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RESEARCH ARTICLE

SEOR SBRT-SG survey on SRS/SBRT dose prescription criteria in Spain

M. J. Perez-Calatayud[1] · A. J. Conde-Moreno[2] · F. J. Celada-Álvarez[2] · C. Rubio[3] · F. López-Campos[4] · A. Navarro-Martin[5] · L. Arribas[1] · M. Santos[6] · J. Lopez-Torrecilla[7] · J. Perez-Calatayud[2,6]

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Abstract

Aim Stereotactic body radiotherapy (SBRT) and stereotactic radiosurgery (SRS) are essential tools in radiation oncology. In Spain, the use of these techniques continues to grow as older linear accelerators (linacs) are replaced with modern equipment. However, little is known about inter-centre variability in prescription and dose heterogeneity limits. Consequently, the SBRT-Spanish Task Group (SBRT-SG) of the Spanish Society of Radiation Oncology (SEOR) has undertaken an initiative to assess prescription and homogeneity in SRS/SBRT treatment. In the present study, we surveyed radiation oncology (RO) departments to obtain a realistic overview of prescription methods used for SBRT and SRS treatment in Spain.

Methods A brief survey was developed and sent to 34 RO departments in Spain, mostly those who are members of the SEOR SBRT-SG. The survey contained seven questions about the specific prescription mode, dose distribution heterogeneity limits, prescription strategies according to SRS/SBRT type, and the use of IMRT–VMAT (Intensity Modulated Radiation Therapy–Volumetric Modulated Arc Therapy).

Results Responses were received from 29 centres. Most centres (59%) used the prescription criteria $D_{95\%} \geq 100\%$. Accepted dose heterogeneity was wide, ranging from 107 to 200%. Most centres used IMRT–VMAT (93%).

Conclusions This survey about SRS/SBRT prescription and dose heterogeneity has evidenced substantial inter-centre variability in prescription criteria, particularly for intended and accepted dose heterogeneity. These differences could potentially influence the mean planning target volume dose and its correlation with treatment outcomes. The findings presented here will be used by the SEOR SBRT-SG to develop recommendations for SRS/SBRT dose prescription and heterogeneity.

Keywords SRS · SBRT · Dose prescription · Clinical dosimetry · External radiotherapy

Introduction

Stereotactic body radiotherapy (SBRT) and stereotactic radiosurgery (SRS) are essential tools in radiation oncology. Interest in these modalities has significantly increased in recent years, particularly in Spain, where many centres have replaced older linacs with more advanced equipment [1], thus facilitating the use of these sophisticated radiotherapy techniques.

As in all areas of medicine, it is essential to develop consensus-based, uniform guidelines in radiation oncology, in part due to the enormous advantages of having common systematic criteria, which permits a reliably compared treatment outcomes. One of the keys to achieving homogeneous criteria in radiotherapy is to establish where and how the prescribed dose is made. This is particularly true in SBRT and SRS due to the high radiation doses. Moreover, to compare clinical results between different centres, it is essential

✉ M. J. Perez-Calatayud
mariajose.perezcalatayud@gmail.com

1 Radiation Oncology Department, Fundacion Instituto Valenciano de Oncologia, C/Beltrán Báguena 8, 46009 Valencia, Spain

2 Radiation Oncology Department, Hospital La Fe, Valencia, Spain

3 Radiation Oncology Department, Hospital HM Sanchinarro, HM Hospitales, Madrid, Spain

4 Radiation Oncology Department, Hospital Ramon Y Cajal, Madrid, Spain

5 Radiation Oncology Department, Hospital Duran I Reynals, Instituto Catalan de Oncología, Barcelona, Spain

6 Radiation Oncology Department, Clinica Benidorm, Alicante, Spain

7 Radiation Oncology Department, Hospital General-ERESA, Valencia, Spain

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to know how the prescription was done; otherwise, there is a high likelihood of comparing different effective doses to the target.

Currently, various scientific societies and bodies are carrying out initiatives to enable realistic comparison of treatment outcomes, to address this important topic. To our knowledge, the focus of most of these initiatives is reporting, while the dose prescription strategy is left to the discretion of the institution. This is the case of the recently published ICRU (International Commission on Radiation Units and Measurements) report 91 [2], an update of the widely used ICRU report 83 [3], focuses on small photon beams. ICRU 83 removed dose prescription to a reference point due to limitations in intensity-modulated radiotherapy (IMRT), recommending instead the use of multiple dose–volume histogram (DVH)-based planning (e.g. $D_{2\%}$ and the $D_{98\%}$) to ensure good homogeneity data. ICRU 83 also recommends prescribing to a DVH parameter such as $D_{50\%}$. However, the $D_{50\%}$ specification is the only data prescription-related data point in that report.

