Assessment of Interfraction Setup Error of Non-Extended Standard Thermoplastic Mask for Head- and- Neck Intensity-Modulated Radiation Therapy Patients

Lalida Tuntipumiamorn, M.Sc., Piyanan Liammookda, M.Sc., Sutee Dechawongsuwan, M.Sc., Satjah Chaikreng, B.Sc., Porntip lampongpaiboon, M.Sc., Chumpot Kakanaporn, M.Sc.

Department Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: Setup accuracy of our head and neck intensity-modulated radiation therapy (IMRT) patients based on the non-extended standard thermoplastic masks was examined using a Varian onboard imaging system.

Methods: Retrospective analysis of thirty head and neck IMRT patients treated during April 2009-July 2010 was performed. All two-dimensional kilovoltage (2DkV) and cone-beam computed tomography (CBCT) images were acquired weekly during the same session and reviewed by oncologists using an offline review 8.6 program on an Eclipse treatment planning system. Couch shifts predicted by software between 2DkV and CBCT images were recorded. The planning target volume (PTV) margin using VanHerk's margin formula was calculated.

Results: Four-hundred and forty-four images of 2DkV and CBCT alignment were analyzed. Positioning errors within \pm 3 mm. were shown in 84.07% of 2DkV radiographs and 85.84% of CBCT images. Average displacement found in anteroposterior (AP), cranio-cuadal (CC) and left-right (LR) axes , were 0.3 ± 2.0 mm , 0 ± 1.7 mm, 0.5 ± 1.5 mm for the 2DkV, and 0.3 ± 2.3 , 0.7 ± 2.1 , 0.4 ± 2.1 mm for the CBCT data set, respectively. Systematic and random variations from both methods which were seen in the range of 0.5-1.8 mm. PTV margins determined from 2DkV pair images, in AP ,CC and LR directions were presented at 4.60, 3.80 and 2.41 mm. when compared to 5.4, 4.32 and 4.35 mm from CBCT, respectively. Adaptive treatment planning on six patients were undertaken as well owing to the great benefit of CBCT to detect the patient's contour changes ,which can be seen in the range of 1.20-3.12 cm.

Conclusion: Based on our immobilization masks and laser-based positioning, the majority of treatment setups were accurate within our acceptable criteria. Both 2DkV and CBCT were shown to be effective methods to reduce the residual setup error. The results from this study will be used as a baseline for further improving the setup accuracy for head and neck IMRT patients at our institution.

Keywords: Setup error, thermoplastic mask, image guided, head and neck, IMRT

Siriraj Med J 2013;65:31-35

E-journal: http://www.sirirajmedj.com

INTRODUCTION

mproving tumor control and keeping a decreased dose to the surrounding healthy tissues is almost a dogma in external beam radiotherapy. With a predominant characteristic in tailoring the treatment dose to match the shape of the targets and so reduce the dose to

avoid normal tissue e structures, intensity modulated radiation therapy (IMRT) has shown highly clinically relevant benefit for head and neck cancer. However, because of a complex anatomy in which many radiation-sensitive organs are in close proximity to the target, as well as treatment plans which must be accurately delivered throughout a six-to-seven week treatment course, it is challenging to keep the daily setup precision and positioning reproducibility for the patients receiving head and neck IMRT.¹

To reposition patients accurately between daily treatment fractions, several parameters including patient- setup procedure, laser alignment accuracy, mechanical stability of the linear accelerator table and gantry, as well as type of

Correspondence to: Lalida Tuntipumiamorn E-mail: Itunti@yahoo.com Received 20 February 2012 Revised 11 May 2012 Accepted 18 May 2012 immobilization device are important. Typically, in brain and head and neck tumors, thermoplastic masks fixed to a carbon fiber base plate have been used for many years to reduce setup uncertainties during treatment delivery.²⁻⁵ Head-to-face masks are used to fix patient's face from the hair line to below the chin. Later, head-to-shoulder masks, are extended to thoroughly immobilize lower head and neck regions. Peer-reviewed data of the facial mask system, showed a range of average positional error which varies from 1 to about 5 mm., and standard deviation as high as 5-8 mm.¹⁻⁹ Setup verifications were also reported on various methods of the alignment correction protocol.¹¹⁻¹⁵

Lately, image-guided radiation therapy (IGRT) has been successfully implemented to maximize treatment accuracy. Movement of the patient during treatment, intrafractional organ motion and anatomical deformation are the main factors for geometric uncertainty. Using the in-room kilovoltage computed tomography technology, high contrast of the two-dimensional kilovoltage (2DkV) and three-dimensional kilovoltage cone-beam computed tomography (3DkV-CBCT) images are provided on the treatment day. When matching these verification images to the reference images of patient or target position on the treatment plan, the positioning deviations can be assessed accurately and consequently corrected for each individual patient.

