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Validation of an Indexed Radiotherapy Head Positioning Device for Use in Dogs and Cats

Authors:

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Abstract:

Setup variability affects the appropriate delivery of radiation and informs the setup margin required to treat radiation patients. Twenty-four veterinary patients with head and neck cancers were prospectively enrolled in this study to determine the accuracy of an indexed board immobilization device for positioning. Couch position values were defined at the first treatment based on setup films. At subsequent treatments, patients were moved to the previously defined couch location, orthogonal films were acquired, table position was modified, and displacement was recorded. The mean systematic displacement, random displacement, overall displacement, and mean displacement values of the three dimensional (3D) vector were calculated. Three hundred thirty-two pairs of orthogonal setup films were analyzed for displacement in cranial-caudal, lateral, and dorsal-ventral directions. The mean systematic displacement was 0.5 mm, 0.8 mm, and 0.5 mm, respectively. The mean random displacement was 1.0 mm, 1.1 mm, and 0.7 mm, respectively. The overall displacement was 1.1 mm, 1.4 mm, and 0.9 mm, respectively. The mean 3D vector value was 1.6 mm with a standard deviation of 1.2 mm. Ninety-five percent of the vectors were <3.6 mm. These values were compared to data obtained with a previously used immobilization device. A t-test was used to compare the two devices, revealing that the 3D vector, the random displacement in all directions, and the overall displacement in the cranial-caudal and dorsal-ventral directions were significantly smaller than displacements with the previous device. The precision and accuracy of the indexed board device is superior to the historical head and neck device.

Introduction:

In radiation therapy, delivery of the radiation dose strictly to the target volume and avoidance of critical surrounding normal tissues require both accurate and precise patient positioning. Although many positioning systems have been evaluated for humans undergoing head and neck radiation therapy, these devices are not always appropriate for veterinary use due to the variation in skull size and shape of veterinary patients.[1-3] It is critical to assess immobilization devices for use in veterinary patients because uncertainties in patient setup have direct impact on the margins used to define the planning target volume. For three-dimensional (3D) radiation planning, delineation of the target and critical organs is executed on individual transverse images obtained from a computed tomography (CT) scanner equipped with simulation accessories (e.g., a flat table, laser lights for positioning, an immobilization device, and image registration). The gross tumor volume (GTV) includes all grossly visible tumor and suspect tumor-related contrast enhancement, while the clinical tumor volume (CTV) encompasses both the GTV and a margin to account for microscopic extension of disease. The planning target volume (PTV) is the additional margin around the CTV to account for uncertainties of mechanical positioning (e.g., beam geometry, collimator leaf width, and light-radiation field coincidence), imaging and quality of imaging, and patient interfraction and intrafraction movement.[4-6] Although intrafraction movement has a small contribution to veterinary patient positioning for the head and neck, in part due to the patients being under anesthesia, interfraction motion is a large contributor to veterinary patient setup error that needs to be minimized by on-board imaging and patient positioning.

