

Scientific Article

First-Year Experience of Stereotactic Body Radiation Therapy/Intensity Modulated Radiation Therapy Treatment Using a Novel Biology-Guided Radiation Therapy Machine



Mengying Shi, PhD,^{a,b} Eric Simiele, PhD,^{a,c} Bin Han, PhD,^a Daniel Pham, PhD,^a Paul Palomares, BS,^a Michaela Aguirre, BS,^a Michael Gensheimer, MD,^a Lucas Vitzthum, MD,^a Quynh-Thu Le, MD,^a Murat Surucu, PhD,^a and Nataliya Kovalchuk, PhD^{a,*}

^aDepartment of Radiation Oncology, Stanford University, Stanford, California; ^bDepartment of Radiation Oncology, University of California, Irvine, Orange, California; and ^cDepartment of Radiation Oncology, University of Alabama, Birmingham, Alabama

Received 17 March 2023; accepted 16 May 2023

Purpose: The aim of this study was to present the first-year experience of treating patients using intensity modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT) with a biology-guided radiation therapy machine, the RefleXion X1 system, installed in a clinical setting.

Methods and Materials: A total of 78 patients were treated on the X1 system using IMRT and SBRT from May 2021 to May 2022. Clinical and technical data including treatment sites, number of pretreatment kilovoltage computed tomography (kVCT) scans, beam-on time, patient setup time, and imaging time were collected and analyzed. Machine quality assurance (QA) results, machine performance, and user satisfactory survey were also collected and reported.

Results: The most commonly treated site was the head and neck (63%), followed by the pelvis (23%), abdomen (8%), and thorax (6%). Except for 5 patients (6%) who received SBRT treatments for bony metastases in the pelvis, all treatments were conventionally fractionated IMRT. The number of kVCT scans per fraction was 1.2 ± 0.5 (mean \pm standard deviation). The beam-on time was 9.2 ± 3.5 minutes. The patient setup time and imaging time per kVCT was 4.8 ± 2.6 minutes and 4.6 ± 1.5 minutes, respectively. The daily machine output deviation was $0.4 \pm 1.2\%$ from the baseline. The patient QA had a passing rate of $97.4 \pm 2.8\%$ at 3%/2 mm gamma criteria. The machine uptime was 92% of the total treatment time. The daily QA and kVCT image quality received the highest level of satisfaction. The treatment workflow for therapists received the lowest level of satisfaction.

Conclusions: One year after the installation, 78 patients were successfully treated with the X1 system using IMRT and/or SBRT. With the recent Food and Drug Administration clearance of biology-guided radiation therapy, our department is preparing to treat patients using positron emission tomography-guidance via a new product release, which will address deficiencies in the current image-guided radiation therapy workflow. © 2023 The Authors. Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Sources of support: This work had no specific funding.
Research data are available upon request to the corresponding author.

*Corresponding author: Nataliya Kovalchuk, PhD; email: natkoval@stanford.edu

<https://doi.org/10.1016/j.adro.2023.101300>

2452-1094/© 2023 The Authors. Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

The RefleXion X1 system (RefleXion Medical, Inc, Hayward, California) is a novel positron emission tomography (PET)–guided radiation therapy machine.^{1,2} The X1 system consists of an 85 cm O-ring gantry linear accelerator (linac) rotating at 60 rpm, a fan-beam kilovoltage computed tomography (kVCT) for image guidance of intensity modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT), and PET for real-time tumor tracking for biology-guided radiation therapy (BgRT).³ The linac consists of a 6 MV flattening filter-free photon beam, a binary multileaf collimator (MLC) with 64 leaves, and 2 pairs of jaws located above and below the MLCs. The width of an MLC leaf is 6.25 mm at isocenter (85 cm from the source). The maximum opening in International Electrotechnical Commission (IEC)-X formed by all MLC leaves retracted is 40 cm. The jaw pairs open 10 or 20 mm at isocenter in International Electrotechnical Commission (IEC)-Y. The nominal beam dose rate is 850 MU/min. The kVCT scanner is located on a plane 61.4 cm superior to the room laser. The linac and PET scanner are located on a plane 100 cm superior to the room laser.

Unlike helical treatment delivery with TomoTherapyTM (Accuray Inc, Sunnyvale, California),⁴ treatment delivery with the X1 system is achieved axially with the couch advancing at discrete intervals of 2.1 mm, making 1 pass through the treated region for IMRT and 4 passes through the treated region for SBRT and BgRT. Detailed introduction of the X1 system can be found in other publications.⁵⁻⁸

The RefleXion X1 system has received Food and Drug Administration (FDA) clearance for conventional kVCT-guided treatment for IMRT and/or SBRT. As of February 2023, the BgRT modality has been FDA-cleared for

patient treatment, expanding the potential applications of the system. Our department was the first to install and commission the RefleXion X1 system for IMRT and/or SBRT in 2020 and has been using it to treat patients since May 2021. In this report, we present a comprehensive performance analysis of the X1 system during its first year of clinical use. The data includes clinical data, technical data, quality assurance (QA) results, machine performance, and results from a user satisfaction survey for X1 v1.0.60.

Methods and Materials

A total of 78 patients were treated on the X1 system between May 17, 2021, and May 20, 2022, comprising 4.1% of all patients treated at our department annually. Seventy-three patients received IMRT, and 5 received SBRT. Treatment sites on the X1 were confined to the head and neck, thorax, abdomen, and pelvis regions.

