



Interobserver Variation in Delineation of Tumor Bed in Postoperative Radiotherapy of Intact Breast and Its Impact on Planning Outcome

Thesis

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ABSTRACT

Background: Radiotherapy following Breast-conservative surgery is a standard treatment for breast cancer, Techniques developed to obtain better target definition, dose homogeneity and coverage, accurate tumor bed localization and delineation is considered the current golden standard.

Objectives: The aim of this work is to evaluate interobserver variability (I.O.V) in tumor bed delineation (evaluated by conformity index) and its effect on planning outcome (e.g homogeneity, coverage and dose distribution).We tried also to define any subgroup with marked I.O.V.

Methods: A total number of fifty female patients included in this study with breast cancer after breast conservative surgery presented for post operative adjuvant radiotherapy. Target volume delineation by observer (1) on the planning system ,the boost was delineated by observer (1) and then observer (2) delineated the boost separately using the same plan put for observer (1)delineation.

Results: Conformity index ranged from 0.50 to 0.83 with mean value $\pm$ SD (0.66 ± 0.09) Percentage of volume receiving 90% of prescribed dose(V90) boost mean value for observer (1) was $= 98.6 \% \pm 2.3 \%$,while for observer (2) $= 95.5 \pm 6.8$ (P value < 0.001). Dose received by 90% of Planning Target Volume (PTV) (D90) boost for observer (1) $= 63.9 \text{ Gy} \pm 2.1 \text{ GY}$ while for observer (2) $= 62 \text{ Gy} \pm 2.9 \text{ GY}$ (P value < 0.001). .Minimal dose received by 2% of PTV(D min)for observer (1) $= 60.5 \text{ Gy} \pm 4 \text{ Gy}$ while for observer (2) $= 57 \text{ Gy} \pm 4.6 \text{ Gy}$ (P value < 0.001). and maximal dose received by 2% of PTV(D max)for observer (1) $= 67.5 \text{ Gy} \pm 1.6 \text{ Gy}$ while for observer (2) $= 67.4 \text{ Gy} \pm 1.7 \text{ Gy}$ (p-value $=0.095$). We failed to define any specific subgroup with marked I.O.V

Conclusion: There was an Interobserver variability in tumor bed delineation between observer (1) and observer (2) , and it has a significant effect on treatment plan outcome i.e (coverage, homogeneity) for tumor bed ,with no subgroup with significant difference.

Keywords : *Breast cancer, Radiotherapy, Interobserver variation.*

CONTENTS

	<i>Page</i>
List of Abbreviations	IV
List of Figures.....	VII
List of Tables	VIII
INTRODUCTION AND AIM OF THE WORK	1
REVIEW OF LITERATURE:	
▪ Chapter I: General outlines in Mangement of Breast Cancer	4
▪ Chapter II: Role of radiotherapy in breast conservative surgery	25
▪ Chapter III: Techniques of Breast Irradiation	41
▪ Chapter IV : Tumor bed delineation and interobserver variability ...	67
PATIENTS AND METHODS	77
RESULTS	88
DISCUSSION	101
SUMMARY	111
CONCLUSIONS	115
RECOMMENDATIONS	116
REFERENCES	117
ARABIC SUMMARY	

List of Abbreviations

AC/TAC	: adriamycin and cyclophosphamide/ taxol, adriamycin and cyclophosphamide
APBI	: accelerated partial breast irradiation
ASTRO	: American Society of Radiation Oncology
BCS	: Breast conserving surgery
BCT	: Breast conserving therapy
CALGB	: Cancer and Leukemia Group B
CI	: Conformity index
CIS	: carcinoma in situ
CMF/CAF	: cyclophosphamide, methotrexate and fluorouracil/ cyclophosphamide, adriamycin and fluorouracil
Co	: Cobalt
COM	: center of mass
CT	: computed tomography
CTV	: Clinical Target Volume
CVS	: Cavity visualization score
DCIS	: Ductal carcinoma in situ
DFS	: Disease-free survival
DRRs	: Digitally reconstructed radiographs
DVH	: Dose volume histogram
EB-APBI	: External beam - accelerated partial breast irradiation
EBCTCG	: Early Breast Cancer Trialists' Collaborative Group
EC/CEF	: epirubicin and cyclophosphamide/ cyclophosphamide, epirubicin and fluorouracil
ECG	: Electriccardiogram
EIC	: Extensive intraductal carcinoma
EORTC	: European Organisation for Research and Treatment of Cancer
EPBI	: External Partial Breast Irradiation
EPID	: Electronic portal imaging devices
ER	: Estrogen receptor
GBT	: Glandular breast tissue
GMI	: Geographical miss index
GTV	: Gross tumor volume