Head and neck tumors are often adjacent to critical normal tissues, and precise and accurate positioning is imperative for normal tissue avoidance and minimizing late complications in those tissues. Moreover, under-treatment of the PTV due to positioning errors may result in local failure and recurrence.[2] Veterinary radiation oncology has experienced a recent increase in the number of facilities able to provide conformal radiation, intensity modulated radiotherapy (IMRT) and stereotactic radiotherapy (SRS).[5] As conformal and IMRT techniques are increasingly used in veterinary patients, thereby creating steep radiation dose gradients in patient tissues, the potential consequences of positioning errors are greatly increased.[7-9] Therefore, the validation of customized patient immobilization devices to provide more accurate and precise positioning of veterinary patients is important.[1] Although parallel-opposed fields with a PTV margin to account for treatment uncertainties are most commonly used for veterinary radiation, conformal 3D radiation involving the use of beam modifiers such as blocks to better shape the beam to the target volume are now frequently used, and treatment plans may have smaller PTV margins for error. Moreover, IMRT plans employing multiple smaller fields and a multi-leaf collimator to conform dose more closely along complex PTV contours should ideally use a PTV margin of only a few millimeters depending on how well a patient can be positioned.[10, 11] Duplicating the setup used for the CT simulation of radiation planning is critical for 3-dimensional radiation planning. Thermoplastic masks, vacuum-locked moldable bags, dental molds for bite blocks, and non-migrating fiducials imbedded in tumors aid in replicating the positioning of the patient and the PTV for subsequent treatments.[12] While fiducial markers help to align the tumor location specifically, external mobilization devices help position the patient body for radiation treatment.[13] Several immobilization systems have previously been described and evaluated for radiotherapy of the head and neck in canines.[14-20] However, not all previous studies have evaluated objective measurements of patient positioning, nor have all studies assessed the systematic and random error associated with those positioning devices. Variability in patient setup is defined in terms of systematic and random components of error, which inform the overall displacement error.[21, 22] Systematic displacement error is a measure of accuracy, while random displacement error is a measure of precision. Sources of systematic error include skin or mask markings, change in fit of masks or bags due to changes in patient contour (weight change, inflammation, and tumor growth or shrinkage) or deflation of the vacuum-locked bag used for positioning. Sources of random error include operator error in setting up the patient in the devices and patient or organ motion (although minimal motion occurs around the head of an anesthetized animal). Systematic displacement error assesses the average position over the treatment course; it is represented by the mean value of the displacement along each coordinate. For a group of patients, systematic displacement error is derived from the standard deviation for the mean displacement values for each patient. Random displacement error is derived from the standard deviation of the difference between the individual daily variation and the systematic displacement.[3, 21] Overall displacement in each direction is found by squaring the systematic displacement and random displacement, then taking the square root of the sum of those squares. The overall displacement can also be estimated by a 3-dimensional (3D) vector calculation.[23] The formulas for each of the above listed quantities have been previously reported.[17]

The purpose of this study was to evaluate the accuracy and precision of a full-body patient immobilization board with a moldable head support cushion and thermoplastic mask, along with a vacuum locked bag, in dogs and cats. This positioning frame is indexed and features Interloc style locks every 14 cm that secure into the notches of the radiation treatment couch. Calculation of the amount of daily interfraction motion that must be accounted for in the PTV margin was also performed. We previously completed a similar study for a non-indexed, head-only positioning board.[17] We hypothesized that the current positioning device would be superior in accuracy and precision when compared to the previously used device. Therefore, the data from the previous head-only device were compared to those for the new positioning device.

Methods:

A prospective study was undertaken with patients of the UC Davis Veterinary Medical Teaching Hospital. This study was Institutional Animal Care and Use Committee and Clinical Trial Review Board approved. Patients were included if they were undergoing radiation therapy for head and neck cancer and received a computer-planned treatment requiring the use of the positioning devices. Patients were excluded if they did not finish at least three treatments. In order to detect a significant difference in error estimates between the current and previous positioning systems, a minimum of 20 patients were required. Calculation of sample size was based on the previously reported mean displacement value and standard deviation of the 3D vector (power of 0.8, type-I error rate of 5%).

Patients were prospectively scheduled for palliative or definitive (4-20 fractions) radiation. All patients had a CT scan performed for treatment planning. Each patient was placed in a vacuum locked bag (SecureVac, Bionix Development Corporation, Toledo, OH) on the indexed board and was fitted with a thermoplastic mask (Klarity standard U-frame, Klarity Medical & Equipment (GZ) Co. Ltd., Lan Yu, China) and a customized polystyrene bead pillow coated in a moisture-cured polyurethane resin (MoldCare pillow, Bionix Development Corporation, Toledo, OH). The thermoplastic mask was modified by cutting out a circular region at the most rostral portion of the thermoplastic to allow the endotracheal tube to pass through the opening for intubation.