Figure 1 shows the RefleXion X1 workflow. It starts with simulation on the computed tomography (CT) scanner. Currently only head-first-supine and feet-first-supine patient orientations are supported. Fusion and contouring are not available in the X1 treatment planning system (TPS); hence, these tasks are performed in Eclipse (Varian Medical Systems, Palo Alto, California) and MIM (MIM Software Inc, Beachwood, Ohio) software at our department. According to our workflow process, each RefleXion treatment plan has a back-up plan generated using Varian Eclipse TPS to be treated on Varian TrueBeam or Trilogy machines (Varian Medical Systems, Palo Alto, California) in the event of RefleXion X1 downtime. The plans are reviewed both in Eclipse and in the X1 by the physicians and physicists. The patient-specific QA measurement is performed using an ArcCHECK device (Sun Nuclear,

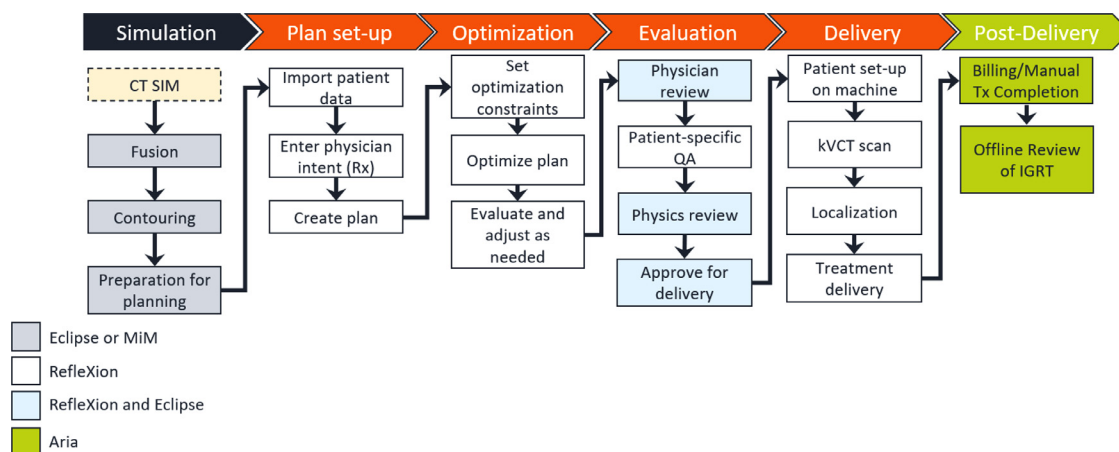


Figure 1 The RefleXion X1 workflow of intensity modulated radiation therapy and stereotactic body radiation therapy. Figure reproduced from the work of Simiele et al.¹⁴ Abbreviations: IGRT = image-guided radiation therapy; IMRT = intensity modulated radiation therapy; kVCT = kilovoltage computed tomography; QA = quality assurance; SBRT = stereotactic body radiation therapy.

Melbourne, Florida) within 3%/2 mm gamma criteria. Treatment scheduling, billing, and image offline review are performed in Aria (Varian Medical Systems, Palo Alto, California).

On the treatment day, the patient is positioned on the couch and aligned with the room laser using skin markers for the initial setup. The patient is then moved superiorly into the bore at the CT scanner plane for image acquisition. Kilovoltage computed tomography images are acquired and registered to the planning CT using manual matching. Couch shifts are calculated and applied in translational and rotational directions. Per our clinic policy, if translations based on image-guided radiation therapy (IGRT) are greater than 10 mm for IMRT treatments or 3 mm for SBRT treatments, kVCT is reacquired to confirm the correct shift. Finally, the couch is moved superiorly to the linac treatment plane, and the treatment starts.

Patient treatment clinical and technical data

The patient treatment data collected for analysis included relevant clinical and technical information such as treatment sites, number of fractions, number of pretreatment kVCT scans, beam-on time, patient setup time, imaging time, monitor unit (MU) values per fraction, and couch shifts in the translational (x, lateral; y, longitudinal; and z, vertical) and rotational (roll, pitch, and yaw) directions.

Quality assurance data

The output stability of the X1 system was evaluated based on daily QA results. The daily QA for the X1 involves delivering 100 MU to a TomoDose QA device (Sun Nuclear, Melbourne, Florida) using a rotational plan with a 100 mm × 20 mm jaw setting at a single couch position. The patient-specific QA results were reported using the ArcCHECK device (Sun Nuclear, Melbourne, Florida) with a gamma criterion of 3%/2 mm.

Machine performance and uptime

During the first year of usage, machine failures were recorded and sorted by the duration of downtime. The

machine uptime was determined by calculating the ratio of total operational time to total treatment time. Additionally, the causes of whole-day downtime were documented.

User survey

A survey was conducted among 5 radiation oncology physicians, 5 medical physicists, 5 dosimetrists, and 4 radiation therapists to gather their feedback on their experience with the X1 system. The survey aimed to assess the ease of learning the X1 treatment planning and delivery system, gauge user satisfaction with the system, and provide the vendor with suggestions for improvement. The survey results were collected and submitted to the vendor for consideration.

Results

The median age of patients was 69 (range, 40-94) years, and 49 (63%) patients were male. The breakdown by treatment region for the 78 treated patients was head and neck (n = 49, 63%), thorax (n = 5, 6%), abdomen (n = 6, 8%), and pelvis (n = 18, 23%). All were conventionally fractionated IMRT treatments except for 5 patients (6%), who received SBRT targeting bony metastases in the pelvis. Each region was further sorted by treatment site, as listed in Table 1. A pie chart in Fig. 2A shows the patient distribution by treatment region.

A total of 1656 fractions were delivered, with 1598 (96.5%) delivered on the X1 system and 58 (3.5%) delivered using TrueBeam or Trilogly linacs. The majority of the fractions delivered were for head and neck treatments (73%), followed by thorax (6%), abdomen (6%), conventionally fractionated pelvis (13%), and SBRT pelvis (2%). The distribution of fractions by treatment region is depicted in Fig. 2B.

