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Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines

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Abstract: Background and purpose: The Global Quality Assurance of Radiation Therapy Clinical Trials Harmonization Group (GHG) is a collaborative group of Radiation Therapy Quality Assurance (RTQA) Groups harmonizing and improving RTQA for multi-institutional clinical trials. The objective of the GHG OAR Working Group was to unify OAR contouring guidance across RTQA groups by compiling a single reference list of OARs in line with AAPM TG 263 and ASTRO, together with peer-reviewed, anatomically defined contouring guidance for integration into clinical trial protocols independent of the radiation therapy delivery technique. Materials and methods: The GHG OAR Working Group comprised of 22 multi-professional members from 6 international RTQA Groups and affiliated organizations conducted the work in 3 stages: (1) Clinical trial documentation review and identification of structures of interest (2) Review of existing contouring guidance and survey of proposed OAR contouring guidance (3) Review of survey feedback with recommendations for contouring guidance with standardized OAR nomenclature. Results: 157 clinical trials were examined; 222 OAR structures were identified. Duplicates, non-anatomical, non-specific, structures with more specific alternative nomenclature, and structures identified by one RTQA group were excluded leaving 58 structures of interest. 6 OAR descriptions were accepted with no amendments, 41 required minor amendments, 6 major amendments, 20 developed as a result of feedback, and 5 structures excluded in response to feedback. The final GHG consensus guidance includes 73 OARs with peer-reviewed descriptions (Appendix A). Conclusion: We provide OAR descriptions with standardized nomenclature for use in clinical trials. A more uniform dataset supports the delivery of clinically relevant and valid conclusions from clinical trials.

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Guidelines

Organ at risk delineation for radiation therapy clinical trials: Global Harmonization Group consensus guidelines

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ABSTRACT

Background and purpose: The Global Quality Assurance of Radiation Therapy Clinical Trials Harmonization Group (GHG) is a collaborative group of Radiation Therapy Quality Assurance (RTQA) Groups harmonizing and improving RTQA for multi-institutional clinical trials. The objective of the GHG OAR Working Group was to unify OAR contouring guidance across RTQA groups by compiling a single reference list of OARs in line with AAPM TG 263 and ASTRO, together with peer-reviewed, anatomically defined contouring guidance for integration into clinical trial protocols independent of the radiation therapy delivery technique.

Materials and methods: The GHG OAR Working Group comprised of 22 multi-professional members from 6 international RTQA Groups and affiliated organizations conducted the work in 3 stages: (1) Clinical trial documentation review and identification of structures of interest (2) Review of existing contouring guidance and survey of proposed OAR contouring guidance (3) Review of survey feedback with recommendations for contouring guidance with standardized OAR nomenclature.

Results: 157 clinical trials were examined; 222 OAR structures were identified. Duplicates, non-anatomical, non-specific, structures with more specific alternative nomenclature, and structures identified by one RTQA group were excluded leaving 58 structures of interest. 6 OAR descriptions were accepted with no amendments, 41 required minor amendments, 6 major amendments, 20 developed as a result of feedback, and 5 structures excluded in response to feedback. The final GHG consensus guidance includes 73 OARs with peer-reviewed descriptions (Appendix A).

Conclusion: We provide OAR descriptions with standardized nomenclature for use in clinical trials. A more uniform dataset supports the delivery of clinically relevant and valid conclusions from clinical trials.

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Introduction

Clinical research in radiation therapy is conducted two-fold: through analysis of high-level evidence generated from well-conducted prospective clinical trials, or retrospective evaluation of real-world data extracted from big data repositories [1,2]. The dosimetric, toxicity, and endpoint reporting parameters from these datasets inform the development of normal tissue complication probability (NTCP) models and define organ at risk (OAR) constraints for future radiation therapy planning protocols [3]. In these approaches, variability in the reporting standards of OAR specific metrics reduces the ability to draw robust conclusions and impacts upon the validity of the recommendations [4–6].

Data pooling from institutions is impeded by inconsistencies in nomenclature [1,7–9]. Inconsistency in contouring guidance for OARs may increase contour variability [10]. Consistency and accuracy in structure nomenclature and contouring guidance not only minimizes variation but also improves departmental workflow and safety [9,11–14], with positive impact on clinician peer-review [9]. Miscommunication and lack of well-defined operating procedures have been highlighted as key causative factors in the origin of radiation incidents, particularly during transfers of care [11–16]. Specific target volume (TV) and OAR radiation therapy errors and near misses were seen in 80/1565 incidents voluntarily reported to Public Health England (PHE) from August to November 2019 [16].

Standardization of terminology facilitates data pooling, scripting, and automation of reports; whether that is for departmental quality assurance (QA), data capture in national registries, or wider inter-institutional radiation therapy research. Data pooling and data sharing agreements between investigators and institutions makes research more efficient and increases the value of the initial clinical trial investment [3]. Standardization of data allows robust derivation of dose constraints and the development of dose–response relationship models [1–7].

The transition from two-dimensional radiation therapy (2D RT) treatment planning and delivery to volumetric three-dimensional conformal radiation therapy (3D CRT), inverse-planned intensity-modulated radiation therapy (IMRT) and proton beam radiation therapy (PBT) has enabled dose-intensification to the TV while sparing dose delivered to the OARs [17,18]. Inverse-planned radiation therapy is driven by user-defined planning objectives. Under-contouring of the OAR leads to inferior OAR sparing [19] with potential for increased or unanticipated toxicity; over-contouring could result in unnecessary dose compromises to the TV. In view of the growing use of sequential and multi-modality anti-cancer therapies, inaccuracies in OAR contouring and hence plan optimization risk inappropriate dose delivery to an OAR, with greater potential for "dose-dumping" in normal tissues and subsequent unanticipated toxicity during a patient's treatment pathway.

The Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) review proposed OAR tolerances and defined OAR constraints; with the acknowledgement that progress in radiation oncology accelerates only when we understand how treatment decisions impact upon patient outcomes [1,3].

The need for consistent language and terminology has been highlighted, as well as the positive impact of consistency on process improvement and workflow management infrastructure [9]. The international radiation therapy community continually promotes a culture of safety. Organizations including, but not limited to, the Pennsylvania Patient Safety Authority (PSA) [11], Radiation Oncology Safety and Education Information System (ROSEIS) [13], Radiation Oncology Incident Learning System (RO-ILS) [15], PHE [16], and American Society of Radiation Oncology (ASTRO) [14] report inaccurate and incomplete communication as causative themes in the origin of radiation incidents [16].

The American Association of Physicists in Medicine (AAPM) has been a driving force for the implementation of improvements in patient safety. AAPM Task Group (TG) reports 113 [20] and 263 [2] both recommend the use of standardized nomenclature, with the latter publishing standardized TV and OAR nomenclature, reducing variability in naming and enabling multi-vendor platforms to interact easily.