Notably, patients were placed in ventral recumbency for mask fitting and treatment, while human patients are conventionally placed in a supine position with this positioning system. The mask was then secured to the carbon fiber body frame (Accufix head and neck device, Qfix, Avondale, PA, USA) with four points of fixation as part of the CT simulation study according to the manufacturer’s instructions (Fig. 1). This body frame was locked onto the diagnostic CT couch, which was fitted with a removal indexing couch top for CT simulation of radiation patients. The CT origin (zero point) was set to the expected isocenter for treatment, and the mask was marked with permanent marker at the crosshairs defined by the lateral and midline longitudinal lasers and cross-table horizontal laser beams of the CT scanner. After the CT scan was completed, Digital Imaging and Communications in Medicine (DICOM) images were imported into the treatment planning system (Eclipse version 8, Varian Medical Systems Inc., Palo Alto, CA). A treatment plan was completed, and two orthogonal view digitally reconstructed radiographs (DRRs) were created with a 4 X 4 cm setup field placed around the treatment isocenter at 0 (dorsal port) and 90 (right port). The images were transferred to the electronic portal imaging software program (Portal Vision Treatment Acquisition Software Version 7.3) for treatment. Patients were induced for all treatment visits with injectable anesthetic agents. They were maintained with isoflurane for those patients with tumors located outside of the cranium, or by a propofol constant rate infusion for the patient with an intracranial lesion. All patients had endotracheal intubation for each treatment.

On the first treatment day, anesthetized patients were placed in the positioning device and were set up by the attending radiation oncologist. The indexed board was affixed to the treatment couch at the appropriate notch, and the mask was locked into place around the patient’s head. The operator then used the room lasers to align to the marks previously made on the mask during the CT scan at origin (i.e., X=0, Y=0, Z=0 if no shifts were needed to reach isocenter). In some cases, the planned isocenter was different from the CT origin. In those cases, the Cartesian coordinate couch shifts (X, Y, and Z) were then performed as defined by the radiation plan to place the isocenter of the treatment plan at the machine isocenter. Two orthogonal digital images were acquired using the electronic portal imaging device and a 6 MV beam (Varian Medical Systems Inc. Portal Vision aS500 Electronic Portal Imaging Device, Varian Medical Systems Inc.). Window and leveling values were adjusted to best visualize the bony landmarks on the images. The images were then compared with the DRR by measuring the distance between the setup field isocenter and a bony structure close to the isocenter. Measurements were made in 2-3 directions on each of the orthogonal images using a digital measuring tool within the software. For example, on anterior-posterior films, 1-2 measurements were performed in the cranial-caudal and lateral directions, while on lateral films measurements were taken in the cranial-caudal and dorsal-ventral directions. Because cranial-caudal was measurable on both images, this directional adjustment was made off of the anterior-posterior film first, and then confirmed on the lateral film. The couch was the adjusted in the cranial-caudal, lateral, and dorsal-ventral directions to match the planned isocenter to the machine isocenter by moving the couch the distances measured on the port films. Once the patient was at the planned isocenter, the mask was then re-marked using permanent marker ink, and these final coordinates were recorded as the baseline couch position for the study.

At each subsequent treatment, the patients were positioned and the table was moved to the Cartesian coordinates established on the first treatment as the baseline couch position. Setup films were then acquired, and the distances were recorded for the required displacement in the cranial–caudal, lateral, and dorsal–ventral direction to match the DRR. For recording, the cranial, right and dorsal values were assigned positive values, and the caudal, left, and ventral displacements were assigned negative values. Table shifts were then made according to the measurements before each patient was treated. Daily patient position displacements were graphed as histograms for each direction. The mean daily displacement for each coordinate and the corresponding standard deviation were calculated for the overall population.