ICRU 91 aims to update the traditional SRS prescription to a covering isodose line to the isodose surface, which should cover an optimal percentage of the planning target volume (PTV) while simultaneously limiting doses to organs-at-risk (OAR) in an optimal manner. As stated in ICRU 91, "the term *optimal* is then strongly depending on the actual treatment situation. For SRS/SBRT of a single brain metastasis away from any OAR, this might mean that close to 100% of the PTV should be covered by the prescription isodose while for lung SBRT only 95% PTV coverage might be safely reached or for spinal SBRT only 80–85% of the PTV can be covered by the prescribed isodose due to the constraints on the spinal cord." ICRU 91 provides recommendations for reporting D_{mean}, D_{median}, $D_{2\%}$, and conformity indices (CI). Like previous ICRU reports, these recommendations are expected to be widely applied by the radiation oncology community.

In addition to the ICRU reports, various medical societies have developed recommendations for specific SRS/SBRT treatments. For example, the ACROP-ESTRO provided recommendation for lung SBRT in 2017 [4]. Those guidelines included detailed recommendations for the prescription and PTV homogeneity, as follows: "at least 95–99% of the PTV should be covered by the prescribed dose and the maximum dose should be 125–150%". The wider tolerance in dose heterogeneity is relevant, which has logical implications for D_{mean} and $D_{50\%}$.

The ACROP-ESTRO recently (2020) published the results of a survey [5] to quantify current variability in the dose prescription practices of the institutions involved in developing the ACROP lung SBRT guidelines. That survey included 15 sample cases from 8 institutions. The results showed that the main focus of some centres is to achieve constant PTV coverage whereas other centres aimed for a constant GTV coverage; one centre prescribed only to the GTV. That study provided more detailed recommendations for dose planning and reporting of lung SBRT, which are in line with ICRU 91, including a minimum PTV $D_{98\%}$ of 100 Gy BED_{10Gy} and minimum GTV/ITV mean dose of 150 Gy BED_{10Gy}, and a $D_{2\%}$ from 60 to 70 Gy. The conclusions of that study emphasised the differences in coverage conditions for the lung PTV and GTV.

In 2017, the Spanish Society of Medical Physics (SEFM) published recommendations on the implementation and use of SBRT [6], separating the recommendations into two categories: "mandatory" or "recommended". According to those guidelines, the prescription to the PTV must be at least 95% ("mandatory"), with overdose up 100% kept within the PTV. The maximum dose ("recommended") should be 125% of the prescribed dose in conventional, C-type linacs, and 135% in robotic linacs, although the dose can be up to 140–145% in both types of linac, always within the PTV. These recommendations show that the heterogeneity window is quite wide.

Finally, some hospitals apply the same policies used in conventional external beam radiation therapy (EBRT) in which PTV homogeneity is a constraint to SBRT and SRS. By contrast, other hospitals apply the classical SRS prescription approach of "prescription isodose", without specifying any % PTV volume or overdose constraint to SBRT.

Given the aforementioned uncertainties and variability in individual hospital strategies, the SEOR SBRT-Spanish Task Group (SBRT-SG) decided to conduct a survey to evaluate the current situation in Spanish hospitals with regard to prescription and homogeneity in SRS/SBRT. Our main aim was to determine the possibility of making recommendations to standardise (to the extent possible) the clinical dosimetry for SRS/SBRT. Given the increasingly widespread implementation of modern linacs in Spain, we believe that this is the time to develop consensus standards to ensure the quality of SRS/SBRT techniques.

In this context, the present study was conducted to survey radiation oncology departments around the country to obtain an overview of current SBRT/SRS prescription practices.

Materials and methods

To assess current prescription practices in Spain for SBRT/SRS, we created a short survey and sent it, gradually from May to June 2020, to a significant number (34) of radiation oncology departments (mainly members of the SEOR SBRT-SG). RO departments without C-type linacs (GammaKnife or CyberKnife) or tomotherapy were excluded due to the logical nature of the dose distribution in those units.