It is crucial for each institution to analyze their own radiation treatment quality employing IMRT and IGRT. At our center, head and neck IMRT patients were routinely fitted with facial masks. This mask fastened the patient's head to face and was extended to the lower neck region without fixation for the shoulders. This type of mask may introduce inadequate rigidity for maximal immobilization. Currently, the head-to-shoulder masks have been implemented, but due to their being doubly more expensive than the conventional ones, they have been applied only to the patients who had no financial or reimbursement issue. Thus, we would like to retrospectively analyze the setup efficacy obtained from using the standard headto-face masking and three points laser alignment as the routine daily setup for our head and neck IMRT patients. We also reviewed and compared the verification images from two different IGRT methods, 2DkV radiographs and 3DkV-CBCT. Results of the setup accuracy on the standard, non-extended thermoplastic masks has been reported and discussed.

MATERIALS AND METHODS

The study population consisted of consecutive thirty head and neck cancer patients receiving IMRT treatment during April 2009 - July 2010. All patients on appropriate neck rests, were aligned and fixed in their treatment position using 2.4 mm thickness, Uni-frame® (35.6 cm) standard perforated thermoplastic masks (CIVCO Medical Solutions, Kalona, IA, USA) as shown in Fig 1. All 3 mm. slice thickness images from Philips Brilliance Bigbore-16 CT simulator (Philips Electronics, Netherland) were imported into the Eclipse 8.6 treatment planning system (Varian Medical Systems Inc., Palo Alto, CA, USA) and

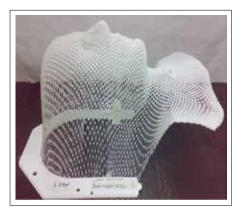


Fig 1. The Uni-frame[®] (35.6 cm) head-to-facial mask used for head and neck IMRT patients in this study.

seven-field sliding window IMRT treatment plans were generated for each patient. Plan delivery was performed by marking three reference points of plan isocenter on the patient's masks using a laser alignment system on Acuity ix simulator (Varian Medical Systems Inc., Palo Alto, CA, USA). Easily seen bony structures, such as mandible, c-spine, orbit and base of skull were outlined by the radiation oncologists on the digitally reconstructed radiographs or simulation images. These bony landmarks would be used as regions of interest for setup verification. (Fig 2)

At the treatment room, IGRT with 2DkV radiographic and 3DkV-CBCT mode, were acquired with a 23 EX linear accelerator (Varian Medical Systems Inc., Palo Alto, CA, USA) equipped with onboard-imaging system. At every pre-treatment, patients were repositioned using the same thermoplastic masks and aligned with treatment room lasers. Based on our routine practice, a pair of 2DkV orthogonal images were firstly acquired and then compared to the reference images using bony structure alignment as the criteria of matching. Setup deviation in three directions (x,y,z) was then assessed from the offline review 8.6 program (Varian Medical Systems Inc., Palo Alto, CA, USA) and consequently corrected for the patient. Each patient was repeated with head and neck CBCT volumetric imaging protocol (120 kVp, 20 mA

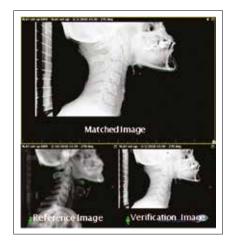


Fig 2. The system software matched the 2DkV verification images with the pre-computed digitally reconstructed radiographs from planning CT or simulation images using bony structure alignment as the criteria of matching.

