



Treatment completion rates and toxicity of 5 fractions of adjuvant radiotherapy over one week in elderly breast cancer patients treated with lumpectomy

Álvaro Flores Sánchez¹, Jorge Contreras Martínez², Remedios Priego Ortiz³

¹Radiation Oncology Department, GenesisCare, Málaga, Spain; ²Radiation Oncology Department, Hospital Regional Universitario Carlos Haya, Málaga, Spain; ³Radiation Oncology Department, GenesisCare, Málaga, Spain

Contributions: (I) Conception and design: Á Flores Sánchez, J Contreras Martínez; (II) Administrative support: Á Flores Sánchez, J Contreras Martínez; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Álvaro Flores Sánchez. Radiation Oncology Consultant, 1Radiation Oncology Department, GenesisCare, Málaga, Spain. Email: alvaro.flores@genesiscare.es.

Background: Elderly patients are usually frail and cannot attend a prolonged radiotherapy course. Many of them undergo mastectomy to avoid adjuvant radiotherapy thinking that they are not going to complete at least 15 fractions. Many studies have suggested hypofractionated radiotherapy in 5 days. We would like to describe the treatment completion rates and toxicity of 5 fractions of 520 cGy delivered within one week in patients over 70 years old treated with tumorectomy.

Methods: Between June 2016 and May 2019 we have analyzed retrospectively 23 patients treated with lumpectomy plus 5 fractions adjuvant radiotherapy. All patients had negative SLNB and aged between 70 and 93 years old. After finishing the RT treatment, follow up was made at 1 month, 3 months, 6 months and a year. This follow up was based on an interview and physical examination.

Results: Independently of their age, the treatment completion rate was 100%. Every patient finished the whole treatment with no interruptions. Regarding cosmetic or toxicity outcomes within one year, there was only one patient with grade I radiation induced dermatitis and 2 patients with pruritus.

Conclusions: Five fractions schedule within one week is well tolerated with no important severe side effects after one year. Elderly patients appreciate to make as short as possible the number of fractions, decreasing the number of days they have to come to clinic, improving patient satisfaction and treatment completion rates.

Keywords: Radiotherapy; oncology; breast cancer; elderly; hypofractionation; 5 days; one week

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Introduction

Breast radiotherapy treatment has been progressively more hypofractionated (1,2) reducing daily visits to radiotherapy centres. Sometimes we receive in our radiotherapy departments, patients coming from far away. This is translated into long travelling times being difficult to reach the radiation oncology service.

If we consider patients in the elderly (3), considered

as above 65 years old, this situation could be a utopia. Furthermore, is common to explain to this category of patients the relevance of the treatment, because they prefer to be more comfortable at home preserving a good quality of life (4,5) even assuming the cost of a worst outcome. Overall survival is not the objective in many patients and they would benefit more from that increased hypofractionation than younger patients.

In 1981 started a common trend in searching a more and more hypofractionated radiotherapy regime to the breast (6,7). According to that, many trials raised. The rationale was the low α/β ratio of the breast and improvements in treatment delivery.

The Yorkshire Breast cancer group run a prospective study (8) with a 4 weeks treatment of 40 Gy in 2.67 Gy per fraction to the breast +/- lymph node area combined with a sequential boost of 15 Gy in 3 Gy per fraction. After 7 years follow up, they showed excellent local control rates and good cosmetic results like other studies did (9,10).

Many studies (8-11) have shown good cosmetic outcomes of 44 Gy in 16 daily fractions after 6.7 years follow up.

The Canada trial (12) in 2002 suggested a more comfortable approach looking for local recurrence as a primary end point and secondary endpoint was cosmesis. After delivering 42.56 Gy in 16 fractions, they conclude that this fractionation would be an acceptable alternative.

