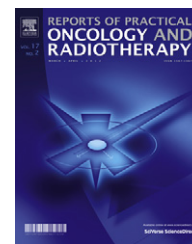


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Original research article

Radiation techniques used in patients with breast cancer: Results of a survey in Spain

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ABSTRACT

Aim: To evaluate the resources and techniques used in the irradiation of patients with breast cancer after lumpectomy or mastectomy and the status of implementation of new techniques and therapeutic schedules in our country.

Background: The demand for cancer care has increased among the Spanish population, as long as cancer treatment innovations have proliferated. Radiation therapy in breast cancer has evolved exponentially in recent years with the implementation of three-dimensional conformal radiotherapy, intensity modulated radiotherapy, image guided radiotherapy and hypofractionation.

Material and Methods: An original survey questionnaire was sent to institutions participating in the SEOR-Mama group (GEORM). In total, the standards of practice in 969 patients with breast cancer after surgery were evaluated.

Results: The response rate was 70% (28/40 centers). In 98.5% of cases 3D conformal treatment was used. All the institutions employed CT-based planning treatment. Boost was performed in 56.4% of patients: electrons in 59.8%, photons in 23.7% and HDR brachytherapy in 8.8%. Fractionation was standard in 93.1% of patients. Supine position was the most frequent. Only 3 centers used prone position. The common organs at risk delimited were: homolateral lung (80.8%) and heart (80.8%). In 84% histograms were used. An 80.8% of the centers used isocentric technique. In 62.5% asymmetric fields were employed. CTV was delimited in 46.2%, PTV in 65% and both in 38.5%. A 65% of the centers checked with portal films. IMRT and hypofractionation were used in 1% and in 5.5% respectively.

Conclusion: In most of centers, 3D conformal treatment and CT-based planning treatment were used. IMRT and hypofractionation are currently poorly implemented in Spain.

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1. Background

Breast cancer is the most common non-cutaneous cancer arising in women, accounting for nearly one-third of cancers diagnosed in females. Most cases are diagnosed in postmenopausal women, with an average age around 60 years. Early detection, when the tumor has not been extended or changed, raise the cure rate up to almost 90%. This has also increased the percentage of breast conservative treatment.¹ Currently, in Spain, 15,000 new breast cancer cases are diagnosed each year, indicating that one in sixteen to eighteen Spanish women will have breast cancer.²

Adjuvant radiotherapy to the breast is now considered part of the standard care in breast conserving therapy. An increasing number of women with early breast cancer in Spain and other countries are treated with breast-conserving therapy, based on the results of trials showing similar efficacy between these techniques and mastectomy.³⁻⁵ In two meta-analyses, radiotherapy after breast-conserving therapy was shown to improve both locoregional control and survival of patients with breast cancer.⁶ The role of radiotherapy in terms of reducing local recurrence and increasing survival after conservative surgery and after a mastectomy has been demonstrated in several randomized trials. A meta-analysis published by the group of the Early Breast Cancer Trialists' Collaborative Group showed that radiation therapy in postoperative loco-regional breast cancer increases breast cancer survival and overall survival of patients.⁷

The demand for cancer care has increased among the Spanish population, as cancer treatment innovations have proliferated. Radiation therapy in breast cancer has evolved exponentially in recent years with the implementation of three-dimensional conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), image guided radiotherapy (IGRT) and hypofractionation. While 3D-CRT has been considered as standard of care, IMRT, IGRT and hypofractionation still need further assessment. To evaluate the state of the implementation of these new techniques, it is essential to define the needs for new units and their characteristics since breast cancer represents 25-30% of patients treated in most radiotherapy departments in our country.² Moreover this study is needed prior to the design of multicenter clinical protocols. There are only a few studies designed to evaluate the radiation therapy technique used in a daily clinical practice cancer care in a country, and in Spain there are no studies on this subject.

A prospective study was proposed by the Breast Cancer Radiation Oncology Spanish Group (GEORM) with the aim to evaluate the resources and techniques used in the irradiation of patients with breast cancer after lumpectomy or mastectomy and the status of implementation of the new techniques and therapeutic schedules in our country.

2. Materials and methods

The objective of the present study was to collect data from treatments between February and March 2009, to learn about the technique and fractionation schedule of radiotherapy in

Spain. For the study to be representative, it was intended to collect data from 1000 cases in over 28 centers and more than 10 regions of Spain. We designed two tools: a database and a questionnaire. There was no financial support for the present study.