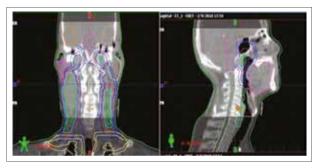


Fig 3. Coronal and sagittal 3DkV-CBCT images were superimposed upon the planning CT images using soft tissue auto-fusion software from the offline review 8.6 program. Couch shifts in three directions were obtained after the contour overlays were visually inspected and manually adjusted by the radiation therapists.

and 25 millisecond, full- fan mode with bowtie filter, 3 mm. slice thickness). The acquired 3DkV-CBCT images on the treatment day were registered with the planning CT images using the soft tissue auto-fusion software. To reduce the residual setup errors, the outlined contour were manually adjusted by radiation therapists until they were matched with the target position. (Fig 3) According to our setup protocol, no couch shifts were performed if the setup errors in three directions were within ± 3 mm. To assess our setup quality, weekly treatment verifications, both of on online 2DkV and offline 3DkV-CBCT images on thirty head and neck IMRT patients, were retrospectively reviewed. Couch shifts presented in three axes, antero-posterior (AP), cranio-cuadal (CC) and leftright (LR) directions, on each image guidance session were collected and quantified for the mean and standard deviation error. Systematic (Σ) and random setup variations (σ) for this study population were calculated. ^{13,22} An appropriate margin for the planning target volume for our head and neck IMRT patients, fitted with the non-extended thermoplastic masks, was defined using Van Herk's margin formula $(2.5* \Sigma + 0.7\sigma)^{20,24}$ Finally, we examined verification efficacy between using 2DkV radiographs and 3DkV-CBCT alignment methods. All CBCT images on each patient were shifted to the precorrected positions and reregistered to the planning CT. Verification procedure on CBCT was repeated and the analyzed results were compared to the 2DkV method. Due to their better representation of 3D anatomy than 2DkV image pairs, couch shifts in 3DkV-CBCT imaging were regarded as reference shifts in this study.

Our study was certified by the Siriraj Institutional Review Board to be in full Compliance with International Guidelines for Human Research Protection (COA Number Si.497/2011).

RESULTS

The total number of 444 scans (composed of 226 pre-correction scans with 2DkV, and 218 post-correction scans with 3DkV-CBCT) with an average of 7.5 images/patient, were analyzed in the context of this study. Fig 4 has shown 87.8% of the patients were verified using both 2DkV and 3DkV-CBCT image guidance technique. Fig 5

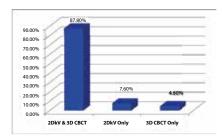


Fig 4. Image guidance technique used on thirty head and neck IMRT patients.



Fig 5. Scatter plot of all observed isocenter displacements seen in any direction from 2DkV and 3DkV-CBCT verification.

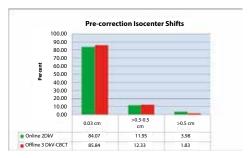


Fig 6. Pre-correction position errors obtained from online 2DkV & offline 3DkV-CBCT images,

has presented scatter plots of the isocenter displacements seen in any direction. Both IG methods in Fig 6, have shown about eighty-five percent of all treatment sessions contained pre-correction position errors within \pm 3 mm. Both 2DkV and 3DkV-CBCT showed similar capability to detect setup errors. Only the setup deviation, which was greater than \pm 5 mm was observed in about 4% of the reviewed data from 2DkV radiographs, compared to 1.8% from the 3DkV-CBCT verification method.

Table 1 has summarized the measured mean and standard deviation of setup uncertainty in any single dimension. Total 3D vector error was presented at 0.58±3.06 mm, on online 2DkV and 0.85±3.72 mm, on offline 3DkV-CBCT image guidance, respectively. Mean and standard deviation of isocenter shifts on the AP and LR direction were similar on both imaging techniques. An exception was in the CC direction, in which mean \pm SD of setup error examined from 3DkV-CBCT verification was found to be 0.68 ± 2.06 mm., when compared to -0.02 ± 1.69 mm. from 2DkV orthogonal radiographs. Appropriate margins calculated from Van Herk's margin formula using the systematic and random variations in this population study have been tabulated in Table 2. Our present data was also compared with the previous published literature as shown in Table 3.

TABLE 1. Mean \pm SD (mm.) of displacement errors (D) from thirty head and neck IMRT patients.

Direction	Online 2DkV	Offline 3DkV-CBCT
AP	0.30 ± 2.04	0.31 ± 2.32
LR	0.50 ± 1.53	0.41 ± 2.06
CC	-0.02±1.69	0.68 ± 2.06
Total vector errors*	0.58 ± 3.06	0.85 ± 3.72

^{*}Total vector errors = $\sqrt{D^2AP + D^2LR + D^2CC}$

TABLE 2. Systematic setup uncertainty (Σ) , random uncertainty (σ) and calculated appropriate margin (in mm.) in any single direction using Van Herk's margin formula.