The survey was limited to seven questions to minimise the time required to complete it, which we hoped would increase the response rate. The survey questions were designed mainly to determine the general prescription approach at each centre. Only descriptive statistics was used. Table 1 shows the survey questions.

The rationale underlying each question is discussed below.

Question #1 was developed to determine whether percentage of the PTV receiving the prescribed dose is accepted or managed. Typical responses should be that 95%, 98%, 99%, or 100% of the PTV receives 95–100% of the prescribed dose. Another aim of question #1 is to ascertain if there are cases in which GTV-ITV coverage (% volume versus dose) is mandatory.

Question #2 aims to determine if there are any other mandatory conditions. For example, ICRU 83 recommends prescribing the dose at D_{50}%; thus, in a typical scenario can be once fulfilled #1 to check $D_{50\%}$. If the DVH curve of the PTV is not sharp (i.e. non-homogenous distribution), the D_{50}% receives the prescription dose once #1 is normalised accordingly.

Question #3 asks respondents to report whether or not the CI must fall within a given interval to be considered acceptable. This question is relevant given the wide diversity of CIs applied by different institutions.

Question #4 is important given that inhomogeneity will affect the D_{50}% and D_{mean} values, and thus dose reporting could be misinterpreted.

For question #5, we expected that, in cases with inhomogeneity > 7–10%, the location would be through the GTV. However, it is essential to understand how overdose volumes are controlled in other cases.

Question #6 aims to detect potential inter-centre differences in prescription heterogeneity according to the type of SRS-SBRT. Commonly, coverage is higher in tumours without adjacent OARs, such as brain SRS non-at the brainstem vicinity or without normal tissue V_{12Gy} compromise. An important example not fulfilling this condition is vertebral SBRT due to the spinal cord constraint.

The aim of question #7 is to determine the use of modulated versus dynamic conformal arc techniques as this has important implications in both radiation equipment and quality assurance procedures.

Results

A total of 29 (85%) centres responded to the questionnaire, but the level of detail provided differed greatly. Some centres provided very interesting details and additional comments. In the following paragraphs, we discuss the results for each question, emphasising inter-centre variability.

1. On what DVH parameters the prescription is based? For example, the % of the PTV (or GTV) covered by a % of the prescribed dose.

A significant proportion of centres (17/29; 58.6%) apply the $D_{95\%} \geq 100\%$ criteria for both SRS and SBRT. However, some centres (4/29; 13.8%) reduce the $D_{95\%} \geq 95\%$ for both SRS and SBRT (or not specified), and in the other cases, only for SBRT (maintaining a higher criteria for SRS). The other centres ($n = 8$) presented substantial diversity of approaches. Two centres (2/29) apply a dose–volume constraint of $D_{100\%} \geq 95\%$, while one centre specified a dose range $D_{95\%} \geq 95$–100%, and another centre indicated a volume range $D_{90–98\%} \geq 100\%$. One centre reported using $D_{98\%} \geq 98\%$. The two centres with the highest coverage aims reported the following values: $D_{100\%} \geq 100\%$ (maximum coverage) and $D_{99.5\%} \geq 100\%$.

Of the four centres that explicitly specified a difference in coverage between SBRT and SRS, two centres reported $D_{98\%} \geq 100\%$ for SRS, while another centre increased the coverage to $D_{99\%} \geq 100\%$ and another maintained the prescription as the PTV covered by the 70–90% isodose.

2. In addition to the DVH parameters referred to in question #1, are there any other parameters that must be met (e.g. $D_{50\%}$ or D_{mean}) ?

Additional conditions were required in 19/29 centres (65.5%); of these, three centres reported that 50% of the dose must be within the PTV volume plus a margin of 2 cm in lung SBRT; four centres indicated only the homogeneity values, as reported in question #4. The remaining centres reported highly diverse criteria. Some centres added other coverage DVH parameter to the PTV ($D_{98\%} \geq 90\%$,

Table 1 Survey questions

1. On what DVH parameters the prescription is based? For example, the % of the PTV (or GTV) covered by a % of the prescribed dose
2. In addition to the DVH parameters referred to in question #1, are there any other parameters that must be met (e.g. $D_{50\%}$ or D_{mean})?
3. Is the conformity index (CI) also considered in the prescription? That is, must the CI fall within a specific range, or merely be reported?
4. Is there any limit to the dose inhomogeneity (D_{max})? If so, what is the limit?
5. If inhomogeneity is greater than 7–10%, is its location conditioned within the GTV-ITV or concentrically through the GTV centre?
6. Are all previous conditions applied in general to SRS-SBRT or are there differences according the type (brain, lung, abdomen, bones, etc.)?
7. Are IMRT or VMAT used in these types of treatments?