2.1. Database

A computerized database was developed which included 51 variables (v) allocated into five groups: demographics (6 v); characteristics of patients (6 v) and tumors (15 v); other treatments (8 v) and radiotherapy (16 v). Most of these questions were closed questions, including quantitative and multiple choice questions. Then, it was sent to departments responsible for breast disease in 40 centers of 12 regions in January 2009. The results were submitted in May 2009. Response was obtained from 28 centers (70%) of 12 regions of Spain (100%).

2.2. Questionnaire

A questionnaire was designed including 46 v questions about techniques and aspects related to the positioning of treatment, immobilizing supports (breastboard, braisserie, etc.), skin references, simulation systems, radiation technique, definition and delineation of GTV and critical organs, dosimetry, histograms and the control system used in the treatment. The questions in this survey were designed to learn about radiation techniques used in breast cancer patients and hence representing the current Spanish practice. This questionnaire was first tested by 3 experts in the field of breast cancer and then adjusted based on their comments. This questionnaire was sent to 28 participants, of which 26 (92.9%) responded.

2.3. Statistics

Quantitative and some categorical variables were considered. Likert scale (categorical variable: never, rarely, sometimes, very often and always) is a psychometric scale commonly used in research using surveys. The statistical analysis included a description of all variables. Intensity factors were calculated as an average of the responses with the following numerical categories: (1) never, (2) rarely, (3) sometimes, (4) very often, and (5) always. The techniques and fractionation schedules were compared on the basis of previous surgeries, i.e., lumpectomy and mastectomy.

3. Results

3.1. Patient and tumor characteristics

This study included 969 patients recruited from 28 centers distributed throughout 12 regions of Spain. The 28 radiation departments completed a database corresponding to a 70% response rate and 100% of autonomous communities on the mailing list. 31.8% of patients came from a screening program. In total, 25.4% were premenopausal, 7.2% perimenopausal and 66.8% postmenopausal. Patients' age was 57.8 ± 12.5 years. Surgical procedures were: 79.3% breast-conserving surgery (C group) including 52.7% lumpectomy and 26.5%

Table 1 – Tumor characteristics (%).

Group	T0	Tis	T1	T2	T3	T4	GI	GII	GIII	N0	N+	RE+	RE–	RP+	RP–	Her2+	Her2–
All	0.6	6.1	51.7	29.7	7.0	4.7	18.7	44.6	28.8	60.2	38.7	74.9	20.8	65.4	29.9	17.1	73.3
C	0.5	7.6	61.3	27.6	2.3	0.7	20.7	46.5	26.4	72	27.4	76.6	19.5	67.7	28.1	15.4	75.0
M	1	0.5	14.9	37.8	24.9	20.4	10.9	37.3	37.8	14.9	83.4	68.7	25.9	56.7	36.8	23.9	61.2

quadrantectomy; and 20.7% mastectomy (M group). The most common histology was infiltrating ductal carcinoma (78.9%) and 6.1% corresponded to intraductal carcinoma. General characteristics of tumors are shown in Table 1. The T stage was different between both groups; basically early tumors were present in the C group and locally advanced in the M group. Similarly, nodes were positive in 27.4% of the C group in comparison to 83.4% in the M group.

3.2. Other treatments

These characteristics are shown in Table 2. Neoadjuvant therapy was: 13.5% chemotherapy, 1.3% hormone therapy and 0.8% others or a combination of chemo and hormone therapy. Adjuvant treatments were: 48.7% chemotherapy, 4.9% hormone therapy and 8.1% others or combinations. Neoadjuvant treatment was more frequent in the M group (38.8%) than in the C group (9.1%); however, the sequential or concurrent adjuvant treatments were similar in both groups. When treatment was sequential, an interval of 3–4 weeks was used. The sentinel lymph node was performed more frequently in the C group than in the M group.

3.3. Radiotherapy

Table 3 shows the differences between both groups (C and M).

