the description of mass margins, and the dynamic enhancement patterns according to the ACR BI-RADS MRI Reporting System (14, 15). Patients with suspicious or indeterminate MRI findings concerning for cancer underwent second-look focused US. If the finding was identified by US, a biopsy was performed under US guidance. If the finding was not seen by US, an MRI-guided biopsy was performed by methods previously described

(16). Final pathology from these biopsies was recorded and correlated retrospectively with the abnormal MRI findings.

Pathology records for the needle biopsies performed by mammographic, US, or MRI guidance were reviewed and categorized as benign or malignant. The number of cancers diagnosed, the method of detection, and the pathologic features were recorded. Descriptive statistics were used to assess the type of breast imaging these patients received, the number of biopsies prompted by each imaging technique, the results of the biopsies, the incidence of breast cancer, and the age and time since HL treatment for those diagnosed with a breast malignancy. Given that the relative risk of developing breast cancer is greatest in those patients who were treated with chest irradiation at the age of 30 years or younger (3, 17–20), the data were also analyzed separately for those treated for HL 30 years of age. Data were also assessed according to the era in which the breast cancer was diagnosed, as breast MRI was not routinely available in most academic centers until 1995 and the ACR guidelines for screening breast MRI were not introduced until 2007 (5).

RESULTS

Between 1961 and 2008, 980 female patients were treated with chest irradiation for HL. Of these, 118 patients had breast imaging performed at our institution consisting of mammography and/or breast MRI. Patient and breast imaging characteristics of these 118 patients, including breast biopsies, are listed in Tables 1 and 2, respectively.

Hodgkin Lymphoma Characteristics

Among this cohort of 118 patients, the median age at the time of HL treatment was 28 years (range 10–69) (Table 1). Twenty-four patients (20%) received radiotherapy alone while 93 patients (79%) underwent combined modality therapy (CMT, radiotherapy and chemotherapy). The median radiotherapy dose was 36 Gy (range 20–45 Gy). The radiotherapy treatment fields consisted of total lymphoid irradiation, subtotal lymphoid irradiation, modified mantle irradiation, supraclavicular irradiation, or splenic irradiation alone.

Ten patients in this cohort (8%) had recurrent HL, with 6 requiring a stem cell transplant. In addition to breast cancer, other secondary malignancies that developed included lung cancer (n=3), anal cancer (n=1), gastric cancer (n=1), colon cancer (n=1), gynecologic cancer (n=1), and non-Hodgkin lymphoma (n=1).

Breast Imaging and Biopsies

Of those who had breast imaging at our institution, 79 survivors of HL (67%) underwent mammography only, 1 (1%) underwent breast MRI only, and 38 (32%) underwent both mammography and breast MRI (Table 2). Of the 38 patients who underwent both mammography and breast MRI, 19 patients (50%) underwent 54 screening breast MRI studies (range per patient = 1-8 MRI studies), 13 (34%) underwent a preoperative breast MRI for workup of a breast cancer that was identified by another modality, and 6 (16%) initiated screening breast MRI of the contralateral breast only after being diagnosed with a breast cancer.

Based on all breast imaging studies, 59 biopsies were performed on 44 women: 47 were prompted by suspicious mammographic findings, 10 by abnormal physical examination (PE) findings, and 2 by suspicious breast MRI findings only. Of the 47 biopsies prompted by mammography, 24 (51%) revealed malignancies while 23 (49%) proved to be benign. All 10 biopsies prompted by abnormal palpable PE findings were consistent with malignancy. Both biopsies prompted by suspicious MRI findings only were benign. One cancer was initially detected by positron emission tomography (PET) for workup of a pleural effusion but was subsequently visualized and biopsied by mammography.

With mammography, there were 34 true positive findings in 32 patients, 23 false positive findings, and 1 false negative finding. With screening MRI (defined as MRI performed as a screening technique without a prior diagnosis of breast cancer), there were 2 false positive findings, one false negative finding, and no true positive findings. All diagnostic MRI studies (defined as preoperative breast MRI studies performed for workup of a breast cancer that was diagnosed by another modality) identified the index lesion.

