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COMPARISON OF HYPOFRACTIONATED EXTERNAL RADIOTHERAPY VS. CONVENTIONAL RADIOTHERAPY IN POST BREAST CONSERVATIVE SURGERY (BCS) CANCER CASES

Oncology

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ABSTRACT

COMPARISON OF HYPOFRACTIONATED EXTERNAL RADIOTHERAPY VS. CONVENTIONAL RADIOTHERAPY IN POST BREAST CONSERVATIVE SURGERY (BCS) CANCER CASES TO DECREASE RADIATION TIME DURATION, COST EFFECTIVENESS WITH PATIENT'S SATSFACTION. STUDY SHOWS EQUAL RESULTS OF TWO PROTOCOLS OF RADIATION, SO HYPOFRACTIONATION IS EQUALLY EFFECTIVE IN BCS PATIENT.

AIMS & OBJECTIVES

AIM: comparing two protocols of radiotherapy in breast cancer after breast conservative surgery for relapse rate, early and late reaction.

OBJECTIVE: -- to study the decrease in radiation treatment time (hospital stay).
--to assess patient's satisfaction in short courses of radiotherapy.
--to assess the cost effectiveness of the treatment.

KEYWORDS

hypofractionation, BCS

INTRODUCTION:

Carcinoma breast has superseded carcinoma cervix as the leading cancer among females in India in terms of incidence as well as mortality. The increasing burden of disease and the availability of limited resources have motivated researchers to investigate the role of hypofractionated protocols in lieu of conventional fractionation for adjuvant radiotherapy in carcinoma breast patients.[11]

Breast cancer, thought to be treated best with 2 Gy or less was considered insensitive to fractionation previously. However, some trials have tested the hypothesis that carcinoma of breast is as sensitive to fraction size as the normal tissues of the breast and underlying rib cage. If confirmed, these findings could indicate that fraction sizes of 2 Gy or lower offer no therapeutic advantage, and that a more effective strategy would be to deliver fewer, larger fractions to a lower total dose.

Multiple randomized trials involving a combined total of more than 7,000 women have compared hypofractionated RT to a standard regimen of 50 Gy in 25 fractions.

The four important trials of hypofractionation in carcinoma breast are discussed below:

(1) Study of the Royal Marsden Hospital and Gloucestershire Oncology Centre (RMH/GOC)[12]

In Royal Marsden Hospital/Gloucestershire Oncology Centre (RMH/GOC) trial between 1986 and 1998 at UK; 1,410 women with invasive breast cancer who had had local tumor excision of early stage breast cancer were assigned to receive adjuvant 50 Gy RT given in 25 fractions, 39 Gy given in 13 fractions, or 42.9 Gy given in 13 fractions, all given over 5 days a week. At 10 years of follow-up, ipsilateral breast tumor recurrence rate was 12.1% in 50 Gy arm, 14.8% in 39 Gy arm, and 9.6% in 42.9 Gy arm. The 3.3 Gy/fraction schedule with a total dose of 42.9 Gy gave the best local control rates both at 5 and 10 years.

(2) Study of the Ontario Clinical Oncology Group (OCOG)[13]

This was the first reported randomized trial (1993-1996); performed by the Ontario Clinical Oncology Group (OCOG) in Canada.It included 1,234 women with lymph node–negative, margin-negative invasive breast cancer treated with breast-conserving surgery and level I and II axillary lymph node dissection. Baseline characteristics were balanced between treatment groups, including use of adjuvant tamoxifen (41%) or chemotherapy (11%), and enrollment was limited to patients with small to moderately sized breasts. In a median follow-up of 12 years, hypofractionated radiation did not compromise local tumor control. The 10-year risk of local invasive recurrence was 6.2% in patients of HF-WBI arm, compared with 6.7% of patients who received CF-WBI. There were no observed differences in terms of breast cancer mortality, death due to other causes such as cardiac events, and overall survival. A trend was noted toward fewer local recurrences in the HF-WBI arm.

(3) The study of the UK Standardisation of Breast Radiotherapy (START) Trial A (START A)[14]

In START A trial between 1998 and 2002; 2,236 women with early breast cancer (pT1-3a, pN0-1, M0) at 17 centers in the UK were randomly assigned after primary surgery (BCS or mastectomy) to receive 50 Gy in 25 fractions of 2 Gy each versus 41.6 or 39 Gy in 13 fractions of 3.2 or 3.0 Gy, respectively. All schemes were delivered over 5 weeks. The 5-year rate of local relapse in the arms receiving 50 Gy, 41.6 Gy and 39 Gy was 3.2%, 3.2% and 4.6%, respectively, whereas the 5-year probability of disease-free survival in the groups receiving 50 Gy, 41.6 Gy and 39 Gy was 86%, 88% and 85%. The absolute 5-year survival was 89% for all groups.