$D_{99\%} \geq 90\%$, $D_{99.5\%} \geq 100\%$) while others applied the condition to the GTV-CTV ($D_{100\%} \geq 100\%$), although the competition with the values reported in question #1 is not clear. In one centre, the PTV $D_{50\%}$ is considered $D_{50\%} \geq 100\%$, thus emphasising that both coverage conditions (questions 1 and 2) must be fulfilled.

3. Is the conformity index also considered in the prescription? That is, must the CI fall within a specific range, or merely be reported?

A substantial proportion of centres (17/29; 58.6%) responded affirmatively to this additional condition, although only three clarified that the CI is evaluated only for SRS. Inter-centre differences in CIs were evident, ranging from the simplest volume quotient of the prescribed dose and PTV to the Paddick CI one, including the particularities of the CI definitions in a given RTOG trials, being unclear its use in function of the SRS or SBRT types.

4. Is there any limit to the dose inhomogeneity (D_{max})? If so, what is the limit?

Four centres reported that they do not limit the maximum dose in SRS or SBRT. Five centres apply different dose inhomogeneity restrictions to SRS compared to SBRT, ranging from 115 to 200%, including one centre with no limit for SRS. For SBRT, the range was 107–110% for those five centres.

Of the centres that apply the same inhomogeneity restriction to SRS and SBRT, we can distinguish two clear groups: eight centres reported small values (107–110%), indicating that the objective is a homogeneous dose distribution. The accepted dose heterogeneity in the other 12 centres was large (120–150%).

5. If inhomogeneity is greater than 7–10%, is its location conditioned within the GTV-ITV or concentrically through the GTV centre?

In most centres (17/29; 58.6%), the maximum dose is located at the GTV-CTV. In the other centres, either no condition was applied ($n = 3$) or only within the PTV.

6. Are all previous conditions applied in general to SRS-SBRT or are there differences according the type (brain, lung, abdomen, bones, etc.)?

Only 5/29 centres (17.2%) reported differences between SRS and SBRT prescriptions. In general, the coverage demand in SRS is higher than SBRT, with a higher dose heterogeneity tolerance. Some centres reported that differences are a function of the target in SBRT, such as in spinal SBRT, where spinal cord constraints condition PTV coverage.

7. Are IMRT or VMAT used in these types of treatments?

With exception of two centres, all others reported using IMRT, mostly VMAT, in SRS-SBRT treatments. In some cases, a dynamic arc technique is considered if the PTV presents a convex outline.

Within the remarkable diversity, the options most adopted are summarised in Table 2

Discussion

This survey detected wide heterogeneity in dose prescription criteria among the participating centres. This finding was not unexpected given that no clear standards have yet been established. In addition to the % PTV covered by the % prescription dose, the condition applied to the ITV-GTV also differed in some cases. Dose inhomogeneity is another important issue and no clear standards are available at present, even though inhomogeneities can have a large influence on mean and median PTV doses.

The heterogeneities found in this survey are consistent with the available literature. For example, Pokhrel et al. [7] recently indicated the following dose prescription conditions for lung SBRT: "at least 95% of the PTV received the prescription dose and the maximum dose to the PTV was limited to 130% (fall within the ITV) of the prescription dose". This approach is common in many studies and recommendations: only the upper dose limit is stated, independently of the specific overdose distribution. Some studies add conditions to the conformity and gradient indices. For example, Pokhrel et al. stated the following: the "conformity index (CI): ratio of prescription isodose volume to the PTV. CI less than 1.2 is highly desirable; CI = 1.2–1.5, acceptable with minor deviations. Gradient index (GI): ratio of 50% prescription isodose volume to

Table 2 Most adopted options

Survey question	Most adopted option	% institutions
PTV prescription	$D_{95} \geq 100\%$	59%
Additional prescription parameters	Lung: 50% of the prescribed dose within PTV + 2 cm	65%
Conformity index consideration in prescription	In SRS	59%
Dose inhomogeneity	≥ 110%	72%
Inhomogeneity location	GTV-CTV	59%
SRS vs SBRT prescription differences	No differences	76%
Treatment technique	IMRT–VMAT	93%

the PTV. GI has to be smaller than 3–6, depending on the PTV".