- (1) *Position and points of reference:* All the centers treated their patients in the supine position, and only 3 centers occasionally treated in the prone position. Forty-six percent of centers treated with one arm in an abduction position, and in 42% of them with two arms in abduction. The breastboard was routinely used in 65% of the centers and only occasionally in 23%. Another type of support and immobilization was used only in a few centers. Temporary cutaneous brands were used only by 8% of the centers, whereas the permanent ones were used by 92%. The majority of the centers used 3 or more brands, usually 3–4. 73.1% of the centers had their own TC and the rest used a TC from Radiology Departments.
- (2) *Delineation of organs at risk:* The organs of risk delimited were: homolateral lung (80.8%), contralateral lung (53.8%); heart (80.8%); head humeral (23.1%); brachial plexus (3.8%); contralateral breast (15.4%). In 84%, histograms were used

for the acceptance of treatment, especially in case of the homolateral lung, using the $V_{20} < 20\%$. Delimitation of critical organs was performed by radiation oncologists (38.5%), radiotherapists from the Radiotherapy Departments (15.4%) or medical dosimetrists from the Medical Physics Departments (19.2%). Dose–volume histograms of delineated OARs were used to decide on plan acceptance in relation to specific criteria in 84% of the responding institutions.

- (3) *Volumes delineation:* Table 3 shows the differences in treated volumes between both groups (C, M). In 46.2% of the centers the radiation oncologists delimited the CTV, in 65% the PTV and in 38.5% both. In 42.3%, the radiopaque surgical brands were helpful for this procedure. When breast target volume delineation was performed, various references and landmarks were used: radiopaque wires visible on CT were usually used in 61.5% of the centers, and 3.8% never used them. For the purpose of boost target volume definition, surgical clips, when available, were used in 42.3% institutions.
- (4) *Energy and dosimetry:* Most patients were treated with megavoltage radiation, with 4–6 MV photons, generally 6 MV. All institutions used CT-based treatment planning. The most common treatment planning method was the three-dimensional conformal treatment, both in breast and in tumor bed. Inverse planning IMRT was performed only in 1% of the cases. The centers used the isocentric technique (80.8%) and asymmetric fields on many occasions (62.5%). A great diversity existed in the number of fields of entry to radiate the mammary volume. In 80% of the occasions more than 2 (segmented fields) were used. The irradiation of the supraclavicular nodes was done by using an anterior field in 42% of the cases, adding a posterior one in 19.2% and in association with another type of field in 38.5% of the centers. The boost in tumor bed was performed in 56.4% of patients and the most commonly used delivery method was electrons in 59.8% of them, followed by photon irradiation in 23.7%, and HDR brachytherapy in 8.8% of the cases.
- (5) *Dose and fractionation schedule:* Total dose and fractionation schedule after breast conservative surgery or after mastectomy was standard in the majority of institutions and for the majority of patients. The fractionation was different in the C group, where 5.5% of patients were treated by using

Table 2 – Other treatments (%).

Group	Lymphadenectomy		Systemic treatment		
	Sentinel	Complete	Neoadjuvant	Concomitant	Adjuvant
All	42.6	52.3	15.6	55.5	71.7
C	54.6	41.4	9.1	57	70.8
M	4.5	94	38.8	60.7	78.1

Table 3 – Radiotherapy technique.

		C group		M group		
		n	%	n	%	
		768	79.2	201	20.7	
Volume	Breast	768	100	–	–	
	Chest wall	–	–	201	100	
	Supraclavicular	130	16.9	167	83.1	
Dosimetry breast or chest wall	Axila	56	7.3	68	33.8	
	IMC	21	2.7	6	3	
	2D	2	0.3	–	1.5	
	3D	758	98.7	–	97.5	
	IMRT	8	1	–	0	
Energy	Cobalt	90	11.7	10	5	
	4–6 MV	643	83.7	160	79.6	
	>6 MV	24	3.1	3	1.5	
	Electrons	–	–	22	10.9	
	Combinations	11	1.4	6	3	
Boost	Yes	522	68	25	12.4	
	No	246	32	176	87.6	
Dosimetry boost	2D	94	18	7	28	
	3D	425	81.6	18	72	
	IMRT	2	0.4	–	–	
Energy boost	Cobalt	40	7.7	–	–	
	Photons	123	23.7	3	12	
	Electrons	311	59.8	22	88	
	HDR	46	8.8	–	–	
Total dose	<46 Gy	59	7.5	9	4.5	
	Breast or chest wall	46–50.4 Gy	704	91.8	188	93.5
Fraction dose	>50.4 Gy	3	0.4	4	2	
	Breast or chest wall	<2 Gy	35	4.6	13	6.5
Total dose boost	Breast or chest wall	2 Gy	675	87.9	180	89.6
		2.5–2.67 Gy	42	5.5	7	3.5
		>5 Gy	14	18.2	1	0.5
		<10 Gy	51	9.7	3	12
Fraction dose boost		10–15 Gy	244	46.3	15	60
		16–20 Gy	174	33	7	28
		<2 Gy	1	0.2	–	–
		2 Gy	422	80.1	22	88
		2.3–2.67 Gy	7	1.3	2–1	8
		3–4.5 Gy	46	8.7	1	4
	5–10 Gy	46	8.7	–	–	