(4) The study of the UK Standardisation of Breast Radiotherapy (START) Trial B (START B)[15]

The START B trial (1999-2001) compared conventional fractionated radiotherapy (50 Gy in 25 fractions over 5 weeks) with a hypofractionated radiotherapy regimen (40 Gy in 15 fractions over 3 weeks). The study at 23 centers in UK included 2,215 women treated with mastectomy or breast-conserving surgery for early-stage breast cancer. The 5-year local recurrence rates in the groups receiving 40 Gy and 50 Gy were 2.0% and 3.3%, respectively. The 5-year disease-free survival rates in the groups receiving 50 Gy and 40 Gy were 86% and 89%, respectively, whereas the 5-year overall survival rates were 89% and 92%, respectively.

The late effects on healthy tissues and breast cosmesis are important issues in hypofractionated schedules.

(1) RMH/GOC trial

The primary endpoint in RMH/GOC trial was the late change in breast appearance compared to postsurgical appearance scored from annual photographs blinded to treatment allocation. It also evaluated the palpable breast induration. The cosmetic outcome was evaluated based on photos and physical examination during annual control visits taken immediately after surgery, then before radiotherapy, annually over 5 years and upon completion of the 10-year treatment. After a minimum 5-year follow-up, the risk of scoring any change in breast appearance after 50 Gy/25 fraction, 39 Gy/13 fraction, and 42.9 Gy/13 fraction was 39.6, 30.3, and 45.7%, respectively. There were significant changes in breast appearance in the groups administered 50 Gy, 42.9 Gy and 39 Gy in 5.6%, 10.1% and 3.4% of patients, respectively at 10 year follow up. The clinical assessment also showed significant differences. The 3.3 Gy/fraction schedule showed the worst cosmetic results whereas the 3 Gy/fraction arm showed the best result.

(2) OCOG trial

In Ontario trial, result of breast cosmesis at a median follow up of >11 years were virtually identical in both treatment arms. There were no significant differences found between the groups in the distribution of causes of death including cardiac deaths.

(3) START A trial

In START A trial, for late change in breast appearance, photographic and patient self-assessments suggested lower rates of late adverse effects after 39 Gy than with 50 Gy, and were comparable in groups receiving 50 Gy and 41.6 Gy. During a median follow up of 5.1 years, the incidence of ischaemic heart disease, rib fractures and symptomatic pulmonary fibrosis was low and similar for all the groups. A lower total dose in a smaller number of fractions could offer similar rates of tumor control and normal tissue damage as the international standard fractionation schedule of 50 Gy in 25 fractions .

(4) START B trial

The UK START B trial recorded a lower rate of change in breast appearance after 40 Gy/15 fractions regimen. Yarnold et al., in their review highlighted a very important observation from START B trial that 40 Gy in 15 fractions is equivalent to 45.5 Gy in 2.0 Gy fractions if α/β ratio = 3.0 Gy so that 40 Gy in 15 fractions is gentler on late reacting normal tissues than 50 Gy in 25 fractions. There were no cases of brachial plexopathy recorded in patients who received supraclavic ular and axilla irradiation in 40 Gy/15 fraction arm at a median follow-up of 6 years. There was low and similar incidence of ischaemic heart disease, rib fracture and pulmonary fibrosis in both the groups.

MATERIALS & METHODS:

SOURCE: Breast cancer cases after breast conservative surgery attending radiotherapy opd in our hospital. Note that all the patient of BCS after surgery already received adjuvant chemotherapy.

SAMPLE SIZE: total 52 patient of BCS. 26 patient in control arm, 26 patient in test arm

CONTROL ARM: External Beam RT 50 Gray/25 fractions delivered in 5 weeks at 2.00 Gray/fraction, f/b electron boost 10 Gray/5 fractions

TEST ARM: Hypofractionated External Beam RT 40.05 Gray/15 fractions delivered in 3 weeks at 2.67 Gray/ fraction , f/b electon boost 10Gray/5 fractions

INCLUSION CRITERIAS:

- K/C/O Ca Breast post-BCS
- Women with operated invasive breast cancer (pT1-3a,pN0-N3a,M0) with clear tumor margin >1 mm
- Age > 18 years and < 70 years

EXCLUSION CRITERIAS:

- Patients with very poor general condition (KPS<50)
- Age < 18 years and > 70 years
- Post MRM patients

EVALUATION FOR ACUTE REACTION: patients evaluated during treatment and monthly for 3 months after treatment for acute reactions or toxicities.