Another example, also for lung SBRT, is the study by Moghanaki et al. [8], conducted to crowdsource and analyse of lung SBRT treatment plans from around the world. Those authors established an interesting metric to describe the "minimum" and "ideal" conditions for the prescription dose (PD):

> Coverage of (98%) of the PTV: min 95% PD, ideal 100% PD.
> Coverage of whole PTV minus 0.03 (cc) min 90%PD, ideal 100%PD.
> Conformation number[1] (95% PD, PTV) min 0.75, ideal 0.95.
> Conformality index[2] (50% PD, PTV) min 5, ideal 4.
> Homogeneity index[3] (100% PD, PTV).
> 1 [Vol PTV covered by 95% PD (cc)]^2/{[Vol PTV (cc)] × [Vol 95% PD (cc)]}.
> 2 [Vol 95% PD (cc)]/[Vol PTV (cc)].
> 3 [D1% PTV (Gy) − D99% PTV (Gy)]/100% PD.

It is worth noting that homogeneity is not included in this metric and that only 0.03 cc is subtracted from the PTV. We selected these two very recent examples, taken from a wide body of recent publications, to illustrate the large difference in prescription criteria and to underscore the fact that dose inhomogeneity is not sufficiently detailed in the literature, having very important influence on D_{mean} and D_{50}.

The publication of ICRU report 91 in 2017 [2] represented a major improvement in establishing standards for SRS-SBRT and in general for small photon fields. ICRU 91 points out the shortcomings of ICRU 83, noting that all relevant aspects of SRS and SBRT are addresses because a single DVH value is insufficient to accurately describe the generally inhomogeneous dose distribution within the target volume. In addition, relevant quality indices (homogeneity, conformity, and gradient indices) were only considered developmental.

ICRU 91 report recommended that reporting for stereotactic treatments should contain the following information (not complete):

- PTV median dose ($D_{50\%}$) and PTV $D_{near\text{-}min}$ and PTV $D_{near\text{-}max}$
- Optionally, the median dose ($D_{50\%}$) for existing GTV/CTV and ITV contours should also be reported (these values must be documented for lung SBRT). For OARs, at least three values should be reported: mean dose, $D_{near\text{-}max}$, and another relevant $V_{D\%}$ value. Dose homogeneity (if available, mean dose to PTV and standard deviation of mean dose to PTV), should also be reported.
- The dose conformity, CI, is given by the volume encompassed by the isodose hypersurface with the prescribed dose (prescription isodose volume [PIV]), the PTV, and the PTV receiving the prescribed dose or more (PTV_{PIV}).
- For brain radiosurgery, the dose gradient index (GI) is given by the volume encompassed by the isodose hypersurface with half the prescribed dose (PIV_{half}) and the volume encompassed by the isodose hypersurface with the prescribed dose (PIV): $GI = PIV_{half}/PIV$
- As an example of CI, the due to Paddick [9] was cited together with other alternative:

$$CI = \frac{PTV \times PIV}{PTV_{PIV}^2}.$$

To standardise the use of CIs, it would be advisable to limit their variety to only those described in ICRU 91.

The near-minimum and near-maximum dose to the PTV ($D_{near\text{-}min}$ and $D_{near\text{-}max}$) were introduced in ICRU report 83 as the $D_{98\%}$ and $D_{2\%}$. However, for very small volumes (< 2 cm^3), which are often present in stereotactic treatments, the PTV $D_{98\%}$ and $D_{2\%}$ indices are close to meaningless, which is why ICRU 91 recommends using $D_{near\text{-}min} = D_{V\text{-}35mm}{}^3$ and $D_{near\text{-}max} = D_{35mm}{}^3$ for volumes < 2 cm^3.

ICRU 91 recommendations for reporting detail both prescription and target dose homogeneity, criteria that should be met by all published studies, clinical trials, and society recommendations. The small value (0.035 cc) implies the need to apply certain special cautions in both contouring and calculations in the treatment planning system, requiring high-resolution volumes, DVH, and a calculation grid. In addition, the volume implications in DVH emphasise the necessity of precise contouring.

In our opinion, homogeneity conditions should receive more attention in the prescription. In most lesions, such as metastases, there is generally no concern about the overdose volume if it is located through the target centre and does not affect normal tissue. However, there are cases, such as arteriovenous malformations, in which the target overlaps with normal tissue and thus overdosing may be of concern.

