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FULL PAPER

Credentialing of radiotherapy centres in Australasia for TROG 09.02 (Chisel), a Phase III clinical trial on stereotactic ablative body radiotherapy of early stage lung cancer

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Objective: A randomised clinical trial comparing stereotactic ablative body radiotherapy (SABR) with conventional radiotherapy for early stage lung cancer has been conducted in Australia and New Zealand under the auspices of the TransTasman Radiation Oncology Group (NCT01014130). We report on the technical credentialing program as prerequisite for centres joining the trial.

Methods: Participating centres were asked to develop treatment plans for two test cases to assess their ability to create plans according to protocol. Dose delivery in the presence of inhomogeneity and motion was assessed during a site visit using a phantom with moving inserts.

Results: Site visits for the trial were conducted in 16 Australian and 3 New Zealand radiotherapy facilities. The tests with low density inhomogeneities confirmed shortcomings of the AAA algorithm for dose calculation. Dose was assessed for a typical treatment delivery including at least one non-coplanar beam in a stationary

and moving phantom. This end-to-end test confirmed that all participating centres were able to deliver stereotactic ablative body radiotherapy with the required accuracy while the planning study demonstrated that they were able to produce acceptable plans for both test cases.

Conclusion: The credentialing process documented that participating centres were able to deliver dose as required in the trial protocol. It also gave an opportunity to provide education about the trial and discuss technical issues such as four-dimensional CT, small field dosimetry and patient immobilisation with staff in participating centres.

Advances in knowledge: Credentialing is an important quality assurance tool for radiotherapy trials using advanced technology. In addition to confirming technical competence, it provides an opportunity for education and discussion about the trial.

INTRODUCTION

Stereotactic ablative body radiotherapy (SABR) is a relatively new treatment modality that utilises image guidance, motion management and many small often non-coplanar radiation beams to deliver very high biological doses of ionising radiation in very few fractions.^{1,2} As it is a non-invasive method of potentially curative treatment for early stage cancers, there has been a lot of interest in particular in the field of lung cancer.^{3,4} However, high level clinical evidence for the equivalence or even superiority of SABR compared to other treatment modalities is still needed. Several trials are currently ongoing,

and despite difficult accrual evidence is starting to emerge.⁵

Stereotactic treatments can be challenging both in terms of patient selection,⁶ dose calculation,⁷ planning⁸ and technical delivery.⁹ In these circumstances, it is common practice to allow only centres that can demonstrate ability to comply with trial requirements and appropriate technical competence to enter patients into clinical trials. These quality assurance activities have been shown to be essential for complex trials¹⁰ and their statistical power.¹¹ Typically, credentialing procedures are tailored to clinical trials

and can assess aspects that could affect the interpretation and outcome of the trial.¹²

One of the randomised Phase III clinical trials comparing SABR with conventional radiotherapy for early stage lung cancer in peripheral location has been conducted in Australia and New Zealand under the auspices of the Trans Tasman Radiation Oncology Group (TROG) is TROG 09.02 “CHISEL”. This trial accrued patients between December 2009 and June 2015. As SABR technology at the commencement of the trial was new to most centres in our region and the techniques used are complex and technologically challenging, a credentialing program was developed for centres wishing to join the trial.

The aim of the present paper is to

- (1) describe the programme that was to assess both planning and delivery aspects of lung SABR, and to
- (2) present the results of the credentialing program with the aim to identify any planning or delivery aspects that could predict for high or low quality of treatment.

METHODS AND MATERIALS

The credentialing program was developed using a prospective risk management approach. [Table 1](#) identifies the main technical aspects that are considered to pose a risk for successful completion of the trial. It takes into consideration that the trial also mandated real-time review of all SABR plans by the trial QA team prior to treatment. This real-time review assessed contouring and dose distribution for the individual patient. The risk rating was decided upon by members of the local trial management committee. The table also identifies the four main tools available in the credentialing process:

- Facility questionnaire
- Planning study
- Phantom irradiation
- Site visit/observation

The facility questionnaire covers contacts, equipment and basic information about the experience in the participating centre. It is provided as part of the [Supplementary Material 1](#), (Supplementary material available online).

Planning study

[Figure 1](#) shows the two scenarios chosen as planning studies. Both test cases feature a single lesion in the left lung with the lesion in Test Case 1 being larger (6.9 vs 2.4 cc) and abutting the chest wall. The deidentified CT scans were acquired as four-dimensional CT¹³ and participating centres were provided with a Digital Imaging and Communications in Medicine (DICOM) image of the average scan. Contours of the internal target volume (ITV),¹⁴ lungs, oesophagus, chest wall, heart spinal cord and brachial plexus were provided to ensure all centres had the same planning challenge. Planning target volume (PTV) margins were originally recommended as 5 mm in axial plane with 10 mm in craniocaudal direction to account for CT slice thickness (max 3 mm) and motion. However, other margins were allowed depending on technology and image-guided radiotherapy

strategy used in participating centres. As the trial also featured real-time review of all SABR plans prior to each SABR treatment, contouring was checked at the time of individual patient plan review.

