

# **RESEARCH ARTICLE**

# HYPOFRACTIONATEDRADIOTHERAPY OF BREAST CANCER IN ELDERLYWOMEN

A. Bouziane<sup>1</sup>, M. Elbaraka<sup>2</sup>, K.EL Kinany<sup>3</sup>, F. Abu Mater<sup>4</sup>, M. Yessoufou<sup>1</sup>, G. Alaoui Chrifi<sup>1</sup>, S. Mhirech<sup>1</sup>, W. Hassani<sup>1</sup>, F. Farhan<sup>1</sup>, Z. Alami<sup>1</sup>, MA. Malhouf<sup>4</sup> and T. Bouhafa<sup>1</sup>

- 1. Department of Radiotherapy, UniversityHospital Center Hassan II Fez, Morocco.
- 2. Physics Unit, RadiotherapyDepartment, Hassan II UniversityHospital, Fez.
- 3. Laboratory of Epidemiology, ClinicalResearch and CommunityHealth of Fez.
- 4. Gyneco-obstetrics department, UniversityHospital Center Hassan II Fez.
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# Manuscript Info

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#### Abstract

**Introduction:**Breast cancer remains the first malignantpathology in women and itsdiagnosis in elderlywomenislate. The aim of ourworkis to evaluate the effectiveness of hypofractionatedradiotherapy in the treatment of breast cancer in elderlywomen.

**Material And Methods:** This is a retrospectivestudy of 171 patients aged over 65 yearsfollowed for invasive breast cancer and whoreceived adjuvant hypofractionatedradiotherapy at the radiotherapydepartment of CHU Hassan II Fez fromJanuary 2012 to December 2016.

Results: The frequency of breast cancer in womenaged over 65 yearswas 7.31%. The averageage of our patients was 70 years (65-88 years) of which 40% wereolderthan 70 years. 8.5% of patients had a familyhistory of breast cancer. The delay of consultation was 10 months. A breast nodule was the revealingsign in all patients withinflammatorysigns in 4.6%; axillaryadenopathywasfound in 20% of All cancers werehistologicallyproven. The cancer patients. wasinfiltratingductal in 90% of cases. 27% of the tumorswereScarff-Bloom and Richardson grade I, 45% grade II, 30% grade III. Hormone receptorswereexpressed in 77% and HER positive in 10% of patients. 83% underwentmastectomywithlymphnode dissection followed by adjuvant radiotherapyaccording to the hypo-fractionatedprotocol: total dose of 42Gy on the wall, of which 32% of patients alsoreceivedlymphnode irradiation, fractionation 2.8Gy/Fr in 15 sessions, spread over 19 days 17% of the patients had conservative surgeryassociated with adjuvant externalradiotherapy on the breastaccording to the same scheme with a boost of 11.8Gy on the tumorbed, spread over 25 days. After a medianfollow-up of 5 years, overallsurvivalwasestimated at 84.2%, locoregionalrecurrence-free survival at 84.7% and metastaticrecurrence-free survival at 83%. Acute toxicityconsisted of radiodermatitis in 81% of patients, and postradiation fibrosis in 15%, and no long-termcardiac or pulmonarytoxicitywasobserved.

**Conclusion:** For elderly patients, adjuvant hypofractionated irradiation seems to be a good alternative, with a good rate of local control, and withoutincreasedtoxicity.

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#### Introduction:-

Adjuvant radiotherapyremains essential in the treatment of early-stage cancers, reducing the risk of locoregional cancer recurrence and breast cancer deaths, including in patients with positive lymphnodestreated with mastectomy and axillary dissection.

For severaldecades, adjuvant radiation therapy programs for these patients have delivered 25 fractions of 2 Gy over 5 weeks. Randomized controlled trials with long-termfollow-up have since confirmed that fewer and larger fractions, giving a lower total dose, are at least as safe and effective as the previously used international standard (1).

# Material and Methods:

This is a retrospectivestudy, involving 171 patients aged over 65 yearsfollowed for invasive breast cancer and whoreceivedhypofractionated adjuvant radiotherapy at the radiotherapydepartment of CHU Hassan II Fez fromJanuary 2012 to December 2016.

Patients receivedthree-dimensional adjuvant radiotherapyaccording to the hypo-fractionatedprotocol: total dose of 42Gy on the wall of which 32% of patients alsoreceivedlymphnode irradiation, fractionation 2.8Gy/ Fr in 15 sessions.

Statistical analyses wereperformed with SPSS version 20 software. The analyses of OS, SSRL PFS and DFS wasestimated by the Kaplan-Meier method, and the coxmethod was used for multifactorial analysis.

#### **Results:-**

Our patients werewomenolder than 65 years with invasive breast carcinoma (pT1-4, pN0-3, M0) after complete microscopic excision of the primary tumor by breast-conserving surgery or master comp. All patients underwent axillary surgery (sentinel node biopsy or axillary dissection)

| Features                   | Number of patients (n=171)(%) |  |
|----------------------------|-------------------------------|--|
| Age (years)                |                               |  |
| Median                     | 70 (65-88)                    |  |
| Under 70 years             | 103 (60)                      |  |
| Over 70 yearsold           | 68 (40)                       |  |
| Laterality n (%)           |                               |  |
| Left / Right               | 60 (35)/ 111 (60)             |  |
| Histological type n (%)    |                               |  |
| Invasive ductal            | 154 (90)                      |  |
| Lobularinfiltrating        | 10 (7)                        |  |
| Other                      | 7(3)                          |  |
| Histological grade         |                               |  |
| SBR I                      | 46 (27)                       |  |
| SBR II                     | 77 (45)                       |  |
| SBR III                    | 51(30)                        |  |
|                            |                               |  |
| Presence of vascularemboli | 46 (27)                       |  |
| Hormone receptors          |                               |  |
| Positive                   | 132 (77)                      |  |
| Her2Neu (%)                |                               |  |
| Positive                   | 18 (11)                       |  |
| Negative                   | 153 (89)                      |  |
| T pathology (AJCC 2010)    |                               |  |
| T1                         | 32(19)                        |  |
| T2                         | 101(59)                       |  |
| T3                         | 26(15,4)                      |  |