The ASTRO Clinical Affairs and Quality Council provides guidance on which OARs should be contoured per anatomical treatment site, defining those essential OARs that consensus *recommends* regardless of treatment scenario providing a basic minimum standard of care, and those OARs which should be *considered* dependent on the clinical situation for contouring in anatomical site-specific clinical trials [18].

The National Radiotherapy Trials Quality Assurance (RTTQA) Group reported on the current provision of OAR specific contouring guidance in United Kingdom (UK) National Institute for Health Research Clinical Research Network (NIHR CRN) portfolio studies [10]. Variation was seen in the OARs contoured across anatomical site-specific clinical trials. The study found that 85.3% of OAR specific descriptions in use within trial documentation provided sub-optimal guidance for contouring [10].

The Global Quality Assurance of Radiation Therapy Clinical Trials Harmonization Group (GHG) (https://rtqaharmonization.com) is a collaborative member group of radiation therapy QA organizations: European Organisation for Research and Treatment of Cancer (EORTC), Imaging and Radiation Oncology Core (IROC), Japan Clinical Oncology Group (JCOG), the National Radiotherapy Trials Quality Assurance (RTTQA) Group, and Trans Tasman Radiation Oncology Group (TROG). The GHG is also associated with the following observer groups: Australian Clinical Dosimetry Service (ACDS), Canadian Cancer Trials Group (CCTG), European Society for Radiotherapy and Oncology (ESTRO), International Atomic Energy Agency (IAEA), National Physical Laboratory (NPL), Quality and Excellence in Radiotherapy and Imaging for Children and Adolescents with Cancer across Europe in Clinical Trials (QUARTET), and the Radiation Dosimetry Services (RDS).

The objective of the GHG is to enhance the quality of radiation therapy in multi-institutional clinical trials through harmonization of QA in order to reduce ambiguity in trial reporting, interpretation and translation of clinical outcomes. The GHG identified an unmet need for the standardization of OAR nomenclature along with peer-reviewed contouring guidance for use in clinical trials involving adult patients with a radiation therapy component.

The GHG OAR Working Group is a multi-professional collaborative initiative, formed of twenty-two members from six international radiation therapy QA groups and affiliated organizations, assuring broad representation across the radiation therapy community.

The objective of the GHG OAR Working Group was to unify OAR contouring guidance across all the QA groups by compiling a single reference list of OARs, together with peer-reviewed, anatomically defined contouring guidance for integration into future clinical trial protocols independent of the radiation therapy delivery technique.

Materials and methods

The GHG OAR Working Group conducted the work in three stages (Fig. 1).

Stage one

Between August and November 2018 representatives of the EORTC, IROC, RTTQA, and TROG QA groups reviewed documenta-

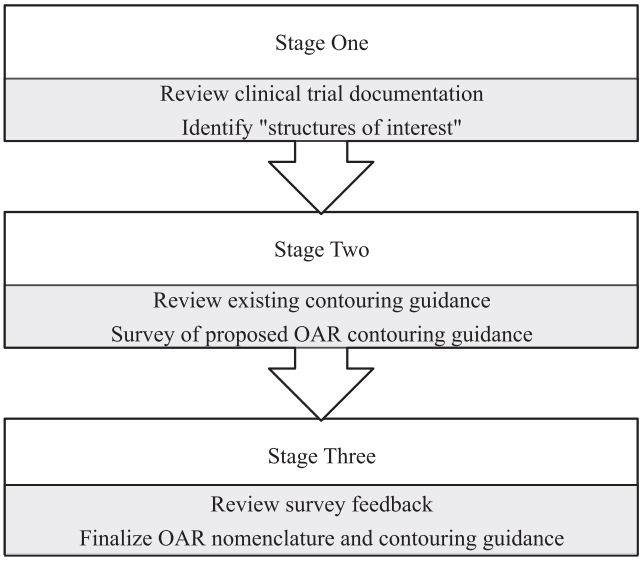

Fig. 1. Work stages one, two, and three.

tion from clinical trials with a radiation therapy QA component, that were either in recruitment or in setup. Data collected included: date of clinical trial opening, radiation therapy technique, anatomical site of radiation therapy delivery, OAR nomenclature, and associated contouring guidance.

Following application of standardized nomenclature [2], OARs in use were collated and combined with those OARs identified as recommended and considered for contouring from the ASTRO Clinical Affairs and Quality Council guidance [18]. Duplicates, non-anatomical, non-specific structures, and structures with more specific alternatives were excluded. Structures identified by two or more radiation therapy QA groups were included, thus creating the "structures of interest".

Stage two

Contouring guidance associated with each structure of interest were collated, whether from the clinical trial protocol, an external reference, or from a pre-existing alternative clinical trial document. The contouring guidance elements were reviewed according to GHG OAR Working Group pre-defined objectives (Fig. 2) and applied to each structure of interest.

Proposed contouring guidance with OAR nomenclature consistent with AAPM TG 263 [2] were created and disseminated to each of the QA groups, who then distributed the proposed nomenclature and contouring guidance to radiation therapy clinical trial investigators within each respective QA network. Investigators participating in the survey were instructed to provide written free-text feedback on the proposed OAR contouring guidance.

Stage three

Anonymized feedback from surveyed individuals was centrally reviewed by the GHG OAR Working Group, reviewed against the pre-defined objectives, and incorporated into consensus OAR contouring guidance. The proposed OAR guidelines were either; accepted, accepted with minor amendment, or accepted with major amendment. Major amendment involved complete revision of the OAR description including modification of borders, whereas minor amendment involved inclusion of omitted landmarks, refinement of borders, or adjustment of sentence structure for user clarity.

1. One name and one description for each OAR[$]
2. OARs are anatomically defined; the same description should be used for all treatment scenarios
3. OAR contouring guidance applies to adults with standard anatomy
4. Laterality is defined on all relevant OARs
5. Contouring guidance incorporates anatomical landmarks and border* definitions. Cranial and caudal terminology used in preference to superior and inferior so guidance is unambiguous regardless of patient positioning
6. Optimal windowing and imaging modality are incorporated into contouring guidance where relevant
7. The clinical trial protocol will define
    a. patient preparation and use of contrast
    b. patient positioning and immobilization
    c. motion management technique(s)
    d. the extent to which the OAR will be delineated beyond the limit of the PTV
8. Consider[$] addition of ~ suffix to denote contouring of a partial structure i.e. SpinalCord~

Fig. 2. Pre-defined objectives for development of the GHG OAR Working Group consensus contouring guidance. [$]consistent with AAPM TG 263 recommendation; *border definitions: cranial, caudal, medial, lateral, anterior, posterior; OAR, Organ at risk; PTV, Planning Target Volume.

The central review process allowed exclusion of OARs and the development of new OAR nomenclature (if not available in AAPM TG 263) and contouring guidance in response to the survey feedback received from the international clinical community.