A total of 1776 kVCT scans were acquired, of which 70% were acquired for head and neck treatment, 7% for thorax, 6% for abdomen, 15% for conventionally fractionated pelvis, and 3% for SBRT pelvis. Overall, the average number of kVCT scans per fraction was 1.20 ± 0.51 (mean ± standard deviation). By treatment region, the average number of kVCT scans per fraction was 1.07 ±

Table 1 Treatment regions and sites (numbers in parentheses refer to the patient number)

Treatment region	Head and neck	Thorax	Abdomen	Pelvis	Pelvis SBRT
Treatment site	Head and neck (44) Scalp (4) Skull (1)	Lung (5)	Gastrointestinal system (5) Pancreas (1)	Rectum (8) Prostate (1) Anal (1) Bladder (1) Pelvic nodes (1) Penis (1)	Bone metastases (5)

Abbreviation: SBRT = stereotactic body radiation therapy.

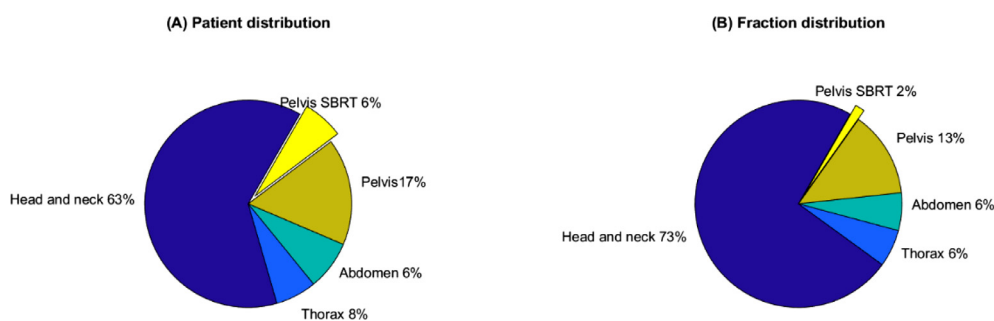


Figure 2 (A) Patient distribution by treatment regions. (B) Fraction distribution by treatment regions.

0.14 for head and neck, 1.24 ± 0.10 for thorax, 1.19 ± 0.08 for abdomen, 1.18 ± 0.17 for conventionally fractionated pelvis, and 2.67 ± 1.52 for pelvis SBRT. The comparisons are plotted in Fig. 3.

For 76 patients (97.4%), a 20 mm y jaw was used for planning, and only 2 patients (2.6%) with glioblastoma multiforme and nasal cavity cancer (where sharp superior and/or inferior dose fall-off was required for optics and neural organs at risk) had plans developed using a 10 mm jaw. The treatment extent in the y direction was 14.1 ± 4.7 cm for all treatments, 14.1 ± 4.4 cm for head and neck, 10.6 ± 1.2 cm for thorax, 16.0 ± 1.4 cm for abdomen, 16.4 ± 4.8 cm for conventionally fractionated pelvis, and 6.7 ± 3.1 cm for pelvis SBRT.

The average beam-on time by treatment region is illustrated in Fig. 4A. The average beam-on time among all treatments was 9.21 ± 3.50 minutes. This number varies with treatment region owing to differences in fraction dose, treatment length, and other relevant factors. The average beam-on time was 8.40 ± 2.41 minutes for head and neck, 6.70 ± 1.27 minutes for thorax, 10.3 ± 1.60 minutes for abdomen, 11.64 ± 5.12 minutes for conventionally fractionated pelvis, and 10.76 ± 5.25 minutes for pelvis SBRT. Based on a recording of 10 patients of various treatment sites, the average patient setup time (from

the moment the patient lies on the couch until the vault door is closed before imaging) was 4.8 ± 2.6 minutes, with a range of 2.5 to 11 minutes. Additionally, the average imaging time per kVCT (from the moment the vault door is closed until the start of treatment) was 4.6 ± 1.5 minutes, with a range of 2.5 to 8 minutes. The total treatment session time can be estimated by the sum of the beam-on time, patient setup time, and imaging time (the product of the imaging time per kVCT and the number of kVCT per treatment). As demonstrated in Fig. 4B, the average treatment session time was 19.5 minutes for all treatment regions, 18.1 minutes for head and neck, 17.2 minutes for thorax, 20.6 minutes for abdomen, 21.9 minutes for conventionally fractionated pelvis, and 27.8 minutes for SBRT pelvis.

The average MU values per fraction, as displayed in Fig. 5A, were 5219 ± 2487 MU for all treatment regions, 4417 ± 1311 MU for head and neck, 3897 ± 837 MU for thorax, 5877 ± 1161 MU for abdomen, 7248 ± 3772 MU for conventionally fractionated pelvis, and 7415 ± 3835 MU for SBRT pelvis. For a more accurate comparison across treatment regions, the MU values were normalized to 200 cGy per fraction and 10 cm treatment length, as depicted in Fig. 5B. The resulting normalized MUs were 2917 ± 786 , 2954 ± 896 , 3042 ± 219 , 3160 ± 562 , 2877

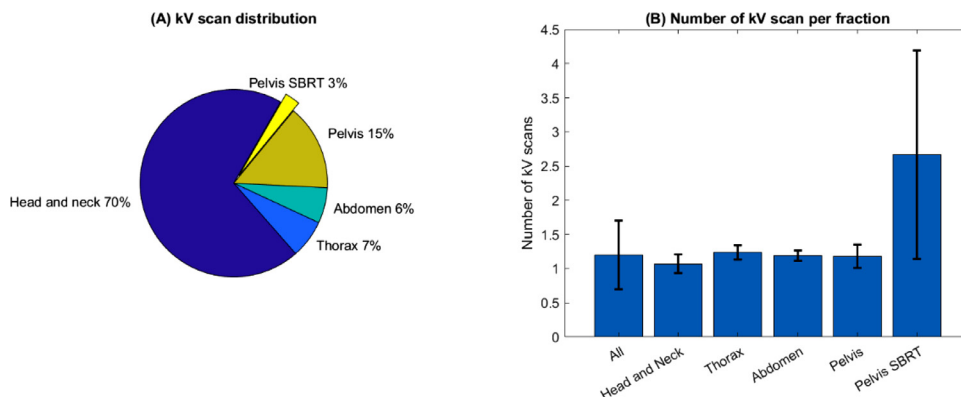


Figure 3 (A) Distribution of kilovoltage computed tomography scans by treatment region. (B) Number of kilovoltage computed tomography scans per fraction. *Abbreviations:* kVCT = kilovoltage computed tomography; SBRT = stereotactic body radiation therapy.

