Published in final edited form as:

Vet Radiol Ultrasound. 2010 ; 51(1): 90–96.

DOSIMETRIC IMPACT OF DAILY SETUP VARIATIONS DURING TREATMENT OF CANINE NASAL TUMORS USING INTENSITY-MODULATED RADIATION THERAPY

Michael A. Deveau¹, Alonso N. Gutiérrez², Thomas R. Mackie¹, Wolfgang A. Tomé¹, and Lisa J. Forrest¹

¹University of Wisconsin School of Medicine and Public Health School of Veterinary Medicine Madison, WI, 53792 USA

²Department of Radiation Oncology School of Medicine Cancer Therapy & Research Center at The University of Texas Health Science Center San Antonio San Antonio, TX 78229 USA

Abstract

Intensity-modulated radiation therapy (IMRT) can be employed to yield precise dose distributions that tightly conform to targets and reduce high doses to normal structures by generating steep dose gradients. Because of these sharp gradients, daily setup variations may have an adverse effect on clinical outcome such that an adjacent normal structure may be overdosed and/or the target may be underdosed. This study provides a detailed analysis of the impact of daily setup variations on optimized IMRT canine nasal tumor treatment plans when variations are not accounted for due to the lack of image guidance. Setup histories of ten patients with nasal tumors previously treated using helical tomotherapy were replanned retrospectively to study the impact of daily setup variations on IMRT dose distributions. Daily setup shifts were applied to IMRT plans on a fraction-by-fraction basis. Using mattress immobilization and laser alignment, mean setup error magnitude in any single dimension was at least 2.5mm (0-10.0mm). With inclusions of all three translational coordinates, mean composite offset vector was 5.9 ± 3.3 mm. Due to variations, a loss of equivalent uniform dose (EUD) for target volumes of up to 5.6% was noted which corresponded to a potential loss in TCP of 39.5%. Overdosing of eyes and brain was noted by increases in mean normalized total dose (NTD_{mean}) and highest normalized dose given to 2% of the volume ($NTD_{2\%}$). Findings suggest that successful implementation of canine nasal IMRT requires daily image guidance to ensure accurate delivery of precise IMRT distributions when non-rigid immobilization techniques are utilized. Unrecognized geographical misses may result in tumor recurrence and/or radiation toxicities to the eyes and brain.

Keywords

canine nasal tumors; tomotherapy; intensity-modulated radiation therapy; setup variations

Introduction

The goal of radiation therapy is to deliver a high tumor dose while sparing normal tissues. With its relatively recent introduction into veterinary medicine yet well-established clinical

Address of Correspondence: Dr. Lisa J Forrest University of Wisconsin School of Veterinary Medicine Department of Surgical Sciences 2060 Veterinary Medicine Building 2015 Linden Drive Madison, WI 53706-1102 U.S.A Tel: 608.263.5668 forrestl@svm.vetmed.wisc.edu.

application in human medicine¹⁻⁵, intensity modulated radiation therapy (IMRT) is a useful tool to better address this goal. IMRT is rapidly reaching its maturity in delivering very precise dose distributions in all three dimensions for various anatomic sites; however, its clinical success is limited by its requirement for motion management and reduction of interfractional setup error.^{6,7}

Typically, the planning target volume (PTV) is commonly obtained by adding a predetermined symmetric margin to the clinical target volume (CTV) which is defined by enlarging the diagnostically identifiable gross tumor volume (GTV). Assessment of the PTV margin is dependent on the type of immobilization and localization devices used. The rationale for the PTV margin is to minimize the effects of geometric (systematic errors) and residual (random errors) uncertainties.⁸

IMRT techniques are capable of highly conforming the prescription isodose volume to the PTV as well as introducing steep dose gradients between adjacent normal tissues and target volumes.⁹ The result of such abilities is the reduction of normal tissue irradiation to high doses. Most IMRT systems achieve this conformity by using multiple beam directions and modulated fields but at the expense of introducing delivery inaccuracies.^{7,10} These inaccuracies in conjunction with superior conformity increases the potential risk of a geographic target miss and increases the possibility of normal tissue injury. Very accurate delivery is often more a challenge because of inter- and intra-fractional variations and patient setup.⁷