Acute reactions mostly occurs in skin and subcutaneous tissue, so during treatment also evaluated especially in hypofractionation arm.

So evaluation done by RTOG(RADIATION THERAPY ONCOLOGY GROUP) and EORTC(EUROPEAN ORGANISATION FOR RESEARCH AND TREATMENT OF CANCER) acute skin reaction grading score.

RTOG /EORTC acute radiation scoring criteria-skin

0	1	2	3	4
No change over base line	Follicular, faint or dull erythema, dry desquamation, decrease sweating	Tender or bright erythema, patchy moist desquamation, moderate edema	Confluent moist desquamation other than skin folds, pitting edema	Ulceration haemorrhage, necrosis

EVALUATION DURING FOLLOW UP:

-After completion of treatment, patients were examined every monthly till 6 months and then 3 monthly for 2 years.

Primary endpoint: was to see for normal tissue effects in breast tissue, skin subcutaneous tissue, arms and shoulder with photographic assessment at baseline post surgery ,pre radiotherapy & 1 year after radiotherapy.

Secondary endpoint: diseases free survival i.e: loco-regional relapse
At each follow-up, patients provided a medical history and underwent a physical examination. Mammography of both breast was performed 6 months after radiation therapy and then yearly then after.

A histo-pathological conformation was required for any local recurrence clinical and laboratory manifestation that suggested recurrent disease were fully investigated.

The criteria for loco-regional relapse was recurrent tumor within the treated whole breast and the regional lymph nodes i.e: ipsilateral axillary , supra clavicular and internal mammary .

LATE RADIATION TOXICITY: was assessed by different radiation oncologists at 2 years used the RTOG / EORTC late radiation morbidity score. The effects of radiation therapy on skin, subcutaneous tissue, brachial plexus, ribs, lungs were graded on the five point scale as:

RTOG / EORTC LATE RADIATION MORBIDITY SCORE

0- no toxicity
1-slight
2-moderate
3-marked
4-severe

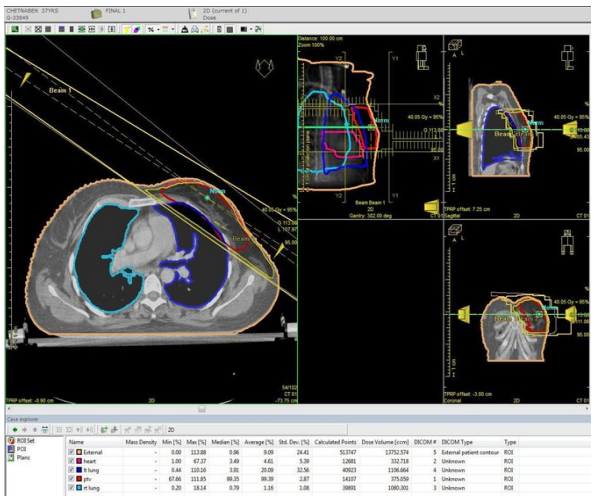
Evaluation of skin and subcutaneous fibrosis: mainly done by clinical examination by different radiation oncologists to overcome subjective variation. evaluation also done by pre and post radiotherapy clinical photographs, and post radiotherapy comparison with opposite normal breast.

Evaluation of arm edema: done by clinical examination. although incidence of arm edema is higher in stage III patients with extensive nodal involvement.

Evaluation of radiation pneumonitis: chest x-ray was done regularly during follow-up to rule out pneumonitis and metastasis. If patient was symptomatic clinically then we have done CECT thorax for final diagnosis of radiation pneumonitis.

Evaluation of brachial plexopathy: done mainly by clinical examination. If patient was having severe symptoms then we have done MRI to rule out brachial plexopathy. But in our study no any patient needs this.

