# Randomized Prospective Study Comparing Conventional Versus Hypofractionated Adjuvant Radiotherapy in Node Positive Breast Cancer

Thesis

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| *AMP* | *Adenosine monophosphate* |
| *ASTRO* | *American Society for Radiation Oncology* |
| *BCS* | *Breast-Conserving Surgery* |
| *CTCAE* | *Common Terminology Criteria for Adverse Events* |
| *D max* | *Maximum dose* |
| *DFS* | *Disease Free Survival* |
| *DVH* | *Dose Volume Histogram* |
| *ECE* | *Extra- Capsular Extension* |
| *EORTC* | *European Organization for research and Treatment* |
| *EQD2* | *Equivalent dose in 2 Gy fractions* |
| *ER* | *Estrogen Receptor* |
| *ERp* | *Estrogen Receptor Positive* |
| *GEC-ESTRO* | *Groupe Europeen de Curietherapie-European Society for Theraputic Radiology and Oncology* |
| *IDC* | *Invasive Ductal Carcinoma* |
| *ILC* | *Invasive Lobular Carcinoma* |
| *IMC* | *Invasive Medullary Carcinoma* |
| *L.Ns* | *Lymph Nodes* |
| *LVI* | *Lymphovascular Invasion* |
| *MRM* | *Modified Radical Mastectomy* |
| *NCCN* | *National Comprehensive Cancer Network* |
| *NSABP* | *National surgical Breast and Bowel Project* |
| *NTCP* | *Normal Tissue Complication Probability* |
| *OS* | *Overall survival* |
| *PMRT* | *Postmastectomy Radiation Therapy* |

# List of Abbreviations (Cont...)

| Abb. | Full term |
|---|---|
| *PR* | *Progesterone Receptor* |
| *RIBP* | *Radiation Induced Brachial Plexopathy* |
| *RNI* | *Regional Nodal Irradiation* |
| *RT* | *Radiation Therapy* |
| *RTOG* | *Radiation Therapy Oncology Group* |
| *SCV* | *Supraclavicular Area* |
| *TCP* | *Tumor Control Probability* |

# ABSTRACT

Our study revealed that Hypofractionated adjuvant radiotherapy in node positive breast cancer patients is equivalent to conventional fractionation, in disease free survival, cosmetic outcome and arm lymphoedema, with decreased early skin reactions; the DFS was 32.4&36.2 months in conventional and hypofractionated arms respectively, (p:0.6),no statistical significant difference in the excellent/good cosmetic score; 46.2%&71.4% in patient scoring respectively (p:0.182), 8%&29% in doctor scoring (p:0.32) respectively, the prevalence of arm lymphoedema was 40% & 22.2% respectively (p:0.149), while hypofractionated radiotherapy significantly lower the incidence of dry desquamation 28.1% in comparison to conventional fractionation 52.9% (p:0.04), with border line significant lowering of skin darkness (p:0.054), but insignificantly lower wet desquamation (p:0.601).

These results are consistent with the results of the main randomized trials comparing hypofractionation radiotherapy versus conventional fractionation in breast cancer, proving that they are equally effective as regard the loco-regional control, systemic metastasis, overall survival, excellent/good cosmetic outcome, radiation induced pneumonitis, ischemic heart disease and radiation predisposed rib fraction, with lower costs and better quality of life; making hypofractionation a preferred choice for early breast cancer management.

***Keywords:*** Radiation Induced Brachial Plexopathy - Regional Nodal Irradiation - Tumor Control Probability

# INTRODUCTION

Breast cancer is the most common cancer among US women, accounting for 30% of all newly diagnosed cancer cases and the second most common cause of death after lung cancer. The American cancer society estimated that 266,120 new cases of invasive breast cancer diagnosed among women in 2018, and approximately 41,400 women are expected to die from breast cancer ***(American Cancer Society, 2018).***