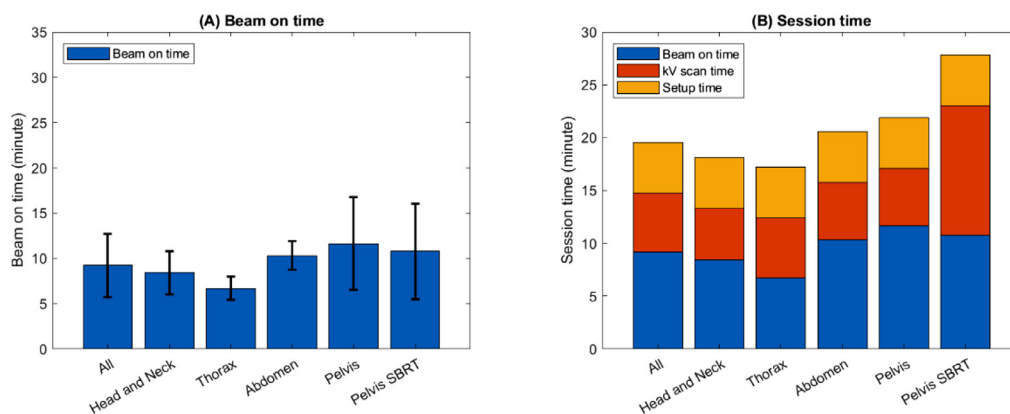


Figure 4 (A) Beam-on time. (B) Session time. *Abbreviations:* kV = kilovoltage; SBRT = stereotactic body radiation therapy.

± 556 , and 2214 ± 454 for all treated sites, head and neck, thorax, abdomen, conventionally fractionated pelvis, and SBRT pelvis, respectively. The results indicate that there is no significant difference in MU (around 3000 MU) between treatment regions for conventionally fractionated IMRT. On the other hand, SBRT treatments required fewer MUs for the same fractionation and treatment length.

The average couch shifts in translations (x, y, and z) and rotations (pitch, roll, and yaw) of all treatments and different regions are plotted in Fig. 6. On average, couch shift for all treatments was 0.4 ± 4.4 mm in the x direction (left-right), 1.0 ± 4.5 mm in the y direction (superior-inferior), and 1.3 ± 4.3 mm in the z direction (anterior-posterior). The averaged couch rotation was $0.1^\circ \pm 0.9^\circ$ for pitch, $0.0^\circ \pm 0.9^\circ$ for roll, and $0.2^\circ \pm 1.2^\circ$ for yaw. The conventionally fractionated pelvis treatment had the largest couch shift in the x, y, roll, and yaw directions. Head and neck treatments had the greatest couch shifts in the z direction, whereas abdomen treatments had the largest couch pitch, and pelvis conventional treatments had the greatest magnitude of translations and rotations.

Quality assurance data

During the first year of using X1 for treatment, daily output was relatively stable, with an average deviation of $0.4 \pm 1.2\%$ from baseline, falling within a range of -1.9% to 2.4% .

Only 1 patient-specific QA for head and neck plan with a low dose per fraction (1.2 Gy/fraction) failed to meet the 90% passing rate at 3%/2 mm gamma criteria, with an absolute passing rate of 84.3%. This patient was treated on TrueBeam instead. In general, the gamma passing rate for all plans was $97.4 \pm 2.8\%$, with a range of 84.3% to 100%.

Machine performance and uptime

A total of 72 machine hardware and/or software failures causing unscheduled downtime occurred during the first year of the clinical treatments with the X1 system. Of these failures, 41 were resolved within an hour, 22 were resolved within 4 hours, and 9 caused a full-day machine downtime. The annual machine downtime was 123 hours, equivalent to approximately 8% of all treatment time,

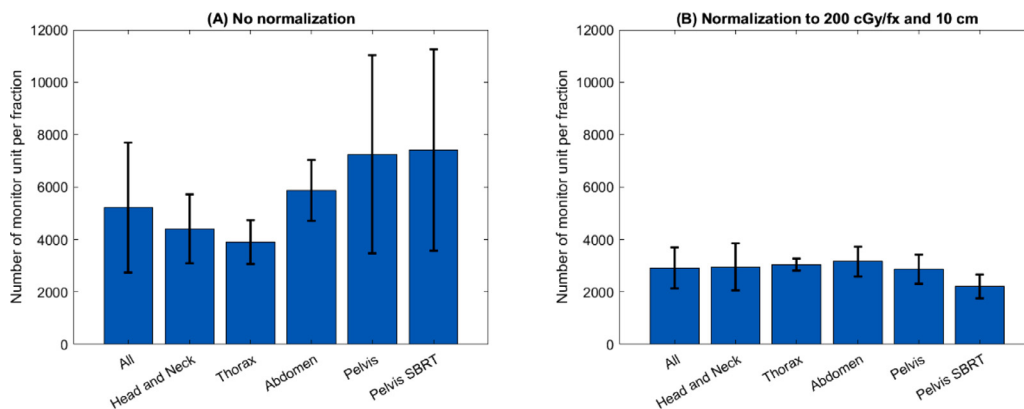


Figure 5 (A) Number of MU per fraction without normalization. (B) Number of MU per fraction normalized to 200 cGy per fraction and 10 cm treatment length. *Abbreviations:* MU = monitor unit; SBRT = stereotactic body radiation therapy.