C group, conservative group; M group, mastectomy group; IMC, internal mammary chain.

the classic hypofractionation schedule and the hypofractionation with dose per fraction of 5 or more Gy was used in 1.82% of patients. In the M group, hypofractionation techniques accounted for only 4%. Sequential delivery of the boost for either some or all patients was used in 94% of the institutions, while a concomitant boost was used in 6% of cases. The most commonly used total boost dose was 10–16 Gy in both groups. However, the doses per fraction were different, 2 Gy being the most frequent in both groups, but the technique in the C group hypofractionation accounted for 18.7% (including HDR) compared to only one case in the M group.

- (6) *Verification procedures*: The 7.7% of institutions reported to use X-ray film for position verification, while 76.9% used electronic portal imaging device (EPID) and in 3.8% of cases both X-ray film and EPI were used. Cone beam CT was used only in 3.8%. 7.8% of them did not provide data.
- (7) *New technologies/strategies*: Specific questions were added to identify the use of partial breast irradiation (PBI),

irradiation in the prone position, and breath-hold techniques. PBI was used in one institution, mostly in selected patients, i.e., patients treated within clinical trials. Irradiation in the prone position is rarely used. None of the centers did respiratory gating in breast cancer patients.

4. Discussion

In Spain, in the last decade, cobalt units have been substituted by linear accelerators at the same time that 2D dosimetry has been replaced by the 3D dosimetry. The results of this survey are based on reports from 28 institutions from 12 regions. In our survey, the response rate to the distributed questionnaire was 92%, which is higher than similar previous surveys which reached response rates of 45%, 65%, 41% and 25%, respectively.^{8–11} The results provide an analysis of the current practice in the institutions participating

and they give a complete picture of practice across the country as reflected by the number of regions participating in the survey. As expected, patients who received radiation after conservative treatment had earlier stage of the disease than those who were treated after mastectomy (Table 2).

In the present study, the most common therapeutical method was to treat the patient in the supine position with one (46%) or two arms (42%) in forced abduction, using some system of immobilization (65% with breastboard) and cutaneous permanent brands (92%). In our study, the prone irradiation position was only occasionally used.

The use of CT has increased rapidly in the last years and all centers now routinely use CT scans for treatment planning. A survey in the United Kingdom, performed between 1997 and 1999, showed that only 2 out of 46 institutions used CT.¹² Australian surveys published in 1999, reported that 3 out of 11 institutions used CT¹³ and in 2001 the numbers increased to 10 out of 20 institutions.⁸ Another survey reporting on the period 1998–2002 showed that 66 out of 102 radiation oncology practices in Australia and New Zealand used CT-based treatment planning.⁹ The survey in EORTC institutions performed in 2008–2009 indicates that CT-based planning is now used as a standard for the delineation of breast target volumes and organs at risk.¹⁴ In the present study, all institutions used CT-based treatment planning. In our survey, 73.1% of centers had TC for planifications and 38.5% used a conventional simulator.

The organs of risk generally delimited are the homolateral lung (80.8%) and the heart (80.8%). Other organs delimited in a few cases were humeral head, contralateral breast and braquial plexus. This illustrates that in current clinical practice, efforts are being made to limit the irradiation dose to organs at risk, thus reducing the risk of side effects. In 38.5% of the centers, the delimitation of organs at risk is performed by radiation oncologists and in the rest by either radiotherapists (15.4%) or medical dosimetrists (19.2%).

The treatment volumes are different after breast conserving treatment than after mastectomy. As expected, the lymph nodes are included more frequently after mastectomy (Table 3). However, in Spain it is very rare to include the internal mammary chain, its radiation being performed only in cases of sentinel lymph node involvement, so the percentage was very similar in both groups. The major differences among centers were the system for delimitation. Some of them already delimit CTV and later they do the expansion to PTV, whereas others continue with the most classic position to delimit directly PTV. With regard to the definition of clinical target volumes, different methods and procedures are used by different institutions. The most frequent method is to use radiopaque wires to delineate the breast target volume. For delineating the boost target volume surgical clips were employed.

