Physics and Imaging in Radiation Oncology 32 (2024) 100652

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

journal homepage: www.sciencedirect.com/journal/physics-and-imaging-in-radiation-oncology

Original Research Article

Results of 2023 survey on the use of synthetic computed tomography for magnetic resonance Imaging-only radiotherapy: Current status and future steps

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ARTICLE INFO

Keywords:
MR-only radiotherapy
MR-only planning
Synthetic CT
Clinical implementation
Deep learning
Artificial intelligence
Survey

ABSTRACT

Background and purpose: The emergence of synthetic CT (sCT) in MR-guided radiotherapy (MRgRT) represents a significant advancement, supporting MR-only workflows and online treatment adaptation. However, the lack of consensus guidelines has led to varied practices. This study reports results from a 2023 ESTRO survey aimed at defining current practices in sCT development and use.

Materials and methods: An survey was distributed to ESTRO members, including 98 questions across four sections on sCT algorithm generation and usage. By June 2023, 100 centers participated. The survey revealed diverse clinical experiences and roles, with primary sCT use in the pelvis (60%), brain (15%), abdomen (11%), thorax (8%), and head-and-neck (6%). sCT was mostly used for conventional fractionation treatments (68%), photon SBRT (40%), and palliative cases (28%), with limited use in proton therapy (4%).

Results: Conditional GANs and GANs were the most used neural network architectures, operating mainly on 1.5 T and 3 T MRI images. Less than half used paired images for training, and only 20% performed image selection. Key MR image quality parameters included magnetic field homogeneity and spatial integrity. Half of the respondents lacked a dedicated sCT-QA program, and many did not apply sanitychecks before calculation. Selection strategies included age, weight, and metal artifacts. A strong consensus (95%) emerged for vendor neutral guidelines.

Conclusion: The survey highlights the need for expert-based, vendor-neutral guidelines to standardize sCT tools, metrics, and clinical protocols, ensuring effective sCT use in MR-guided radiotherapy.

1. Introduction

The introduction of synthetic computed tomography (sCT) in clinical practice has advanced radiotherapy (RT) workflows by enabling more accurate and patient-specific treatment planning. Traditionally, CT has been integral to treatment planning, providing electron density data

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https://doi.org/10.1016/j.phro.2024.100652
Received 31 May 2024; Received in revised form 11 September 2024; Accepted 16 September 2024
Available online 26 September 2024

crucial for accurate dose calculations. Magnetic resonance imaging (MRI), on the other hand, offers superior soft-tissue contrast but lacks the electron density information that CT provides. This advancement with sCT has led to enhanced precision in dose delivery, reduced reliance on traditional CT imaging, and streamlined workflows that improve staff efficiency and reduce overall treatment costs. This technique represents a shift in radiotherapy, particularly in integrating MRI-only workflows, which allows for better soft-tissue contrast and more accurate tumor targeting. The integration of sCT addresses these challenges by combining the strengths of both CT and MRI, thereby optimizing treatment planning and delivery [1–6].

The transition to sCT, while innovative, requires careful consideration during the commissioning and implementation phases, as it eliminates the use of the gold-standard CT from the RT workflow. This shift necessitates rigorous validation and quality assurance to ensure that MRI-only workflows can achieve the same or improved levels of accuracy and safety [7]. The development and clinical implementation of sCT is a complex process, hindered by the lack of guidelines necessary for its consistent and effective use in clinical settings. This absence of standardization has led to considerable variability in practices between institutions [8–11]. Such discrepancies are mainly attributed to the multidisciplinary nature of sCT development, which involves medical physicists, engineers, and clinical end-users, each bringing different perspectives and methodologies.

As a result, there is a need for sCT practices standardization, and a unified approach is essential to ensure the optimal and safe use of this technology in patient care. To address these challenges, a working group arising from the 2022 European Society for Radiotherapy and Oncology (ESTRO) Physics Workshop launched a comprehensive survey on the use of sCT in MRI-only RT, involving experts from various fields. The primary goal of this survey was to outline the current landscape of sCT usage within MRI-only RT, to provide a detailed snapshot of the technical development and clinical application of sCT. This comprehensive overview serves as a foundational step toward identifying key areas where standardization is necessary. Although the survey itself does not establish standardized guidelines, it highlights critical aspects that require uniformity and lays the groundwork for future discussions and the development of vendor-neutral guidelines and operational protocols. These efforts will ultimately support the creation of practical guidelines and protocols that can standardize sCT practices across different clinical settings.