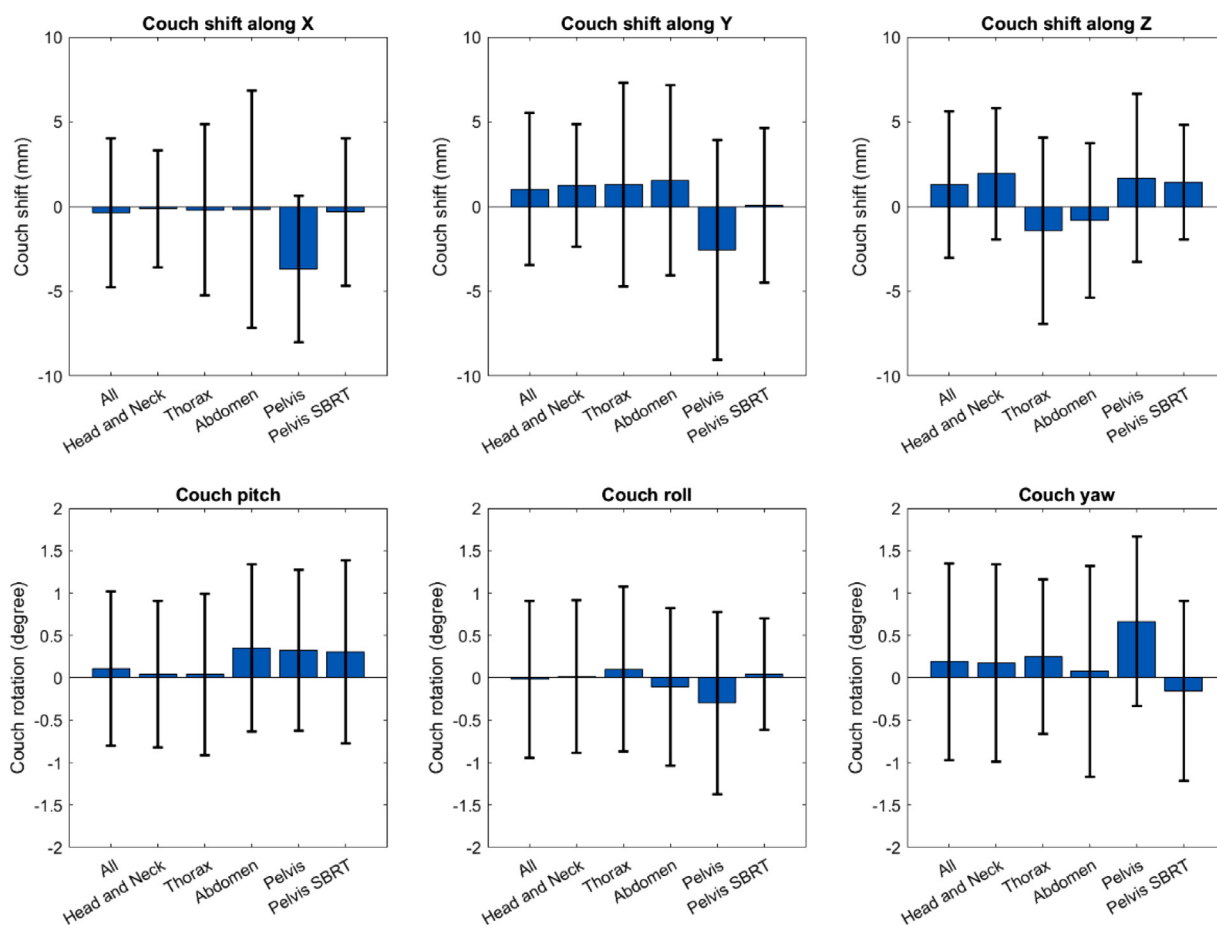


Figure 6 Mean couch shifts in translational and rotational directions associated with different treatment sites, as well as their corresponding standard deviations. The top row shows the couch shift along the X, Y, and Z axes, and the bottom row shows the couch pitch, roll, and yaw. Each plot includes a bar representing the mean shift/rotation and error bars representing the standard deviation. *Abbreviations:* SBRT = stereotactic body radiation therapy.

considering 257 days with 6 hours of treatment per day. This resulted in a machine uptime of 92%.

The full-day failures were caused by issues with the magnetron, cooling ring, kVCT scanner, couch, beam generation system, and circuit breaker. Treatment affected by those failures were delivered on TrueBeam or Trilogy linacs using the backup plans or delayed. Out of 1656 fractions delivered, 58 (3.5%) were delivered on TrueBeam or Trilogy linacs during X1 downtime.

Satisfaction survey results

The response rate for the satisfaction survey was 100%. [Figure 7](#) presents the satisfaction levels of physicians, physicists, dosimetrists, and therapists with different aspects of the X1 system. All of the respondents were either satisfied, highly satisfied, or neutral regarding the ease of learning the X1 system. For physicians, 100% were either highly satisfied or satisfied with kVCT image quality, but 100% were dissatisfied with the IGRT workflow,

owing to the lack of auto-matching tools, and 80% were satisfied with the plan quality. Among physicists, 60% reported being satisfied with the output stability and machine uptime, although 60% were neutral with regards to the periodic QA process. Most of the dosimetrists were neutral regarding the workflow, planning process, and plan quality. For therapists, 75% were dissatisfied with the treatment workflow, owing to the lack of auto-match IGRT tools and no ability to reimage after large table offsets without exiting the treatment session, whereas 75% were highly satisfied with the daily QA process.