Participating centres were able to download the DICOM data sets from a central database at TROG and were asked to create plans that would meet the dosimetric criteria required for the plan. [Table 2](#) shows the dose volume constraints for critical structures as required in the trial protocol. The prescription method was chosen to ensure that the PTV in both conventional and hypofractionated arms receive a minimum of 95% of the prescribed dose. Lungs were to be contoured as whole lung excluding the ITV and a contouring atlas for brachial plexus was provided as part of the protocol.

Plans were to be created using megavoltage photons with a maximum energy of 10 MV and >7 conformal radiation fields. Following the practice at the commencement of the trial and the uncertainty about the potential for interplay effect intensity modulated radiation therapy¹⁵ was not allowed. The plan evaluation was performed using SWAN plan evaluation software.¹⁶ Due to differences in volume sampling, which is particularly noticeable for small volumes,¹⁷ the minimum dose to the PTV was calculated as dose to 99%. Conformity indices were not mandated and reported in the study.

Site visit and phantom study

[Figure 2](#) shows the Perpex phantom (QUASAR, Modus Medical, London, ON) which was modified to accommodate a moving cylinder with programmable motion.¹⁸ The dimensions of the phantom and experimental set ups are shown in [Figure 3](#).

The measurements during site visit were divided into two main components. The first is a series of measurements with the isocentre of the linear accelerator in the centre of the phantom as shown in [Figure 3a](#). Initially, a measurement with an ionisation chamber (CC13 IBA/Wellhoefer, Schwarzenbruck, Germany) in a 10 × 10 cm² field verifies output and can be used to correct all other ionisation chamber measurements for the relative output on the day. The setup is also used to expose two standards for radiochromic film (EBT2 and later in the study EBT3, ISP, Wayne, NJ). This is followed by measurements in a 5 × 5 cm² field, first at isocentre and then 6 cm below as indicated in [Figure 3a](#). The centre cylinder of Perspex is then replaced by a lung equivalent wooden cylinder and later by air to assess the ability of the participating centre to calculate dose in the presence of inhomogeneities.

The second set of measurements consists of a “realistic” treatment of the phantom as shown in [Figure 3b](#). The treatment was delivered four times in total, to facilitate ion chamber and film measurements in static and moving phantom. In several instances, the ion chamber measurement in the moving phantom was omitted due to time constraints and technical issues. The centre was provided with an average and maximum intensity CT scan of the phantom prior to the site visit or alternatively could acquire CT scans during the site visit. The

Table 1. Technical risk management matrix for TROG O9.02

Identified risk	Tools for credentialing				Risk rating	Comments
	Facility questionnaire	Planning study	Phantom irradiation	Site visit/ observation		
Patient positioning/immobilisation	X			X	Low	Treatment time can be longer than conventional
Contouring/margins		(X)			Medium	ITV contours provided in planning study; atlas for brachial plexus provided; the planning study tested handling of structures such as Boolean operations; the main test of contouring was done on a patient by patient case during real-time review
Planning/approach		X	(X)		Medium	IMRT/VMAT not allowed; real-time review mitigates additional risk; the phantom irradiation provided another check of planning approach in a very simple scenario
Dose calculation/small fields/inhomogeneity		X	X		High	Small field dosimetry in presence of lung difficult due to lateral charged particle disequilibrium
Motion management planning	X			(X)	High	4DCT mandatory in the trial but not widely used clinically at start of trial. Bringing the phantom on site allowed for a discussion of motion management
Motion management treatment	X		X	(X)	Medium	In practice, risk was 'low' as ITV concept was used throughout the trial. Bringing the phantom with moving carriage on site allowed for a discussion of motion management
Image guidance	X		X	X	Medium	Must include some assessment of motion
Dose delivery/collision	X			X	Low	Higher collision risk due to non-coplanar fields

4D-CT, four-dimensional CT; IMRT, intensity modulated radiotherapy; ITV, internal target volume; TROG, Trans Tasman Radiation Oncology Group; VMAT, Volumetric Modulated Arc Therapy. Marks in brackets indicate that aspects of the risk are tested.

Figure 1. Illustration of the two test cases used for credentialing of centres. Shown is the dose distribution from a typical 3D conformal plan with non-coplanar beams. 3D, three-dimensional.

imaging for treatment planning was performed with a Perspex cylinder including a water filled 2 cm diameter sphere with iodinated contrast on the left of the phantom. During imaging, the cylinder was moved with sinusoidal motion (1 cm amplitude, 4 s period). The centre was asked to develop a treatment plan for the lesion with a 0.5 cm ITV to PTV margin using

Figure 2. Perspex body phantom with three inserts. The left one can be moved using programmable amplitudes and breathing patterns. The insert shows a CT image of the phantom with a lung inhomogeneity on the right (light wood) and a cylinder with an insert for radiochromic film on the left.

at least one non-coplanar beam, even if this would not necessarily be needed in the scenario to achieve an acceptable dose distribution. The plan was then delivered four times to the phantom facilitating ionisation chamber and radiochromic film measurements in a stationary and moving phantom.