Three separate methods were used for evaluating displacements. For the first method, a 3D vector representing the maximum distance variation between the DRR and each daily setup image was calculated according to the previously described formula:

$$D_{3d} = \sqrt{d^2_{Cr-Ca} + d^2_{Lat} + d^2_{DV}}$$

where dCr–Ca is the measured value in the cranial-caudal direction, dLat is the measured value in the left right direction, and dDV is the measured value in the dorsal–ventral direction.[17] For the second method, the overall displacement was calculated by derivation of the systematic displacement and random displacement. The standard deviation of the mean of the displacements for each patient for each direction was calculated to represent the systematic displacement. To calculate the random portion of displacement in each direction, the mean of the displacement for a patient was subtracted from the daily position displacement, and the standard deviation for the group was calculated. The overall distribution of the displacement is related to the systematic and random components of displacement by the previously described formula.[17] For the third method, a previously described margin recipe based on the systematic and random errors for patient positioning was used.[24] In this recipe, the nomenclature varies from our study, and Σ represents the standard deviation of the systematic error, which is equivalent to our described systematic displacement error. The recipe also describes σ as the standard deviation of the random error, which is equivalent to our described random displacement error. This recipe for margins was used to derive recommended margins for each of the three directions for both the previously used and current positioning devices: recommended margin = 2.5 Σ + 0.7 σ. Data for the previously published head positioning device were derived by the first two methods.[17] Both the previously reported data and currently acquired data were assessed for normality. These data sets were evaluated using a t-test to compare differences in the means for each parameter measured. $P \leq 0.05$ was considered significant.

All graphing and calculations were prepared with commercially available statistics and graphing programs (STATA 10.0, Stata Corporation, College Station, TX. Microsoft Excel 2008 for Mac, Version 12.1, Microsoft Corporation, Redmond, WA) by Hansen and Kent. Data were confirmed to be normal by visually assessing histograms of the data.

Results:

Twenty-two dogs and two cats undergoing fractionated radiation therapy for a head or neck mass met the inclusion criteria for the study. Nine dogs had nasal tumors (one osteosarcoma, two chondrosarcomas, three carcinomas, one lymphoma, one sarcoma, and one suspected sarcoma), eight dogs had oral tumors (two maxillary squamous cell carcinomas, one maxillary sarcoma, three mandibular sarcomas, one mandibular osteosarcoma, one mandibular oral melanoma), and one dog each had the following tumor types: glioma, frontal bone osteosarcoma, carotid body chemodectoma, multiple fibromas, and mast cell tumor. One cat had nasal lymphoma and one cat had aural adenocarcinoma.

Three hundred thirty-two pairs of orthogonal portal films were acquired and analyzed. When analyzing all the images from all patients, the mean displacement in the cranial–caudal, lateral, and dorsal–ventral direction was -0.07 mm (standard deviation—1.2 mm, range -4 to 5 mm),

-0.03 mm (standard deviation—1.4 mm; range -4 to 7 mm) and -0.05 mm (standard deviation—1.0 mm; range -4 to 3 mm), respectively. The mean displacement value of the 3D vector for all patients was 1.6 mm (standard deviation —1.2 mm) with 95% of all vectors being ≤ 3.6 mm (Fig. 2).

The mean systematic displacement in the cranial–caudal, lateral, and dorsal–ventral direction was 0.5 mm, 0.8 mm, and 0.5 mm, respectively (Table 1). The mean random displacement was 1.0 mm, 1.1 mm, and 0.7 mm, respectively. The overall displacement was 1.1 mm, 1.4 mm, and 0.9 mm, respectively (Table 1).

These values were compared to historical values for a previous head-only immobilization board. A two-way analysis of variance comparing to the historical study revealed that the 3D vector ($p = 0.002$), the random displacement in the cranial-caudal ($p < 0.0001$), dorsal-ventral ($p < 0.0001$) and lateral ($p = 0.03$), and the overall displacement in the cranial-caudal ($p = 0.0002$) and dorsal-ventral directions ($p = 0.05$) were significantly smaller than displacements with the previous device (Fig. 3 a-c). The range of mean 3D vector lengths for the previous immobilization board was 1.32 – 4.60 mm, and the range of the mean 3D vector lengths for the current positioning device was 0.59 – 2.56 mm.