RADIOTHERAPY PLANNING BY 3DCRT PLANNING



OBSERVATION & RESULTS

Table no. 1 – Age and Habitat wise distribution of the patients in control arm

Age (years)	urban	rural
<40	3	9
41-50	5	4
51-60	1	1
>60	1	2
Total	10	16

Value of x^2=2.176 , dof=3 , p value=0.53, insignificant

After applying chi-square test there is no significant association between age and habitat in control arm (p >0.05)

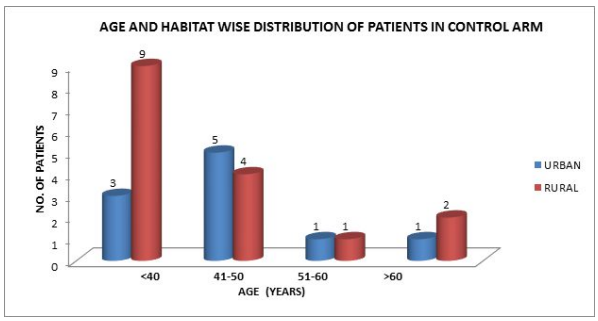


Table no.2- Age and Habitat wise distribution of patients in test arm

Age (years)	urban	rural
<40	3	6
41-50	5	4
51-60	2	3
>60	0	3
total	10	16

Value of x^2=3.09 , dof=3 , p value=0.37, insignificant

After applying chi-square test there is no significant association between age and habitat in test arm (p >0.05)

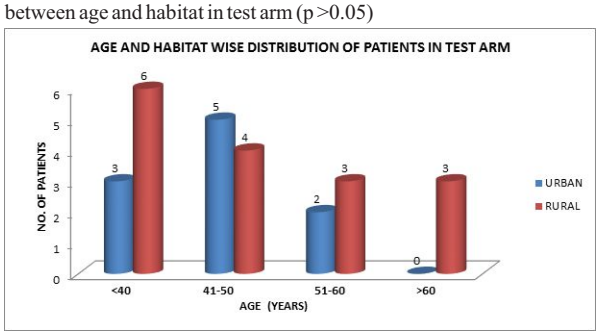


Table no.3- stage wise distribution of patients in control arm and test arm

stage	Control arm	Studyarm
I	7	7
II	18	14
III	1	5
total	26	26

Value of x^2=3.16 , dof=2 , p value=0.2053, insignificant

After applying chi-square test there is no significant association between stage and patients in control arm and test arm (p >0.05).
Although majority of patients in both arms were in stage II

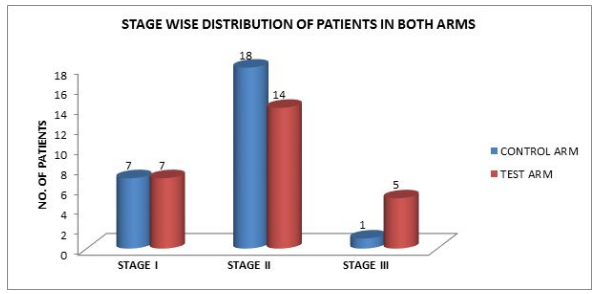


Table no 4- distribution of patients according to acute skin reaction in control arm and test arm

Skin Reaction grade	Control arm	Test arm
0	0	2
I	12	14
II	9	6
III	5	4
IV	0	0
total	26	26

Value of x^2=2.86 , dof=3 , p value=0.4129, insignificant

After applying chi-square test there is no significant association between acute skin reaction and patients in control arm and test arm (p >0.05)

Although acute skin reaction wise both arms have almost same results.

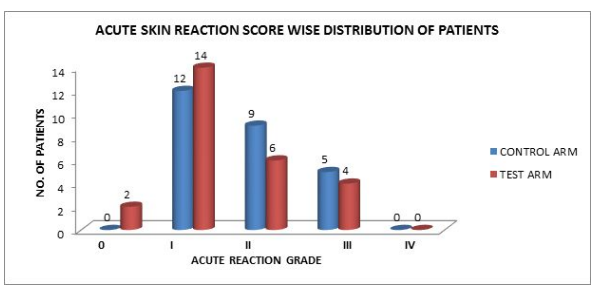


Table no.5- distibution of patients according to late radiation toxicity in control arm and test arm

Late Radiation toxicity	Control arm	Test arm
Skin/sub.cut.fibrosis	16	12
Arm edema	3	2
Radiation pneumonitis	0	0
Brachial plexopathy	0	0
No late toxicity	7	12

Value of x^2=2.087 , dof=2 , p value=0.35, insignificant

After applying chi-square test there is no significant association between late radiation toxicity and patients in control arm and test arm (p >0.05)

Although both arms have same results, but patients with no late reaction (grade 0 score) were higher in test arm.