Direction	Online 2DkV			Offline 3DkV-CBCT		
	$oldsymbol{\Sigma}$	σ	Margin	$oldsymbol{\Sigma}$	σ	Margin
AP	1.4	1.5	4.6	1.7	1.7	5.4
LR	0.5	1.6	2.4	1.2	1.8	4.4
CC	1.1	1.4	3.8	1.2	1.8	4.3

DISCUSSION

This study was undertaken to examine daily setup variation in the IMRT treatment of head and neck cancer patients using conventional applied masks immobilization and laser alignment technique. With weekly IGRT, the interfractional setup-errors of this population (n=30) showed the systematic error in the range of 0.5-1.7 mm and 1.3-1.8 mm for the random errors. This finding, when compared to the previous studies in Table 3, was found to be acceptable. We also noticed that the systematic uncertainty which carry a greater dosimetric impact was

likely to be less than or equal to the random setup error and 98% of all observations contained setup deviation within 5 mm in this investigation.²³

Verification based on 3D- CBCT was found more sensitive in detecting setup errors than 2DkV images. Setup uncertainty in the CC direction from 3DkV-CBCT as shown in Table 1 presented itself as higher than 2DkV alignment. The study of Li H et al., 25 also reported a stronger correlation between 2D and 3D registration technique on AP and LR direction than CC direction. They pointed out that this might be because planning CT has lower resolution in the CC direction and therefore a higher uncertainty. Thus, the discrepancy is most likely from using the different registration techniques between the two alignment techniques. In twenty-one patients, the systematic and random errors were < 1.6 mm for both 2DkV and kV-CBCT, as well as the couch shifts were >3 mm, 18.7% for all CBCT whereas for 2DkV 11.2%, were reported. This study showed, couch shifts within 3 and 5 mm, which were comparable to both 2DkV and 3D-CBCT techniques. However, reviewing all the CBCT verification images suggested the advantage of detecting the patient's contour changes, which in this study was found on six patients in the range of 1.20-3.12 cm. All patients received adaptive radiation therapy, and benefited from volumetric CBCT images.

Several investigations reported the smaller SDs on the head-to-shoulder masks than the non-extended ones. ^{10,26,30} Hong TS et al., ³¹ also concluded that the rigorous immobilization device such as head, neck and shoulder immobilization shell may be a prerequisite for highly conformal radiation therapy such as IMRT

TABLE 3. Systematic setup uncertainty (Σ) , random uncertainty (σ) and displacement errors of various series compared to the present study.

~ •				D1 1
Series	$oldsymbol{\Sigma}$	σ	Type of Mask	Displacement Errors
Gilbeau, 2001 (10)	2.3-3.1	0.7-0.9	head-to-face	4.5-5.5 mm. for 90%
	1.7-2.4	0.9-1.0	head-to- shoulder	probability of target coverage
			(4-points masks)	
De Boer, 2001 (30)	1.5-2.0	1.5-2.0	head-to-face	Probability values not specified
Humphreys, 2005 (26)	0.02-0.9	0.4-0.7	head-to- shoulder	3 mm. for 95% of the errors
				5 mm, for 99% of errors
Hong, 2005 (31)	2.7-4	2.3-2.8	head-to-face	Setup errors cause underdosing 1%
				of tumor subvolume by 20%
				can lead to a loss of 11% in expected
				TCP
Zhang, 2006 (27)	1.5-3.2	1.1-2.9	head-to- shoulder	5.5 mm, for 90%
				probability of target coverage
Zusuki, 2006 (28)	0.7-1.3	0.7-1.6	head-to- shoulder	5 mm. margin for PTV
				and 3 mm. for PRV.
				Probability values not specified
Rotondo RL, 2008 (15)	$2.6-3.0^{a}$	0.9-1.0	head-to-face	PTV margin for upper head &
	5.7-10.2 ^b	2.4-7.2		neck target <4 mm.
	2.9-3.6 ^a	1.2-2.1	head-to- shoulder	Probability values not specified
	5.1-10.0 ^b	2.1-6.1		•
Present study	1.2-1.7°	1.7-1.8	head-to-face	3 mm, for 85% of the errors
•				5 mm, for 98% of errors
Present study			head-to-face	

TCP: tumor control probability, PTV: planning target volume, PRV: planning organ at risk volume

^a Data from upper neck region, ^b Data from lower neck, ^c Data from 3DkV-CBCT method

or three dimensional conformal technique for head and neck tumors. However, it should be kept in mind that the important factors for reproducibility of patient positioning also came from the quality of infrastructure as well as the experience and efforts of treatment staff. There was no significant difference of setup accuracy between the conventional and head- to-shoulder masks. ¹⁵ The study concluded that the non-extended masks were found equivalent to the head-to-shoulder masks in terms of setup accuracy, comfort level and setup time.