Ethical approval was not required when producing this consensus report.

Results

One hundred and fifty seven clinical trials including radiation therapy were identified from the QA groups as recruiting or in setup: 14 (8.9%) from EORTC, 38 (24.2%) from IROC, 84 (53.5%) from RTTQA, and 21 (13.4%) from TROG.

The earliest clinical trial included in this analysis opened in November 2004. Overall, 2 clinical trials included 2D RT, 61 included 3D CRT, and 103 included IMRT as the permitted radiation therapy technique(s). Stereotactic Body Radiation Therapy (SBRT), Stereotactic Radiosurgery (SRS), and PBT were included in the randomization(s) in 29, 3, and 7 clinical trials respectively (Table 1).

Two hundred and six instances of OARs were identified from the clinical trial documentation. When combined with the recommended and consider ASTRO structures, 16 additional structures were highlighted as listed within ASTRO guidance, but not identified within clinical trial documentation. Following the exclusion of duplicates (Table 2), 117 distinct structures remained. Exclusion of non-anatomical, non-specific structures, structures with more specific alternatives, and structures specified in clinical trials monitored by one or fewer radiation therapy QA groups resulted in 58 structures of interest.

Table 2
Examples of excluded structures.

Reason for exclusion	Structure	Comment
Non-anatomical	Bag_ostomy	Ostomy bag
	Pacemaker	
Non-specific	Bronchus_Adj	Bronchus adjacent to PTV
	RVR	Remaining volume at risk
More specific alternative nomenclature	Bronchus_Main	Incorporated into Trachea and Bronchus_Prox
	Bronchus_L/R	
	Reprod^Female	Encompassing structure of the ovary, uterus, and vagina
Identified by one radiation therapy QA group	Ear_L/R	
	Liver^Ves	Liver vessels

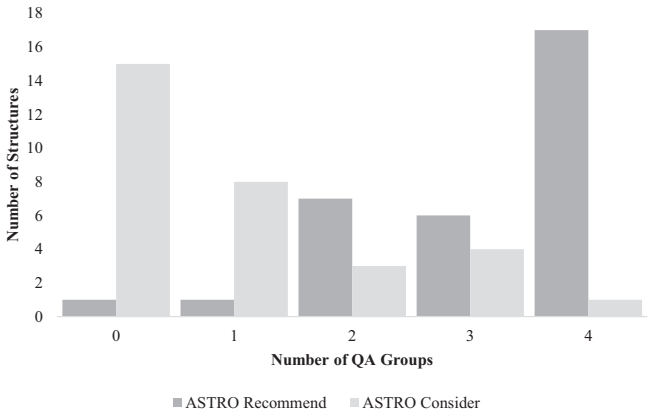

Fig. 3. QA Groups identifying each ASTRO structure.

Structures of interest

Of the 58 structures of interest, 39 (67.2%) were consistent with the ASTRO recommended and consider OAR structures [18]. Sixteen structures were identified for contouring in the ASTRO guidance, but were not included within clinical trial documentation from the QA groups. The cauda equina was the only structure (Fig. 3) listed as recommended for contouring by ASTRO, which was not described in clinical trial documentation across the QA groups.

The brachial plexus was identified by all four radiation therapy QA groups for contouring, but recognized as a structure only to be considered for contouring by ASTRO for treatment involving the cervical spine, nasopharynx, oropharynx, larynx, hypopharynx, cervical esophagus, neck, breast, supra-clavicular fossa, axilla, or lung.

Of the 32 ASTRO recommended structures, 30 (93.8%) were identified in trials monitored by two or more QA groups; 17 structures (53.1%) were identified in trials monitored by all four QA groups (Fig. 3). The ASTRO considered structures of the breast, chest wall, great vessels, and trachea were identified by three QA groups; genitals, hippocampus, and ovary were identified by two QA groups.

Survey

Forty-one radiation oncologists and 6 radiation therapists (RTT) from 38 institutions across 15 countries participated in the survey and commented on the 58 structures of interest. The mean number of responses per OAR was 17.72 (IQR 14–21); the surveyed participants varied by specialist site: 9 gastro-intestinal and head and neck malignancies respectively, 7 lung, 6 breast, central nervous system, and urological malignancies respectively, 5 sarcoma, and 4 gynae-oncology.

On review of survey responses, 6 OAR descriptions were accepted with no amendments, 41 were accepted with minor amendments, and 6 underwent major amendment (Fig. 4). The existing nomenclature choices within AAPM TG 263 did not fulfill requirements for 3 of the surveyed structures, and so new nomen-

Table 1
Anatomical treatment site and permitted radiation therapy delivery technique(s).

	CNS	H&N	Thorax	Abdomen	Pelvis	Any*
2D RT						2
BT					1	
3D CRT	11	3	16	9	12	10
IMRT	15	24	20	9	31	4
SBRT			6	6	5	12
SRS	3					
PBT	2	1	2	2		

*Radiation therapy delivery to any anatomical site; BT, Brachytherapy; CNS, Central Nervous System; H&N, Head and Neck; IMRT, Intensity-Modulated Radiation Therapy; PBT, Proton Beam Radiation Therapy; SBRT, Stereotactic Body Radiation Therapy; SRS, Stereotactic Radiosurgery; 2D RT, Two-dimensional Radiation Therapy; 3D CRT, Three-Dimensional Conformal Radiation Therapy.