Unlike other areas of the body, lesions in the head-and-neck are, in general, assumed to be rigidly attached to underlying bony anatomy making the introduction of an error due to target deformation or motion less likely.¹¹ Expansion of the CTV into the PTV in these patients is largely to account for setup uncertainty throughout the course of treatment. In humans, several authors have demonstrated the potential consequence of setup uncertainties using various immobilization and localization techniques in head and neck IMRT.¹²⁻¹⁶ As with human radiation oncology, systematic clinical data analysis regarding daily setup variation, accounting for all six degrees of freedom, is lacking in veterinary medicine. Setup variations have been examined in animals undergoing radiation therapy using multiple immobilization techniques (mattress, bite blocks, thermoplast masks, etc) and forms of localization (predominantly weekly port films),¹⁷⁻¹⁹ but the dosimetric effect of these setup uncertainties in canine head and neck patients treated with IMRT delivery techniques has not been characterized. The purpose of this study was to investigate and characterize the dosimetric impact on normal tissue sparing and target coverage due to the localization accuracy of solely using a laser-based localization technique during the treatment of canine nasal tumor with IMRT.

Materials and Methods

Ten dogs (n=10) with nasal tumors of varying PTV size (63-228 cm³, median 155 cm³), stage (Theon: 4 stage T1, 3 stage T2, 3 stage T3) and location (4 right-sided, 2 left-sided, 4 bilateral) previously treated with a tomotherapy Hi-ART™ unit (TomoTherapy Inc., Madison WI) were re-planned and analyzed retrospectively. Patients for the original study were in sternal recumbency in a Vac-Lok™ mattress (CIVCO, Orange City IA) and scanned by a computed tomography (CT) system (GE Medical, Milwaukee WI) using 3.0 to 5.0 mm slice thickness over the head region. In accordance with the study selection, all tumors were contained within the nasal cavity and/or frontal sinus with no evidence of disease extension through the cribriform plate.

CT image sets were transferred to the treatment planning system (TPS) Pinnacle3® (Philips Medical System, Las Milpitas, CA) where the PTV, brain and eyes were contoured. For each

dog the GTV was defined as gross, identifiable disease on the planning CT. The CTV was defined as the entire nasal cavity and incorporated portions of the frontal sinuses when evidence of disease was present. For each of the ten dogs, the PTV was defined as the CTV to simulate tight margins as are appropriate for high quality patient setup that is accomplished by either using rigid immobilization and/or volumetric image guidance. Acceptable treatment plans were generated using the TomoTherapy TPS (TomoTherapy Inc., Madison, WI), and delivered. Prescription doses were 42.0 Gy to 95% volume of the PTV with dose to the organs at risk (OAR) typically constrained to no more than 50% of the brain and eyes receiving more than 10 Gy. This dose fractionation schedule was chosen so dogs treated in the conformal avoidance study could be compared to historical controls.²⁴ Initial localization for each treatment was performed using a thorough 3-point laser alignment which was referenced to anatomic landmarks and marks on an immobilization mattress. After laser-based localization, a volumetric mega voltage CT (MVCT) was acquired. The planning kVCT and MVCT images were fused within the tomotherapy software and spatial discrepancies between the kVCT and MVCT were applied to the patient as final shifts. Consequently, these final shifts were also residual shifts with regard to the initial set up and inherently define the localization accuracy of the laser-based localization technique used. With knowledge of these residual shifts, the dosimetric impact due to the limited accuracy of laser-based localization techniques can be characterized. In total, 60 individual residual shifts were obtained over the course of treatment (10 treatment days $\times$ 6 degrees of freedom) for each dog.

These ten patients were replanned retrospectively with the Pinnacle³® TPS using a five-field, 6 MV photon, 'step and shoot' IMRT technique. Plans were optimized and normalized to deliver 42.0Gy to 95% of the PTV. Dose to the eyes, brain, and hard palate were minimized during optimization. The previously recorded daily residual shifts from each patient were applied to their corresponding IMRT plans on a fraction-by-fraction basis. Dose distributions accounting for the daily residual shifts for each fraction were summed. The actualized plans were compared against the idealized plans.