2. Materials and methods

In April 2023, an online survey consisting of 98 questions was distributed to all ESTRO members. The survey was structured into four sections, each focusing on distinct technical aspects of sCT generation algorithms and their clinical applications (Table 1 and Supplementary Materials).

The first section of the survey is composed of 9 questions aimed at capturing the overall patterns of sCT use. This section identified the MRI/MRI-Linac devices available in each institution and their potential applications for MRI-only RT and treatment adaptation.

The second section, comprising 19 targeted questions, was designed for developers. Notably, this section focused solely on in-house deep learning-based sCT algorithms, excluding commercial solutions. This section explored the technical development of sCT algorithms, starting with the MRI data used as input and its associated device-specific QA. Details on the training sets, including the paired/unpaired image approaches, image selection, preprocessing, and the number of acquisition devices involved, were collected. This section also inquired the sizes of the training, validation, and test sets. Furthermore, it delved into the AI based network architecture and training strategies, including fine-tuned hyperparameters, data augmentation, and overfitting prevention techniques, as detailed specified in literature [7–10].

The third section of the survey examined sCT usage across five primary anatomical regions: pelvis, brain, thorax, head-and-neck, and abdomen, consisting of 11 questions per site that focused on clinical commissioning, routine quality assurance (QA), and usage patterns. Specifically, this section assessed the accuracy and performance of sCT by analyzing both intensity-based and dosimetry-based metrics. Intensity-based metrics, including Mean Absolute Error (MAE) and Mean Error (ME), were used to quantify the accuracy of sCT images in Hounsfield units (HU) compared to reference CT images, with MAE reflecting the overall error and ME highlighting any systematic biases in sCT generation. Additionally, dosimetry-based metrics, such as dose volume histograms (DVH) and gamma indices (and details on metrics like threshold, and if local or global), were employed to evaluate the dose distribution accuracy and spatial agreement between sCT and reference CT images. Only the two anatomical sites with the highest number of responses along all questions in the section are reported in the results. The fourth and final section focused on the clinical implementation of sCT. It assessed operational standards and QA practices to ensure the efficacy and safety of sCT use in patient care. Additionally, it gathered information on specific tumor sites and treatments involving sCT generation. The survey finally investigated exclusion criteria as well as the rate of patients who cannot benefit from MR-only RT because of failure to generate a sCT.

The survey was designed to reach both clinical users and developers. The target audiences vary throughout the survey (see Table 1), and some questions can only be answered by developers, while all others can be answered by all participants.

Table 1
Survey sections and associated investigation topics.

Section	Section Description	Investigation Topics
1	General information on the use of MRI Target audience: all	Use of MRI for RT, use of MRI-Linac, MRI-only RT and MRgRT
2	Algorithm development Target audience: developers	MRI data and QA, training set composition, patients split into training, validation, and test sets, neural network architecture and training strategy
3	sCT evaluation Target audience: all	Specific to a given anatomical site (investigated sites: pelvis, thorax, brain, abdomen, head-and-neck), intensity-based metrics including the mean absolute error and mean error, dosimetry-based metrics including dose volume histograms and gamma indices
4	sCT clinical implementation Target audience: all	Sanity check, QA, exclusion criteria

Abbreviations: MRI: magnetic resonance imaging; RT: radiation therapy; MRI-Linac: MRI-linear accelerator; MRgRT: MR-guided RT; QA: quality assurance; sCT: synthetic CT.

3. Results

By June 2023, a total of 100 centers participated in the survey, but only 98 answers were included in the final analysis after excluding two responses due to incompleteness and inconsistencies. These exclusions were necessary to ensure the accuracy and reliability of the analysis. Response rates varied across the four sections and reflected diverse clinical experiences (8 % MRgRT, 40 % MRI-only workflow, 12 % both) and roles either as developers (10 %), clinical users who are not developers (55 %), or both (9 %).