Table 2. Dose volume constraints for TROG 09.02 (CHISEL)

Organ	Parameter	Conventional arm	Investigational hypofractionated arm	Comments
PTV	ICRU reference point	66 Gy in 33 fractions or 50 Gy in 20 fractions		As per institutional preference
	Covering isodose		95% of prescription dose	Prescription dose 54 Gy (48 Gy if lesion close to the chest wall)
Lung	V20	35%	15%	Lung contour excludes ITV
	Mean dose	20 Gy		
Heart	Maximum dose	65 Gy	30 Gy	Dose per fraction in the hypofractionated arm as per fractionation
Oesophagus	Maximum dose	65 Gy	27 Gy	Dose per fraction in the hypofractionated arm as per fractionation
Spinal canal	Maximum dose	45 Gy	18 Gy	Dose per fraction in the hypofractionated arm as per fractionation
Brachial plexus	Maximum dose	65 Gy	24 Gy	Dose per fraction in the hypofractionated arm as per fractionation
Skin and chest wall	Maximum dose	65 Gy		
	D70 cc		30 Gy	Dose per fraction in the hypofractionated arm as per fractionation. At commencement of the trial the limit was applied to 30 cc. D30 cc $\leq$ 30 Gy
Liver	V20, V30			No constraint but dose-volume parameters to be documented

ICRU, International Commission on Radiation Units and Measurements; PTV, planning target volume; TROG, Trans Tasman Radiation Oncology Group.

Maximum doses to a voxel to be defined as 0.035 cc.

Figure 3. Measurement set up for ionisation chamber and radiochromic film measurements during the site visit for credentialing. (a) Assessment of output, field size factor and dose calculation in the presence of inhomogeneities. (b) Delivery of a SABR plan to a stationary and moving target. SABR, stereotactic ablative body radiotherapy.

Image guidance was performed as per institutional practice and an ionisation chamber reading taken to verify the order of magnitude of dose during imaging. Due to time constraints during the site visit, measurements with the moving phantom were restricted to film measurements in approximately half the cases.

Radiochromic film was scanned using an EPSON 700 film scanner (EPSON, Nagano, Japan) in transmission mode and evaluated in red and green colour using ImageJ (National Institute of Health, Bethesda) and MS Excel software. Using 50 dpi spatial resolution, the measurement uncertainty is of the order of 1 mm. The 95 and 70% isodose lines were compared between treatment plan and film dosimetry.

RESULTS

A total of 22 sites in Australia and New Zealand expressed an interest in participating in the trial. A summary of characteristics of participating centres and their credentialing activities is shown in Table 3.

Table 3. Characteristics of centres participating in the TROG 09.02

• Total expressions of interest: 22
• Participation in planning studies: SABR techniques, 17; conventional fractionation, 1
Treatment planning: Varian eclipse $n = 7$ (v. 7 to 11—all AAA dose calculation); ADAC/Philips Pinnacle $n = 5$ (v. 9—convolution dose calculation); CMS/Elekta XiO $n = 9$ (v. 4.5 to 4.8—superposition and CCC); Brainlab iPlan $n = 1$ (v. 4.1-Monte Carlo)
• Site visits: Australia 16; New Zealand 3
Linear accelerators: Varian 15 (21 series: 6; Trilogy: 7; Truebeam: 2); Elekta 5 (Synergy: 3; Infinity 1; Axesse 1); Siemens Artiste 1; Varian/Brainlab Novalis 1
• Credentialed for participation in the trial: Australia 14; New Zealand 3

AAA, anisotropic analytical algorithm; SABR, stereotactic ablative body radiotherapy; TROG, Trans Tasman Radiation Oncology Group.

Planning study

All but one centre were able to download and plan the two DICOM test cases. One centre did submit two similar planning cases of their own *in lieu*. The review of plans for credentialing was centralised. Due to sampling differences, dose volume parameters differed slightly between the respective treatment planning system and the review software. For the credentialing, the results as shown by the review software were evaluated. They are shown in Figure 4 which shows maximum dose (D_{max}) and dose to 95% of the target volume (D_{95}) as a function of the minimum dose. According to the protocol, the minimum dose must not be less than 95% of the prescription dose to ensure the SABR and a conventional plan prescribed according to ICRU

Figure 4. Maximum dose (D_{max}) and dose to 95% of the PTV (D_{95}) for the test plans as a function of the minimum covering isodose line in % of the prescription. The vertical line indicates the minimum dose to cover the target according to protocol. Variations from this dose can be due to differences between planning and review software and in case of higher dose may reflect a choice of the centre. For the evaluation a covering isodose line to 0.2 cc was considered. PTV, planning target volume.

recommendations (target dose between 95 and 107% of prescription)¹⁹ share the same dose minimum.