To assess the impact of these residual shifts on target volumes and critical structures, the equivalent uniform dose (EUD) was calculated for the target volume using the following model parameters: $SF_2 = 0.48$ & $\alpha/\beta = 10\text{Gy}$.^{20,21} The EUD is defined as the uniform dose which induces the same biological effect as an inhomogeneous dose distribution. The mean normalized total dose (NTD_{mean}) and $NTD_{2\%}$ were calculated for the evaluated normal tissues. NTD_{mean} is the mean dose to a structure when delivered in standard fractionation—i.e. 2Gy fractions.²² $NTD_{2\%}$ represents the highest dose given to the hottest 2% of the volume of tissue evaluated when delivered in standard fractionation. The $NTD_{2\%}$ is a better descriptor of the maximum dose to a volume than just simply the maximum dose value when using IMRT due to the possibility of a single voxel possessing an unrealistic large dose during IMRT optimization. Additionally, to model the possible clinical impact to the tumor volume, tumor control probability (TCP) calculations were performed using the logistic dose-response model ($\gamma_{50} = 2.0$ & $TCD_{50} = 58.2\text{Gy}$) with model parameters derived from clinical data in a previous trial at our institution.²³

Results

The systematic and random errors in the six degrees of motion for each patient using MVCT and the associated displacement vector are listed in Table 1. The mean setup deviation in any single dimension was at least 0.5 mm (range: 0.5-8.3mm) and 0.1° (0.1 - 5.4°) during the entire course of treatment. The mean setup deviations for all patients in the lateral, longitudinal, and vertical directions were 2.9, 3.0, and 2.5mm, respectively. There was no apparent preferential direction for shifting being that the mean setup deviations in any given direction were within the standard deviation of one another. When all three translational coordinates were analyzed,

a mean composite displacement vector of 5.9 ± 3.3 mm (2.8–8.9 mm) was obtained for all patients.

To evaluate if the magnitude of setup deviations changed over the course of treatment, patient setup histories were analyzed for drift. Figure 1 illustrates the absolute mean displacement vector for each patient on a fractional basis. Although individual daily vector displacements for each patient varied throughout the course of treatment, there was no net accumulation of displacement, and the absolute mean displacement vector remained relatively constant over the ten fractions. The group mean displacement vector curve in Figure 1 exemplifies this point.

To characterize the expected impact on treatment, daily setup variations were applied to idealized IMRT plans for each patient on a fraction-by-fraction basis. As an example, Figure 2 illustrates daily isocenter offsets in relation to the ideal isocenter superimposed on a digitally reconstructed radiograph (DRR) for a sample patient over the course of treatment. Figure 3 depicts a clinician-approved ideal IMRT plan and the shifted IMRT plan resulting from the incorporation of the daily positional isocenter offsets in the dose calculation. As seen in Figure 3, the daily positional offsets deteriorate the conformation of the prescription isodose lines and cause a loss of PTV coverage. Moreover, an increase in dose to the right eye is apparent. Figure 4 further illustrates the impact of the setup deviations on the cumulative, normalized dose volume histogram (DVH). From the DVH, a loss in dose coverage of the PTV is seen as a decrease in the minimum dose. As for the right eye, the DVH curve shifts significantly to the right and eliminates much of the sparing abilities of IMRT. Consequently, because of the symmetry of the target and regional anatomy, the overdosing of the right eye leads to a sparing of the left eye. This effect was common in many of the patients in the study.

For all the patients, the EUD was computed for the ideal and actualized IMRT treatment plan. Figure 5 shows the percent deviation of the EUD between the ideal and actualized IMRT treatment plans as well as the impact of the actualized plan on the TCP. From the figure, it is noted that the percentage change of the EUD for all patients is rather small (maximum deviation value equal to 5.6%). Moreover, for some patients—i.e. Patient 2 and 9—a small increase in EUD was noted with the actualized plans. However, being that the doses delivered lie on the steepest portion of the dose response curve, these small changes in EUD between ideal and actualized plans equate to significant differences in TCP—i.e. deviations up to almost a 40% loss in TCP with a 5 percent loss of EUD.

With respect to normal tissue, Table 2 shows the percent changes between the ideal and actualized IMRT treatment plans for the eyes, brain, and hard palate. From the table, a significant increase in the NTD_{mean} was noted for the eyes. As previously mentioned some of the patients exhibited a decrease in dose to one eye but experienced an increase in the contralateral eye. This effect is solely due to the geometry and nature of the target being irradiated. In terms of the $NTD_{2\%}$, percent changes followed the pattern observed with the NTD_{mean} . For the brain and hard palate, a percent decrease was noted for both the NTD_{mean} and $NTD_{2\%}$ likely due to the decrease in prescription dose coverage of the target and consequential sparing of these structures.