3.1. Section 1 (General Information)

The survey results indicated that 46 % of respondents reported having one MRI scanner in their institution, 18 % reported having two, 10 % had three, and 26 % had more than three MRI scanners. The majority (94 %) used these MRI scanners for RT purposes, among which 64

% have MRI scanners equipped for treatment simulation (flat couch, laser). Among responders, 29 % indicated that their institutions were equipped with an MRI-Linac, while 39 % had implemented an active MRI-only workflow. Most responses (89 %) were from European centers, reflecting the survey's focus on institutions within ESTRO network.

3.2. Section 2 (Algorithm Development)

A total of 19 centers responded to the survey and identified themselves as developers; 9 of them are both developers and user of sCT algorithms. In terms of MRI sequences used for sCT generation, 52 % of developers reported a preference for T2-weighted MRI as the primary input for their algorithms. T1-weighted images were utilized by 40 % of the respondents, indicating a diversity in image preferences depending on the specific clinical application and the anatomical site under consideration. Regarding the magnetic field strength, 50 % of respondents used 3 T MRI scanners, while 30 % relied on 1.5 T scanners, and 20 % used 0.35 T scanners. These variations reflect the adaptability of sCT algorithms to different imaging environments. The survey highlighted the magnetic field homogeneity and the spatial integrity as the main quality parameters, with 68 % and 79 % of developers respectively identifying them as crucial.

An interesting finding was that a quarter of the developers used paired images to develop the deep learning model. Furthermore, a similar proportion conducted image selection primarily to circumvent issues such as metal artifacts, and secondarily to check the anatomic correspondence as well as the noise-based images quality. A minority of respondents checked and corrected for air pockets (2 responders). Developers implemented various preprocessing techniques to enhance the quality of MRI data before it was fed into the sCT generation algorithms as shown in Fig. 1. In most of the cases (72 %), the images were acquired on the same MRI scanner.

The survey responses highlighted a clear preference for generative adversarial networks (GAN) with 80 % of developers utilizing this architecture. The number of 3D image pairs used for training varied significantly among respondents, ranging from 70 to 500. Typically, 70 % of the data was allocated to the training set, while 10 % to 20 % was used for both validation and testing. This variation underscores the flexibility in data requirements depending on the specific sCT generation task and the available datasets. For the hyper-parameters, the learning rate, the number of epochs and the batch size were modified by 50 %, 65 % and 65 % of the respondents. (See Fig. 1). To mitigate the risk of overfitting during model training, 50 % of respondents employed early stopping, a technique where training is halted once the model's performance on the validation set no longer improves. Other strategies included using dropout layers, regularization techniques, and data augmentation to enhance model generalization.

3.3. Section 3 (Site-Specific Questions)

The site-specific analysis focused primarily on the pelvis, as it was the most frequently reported site with 43 respondents providing detailed data. Brain was the second most reported site, with 10 respondents contributing to this analysis. While some data for other anatomical sites, such as Thorax (6), Abdomen (8), and Head-and-Neck (4) were collected, not all respondents answered every required question for these sites. This limited the completeness and robustness of the analysis for these areas. Consequently, detailed findings are presented for the Pelvis and Brain in this paper.

3.3.1. Pelvis site-specific findings

Respondents employed various metrics to evaluate the image quality and dosimetric accuracy of sCT. The use of the MAE and the ME, both in Hounsfield units (HU), was common, but a significant proportion also used other methods like check density in specific ROI, visual inspection, or geometric accuracy. Fig. 2 illustrates the different metrics used by respondents for evaluating image quality and dosimetric accuracy.