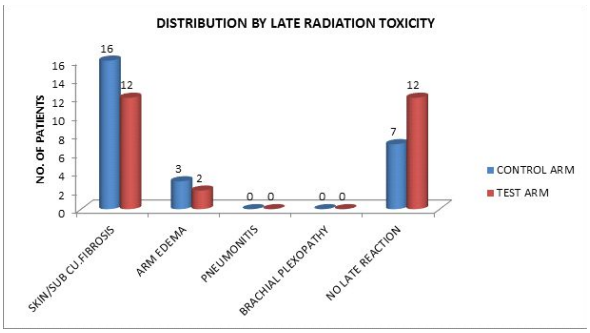
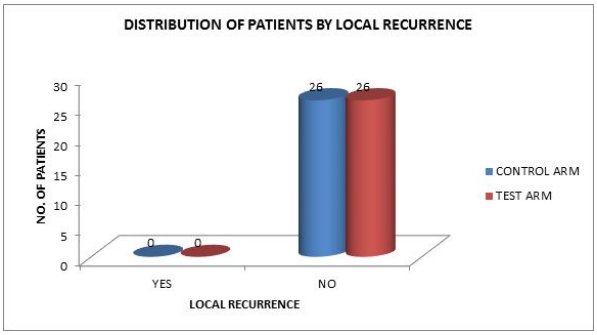


Table no.6-distribution of patients according to local recurrence in control arm and test arm

Local recurrence	Control arm	Test arm
yes	0	0
no	26	26

Due to '0' value in table ,chi- square test not done.

To asses the local recurrence our follow up period is short, but according to median follow-up both arms have same results and none of the patients having local recurrence.



DISCUSSION

A revolutionary breakthrough might be on the horizon in breast carcinoma treatment. This disease is the leading cancer in women, and radiation therapy is an integral part of management for a large percentage of post-breast conservative surgery patients. Throughout the world, radiation therapy centers are struggling to keep pace with the ever- growing need for radiation therapy in patients with breast carcinomas. The beneficial effect of radiotherapy after surgery has been unequivocally demonstrated in randomized trials. Radiotherapy therapy after surgery not only improves local recurrence rates but also improves survival. Conventional radiotherapy after surgery usually implies giving a dose of 50 Gy in 25 fractions i.e. 2 Gy per fraction over 5 weeks.

In this regard, there has been recent interest in hypofractionation, which means giving higher dose per fraction to target area and thereby allowing a lesser overall treatment time. This concept is similar to the accelerated partial breast irradiation, which too has the basic advantages of drastically reducing overall treatment time. However unlike accelerated partial breast irradiation, which is used in highly selected group of patients. hypofractionation has wider applicability and can be used in most stages of loco-regionally confined breast cancer.

A typical course of radiation therapy lasts nearly for 5-6 weeks in post breast conservative surgery patients. Conventionally, a dose per fraction per day of 1.8 to 2Gy has been used in treatment of breast cancer, stemming from concern that fraction sizes of larger than 2Gy might increase the likelihood of the late effects on healthy tissue toxicity in breast cancer patients. A number of reports of with schedules using 1.8Gy to 2.2Gy per fraction have been published with 60% to 90% of patients reporting high recurrence free survival and overall survival.

Therefore, a technique which reduces the treatment time by half (3 weeks instead of the present 6 weeks) while maintaining local control rates needs to be viewed with great interest. Recent studies examining 13 to 16 fractions of hypofractionated radiation therapy (using larger dose per fraction) compared with the present 25 fractions are providing crucial supportive evidence.[19,20,21]

This study provide follow-up of patients of Breast Carcinoma treated with three different types of radiation therapy schedules i.e. conventional and hypofractionated radiotherapy schedules. In START TRIAL B Breast cancer patients were randomly assigned after primary surgery to receive 50Gy in 25 fractions of 2.0Gy over 5 weeks or 40Gy in 15 fractions of 2.67Gy over 3 weeks. Median follow-up was 9.9 years (IQR 7.5-10.1), after which 95 local-regional relapses had occurred. The proportion of patients with loco-regional relapse at 10 years did not differ significantly between the 40Gy group (4.3%, 95% CI 3.2-5.9) and the 50Gy group (5.5%, 95% CI 4.2-7.2; HR 0.77, 95% CI 0.51-1.16; p=0.21). In CANADIAN Trial Breast cancer patients were randomly assigned after primary surgery to receive 50GY in 25 fractions of 2.0GY over 5 weeks or 42.5GY in 16 fractions of 2.6GY over 3 ½ weeks. The risk of local recurrence at 10 years was 6.7% among the 612 women assigned to standard irradiation as compared with 6.2% among the 622 women assigned to the hypofractionated regimen(absolute difference, 0.5 percentage points; 95% confidence interval [CI],-2.5 to 3.5).