According to the positioning error, the setup margin of the clinical target volume (CTV) to defined planning target volume (PTV), was universally accepted as the benchmark of radiation therapy. Several recommendations included the International Commission on Radiation Units and Measurements (ICRU) Report 62²¹, Stroom's^{22,23} and van Herk's^{20,24} indicated that the PTV margin should be calculated based on the data of the population systematic and random errors. Using this concept, the appropriate PTV margin in this population study was found to be about 5 mm. which was consistent with our current head and neck IMRT practice guideline, except for the direction adjacent to the brain stem.

In conclusion, prior to adopting any published margin formula, factors that can potentially impact upon margins should be taken into consideration to ensure adequacy of target volume coverage. Our study presented here was a report of the set-up accuracy obtained from using the conventional, head-to-face masks for head and neck patients receiving IMRT radiotherapy. The results compared well with published set-up error data with ninety eight percent of translational displacements being within 5 mm. Optimal setup margins were detected at about 5 mm in all three directions with this type of mask. The online correction procedure from the IGRT system has enabled an additional reduction of both systematic and random deviation for application of this mask to the patients.

REFERENCES

- Manning MA, Wu Q, Cardinale RM, Mohan R, Lauve AD, Kavanagh BD, 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 Dec 1;51(5): 1400-9
- Niewald M, Lehmann W, Uhlmann U, Schnabel K, Leetz HK. Plastic material used to optimize radiotherapy of head and neck tumors and the mammary carcinoma. Radiother Oncol. 1988 Jan;11(1):55-63.
- Bentel GC, Marks LB, Sherouse GW, Spencer DP. A customized head and neck support. Int J Radiat Oncol Biol Phys. 1995 Apr 30;32(1):245-8.
- Weltens C, Kesteloot K, Vandevelde G, van den Bogaert W. Comparison of plastic and Orfit masks for patient head fixation during radiotherapy: Precision and costs. Int J Radiat Oncol Biol Phys. 1995 Sep 30;33(2):499-507.
- Bentel GC, Marks LB, Hendren K, Brizel DM. Comparison of two head and neck immobilization systems. Int J Radiat Oncol Biol Phys. 1997 Jul 1:38(4):867-73.
- Hunt M, Kutcher GJ, Burman C, Fass D, Harrison L, Leibel S, et al. The effect of uncertainties on the treatment of nasopharynx cancer. Int J Radiat Oncol Biol Phys. 1993 Sep 30;27(2):437-47.
- Kortmann RD, Hess CF, Jany R, Meisner C, Bamberg M. Reproducibility of field alignment in difficult patient positioning. Int J Radiat Oncol Biol Phys. 1994 Jul 1;29(4):869-72.
- Hess CF, Kortmann RD, Jany R, Hamberger A, Bamberg M. Accuracy
 of field alignment in radiotherapy of head and neck cancer utilizing face
 mask immobilization: A retrospective analysis of clinical practices. Radiother Oncol. 1995 Jan;34(1):69-72.
- Yan D, Wong J, Vicini F, Michalski J, Pan C, Frazier A, et al. Adaptive modification of treatment planning to minimize the deleterious effects of