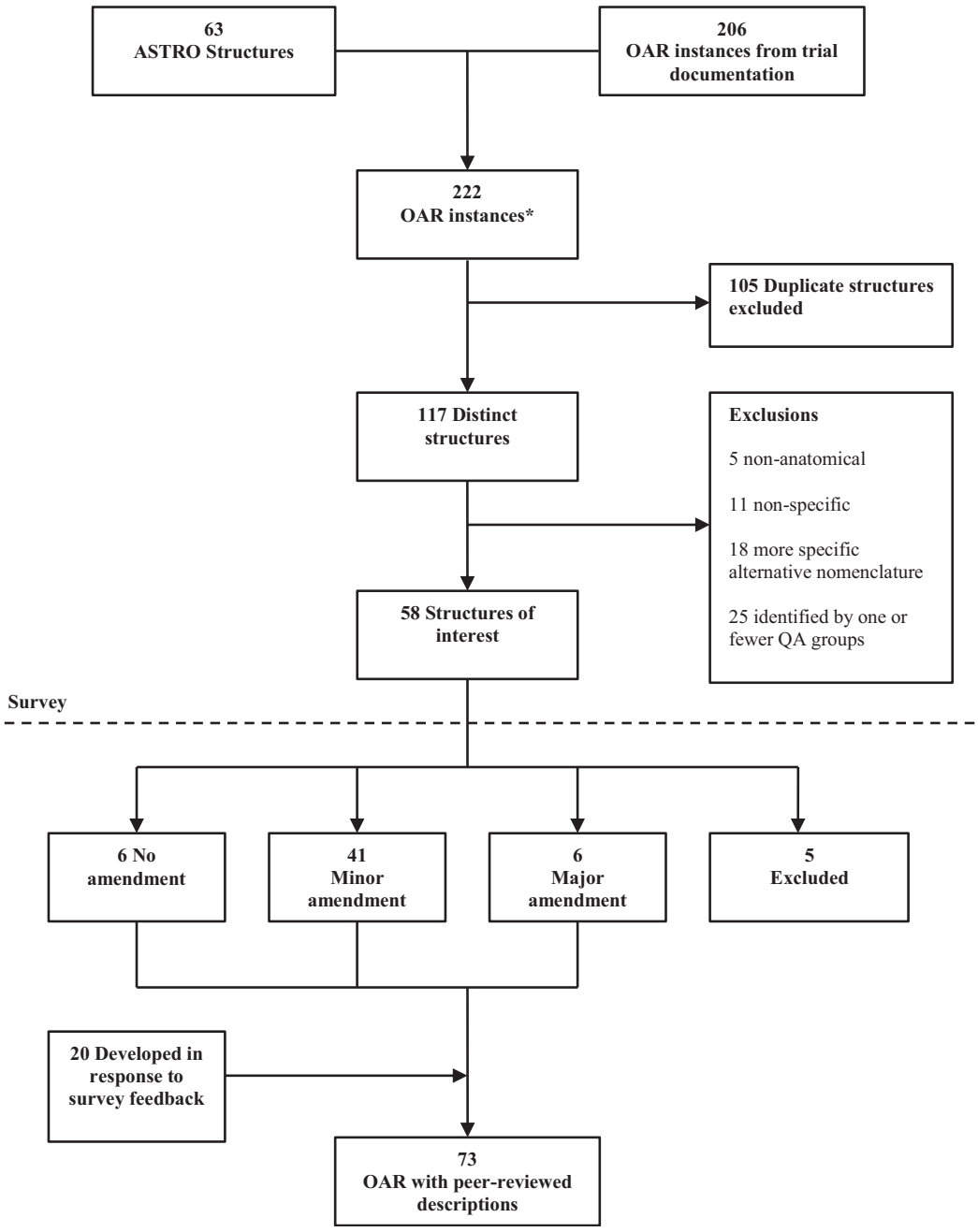

Fig. 4. OAR description survey and feedback responses. *Includes 206 OAR instances and 16 OAR structures listed within ASTRO [18] consensus guidance, which did not appear in clinical trial documentation.

clature were created: *Bronchus_Prox, FemurHeadNeck_L/R,* and *LumbsacPlexs (LumbSacPlex_L/R* with laterality designation). Twenty descriptions were developed in response to survey feedback (Fig. 5), 7 of which did not have standardized nomenclature pre-defined by AAPM TG 263 [2].

Heart

The description for the cranial border of the heart differed between clinical trials. Six landmarks for the cranial border are in use: superior aspect of the pulmonary artery, aorta-pulmonary window, origin of the ascending aorta, inferior to the left pulmonary artery, point at which the pulmonary trunk and right pulmonary artery are seen as separate structures, and the infundibulum of the right ventricle, respectively. The upper most cranial borders were predominantly used in clinical trials pertaining to fractionated radical radiation therapy for lung cancer or SBRT to the lung for either primary lung cancer or oligo-progressive disease, or oligometastatic disease from any primary cancer. The point at which the pulmonary trunk and right pulmonary artery were seen as separate structures was used in clinical trials for lymphoma and primary tumors arising from the breast.

AAPM TG report 101 [21] and UK Consensus on Normal Tissue Dose Constraints [22] recommend the toxicity end-point for heart irradiation in the setting of SBRT is ≥grade 3 pericarditis. To ensure the pericardium is encompassed fully, in the context of SBRT, the cranial heart border is extended to the top of the pulmonary artery to include the attachment of the fibrous pericardium at the adventitia of the great vessels [23].

