Evaluation of radiation exposure to the humeral head and its correlation with patient-reported outcomes in patients undergoing radiotherapy for early breast cancer

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Introduction

Research indicates that up to two-thirds of patients with early breast cancer experience arm or shoulder pain or other symptoms following surgery and radiotherapy. The relationship between morbidity and dose administered to the humeral head is still not fully understood. We seek to determine if the radiation dose to humeral head, radiation technique (3D-CRT versus IMRT/VMAT), and fractionation schedule—correlates with the patient-reported outcomes measures (PROMs).

Methods and Materials

We identified patients who underwent surgery and postoperative radiation therapy for early breast cancer and were included in the institutional prospective database of the Early Individualized Integrated Rehabilitation Program – OREH between November 2019 and April 2023. These patients had completed the EORTC QLQ-C30 and BR23 questionnaires prior to surgery/at baseline and 12 months after the start of treatment. Retrospective delineations of the humeral head and humeral head PRV with a 1 cm safety margin were implemented for each case (**Figure 1**). The treatment planning parameters for all treatment plans were subsequently obtained.

The associations between categorical variables were investigated using Pearson's chi-square test and multivariate analysis. A two-tailed test was used to identify significant differences with a p-value of ≤0.05. The mean values were compared using the non-parametric Kruskal-Wallis test.

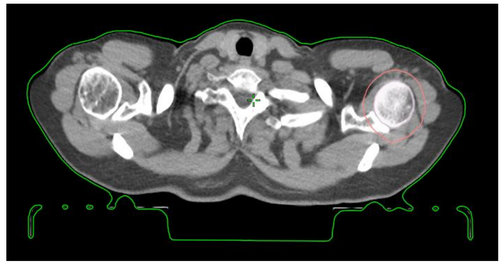


Figure 1: Delineation of the humeral head and humeral head PRV.

Results

We enrolled 298 patients in this study. The majority of patients were treated with breast conserving surgery (N=210; 70.5%) and sentinel lymph node biopsy (N=200; 67.1%). The majority of patients (N=194, 65.1%) underwent moderate hypofractionation consisting of 15-16 fractions of 2,67 Gy with or without tumor bed boost. Regional nodal irradiation (RNI) to levels I-IV with or without internal mammary lymph nodes irradiation was delivered to 121 (40.6%) patients. Patient, tumor and treatment characteristics are presented in **Table 1**. Dosimetric-volumetric parameters of irradiation of the humeral head and humeral head PRV are presented in **Table 2**.

Any pain in arm or shoulder was reported by 110 (36.9%) and 189 (63.4%) patients at baseline and 12 months after treatment start, respectively.

Variable	Humerus	Humerus PRV
D_2, median (range) [Gy]	14.7 (0-51.0)	30.6 (0.1-58.0)
D_{98}, median (range) [Gy]	0.7 (0-14.5)	0.4 (0-2.6)
D_{mean}, median (range) [Gy]	2.3 (0-34.0)	3.6 (0-30.0)
V_{50}, median (range) [cm^3]	0 (0-0)	0 (0-5.7)
V_{45}, median (range) [cm^3]	0 (0-3.4)	0 (0-21.3)
V_{30}, median (range) [cm^3]	0 (0-41.1)	1.5 (0-60.2)
V_{20}, median (range) [cm^3]	0 (0-62.8)	5.4 (0-85.9)
V_{10}, median (range) [cm^3]	1.6 (0-78.2)	15.1 (0-131.6)

Table 2: Dosimetric-volumetric parameters of irradiation of the humeral head and humeral head PRV. Legend: Humerus – humeral head, Humerus PRV –humeral head planning organ at risk volume, Dx - dose received by x % of the target volume, Dmean - mean absorbed dose within a target volume, Vx - volume receiving x Gy.

Pain

Median D_{mean} doses to humeral head and humeral head PRV were 2.3 Gy (range 0–34 Gy) and 3.6 Gy (range 0–30 Gy), respectively. Multivariate ordinal regression model analysis confirmed a statistically significant association between the dose received by 2% of the humeral (D2%) (p=0.044), volume of humeral head receiving ≥10 Gy (V10Gy) (p=0.028) and V20 Gy (p=0.045) and any pain in arm or shoulder 12 months after diagnosis.

Arm mobility

At baseline and 12 months after treatment initiation, 39 (13.1%) and 142 (47.7%) patients, respectively, reported any difficulties in raising or moving their arm sideways. This was correlated with humeral head V20 Gy (p=0.029) and V30 Gy (0.035) in a multivariate analysis.

Irradiation to lymph node regions, radiation technique (3D-CRT versus IMRT/VMAT), fractionation schedule (hypofractionation versus conventional fractionation), type of breast and axillary surgery were not correlated with arm or shoulder pain (or other symptoms) and PROMs.

Characteristics		
Age, median ([IQR]) [years]		51.1 (44–58)
BMI, median ([IQR]) [kg/m2]		25.9 (22.3–28.4)
Stage, n (%)	Not defined	5 (1.7)
	I	132 (44.3)
	II	112 (37.6)
	III	49 (16.4)
Locoregional treatment		
Surgery, n (%)	No surgery	1 (0.3)
	Lumpectomy	210 (70.5)
	Mastectomy	87 (29.2)
LN surgery, n (%)		
	Sentinel LN biopsy	209 (70.1)
	Axillary dissection	89 (29.9)
N of positive LN, median ([IQR])		0 (0-36)
N of removed LN, (median ([IQR])		2 (0-42)
Radiation therapy, n (%)	Yes	298 (100)
Volume of radiation, n (%)	WBRT/Chest Wall only	177 (59.4)
	Levels I-IV ± IMN	121 (40.6)
Boost, N (%)	No	164 (55)
	Yes - SIB	86 (28.9)
	Yes - Electrons	44 (14.8)
	Yes - Photons	4 (1.3)
Radiation technique, n (%)	3D-CRT	198 (66.4)
	IMRT	100 (33.6)
Total radiation dose, median ([IQR]) [Gy]		44.6 (40.1–50)
N of fractions, median ([IQR])		19 (15–25)
Fractionation		
	Conventional fractionation	104 (34.9)
	Moderate hypofractionation	194 (65.1)
Systemic treatment		
Chemotherapy, n (%)		
	Yes	160 (53.7)
	No	138 (46.3)

Table 1. Patient, tumor and treatment characteristics of the patient cohort (n = 298).
Legend: IQR – interquartile range, BMI – body mass index, N – number, LN – lymph nodes, SIB –simultaneous integrated boost, 3D-CRT – three-dimensional conformal radiation therapy, IMRT – intensity-modulated radiation therapy.

Conclusions

The irradiation of the humeral head correlates with the development of arm or shoulder symptoms following surgery and radiotherapy for early breast cancer. More research is needed toward identifying dose to organs at risk that will be considered when planning future radiation therapy.

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