Breast Cancer in Survivors of HL

Thirty-three patients (28%) developed 35 breast cancers (2 bilateral breast cancers) (Table 3). The median age at the time of HL treatment was 24 (range, 10–48), and the median age at the time of breast cancer diagnosis was 44 (range, 34–79). The median time from HL treatment until a diagnosis of breast cancer was 21 years (range, 6–36). Twenty-three breast cancers (66%) were detected by mammographic screening, 10 (28%) by a clinically palpable abnormality, 1 (3%) at the time of prophylactic mastectomy after a negative mammogram and MRI, and 1 (3%) as an incidental finding on PET imaging for workup of a pleural effusion. Of the 10 cancers detected by palpable abnormalities, 7 were interval cancers that appeared in between screening mammography. The remaining developed in women who had not yet initiated screening mammography. Twenty-four cancers were invasive ductal carcinoma with (n=8) or without (n = 16) ductal carcinoma in situ (DCIS). Eleven (31%) were DCIS only. No patients in this cohort were diagnosed with invasive lobular carcinoma.

Of the patients 30 years of age at the time of HL treatment (n= 70), 26 breast cancers were diagnosed in 24 patients (34% of the younger patients) (Table 3). The median age at the time of HL treatment was 21 (range, 10–30) and the median age at the time of breast cancer diagnosis was 43 (range, 34–66). The median time from HL treatment until a diagnosis of breast cancer was 21 years (range, 9–36). Sixty-five percent (17/26) of these cancers were detected by mammography, while 27% (7/26) of cancers were detected by palpation (Table 4). Of the 48 patients > 30 years of age at the time of HL treatment, 9 (19%) developed breast cancer. The median age at the time of HL treatment in the older cohort was 35 (range, 31–48) and the median age at the time of breast cancer diagnosis was 53 (range, 42–79). The median time from HL treatment until a diagnosis of breast cancer was 18 years (range, 6–29). Similar to the younger cohort, 67% (6/9) of these cancers were detected by mammography, while 33% (3/9) of cancers were detected by palpation. There were more patients in the younger cohort who were diagnosed with DCIS (38%, 10/26) than in the older cohort (11%, 1/9). The clinical and pathologic features for all 33 patients diagnosed with breast cancer are listed in Table 5.

Breast Cancer Detection and Era of Breast Imaging

Given that most academic centers only began to utilize breast MRI in 1995, and that the ACR guidelines for screening breast MRI were not introduced until 2007, the dates in which patients were diagnosed with breast cancer were reviewed (Table 6). Of the 35 cancers diagnosed in 33 patients, 1 (3%) was diagnosed before 1995. This cancer was diagnosed by screening mammography, with no screening MRI studies performed prior to 1995. Between 1995 and 2007, 62 screening mammograms and 8 screening breast MRI studies were performed. Twenty-one cancers (60%) were diagnosed during this time, with 6 diagnosed by palpation, 14 by screening mammograms and 24 screening breast MRI studies were performed in this cohort. Thirteen cancers (37%) were diagnosed after 2007, with 2 by palpation, 10 by screening mammography, and 1 by prophylactic mastectomy.

DISCUSSION

It is well documented that young women treated with chest irradiation for HL have an increased risk of breast cancer, particularly those treated before the age of 30 years (2, 21). Since this risk appears to increase as early as 8 years after radiotherapy treatment, experts have recommended that these women initiate screening mammography at age 25 or 8 years after treatment (2, 3, 22, 23). Many women in this risk category, however, are unaware of their increased risk and do not undergo regular screening mammography (24, 25). Even with the earlier initiation of screening mammography, many breast cancers are still detected by palpable findings on clinical examination (26).

More recently, screening breast MRI has been recommended for this patient population as an adjunct to mammography based on the observed risk (5–6). While breast MRI has a high sensitivity for detecting breast cancer, particularly for those with increased breast density, its routine use has been controversial given the modest specificity that may result in false positive findings and benign biopsies (27, 28). Since the establishment of these guidelines in 2007, there have been limited data regarding patient compliance, biopsy rates, and cancer detection rates in survivors of HL. The current study was designed to evaluate breast imaging practice patterns in this patient population at our institution leading up to the ACR guidelines for screening breast MRI.

We found that despite the introduction of breast MRI in 1995, only 21% of the patients in our cohort underwent screening breast MRI, with 5% undergoing screening breast MRI only after having been diagnosed with a contralateral breast cancer. An additional 12% underwent preoperative MRI for workup of a breast cancer that had been established by another modality, while the remaining 67% underwent mammography only. These data suggest slow adoption of breast MRI in this cohort compared to its use in other high-risk patient groups (7).