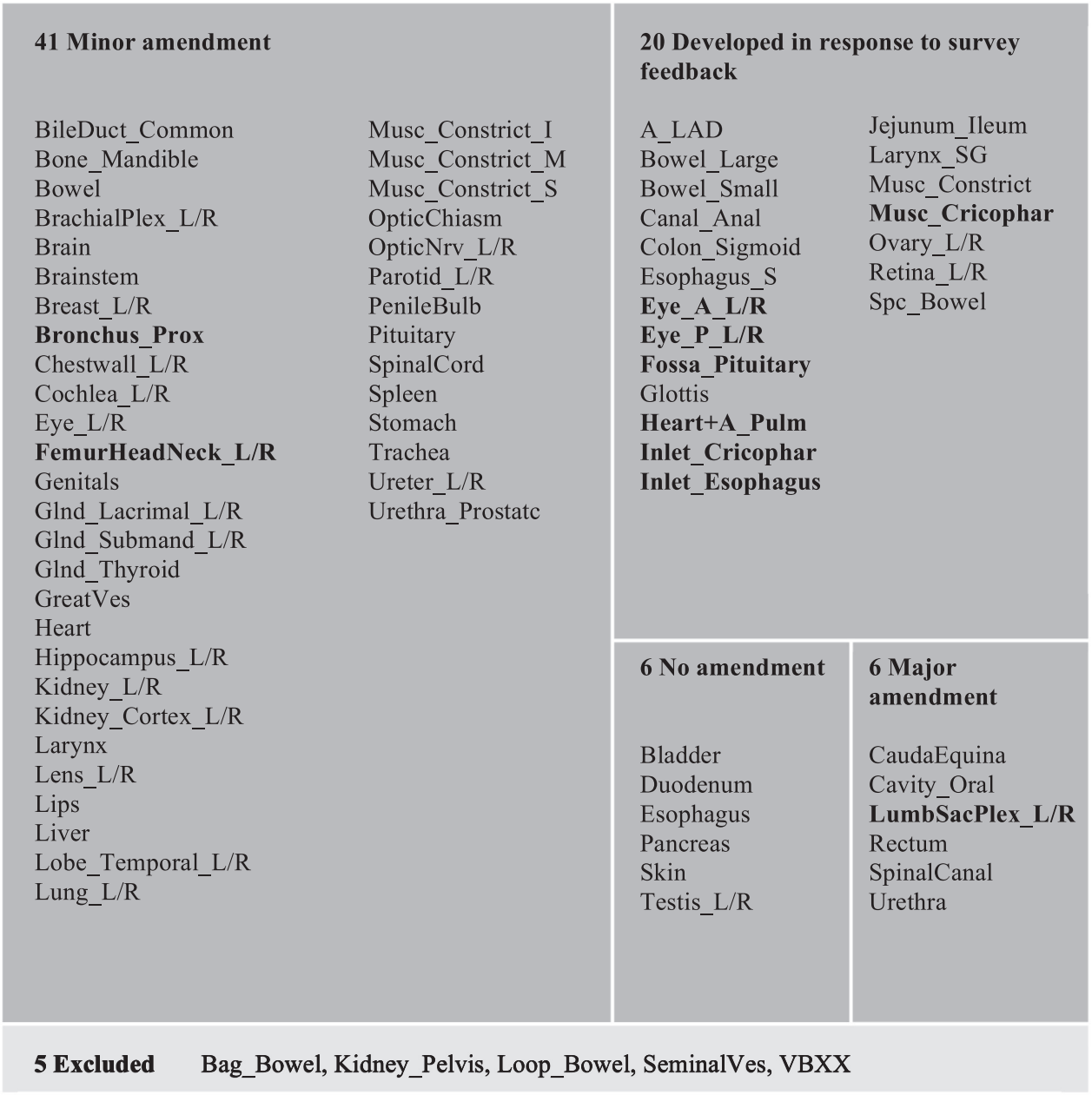

Fig. 5. GHG consensus OAR. Treemap displaying the 73 GHG consensus OAR in dark grey and 5 excluded OAR in light grey, with classifications of no amendment, minor amendment, major amendment, and developed in response to survey feedback. Structures in bold denote nomenclature not pre-existing within AAPM TG 263.

Considering the information above, surveyed investigators had a preference for two of the cranial heart borders described: the superior aspect of the pulmonary artery and the point at which the pulmonary trunk and right pulmonary artery are seen as separate structures. In response to survey feedback and as an exception to the pre-defined objectives (Fig. 2) two distinct heart structures are defined within the GHG OAR consensus guidance, *Heart +A_Pulm* and *Heart*.

Skin

The skin structure was highlighted in clinical trial documentation or external references as "should be outlined", "exclude", or "include"; either in support of the radiation therapy planning and optimization process or as a distinct OAR. This request was seldom accompanied by contouring guidance. Review of clinical and dosimetric evaluation studies demonstrates variation in practice [24–32]. Recommended skin thickness for contouring from clinical trial documentation ranged from 3 to 6 mm; anatomically the thickness of the skin is dependent on the location, ranging from 1.5 to 5 mm [33]. Contouring guidance specifies the skin structure as a 5 mm inner rind automatically created from the external contour [34]; GHG OAR consensus guidance reflects the published contouring guidance, with the caveat that skin thickness will vary dependent on region of interest.

Bowel

The survey distributed to investigators described the bowel as an encompassing structure from the pylorus to the recto-sigmoid

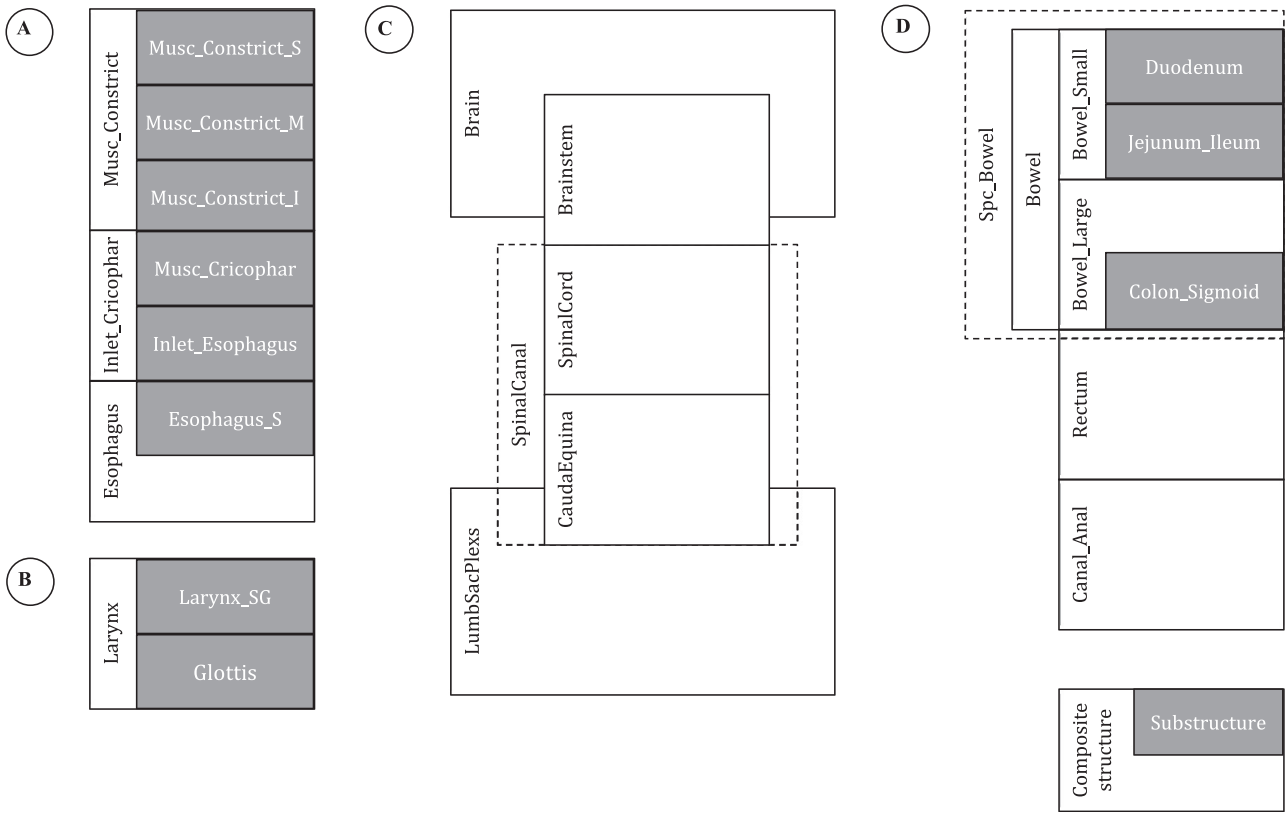

Fig. 6. Relationship between composite and individual substructures. A, swallowing structures of the neck; B, laryngeal structures; C, the central nervous system; D, the sub-diaphragmatic gastro-intestinal tract.

junction; the composite structure was reflective of the current contouring practice [10]. The overwhelming feedback from the radiation therapy community was to allow the bowel to be contoured as individual substructures, and so *Jejunum_Ileum, Bowel_Small, Bowel_Large, Colon_Sigmoid,* and *Canal_Anal* were defined, whilst retaining the original *Duodenum* and *Bowel* structure. Investigators are encouraged to choose the most appropriate structures to contour within a given treatment protocol.

Bag_Bowel nomenclature was excluded in favour of *Spc_Bowel* as the nomenclature for the former was inconsistent with the associated contouring guidance [10,35].