In 2008, Start trials (A and B) (13,14) examined 41.6 Gy in 3.2 Gy fractions and 40 Gy in 15 fractions of 2.67 Gy each. In both trials there is a similar local-regional tumor control rate and late radiation induced side effects compared with the standard fractionation of 50 Gy in 25 days.

More recently, the UK FAST trial and the UK Fast-Forward trial (15,16) tested 5 weekly fractions of 5.7 Gy and 6 Gy, and 26 Gy or 27 Gy within a week respectively. Both suggested mild acute skin side effects being similar to the standard fractionation ones. Results in terms of recurrence rates and local control are pending.

Methods

Patients included

We have analysed retrospectively 23 patients treated between June 2016 and May 2019 with lumpectomy plus negative sentinel node biopsy and adjuvant radiotherapy to the breast.

First of all, we evaluated if they were appropriate candidates for treatment selection (17,18). We included initially only those patients above 70 years old. There were only 3 exceptions to that. Those 3 patients were coming from far away in rural areas. They refused 15 days of treatment being translated in long journeys and below 70 y.o. Adjuvant radiotherapy was denied after full explanation of its consequences, so we considered to offer them at least the 5 days schedule taking into account the relevance of avoiding any adjuvant radiotherapy. In such

cases, they would be offered mastectomy from a beginning instead of consider highly hypofractionated radiotherapy regimes (19-21).

Another relevant aspect is that all patients who were offered 5 days of radiotherapy treatment or 15 days, chose the 5 fraction approach (22).

Regarding pathological characteristics of patients, 8 were intraductal carcinoma, 11 Infiltrating ductal carcinoma, 2 Infiltrating Lobular carcinoma, 1 papillary carcinoma and 1 intracystic papillary carcinoma.

Considering clinical characteristics all patients were women between 61 and 93 years old, with an average age of 76 years old and Caucasian race.

We selected all patients without radiotherapy indication to the axilla or supraclavicular lymph nodes. We exclude those with positive lymph nodes based on fine needle aspiration (FNA), mammogram, MRI, clinically positive on examination, positive after sentinel lymph node biopsy (SLNB) or axillary clearance.

Other exclusion criteria were the TNM classification of pT3 or pT4, metastatic disease, mastectomy surgery, bilateral breast cancer or positive margins after lumpectomy. Positive margins were considered below 2 mm. Surgery was performed by experienced breast surgeons.

CT simulation

All patients were simulated in a Siemens Healthineers Somatom CT scan with 3D simulation. We estimated 3 mm slices as enough thickness assuring a proper image quality and treatment design.

The table for simulation and treatment was the same Elekta model.

Immobilization was performed with the Siho Comfort Thorax system[®], supine position and head to the middle. All patients tolerated their arms holding the brace.

Radiotherapy treatment

Radiotherapy treatment was always delivered within 2 months after performing surgery. All radiotherapy treatments were delivered from Monday to Friday or Tuesday to Saturday, five days per week.

We used VMAT technique in all cases with 6 MV photons. The LINAC used was a VersaHD accelerator with 5 mm wide leaf. XVI was acquired on daily basis during radiotherapy treatments.

For treatment design, we used Pinnacle V.3. All treatments were delivered with VMAT technique using 6 MV photons and 2 arcs. Daily XVI image verification was done for positioning prior to treatment. There was no need for Hexapod based on the minimal rotation movements required by the XVI fusion.

All PTV volumes were the breast anatomy with the limited external border of the skin, considered as 0.5 cm from the patient's surface anatomy. No boost was delivered to the surgical clips. However, if the clips were outside the initial PTV volume, it was contoured as part of the PTV.

Organs at risk (OAR) were contoured by radiotherapists with the posterior evaluation of the radiation oncologist. OAR included were contralateral breast, spinal cord, lungs, heart and coronary arteries. They were contoured with the auto contouring Pinnacle tool.

Clinical evaluation

All patients were evaluated by the Clinical Nurse Specialist (CNS) during RT treatment on daily basis providing the skincare recommendations.

