Variability of Medial and Lateral Borders Delineation in Guidelines for Postmastectomy Irradiation Significantly Affects Radiation Dose Received by Left Lung and Heart

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Abstract:

Background: Post-operative chest wall irradiation improves local control & survival with higher techniques (conformal & intensity modulated) are recommended in left side. These techniques involve mastectomy bed Clinical Target Volume (CTV) delineation which varied clearly among guidelines especially for the lateral margin with subsequent possible effects on dose received by lung & heart (in left sided cases). Aim of work: Comparison between American & European guidelines to a more anatomical (from our point of view) method using wire following anatomical lines regarding post left mastectomy chest wall CTV volume & doses received by the heart & left lung.
Methodology: One oncologist had delineated 10 cases referred for radiation therapy of the chest wall & peripheral lymphatics following left modified radical mastectomy. He delineated every case according to Radiation Therapy Oncology Group (RTOG), European Society of Therapeutic Radiology and Oncology (ESTRO) & according to an anatomically set wire during scanning. Plans were set for each delineation by an expert radiation physicist. Results of the 3 plans were compared regarding coverage, homogeneity of CTV & doses to risk organs.
Results: The three CTVs were well covered & homogeneously treated. Statistically significant less left lung V20Gy & V30Gy for anatomical wire based delineation (16.0 +/- 4.1% &12.75 +/- 2% respectively) compared to ESTRO (19.1 +/- 1.73 & 15.2 +/- 5.1 respectively) & RTOG (18.22 + 1.6 & 14.52 + 5.3 respectively), p=0.001 for V20Gy & 0.01 for V30Gy. Cardiac D50% was statistically significantly lower (101.6 + 41.2cGy) vs (141 +/- 81cGy & 132 +/- 93 cGy, p= 0-00001) for ESTRO & RTOG respectively.
Conclusion: Delineation of left mastectomy chest wall CTV based on anatomical landmarks guided by wire set during patient scanning may reduce cardiac & pulmonary doses compared to ESTRO & RTOG. Clinical follow up of cases treated based on this delineation is highly recommended specially to evaluate local recurrence.

Key words: Left breast cancer, Conformal radiotherapy, delineation lateral border.

Received: 29 August 2021
Accepted: 1 September 2021

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Introduction:

Delineation of Clinical Target Volume (CTV) is the main step in three Dimensional Conformal (3DCRT) [1]. Mastectomy is still a commonly used breast cancer surgery especially in developing countries, including Egypt [2-4]. CTV is defined as the demonstrable tumor plus the microscopic disease or only microscopic & sub-microscopic disease if tumor was removed (ICRU report 52 & 60) [5,6]. A remarkable differences however exists among variable guidelines in delineation of chest wall CTV specially for the lateral margin which is defined as mid-axillary line or anterior end of latissimus dorsi muscle by Radiation Therapy Oncology Group (RTOG) [7], while the European Society of Therapeutic Radiology and Oncology (ESTRO) defined it as same level of lateral end of contralateral breast [8]. Even, many experts used wire localization for the anatomical delineation of the surgically removed breast [9]. It is expected that lateral margin delineation will

affect the standard tangential fields and therefore the ipsilateral lung & heart (in left side) volumes received irradiation to high doses. It is established that these volumes are significant indicators of subsequent late side effects [10]. A decrease of these volumes can improve toxicity, quality of life & even survival through reduction of cardiac mortality [11]. To our knowledge, no study evaluated the effect of using various guidelines for CTV delineation on outcome regarding doses received by various Organs At Risk (OAR) nor compared these guidelines to the more anatomical based wire localization we believe in.

Aim of work:

To examine the effect of using different guidelines for chest wall CTV delineation on the outcome regarding doses received by heart and left lung (in post left mastectomy irradiation) and compare these outcomes to that of wire based delineation.