Discussion

The study was undertaken to examine the potential impact of residual shifts on the integrity of optimized IMRT canine nasal tumor treatment plans using conventionally applied Vac-Lok mattress immobilization and laser-based localization techniques. These conventional mattress immobilization and laser alignment techniques, also in combination with bite blocks, dental molds, and/or thermoplast masks, provide reproducible and accurate positioning for both human and animal patients.^{10,12,17–19} In canine head and neck cancer patients, the average

positional offset ranged from 0.5mm to 9.5mm depending on the type of immobilization and the use of weekly port film measurements.¹⁷ Our data falls well within these published results, with a 2.5mm absolute average setup error. However, the advantage of daily volumetric imaging is the ability to elucidate the setup error in three-dimensional space.⁷ Based on the analysis of MVCT, our patients mean composite vector setup error during the 2 week treatment course was 5.9 ± 3.3 mm. This corresponds with one-dimensional positional setup errors that could range less than 2mm. Such a small shift may go unnoticed and exemplifies why weekly orthogonal portal films may not be sensitive enough to adequately represent the magnitude of a three-dimensional error. In addition, accounting for such errors could require an expansion of the treatment field in multiple dimensions of at least 10mm—negating the potential benefits of IMRT delivery techniques.

The effects of setup uncertainty on ideal, clinician approved, human head-and-neck IMRT plans has been characterized.¹²⁻¹⁶ In 3 patients, the mean dose to the observed organ at risk varied significantly with each 5mm isocenter shift.¹⁵ This is of critical importance particularly when IMRT is used for conformal avoidance, such as parotid sparing or ocular sparing, as in our study. Even a slight shift will impact the dose to these structure due to the large size of the target volume.

Similarly, with 5mm systematic setup errors along each Cartesian axis, target coverage was sensitive to the quality of the unshifted plan while OAR depended primarily on the dose gradient outside the critical structure.¹⁶ Also, with analyzing daily IMRT setup variation based on an optical guidance system, partial geographical tumor miss and normal tissue overdosing was common.¹² Similar to these human studies, our data recapitulates the negative effects of actual canine patient positional offsets on dose distribution when these misalignments are not corrected.

As previously noted, many IMRT strategies rely on multiple beam directions and modulated fields to highly conform prescription dose to the target while creating steep dose gradients to reduce normal tissue toxicity.^{7,10} While this allows for the creation of precise dose distributions, it also demands the incorporation of volumetric imaging prior to each fraction delivery to ensure accurate setup. Any inaccuracies in localization may induce radiation effects not accounted for in the idealized treatment plan. This is especially the situation with conformal avoidance techniques since IMRT generates excellent conformity in all three spatial dimensions.

To minimize the effect of the dose margin in this study, the PTV margin was defined as a clone of the CTV to simulate the tightest margin theoretically possible. Initially, this may seem unorthodox. However, CTV to PTV margin expansions are applied to treatment plans to incorporate a specified level of tolerance for sensitivity to various geometrical and patient setup errors. Utilizing typical margin formulas tend to over compensate for setup errors because dosimetric margins extend unrecognized past the CTV to PTV margin.²⁷ This is exacerbated when the dose distribution delivered is limited by the number of coplanar beams as the exit dose is less spread out. Because of the vicinity of the brain and eyes to the nasal cavity and the proclivity of these tumors for cribriform plate invasion, tight margins are necessary as doses deliverable to these tumors are strictly governed by normal tissue toxicities. This study illustrated that without daily image guidance, compensatory margins would have to be much larger which may thus partially negate the benefit of IMRT.

The consequences of not accurately delivering precise dose distributions may be severe. Based on a four-bin DVH model, it was concluded that a dose deficit to only 1% volume of the target that is larger than 20% of the prescription dose may lead to a loss of expected TCP, even if a large volume (80%) of the target is boosted (10%) above the prescription dose.²⁶ We

demonstrated that small, yet significant volumes of cold spots are generated from daily positional setup errors throughout a short 2-week course of treatment.