The consultant radiation oncologist made an evaluation the last day of treatment, at one month, three months, six months and a year after finishing.

Both evaluations were based on interview and physical evaluation. The reference method for side effects evaluation was the standard and widely accepted Common Terminology Criteria for Adverse events (version 5.0).

Results

In June 2016 we started offering the 5 fraction treatment. Since that moment, we gave patients the opportunity to choose between the 5 fraction treatment or the standard 15 days as per UK START after knowing that they were refusing 15 fractions.

All 23 patients who were offered both treatment options, completed the 5 days treatment, so we saw a 100% completion treatment rate.

The end of treatment day, only one patient experienced radiation induced dermatitis (4%) and two patients pruritus (9%). There were not any other side effects described or commented.

One month later, there were two patients describing "pins and needles" (9%).

Three out of 23 (13%) described pruritus. Two of them

didn't described it at the end of treatment and the other one didn't improve from the end of treatment.

Regarding radiation induced dermatitis only two patients (9%) presented with Grade I by the CTCAE v.5 scale. One of them showed that at the end of treatment with the addition of one new patient.

After three months of treatment, one patient (4%) described grade 1 erythema in the inframammary fold. She attributed that to an increased sweating due to summer season. This patient presented with pruritus from the end of treatment.

Two patients (9%) started with pruritus. They were different ones from the previous who presented that symptom.

Three out of 23 patients didn't come to clinic, as they were living too far. In those cases, we made the interview by phone and examination sent by pictures taken of the breast and sent to our clinic.

After 6 months of treatment completion, none of the patients described pruritus or radiation induced dermatitis.

For the one year follow up, we only get information from 16 patients. Three of them were contacted by phone and thirteen were coming to the clinic. None of them described pruritus or radiation induced dermatitis. We couldn't contact 4 patients and 3 did not reach one year after RT treatment.

All patients asked were satisfied with the treatment and they would choose it if they were asked again.

Discussion

In a beginning, we saw that many patients refused adjuvant treatment after lumpectomy. The majority of them were elderly patients coming from rural areas and different hospital trusts than ours, were multidisciplinary oncology meetings are not well established due to the lack of radiation oncology consultants or medical oncologists. Treatment decision for patients coming directly to the surgeons in our unit, was made in an oncology multidisciplinary meeting between experienced oncology surgeons, radiation oncologists and medical oncologists.

All patient circumstances were considered in treatment decision. Age, comorbidities, location and patient's opinion were important factors in decision make. Elderly patients refusing coming for 15 radiotherapy treatments after lumpectomy were offered mastectomy.

Nevertheless, we received many patients after lumpectomy

for adjuvant radiotherapy. They were not told in the initial centre about the number of radiotherapy treatments, location, length and benefits. After explaining them all these considerations and after further assessment, we saw that many of them were refusing radiotherapy treatment.

After reviewing the literature with all this new highly hypofractionated approaches, we decided to offer them at least this 5 treatment schedule. We were surprised knowing that all patients refusing 15 days of treatment, accepted the five fractions treatment.

This reinforces the concept that elderly patients give more relevance to other matters apart from local recurrence rates, overall survival in favour of quality of life and living the rest of their life a little bit more relaxed.

After seeing the side effects from this 5 fraction treatment, they were quite happy of their choice.

Conclusions

We would qualify as satisfactory this treatment approach for highly selected patients like we described. This could not be established as standard treatment as there is not enough evidence to support that. However, it seems to be a reasonable option for elderly patients with no standard requirements.

Further investigations and the results of the UK FAST Forward trial in terms of local control and overall survival are needed to standardize this treatment approach.

Nevertheless, there are many other fractionation alternatives as could be the FAST trial with longer follow up and reporting excellent local control and overall survival rates.

Nowadays, we can consider standard fractionation the 15 hypofractionated radiotherapy regime.

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Footnote

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