In this study, 172 breast cancer patients were recruited within 2 years period. In our study four patients experienced local breast cancer recurrence as a first event: 2 in the study group 1, 1 in study group 2 and 1 in the control group. At 2 years, local recurrence-free survival was 96.42% in the study group 1, 98.24% in study group 2 and 98.3% in the control group. 6% & 8% of patients died due to metastatic disease in study & control group respectively. Not a single patients had developed radiation pneumonitis as a late complication in both study & control group respectively.

These results do suggest that the intended short 3-week schedule of radiotherapy has achieved a high level of local control.

The following table shows summary of hypofractionated regimens used in different trials.[14,15,22,23].

Trials	Endpoints	No of patients	Dose/No (Gy/#)	OTT (WKS)	5-YRS LRR
STUDY	LRR,QOL	216	2.67	5&3	3.57 & 1.75 (2 Yrs)
U.K. START A	LRR	749	2	5	3.6
	Late effects	750	3	5	5.2
	QOL	737	3.2	5	3.5
U.K. START B	LRR	1105	2	5	3.3
	Late effects	1110	2.67	3	2.2
RMH/GOC Trial	LRR	470	2	5	7.9
	Late effects	466	3	5	9.1
	QOL	474	3.3	3	7.1
Canadian Trial	LRR	612	2	5	3.2
	Late effects	622	2.65	3	2.8

Two important randomized trials have evaluated the issue of hypofractionation in breast cancer. The first randomized trial by Whelan et a14 studies 1,234 patients with early-stage, lymph node-negative breast cancer treated in which they compared two fractionation schedules (42.5Gy in 16 fractions and 50Gy in 25 fractions) with does per fraction of 2.6Gy and 2Gy, respectively. Their study supported the use of a shorter course of radiation therapy for patients with the most favorable infiltrating ductal carcinomas.

The effect of increasing the dose per fraction result in a biologically equivalent dose that is different for breast cancer cells and normal tissue cells (Skin, subcutaneous tissue, muscle, brachial plexus, lung and heart). Biologically equivalent dose in turn depends not only on dose per fraction but also on α/β value for each tissue. This value is an index of sensitivity of a particular tissue to effect of RT fraction. A higher value makes tissue less sensitive to effect of fractionation while a lower value increases the sensitivity of tissue to fraction size. If breast cancer is generally as sensitive to fraction size as are the late reacting healthy tissues of the breast, muscle and underlying rib cage (i.e., an α/β value of 3-5Gy compared with $\geq$ 10Gy for squamous carcinomas), larger fraction sizes will be more effective than previously though. The

first indication that breast cancer could be safely and effectively treated with using hypofractionation was first raised more than three decades ago when biological models were applied to clinical data derived from restrospective studies.

The first randomized trial of hypofractionated radiotherapy in breast cancer was reported from Canada. This study had 1234 patients with early-stage, lymph node negative breast cancer. The patients were randomized to two fractionation schedules 42.5Gy in 16 fraction and 50Gy in 25 fractions) with does per fraction of 2.65 and 2Gy, respectively. Both the local recurrence rate and the cosmetic outcome in the two arms were comparable. Yarnold et.al. have analyzed the effect of hypofractionated radiotherapy in successive trials testing the effect of different regimens on local control, overall survival and cosmesis. The study was planned with late effect of normal tissue as the primary endpoint and tumour recurrence and palpable fibrosis as the secondary endpoint after a minimum five years follow-up, the risk of scoring and change in breast appearance after 50Gy/25#, 39Gy/13# and 42.9Gy/13# was 39.6, 30.3 and 45.7% from which an α/β value of 3.6Gy was estimated. This study proved the hypothesis that radiobiology of breast cancer was different from other tumours in general and hypofractionated radiotherapy (Compare to conventional fractionation) would possibly improve local control rates.

START A Trial randomized 2236 patients (at 17 centre's in UK) with early breast cancer after primary surgery to receive radiotherapy with 2Gy (45Gy/25#) versus 3Gy (39Gy/13#) versus 3.2Gy (41.6Gy/13#) in same treatment time of 5 weeks. After a median follow-up of 5 years, the estimated absolute difference in 5 years locoregional relapse rates compared with 50Gy were 0.2%(95% CI-1.3% to 2.6%) after 41.6Gy and 0.9% (95% CI=0.8% to 3.7%) after 3.9Gy.