The X1 machine received feedback from physicians regarding several areas of improvement, including variable jaw size plans, better IGRT viewing tools, and KV-planar imaging capability for patient alignment. Physicians suggested optimizing multiple plans for patients at the same time, replacing film tests with megavoltage port imaging, implementing motion management for SBRT, and enabling adaptive planning based on kVCT. Dosimetrists emphasized the need for a customizable planning interface, interactive optimization, and contouring tools

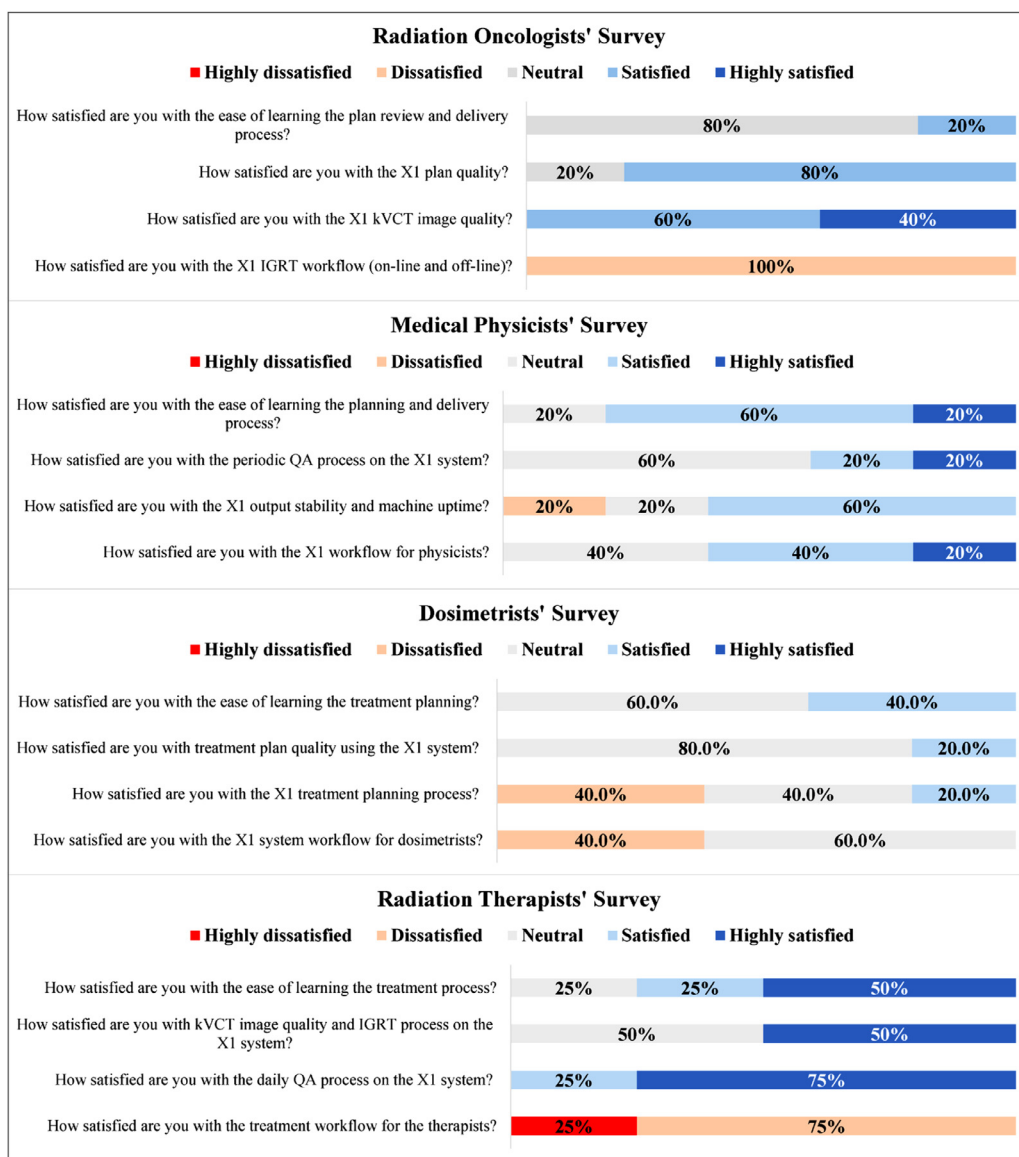


Figure 7 Initial user satisfaction survey results. *Abbreviations:* IGRT = image-guided radiation therapy; QA = quality assurance; kVCT = kilovoltage computed tomography.

in TPS. Therapists suggested streamlining and automating the offline review process, improving the IGRT matching display, and adding an auto-match feature. They also expressed the need for any therapist to sign off on “Resume Treatment” and improved X1 system interoperability with Aria. Data and comments from this survey were submitted to the vendor to guide the future development and improvement of the X1 system.

Discussion

This study reports the first-year treatment experience with the RefleXion X1 system at our department. Seventy-eight patients were treated using IMRT and SBRT modalities over 4 different anatomic sites. To thoroughly

evaluate the system’s performance, we collected a comprehensive array of information, including clinical data, technical data, machine quality assurance results, and machine performance. Additionally, a user satisfaction survey was conducted to gather feedback from different groups who use the system. The aim of this study was to provide valuable insights and guidance to clinicians and researchers who are interested in exploring the X1 system and its potential applications in clinical and research settings.

