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Dosimetric Effect When Treating Multiple Lesion SRS Using VMAT With and Without Jaw Tracking

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Abstract

Introduction

The main purpose of this study was to determine if jaw tracking or non-jaw tracking is the superior technique for patients with multiple brain metastasis that are treated with Volumetric Modulated Radiation Therapy (VMAT) Stereotactic Radiosurgery (SRS). Doses to the organs at risk (OAR) and the target volumes were analyzed using the dose volume histogram (DVH) and dose statistics for each plan. The goal of this study included analyzing the dosimetric effect on the organs at risk and the normal tissue when using jaw tracking versus non jaw tracking. The pros and cons for each technique were identified as well as which situations were most positively or negatively affected using each technique.

Methods

Two different techniques of VMAT SRS treatment were compared for 10 Radiation Therapy patients with multiple metastatic brain lesions treated within a single isocenter. Treatment plans of patients who have been previously treated with VMAT SRS were retrospectively studied. The initial jaw tracking plan for each patient was edited to remove the jaw tracking component while keeping all other parameters the same. The non-jaw tracking plan was created by taking the maximum field size from the jaw tracking plan and locking it in as the new field size. The new plan was then optimized with the same objectives to obtain a comparable non-jaw tracking plan.

Results

Based on the DVH and dose statistics it was determined that the only statistically significant difference between the jaw tracking and non-jaw tracking methods was for the maximum dose to the optic chiasm, which had decreased maximum doses for 9 out of 10 patients when using the jaw tracking plan. The structures that benefited from the jaw tracking technique had the most impact in the low dose regions, mainly in the volumes receiving 2- 6 Gray (V_2-V_6). Jaw tracking also decreased the global maximum dose in 9 out of 10 patients by 0.4%- 2.5%.

Conclusion

Similar target coverage can be obtained with both jaw tracking and non- jaw tracking plans. The benefit comes from the jaw tracking plan having the ability to close the jaws continuously to match the shape of the multi- leaf collimator (MLC) as it rotates around the patient. There was some benefit in dose reduction to OARs with jaw tracking over non jaw tracking, but with SRS the smaller tumor volumes in addition to the distance to OARs caused this study to not provide statistically significant results. The OARs saw the most sparing in the low dose region in the normal tissue further from the target volumes. The jaw tracking technique would likely produce more significant results with larger target volumes that are closer to or even abutting the OARs.

Introduction

Brain Metastasis (BM) is a condition that affects approximately 200,000 people each year in the United States, affecting men and women equally.[1,2] Brain metastasis occurs when cancer cells from a primary tumor site spread to the brain.[3] The cancers that spread to the brain most frequently are lung, which accounts for up to 20% of BM, breast, melanoma, renal, and colorectal.[2,4] The incidence of BM is 10 times more common than primary brain tumors; one in every three adults with cancer will be affected with BM at some point. [1] Cancer patients are living longer due to advances in detection and treatment, so the frequency of BM is on the rise.[2] Advances in systemic therapy have played a large role in the length of survival, but due to the nature of the blood brain barrier those agents are unable to reach the brain to protect it against disease.[1]

In the past, the presence of BM was considered a poor prognostic indicator, and it was viewed as the end stage of cancer with only 1 month of life expectancy with no treatment at all. Then, the addition of steroids extended life expectancy to 2 months, and in the 1980s the addition of whole brain radiotherapy (WBRT) with steroids further increased survival to 4–6 months.[2,5] More recently, Yamamoto et al determined that the extent of a patient's systemic disease and how well it responds to systemic treatment are more likely to affect survival rates than the presence of BM.[1] In 2012, a new prognostic index was developed for BM that is unique to the type of primary cancer. The Disease Specific- Graded Prognostic Assessment (DS-GPA) now takes more components into account such as extracranial disease status, patient age, amount of brain metastases, functional status, and for breast cancer, the molecular subtype.[1] Due to the increase in life expectancy in patients with BM there is an increasing need to spare the organs at risk (OAR) to lower their risk of developing secondary neoplasm or late side effects such as

myelitis and cataracts. [6,7] Over the years several radiation therapy techniques have been used for the treatment of BM, each one aiming to decrease dose to the OAR more than the last.

The original standard of treatment for brain metastases was WBRT alone since WBRT could be started quickly, was convenient, and could treat both detectable and undetectable BM. [1,5] The standard dose-fractionation scheme for WBRT is treatment to a total of 3000 centi-gray (cGy) over the course of 10-12 days.[1] The main objectives of treatment included alleviation of neurologic symptoms, increasing local control, increasing life expectancy and increasing the quality of life. [2,5] Although WBRT had many benefits it was also known to cause increased fatigue and decreased neurocognitive function. [1,2] In the 1990s multiple clinical trials agreed that upfront resection of symptomatic solitary brain metastasis in addition to WBRT resulted in a longer progression-free survival and increased local control compared to using WBRT alone. Other advantages included the ability to obtain a histological diagnosis when necessary, and avoid the long-term use of steroids which can cause side effects such as myopathy, immunosuppression, osteoporosis, and gastrointestinal complications.[1,2,8] The use of surgical resection for brain metastasis has made many advances over the past two decades and remains an important regimen for the treatment of solitary metastatic brain lesions larger than 3 cm that cause neurologic deficits.[1,2] Although surgery has proved to be beneficial in the treatment of solitary metastatic brain lesions, there is inadequate sound documentation assessing the role of surgery for multiple metastatic brain lesions.[2]

In the 1980s a less-invasive approach, stereotactic radiosurgery (SRS), was implemented clinically. [1] SRS is defined by the American Association of Neurological Surgeons (AANS) and the American Society for Therapeutic Radiology and Oncology (ASTRO) as “a distinct neurosurgical discipline that utilizes externally generated ionizing radiation to inactivate or

eradicate defined targets in the head or spine without need to make an incision."[2] Credited to the neurosurgery field, SRS was probably the single most important development for the treatment of BM.[5] Since the implementation of SRS there have been great advances in imaging, radiation treatment planning, and radiation treatment machines which have led to SRS evolving into one of the most predominant neurosurgical treatment methods for multiple brain conditions.[2,5] In the early stages SRS was used to treat single BM lesions in a single fraction, but more recently, due to the above mentioned advances, the cutoff for number of lesions treated simultaneously is becoming less crucial.[1] The implementation of SRS now allows for precise planning and conformal treatment of the BM without having to treat the whole brain.[5] There are many advantages of using SRS including shorter treatment duration, high likelihood of treated-lesion control, minimal delay in resuming systemic therapy, less cognitive function loss, and minimal adverse effects to normal tissue when following standard dose/volume recommendations.[1,5] In the instance of recurrence, SRS for salvage purposes is another advantage for patients previously treated with SRS and/or WBRT.[5]