A total of 40 plans were uploaded by participating centres for review over a period of nearly 3 years (2010–2013). 4 of these planning studies were for the conventional arm (two centres intending to contributing only to the conventional arm with a partnered SABR centre), 10 for 48 Gy in 4 fractions (9 of them for case 1 as it proved more difficult to meet the criteria at 54 Gy) and 26 for 54 Gy in 3 fractions. Three plans were repeat submissions due to corrections made following the review. Nine submitted plans were returned with comments with the prescription dose (D100 = 95% of prescription) being the most common issue. Being a three-dimensional conformal approach, the plan was accepted and the centre informed if scaling the plan up by less than 5% would have made it acceptable. Critical structure doses were then evaluated using the rescaled dose. Figure 4 includes these as well as data for the centre that submitted two planning studies from their own patient library, as they were not able to download the DICOM data from the TROG webpage.

Other issues found and communicated back to the respective facility were handling of contours (one centre used lung minus PTV instead of ITV for reporting) and beam placement. Beam placement was considered suboptimal, if beam paths were unnecessarily passing through critical structures such as the heart prior to reaching the target. Centres were also alerted to beams that may have collision risk or that would pass through rails as part of the treatment couch. The latter was also tested during the phantom irradiation at the site visit.²⁰

Figure 5 shows dose-volume histogram parameters for organs at risk as a function of D95. The two cases for which the participating centre used cases from their own library are not included. As can be seen, there is a trend towards lower doses for organs at risk with increasing target dose indicating an improvement in plan quality rather than a trade-off of objectives.

Within the uncertainty of the assessments due to handling of contours and isodose lines in different planning systems and the variability in planning approaches there was no difference between the planning systems used. Omission of non-coplanar

beams ($n = 7$ across the 32 plans in the evaluation) did not affect plan quality.

Site visit and phantom study

Site visits were conducted in 16 Australian and 3 New Zealand radiotherapy facilities. Overall, the site visit took approximately 3 h of time on the treatment unit and a similar amount of time to review immobilisation equipment, motion management and procedures including discussion of the protocol. Site visits also included a formal presentation to staff discussing the trial and its dosimetry requirements. Output measurements in the phantom confirmed good overall agreement in reference dosimetry with an average output of 1.004 ± 0.006 cGy per monitor unit at the dose normalisation point ($n = 19$). Measurements were performed three times and ratios take the output measured by the centre on the day of site visit into account where applicable. Within the uncertainty of the ionisation chamber measurements (estimated as $\pm 2\%$ 1 standard deviation dominated by Type B uncertainty), all centres delivered doses comparable to the chamber calibration at the reference centre.

Figure 6 shows the key results for the ionisation chamber measurements expressed as ratios between measurement and plan. Shown are the assessments of dose behind an 8-cm diameter inhomogeneity as part of the small field and inhomogeneity assessment per geometry shown in Figure 3a. The results are corrected for the output measured on the day. A more detailed summary of these results is shown in Figure 7, where the ratio of planned vs measured dose for all measurements is broken down by planning system (Eclipse $n = 5$; iPlan $n = 1$; Pinnacle $n = 4$; XiO $n = 9$). Except for the Eclipse results [v. 8.6 to 11.0; all AAA (anisotropic analytical algorithm)], in the presence of the inhomogeneity, all measurements were within the acceptable range of unity $\pm 3\%$.

Figure 7 shows a frequency histogram of the comparisons between plan prediction and measurement corrected for output of the day in a SABR plan delivered to a stationary and moving phantom as illustrated in Figure 3b. Also, included in the histogram is the frequency distribution for the ratios between dose measured in small fields behind lung and the dose predicted by

Figure 5. DVH parameters for organs at risk in the planning study as a function of D95 to the PTV. (a) Mean lung dose for the two test cases. For Case 1, a distinction was made between the two allowable fractionation schemes while for test Case 2, all centres used 54 Gy in 3 fractions. The line shows the best linear fit for case 2 ($R^2 = 0.189$). (b) Volume of lung receiving 20 Gy as a function of the maximum dose in the target. The line shows the best linear fit for Case 2 ($R^2 = 0.265$). (c) DVH parameters for spinal cord maximum dose and dose to 70 cc of the chest wall. Only data for cases planned for 54 Gy in three fractions is shown. No variation of cord dose with D95 was shown, while there was a trend for reduced D70 in the chest wall with increasing PTV dose indicated by the regression line shown for Case 2 ($R^2 = 0.241$). DVH, dose-volume histogram; PTV, planning target volume.