In the course of treatment on the RefleXion X1 system, it is common to require more than 1 kVCT scan. This is because of the need for verification scans in the event of couch shifts exceeding 10 mm for IMRT or 3 mm for SBRT, or when treatment is interrupted by machine issues. However, it is important to note that in the initial

version of the X1 system, reacquiring a CT scan during the same treatment session is not possible on the X1 system; thus, a new treatment session must be performed, and the patient needs to be shifted outside the bore to restart the process. The duration of beam-on time and treatment session time varies greatly depending on factors such as the treatment region, patient condition, and machine performance. For example, pelvis SBRT treatments tend to have the longest treatment session time, owing to the tighter thresholds for the need to reimage after couch offsets and the longer beam-on time, and thorax treatments typically have the shortest. At our department, a 30-minute appointment slot is reserved for conventionally fractionated IMRT treatments, whereas 45 minutes are reserved for SBRT treatments.

The RefleXion X1 system has demonstrated promising results in various aspects of radiation therapy. The kVCT image quality, which is close to diagnostic quality, is appreciated by the physicians and therapists and can potentially be used for adaptive radiation therapy. However, there are several areas where the system could be improved to further enhance the treatment experience for patients and health care providers. For example, some users have reported dissatisfaction with the image guidance workflow with the lack of auto-match image registration tools and lack of ability to reimage the patient after shifts and during treatment. There have been instances where machine uptime, output stability, and planning process have been a concern. To address these issues, the vendor is preparing the next software and hardware upgrade. Currently, the X1 system lacks motion management capabilities. This poses a challenge for treatments that are affected by respiratory motion, such as thorax treatments. Our previous phantom study found the presence of an interplay effect when treating targets moving along the direction of table motion.⁸ To prevent the interplay effect, only tumors with an amplitude of motion of <2 cm are treated based on the motion-inclusive target volume. During treatment, a slow couch speed CT scan is acquired to maintain the target motion information and enable accurate patient positioning. To ensure backup options, each RefleXion treatment requires an additional linac plan, which can put extra demands on planning resources, even though we found that only 3.5% of fractions were treated on the backup machine. Additionally, the X1 system offers limited integration with Aria Record-and-Verify system that makes scheduling, tracking of delivered dose, and offline image review process more labor intensive.

Machine uptime plays a crucial role in determining the quality of radiation therapy. According to reports from 2 different groups studying linac performance,^{9,10} the machine uptime (converted from the reported downtime) can range from 64% to 99.3%, with a mean and standard deviation of $91 \pm 8\%$. The X1 system has a comparable machine uptime (92%) to that of other linac systems.

The results of the satisfaction survey indicated a 100% response rate, with physicians expressing high satisfaction with the kVCT image quality but dissatisfaction with the IGRT workflow owing to the lack of auto-match tools. Physicists were satisfied with the output stability and machine uptime. Dosimetrists were generally neutral regarding the workflow, planning process, and plan quality. Therapists were dissatisfied with the treatment workflow owing to the lack of auto-match IGRT tools and the inability to reimage after large table offsets without exiting the treatment session, but they were highly satisfied with the daily QA process. All groups were satisfied with the ease of learning RefleXion X1 system. Overall, the satisfaction levels suggest that improvements can be made to the IGRT workflow and the treatment workflow. High satisfaction levels with the kVCT image quality indicate the potential for RefleXion X1 to become an excellent platform for adaptive radiation therapy.

One of the main advantages of the X1 system is its real-time tracking of the tumor using a PET signal, which allows for more targeted delivery of radiation. Unfortunately, this work does not report on BgRT, as it was just recently FDA-approved and not yet enabled on our clinical X1 system. Additionally, the use of tumor-specific PET agents to guide the treatment, and to adapt and predict the outcomes can open the door to improving the therapeutic ratio in radiation oncology. A new long-living PET agent is currently being tested at our institution that would require only one PET injection for the entire course of BgRT.^{11,12} This could significantly reduce the burden on patients and improve the efficiency of treatment. In terms of IMRT and/or IGRT advantages, the near-diagnostic imaging quality of the X1 system enables patient-specific autosegmentation on daily kVCT images, which has the potential for adaptive therapy.¹³ Some disadvantages include the longer treatment delivery times than those of C-arm linacs treating with volumetric-modulated arc therapy and limited integration with external record and verify systems (RVSS). The vendor is actively working to improve the X1 system. The most recent X1 upgrade has introduced increased dose rates to improve treatment delivery times, enabled IGRT auto-matching, and enabled reimaging after shift tools to streamline the treatment delivery workflow.

Since the introduction of the X1 system at our department, several studies have been conducted to assess its clinical and research applications, exploring the novel capabilities of this device. Han et al reported the results of the beam commissioning for the X1 system.⁵ The study found that the source misalignments and MLC misalignment were minimal, and the difference between the measured and modeled output factors was within 0.8%. Simiele et al reported on the results of the commissioning of the X1 TPS.⁸ The results showed that the TPS met the specified tolerances for dose calculation accuracy and data transfer for targets >1.5 cm in diameter. The end-to-end

testing showed small targeting errors for both isocentric and off-axis treatments. Shi et al have measured the small-field dosimetry results and validated a Monte Carlo model of the X1 system.⁷ Output correction factors for Edge detector ranging from 0.958 to 1 were reported. Pham et al have evaluated the treatment plan quality and delivery efficiency of the X1 system in comparison to 2 traditional linacs (TrueBeam and Trilogy) for 42 patient cases across 6 different cancer sites.⁶ The study found that the X1 TPS generated treatment plans with similar or better quality than the traditional systems and was considered acceptable for treatment. Although the X1-20 mm plans were deemed acceptable for treatment, the Eclipse VMAT and X1-10 mm plans yielded superior plan quality and sharper dose fall-off superior and/or inferior to targets. The beam-on time reported for X1 20 mm jaw plans was comparable to the data collected in this study for anus (10.1 minutes vs 11.7 minutes) and head and neck (8.3 minutes vs 8.4 minutes).