In this study, daily volumetric image guidance was used to identify interfractional shifts. We are cognizant that most veterinary facilities do not have access to integrated volumetric image guidance largely due to the cost of implementation; however, other strategies can be incorporated. Utilization of indexed, rigid immobilization techniques, such as bite blocks that are indexed to the treatment couch or linked to optical guidance systems to aid in the localization process can be used to reduce inter fraction setup errors.²⁸ Optical guidance systems allow one to control for possible intra fraction motion.^{29,30} Migration away from the conventional or standard methodologies of weekly port films to that of daily orthogonal portal imaging for pretreatment patient setup assessment could also allow patient registration in three dimensions. Such techniques are of much more significance if IMRT is used in conjunction with small set up margins, conformal dose distributions, and steep dose gradients. Regardless of the strategy chosen, pretreatment patient positioning constitutes a major element in determining treatment accuracy and aggressive steps should be taken to reduce setup errors.

Findings suggest that successful implementation of canine nasal IMRT requires daily image guidance to ensure accurate delivery of precise IMRT distributions with non-rigid immobilization techniques. Unrecognized geographical miss can result in pronounced underdosing of targets and overdosing of normal structures. Conventional techniques such as mattress immobilization, single user setup, multi-laser alignment, and intermittent 2 dimensional orthogonal port films are not sufficient to ensure the reproducibility and precision of IMRT treatment plans.

Acknowledgments

Authors gratefully acknowledge support of NIH National Cancer Institute Grant 1P01 CA99060. T.R.M. has financial interest in TomoTherapy, Inc., and therefore has a potential conflict of interest.

References

1. Kippenes H, Gavin PR, Parsael H, et al. Spatial accuracy of fractionated imrt delivery studies in canine paraspinal irradiation. *Vet. Radiol Ultrasound* 1993;34:126–133.
2. Vaudaux C, Schneider U, Kaser-Hotz U, et al. Potential for Intensity-modulated radiation therapy to permit dose escalation for canine nasal cancer. *Vet. Radio Ultrasound* 2007;48:475–481.
3. Forrest LJ, Lawrence JA, Miller PE, et al. Ocular sparing using image-guided helical tomotherapy (IGHT) in spontaneous sino-nasal tumors in dogs. *Int J Radiat Oncol Biol Phys* 2006;66(3):S425.
4. Bortfeld T. IMRT: a review and preview. *Phys. Med. Biol* 2006;51:R363–R379. [PubMed: 16790913]
5. Mell LK, Mehrotra AK, Mundt AJ. Intensity-modulated radiation therapy use in the U.S. 2004. *Cancer* 2005;104:1296–303. [PubMed: 16078260]
6. Purdy JA. Dose-volume specification: New challenges with intensity-modulated radiation therapy. *Semin Radiat Oncol* 2002;12:199–209. [PubMed: 12118385]
7. Mackie TR, Kapatoes J, Ruchala K, et al. Image guidance for precise conformal radiotherapy. *Int J Radiat Oncol Biol Phys* 2003;56:89–105. [PubMed: 12694827]
8. ICRU. Prescribing, Recording and Reporting Photon Beam Therapy ICRU Report No 50. ICRU; Bethesda, MD: 1993.
9. Brahme A. Optimization of stationary and moving beam radiation therapy techniques. *Radiother Oncol* 1988;12(2):129–40. [PubMed: 3406458]
10. Welsh JS, Lock M, Harari PM, et al. Clinical implementation of adaptive helical tomotherapy: a unique approach to image-guided intensity modulated radiotherapy. *Tech. Canc. Resea. Treat* 2006;5(5):465–479.
11. Eisbruch A. Intensity-modulated radiotherapy of head-and-neck cancer: encouraging early results. *Int. J. Radiat. Oncol. Biol. Phys* 2002;53:1–3. [PubMed: 12007933]