In the evaluation of gamma criteria indices, most participants (60 %) used a 2 %/2mm criterion, while 25 % employed a 3 %/3mm criterion, and only 15 % opted for a 1 %/1mm criterion. When considering acceptance criteria, 90 % of users adhered to a 95 % gamma passing rate, with just 10 % accepting a 90 % passing rate. For low-dose evaluation, the most common threshold was 10 %, used by 50 % of participants, followed by 20 % (35 %), 30 % (10 %), and higher thresholds

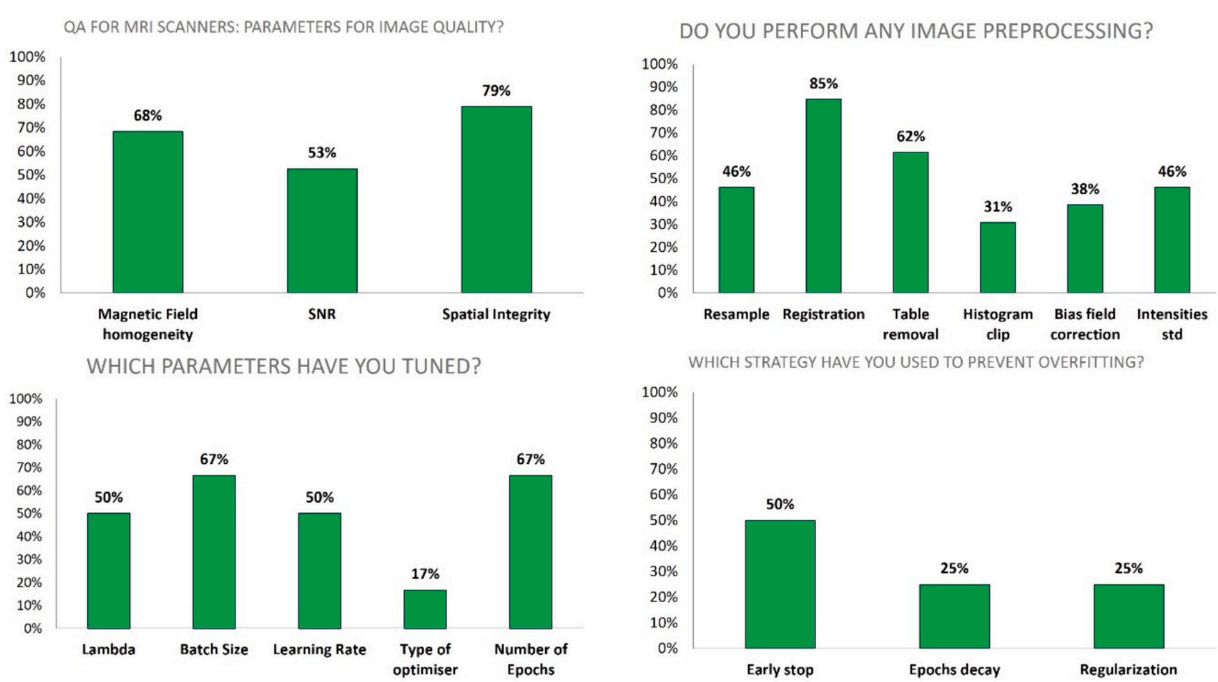

Fig. 1. *Insights from developers: parameters considered crucial for image quality before training (a); preprocessing steps used by developers, multiple choice allowed (b); parameters tuned during the training and validation of the NN (c); strategy used to prevent overfitting during the training (d).* Abbreviations: SNR: signal to noise ratio; Intensity std: Histogram intensity standardization.