Yet with the establishment of the ACR guidelines in 2007, there has been increased awareness of the potential benefit of screening breast MRI in addition to screening mammography. In a cohort of 91 women with a history of chest irradiation, Sung et al. at Memorial Sloan-Kettering Cancer Center identified 4 mammographically occult cancers

Interestingly, 11 of the 35 cancers detected in our series (31%) were DCIS, which appeared as calcifications on mammography. This is similar to Sung et al, where 3 of 10 cancers (30%) identified were in situ carcinomas detected on screening mammography only (29). The results of both series support the recommendation that MR imaging should be used as an adjunct to, and not in place of, mammography in this patient population.

Our study is limited by its retrospective nature from a single institution and its small sample size with a limited number of breast MRI studies. It also is limited by potential selection bias, as we did not have complete information about the other female HL survivors who did not have breast imaging performed at our institution to verify that the study population is not a biased population. In addition, we did not have breast imaging studies that may have been performed at outside institutions. Our results, however, provide preliminary information for the design of future studies.

An ongoing study by Ng et al at the Brigham and Women's Hospital and Dana-Farber Cancer Center is prospectively evaluating the role of screening breast MRI in women previously treated with mantle irradiation for HL at age 35 and more than 8 years beyond treatment (31). Preliminary results of 148 women demonstrated that while the addition of screening breast MRI contributed to the detection of an additional 5 cancers that would have otherwise been missed by mammography, it also resulted in 18 unnecessary biopsies in 14 women. Similar to our series, Ng et al reported one cancer (DCIS) that was identified on prophylactic mastectomy but was missed by imaging, further highlighting the need for even more improvements in breast imaging.

Finally, when evaluating the use of breast MRI in this population, a main limitation is the era in which patients are evaluated and the time delay between introduction of an imaging modality and its adoption into clinical practice. As our cohort only included imaging studies up until 2008, we were not able to evaluate the impact of the 2007 guidelines on the use of breast MRI. Future studies will explore breast MRI after 2008 and its effect on breast cancer detection.

CONCLUSIONS

The role of screening breast MRI in women previously irradiated for Hodgkin Lymphoma is evolving. Further education of patients and physicians is important to increase awareness of more sensitive breast cancer screening modalities in this high-risk population. Additional studies are warranted to determine the optimal timing and frequency of screening breast MRI with the goal of earlier detection and improved breast cancer outcomes in these women.

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Hodgkin Lymphoma (HL) Patient Characteristics (n=118)

| | n (%) |
|---------------------------------|----------|
| Age at HL Diagnosis (years) | |
| Median | 28 |
| Range | 10–69 |
| HL Treatment | |
| Radiotherapy Only | 24 (20%) |
| Combined Modality Therapy (CMT) | 93 (79%) |
| Unknown | 1 (1%) |
| Radiotherapy Dose | |
| Median | 36 Gy |
| Range | 20–45 Gy |
| Radiotherapy Treatment Fields | |
| TLI | 13 (11%) |
| STLI | 29 (24%) |
| Mantle | 39 (33%) |
| Modified Mantle | 18 (15% |
| SCV | 2 (2%) |
| Spleen | 1 (1%) |
| Left Axilla | 1 (1%) |
| SCV and Axilla | 1 (1%) |
| Unknown | 14 (12%) |
| Chemotherapy used in CMT | |
| Stanford V | 38 (32%) |
| MOPP | 17 (14%) |
| ABVD | 10 (9%) |
| VBM | 5 (4%) |
| PAVe | 12 (10%) |
| ABVD/MOPP | 2 (2%) |
| None | 24 (20%) |
| Unknown | 10 (9%) |

TLI = total lymphoid irradiation; STLI = subtotal lymphoid irradiation; SCV = supraclavicular; Stanford V = mustargen, adriamycin, vinblastine, oncovin, bleomycin, etoposide, prednisone; MOPP = mustargen, oncovin, procarbazine, prednisone; ABVD = adramycin, bleomycin, vinblastine, dacarbazine; VBM = vinblastine, bleomycin, methotrexate; PAVe = procarbazine, alkeran, vinblastine