Hypofractionated SRS has been increasingly utilized to help spare normal tissues when treating bulky, unresectable lesions and lesions located near radiosensitive structures. Hypo fractionated SRS is also called hypo fractionated stereotactic radiotherapy (SRT), and it allows the treatment duration to be spread out over 3-5 treatments on consecutive days, or every other day. One of the reasons for spreading the treatment over more days allows the normal tissues a chance to recover in order to reduce toxicity. The SRT regimens that are most commonly used are 25 Gray (Gy) in 5 fractions, and 21 Gy in 3 fractions, although the optimal dose/fractionation scheme for SRT is undefined.[1]

There was once a treatment scheme that included WBRT in addition to SRS. [1] SRS can increase the local control rate, but with the addition of WBRT the local control rate could increase even more, although toxicity from WBRT was still a concern.[1,2] In 2006-2011, three studies tested whether WBRT could be eliminated from patients receiving SRS. The results of these trials proved the addition of WBRT for up to 4 BM decreased local recurrence and provided prophylaxis against distant recurrence while SRS alone resulted in an increase of distant recurrence. Although there was an increase of distant brain metastases in patients treated with SRS alone, 25% of patients with upfront WBRT also developed new distant BM following WBRT. It was determined that withholding WBRT lowered the risk of cognitive impairment and did not affect survival. In response to this new information, ASTRO issued a recommendation in 2014 discouraging the addition of WBRT to SRS for patients with limited BM.[1]

In addition to the evolution of BM treatment techniques, the treatment machines themselves have evolved. Within the head of a modern-day linear accelerator (linac) is a set of jaws which provide secondary collimation of the treatment field size, and under the jaws is a tertiary collimation called the multileaf collimator (MLC). [7] Depending on the linac model, the MLCs are made of up to 120- 160 individual leaves that can move during treatment to continuously shape the field to the size of the tumor.

MLCs are essential for modern external beam radiation therapy.[7] For the treatment of WBRT, 3D conformal technique is used in which the MLC leaves for the treatment fields are fixed in a position that correspond to the projection of the target volume from the beams eye view. Fixed MLC leaves were the standard until the development of Intensity Modulated Radiation Therapy (IMRT). IMRT allows for modulation of dose across each of multiple treatment fields by using dynamic MLCs. With sliding window IMRT, the MLCs move

continuously during the treatment of each field and then the gantry of the linac is moved manually to the next treatment position. The introduction of Volumetric- Modulated Arc Therapy (VMAT) in 2008 enhanced this technology by adding the ability for the modulation of dose rate and MLC position as the gantry simultaneously rotates around the patient. [9]

Prior to recent advances in SRS, each BM was given its own isocenter. For patients with multiple BM this could result in very long treatment times, up to several hours in some cases. More recently VMAT has allowed for the treatment of multiple BM within a single isocenter, which can drastically decrease the treatment time to a few minutes without sacrificing accuracy.[1] This is a huge advancement for the comfort of the patient alone. The goal of radiation therapy is to deliver maximum dose to a tumor while minimizing doses to normal structures. The implementation of VMAT for SRS has proven to be exceptional in achieving this goal while improving SRS outcomes.[9,10] Although advanced, VMAT still delivers a low nominal dose due to the interleaf leakage of the MLCs.[10] The solution to this problem is Jaw Tracking.

Jaw tracking is a technique that was developed by Varian for the True Beam linear accelerator; it was implemented starting in the Eclipse V.10.0 treatment planning software (TPS).[10,11] Jaw tracking adds the ability of the main collimator jaws to continually adjust and track the shape of the MLCs during treatment, minimizing the radiation leakage through the MLC leaves. [7,10,11] This allows for increased shielding of the normal tissues around the tumor.[10,11] Since jaw tracking plans have been shown to better spare the OAR, the probability of developing a secondary neoplasm or late side effects may decrease.[6,7] Jaw tracking has also proven to be advantageous for treatment of patients who have local recurrence or a second primary malignant neoplasm in or beside a previously treated area.[6]

The significance of jaw tracking is all about minimizing unnecessary interleaf leakage. Cadman et al., found that the transmission through the MLC and jaws combined is less than 0.1% of the original intensity.[12] Losasso et al., found that MLC transmission increases with an increase in jaw field size and beam energy.[13] For various jaw sizes the transmitted dose rate when shielded by MLCs alone could be 0.90%- 4.40% for 6MV and 1.14-7.00% for 18MV, higher than that shielded by jaws or both MLC and jaws.[7] The Eclipse TPS has a dose calculation algorithm that takes the collimator scatter during jaw movement into account.[10]

Many studies have shown the potential of jaw tracking in reducing radiation doses to normal organs by using different radiation delivery techniques.[10] Yao et al., compared the dosimetric differences between jaw tracking and no jaw tracking in 16 static IMRT plans. This study included 8 plans with large tumor volumes that were compared with 8 plans with small tumor volumes. This study concluded that jaw tracking can reduce the dose to OAR, and the plans with large tumor volumes showed more significant results than the plans with small tumor volumes.[11] Feng et al., compared dynamic IMRT versus static jaw IMRT on 28 different plans with various tumor locations. This study showed that the jaw tracking plans resulted in lower mean doses in the whole body as well as in the low dose regions such as the V_5,V_{10}, V_{20}, V_{30}, and V_{40}.[6]

In addition to IMRT, the effects of jaw tracking in VMAT plans have also been explored. Thongsawad et al., compared the effects of jaw tracking versus non-jaw tracking in prostate, lung, and nasopharynx VMAT plans. With jaw tracking, it was observed that there was a decrease in the low dose regions of V_5 and V_{10} for the OAR, and an overall decrease in mean dose to the lung. For integral dose there was a significant decrease in almost all of the treatment plans by using jaw tracking, and a large reduction was seen in the V_5.[10] Wu et al., compared

identical VMAT plans with and without jaw tracking while keeping all other plan details constant. Jaw tracking resulted in decreased doses to both the tumor volume and OAR without sacrificing the delivery efficiency of the VMAT plans.[7]

Most publications discussed the dose changes in several kinds of tumors, but very few studied the impact of tumor sizes. Schmidhalter et al., indicated that integral-dose reduction was dependent on the tumor size; for example, a large size difference between anterior and lateral views in a head and neck tumor can create larger range of jaw movement.[14] In multiple lesion VMAT SRS, the tumor volumes will likely be small, but considering there can be multiple targets treated by one isocenter, the maximum jaw width at different angles is likely to produce significant results when using jaw tracking versus non jaw tracking.