Similarly START B trial randomized 2215 patients of early breast cancer (at 23 centre's in UK) to receive 50Gy/25# at 2Gy /# over 5 weeks versus 40Gy/16# at 2.67Gy /# over 3 weeks. After a median follow-up of 10 years, locoregional tumor relapse rate were comparable in hypofractionated arm. Fraction size of 3.3 Gy/# was superior in terms of local control in START A, although it yielded inferior cosmetic outcomes. Any fraction size of 3.2Gy or less as seen in both START A and B trials led to similar results a terms of both local control and cosmesis. Interestingly, the hypofractionated arm in the START B trial had lower rate of distant metastasis and overall mortality compared with the conventional fractionation arm.

The result of these trials has tremendous implications for both the patients of breast cancer and health care system. It is a known fact that prolonged daily treatments make a substantial impact on reduction of quality of life experienced by women with breast cancer, treated with radiotherapy as shown by randomized trial. Apart from quality of life benefits because of convenience and less time in the hospital. It has a tremendous logistic advantage. Presently radiotherapy for breast cancer accounts for 25-30% of all radiation therapy burden.24 The shorter schedule also will permit more efficient use of resources. In that up to 50 more women can be treated with existing equipments and personnel.

CONCLUSION

Breast cancer is the leading cancer in women, and radiation therapy is an integral part of management and for a large percentage of breast conservative surgery patients. throughout the world radiation therapy centers are struggling to keep pace with the ever growing need of radiation therapy in patients with breast carcinomas.

Hypofractionation is a technique which reduces the treatment time by half 3 wks instead of the present 6 wks, while maintaining cosmetic and control rates, needs to be viewed with great interest.

Hypofractionated radiotherapy after surgery not only improves local recurrence rates but also improves survival.

Intended short course radiotherapy have tremendous implication for both the patients of breast cancer and health care system. it is a known fact that prolonged daily treatments make a substantial impact on reduction of quality of life experienced by women with breast cancer treated with radiotherapy as shown by randomized trial.

Apart from quality of life benefits because of convenience and less time in the hospital, it has a tremendous logistic advantage. Presently radiotherapy for breast cancer accounts for 25-30% of radiotherapy burden. the shorter schedule also will permit more efficient use of resources, in that up to 50% more women can be treated with existing equipments and personnel.

In this study 52 patients were randomly assigned to receive hypofracti onated radiotherapy (test arm) and conventional radiother apy (control arm).

Hypofractionated radiotherapy was given in a dose of 40.05 Gy in a 15 fractions over a period of 3 wks and conventional radiotherapy was given in a dose of 50 Gy in 25 fractions over a period of 5 wks.

Both group patients already received adjuvant chemotherapy before starting radiotherapy.

Majority of the patients were in the age group of 30-50 years.
Patients recorded in the study were 60% from rural area and 40% from urban areas.

Majority of patients from both group is stage II patients.
Almost 70% of patients from both group were premenopausal and received hormonal therapy according to hormonal status.

All the patients tolerated radiation well and took the treatment without interruption.

Grade 1 acute skin reaction were almost same in control arm (48%) as compared to test arm (52%). Grade 3 acute skin reaction also same in both arms 5 patients in control arm and 4 patient in test arm. It concluded that hypofractionation is not inferior to conventional radiotherapy in view of acute skin reaction.

Late radiation toxicity is evaluated by regular follow up of patients in view of skin and subcutaneous tissue fibrosis, arm edema, radiation pneumonitis, brachial plexopathy. Some patients have no late side effects also evaluated. Late toxicity was evaluated by RTOG and EORTC late morbidity score. Radiation Pneumonitis and Brachial Plexopathy were not seen in any patients of either arms. Skin and subcutaneous tissue fibrosis grade 1 was seen slightly low in test arm. 61% of patient in control arm and 46% of patients of test arm having skin and subcutaneous tissue fibrosis.

Arm edema was seen in 3 patients of control arm and 2 patients of test arm. 26% of patients in control arm and 46% of patients in test arm having no any late radiation toxicity. Apart from this we can say that hypofractionation is non inferior to conventional radiotherapy.

Out of 26 patients in both arms none of the patients having local recurrence. When local recurrence is concerned actually we need long follow up, but in our study approx. median follow- up of 14 months is slight short, till now no any patient from either arm having local recurrence.