 Table I:- Patient characteristics.

| T4                              | $\mathcal{Q}(A,\mathcal{L})$ |
|---------------------------------|------------------------------|
| 14                              | 8(4,0)                       |
| N pathology (AJCC 2010)         |                              |
| N0                              | 64 (38)                      |
| N1                              | 72 (42)                      |
| N2                              | 26 (15)                      |
| N3                              | 9 (5)                        |
| Stade (AJCC 2010)               |                              |
| IIA                             | 10                           |
| IIB                             | 25                           |
| IIIA                            | 32                           |
| IIIB                            | 12                           |
| IIIC                            | 9                            |
| Surgery                         |                              |
| Mastectomy                      | 142 (83)                     |
| Conservative                    | 29 (17)                      |
| Lymphnode dissection            | 171                          |
| Systemictreatments              |                              |
| Chemotherapy                    | 50                           |
| Adjuvant                        | 46 (92)                      |
| Neoadjuvant                     | 4 (8)                        |
| Hormone therapy                 | 132 (77)                     |
| Anti HER2 therapy (trastuzumab) | 18 (10)                      |
| Radiotherapy                    |                              |
| (Boost): Photon                 | 15 (8)                       |

The patients received three-dimensional adjuvant radio therapy according to the hypo-fractionated protocol: total dose of 42Gy on the wall of which 32% of the patients also received lymphnode irradiation, fractionation 2.8Gy/ Fr in 15 sessions (Figure 1).



Figure 1:- Axial scan section showing the dose distribution duringchestwall irradiation.

#### Survival and relapse:

After a medianfollow-up of 5 years, overallsurvivalisestimated at 84.2% (Figure2);locoregionalrecurrence-free survival at 84.7% and metastaticrecurrence-free survival at 83%.



IC: (67,5-76,12),m=71,86

Figure 2:- Overallsurvivalcurve.

#### **Toxicity:**

Acute toxicityconsisted of radiodermatitis in 81% of patients, and post-radiation fibrosis in 15% patients, and no long-termcardiac or pulmonarytoxicitywasobserved.

| skin toxicity | Number(%) | Type and grade        |
|---------------|-----------|-----------------------|
| acute         | 139 (81)  | radiodermatitis:      |
|               |           | Grade 1: 85(61%)      |
|               |           | Grade 2: 51(37%)      |
|               |           | Gade 3: 3(2%)         |
| chronicle     | 36 (21%)  | Fibrosis: 14%         |
|               |           | Telangiectasia: 7%    |
|               |           | Hyperpigmentation: 1% |

**Table II:-** Distribution of patients by toxicity.

# **Discussion:-**

Our objective was to determinewhetherwhole-breast irradiation after conservative surgery or mastectomycouldbesafe and effective whendelivered at a higher dose per fraction and over a shorterperiod of time in elderlywomenthan in the standard regimen.

Standard treatmentdelivering 50 Gy in 25 fractions to the breast or wall and or not to the lymphnodes and or not to the tumorbedwith 10 to 16 Gy of additional radiation in conventional fractionation is relatively long and restrictive, especially for elderly patients and/or patients with long tracts (2). In 2000, in a study in the United States, Athas et al. showed that up to 33% of womentreated with conservative surgerydid not receive the adjuvant radiotherapy they should have had, mainly because of age over 70 years and distance to the radiotherapy center [3].

Variousaccelerated and non-accelerated hypofractionated irradiation regimens have been tested to address this issue. Data from four large phase III non-inferiority trials, showed, with level of evidence IA, that hypofractionated breastradio therapy was non-inferior to normofractionated radio therapy, both in terms of efficacy and toxicity [4-6].

The randomized phase III Fast-Forward trial showed non-inferiority of the 27Gy and 26Gy 5-fraction regimens compared with 40Gy 15-fraction regimen, with the incidence of local relapse at 5 years after hypofractionated radio therapy given in five fractions being no lower than the standard 3-week regimen. The 26 Gy dose level is similar to the 40 Gy 15-fraction dose level in terms of patient-rated normal tissue effects, clinician-rated normal tissue effects, and breast appearance change. The consistency of the FAST-Forward results with previous hypofractionation trials supports the adoption of 26 Gy in five daily fractions as the new standard for women with operable breast cancer requiring adjuvant radiation therapy (1).

Since 2011, the American Society of Radiation Therapy (ASTRO) has published recommendations for the use of hypofractionated regimens, in patients at least 50 years of age, with stage pT1-2, pN0 breast cancer, without adjuvant chemotherapy, with no indication for additional tumor bed irradiation [7]. Since then, several national and international guidelines have also followed [8-14]. In the United Kingdom, as in manyother countries, 40 Gy in 15 fractions has become the standard treatment for breast or even parietal irradiation, with or withoutlymphnode irradiation [15].

# **Conclusion:-**

In thisseries evaluating a hypofractionated regimen in elderly patients with invasive breast carcinoma, the results are promising both in terms of locoregional control and toxicity. This hypofractionated regimenallows to decongest the treatment machines and to shorten the waiting time for our patients.

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