The following recommended error margins were calculated for the full-body board using the margin recipe: 2 mm in the cranial-caudal direction, 1.7 mm in the dorsal-ventral direction, and 2.8 mm in the lateral directions. The following recommended error margins were calculated for the head-only board: 3.3 mm in the cranial-caudal direction, 3.1 mm in the dorsal-ventral direction, and 3.6 mm in the lateral directions.

Discussion:

In order to deliver the prescribed radiation dose, it is critical to quantify daily positioning variation and minimize patient movement. In this study, we found that our current immobilization device had significantly smaller random displacement values in all directions, significantly smaller overall displacement values in the cranial-caudal and dorsal-ventral directions, and a significantly smaller 3D vector value when compared to the previous head-only immobilization board. Recommended error margins were also calculated for use with the current immobilization device. Compared to the previously assessed head-only positioning device, the system described in this study uses the same disposable cushion and mask while having the added benefit of indexing and locking into the patient couch.

It is critical to calculate systematic and random displacement error values for radiation positioning because mean displacement values over a course of radiation tend to cancel out daily error in opposing directions. Mean 3D displacement vectors give an even better understanding of the potential for setup error because they better define the potential magnitude of setup error.

There appears to be little systematic displacement error difference between the previously used and current immobilization systems. This minimal change in systematic displacement makes sense because the sources of systematic error are unlikely to be changed by the current positioning system. It is also logical that the random displacement is different between the two positioning systems, because sources of random error, such as operator error in setting up the patient, are likely reduced by the indexed device that locks into the treatment couch.

There does not appear to be a directional bias in our data. Should systematic displacements be found toward a particular direction (e.g., left or right) one may be able to deduce that there is a consistent issue with the positioning device placement compared to the CT simulation. Issues with how the patient sits in the device, changes in patient contour, how the device locks into the couch, or how the therapist sets up the patient may be found as causes of directional displacements.

The improved positioning with this indexed device when compared to the previous device may be derived from several sources. The use of a vacuum-locked bag that not only molds to the patient, but also to the pelvic portion of the board, helps to keep the patients entire body in a more predictable position. The body position tends to affect the neck position, which has many degrees of freedom around the cervical spine; there may be less variability in the angle of the head and neck as it sits in the currently tested mask, although yaw was not directly measured in this study. Perhaps the most critical improvement is that the board is indexed and therefore locks onto the couch. This indexing keeps the board centered and aligned with the couch, minimizes lateral displacement, and prevents yaw of the entire positioning system.

Based on the calculated 3D vector displacement, the PTV margin can be reduced to < 4 mm with this immobilization system to guarantee coverage of 95% of the tumor volume. Alternatively, the margin recipe demonstrates that a 3 mm PTV can be applied in the lateral directions, while a 2 mm PTV is sufficient in the cranial-caudal and dorsal-ventral directions for the currently tested positioning device. The PTV may be further reduced by the use of daily imaging prior to treatment, and daily imaging is recommend for all patients with small PTVs (i.e., patients with IMRT plans, SRS plans, and complex 3D conformal plans). The use of on-board cone-beam imaging, in particular, helps minimize patient positioning uncertainty. Thus, this study confirms the importance of on-board imaging for head and neck radiation patients.[16, 17, 20, 25, 26] Errors in patient position due to therapist or radiation oncologist errors in positioning, poor fit of the radiation mask or other devices, or due to changes in tumor contours during the course of treatment contribute to the need for on-board imaging of patients to maximize accuracy and precision of radiation delivery in addition to the use of positioning devices. Image guidance with on-board CT imaging may also allow the user to adapt treatment plans to the changes in tumor contour or normal tissue contour that may occur during the treatment period, which may further reduce normal tissue dose while maximizing tumor dose coverage.[27] Additionally, on-board CT images can be used to compare delivered dose to planned dose for adaptive radiotherapy.[28]

With portal radiography, there is very little ability to detect positioning errors in pitch or yaw, and no ability to effectively detect roll; therefore, these rotational errors may be present and unaccounted for in this study.[9] The indexing on the positioning board may limit yaw and pitch of the entire immobilization system compared to non-indexed devices; however, there is still the possibility for rotational errors within the cushion and mask. As discussed in previous literature, drift of the portal radiograph plate and gantry rotation are minimized by quality assurance but do exist; therefore, despite the resolution of digital portal radiographs being submillimeter, the imaging system may still contribute to some error.[17, 29, 30] Our EPID center position and crosshair was checked at least quarterly during the year. Light field – radiation field coincidence was assessed annually.