The main purpose of this study was to determine the potential advantages of using jaw tracking with VMAT SRS for the treatment of multiple metastatic brain lesion within a single isocenter. The goals of this study include analyzing the dosimetric effects on the organs at risk and the normal tissue, change in MU, and difference in max field width when using jaw tracking versus non jaw tracking.

Null hypothesis (Ho): In VMAT SRS for patients with multiple brain metastases jaw tracking will not show a lowered dose to organs at risk and normal tissue compared to using non jaw tracking.

Alternative hypothesis (Ha): In VMAT SRS for patients with multiple brain metastases jaw tracking will show a lowered dose to organs at risk and normal tissue compared to using non jaw tracking.

Methods and Materials

Patient Selection

This is a retrospective study that includes 10 male and female patients who were previously treated at a Southeast hospital for multiple lesion brain metastases using the VMAT SRS technique with jaw tracking. A list was obtained from the billing department that outlined patients who had been previously charged for an SRS treatment. From the list, patients were selected for the study if they met a certain criterion. They were all treated previously using the VMAT SRS technique with jaw tracking, had multiple metastatic brain lesions treated in one isocenter, had the same critical structures delineated by the same dosimetrist, and had the same prescription which utilized the 10MV FFF beam on the Varian True Beam linear accelerator. A new plan was created based off the previous plan to do a comparison. There was no harm to the patient because the new plan was only created for the purpose of data collection, and it was not meant to be implemented clinically.

IRB

Prior to seeking the approval from the Institutional Review Board (IRB), the required CITI program courses were completed through Grand Valley State University. The research proposal was presented to the hospital IRB board. Details about the study were presented along with the plan for handling Protected Health Information (PHI). The hospital approved this study under the exempt status. In order to comply with the Health Insurance Portability and Accountability Act of 1996 (HIPPA), the hospital implemented a "Data Management Procedure" for all research investigators to follow. This agreement involved guidelines for safely acquiring and storing PHI. To safely store patient data, the hospital created a confidential folder on the network that could only be accessed by the research investigators. After obtaining IRB approval from the hospital, the

IRB board at Grand Valley State University also approved this study as exempt. During the study, all patient data was stored in the confidential network folder with patient identifiers removed

Each patient was simulated in a GE LightSpeed RT Wide Bore 16 Slice CT simulator. A QFix Portrait Intracranial Head & Neck Device was indexed on the CT Simulator table with a CIVCO lockbar. The patients laid in the supine position with their head rested on a customized QFix cushion which was supported underneath by a clear headrest. A 3.2mm QFix Assure Open View U-frame aquaplast mask was custom made for each patient, and then it was immobilized to the treatment table. All patients kept their arms by their side and were given a knee cushion for support. After the fabrication of all devices, each patient was scanned with 1.25 mm slice thickness in the head-first supine (HFS) position. Prior to releasing the patient, the Radiation Oncologist verified the set-up and reviewed the CT Simulation scan.

Planning

Post simulation, Eclipse treatment planning System (TPS) version 15 was utilized for the reconstruction and planning of each patient. To maintain consistency, all plans that were chosen for this study were created and contoured by the same Dosimetrist, and planned on the same LINAC, the Varian True Beam. All prior imaging studies were fused, and all critical structures were delineated by the Dosimetrist prior to the Radiation Oncologist setting an isocenter and contouring the Gross Tumor Volumes (GTV). After the GTVs were delineated, the Dosimetrist followed the same planning technique for each patient. First, the GTVs were all combined to create a "Total GTV" structure that would be used for planning purposes only. From the GTV there were three rings added, an inner control, middle control, and outer control as seen in Figure 1 in the appendix. Starting at the edge of the GTV, a 5mm inner control ring was created. From the outer edge of the inner control ring, a 5 mm margin was added to create the middle control ring. Then,

the outer control ring was created by adding a 5mm ring starting at the outer edge of the middle control ring.

After all planning structures were completed, 10 MV Flattening Filter Free (FFF) SRS Rapid Arc fields were added to each plan and MLCs were fit to the "GTV Total" planning volume to optimize the collimator jaws. Each field was visualized in the beams eye view (BEV) window and the parameters, including the collimator, were set with the goal of minimizing the maximum field size and minimizing island blocking. Each patient in this study was prescribed a hypofractionated regimen of 3000 cGy over the course of 5 fractions. The plans were optimized as shown in Table 1, then calculated using the Anisotropic Analytical Algorithm (AAA) and a dose grid size of 0.15 cm. After calculation, all plans were normalized at 100% to the lesion with the least coverage. When evaluating each plan, special attention was placed on producing a plan with a conformality index less than 1.5, gradient between 3-5, and dose bridging the 50% isodose line between lesions was avoided if possible. The International Commission on Radiation Units and Measurements (ICRU) 62 calculates the conformality index as the ratio of the volume enclosed by the prescription isodose surface (V_{Rx}) to the volume of the PTV (V_{PTV}). The conformality index defines how well the tumor volume is being covered by the treatment. Gradient index (GI) is a tool to evaluate intermediate dose fall off, is the ratio of the volume enclosed by half of the prescription isodose and the prescription isodose volume. [15]

For the evaluation of both plans, an SRS protocol from the University of Alabama at Birmingham (UAB) was followed in which constraints were defined for organs at risk. The constraints that were followed were for hypofractionated SRS treatment when treating 4-6 Gy per fraction in 5 fractions. Dose constraints are as follows: brain minus PTV- maximum dose < 20 Gy, mean dose < 6 Gy, brainstem- maximum dose < 31 Gy, V_{26} Gy < 1cc, chiasm and optic nerve-

maximum dose < 25 Gy, V_{20} Gy < 0.2cc, cochlea- max dose < 27.5 Gy, lens- max dose < 3-7 Gy, and spinal cord- max dose < 30 Gy, $V_{22.5}$ < 0.25cc (Table 2).