12. Hong T, Tomé W, Chappell R, et al. The impact of daily setup variations on head-and-neck intensity-modulated radiation therapy. *Int. J. Radiat. Oncol. Biol. Phys* 2005;3:779–88. [PubMed: 15708257]
13. Hunt MA, Kutcher GJ, Burman C, et al. The effect of setup uncertainties on the treatment of nasopharynx cancer. *Int. J. Radiat. Oncol. Biol. Phys* 1993;127:437–47. [PubMed: 8407420]
14. Siebers JV, Keall PJ, Wu Q, et al. Effect of patient setup errors on simultaneously integrated boost head and neck imrt treatment plans. *Int. J. Radiat. Oncol. Biol. Phys* 2005;63(2):422–433. [PubMed: 16168835]
15. Manning MA, Wu Q, Cardinale RM, et al. The effect of setup uncertainty on normal tissue sparing with IMRT for head-and-neck cancer. *Int J. Radiat. Oncol. Biol. Phys* 2001;51:1400–1409. [PubMed: 11728701]
16. Samuelsson A, Mercke C, Johansson KA. Systematic set-up errors in IMRT in the head and neck region: Effect on dose distribution. *Radiother Oncol* 2003;66:303–311. [PubMed: 12742270]
17. Kippenes H, et al. Comparison of the accuracy of positioning devices for radiation therapy of canine and feline head tumors. *Vet. Radiol. Ultrasound* 2000;41(4):1–376.
18. Green EM, Forrest LJ, Adams WM. A vacuum-formable mattress for veterinary radiotherapy positioning: comparison with conventional methods. *Vet. Radiol. Ultrasound* 2003;44(4):476–479. [PubMed: 12939068]
19. Bley CR, Blattmann H, Roos M, et al. Assessment of a radiotherapy patient immobilization device using single plane radiographs and a remote computed tomography scanner. *Vet. Radiol. Ultrasound* 2003;44(4):470–75. [PubMed: 12939067]
20. Niemierko A. Reporting and analyzing dose distributions: a concept of equivalent uniform dose. *Med Phys* 1997;24:103–10. [PubMed: 9029544]
21. Suit H, Skates S, Taghian A, et al. Clinical implications of heterogeneity of tumor response to radiation therapy. *Radiat Oncol* 1992;25:251–260.
22. Lebesque JV, Keus RB. The simultaneous boost technique: the concept of relative normalized total dose. *Radiother Oncol* 1991;22:45–55. [PubMed: 1947212]
23. Gutierrez AN, Deveau MA, Forrest LJ, et al. Radiobiological and treatment planning study of a simultaneously integrated boost for canine nasal tumors using helical tomotherapy. *Vet. Radiol. Ultrasound* 2007;48(6):594–602. [PubMed: 18018736]
24. Adams WM, Miller PE, Vail DM, et al. An accelerated technique for irradiation of malignant canine nasal and paranasal sinus tumors. *Vet. Radiol. Ultrasound* 1998;39(5):475–481. [PubMed: 9771602]
25. Theon AP, Madewell BR, Harb MF, et al. Megavoltage irradiation of neoplasms of the nasal and paranasal cavities in 77 dogs. *J Am Vet Med Assoc* 1993;202:1469–1475. [PubMed: 8496103]
26. Tomé WA, Fowler JF. On cold spots in tumor subvolumes. *Med. Phys* 2002;29:1590–1598. [PubMed: 12148742]
27. Gordon JJ, Siebers JV. Evaluation of dosimetric margins in prostate IMRT treatment plans. *Med Phys* 2008;35(2):569–575. [PubMed: 18383678]
28. Bova FJ, Buatti JM, Friedman WA, et al. The University of Florida Frameless High-Precision Stereotactic Radiotherapy System. *Int J Radiat Oncol Biol Phys* 1997;38:875–882. [PubMed: 9240657]
29. Tomé WA, Meeks SL, et al. A High Precision System for conformal intracranial radiotherapy. *Int. J. Radiat Oncol Biol Phys* 2000;47(4):1137–1143.
30. Tomé WA, Meeks SL, McNutt TR, et al. Optically Guided Intensity Modulated Radiotherapy. *Radiother Oncol* 2001;61(1):33–44. [PubMed: 11578726]

Figure 1.

Absolute vector displacement scatter plot for each patient as a function of delivery fraction evaluated over the entire 10 fractions. Mean vector displacement of group is also illustrated in solid line.

Figure 2.
Daily isocenter offsets throughout the course of treatment superimposed on a digitally reconstructed radiograph (DRR) in relation to the ideal isocenter (center of the crosshairs) for a sample patient.

Figure 3.

Adverse impacts on treatment plan quality when daily setup variations are applied to an idealized IMRT on a fraction-by-fraction basis. Clinician-approved ideal IMRT plan developed to treat a canine nasal tumor patient (left-A) and the ideal IMRT plan with the fractional isocenter offsets depicted (right-B). Note the loss of PTV coverage with the prescription isodose line (42.0Gy) shifted to the right (white arrows) and the increased dose to the right eye (asterisks placed on the 20.0Gy isodose line).