Characteristics of Breast Imaging and Breast Biopsies (n= 118 patients; 59 biopsies)

| | n (%) |
|---|-----------|
| Number of Survivors of HL with Breast Imaging | (n= 118) |
| Mammography Only | 79 (67%) |
| Breast MRI Only | 1 (1%) |
| Mammography and Breast MRI | 38 (32%) |
| Number of Biopsies (n= 59) | |
| Based on Abnormal Mammogram | 47 (80%) |
| Based on Physical Exam | 10 (17%) |
| Based on Abnormal Breast MRI Only | 2 (3%) |
| Number of Benign Biopsies (n= 25) | |
| Performed by Mammographic Guidance | 23 (39%) |
| Performed by Breast MRI Guidance | 2 (3%) |
| Number of Malignant Biopsies (n= 34) | |
| Performed by Mammographic Guidance | 24* (41%) |
| Performed by Palpation | 10 (17%) |
| Performed by Breast MRI Guidance | 0 (0%) |

one cancer detected initially by PET and biopsied under mammographic guidance

Characteristics of those who developed Breast Cancer according to age at time of HL treatment (n= 33 patients)

| Pati | ents 30 years at HL treatment (n=24) | Patients >30 years at HL treatment (n=9) |
|-------------------------|---|--|
| Age at HL Diagnosis (ye | ears) | |
| Median | 21 | 35 |
| Range | 10–30 | 31–48 |
| Radiotherapy Dose | | |
| Median | 44 Gy | 44 Gy |
| Range | 36–45 Gy | 30–45 Gy |
| Chemotherapy | | |
| Stanford V | 2 (7%) | 1 (11%) |
| MOPP | 6 (25%) | 2 (22%) |
| ABVD | 3 (13%) | 2 (22%) |
| PAVe | 3 (13%) | 1 (11%) |
| ABVD/MOPP | 1 (4%) | 0 (0%) |
| None | 6 (25%) | 3 (33%) |
| Unknown | 3 (13%) | 0 (0%) |
| Age at Breast Cancer Di | agnosis (years) | |
| Median | 43 | 53 |
| Range | 34–66 | 42–79 |
| Time from HL Treatmen | t until Breast Cancer Diagnosis (years) | |
| Median | 21 | 18 |
| Range | 9–36 | 6–29 |

Imaging and Pathology of Breast Cancers according to patient age at time of HL treatment (n= 35 cancers in 33 patients)

| | Cancers in Patients 30 years at HL treatment (n=26) | Cancers in Patients >30 years at HL treatment (n=9) |
|-------------------------------------|--|--|
| Method of Detection | | |
| Mammography | 17 (65%) | 6 (67%) |
| Screening Breast MRI | 0 (0%) | 0 (0%) |
| Palpation | 7 (27%) | 3 (33%) |
| PET | 1 (4%) | 0 (0%) |
| Prophylactic Mastectomy | 1 (4%) | 0 (0%) |
| Histologic Diagnosis | | |
| Invasive Ductal Carcinoma | 9 (35%) | 7 (78%) |
| Invasive Ductal Carcinoma with DCIS | 7 (27%) | 1 (11%) |
| Invasive Lobular Carcinoma | 0 (0%) | 0 (0%) |
| Ductal Carcinoma in situ (DCIS) | 10 (38%) | 1 (11%) |

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Clinical and pathologic features for all 33 patients diagnosed with breast cancer