For this study, each plan was copied into a new course labeled "Research". The previously treated plan was labeled as "Jaw Tracking" (JT) and it was duplicated to create a non-jaw tracking (NJT) plan. For the NJT plan the MLCs were deleted and re-created by using the maximum field size from the JT plan. This is the only change that was made prior to optimization. Once in the optimization window, the jaw tracking feature was turned off and each plan was re-run starting in level 1. To have consistency between the two plans, the optimization objectives were left the same. The plans were calculated once again using the AAA and a dose grid size of 0.15 cm. After calculation, each plan was once again normalized at 100% to the lesion with the least coverage.

In the Eclipse treatment planning software, a plan comparison was created for each patient. The DVH and dose statistics provided in this plan comparison were analyzed for 10 different critical structures. The maximum dose and mean dose for brain-PTV, brainstem, spinal cord, left cochlea, right cochlea, left lens, right lens, left optic nerve, right optic nerve, and optic chiasm were all evaluated. Due to variations in size and number of tumors in each patient the brain was not evaluated. Instead brain-PTV was created by combining the planning target volumes (PTV) of each patient to create a total PTV structure. This total PTV structure was then subtracted from the brain volume which resulted in the brain- PTV structure that was evaluated.

Statistical analysis was performed in consultation with Grand Valley State University's Statistics Center using IBM SAS version 9.4 software. Due to the small sample size, nonparametric tests were used to see if the median dose for each critical structure differed when using the jaw tracking technique and the non-jaw tracking technique. Nonparametric tests are used on data that is either counted or ranked, and they are based on fewer assumptions. A nonparametric test can be

used if there is a deviation from normal distribution, a difference in the number of subjects in each group, and a small sample size.[16] Boxplots and histograms were created to analyze symmetry and detect outliers. Outliers were observed and symmetry could not be assumed so the sign test was performed for the comparison of variables. For this study, the median of each data set was used to measure central tendency. The sign test is used to compare differences between two sets of data for each patient. When it is not possible to acquire quantitative measures, but rank measures are able to be obtained between members of a pair, the sign test is a great tool to use. [16]

Results

The main purpose of this study was to determine if there were any advantages of using jaw tracking with VMAT SRS for the treatment of multiple metastatic brain lesion within a single isocenter. The main goal of this study is to obtain a better understanding of the dose effects on normal tissues when utilizing the jaw tracking technique as opposed to not using jaw tracking, and to determine if there is a significant impact when using one technique over the other. The 10 previously treated male and female patients were selected for this study with varying amounts of brain metastases ranging from 3- 14 lesions within a single isocenter.

Brain- GTV

The mean doses and max point doses for brain - GTV were evaluated for both plans as seen in Table 3 and Table 4. For the jaw tracking plan the mean doses across all 10 subjects ranged from 198 cGy- 652 cGy with a median of 479.4 cGy as seen in. For the non- jaw tracking plan the mean dose across all subjects ranged from 221.8- 711.8 cGy with a median of 492.2 cGy. The median brain – GTV mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for brain - GTV, p= 0.3438. For the jaw

tracking plan the maximum point doses for the brain – GTV across all 10 subjects ranged between 3040.8- 3695.4 cGy with a median dose of 3442 cGy. For the non- jaw tracking plan the maximum doses across all 10 subjects ranged from 3070.8- 3720.8 cGy with a median dose of 3470.9 cGy. The median brain – GTV maximum dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum dose for brain - GTV, $p = 0.2891$.

Brainstem

The mean doses and max point doses for the brainstem were evaluated for both plans. For the jaw tracking plan the mean brainstem doses across all 10 subjects ranged from 79.9- 1118.1 cGy with a median dose of 391.3 cGy. For the non- jaw tracking plan the mean brainstem dose across all subjects ranged from 94.2-1145.9 cGy with a median of 398 cGy. The median brainstem mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the brainstem, $p = 0.3438$. For the jaw tracking plan the maximum point doses for the brainstem across all 10 subjects ranged between 217.2-2974.2 cGy with a median of 826.4 cGy. For the non- jaw tracking plan the maximum brainstem doses across all 10 subjects ranged from 231.4- 2953.3 cGy with a median dose of 1009 cGy. The median brainstem max point dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the brainstem, $p = 0.3438$.

Spinal Cord

The mean doses and max point doses for the spinal cord were evaluated for both plans. For the jaw tracking plan the mean spinal cord doses across all 10 subjects ranged from 10-388.3 cGy with a median dose of 128.7 cGy. For the non- jaw tracking plan the mean spinal cord dose across all subjects ranged from 13- 442.4 cGy with a median dose of 117.3 cGy. The median spinal cord mean dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the spinal cord, p= 0.3438. For the jaw tracking plan the maximum point doses for the spinal cord across all 10 subjects ranged between 24.7- 1552.2 cGy with a median dose of 363.7 cGy. For the non- jaw tracking plan the maximum spinal cord doses across all 10 subjects ranged from 36- 1713.2 cGy with a median dose of 329.5 cGy. The median spinal cord max point dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the spinal cord, p= 0.3438.

Optic Chiasm

The mean doses and max point doses for the optic chiasm were evaluated for both plans. For the jaw tracking plan the mean optic chiasm doses across all 10 subjects ranged from 158.6-525.1 cGy with a median dose of 251.3 cGy. For the non- jaw tracking plan the mean optic chiasm dose across all subjects ranged from 214.3-521.5 cGy with a median of 262.7 cGy. The median optic chiasm mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the optic chiasm, p= 0.7539. For the jaw

tracking plan the maximum point doses for the optic chiasm across all 10 subjects ranged between 283.5-647.4 cGy with a median dose of 402.7 cGy. For the non- jaw tracking plan the maximum optic chiasm doses across all 10 subjects ranged from 340.4- 757.4 cGy with a median of 464.8 cGy. The median optic chiasm max point dose was higher the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the optic chiasm, p= 0.0215.

Left Optic Nerve

The mean doses and max point doses for the L optic nerve were evaluated for both plans. For the jaw tracking plan the mean L optic nerve doses across all 10 subjects ranged from 58.3-357 cGy with a median of 193.1 cGy. For the non- jaw tracking plan the mean L optic nerve dose across all subjects ranged from 50.6-362.7 cGy with a median dose of 199.6 cGy. The median L optic nerve mean dose was higher the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the L optic nerve, p= 1.0. For the jaw tracking plan the maximum point doses for the L optic nerve across all 10 subjects ranged between 78.8-534.1 cGy with a median dose of 298.4 cGy. For the non- jaw tracking plan the maximum L optic nerve doses across all 10 subjects ranged from 72.8-540.2 cGy with a median of 304.8 cGy. The median L optic nerve point dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the left optic nerve, p=0 .7539.