Figure .7 Histogram of the ratios of ionisation chamber measurements obtained during the site visits compared to the respective planning data. Shown is the assessment of dose behind an 8 cm diameter inhomogeneity (geometry as shown in Figure 3a) as well as the comparison between plan prediction and measurement corrected for output of the day in a SABR plan delivered to a stationary and moving phantom as illustrated in Figure 3b. Only a limited number of measurements in the moving phantom ($n = 8$) were available for evaluation. SABR, stereotactic ablative body radiotherapy.

the planning system. One can clearly see that the dose delivered in the full treatment plan to the stationary phantom is closest to unity and has the least spread.

Figure .6 Ratios between ion chamber measurement and prediction of the treatment planning system assessed during site visit using the Perspex body phantom shown in Figure 2. The first five set of bars show results taken in the geometry depicted in Figure 3a. The last set of bars termed “plan” shows the combined results from the ion chamber measurement, when a SABR plan was delivered to the phantom (geometry as per Figure 3b). Bars for selected measurements indicate the variability between different centres. The algorithms used by the planning systems were: Eclipse: AAA; iPlan: Monte Carlo; Pinnacle: CCC; XiO: Superposition. Selected uncertainty bars show single standard deviation of measurements performed in different institutions. AAA, anisotropic analytical algorithm; SABR, stereotactic ablative body radiotherapy.

The average ratio between dose measurements in the moving and stationary phantom was 0.995 ± 0.005 ($n = 8$) with all ratios ≤ 1 and the lowest being 0.974. Within the uncertainty of the measurements no difference between planning systems and approaches could be found. Also, the choice of treatment unit (Varian $n = 12$; Elekta $n = 5$, Siemens and Brainlab 1 each) and width of the multileaf collimator (all 5 mm except for one each 2.5, 3 and 10 mm) did not affect the assessable outcome.

The film measurements in the stationary phantom demonstrated that both 95 and 70% isodose lines on plan and delivery for the ITV were within 3 mm. A typical film measurement is shown in the supplementary material. No γ analysis was performed. The assessments with film in the moving phantom confirmed the reduction of coverage in direction of motion (superior/inferior). In nine evaluable measurements, the reduction of coverage in the 70% isodose was 11.5 ± 3.2 mm (mean ± 1 standard deviation) for a sinusoidal motion of 20 mm peak to peak motion.

DISCUSSION

Credentialing programs incorporating site visits have a long tradition in Australia and New Zealand.^{21–23} However, they are resource intensive and time consuming and in regions with many more participating centres mail based and electronic credentialing programs are more common.^{8,24,25} The resources that can be invested into the credentialing of a trial depend on the risk that variations from the protocol can pose for the successful conduct of the trial (and of course also the safety of participants). In the development phase of the TROG 09.02 trial on SABR in lung cancer in 2008, it was decided that the risks posed by technology to the trial outcomes was large enough to warrant inclusion of a comprehensive credentialing program including site visits, and the Cancer Australia grant supporting the trial included an allocation for this program. Given the difficulty of accruing to randomised trials of SABR,⁵ it was also felt to be imperative to aim for high quality and standardised technical delivery to ensure the power of the trial is adequate with a modest number of overall participants.¹¹

A risk assessment was performed by a small group of professionals as per Table 1. Data collection via a facility questionnaire constituted a starting point but a planning study and a site visit including a phantom irradiation were the most important aspect of the technical credentialing program. The results of the planning study demonstrated that all participating centres were able to create treatment plans that complied with the protocol, some after corrections. Major protocol variations required participating centres to create a new plan, while minor variations were communicated to the centre for future consideration. The prescription method of the trial proved to be the main issue in the planning studies. Dose to PTV was to be prescribed in a way that no part of the PTV would receive less than 95% of the prescription dose. In the case of three-dimensional conformal radiotherapy, this would typically mean that the covering isodose for the target is 95%, which ensures that in comparison with a conventional treatment planned using ICRU 50 guidelines both plans have a minimum target dose not below 95%.^{19,26}

Unfortunately, this prescription method caused some misunderstanding in the planning study as can be seen in Figure 4, where six plans did not meet the prescription guidelines.

Ideally, all plans in Figure 4 should be on the vertical dotted line with variations in the other axis illustrating dose homogeneity. The planning studies also demonstrated that all centres could upload plans as required for the real-time review^{27,28} that was part of the trial for all SABR patients. For the purpose of the trial during real-time review of plans, the report of the planning system (as signed by the oncologist) was taken as ground truth. The present credentialing study reports the data as shown by the review software, which can lead to small differences, particularly for the covering isodose volume for target structures (D100) as can be seen in Figure 4.¹⁷

The planning results shown in Figures 4 and 5 demonstrate that different planning approaches can yield differences in dosimetric outcomes reflecting trade-offs between critical structure and target dose. The reduction in volume of lung receiving 20 Gy (V20) is the closest the present study comes to assessment of conformity indices, which were not considered an important aspect of treatment plan evaluation at the time of the set up of the credentialing study.^{29,30} Not surprisingly, V20 is reduced as the dose inhomogeneity in the target (expressed by maximum dose) increases. This is shown in Figure 5b. As these results represent plans created for the same test cases, this is not due to variations in target size which has been reported for the conformity index.^{7,31}