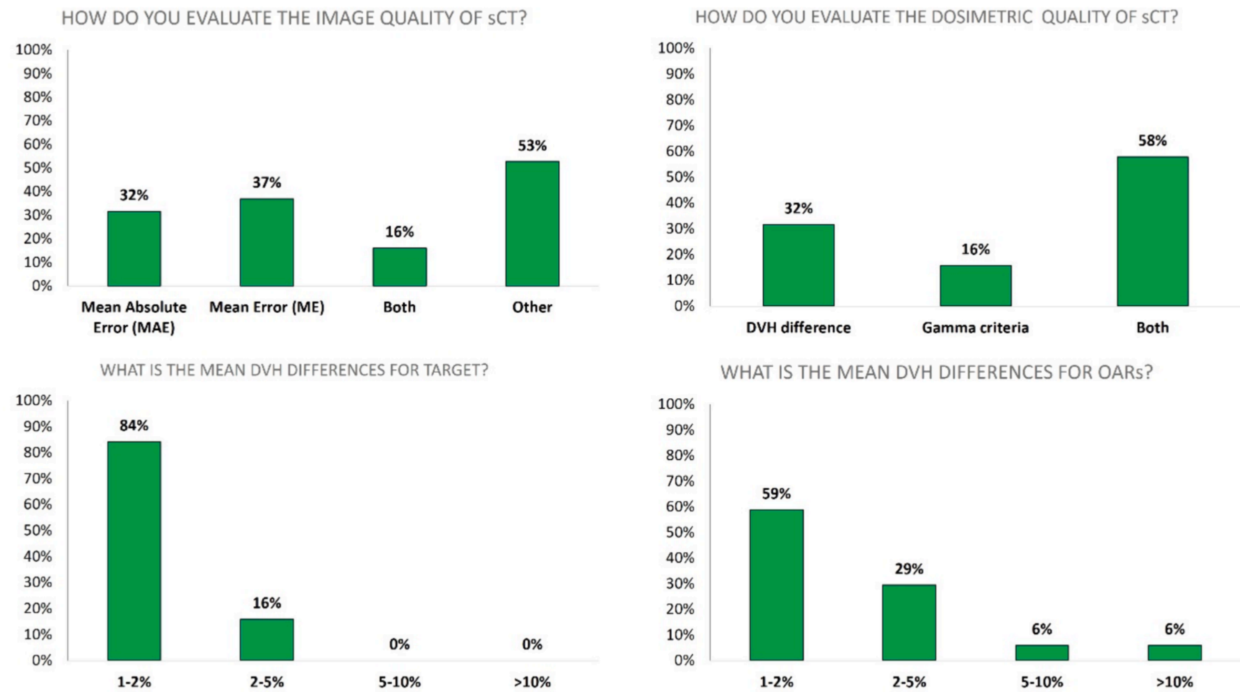

Fig. 2. Metrics used to evaluate the image quality and the dosimetric accuracy.

(>50 %) being relatively rare (5 %). Lastly, when choosing between global or local gamma criteria, 65 % of the respondents preferred local criteria, while 35 % utilized global criteria.

3.3.2. Brain site-specific findings

A total of 10 participants shared responses on the use of sCT in brain. Fig. 3 shows the most interesting results regarding sCT validation metrics, which were slightly different from the pelvis site (Fig. 3.). The use of the MAE and the ME was common, but a significant proportion also used other methods like check density of the brain or only dosimetric evaluations. Fig. 3. illustrates the different metrics used by respondents for evaluating image quality and dosimetric accuracy.

In the evaluation of gamma criteria indices, most participants (80 %) used a 2 %/2mm criterion, while 20 % employed a 3 %/3mm criterion. When considering acceptance criteria, 80 % of users adhered to a 95 % gamma passing rate, with just 20 % accepting a 90 % passing rate. For low-dose evaluation, the most common threshold was 10 %, used by 60 % of participants.