Right Optic Nerve

The mean doses and max point doses for the R optic nerve were evaluated for both plans. For the jaw tracking plan the mean R optic nerve doses across all 10 subjects ranged from 42.2-292.2 cGy with a median of 181.9 cGy. For the non- jaw tracking plan the mean R optic nerve dose across all subjects ranged from 42.7-292.8 cGy with a median of 209 cGy. The median R optic nerve mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the R optic nerve, p= 0.1094. For the jaw tracking plan the maximum point doses for the R optic nerve across all 10 subjects ranged between 146.9-529.9 cGy with a median of 391.5 cGy. For the non- jaw tracking plan the maximum R optic nerve doses across all 10 subjects ranged from 75.9-513.9 cGy with a median of 372.4 cGy. The median R optic nerve point dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the R optic nerve, p= 0.3438.

Right Lens

The mean doses and max point doses for the R lens were evaluated for both plans. For the jaw tracking plan the mean R lens doses across all 10 subjects ranged from 16-150.8 cGy with a median of 67.6 cGy. For the non- jaw tracking plan the mean R lens dose across all subjects ranged from 23-142.2 cGy with a median of 82.2 cGy. The median R lens mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the R lens, p= 0.3438. For the jaw tracking plan the maximum point doses for the R lens across all 10 subjects ranged between 18.6-183.2 cGy with a median of 105.3 cGy. For the non-

jaw tracking plan the maximum R lens doses across all 10 subjects ranged from 28.6-174.2 cGy with a median of 115.6 cGy. The median R lens max point dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the R lens, p= 0.7539.

Left Lens

The mean doses and max point doses for the L lens were evaluated for both plans. For the jaw tracking plan the mean L lens doses across all 10 subjects ranged from 55.7-129.2 cGy with a median of 85.9 cGy. For the non- jaw tracking plan the mean L lens dose across all subjects ranged from 47.2-142 cGy with a median of 82.1 cGy. The median L lens mean dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking mean dose for the L lens, p= 0.3438. For the jaw tracking plan the maximum point doses for the L lens across all 10 subjects ranged between 87.9-161.3 cGy with a median of 118.7 cGy. For the non- jaw tracking plan the maximum L lens doses across all 10 subjects ranged from 72.9-208.2 cGy with a median of 97.9 cGy. The median L lens max point dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the L lens, p= 0.3438.

Right Cochlea

The mean doses and max point doses for the R cochlea were evaluated for both plans. For the jaw tracking plan the mean R cochlea doses across all 10 subjects ranged from 59.1-618.5

cGy with a median of 259 cGy. For the non- jaw tracking plan the mean R cochlea dose across all subjects ranged from 63.7-723.9 cGy with a median of 562.4 cGy. The median R cochlea mean dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non-jaw tracking mean dose for the R cochlea, p= 0.3438. For the jaw tracking plan the maximum point doses for the R cochlea across all 10 subjects ranged between 80.3-1073.5 cGy with a median of 326.2 cGy. For the non- jaw tracking plan the maximum R cochlea doses across all 10 subjects ranged from 106.4-1191.9 cGy with a median of 338.1 cGy. The median R cochlea max point dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did/ did not indicate a statistical difference between the median jaw tracking and non- jaw tracking maximum point dose for the R cochlea p= 0.1094.

Left Cochlea

The mean doses and max point doses for the L cochlea were evaluated for both plans. For the jaw tracking plan the mean L cochlea doses across all 10 subjects ranged from 105.2- 675.7 cGy with a median of 258.8 cGy. For the non- jaw tracking plan the mean L cochlea dose across all subjects ranged from 143.1-549.2 cGy with a median of 249 cGy. The median L cochlea mean dose was lower in the non- jaw tracking plan than the jaw tracking plan. A sign test was performed and did not indicate a statistical difference between the median jaw tracking and non-jaw tracking mean dose for the L cochlea, p= 1.0. For the jaw tracking plan the maximum point doses for the L cochlea across all 10 subjects ranged between 113.5-882.4 cGy with a median of 318 cGy. For the non- jaw tracking plan the maximum L Cochlea doses across all 10 subjects ranged from 167.6-827.9 cGy with a median of 320.1 cGy. The median L cochlea max point dose was higher in the non- jaw tracking plan than the jaw tracking plan. A sign test was

performed and did not indicate a statistical difference between the median jaw tracking and non-jaw tracking maximum point dose for the L cochlea p= 0.7539.

This study demonstrates that the median values of the mean doses to brain-GTV, brainstem, optic chiasm, optic nerves, lenses, cochlea, and spinal cord are not significantly different in the two plans (all p values > 0.05) as shown in Table 3. Jaw tracking resulted in a 1.7% - 54% decrease in the median value of the mean doses to OARs in 7 out of 10 patients. With the jaw tracking plan, the right cochlea had the largest decrease in mean dose at 54%.

Also shown in this study is that the median values of the maximum doses to brain-GTV, brainstem, optic nerves, lenses, cochlea, and spinal cord are not significantly different in the two plans (all p values > 0.05), as shown in Table 4. Jaw tracking resulted in a 0.7% to 18.1% decrease in the median maximum dose to OARs in 7 out of 10 patients. The only OAR which showed a statistically significant difference between the two plans was the maximum dose to the optic chiasm (p value = 0.0215). In addition to OAR comparisons, the global maximum dose to the whole body was evaluated for all plans. The data in Table 5 shows that the jaw tracking plan decreased the global maximum dose by 0.4%- 2.5% in 9 out of 10 plans. In the other plan the global maximum doses were the same.

Discussion

The purpose of this study was to analyze two different treatment planning techniques when treating multiple metastatic brain lesions in one isocenter with VMAT SRS. The two techniques, jaw tracking and non- jaw tracking were created and the dosimetric effects to organs at risk and normal tissues were evaluated. For this study, the mean and maximum doses to the OARs, global maximum dose, and DVH were evaluated.

OAR Maximum and Mean Dose

Out of the maximum doses, using the jaw tracking technique resulted in lower median values for brain- GTV, optic chiasm, left optic nerve, right lens, right cochlea, and left cochlea. Using the non-jaw tracking technique resulted in lower median values for the brainstem, right optic nerve, left lens, and spinal cord. Out of the mean doses, using the jaw tracking technique resulted in lower median values for brain- GTV, brainstem, optic chiasm, left optic nerve, right optic nerve, right lens, and right cochlea. Using the non- jaw tracking technique resulted in lower median values for the left lens, left cochlea, and cord. The optic chiasm was the only structure to have a lower maximum dose in all 10 jaw tracking plans which resulted in it being the only structure with a statistically significant decrease.