Given the relatively small number of centres credentialed and the variety of equipment used, it was not possible to identify any issues that could predict for a particularly good or bad plan or delivery. The tests with lung and air inhomogeneities shown in Figure 7 confirmed known shortcomings of the AAA algorithm for dose calculation behind inhomogeneities.^{32–34} As can be seen in Figures 6 and 7, this does not affect the overall treatment plan as delivered to a phantom. This was confirmed in investigations by the trial QA team that resulted in a document accompanying credentialing information and endorsed by the trial management committee and TROG. This document “On the use of dose calculation algorithms for radiotherapy treatment planning in TROG 09.02 (CHISEL)” is provided as Supplementary material 3. In summary, centres were alerted to the potential impact of the dose calculation algorithm and the dosimetric aspect of the credentialing process passed if the ratio between measured and planned dose behind the inhomogeneity was 0.97 ± 0.03 for Eclipse AAA users. The use of more advanced dose calculation algorithms such as Acuros XB³⁵ was encouraged towards the end of the trial as it became more widely available.

Cost for the site visits were included in the trial budget and the staff time absorbed by participating institutions. Independent dosimetric assessment in phantoms has been demonstrated to be an important part of trial credentialing³⁶ and high passing rates are not a given even with relatively wide acceptance criteria.^{37,38} In the present study, the phantom irradiation was included into the site visit which allowed also for a basic assessment of image guidance through observation. The site visit, which has the largest resource implications, also gave an opportunity to provide education about the trial and discuss technical issues such as four-dimensional CT, small field dosimetry and patient immobilisation with staff in participating centres. Overall, the site visit was well-received by participating staff and made communications between the dosimetric QA review team and participating centres during the real-time review more effective.

CONCLUSION

The credentialing process based on planning studies and a dosimetric audit during a site visit documented that participating centres were able to deliver dose as required in trial on SABR for early stage lung cancer. It is one of the possible approaches highlighted in a recent review of SABR credentialing by Clark et al³⁹. For several facilities, it proved to be a useful step in the process of developing a SABR program.

Supplements (online only)

- (1) Facility questionnaire.
- (2) Dosimetric statement: on the use of dose calculation algorithms for radiotherapy treatment planning in TROG 09.02 (CHISEL).
- (3) Example of film results.

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REFERENCES

1. Timmerman RD, Kavanagh BD, Cho LC, Papiez L, Xing L. Stereotactic body radiation therapy in multiple organ sites. *J Clin Oncol* 2007; 25: 947–52. doi: <https://doi.org/10.1200/JCO.2006.09.7469>
2. Martin A, Gaya A. Stereotactic body radiotherapy: a review. *Clin Oncol* 2010;