The DEGRO/DGMP (German Society for Radiation Oncology/German Society for Medical Physics) working group on stereotactic radiotherapy and radiosurgery reviewed the ICRU 91 report and emphasised the importance of consulting with experts when starting a new stereotactic radiotherapy programme [10]. Continuous communication and collaboration between centres, in the framework of working groups or multicentre trials, will further support and improve the quality of stereotactic treatments [11, 12]. However, as the DEGRO/DGMP working group observed, ICRU 91 does not provide specific prescription recommendations.

Perhaps the most notable finding of the present survey is the wide inter-centre range in accepted or intended dose heterogeneity, which ranges from homogenous approaches (maximum 107%) to very high overdose volumes (up to 200%). This dose inhomogeneity will affect the $D_{50\%}$ and D_{mean}, and thus dose reporting could be misinterpreted.

Klement et al. [13] recently evaluated a large number ($n = 1500$) of lung SBRT treatment plans, finding that prescription and dose inhomogeneity for SBRT vary widely in early-stage non-small cell lung cancer. The authors demonstrated that BED_{ave} (the average between near-minimum and near-maximum doses) was generally better correlated with the probability of tumour control than either BED_{max} or BED_{min}. Since the BED_{ave} was highly correlated with the mean gross tumour volume dose, they concluded that the latter could be used as a prescription target. Consequently, the inhomogeneous dose distribution plays a key role.

Quality and accuracy are both crucial in radiation oncology, particularly in SRS/SBRT techniques in which many significant challenges are present, including: small beam dosimetry and delivery aspects; setup margins (in lung or abdominal SBRT); dose calculation issues in lung treatments; and delivery cautions when IMRT–VMAT techniques are used due to interplay and other issues.

The impact of contouring on DVH prescription parameter is important. Assuming spherical PTVs with volumes of 10, 100, and 200 cc; the corresponding radii are 13.37, 28.79, and 36.28 mm, respectively. If the volume is reduced to 95%, the resulting radii show a negative increase of 0.13, 0.48, and 0.62 mm, respectively. Thus, reducing coverage from 100 to 95% implies an approximate variation of 0.5 mm, even for a 200 cc spherical target. These figures illustrate the very small differential thickness when using the 95 or 98% dose prescription. Indeed, this underscores the crucial importance of ensuring that PTV contouring is performed with the appropriate imaging modality by an experienced, well-trained radiation oncologist to minimise interobserver variation, as has been evidenced elsewhere [14–16].

The SEOR and SEFM continue their ongoing efforts to develop protocols, recommendations, and guidelines to help address these fundamental issues. Moreover, as older machines are replaced with more modern equipment in Spain, the role of these professional associations will become even more important for new and future users.

An important limitation of this study is that the participating centres have widely different experience levels. Some centres are just starting to apply SRS/SBRT treatments, while others have many years of experience. In addition, some centres administer SBRT but not SRS, or do not offer all SBRT indications, such as spinal treatments in which coverage must consider spinal cord sparing. In this regard, representatives from one experienced centre suggested that the prescription criteria could be modified according to the level of experience.

We believe it is important to emphasise the modest aims of this study: to collect data to confirm the assumed heterogeneity in clinical practice in terms of SBRT and SRT parameters. In this context, even though we did not survey all RO departments in Spain, this was not necessary because the purpose was simply to collect a representative sample of data from centres throughout the country to confirm the diversity in prescription practices among Spanish RO departments. Nonetheless, we sought to include all centres that offer SRS-SBRT, both experienced and less experienced centres. We purposely designed a very simple questionnaire to ensure a sufficient response rate to investigate only two main issues: prescription and dose inhomogeneity.

Our aim was to obtain evidence to promote future initiatives by the SEOR, and specifically its SBRT-SG, to help in standardise the current prescription and dose inhomogeneity scenario and to produce an important guide for the significant number of departments that are starting (or will soon start) to apply SRS/SBRT treatments.

Conclusions

The present survey was carried out to assess SRS/SBRT prescription and dose heterogeneity in radiation oncology departments in Spain. Our finding show significant inter-centre variability in criteria, particularly for the intended or accepted dose heterogeneity, which ranged from 107 to 200%. These differences in criteria could influence the mean PTV dose and potentially its correlation with treatment outcomes. The findings of this study will be used to promote an initiative within the SEOR SBRT-SG to develop recommendations for SRS-SBRT dose prescription and heterogeneity.

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Compliance with ethical standards

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