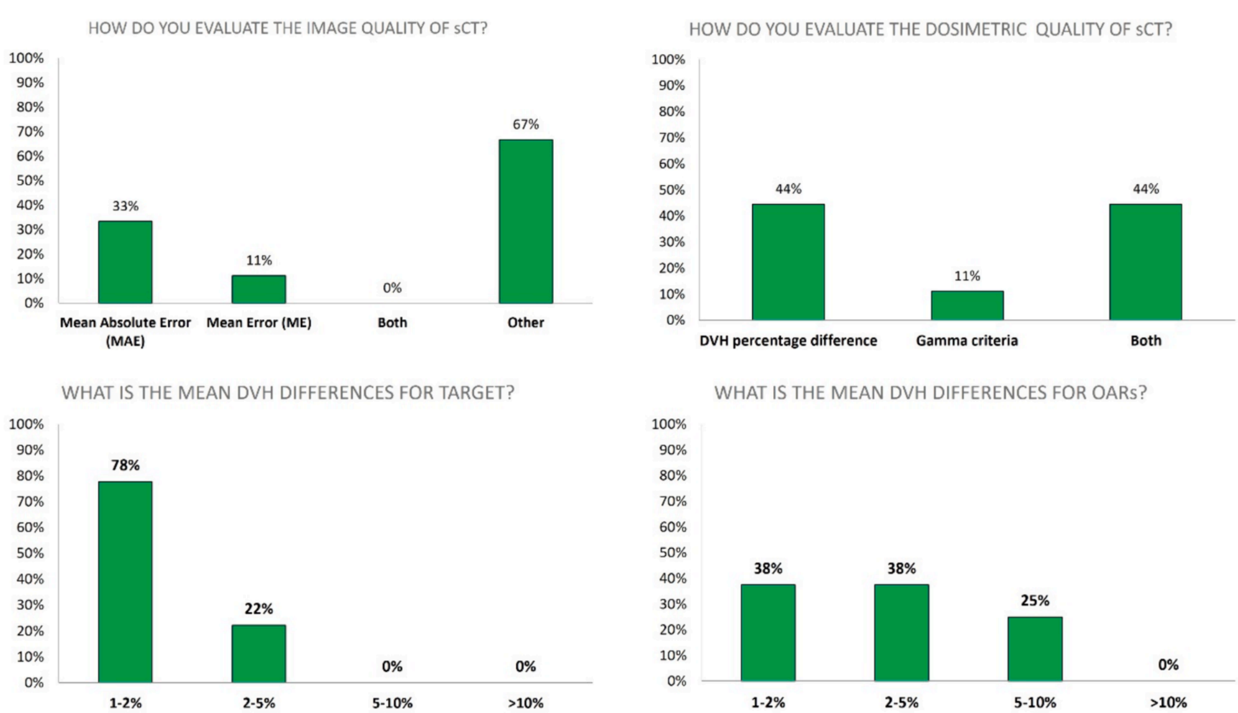

Fig. 3. Details of Gamma Criteria and pass rates.

3.4. Section 4 (sCT implementation into clinics)

The survey revealed that 50 % of the respondents reported the absence of a dedicated sCT QA program in their institutions. This finding is highlighting the need for more standardized and robust QA practices across institutions to ensure the safe and effective implementation of sCT in clinical workflows. When implemented, QA strategies vary among respondents: from QA on MRI images to recalculation on CBCT, to visual inspection.

Most of the respondents (60 %) reported applying specific selection criteria before enrolling patients in an MRI-only workflow. These criteria included factors such as patient age, the presence of metal implants, and anatomical considerations (primarily based on body mass index) that may affect the accuracy of sCT generation. The survey revealed that the presence of metal implants was the most applied criterion, considered by 70 % of respondents, followed by patient weight (40 %) and age (30 %). Other factors, including patient position, were also noted but to a lesser extent.

Despite these selection criteria, a significant proportion of patients—ranging from 1 % to over 40 %, depending on the institution—were deemed unsuitable for sCT-based treatments and instead required conventional CT-based workflows.

The survey results indicate that sCT is predominantly used for conventional fractionation treatments (>5 fractions), with 68 % of respondents reporting its use in this context. In contrast, 40 % of respondents reported using sCT for hypofractionated stereotactic body radiotherapy (SBRT), which involves fewer fractions and higher doses per fraction. The lower utilization in SBRT may reflect the higher precision required in these treatments, where the accuracy of sCT must be rigorously validated to ensure patient safety. These findings suggest that while sCT is well-integrated into conventional fractionation workflows, its application in hypofractionated treatments may require further development and validation. Less experiences are reported in case of palliative treatments or particle therapy (25 % and 5 % respectively). Sanity checks, which include visual inspections of body contour and artifacts, were performed by less than half of the respondents (46 %). This low percentage suggests that more rigorous protocols for sanity checks are needed to ensure the accuracy and safety of sCT-generated images. Implementing standardized sanity checks across institutions could mitigate the risk of errors in MRI-only workflows, further enhancing the reliability of sCT in clinical practice. A compelling 95 % of respondents emphasized the need for vendor-neutral international guidelines for sCT use. From answers emerged also the need for dedicated phantoms for end-to-end test from MRI to Linac, simplified workflows, and specific topics like robust fiducial detection to improve image guidance.