**Estimated New Cases**

| Males | | | | Females | | |
|---|---|---|---|---|---|---|
| Prostate | 164,690 | 19% | | Breast | 266,120 | 30% |
| Lung & bronchus | 121,680 | 14% | | Lung & bronchus | 112,350 | 13% |
| Colon & rectum | 75,610 | 9% | | Colon & rectum | 64,640 | 7% |
| Urinary bladder | 62,380 | 7% | | Uterine corpus | 63,230 | 7% |
| Melanoma of the skin | 55,150 | 6% | | Thyroid | 40,900 | 5% |
| Kidney & renal pelvis | 42,680 | 5% | | Melanoma of the skin | 36,120 | 4% |
| Non-Hodgkin lymphoma | 41,730 | 5% | | Non-Hodgkin lymphoma | 32,950 | 4% |
| Oral cavity & pharynx | 37,160 | 4% | | Pancreas | 26,240 | 3% |
| Leukemia | 35,030 | 4% | | Leukemia | 25,270 | 3% |
| Liver & intrahepatic bile duct | 30,610 | 4% | | Kidney & renal pelvis | 22,660 | 3% |
| **All Sites** | **856,370** | **100%** | | **All Sites** | **878,980** | **100%** |

**Estimated Deaths**

| Males | | | | Females | | |
|---|---|---|---|---|---|---|
| Lung & bronchus | 83,550 | 26% | | Lung & bronchus | 70,500 | 25% |
| Prostate | 29,430 | 9% | | Breast | 40,920 | 14% |
| Colon & rectum | 27,390 | 8% | | Colon & rectum | 23,240 | 8% |
| Pancreas | 23,020 | 7% | | Pancreas | 21,310 | 7% |
| Liver & intrahepatic bile duct | 20,540 | 6% | | Ovary | 14,070 | 5% |
| Leukemia | 14,270 | 4% | | Uterine corpus | 11,350 | 4% |
| Esophagus | 12,850 | 4% | | Leukemia | 10,100 | 4% |
| Urinary bladder | 12,520 | 4% | | Liver & intrahepatic bile duct | 9,660 | 3% |
| Non-Hodgkin lymphoma | 11,510 | 4% | | Non-Hodgkin lymphoma | 8,400 | 3% |
| Kidney & renal pelvis | 10,010 | 3% | | Brain & other nervous system | 7,340 | 3% |
| **All Sites** | **323,630** | **100%** | | **All Sites** | **286,010** | **100%** |

**Figure (1):** Ten main Cancer Types for the Estimated New Cancer Cases and Deaths by Sex, United States, 2018 ***(Siegel et al., 2018).***

In Egypt, according to the population-based cancer registry, the estimated incidence rates of breast cancer among females in Lower, Middle, and Upper Egypt are 53/100000 (33.8%) in 2009-2011, 35.6/100000 (26.8%) in 2009 and 64.5/100000 (38.7%) in 2008, respectively ***(Amal et al., 2014).***

The estimated total number of breast cancer patients in the department of Clinical Oncology & Nuclear medicine, Ain Shams University Hospitals in the period between Jan 2010 to December 2014 was 1906 patients, 1412(74%) of them in the adjuvant setting including 1087 (57%) patients with node positive disease ***(Gado et al., 2017).***

While in the United States it is estimated that 93% of breast cancer cases are diagnosed with localized and regional stage with 31 % representing the node positive cases ***(Siegel et al., 2018).***

Therefore those patients with node positive disease constitute a big load to the radiotherapy department which led us to think to apply a shorter course of radiation which would result in considerable decrease in machine time, working hours and less patients visits so as to perform our task efficiently without compromising either the locoregional control and the overall survival benefit proven for adjuvant radiotherapy or increasing its toxicity leading to impairing the quality of life.

# Aim of the Work

The aim of our study is to prospectively compare between node positive breast cancer patients operated with modified radical mastectomy or breast conservative surgery and axillary clearance receiving adjuvant conventional radiotherapy versus hypofractionated radiotherapy for chest wall or whole breast and regional lymphatic areas, in terms of the locoregional control, disease free survival, cosmetic outcome, arm lymphoedema and acute skin reactions. To explore the best options across the continuum of care for patients at Ain Shams University Hospitals.