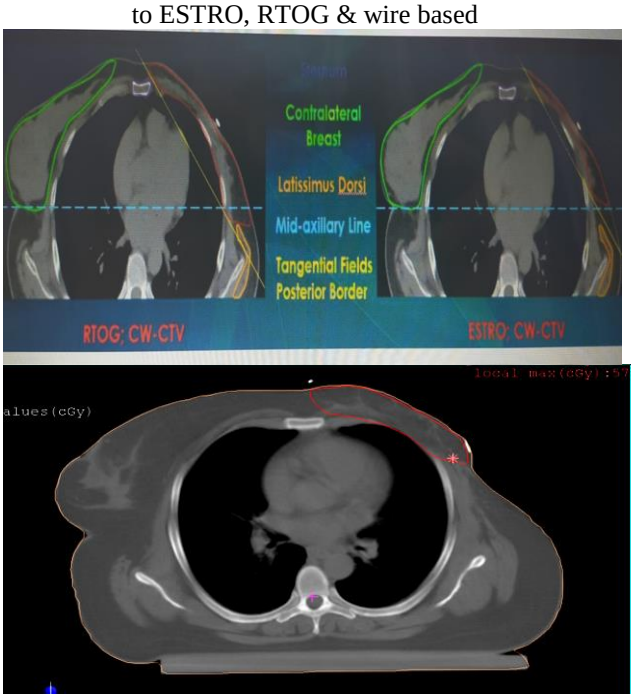
Methodology:

Ten patients with left mastectomy indicated for post-operative irradiation to chest wall (T3, T4 or N+) were CT scanned in treatment position with slice thickness of 5 mm. from 4th cervical vertebra (C4) to below costo-phrenic angles. Wire was placed on patient skin anatomically followed presumed breast insertion from upper border of 2nd rib above to medial border of sternum medially till 4th rib where the wire was shifted laterally till lower border of the 6th rib in a mirror image fashion to the right breast. Wire reached lower border of 6th rib below and followed the anterior axillary line laterally from 6th rib below to lower border of 3rd rib above then it was shifted laterally to mid-axillary line till the level of upper border of 2nd rib anteriorly to cover the presumed breast tail (the exact anatomical lateral extension). CT scan was sent to Treatment Planning System (TPS) ECLIPS v.11. Delineation by one radiation oncologist followed 2 different guidelines namely RTOG [7] & ESTRO [8] in addition to delineation of chest wall underlying the wire from skin to rib-pleural interface (figure-1). All CTVs were delineated in the same day. Accordingly, 3 CTVs for chest wall were presented to the same medical radiation physicist. Three tangential plans were accomplished (plan for each CTV) aiming at 50Gy in 25 fractions homogenously to CTV with maximum sparing of OAR mainly heart & left lung. The three plans were compared to each other.

Statistical Analysis:

Data were statistically described in terms of range, mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

Figure-1: Delineation of chest wall CTV according to ESTRO, RTOG & wire based



Chest wall - WBD

Results:

CTVs:

The volume of chest wall CTVs showed statistically significant difference with mean volumes of 610.5 +/- 192cc, 600.4 +/- 188.8 & 536.07 + 168.65 for ESTRO, RTOG & wire based delineation respectively (Table"1"). The dose coverage & homogeneity of the CTVs were not statistically different as assessed by D95%,V45Gy, Dmin&Dmax for the different CTVs (Table"2").

Table (1): different chest wall volumes based on different delineation guidelines

Guideline for delineation	Chest wall CTV volume(cc)	p-value
RTOG	610.5 +/- 192	
ESTRO	600.4 +/- 188.8	0.000000
Wire based	536.07 ± 168.65	

RTOG; Radiation Therapy Oncology Group
ESTRO; European Society of Therapeutic Radiology and Oncology

Table (2): The dose coverage & homogeneity of the CTVs based on different guidelines

Guideline	ESTRO (mean +/- SD)	RTOG(mean +/- SD)	Wire based(mean +/- SD)	p-value
V45Gy (%)	96.9 +/- 2.15	98.5 +/- 2.2	98.7 +/- 0.9	0.616
D95%(Gy)	47.5 +/- 1.67	48.3 +/- 1.7	48.3 +/- 0.7	0.801
Dmax. (Gy)	52.3 +/- 1.08	53.2 +/- 1.1	52.9 +/- 0.8	0.265
Dmin. (Gy)	44.5 +/- 1.47	45.2 +/- 1.5	45.1 +/- 1.7	0.788

D95%,V45Gy, Dmin & Dmax definitions according to ICRU report 60

➢*OAR:*

1- left Lung dose (Table-3): The V20Gy & V30Gy were significantly lower in wire based delineation than both ESTRO & RTOG guidelines based delineation. V20Gy & V30Gy received by lt. lung for plans based on WBD was 16.0 +/- 4.1% &12.75 +/- 2% respectively vs those based on ESTRO (19.1 +/- 1.73 & 15.2 +/- 5.1 respectively) or RTOG guidelines (18.22 + 1.6 & 14.52 + 5.3 respectively), p=0.001 for V20Gy & 0.01 for V30Gy.