4. Discussion

The survey revealed significant variation in sCT practices among institutions, highlighting the need for standardized, vendor-neutral guidelines to ensure consistent quality assurance and effective clinical integration. Despite the relatively limited number of responses, these results are representative given the early adoption stage of MRI-only workflows, particularly considering that sCT technology has only been available since 2016 and there are around 180 MRI-Linacs installed globally. As these technologies becomes more widespread, the number of users is expected to grow.

The transition from CT to sCT presents technical and QA challenges, as highlighted in recent studies [2,7,8–11], emphasized the need for robust QA practices in MRI-only workflows, reflecting the broader challenge of ensuring sCT reliability. Our survey confirmed this, with 60 % of respondents lacking a dedicated sCT QA program, underscoring the need for comprehensive testing and patient-specific QA protocols.

Deep learning algorithms, particularly GANs, have proven effective in generating sCT, with 80 % of developers favoring GANs over U-Nets consistent as widely reported also in literature [12–38]. However, the interpretability and reliability of these models, especially for new patient characteristics, remain areas of active research. Emerging architectures such as transformers and diffusion models are beginning to show promise in medical imaging applications, including sCT generation, and may soon surpass GANs as the state-of-the-art in this domain [39,40].

A multidisciplinary approach is essential for sCT development and implementation, as highlighted by the collaborative spirit of the ESTRO Physics Workshop 2022. Open questions remain about the roles within this multidisciplinary team where medical physicist should be responsible [41]. The survey also revealed that 60 % of respondents apply specific patient selection criteria, such as age and metal implants, underscoring the need for backup CT workflows. However, sCT usage is still limited to certain treatments, with only 68 % using it for conventional fractionation, and fewer for hypofractionated SBRT or other therapies. Additionally, sanity checks are performed by less than half of the respondents, indicating the need for more rigorous protocols.

Future research should prioritize the validation of sCT technology through multicentric studies. These studies will be crucial in assessing the performance and generalizability of sCT across diverse clinical environments, enabling a realistic evaluation of its effectiveness in routine practice. Additionally, there is a pressing need to establish shared quality assurance (QA) frameworks for the commissioning and periodic QA of sCT systems. Standardized QA protocols, developed through discussion among experts, will ensure consistent performance and safety across institutions. Another critical future step is the creation of a shared dataset that can serve as a benchmark for sCT performance. A well-curated, publicly available dataset would allow researchers and clinicians to test and compare different sCT algorithms under standardized conditions, facilitating the development of more robust and generalizable models. Such a resource would also support the ongoing refinement of sCT technology and help to accelerate its integration into clinical practice, as provided for example by 2023 SynthRad Grand Challenge [42,43].

This study has several limitations that must be considered when interpreting the findings. First, the reliance on self-reported data introduces the potential for response bias. Additionally, the geographic concentration of respondents, with approximately 90 % from European institutions, limits the generalizability of the results to other regions.

The focus on the pelvis and brain does not fully represent sCT use in other anatomical sites, and the rapid evolution of technology may render these findings outdated. Other limitations are related to more technical questions, regarding details on acquisition sequences for NN training, or about details in validation metrics, like Gamma Index, that is not explained if it 2D or 3D.

This survey highlights the need for standardized, vendor-neutral guidelines in the development and clinical use of sCT. The variability in current practices underscores the importance of consistent quality assurance and robust patient selection criteria. Future efforts should focus on practical education, developing commercial tools, and conducting studies to evaluate their impact. Achieving consensus on key metrics will be crucial for advancing sCT integration into radiotherapy workflows.

CRediT authorship contribution statement

M. Fusella: Conceptualization, Methodology, Formal analysis, Writing – original draft. **E. Alvarez Andres:** Conceptualization, Methodology, Formal analysis, Writing – original draft. **F. Villegas:** Methodology, Writing – review & editing. **L. Milan:** Methodology, Writing – review & editing. **TM. Janssen:** Methodology, Writing – review & editing. **R. Dal Bello:** Methodology, Writing – review & editing. **C. Garibaldi:** Methodology, Writing – review & editing. **L. Placidi:** Methodology, Writing – review & editing, Supervision. **D. Cusumano:** Methodology, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2024.100652.

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