Locoregional recurrence in patients with node negative early breast cancer who received adjuvant hypofractionated radiotherapy regimen vs. conventional fractionation regimen after breast conservative surgery retrospective study

Thesis

Submitted for Partial Fulfillment of Master Degree in
Clinical Oncology and Nuclear Medicine

By

Engy Salah Ramzy Todary

M.B.B.C.H

Under Supervision of

Prof.Dr.Hany Mohammed Abd Elaziz

Professor of clinical Oncology and Nuclear Medicine
Faculty of Medicine -Ain-Shams University

Prof. Dr. Dina Ahmed Salem

Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine -Ain-Shams University

Dr. Amr Shafik Tawfik

Assistant Professor of Clinical Oncology and Nuclear Medicine
Faculty of Medicine Ain-Shams University

Faculty of Medicine
Ain Shams University
2019

Acknowledgment

First, and foremost, I feel always indebted to Allah, the Most Kind and the Most Merciful.

*Words can never express my hearty thanks and indebtedness to **Prof. Dr. Hany Mohammed Abd Elaziz,** Professor of clinical Oncology and Nuclear Medicine , Faculty of Medicine -Ain-Shams University, for his great support and continuous encouragement and guidance to complete this work. It was a great honor to work under his guidance and supervision.*

*I wish also to express my gratitude to **Prof. Dr. Dina Ahmed Salem,** Professor of Clinical Oncology and Nuclear Medicine, Faculty of Medicine -Ain-Shams University, for her great efforts, kind advice, support and encouragement throughout the whole work.*

*My deepest appreciation and grateful thanks to **Dr. Amr Shafik Tawfik,** Assistant Professor of Clinical Oncology and Nuclear Medicine Faculty of Medicine Ain-Shams University, for his meticulous supervision, continuous guidance, and constructive criticism.*

*Last but not least, I can't forget to thank all members of my Family, specially my **Parents**, and my **Friends,** for their great support and pushing me forward in every step of my life.*

Engy Salah Ramzy Todary

List of Contents

List of Abbreviations

Abbrev.	Full-term
ABUS	: Automated Breast Ultrasound System
AIs	: **A**romatase Inhibitors
ALN	: Axillary Lymph Node
AR	: Axillary Recurrence
ASTRO	: American Society of Radiation Oncology
BCS	: Breast Conservative Surgery
BCT	: Breast Conservative Therapy
BSGI	: Breast Specific Gamma Imaging
CEDM	: Contrast Enhanced Digital Mammography
CESM	: Contrast Enhanced Spectral Mammography
CFRT	: Conventional Fractionation Radiotherapy
CMF	: Cyclophosphamide, Methotrexate and Fluorouracil
DCIS	: Ductal Carcinoma In Situ
DFS	: Disease Free Survival
DWI	: Diffusion-Weighted Image
EBCTCG	: Early Breast Cancer Trialists’ Collaborative Group
EQD2	: Equivalent Dose Delivered in 2 Gy fractions
ER	: ER receptor
F	: Fraction
G	: Grade
HER2	: Human epidermal growth factor receptor 2
HFRT	: Hypofractionated Radiotherapy
HHUS	: Hand-Held US
HP	: Herceptin/Perjeta
IHC	: Immunohistochemistry

ILC	: Invasive Lobular Carcinoma
IMRT	: Intensity Modulated Radiation Therapy
IORT	: Intra-Operative Radiotherapy
LCIS	: Lobular Carcinoma In-Situ
LRR	: Locoregional Recurrence
LVI	: lymphovascular Invasion
MRI	: Magnetic Resonance Imaging
NCCN	: National Comprehensive Cancer Network
NICE	: National Institute for Health and Care Excellence
OS	: Overall Survival
PEM	: Positron Emission Mammography
PR	: Progesterone Receptor
ROR	: Risk Of Recurrrence
RS	: Recurrence Score
SD	: Standard deviation
SLN	: Sentinel Lymph Node
SLNB	: Sentinel Lymph Node Biopsy
SPSS	: Statistical Package for the Social Sciences
TNBC	: Triple Negative Breast Cancer
US	: Ultrasound
WBI	: Whole Breast Irradiation

List of Tables

List of Figures

Introduction

Worldwide, breast cancer is the most frequently diagnosed cancer accounting for more than a million cases each year **(Globocan, 2012)**, including low and middle income countries **(WHO 2013),** incidence rates are higher in north America, Australia, western and northern Europe, and lowest in Asia and sub-Saharan Africa **(Torre et al., 2015),** these international variation is likely attributed to societal changes as a consequence of industrialization such as changes in fat intake, body weight, age at menarche, reproductive patterns of fewer pregnancies and later age at first birth (**Siegel et al., 2018**). Breast cancer mortality rates have been decreasing since the 1970s which is likely attributed to improved screening modalities and adjuvant therapies (**Kohler et al., 2015).**

Breast cancer is treated with a multidisciplinary approach that involves surgical oncology, radiotherapy and medical oncology; these combined modalities have been associated with a reduction in breast cancer mortality **(Kesson et al., 2012).**

patients with early-stage breast cancer undergo primary surgery (lumpectomy or mastectomy) with or without radiation therapy (RT), followed by adjuvant systemic therapy based on primary tumor characteristics, such as tumor size, grade, number of involved lymph nodes, the status of estrogen (ER) and progesterone receptors (PR), and expression of the human epidermal growth factor 2 receptor (HER2) **(Taghian et al., 2019).**

Breast conserving therapy (BCT) is comprised of breast-conserving surgery (BCS) plus radiation therapy, randomized trials have demonstrated equivalent disease-free and overall survival (OS) between mastectomy and BCT **(Litière et al., 2012)**.

The objective of adjuvant radiotherapy is the eradication of any tumor deposits remaining after surgery which reduces the risk of Locoregional recurrence (LRR) and improves breast cancer specific and overall survival **(Darby et al., 2011)**.

Conventional Whole-Breast Irradiation (WBI) delivers 1.8 to 2 Gy daily fractions (F) over 4.5 to 5 weeks to a total dose of 45 to 50 Gy with or without a 10 to 16 Gy boost to the tumor bed over 5 to 8 fractions for a total dose of 60 to 66 Gy delivered over 6 to 7.5 weeks, while hypofractionated schedule, delivers more radiation per dose, but the overall treatment duration is shorter (40 to 42.5 Gy in approximately three to five weeks with or without a boost. The American Society for Radiation Oncology (ASTRO) strongly encourage the use of hypofractionated regimen in women with invasive breast cancer receiving WBI with or without inclusion of the low axilla, the preferred dose-fractionation scheme is hypofractionated WBI to a dose of 4000 cGy in 15 fractions or 4250 cGy in 16 fractions (**Benjamin et al., 2018)**. Cosmetic and disease outcomes have been found to be equivalent between both hypofractionated and conventional schedules as demonstrated in a meta-analysis of four randomized trials, in which 7095 patients were enrolled (**James et al., 2010).**

A boost to the tumor bed is recommended for patients with invasive breast cancer with any of the following criteria: age ≤ 50 years with any histopathological grade, or if AGE 51 to 70 years with high grade or a positive margin **(Benjamin et al., 2018).**

WBI is associated with acute toxicities that involve the area treated such as skin, muscle, and internal organs. Also it may cause long-term complications, including cardiotoxicity, lung injury, and second malignancies **(Taylor et al., 2017).**