Figure 4. Normalized, cumulative DVH for the idealized IMRT (solid lines) and actualized IMRT (dashed lines) plans. With the actualized plan the prescription dose coverage of the PTV is compromised and an increase in the dose to the right eye is seen.

Figure 5.

Impact of daily setup variations on tumor control probability (TCP) values. Percent change of equivalent uniform dose (EUD) are shown on for each patient.

Table 1
Mean Setup Deviations in each of the 6 Degrees of Freedom for each Patient Using MVCT.

Patient	Lateral [mm]	Longitudinal [mm]	Vertical [mm]	Pitch [°]	Roll [°]	Yaw [°]	Vector [mm]
1	4.5 (2.8)	1.1 (1.1)	2.0 (2.3)	0.0 (0.0)	3.6 (1.7)	0.0 (0.0)	5.7 (2.6)
2	1.0 (1.0)	1.0 (0.7)	3.1 (2.2)	0.0 (0.0)	1.4 (1.1)	0.0 (0.0)	3.7 (2.1)
3	2.3 (1.2)	0.5 (0.8)	0.8 (0.7)	0.0 (0.0)	4.3 (1.8)	0.0 (0.0)	2.8 (1.0)
4	3.7 (3.3)	3.2 (1.5)	2.2 (2.3)	0.0 (0.0)	1.4 (1.4)	0.4 (1.3)	5.8 (3.7)
5	2.9 (2.0)	1.1 (2.6)	4.4 (2.9)	0.6 (1.9)	2.7 (3.9)	0.1 (0.3)	6.0 (3.4)
6	3.6 (3.0)	1.9 (1.4)	1.7 (1.4)	0.0 (0.0)	3.1 (2.9)	0.4 (1.0)	4.9 (2.9)
7	1.4 (1.0)	8.3 (5.0)	2.3 (1.4)	0.0 (0.0)	1.2 (1.2)	0.0 (0.0)	8.9 (5.0)
8	4.4 (3.4)	4.6 (2.5)	3.0 (2.2)	0.4 (1.0)	3.9 (3.9)	1.4 (2.3)	8.2 (1.8)
9	3.6 (3.1)	4.5 (0.7)	2.6 (2.1)	0.0 (0.0)	5.4 (1.8)	0.0 (0.0)	7.0 (2.4)
10	1.9 (1.0)	4.0 (2.3)	3.1 (1.7)	0.0 (0.0)	1.8 (0.6)	0.0 (0.0)	5.8 (2.0)
Group	2.9 (2.6)	3.0 (3.2)	2.5 (2.0)	0.1 (0.7)	2.9 (2.6)	0.2 (1.0)	5.8 (3.3)

Abbreviations: Standard deviation shown in parentheses

Table 2
Percent Changes in NTD_{mean} and NTD_{2%} for Critical Structures between Idealized and Actualized IMRT Plans.

Pt.	NTD _{mean}				NTD _{2%}			
	OS [%]	OD [%]	Brain [%]	Palate [%]	OS [%]	OD [%]	Brain [%]	Palate [%]
1	-15.7	31.0	0.0	-1.0	-30.3	15.1	-3.2	-1.0
2	0.0	16.7	3.8	2.7	0.0	10.8	6.0	-4.1
3	30.1	21.0	-3.8	-0.4	-28.2	14.0	-0.4	-2.1
4	-36.8	25.0	-8.1	-5.3	-39.1	9.4	-4.8	-7.0
5	-3.7	27.0	-4.6	-5.5	-8.0	14.5	-5.4	-7.5
6	24.3	-19.7	-5.8	-1.4	9.3	-30.5	6.0	0.3
7	22.9	33.4	29.7	-11.4	6.8	11.3	1.9	-9.5
8	17.8	-7.7	-4.8	0.7	3.5	-29.6	-8.6	-10.1
9	10.5	10.8	-19.4	-0.4	1.2	-2.1	-0.8	-6.3
10	-2.0	6.7	-1.8	-2.6	-26.0	-8.7	-5.0	-1.1

Abbreviations: OS - left eye ; OD- right eye ; Brain - hard palate ventral to the nasal cavity.