HDR	: High dose rate
HER2	: Human Epidermal Growth Factor Receptor 2
HR	: Hazard Ratio
ICRU	: International Commission on Radiation Units
IDC	: Invasive ductal carcinomas
ILC	: Invasive lobular carcinoma
IMN	: Internal Mammary Nodes
IMRT	: Intensity modulated radiotherapy
IMs	: Internal margins
IMV	: Internal mammary vessels
IORT	: Intraoperative radiotherapy
ITV	: Internal target volume
JCRT	: Joint Center for Radiation Therapy
LC	lumpectomy cavity
LCIS	: lobular carcinoma in situ
LDR	: Low Dose rate
LFR	: Limited field radiation
LR	: Local recurrence
LRR	: Local recurrence rate
MBC	: Metastatic breast cancer
MLC	: Multi leaf collimator
MR	: Magnetic resonance
MRI	: Magnetic resonance imaging
mTOR	: Mammalian target of rapamycin
NCCN	: National Comprehensive Cancer Network
NCI	: National cancer institute
NCT	: Neoadjuvant chemotherapy
NSABP	: National Surgical Adjuvant Breast and Bowel Project Experience
NTI	: Normal tissue index
OAR	: Organ at risk
PBI	: Partial breast irradiation
PBT	: Proton beam therapy
PD	: Prescribed dose
PET	: Positron emission tomography
PMRT	: Postmastectomy radiation therapy

PRV	: Planning at risk volume
PTV	: Planning Target Volume
RT	: radiotherapy
RTOG	: Radiation Therapy Oncology Group
SCLN	: Supraclavicular Lymph nodes
SIB	: Simultaneous Integrated Boost
SLNB	: Sentinel lymph node biopsy
SM	: Setup margin
SPECT	: Single photon emission computed tomography
SPSS	: Statistical Package for the Social Science
TC	: Technetium
TC/TCH	: Taxotere and cyclophosphamide/ taxotere, cyclophosphamide and herceptin
Uk	: United kingdom
UV	: Ultraviolet
VBV	: Visible boost volume
VEGF	: Vascular endothelial growth factor
WBI	: Whole breast irradiation
3DCRT	: three dimensional conformal radiotherapy
4D	: four-dimensional
5-FU	: 5-fluorouracil

LIST OF FIGURES

Fig. No.	Title	Page
1.	Statistical representation of cancer cases and deaths	4
2.	Targeting hallmarks of cancer for therapy	11
3.	Sentinel lymph node biopsy	13
4.	survival curves according to treatment assignment in node negative and node positive women	39
5.	Treatment and mortality in women aged 40–69 with T1 or T2 node-negative or node-positive non-metastasized breast cancer treated by breastconserving surgery and axillary dissection.	40
6.	Axial CT image of breast tissue	63
7.	Definitions of conformity index, geographical miss index and normal tissue index	63
8.	Mri- versus ct-based volume delineation of lumpectomy cavity	71
9.	Beam arrangements for three-dimensional conformal radiotherapy, intensity-modulated radiotherapy and proton beam therapy	72
10.	Dose distribution of three-dimensional conformal radiotherapy, intensity-modulated radiotherapy, helical tomotherapy, and proton beam therapy in the axial plane.	76
11.	Delineation of Heart, Lungs, Contra lateral breast & Spinal Cord	80
12.	Delineation of Thyroid gland & Spinal Cord	80
13.	Delineation of Planning Target Volume Breast "in conservative surgery	81
14.	Delineation of Supraclavicular Lymph Nodes	82
15.	Interobserver variation between the delination of tumor bed between observer (1) and observer (2)	83
16.	Plan Evaluation	85
17.	Age group of patients	90
18.	Body mass index of patients	90
19.	Menopausal state of patients	91
20.	Pathological Type in patients	94
21.	T Stage Of tumour	94
22.	Conformity Index of patients	96
23.	Dosimetric Data of patients	99
24.	DVH of boost of observer (1) and boost of observer (2)	100

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page</i>
1.	Risk Factors for breast cancer	5
2.	Effect of age and radiotherapy on local recurrence in patients who underwent breast-conserving therapy	32
3.	10-year actuarial local recurrence with and without supplementary radiotherapy in patients who underwent breast-conserving surgery for early breast cancer	32
4.	Demographic data of patients	88
5.	Pathological data of patients	92
6.	Breast measurements in the fifty patients studied with breast cancer	95
7.	Treatment adapted in fifty studied patients	95
8.	Conformity Index Between the 2 observers	96
9.	Conformity Index in subgroups of the fifty studied patients	97
10.	Dosimetric Data Comparison between the 2 Observers And effect on plan outcome	98
11.	Dose received by risk structures	100

INTRODUCTION

Breast cancer is the most common female malignancy in women in almost all Arab countries (**Salim et al, 2009**).