REFERENCES:

1. Globacon:http//globacon.iarc.fr
2. (Altekruse et. Al. 2009). Altekruse SF, Kosary CL, Krapcho M, Neyman N et.al. SEER cancer statistic Review,1975-2007.,National Cancer Institute.
3. Nair et. al. 2005) Nair MK, Varghese C, Swaminathan A. Cancer : current scenario intervention strategies and projection for 2015. Burden of disease in india. background papers. National commission for microeconomics and health, ministry of health and family welfare ,Govt. of India, New Delhi. PP218-25,2005.
4. WHO (World Health Organisation) data of 2012 on Breast cancer incidence in the world and india.
5. Jemal A ,Siegel R, Ward E (2007) Cancer statistics, 2007.CA Cancer J Clin 57:43-66
6. Anatomy and Lymphatic drainage of breast: Decision Making in Radiation Oncology part 1 : with permission from Elsevier.
7. Satyanarayana and Asthana, 2008). Satyanarayana L, Asthana S, Life Time Risk for development of ten major cancers in india and its trends over the years from 1982 to 2000. Ind J Med Sci 2008; 62:35-44
8. Practical Radiotherapy planning 4th Edition @ 2009 Ann Barrett, Jane Dobbs, Stephen Morris and Tom Roques chapter 22 p.265.
9. Danish Breast Cancer Trials Group (DBCG) report on advantage of radiotherapy in post mastectomy patient in loco regional control.
10. Yarnold JR, Price P, Steel GG. Non surgical management of early breast cancer in the United Kingdom: radiotherapy fractionation practices. Clin Oncol 1995;7:223-6
11. Yeole et. al.2004). Yeole BB, Kumar AVR, Kurkure A, Sunny L, (2004). Population based survival from cancer of breast cervix and ovary in women in Mumbai, India. Asian Pac J Cancer Prev. 5,308-315.
12. Royal Marsden ,2006 Owen JR (2006) Effect of radiotherapy fraction size on tumour control in patient with early stage breast cancer after local tumour excision: long term results of a randomized trial. Lancet Oncol 7(6) : 467-471 Egypt NCI ,2004
14. The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomized trial. Lancet oncol 2008a;9(4):331-341.Bentzen SM, Agrawal RK, Aird EG, et.al.

15. The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomized trial. Lancet oncol 2008;371(9618):1098-1107
16. Early Breast Cancer Trialists' collaborative group (EBCTCG) report on conventional radiotherapy and hypofractionated radiotherapy.
17. EL Sayed et.al. at Egypt report on two different schedule of radiotherapy.
18. UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015) Radiotherapy & Oncology 100 (2011) 93-100 www. thegreenjou rnal.com
19. Canada, 2002 Whelan T et al (2002) Randomized trial of breast irradiation schedule after lumpectomy for women with lymph node negative breast cancer. J Natl Cancer Inst 94 (15) :1143-1150
20. Royal Marsden ,2006 Owen JR (2006) Effect of radiotherapy fraction size on tumour control in patient with early stage breast cancer after local tumour excision: long term results of a randomized trial. Lancet Oncol 7(6) : 467-471 Egypt NCI ,2004
21. Taher AN (2004) Hypofractionation versus conventional fractionation radiotherapy after conservative treatment of breast cancer: early skin reaction and cosmetic results. J Egypt Natl Canc Inst 16 (3):178-187
22. Suit H, Skates S, Taghian A, et.al. Clinical Implication of heterogeneity of tumour response to radiation therapy. Radiother Oncol 1992;25:251-60
23. Brenner DJ. Hypofractionation for prostate cancer radiotherapy –what are the issue ? Int J Radiat Oncol Biol Phys 2003;57:912-4
24. Mackillop WJ ,Zhou S, Groome P, Dixon P, Cummings BJ ,Hayter C, Changes in the use of radiotherapy in Ontario 1984-1995. Int J Radiat Oncol Biol Phys 1999;44:355-62
25. Schinitt SJ, Guidi AJ. Pathology of invasive breast cancer. In : Harris JR , Lippman ME, Morrow M, Osborne CK, eds. Diseases of the breast, 3rd ed. Philadelphia: Lippincott Williams & Wilkins , 2004:541
26. The World Health Organization histological typing of breast tumours, 2nd ed. The World Organisation. Am J Clin Pathol 1982; 78(6):806.
27. Greene et al. (2002) Greene F, Page D, Fleming I et al.(2002) AJCC cancer Staging Manual, 6th edn. Springer, Berlin Heidelberg New York.