Global Maximum Dose

Global maximum dose was also evaluated for both techniques. Out of the 10 patients, 9 saw a 0.4%- 3.1% reduction in the global maximum dose when using the jaw tracking technique. The remaining patient had no change in global maximum dose when going from one plan to the other. The reduction in global maximum dose when using the jaw tracking technique is possibly due to the jaws closing down to block any unnecessary radiation from reaching the patient caused by inter- and intra- leaf leakage as the MLCs continuously reposition to align with the targets. Figure 2 illustrates the MLC and jaw configuration for the same lesions at the same gantry angle for both jaw tracking and non-jaw tracking techniques. This shows the jaws remaining in the fixed position for the maximum field size needed for the non- jaw tracking plan compared to how much it can be closed when using jaw- tracking.

DVH Analysis

DVH analysis for each patient showed the biggest difference in dose between jaw tracking and non- jaw tracking occurs in the V2- V5 region as shown in Figure 3. This means the low doses further from the target volume can be better spared by jaw tracking. In this study the patients had small, spherical lesions which created small openings in the MLCs. This study showed there was not a significant difference when using jaw tracking versus non- jaw tracking in VMAT SRS for multiple brain lesions. This study did show that the same findings, although small, can be applied to other situations and likely show a more significant response. Thongsawad et al. indicated that a reduction in integral dose is dependent on the tumor shape; for example a large size difference between the anterior and lateral views in a large, irregular shaped lung tumor could create a bigger difference in jaw positions. [10] With irregular shaped tumors the jaw tracking would be able to close the jaws simultaneously with the MLCs as the gantry rotates around the patient. With large, irregular shaped volumes, the beam's eye view (BEV) of the target volume can be smaller at some gantry angles and larger as it rotates around. Jaw tracking allows the jaws to close when the gantry reaches the smaller BEV of the volume, and in a chest patient the difference between these two treatment techniques should be more pronounced. Another instance that jaw tracking would be beneficial is in the treatment of young patients, or patients who are treated for something curative such as lymphoma. Because jaw tracking has shown to benefit the low dose regions, this could help prevent secondary malignancies such as breast cancer, lung cancer, soft tissue sarcomas, thyroid cancer, and cardiovascular diseases from forming due to radiation treatment. [17]

The main differences in the two techniques were likely due to the MLC leakage created in the periphery through the beam shaping process. The jaw tracking plan is able to continuously

adjust the jaws to the edge of the MLCs whereas the jaws in the non- jaw tracking plan stay fixed at the maximum field size needed to cover the widest point in the target. Yao et al. concluded there was a correlation between field size and dose reduction to OARs when using jaw tracking versus non- jaw tracking. “With small lesions, the field size is small, so the leakage to the OARs is also small. The impact of jaw tracking is more obvious in large tumors because the jaw tracking technique can block more MLC transmission in large field sizes and reduce the dose to out-of-field OARs.” [11] These results agree with the findings of this study.

Limitations and future research

Limitations of this study include having a small sample size as well as it being conducted retrospectively. Due to the small sample size of 10 patients, non-parametric measures had to be utilized for analysis. Another limitation is the volume of the lesions being small and spherical. Due to the small, spherical volumes there were times when certain MLC leaves did not have to move or modulate as much as they did when larger lesions were involved. Also, most OARs were far enough away from the GTV that they did not seem to be affected as much as they would if they had been in closer proximity.

Further research could include analysis of tumor volumes in the treatment of multiple metastatic lesions when treated with VMAT SRS. These volumes could be compared using jaw tracking versus non- jaw tracking to determine if dose to OARs were significantly different between the two techniques when volume is considered. Output for these plans could also be compared to see if they correlate with the findings from the dose statistics and DVH. Further research could compare jaw tracking versus non- jaw tracking when using VMAT to treat other areas in the body which could contain larger, irregular shaped fields that are in closer proximity to OARs.

Conclusion

Similar target coverage, conformality, and gradient can be obtained with both jaw tracking and non- jaw tracking plans. The benefit comes from the jaw tracking plan having the ability to close the jaws continuously to match the shape of the multi- leaf collimator (MLC) as it rotates around the patient. There was some benefit in dose reduction to OARs with jaw tracking over non jaw tracking, but with SRS the smaller tumor volumes in addition to the distance to OARs caused this study to not provide statistically significant results. The OARs saw the most sparing in the low dose region between $V_{2-}V_5$ in the normal tissues further from the target volumes. This could be beneficial in preventing secondary cancers when treating young or curative patients. The jaw tracking technique would likely produce more significant results with larger target volumes that are closer to or even abutting the OARs.