Additional studies were also performed. Simiele et al has conducted a study that applied Six Sigma methodology and failure mode and effect analysis to improve the X1 IMRT and/or SBRT treatment planning process.¹⁴ The team identified and ranked the potential failure modes and developed scripts to improve the efficiency and safety of the process. After 12 months of clinical use, only 3 errors were reported, and the average risk priority number decreased significantly, indicating a safer process. The study concluded that using the Six Sigma methodology was effective in minimizing errors in the implementation of the novel X1 system. An autosegmentations study was also conducted to explore the use of deep learning for patient-specific auto-segmentation on the X1 kVCT images.¹⁵ A population network was learned on a data set of 67 patient cases on auto-segmentation of esophagus, larynx, and pharynx. The pretrained network was then adapted to a specific patient using a transfer learning method. The results showed that the patient-specific network outperformed the population network and the clinical registration method in terms of contouring and dosimetric accuracy.

The results of this study are limited by its sole representation of the experiences from 1 institution, which may not accurately reflect the larger trend in X1 system usage and performance owing to potential biases arising from institutional treatment practices. To truly evaluate the effectiveness and efficiency of the X1 system, further studies involving multiple institutions are necessary. Additionally, the sample size for treatment of thorax, abdomen, and SBRT regions was limited, which may not fully reflect the capability of the X1 system in these areas. Future directions of study will include using the system's strengths of high-quality kVCT imaging to evaluate treatment response and consider adaptation. Although we did not report clinical outcomes in this study, we are actively collecting data on patient response to treatment with RefleXion and plan to report these findings in future studies.

Conclusion

This study provides valuable insights into the first-year treatment experience with the RefleXion X1 system at our department. It represents the first clinical study of the device's treatment performance and presents relevant clinical and technical data. Despite being a single-institution study, the results provide a useful starting point for further investigation into the use of the X1 system in clinical settings. With the recent FDA clearance of BgRT, our department is preparing to treat patients using PET-guidance via a new product release, which should also address deficiencies in the current IGRT workflow.

Disclosures

Nataliya Kovalchuk reports a relationship with RefleXion Medical that includes funding grants.

Acknowledgments

We acknowledge the whole radiation oncology team at Stanford radiation oncology department that helped with the RefleXion commissioning and patient treatments.

References

1. Shirvani SM, Huntzinger CJ, Melcher T, et al. Biology-guided radiotherapy: Redefining the role of radiotherapy in metastatic cancer. *Br J Radiol.* 2021;94:20200873.
2. Oderinde OM, Shirvani SM, Olcott PD, Kuduvali G, Mazin S, Larkin D. The technical design and concept of a PET/CT linac for biology-guided radiotherapy. *Clin Transl Radiat Oncol.* 2021;29:106-112.
3. Hu Z, Bieniosek M, Ferri V, et al. Image-mode performance characterisation of a positron emission tomography subsystem designed for biology-guided radiotherapy (BgRT). *Br J Radiol.* 2023;9:20220387.
4. Mackie TR. History of tomotherapy. *Phys Med Biol.* 2006;51:R427-R453.
5. Han B, Capaldi D, Kovalchuk N, et al. Beam commissioning of the first clinical biology-guided radiotherapy system. *J Appl Clin Med Phys.* 2022;23:e13607.
6. Pham D, Simiele E, Breikreutz D, et al. IMRT and SBRT treatment planning study for the first clinical biology-guided radiotherapy system. *Technol Cancer Res Treat.* 2022;21:15330338221100231.
7. Shi M, Chuang CF, Kovalchuk N, et al. Small-field measurement and Monte Carlo model validation of a novel image-guided radiotherapy system. *Med Phys.* 2021;48:7450-7460.
8. Simiele E, Capaldi D, Breikreutz D, et al. Treatment planning system commissioning of the first clinical biology-guided radiotherapy machine. *J Appl Clin Med Phys.* 2022;23:e13638.
9. Peiris GS, Pawiro SA, Kasim MF, Sheehy SL. Failure modes and downtime of radiotherapy LINACs and multileaf collimators in Indonesia. *J Appl Clin Med Phys.* 2023;24:e13756.
10. Wroe LM, Ige TA, Asogwa OC, et al. Comparative analysis of radiotherapy linear accelerator downtime and failure modes in the UK.

- Nigeria and Botswana. *Clin Oncol (R Coll Radiol)*. 2020;32:e111-e118.
11. Natarajan A, Khan S, Liang X, et al. Preclinical evaluation of (89)Zr-panitumumab for biology-guided radiation therapy. *Int J Radiat Oncol Biol Phys*. 2023;116:927-934.
 12. Lee YJ, van den Berg NS, Duan H, et al. 89Zr-panitumumab combined with 18F-FDG PET improves detection and staging of head and neck squamous cell carcinoma. *Clin Cancer Res*. 2022;28:4425-4434.
 13. Chen Y, Gensheimer MF, Bagshaw HP, et al. Patient-specific auto-segmentation on daily kVCT images for adaptive radiotherapy [e-pub ahead of print]. *Int J Radiat Oncol Biol Phys*. 2023. <https://doi.org/10.1016/j.ijrobp.2023.04.026>. Accessed July 18, 2023.
 14. Simiele E, Han B, Skinner L, et al. Mitigation of IMRT/SBRT treatment planning errors on the novel RefleXion XI system using FMEA within six sigma framework. *Adv Radiat Oncol*. 2023;8:101186.
 15. Chen Y, Yu L, Zhou Y, et al. Systematic study of patient-specific organs at risk auto-segmentation on daily kVCT images for adaptive head and neck radiotherapy. *Int J Radiat Oncol Biol Phys*. 2022;114:e590.