The schematic (Fig. 6) demonstrates the relationship between composite e.g. *Bowel* and individual substructures of the neck, central nervous system, and sub-diaphragmatic gastro-intestinal tract e.g. *Jejunum_Ileum, Colon_Sigmoid*.

New nomenclature

The GHG OAR Working Group adopted AAPM TG 263 [2] recommendations as the nomenclature standard for this work. The existing nomenclature choices did not fulfill requirements for 10 structures; the GHG OAR central reviewers established new nomenclature to align with currently contoured OAR (Table 3).

GHG consensus guidance on 73 OARs with standardized nomenclature and peer-reviewed descriptions are detailed in Appendix A; with an example of implementation of the guidance into a clinical trial protocol.

Table 3
New nomenclature and AAPM TG 263 anatomic group.

	AAPM TG 263 Anatomic Group	New Nomenclature	OAR
1	Eye	Eye_A_L Eye_A_R	Anterior segment of the eye
2	Eye	Eye_P_L Eye_P_R	Posterior segment of the eye
3	Head & Neck	Fossa_Pituitary	Pituitary fossa
4	Head & Neck	Inlet_Cricophar	Cricopharyngeal inlet
5	Head & Neck	Inlet_Esophagus	Esophageal inlet
6	Head & Neck	Musc_Cricophar	Cricopharyngeal muscle
7	Thorax	Bronchus_Prox	Proximal bronchial tree
8	Thorax	Heart+A_Pulm	Heart (extended cranial border)
9	Pelvis	FemurHeadNeck_L FemurHeadNeck_R	Femoral head and neck
10	Pelvis	LumbSacPlex_L LumbSacPlex_R LumbSacPlexs	Lumbar-sacral plexus with laterality, bilateral lumbar-sacral plexus

Discussion

With the advances in the precision and delivery of radiation therapy, the importance of accurate and consistent OAR delineation cannot be understated. This GHG OAR Working Group report from an international collaborative network of radiation therapy QA groups provides consensus guidance on the OAR descriptions and nomenclature for use in clinical trials, with the aim of promoting consistency in OAR contouring and dosimetric reporting.

Seventy-three OARs have been defined the GHG OAR Working Group; 48 (65.8%) are included in the ASTRO Clinical Affairs and Quality Council guidance [18]. Thirty (93.8%) of the ASTRO recommended structures were identified by two or more QA groups; 17 structures (53.1%) were identified by the four QA groups (Fig. 3), thereby validating the consensus guidance and OAR contouring recommendation provided by ASTRO [18].

Six OAR descriptions underwent major amendment following review of survey feedback (Fig. 5); the rectum, a commonly contoured OAR in urological and gynaecological clinical trials, was one such structure. Existing rectal contouring guidance varied in the cranial and caudal border, with use of the ischial tuberosities as a bone surrogate for the caudal border [10]. With the move away from 2D orthogonal radiation therapy planning, it is inaccurate to identify soft tissue structures based on variably positioned bone surrogates, the GHG OAR consensus guidance identifies the levator muscles, the pubo-rectalis sling, and the disappearance of perirectal fat as landmarks for the caudal rectal border.

Five OARs were excluded in response to survey feedback; reasons for exclusion were incorporation of the OAR into alternative nomenclature or survey respondents deeming the structure as a TV as opposed to an OAR.

New OAR nomenclature was created for 10 structures (Table 3). For clarity, the femoral head and neck structure is renamed as *FemurHeadNeck_L/R*, the *Cricopharyngeus* structure is renamed as the encompassing *Inlet_Cricophar* with division to the substructures *Musc_Cricophar* and *Inlet_Esophagus* to discriminate between the muscle and inlet components (Fig. 6). The eye is subdivided into anterior and posterior components with nomenclature consistent with AAPM TG 263 [2] guidance. The *Fossa_Pituitary* defines the inner bony limits of the sella turcica, which in clinical practice is used as an alternative structure for the *Pituitary* gland. The *Bronchus_Prox* describes the proximal bronchial tree, a well-established structure when delivering SBRT to the thorax. *LumbSacPlexs* replaces *SacralPlex* as established contouring guidance is available for the former.

The GHG OAR Working Group pre-specified objectives for the development of consensus OAR descriptions (Fig. 2). One name and one description should be used for each OAR. The GHG OAR Working Group was unable to meet this objective for the heart structure due to the variation in contouring guidance across clinical trials. As an exception, the GHG OAR Working Group has provided two heart OAR descriptions with distinct nomenclature: *Heart+A_Pulm* and *Heart*. Clinical trial protocols and investigators must be clear on which heart contour is used within the respective clinical trial and use the appropriate nomenclature.

The heart as an OAR is of increasing importance. Historical series of Hodgkin's Lymphoma survivors quantify the risk of heart toxicity following large-field mediastinal radiation therapy [36,37]. The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) review of Surveillance Epidemiology and End Results (SEER) cancer registries identified an excess of cardiac deaths following left sided versus right sided 2D planned tangential breast radiation therapy (cardiac mortality ratio 1.58 95% CI 1.29–1.95 $p = 0.03$) [38]. In the context of contemporary 3D planned radical radiation therapy delivered in the treatment of non-small cell lung cancer and esophageal cancer, big-data analyses imply residual shifts towards the mediastinum [39] and dose to the base of the heart structure [40] negatively impact on overall survival. The GHG OAR Working Group anticipates dose constraints to heart substructures: the ventricles, atria, valves, and conduction pathways [41,42] to be prospectively evaluated in forthcoming clinical trials.

The RTTQA Group identified the lack of OAR laterality in 54.2% of instances of relevant nomenclature within United Kingdom clinical trials, the predominance of these OAR were within the head and neck anatomical site [10]. AAPM TG 263 recognizes the inconsistent approach when designating OAR laterality and recommends the use of the suffix _L or _R following the primary structure name [2]. The GHG OAR Working Group unanimously agrees with AAPM TG 263 with the inclusion of the laterality suffix on paired OAR over contra- or ipsi- prefix, as laterality is unambiguous, avoids non-formalized assumptions, and is logical for all multi-professional members of a radiation oncology department. The application of contra- or ipsi- prefix is uncertain for midline or bilateral TV, and laterality designation provides user clarity in the event of TV re-irradiation.

Automated tools implementing AAPM TG 263 nomenclature, either applied retrospectively or prospectively to institutional datasets improve structure name compliance, with structure naming consistency reported as greater than 99.0% [43,44]. Consistency of the guidance underlying the nomenclature choices was not evaluated; this GHG OAR consensus guidance aims to internationally and prospectively implement a globally agreed standard for OAR contouring.