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Appendix

Figure 1. Dose control rings used in optimization

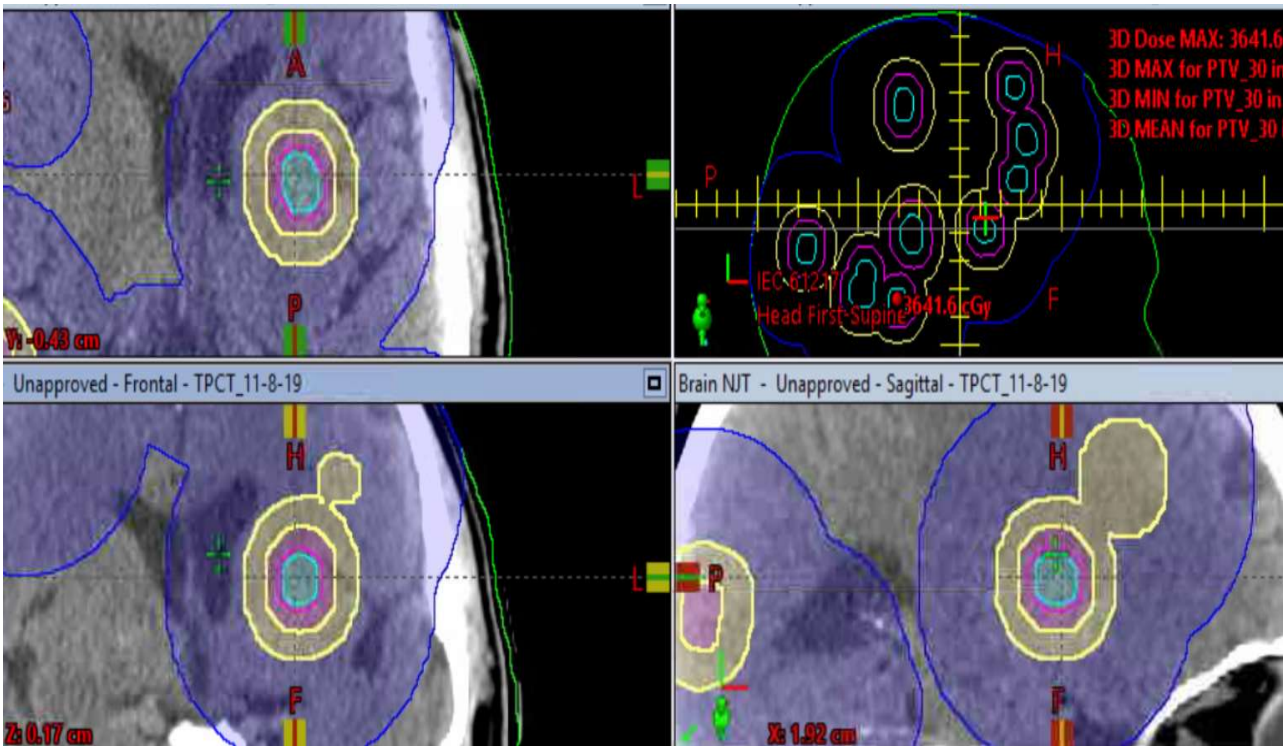


Table 1. Dose Objectives

Structure	Objective Type	Percent of Prescription	Priority
Target	lower objective	102% of Rx	100%
Inner Control	upper objective	98% of Rx	150%
Middle Control	upper objective	50% of Rx	100%
Outer Control	upper objective	40% of Rx	100%
Brain-GtV	* include in cost function		

Table 2. CNS Normal Tissue Constraints

Hypofractionation (4.0- 6.0 Gy per fraction)

Organ	Constraint
Brain	5 fractions: Max dose 20 Gy Mean dose 6 Gy[1]
Brainstem	3 fractions: Max dose 23 Gy, V18 Gy < 1cc 5 fractions: Max dose 31 Gy, V26 Gy < 1cc
Chiasm/ Optic Nerve	3 fractions: Max dose 19.5 Gy, V15 Gy < 0.2 cc 5 fractions: Max dose 25 Gy, V20 Gy < 0.2 cc
Cochlea	3 fractions: Max dose 20 Gy 5 fractions: Max dose 27.5 Gy
Lens	Max dose 3-7 Gy
Retina	Max dose 5-15 Gy
Spinal Cord	3 fractions: Max dose 18-20 Gy 4 fractions: Max dose 26 Gy, V20.8 < 0.35cc 5 fractions: Max dose 30 Gy, V22.5 < 0.25cc

[1]***As more lesions are added this may be hard to achieve.***

Table 3. Mean Dose to Organs at Risk

	Jaw Tracking			Non- Jaw Tracking			Sign Test
	Min	**Max**	**Median**	**Min**	**Max**	**Median**	***p* Value**
Brain-GTV	198 cGy	652 cGy	479.4 cGy	221.8 cGy	711.8 cGy	492.2 cGy	1
Brainstem	79.9 cGy	1118.1 cGy	391.3 cGy	94.2 cGy	1145.9 cGy	398 cGy	0.3438
Optic Chiasm	158.6 cGy	525.1 cGy	251.3 cGy	214.3 cGy	521.5 cGy	262.7 cGy	0.7539
L. Optic Nerve	58.3 cGy	357 cGy	193.1 cGy	50.6 cGy	362.7 cGy	199.6 cGy	1
R. Optic Nerve	42.2 cGy	292.2 cGy	181.9 cGy	42.7 cGy	292.8 cGy	209 cGy	0.1094
R. Lens	16 cGy	150.8 cGy	67.6 cGy	23 cGy	142.2 cGy	82.2 cGy	0.3438
L. Lens	55.7 cGy	129.2 cGy	85.9 cGy	47.2 cGy	142 cGy	82.1 cGy	0.3438
R. Cochlea	59.1 cGy	618.5 cGy	259 cGy	63.7 cGy	723.9 cGy	562.4 cGy	0.3438
L. Cochlea	105.2 cGy	675.7 cGy	258.8 cGy	143.1 cGy	549.2 cGy	249 cGy	1
Spinal Cord	10 cGy	388.3 cGy	128.7 cGy	13 cGy	442.4 cGy	117.3 cGy	0.3438

Table 4. Maximum Dose to Organs at Risk

	Jaw Tracking			Non- Jaw Tracking			Sign Test
	Min	**Max**	**Median**	**Min**	**Max**	**Median**	***p* Value**
Brain-GTV	3040.8 cGy	3695.4 cGy	3442 cGy	3070.8 cGy	3720.8 cGy	3470.9 cGy	0.2891
Brainstem	217.2 cGy	2974.2 cGy	826.4cGy	231.4 cGy	2953.3 cGy	1009 cGy	0.3438
Optic Chiasm	283.5 cGy	647.4 cGy	402.7 cGy	340.4 cGy	757.4 cGy	464.8 cGy	0.0215
L. Optic Nerve	78.8 cGy	534.1 cGy	298.4 cGy	72.8 cGy	540.2 cGy	304.8 cGy	0.7539
R. Optic Nerve	146.9 cGy	529.9 cGy	391.5 cGy	75.9 cGy	513.9 cGy	372.4 cGy	0.3438
R. Lens	18.6 cGy	183.2 cGy	105.3 cGy	28.6 cGy	174.2 cGy	115.6 cGy	0.7539
L. Lens	87.9 cGy	161.3 cGy	118.7 cGy	72.9 cGy	208.2 cGy	97.9 cGy	0.3438
R. Cochlea	80.3 cGy	1073.5 cGy	326.2 cGy	106.4 cGy	1191.9 cGy	338.1 cGy	0.1094
L. Cochlea	113.5 cGy	882.4 cGy	318 cGy	167.6 cGy	827.9 cGy	320.1 cGy	0.7539
Spinal Cord	24.7 cGy	1552.2 cGy	363.7 cGy	36 cGy	1713.2 cGy	329.5 cGy	0.3438