- 22: 157–72. doi: <https://doi.org/10.1016/j.clon.2009.12.003>
3. Senan S, Paul MA, Lagerwaard FJ. Treatment of early-stage lung cancer detected by screening: surgery or stereotactic ablative radiotherapy? *Lancet Oncol* 2013; **14**: e270–e274. doi: [https://doi.org/10.1016/S1470-2045\(12\)70592-2](https://doi.org/10.1016/S1470-2045(12)70592-2)
4. Timmerman R, Paulus R, Galvin J, Michalski J, Straube W, Bradley J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010; **303**: 1070–6. doi: <https://doi.org/10.1001/jama.2010.261>
5. Chang JY, Senan S, Paul MA, Mehran RJ, Louie AV, Balter P, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *Lancet Oncol* 2015; **16**: 630–7. doi: [https://doi.org/10.1016/S1470-2045\(15\)70168-3](https://doi.org/10.1016/S1470-2045(15)70168-3)
6. Timmerman R, McGarry R, Yiannoutsos C, Papiez L, Tudor K, DeLuca J, et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. *J Clin Oncol* 2006; **24**: 4833–9. doi: <https://doi.org/10.1200/JCO.2006.07.5937>
7. Xiao Y, Papiez L, Paulus R, Timmerman R, Straube WL, Bosch WR, et al. Dosimetric evaluation of heterogeneity corrections for RTOG 0236: stereotactic body radiotherapy of inoperable stage I-II non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2009; **73**: 1235–42. doi: <https://doi.org/10.1016/j.ijrobp.2008.11.019>
8. Al-Hallaq HA, Chmura SJ, Salama JK, Lowenstein JR, McNulty S, Galvin JM, et al. Benchmark credentialing results for NRG-BR001: the first national cancer institute-sponsored trial of stereotactic body radiation therapy for multiple metastases. *Int J Radiat Oncol Biol Phys* 2017; **97**: 155–63. doi: <https://doi.org/10.1016/j.ijrobp.2016.09.030>
9. Benedict SH, Yenice KM, Followill D, Galvin JM, Hinson W, Kavanagh B, et al. Stereotactic body radiation therapy: the report of AAPM Task Group 101. *Med Phys* 2010; **37**: 4078–101. doi: <https://doi.org/10.1118/1.3438081>
10. Peters LJ, O'Sullivan B, Giral J, Fitzgerald TJ, Trotti A, Bernier J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: results from TROG 02.02. *J Clin Oncol* 2010; **28**: 2996–3001. doi: <https://doi.org/10.1200/JCO.2009.27.4498>
11. Pettersen MN, Aird E, Olsen DR. Quality assurance of dosimetry and the impact on sample size in randomized clinical trials. *Radiother Oncol* 2008; **86**: 195–9. doi: <https://doi.org/10.1016/j.radonc.2007.07.001>
12. Kron T, Pham D, Roxby P, Rolfo A, Foroudi F. Credentialing of radiotherapy centres for a clinical trial of adaptive radiotherapy for bladder cancer (TROG 10.01). *Radiother Oncol* 2012; **103**: 293–8. doi: <https://doi.org/10.1016/j.radonc.2012.03.003>
13. Clements N, Kron T, Franich R, Dunn L, Roxby P, Aarons Y, et al. The effect of irregular breathing patterns on internal target volumes in four-dimensional CT and cone-beam CT images in the context of stereotactic lung radiotherapy. *Med Phys* 2013; **40**: 021904. doi: <https://doi.org/10.1118/1.4773310>
14. ICRU. Prescribing, recording, and reporting photon beam therapy (supplement to ICRU report 50) Report No: ICRU report 62. Bethesda: International Commission on Radiological Units and Measurements; 2000.
15. Bortfeld T, Jiang SB, Rietzel E. Effects of motion on the total dose distribution. *Semin Radiat Oncol* 2004; **14**: 41–51. doi: <https://doi.org/10.1053/j.semradonc.2003.10.011>
16. Ebert MA, Haworth A, Kearvell R, Hooton B, Coleman R, Spry N, et al. Detailed review and analysis of complex radiotherapy clinical trial planning data: evaluation and initial experience with the SWAN software system. *Radiother Oncol* 2008; **86**: 200–10. doi: <https://doi.org/10.1016/j.radonc.2007.11.013>
17. Ebert MA, Haworth A, Kearvell R, Hooton B, Hug B, Spry NA, et al. Comparison of DVH data from multiple radiotherapy treatment planning systems. *Phys Med Biol* 2010; **55**: N337–N346. doi: <https://doi.org/10.1088/0031-9155/55/11/N04>
18. Dunn L, Kron T, Johnston PN, McDermott LN, Taylor ML, Callahan J, et al. A programmable motion phantom for quality assurance of motion management in radiotherapy. *Australas Phys Eng Sci Med* 2012; **35**: 93–100. doi: <https://doi.org/10.1007/s13246-011-0114-0>
19. ICRU. Prescribing, recording, and reporting photon beam therapy Report No: ICRU report 50. Bethesda: International Commission on Radiological Units and Measurements; 1993.
20. Hardcastle N, Clements N, Chesson B, Aarons Y, Cramb J, Siva S, et al. Results of patient specific quality assurance for patients undergoing stereotactic ablative radiotherapy for lung lesions. *Australas Phys Eng Sci Med* 2014; **37**: 45–52. doi: <https://doi.org/10.1007/s13246-013-0239-4>
21. Healy B, Frantz J, Murry R, Martin J, Plank A, Middleton M, et al. Results from a multicenter prostate IMRT dosimetry intercomparison for an OCOG-TROG clinical trial. *Med Phys* 2013; **40**: 071706. doi: <https://doi.org/10.1118/1.4808151>
22. Kron T, Hamilton C, Roff M, Denham J. Dosimetric intercomparison for two Australasian clinical trials using an anthropomorphic phantom. *Int J Radiat Oncol Biol Phys* 2002; **52**: 566–79. doi: [https://doi.org/10.1016/S0360-3016\(01\)02682-7](https://doi.org/10.1016/S0360-3016(01)02682-7)
23. Ebert MA, Harrison KM, Howlett SJ, Cornes D, Bulsara M, Hamilton CS, et al. Dosimetric intercomparison for multicenter clinical trials using a patient-based anatomical pelvic phantom. *Med Phys* 2011; **38**: 5167–75. doi: <https://doi.org/10.1118/1.3626484>
24. Ibbott GS, Followill DS, Molineu HA, Lowenstein JR, Alvarez PE, Roll JE. Challenges in credentialing institutions and participants in advanced technology multi-institutional clinical trials. *Int J Radiat Oncol Biol Phys* 2008; **71**(1 Suppl): S71–S75. doi: <https://doi.org/10.1016/j.ijrobp.2007.08.083>
25. Weber DC, Vallet V, Molineu A, Melidis C, Teglas V, Naudy S, et al. IMRT credentialing for prospective trials using institutional virtual phantoms: results of a joint European organization for the research and treatment of cancer and radiological physics center project. *Radiat Oncol* 2014; **9**: 123. doi: <https://doi.org/10.1186/1748-717X-9-123>
26. ICRU. Prescribing, recording, and reporting of IMRT Report No: ICRU report 83. Bethesda: International Commission on Radiological Units and Measurements; 2008.
27. Trada Y, Kneebone A, Paneghel A, Pearse M, Sidhom M, Tang C, et al. Optimizing radiation therapy quality assurance in clinical trials: a TROG 08.03 RAVES substudy. *Int J Radiat Oncol Biol Phys* 2015; **93**: 1045–51. doi: <https://doi.org/10.1016/j.ijrobp.2015.08.029>
28. Gondi V, Cui Y, Mehta MP, Manfredi D, Xiao Y, Galvin JM, et al. Real-time pretreatment review limits unacceptable deviations on a cooperative group radiation therapy technique trial: quality assurance results of RTOG 0933. *Int J Radiat Oncol Biol Phys* 2015; **91**: 564–70. doi: <https://doi.org/10.1016/j.ijrobp.2014.10.054>
29. Giglioli FR, Strigari L, Ragona R, Borzi GR, Cagni E, Carbonini C, et al. Lung stereotactic ablative body radiotherapy:

- a large scale multi- institutional planning comparison for interpreting results of multi-institutional studies. *Phys Med* 2016; **32**: 600–6. doi: <https://doi.org/10.1016/j.ejmp.2016.03.015>
30. Pokhrel D, Sood S, Badkul R, Jiang H, McClinton C, Lominska C, et al. Assessment of Monte Carlo algorithm for compliance with RTOG 0915 dosimetric criteria in peripheral lung cancer patients treated with stereotactic body radiotherapy. *J Appl Clin Med Phys* 2016; **17**: 277–93. doi: <https://doi.org/10.1120/jacmp.v17i3.6077>
 31. Hurkmans CW, Cuijpers JP, Lagerwaard FJ, Widder J, van der Heide UA, Schuring D, et al. Recommendations for implementing stereotactic radiotherapy in peripheral stage IA non-small cell lung cancer: report from the quality assurance working party of the randomised phase III ROSEL study. *Radiat Oncol* 2009; **4**: 1. doi: <https://doi.org/10.1186/1748-717X-4-1>
 32. Dunn L, Lehmann J, Lye J, Kenny J, Kron T, Alves A, et al. National dosimetric audit network finds discrepancies in AAA lung inhomogeneity corrections. *Phys Med* 2015; **31**: 435–41. doi: <https://doi.org/10.1016/j.ejmp.2015.04.002>
 33. Ono K, Endo S, Tanaka K, Hoshi M, Hirokawa Y. Dosimetric verification of the anisotropic analytical algorithm in lung equivalent heterogeneities with and without bone equivalent heterogeneities. *Med Phys* 2010; **37**: 4456–63. doi: <https://doi.org/10.1118/1.3464748>
 34. Van Esch A, Tillikainen L, Pyykkonen J, Tenhunen M, Helminen H, Siljamäki S, et al. Testing of the analytical anisotropic algorithm for photon dose calculation. *Med Phys* 2006; **33**: 4130–48. doi: <https://doi.org/10.1118/1.2358333>
 35. Fogliata A, Nicolini G, Clivio A, Vanetti E, Cozzi L. Critical appraisal of Acuros XB and anisotropic analytic Algorithm dose calculation in advanced non-small-cell lung cancer treatments. *Int J Radiat Oncol Biol Phys* 2012; **83**: 1587–95. doi: <https://doi.org/10.1016/j.ijrobp.2011.10.078>
 36. Science Council and Therapy Physics Committee of the American Association of Physicists in Medicine. Independent phantom irradiation is both necessary and cost effective for clinical trial credentialing. *Int J Radiat Oncol Biol Phys* 2015; **92**: 501–3. doi: <https://doi.org/10.1016/j.ijrobp.2015.01.021>
 37. Carson ME, Molineu A, Taylor PA, Followill DS, Stingo FC, Kry SE. Examining credentialing criteria and poor performance indicators for IROC Houston's anthropomorphic head and neck phantom. *Med Phys* 2016; **43**: 6491–6. doi: <https://doi.org/10.1118/1.4967344>
 38. Molineu A, Hernandez N, Nguyen T, Ibbott G, Followill D. Credentialing results from IMRT irradiations of an anthropomorphic head and neck phantom. *Med Phys* 2013; **40**: 022101. doi: <https://doi.org/10.1118/1.4773309>
 39. Clark CH, Hurkmans CW, Kry SE, Global Quality Assurance of Radiation Therapy Clinical Trials Harmonisation Group. The role of dosimetry audit in lung SBRT multi-centre clinical trials. *Phys Med* 2017; **44**: 171–6. doi: <https://doi.org/10.1016/j.ejmp.2017.04.003>