Auto-segmentation for OAR contouring, particularly based on deep learning algorithms are attractive; as once they have achieved a reliable and consistent quality in OAR contouring these processes may offer time saving efficiencies during the radiation therapy planning process. Deep learning is reliant on consistent expert contours over the normal variation of patient anatomies; this GHG OAR consensus guidance defines OAR anatomically, which could aid the generation of robust auto-segmentation models [45,46].

The impact of standardized nomenclature on treatment planning systems (TPS) and end-to-end accuracy has been estimated. AAPM TG 263 limit OAR nomenclature to 16 characters to ensure compatibility with the majority of TPS [2]. Three TPS compatible special characters have been included in this consensus report: plus, included in *Heart+A_Pulm* nomenclature; underscore, distinguishing OAR laterality from the primary or root name; and tilde, designating where a structure has not been contoured in entirety (Fig. 2). User uptake of these special characters and the impact on compatibility between multi-vendor platforms and end-to-end accuracy will be recorded with ongoing audit.

There are limitations to this work. The GHG OAR Working Group elected to exclude structures which were not listed within ASTRO contouring consensus guidance and were identified by one or fewer radiation therapy QA groups; structures not frequently contoured such as the *Ear_L/R* and the *Liver^Ves* were excluded from the stage two investigator survey. The consensus OAR are defined in entirety; the consensus guidance may not be suitable when overarching structures are used for optimization and dose-reporting of substructures of variable radio-sensitivities e.g. optimizing to the *SpinalCanal* structure using the dose-constraint of either the underlying *SpinalCord* or *CaudaEquina*. In these circumstances, the GHG OAR Working Group recommend either use of the GHG consensus contouring guidance and nomenclature or development of situation-specific clinical trial nomenclature.

The GHG OAR Working Group consensus guideline provides peer-reviewed contouring guidance alongside standardized nomenclature for implementation in clinical trials. In addition to this consensus guidance, users should employ good practice and confirm the structure contour on all viewing planes. Image co-registration inaccuracies and artefacts affecting image quality impact upon contouring accuracy and precision; users should be aware of these potential sources of error and review the final contours on the primary dataset. This consensus guidance describes each OAR in entirety; in practice, clinical trial protocols may either specify partial OAR contouring or define the extent to which the OAR will be contoured beyond the planning target volume (PTV). The tilde suffix discriminates between a complete and partially contoured OAR and on data analysis identifies the contour to researchers as suitable for point dose measurement reporting, and not suitable for volumetric dose reporting.

The OAR structures within this report are anatomically defined; the GHG OAR consensus contouring guidance of whole organs is unlikely to change. Further work and dosimetric research will

identify radiosensitive OAR substructures with respective dose constraints; contouring guidance for these newly identified substructures should be developed with the engagement of the international radiation therapy community.

Conflict of interest

Authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2020.05.038.