Table 5. Global Body Maximum Dose in cGy

	JT Max Dose	**NJT Max Dose**	**Percent (%) Change**
Patient 1	3837 cGy	3837 cGy	No change
Patient 2	3583 cGy	3644 cGy	1.7% reduction with JT
Patient 3	3696 cGy	3798 cGy	1.1% reduction with JT
Patient 4	3727 cGy	3807 cGy	2.2% reduction with JT
Patient 5	3523 cGy	3600 cGy	2.2% reduction with JT
Patient 6	3568 cGy	3661 cGy	2.5% reduction with JT
Patient 7	3606 cGy	3721 cGy	3.1% reduction with JT
Patient 8	3693 cGy	3707 cGy	0.4% reduction with JT
Patient 9	3616 cGy	3642 cGy	0.8% reduction with JT
Patient 10	3645 cGy	3680 cGy	1.0% reduction with JT

Figure 2. Same patient with identical treatment parameters- Jaw Tracking vs. Non- Jaw Tracking

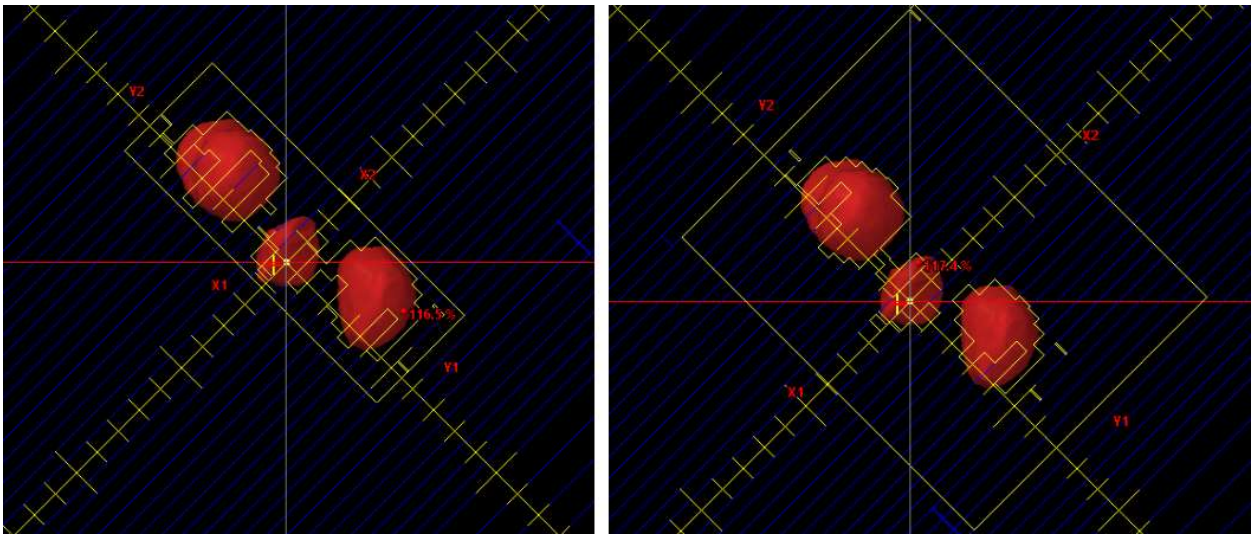
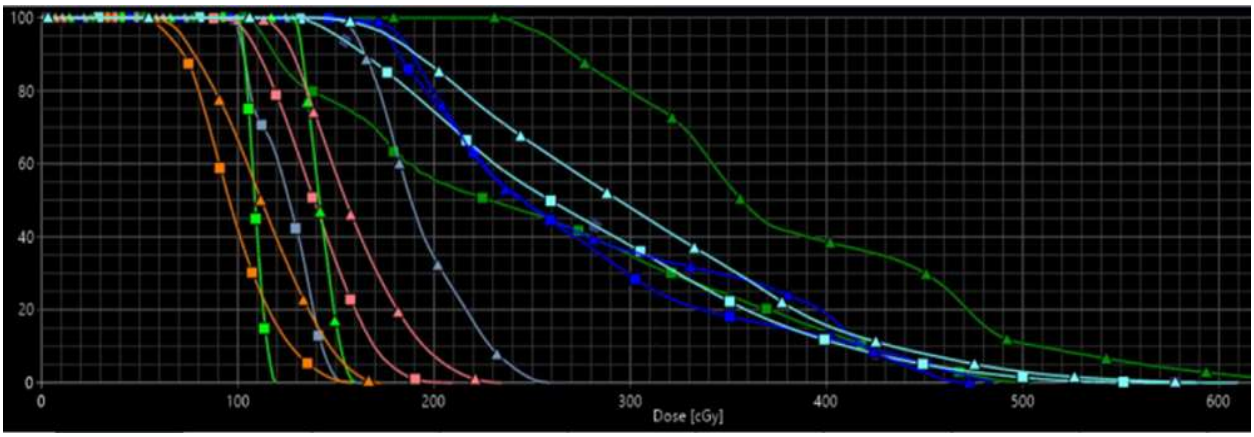


Figure 3. DVH showing the low dose region of the OARs for jaw tracking and non-jaw tracking



Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[...	Min Dose [cGy]	Max Dose [cGy]	Mean Dose [cGy]
☑	Optic Nerve R	Approved	JT	Research	0.9	100.0	100.1	136.9	485.6	270.4
☑	Optic Nerve R	Approved	NJT	Research	0.9	100.0	100.1	145.3	474.5	282.1
☑	Optic Nerve L	Approved	JT	Research	0.8	100.0	100.2	97.2	164.3	124.1
☑	Optic Nerve L	Approved	NJT	Research	0.8	100.0	100.2	146.0	259.8	193.2
☑	Optic Chiasm	Approved	JT	Research	0.6	100.0	99.6	104.1	505.6	252.7
☑	Optic Chiasm	Approved	NJT	Research	0.6	100.0	99.6	232.7	659.3	384.5
☑	Lens R	Approved	JT	Research	0.2	100.0	100.3	100.0	119.4	109.0
☑	Lens R	Approved	NJT	Research	0.2	100.0	100.3	127.9	160.4	142.2
☑	Eye Right	Approved	JT	Research	7.8	100.0	100.1	66.3	209.6	139.7
☑	Eye Right	Approved	NJT	Research	7.8	100.0	100.1	82.6	235.1	158.5
☑	Eye Left	Approved	JT	Research	7.9	100.0	100.1	49.9	158.5	97.8
☑	Eye Left	Approved	NJT	Research	7.9	100.0	100.1	55.0	173.3	112.4
☑	BrainStem	Approved	JT	Research	21.7	100.0	100.1	124.5	589.1	275.4
☑	BrainStem	Approved	NJT	Research	21.7	100.0	100.1	136.4	609.9	304.2