Beyond the limitations of portal radiography, there are other limitations of this study. Due to the schedule of patient treatments and consultations, three observers were involved in taking the measurements. Therefore, there could be inter-observer biases or inconsistencies, although all observers were trained in the same manner. Moreover, our historical population was comprised of a similar population of patients, but an identical set of patients using both devices would be more ideal. However, it is difficult to justify placing client-owned patients under anesthesia for the extra time required to assess both sets of equipment at each treatment visit, so the use of a comparable population with data already collected was used as a compromise. The users had experience with the portal imaging and DRRs prior to the first study; therefore, it is less likely that the improved set up error was only due to user experience with the imaging software. In our practice, we generally add a 3 mm margin as a PTV when using this immobilization system with daily portal radiographs for head patients (when reliably positioned bony landmarks are available). However, for neck treatments, a 5 mm PTV is often employed due to more variability in daily position of tissues within the neck (e.g., lymph node location), whereas the tissues of the skull are generally restricted to bony confines and have less movement.[10] Recently, standard of care at our institution has included the use of a mouth block with dental molding along with the indexed positioning system to improve reproducibility of the jaw angle.[14] Further analysis of dental mold blocks for use with commercially available masks should be performed to assess for improvement in precision and accuracy.

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Table 1: Summary of Displacements with the Full-Body, Indexed Board Vs. the Previous, Head-Only Board.

<table>
<tr><th></th><th colspan="2">Cranial-Caudal</th><th colspan="2">Dorsal-Ventral</th><th colspan="2">Lateral</th></tr>
<tr><th></th><th>Full-body</th><th>Head-only</th><th>Full-body</th><th>Head-only</th><th>Full-body</th><th>Head-only</th></tr>
<tr><td>Mean SD[*]</td><td>0.5 mm</td><td>0.8 mm</td><td>0.5 mm</td><td>0.9 mm</td><td>0.8 mm</td><td>1.0 mm</td></tr>
<tr><td>RD[†]</td><td>1.0 mm[§]</td><td>1.9 mm</td><td>0.7 mm[||]</td><td>1.2 mm</td><td>1.1 mm[¶]</td><td>1.5 mm</td></tr>
<tr><td>OD[‡]</td><td>1.1 mm[#]</td><td>2.1 mm</td><td>0.9 mm[**]</td><td>1.5 mm</td><td>1.4 mm</td><td>1.8 mm</td></tr>
</table>

[*] Systematic displacement
[†] Random displacement
[‡] Overall displacement
[§] p=0.0001
[||] p<0.0001
[¶] p=0.03
[#] p=0.0002
[**] p=0.05

Table 2: Mean 3D Vector Values for the Full-Body, Indexed Board and the Previous, Head-Only Board.

3D Vector	
Full-body	Head-only
1.59 mm (standard deviation 1.2 mm)*	2.4 mm (standard deviation 2.1 mm)
95% of 3D vectors < 3.6 mm	95% of 3D vectors < 6.3 mm

* p=0.002

Figures Legends:

Figure 1: Indexed positioning frame with pillow and thermoplastic mask used for head and neck radiation patients.

Figure 2: Mean 3D vectors comparing a full-body indexed positioning board to a previously published head-only positioning board. Histograms demonstrate that the mean 3D vectors for the different positioning boards were smaller with the full-body positioning board and had smaller standard deviations.

Figure 3: Overall displacements comparing a full-body indexed positioning board to a previously published head-only positioning board. The overall displacements were smaller for the full-body positioning board when compared to the previous head-only positioning board. Histograms for the different positioning boards in the A) cranial-caudal directions, B) dorsal-ventral directions, and C) lateral directions are shown.