In spite of the majority of the cobalt units having been replaced by liner accelerators, 11.7% of conservative and 5% of post-mastectomy treatments were still performed with these units. This is due to the need for optimization of resources. The electrons are used only in 10.9% of cases in the irradiation of the chest wall.

With regard to treatment techniques, wedge filters are being replaced by segmentation of fields. Eighty percent of

centers used more than two fields of treatment, 80.8% used the isocentric technique. In relation to supraclavicular area, 42% of centers normally used one anterior field, 19.2% added a posterior field and 38.5% used other fields. Although previous studies have demonstrated that IMRT generally improves dose homogeneity in clinical target volumes, reduces the dose delivered to normal tissue and limits the incidence of acute and late skin toxicity and oedema,^{15–19} it seems that its actual implementation in clinical practice is still limited. This might be explained by the fact that the implementation of IMRT may require additional personnel, special training and dedicated equipment.

In our survey, the use of electron irradiation was the most common method used for the boost treatment. We use a direct field of electrons in 59.8%, followed by 23.7% by photons and 8.8% with HDR. The variability in the modality of boost treatment among institutions can be probably explained in terms of comfort for patients, the electrons being the best choice in this regard, and availability, since not all the services have HDR units.²⁰ In our study, there were no cases treated with MammoSite®.²¹

The predominant dose per fraction size for breast irradiation was 2 Gy, which was used in 5.5% of treatments in the C group with a fractionation schedule of 15 fractions of 2.67 Gy, which is the same fractionation schedule as that used in the UK START B trial.²² In the UK START A trial, a dose of 41.6 Gy was delivered in 13 fractions,²³ while a dose of 42.5 Gy was delivered in 16 fractions in a Canadian trial, which only included node-negative patients.²⁴ All these trials, including the updated results of the Canadian trial²⁵ with a median follow-up of 10 year, confirm that hypofractionation is associated with excellent local control and toxicity; similar to the conventional schedule of 50 Gy delivered in 2 Gy-fractions. In our country, a 1.8% of cases were treated with weekly hypofractionation schemes, with fractions greater than or equal to 5 Gy. In the M group, the daily hypofractionation scheme decreased to 3.5% and the weekly hypofractionation scheme was only applied in 0.5% of cases weekly. To the boost it is only given with hypofractionation scheme in 1.3% of cases. Although this survey indicates that hypofractionation is currently poorly implemented in Spain, it can be expected that in the near future an increasing number of patients in Spain will be treated with a higher dose per fraction. Also, the survey shows that the use of partial breast irradiation is very unusual; the majority of patients being included in a clinical trial.

The majority of Spanish institutes apply a sequential boost with a fraction size for boost irradiation of 2 Gy. At the same time, integrated boost (SIB) is used in a few institutions in Spain.

76.9% of the institutions reported to use Electronic Portal Imaging (EPI) for patient set-up verification²⁶ and 7.7% used X-ray check. The Cone-Beam is available only in 3.8% of the centers. There were important differences in the results from a UK survey published in 2002, when only half of the institutions performed set-up verification.¹² The results of EORTC-Radiation Oncology Group conducted in the years 2008 and 2009 showed that 92% of the institutions used EPI for patient set-up.¹⁴

5. Conclusions

This survey among the Breast Cancer Radiation Oncology Spanish Group indicates that the technique used for treatment of breast cancer with radiotherapy is very homogeneous in Spain. Broad adoption of new techniques and developments is in progress.

All responding institutions reported to use CT-based treatment planning. Three-dimensional conformal radiotherapy and EPI based patient set-up verification are now in mainstream use, with IMRT techniques being used only in a few institutions. The boost is applied sequentially in the majority of the responding institutions.

The future is to delegate the delineation of the organs at risk to technologists, and to increase hypofractionation schedules and partial breast irradiation.

Contributors

Manuel Algara: Study design, Data collection, Statistical analysis, Prepared Manuscript; Meritxell Arenas, Dolores De las Peñas, Eloisa Bayo and Julia Muñoz: Study design, Data collection, Prepared Manuscript; José Antonio Carceller, Juan Salinas, Ferran Moreno, Francisco Martínez and Ezequiel González: Study design, Data collection; Ángel Montero: Study design, Data collection, Prepared Manuscript.

Conflict of interest

None declared.

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