| Patient | Age at HL tx | XRT Dose (Gy) | Chemo | Age at BC | Attribution | Histology | Grade | Tumor (cm) | ER status | PR Status | Her2/neu status |
|---------|--------------|---------------|------------|-----------|-------------|-----------------|-------|------------|-----------|-----------|-----------------|
| 1 (L) | 10 | *. | None | 37 | mammo | DCIS | 2 | 6.3 | neg | neg | ī |
| 1 (R) | 10 | ı | None | 37 | palpation | IDC | ı | 3.0 | neg | neg | sod |
| 2 | 13 | I | | 34 | mammo | DCIS | 2 | 9.7 | sod | sod | ı |
| 3 | 14 | I | None | 47 | mastectomy | IDC | 7 | 1.0 | sod | sod | neg |
| 4 | 16 | ı | PAVe | 35 | mammo | IDC | ю | 2.1 | neg | neg | ı |
| 5 | 16 | I | ABVD | 42 | mammo | DCIS | 2 | 1.4 | sod | sod | neg |
| 9 | 17 | 44 | MOPP | 44 | mammo | IDC | 1 | 2.2 | sod | sod | neg |
| 7 | 18 | 44 | ABVD | 34 | mammo | DCIS | | ı | ı | ı | ı |
| 8 | 21 | 44 | | 54 | mammo | DCIS | 3 | 1.8 | sod | sod | ı |
| 6 | 21 | 44 | None | 42 | mammo | IDC | б | 1.2 | neg | neg | neg |
| 10 | 21 | ı | None | 38 | mammo | DCIS | ю | 1.5 | sod | sod | ı |
| 11 (L) | 21 | 44 | MOPP | 53 | palpation | IDC/DCIS | б | 3.0 | neg | neg | neg |
| 11 (R) | 21 | 44 | MOPP | 53 | palpation | IDC/DCIS | 7 | 1.2 | sod | sod | neg |
| 12 | 21 | 36 | Stanford V | 35 | palpation | IDC/DCIS | 7 | 2.0 | sod | sod | neg |
| 13 | 22 | 44 | PAVe | 53 | mammo | IDC | 2 | 1.8 | sod | neg | neg |
| 14 | 23 | ı | ABVD | 44 | mammo | IDC/DCIS | 7 | 1.0 | sod | sod | neg |
| 15 | 23 | 44 | MOPP | 58 | PET | IDC | 7 | 1.3 | neg | neg | neg |
| 16 | 24 | 44 | None | 50 | palpation | IDC/DCIS | 1 | 1.8 | sod | neg | ı |
| 17 | 24 | 43.2 | MOPP | 43 | mammo | IDC | 7 | 1.8 | sod | sod | neg |
| 18 | 25 | 43.8 | PAVe | 41 | mammo | DCIS | 3 | 0.5 | ı | ı | ı |
| 19 | 25 | 44 | None | 61 | mammo | DCIS | б | 3.5 | sod | sod | ı |
| 20 | 27 | 45 | ABVD/MOPP | 36 | palpation | IDC | 7 | 1.5 | neg | neg | ı |
| 21 | 28 | I | | 46 | palpation | DCIS | 3 | 2.7 | ı | ı | ı |
| 22 | 29 | 36 | Stanford V | 40 | mammo | DCIS | б | 1.8 | neg | neg | ı |
| 23 | 30 | 44 | MOPP | 99 | mammo | IDC/DCIS | ю | 4.0 | sod | sod | neg |
| 24 | 30 | 44 | | 50 | mammo | IDC/DCIS | 7 | 1.4 | sod | sod | neg |
| 25 | 31 | 44 | MOPP | 56 | mammo | IDC | 7 | 1.8 | neg | neg | neg |
| 26 | 32 | 44 | None | 50 | palpation | IDC | ю | 1.5 | neg | neg | |

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| Patient | Age at HL tx | atient Age at HL tx XRT Dose (Gy) | | Age at BC | Attribution | Histology | Grade | Tumor (cm) | ER status | PR Status | Chemo Age at BC Attribution Histology Grade Tumor (cm) ER status PR Status Her2/neu status |
|----------------|--------------------------|-----------------------------------|------------|-----------|-------------|-----------------|-------|------------|-----------|-----------|--|
| 27 | 33 | 43.6 | ABVD | 44 | palpation | IDC | 1 | 2.2 | neg | neg | neg |
| 28 | 33 | 45 | PAVe | 57 | mammo | IDC | 3 | 2.0 | sod | neg | neg |
| 29 | 33 | 44 | None | 42 | palpation | IDC | 2 | 2.0 | neg | neg | neg |
| 30 | 34 | 44 | None | 51 | mammo | IDC/DCIS | 2 | 0.6 | neg | neg | sod |
| 31 | 35 | 44 | ABVD | 57 | mammo | IDC | 2 | 1.2 | sod | sod | neg |
| 32 | 38 | 30 | Stanford V | 44 | mammo | IDC | 2 | 3.3 | sod | sod | neg |
| 33 | 48 | 44 | MOPP | 79 | mammo | DCIS | 7 | 0.2 | sod | sod | I |
| * Informati | ormation was unavailable | le | | | | | | | | | |

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Breast Cancer Detection and Imaging Era

| | Before 1995 (n=1 cancer) | Before 1995 (n=1 cancer) 1995–2007 (n=21 cancers) After 2007 (n=13 cancers) | After 2007 (n=13 cancers) |
|-------------------------|--------------------------|---|---------------------------|
| Palpation | 0 (0%) | 6 (28%) | 2 (15%) |
| Screening Mammography | 1 (100%) | 14 (67%) | 10 (77%) |
| Prophylactic Mastectomy | 0(0%) | 0 (0%) | 1 (8%) |
| PET | 0 (0%) | 1 (5%) | 0 (0%) |
| Screening Breast MRI | 0 (0%) | 0 (0%) | 0(0)(0) |