Table-3: Left lung dose (V20Gy & V30Gy) for different plans based on ESTRO, RTOG guidelines & wire based delineation

Guideline	ESTRO (mean +/- SD)	RTOG (mean +/- SD)	Wire based(mean +/- SD)	p-value
V20Gy(%)	19.1 +/- 1.73	18.22 ± 1.6	16.0 +/- 4.1	0-0001
V30Gy (%)	15.2 +/- 5.1	14.52 ± 5.3	12.75 +/- 2	0.01

V20Gy, V30Gydefinitions according to ICRU report 60

2 Cardiac dose (Table-4): The D50%, V50Gy & V40Gy were significantly lower in wire based delineation than both ESTRO & RTOG guidelines based delineation. A statistically significant lower D50% received by the heart in plans based on WBM delineation (101.6 + 41.2 Gy) compared to plans based on ESTRO & RTOG guidelines based CTV (141 +/- 81cGy & 132 +/- 93 cGy respectively, p= 0-00001). However, no significant difference detected regarding both V40Gy & V50Gy.

Table-4: Cardiac dose (MHD, D50% & V40Gy) for different plans based on ESTRO, RTOG guidelines & wire based delineation. Guideline ESTRO (mean +/- SD)

Guideline	ESTRO (mean +/- SD)	RTOG (mean +/- SD)	Wire based (mean +/- SD)	p-value
V50Gy (%)	0.29 +/- 0.08	0.28+/-0.07	0.22 ± 0.7	0.8
V40Gy (%)	3.1 +/- 0.8	3 +/- 0.7	2.33 ± 0.9	0.07
D50% (Gy)	141 +/- 81	132 +/- 93	101.6± 41.2	0.0000

V40Gy, V50Gy & D50% definitions according to ICRU report 60

Discussion:

The notable variation in CTV delineation exists among different guidelines in delineation of chest wall CTV specially for the lateral margin [7-9] is thought to much affect the ipsilateral lung & heart (in left side) volumes irradiated to high dose which may result in subsequent late toxicities [10], negative impact in quality of life & even increase in cardiac mortality [11]. This is the 1st study evaluated the effect of using various guidelines for CTV delineation on outcome and compared these guidelines to the more anatomical based wire localization we believe in. Ten patients with left mastectomy indicated for post-operative irradiation to chest wall (T3 or T4) were studied to show the effect of chest wall CTV delineation protocols on doses received by heart and left lung. The WBD was more anatomically based from our point of view especially the 2 international guidelines have shown much variation in the lateral margin. Delineation was established by one radiation oncologist & in the same day to avoid the effect of inter observer variability in CTV delineation which showed great variation in the literature [12]. All plans were generated by senior medical radiation physicist (PhD holder). The resultant CTV for the more anatomically based WBD was significantly smaller than those resulting from delineations based on ESTRO & RTOG guidelines which could be attributed to reduced volume of wire based CTV below 4th rib medially & laterally specially below the 3rd rib. All homogeneity & coverage parameters were acceptable for all plans generated for each CTV with no statistically significant difference as shown in table (2). However, a significant reduction in doses received by OAR have been noticed (tables 3 & 4), which could be explained by reduced volume of wire based CTV. To our knowledge, no study evaluated the effect of reduction of lateral border to the anatomically oriented WBD we used on dose to OAR. This reduction in dose to OAR warrants further studies and clinical follow for recurrences & clinical toxicity.

Conclusion:

Wire based delineation of post left mastectomy chest wall CTV delineation significantly reduced high dose volume received by heart & left lung. Larger trial with clinical follow up to evaluate for being not inferior to ESMO &/or ESRTO guidelines based treatment regarding local recurrence.

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