References

[1] Deasy JO, Bentzen SM, Jackson A, Ten Haken RK, Yorke ED, Constine LS, et al. Improving normal tissue complication probability models: the need to adopt a "data-pooling" culture. IJROBP 2010;76:s151–4.
[2] Mayo CS, Moran JM, Bosch W, Xiao Y, McNutt T, Popple R, et al. American Association of Physicists in Medicine Task Group 263: standardizing nomenclatures in radiation oncology. IJROBP 2018;100:1057–66.
[3] Jackson A, Marks LB, Bentzen SM, Eisbruch A, Yorke ED, Ten Haken RK, et al. The lessons of QUANTEC: recommendations for reporting and gathering data on dose-volume dependencies of treatment outcome. IJROBP 2010;76:s155–60.
[4] Jadon R, Higgins E, Hanna L, Evans M, Coles B, Staffurth J. A systematic review of dose-volume predictors and constraints for late bowel toxicity following pelvic radiotherapy. Radiat Oncol 2019;14:57.
[5] Holyoake DLP, Partridge M, Hawkins MA. Systematic review and meta-analysis of small bowel dose-volume and acute toxicity in conventionally-fractionated rectal cancer radiotherapy. Radiother Oncol 2019;138:38–44.
[6] Draeger E, Sawant A, Johnstone C, Koger B, Bcker S, Vujaskovic Z, et al. A dose of reality: how 20 years of incomplete physics and dosimetry reporting in radiobiology studies may have contributed to the reproducibility crisis. IJROBP 2020;106:243–52.
[7] Santanam L, Hurkmans C, Mutic S, van Vliet-Vroegindeweij C, Brame S, Straube W, et al. Standardising naming conventions in radiation oncology. IJROBP 2011;83:1344–9.
[8] Evans SB, Fraass BA, Berner P, Colins KS, Nurushev T, O'Neill MJ, et al. Standardizing dose prescriptions: an ASTRO white paper. PRO 2016;6:e369–81.
[9] The Royal College of Radiologists. Radiotherapy target volume definition and peer review – RCR guidance. London: The Royal College of Radiologists, 2017.
[10] Yang H, Mir R, Diez P, Tsang Y, Conibear J, Simoes R, et al. Provision of organ at risk contouring guidance in UK radiotherapy clinical trials. Clin Onc 2020;32:e60–6.
[11] Errors in radiation therapy. Pennsylvania Patient Safety Advisory 2009; 6: 87-92.
[12] Santanam L, Brame RS, Lindsey A, Dewees T, Danieley J, Parikh P, et al. Eliminating inconsistencies in simulation and treatment planning orders in radiation therapy. IJROBP 2013;85:484–91.
[13] Cunningham J, Coffey M, Knoos T, Holmberg O. Radiation Oncology Safety Information System (ROSIS) profiles of participants and the first 1074 incident reports. Radiother Oncol 2010;97:601–7.
[14] Web Exclusive: ASTRO commits to six-point patient protection plan. ASTRO news posted February 3, 2010.
[15] American Society for Radiation Oncology (ASTRO). "2017 RO-ILS Year in Review." https://www.astro.org/uploadedFiles/_MAIN_SITE/Patient_Care/Patient_Safety/RO-ILS/2017YIR.pdf.
[16] Radiotherapy Errors and Near Misses Data Report No 5. (December 2015 to November 2017). May 2019, Public Health England.
[17] Transition from 2-D Radiotherapy to 3-D Conformal and Intensity Modulated Radiotherapy. May 2008 IAEA.
[18] Wright JL, Yom SS, Awan MJ, Dawes S, Fischer-Valuck B, Kudner R, et al. Standardizing normal tissue contouring for radiation therapy treatment planning: an ASTRO consensus paper. PRO 2019;9:65–72.
[19] Delaney AR, Dahele M, Slotman BJ, Verbakel WFAR. Is accurate contouring of salivary and swallowing structures necessary to spare them in head and neck VMAT plans?. Radiother Oncol 2018;127:190–6.
[20] Moran JM, Molineu A, Kruse JJ, Urie MM, Oldham M, Drzymala RE, Jeraj R, Galvin JM, Palta JR, Purdy JA, Olch AJ. AAPM Report Task Group 113: improving physics practices for external beam radiation therapy clinical trials. Alexandria, VA: American Association of Physicists in Medicine
[21] 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;37:4087–101.
[22] Hanna GG, Murray L, Patel R, Jain S, Aitken KL, Franks KN, et al. UK consensus on normal tissue dose constraints for stereotactic radiotherapy. Clin Onc 2018;30:5–14.
[23] Tabaksblat MY, Halpern DG, Argulian E, Herzog E. Anatomy and Physiology of the Pericardium. 2014. Management of Pericardial Disease. Springer, Cham https://doi.org/10,1007/978-3-319-06124-5_1
[24] Astreinidou A, Bel A, Raaijmakers CPJ, Terhaard CHJ, Lagendijk JJW. Adequate margins for random setup uncertainties in head-and-neck IMRT. IJROBP 2005;61:938–44.
[25] ICRU Report 83: Prescribing, recording and reporting photon-beam intensity-modulated radiation therapy. J Int Commission Radiat Units Measurements 2010; 10.
[26] Bahig H, Roberge D, Bosch W, Levin W, Petersen I, Haddock M, et al. Agreement among RTOG sarcoma radiation oncologists in contouring suspicious peritumoral edema for preoperative radiation threapy of soft tissue sarcoma of the extremity. IJROBP 2013;86:298–303.
[27] Nielsen MH, Berg M, Pedersen AN, Andersen K, Glavicic V, Jakobsen EH, et al. Delineation of target volumes and organs at risk in adjuvant radiotherapy of early breast cancer: national guidelines and contouring atlas by the Danish Breast Cancer Cooperative Group. Acta Oncol 2013;52:703–10.
[28] Baldini EH, Abrams RA, Bosch W, Roberge D, Haas RLM, Catton CN, et al. Retroperitoneal sarcoma target volume and organ at risk contour delineation agreement among NRG Sarcoma Radiation Oncologists. IJROBP 2015;92:1053–9.
[29] Offersen BV, Boersma LJ, Kirkove C, Hol S, Aznar MC, Sola AB, et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer version 1.1. Radiother Oncol 2016;11:205–8.
[30] Aznar MC, Girinsky T, Berthelsen AK, Aleman B, Beijert M, Hutchings M, et al. Interobserver delineation uncertainty in involved-node radiation therapy (INRT) for early-stage Hodgkin lumphoma: on behalf of the Radiotherapy Committee of the EORTC lymphoma group. Acta Oncol 2017;56:608–13.
[31] Kovtun KA, Yeo WP, Philips CH, Viswanathan A, Baldini EH. Ovary-sparing radiation planning techniques can achieve ovarian dose reduction for soft tissue sarcoma of the buttock and thigh. Sarcoma 2017;2796925.
[32] Kristensen I, Nilsson K, Agrup M, Belfrage K, Embring A, Haugen H, et al. A dose based approach for evaluation of inter-observer variations in target delineation. TIPSRO 2017;3:41–7.
[33] Standring S. Gray's Anatomy: The anatomical basis of clinical practice. 40th Edition. 2016. Elsevier Ltd.
[34] Eekers DB, In 't Ven L, Roelofs E, Postma A, Alapetite C, Burnet NG, Calugaru V, Compter I, Coremans IEM, Hoyer M, Lambrecht M, Nystrom PW, Mendez Romero A, Paulsen F, Perpar A, de Ruysscher D, Renard L, Timmermann B, Vitek P, Weber DC, van der Weide HL, Whitfield GA, Wiggenraad R, Troost EGC. The EPTN consensus-based atlas for CT- and MR-based contouring in neuro-oncology. Radiother Oncol 2018; 128: 37-43.
[35] Gay HA, Barthold HJ, O'Meara E, Bosch WR, El Naqa I, Al-lozi R, et al. Pelvic normal tissue contouring guidelines for radiation therapy: a Radiation Therapy Oncology Group Consensus Panel Atlas. IJROBP 2012;83:e353–62.
[36] van Nimwegen FA, Ntentas G, Darby SC, Schaapveld M, Hauptmann M, Lugtenburg PJ, et al. Risk of heart failure in survivors of Hodgkin lymphoma: effects of cardiac exposure to radiation and anthracyclines. Blood 2017;129:2257–65.
[37] Hahn E, Jiang H, Ng A, Bashir S, Ahmed S, Tsang R, et al. Late cardiac toxicity after mediastinal radiation therapy for Hodgkin Lymphoma: contributions of coronary artery and whole heart dose-volume variables to risk prediction. IJROBP 2017;98:1116–23.
[38] Darby SC, McGale P, Taylor CW, Peto R. Long-term mortality from heart disease and lung cancer after radiotherapy for early breast cancer: prospective cohort study of about 300,000 women in US SEER registries. Lancet Oncol 2005;6:557–65.
[39] Johnson-Hart CN, Price GJ, Faivre-Finn C, Aznar MC, van Herk M. Residual setup errors towards the heart after image guidance linked with poorer

survival in lung cancer patients: do we need stricter IGRT protocols?. IJROBP 2018;102:434–42.
[40] McWilliam A, Kennedy J, Hodgson C, Vasquez Osorio E, Faivre-Finn C, van Herk M. Radiation dose to heart base linked with poorer survival in lung cancer patients. EJC 2017;85:106–13.
[41] Vivekanandan S, Landau DB, Counsell N, Warren DR, Khwanda A, Rosen SD, et al. The impact of cardiac radiation dosimetry on survival after radiation therapy for non-small cell lung cancer. IJROBP 2017;99:51–60.
[42] Hotca A, Thor M, Deasy JO, Rimner A. Dose to the cardio-pulmonary system and treatment-induced electrocardiogram abnormalities in locally advanced non-small cell lung cancer. CTRO 2019;19:96–102.
[43] Schuler T, Kipritidis J, Eade T, Hruby G, Kneebone A, Perez M, et al. Big data readiness in radiation oncology: an efficient approach for relabeling radiation therapy structures with their TG-263 standard name in real-world data sets. Adv Rad Onc 2019;4:191–200.
[44] Cardan RA, Covington EL, Popple RA. Technical note: an open source solution for improving TG-263 compliance. J Appl Clin Med Phys 2019;20:163–5.
[45] Yang J, Veeraraghavan H, van Elmpt W, Dekker A, Gooding M, Sharp G. CT images with expert manual contours of thoracic cancer for benchmarking auto-segmentation accuracy. Med Phys 2020. https://doi.org/10.1002/mp.14107. in press.
[46] Wong J, Fong A, McVicar N, Smith S, Giambattista J, Wells D, et al. Comparing deep learning-based auto-segmentation of organs at risk and clinical target volumes to expert inter-observer variability in radiotherapy planning. Radiother Oncol 2020;144:152–8.