One of the very important factors in reducing the impact of breast cancer is effective loco regional therapy (**Donovan et al, 2006**)

Treatment should be based on clinical extent and pathologic characteristics of the tumor ,biologic prognostic factors ,patient age ,menopausal status ,and the preference and psychological profile of the patient, Breast conservation therapy is preferred by many for T1,T2,and selected T3 tumors ,Since the results of large randomized clinical trials confirmed that the type of surgical procedure (modified radical mastectomy or conservative) has no effect on the survival time of women with stage I and II breast cancer, breast conserving surgery has been used world wide (**Luini et al., 2006**)

Breast-conserving radiotherapy (RT) is the standard treatment for breast cancer ,Over recent years, new techniques have been developed to obtain better target definition, dose homogeneity and conformity , Radiation oncologists have three main objectives: definition of treatment volumes (breast, axilla, supraclavicular lymph nodes (SCLNs) and infraclavicular lymph nodes (ICLN)), homogeneous coverage of these volumes and avoidance of organs at risk (OAR) to reduce early and late complications (**Gonzales et al., 2006**).

Accurate delineation of target volumes and OARs is prerequisite and critical for conformal RT, as all subsequent decisions on treatment

planning and delivery are based on these volumes. A few previous studies have reported that there are significant variations in defining target volumes for breast RT, For example, Hurkmans et al (2001) observed, in a single institutional study, that the clinical target volume (the breast volume) delineated based on CT by multiple observers varied by 17.5%.

In another single institutional study, **Struikmans et al (2005)** showed that two volumes delineated by different observers overlapped on an average of 87% or 56% for breast or boost volumes, respectively. **Landis et al (2007)** reported large variations in delineating the lumpectomy cavity among four academic radiation oncologists who specialize in breast RT. It has been shown in some of these studies that detailed delineation instruction and/or training can improve delineation consistency.

AIM OF THE WORK

1. To evaluate interobserver variability in tumor bed delineation which is evaluated by conformity index and determination of factors affecting the variability e.g age ,menopausal state ,obesity and tumor size.
2. To evaluate the effect of interobserver variability on planning outcome (e.g homogeneity ,coverage and dose distribution).
3. To evaluate the effect of interobserver variability among different groups of patients e.g menopausal state, obesity, age, tumor size and effect on plan outcome.

CHAPTER I

General outlines in Management of Breast Cancer

Introduction:

The global burden of cancer continues to increase mostly because of the aging, factors like exposure to UV radiation, pollution and a rise in the adoption of cancer causing behaviors (obesity, poor diet, smoking habits etc.). Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer death among females (Jemal et al, 2011).

Statistics estimated almost 230,480 new cases of the invasive breast cancer occurring among women during 2011 and about 2,140 new cases in men. For the year 2012, almost 39,970 deaths due to breast cancer are expected along with 226,870 new cases (Cancer Facts & Figures, 2011).

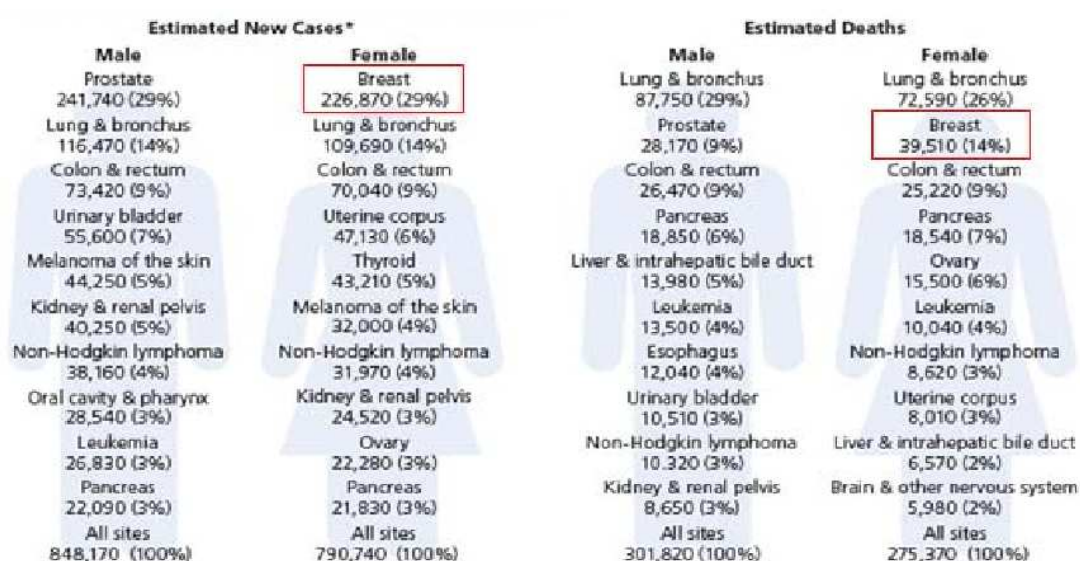


Figure (1): Statistical representation of cancer cases and deaths (Cancer Facts & Figures, 2011).