- treatment setup errors. Int J Radiat Oncol Biol Phys. 1997 Apr 1;38(1):197-206
- Gilbeau L, Octave-Prignot M, Loncol T, Renard L, Scalliet P, Grégoire V. Comparison of set up accuracy of three different thermoplastic masks for the treatment of brain and head and neck tumors. Radiother Oncol. 2001 Feb;58(2):155-62.
- Mitine CA, Dutreix A, van der Schueren E. Black and white in accuracy assessment of megavoltage images. The medical decision is often grey. Radiother Oncol. 1993 Jul;28(1):31-6.
- Bel A, Keus R, Vijibrief RE, Lebesque JV. Setup deviations in wedged pair irradiation of parotid gland and tonsillar tumors, measured with electronic portal imaging device. Radiother Oncol. 1995 Nov;37(2):153-9.
- Hurkmans CW, Remeijer P, Lebesque JV, Mijnheer BJ. Setup verification using portal imaging, review of current clinical practice. Radiother Oncol. 2001 Feb;58(2):105-20.
- van Lin EN, van der Vight L, Huizenga H, Kaanders JH, Visser AG. Set-up improvement in head and neck radiotherapy using a 3D off-line EPIDbased correction protocol and a customized head and neck support. Radiother Oncol. 2003 Aug;68(2):137-48.
- Rotondo RL, Sultanem K, Lavoie I, Skelly J, Raymond L. Comparison of repositioning accuracy of two commercially available immobilization systems for treatment of head-and-neck tumors using simulation computed tomography imaging. Int J Radiat Oncol Biol Phys. 2008 Apr 1;70(5):1389-96.
- Jaffray DA, Siewerdsen JH, Wong JW, Martinez AA. Flat-panel cone-beam computed tomography for image-guided radiation therapy. Int J Radiat Oncol Biol Phys. 2002 Aug 1;53(5):1337-49.
- Gong Y, Wang J, Bai S, Jaing X, XU F. Conventionally-fractionated image-guided intensity modulated radiotherapy (IG-IMRT): a safe and effective treatment for cancer spinal metastasis. Radiat Oncol. 2008 Apr 22;3:11.
- Meyer J, Wilbert J, Baier K, Guckenberger M, Richter A, Sauer O, et al. Positioning accuracy of cone-beam computed tomography in combination with a Hexa-POD robot treatment table. Int J Radiat Oncol Biol Phys. 2007 Mar 15;67(4):1220-8.
- Oldham M, Létourneau D, Watt L, Hugo G, Yan D, Lockman D, et al. Cone-beam CT guided radiation therapy: A model for on-line application. Radiother Oncol. 2005 Jun;75(3):271-8.
- van Herk M, Remeijer P, Lebesque JV. The probability of correct target dosages: Dose-population histograms for deriving treatment margins for radiotherapy. Int J Radiat Oncol Biol Phys. 2000 Jul 1:47(4):1121-35.
- International Commission on Radiation Units and Measurements ICRU Report, 62. Bethesda, MD: ICRU Publications; 2000. Prescribing, recording and reporting photon beam therapy (Supplement to ICRU report 50).
- Stroom JC, Heijmen BJ. Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report. Radiother Oncol. 2002 Jul;64(1):75-83.
- Stroom JC, de Boer HC, Huizenga H, Visser AG. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. Int J Radiat Oncol Biol Phys. 1999 Mar 1;43(4):905-19.
- Van Herk M, Errors and margins in radiotherapy. Semin Radiat Oncol. 2004;14:52-64
- Li H, Zhu XR, Zhang L, Dong L, Tung S, Ahamad A, et al. Comparison of 2D radiographic images and 3D cone beam computed tomography for positioning head- and- neck radiotherapy patients. Int J Radiat Oncol Biol Phys. 2008 Jul 1;71(3):916-25.
- Humphreys M, Guerrero Urbano MT, Mubata C, Miles E, Harrington KJ, Bidmead M, et al. Assessment of customized immobilization system for head and neck IMRT using electronic portal imaging. Radiother Oncol. 2005 Oct;77(1):39-44.
- Zhang L, Garden AS, Lo J, Ang Kian K, Ahamad A, Morrison WH, et al. Multiple regions-of-interest analysis of setup uncertainties for head-and – neck cancer radiotherapy. Int J Radiat Oncol Biol Phys. 2006 Apr 1;64(5): 1559-69.
- Suzuki M, Nishimura Y, Nakamatsu K, Okumura M, Hashiba H, Koike R, et al. Analysis of inter-fractional set up errors and intrafractional organ motion during IMRT for head and neck tumours to define an appropriate planning target volume (PTV) and planning organ at risk volume (PRV) margins. Radiother Oncol. 2006 Mar;78(3):283-90.
- de Boer HC, van Sörnsen de Koste JR, Creutzberg CL, Visser AG, Levendag PC, Heijmen BJ. Electronic portal image assisted reduction of systematic set up errors in head and neck irradiation. Radiother Oncol. 2001 Dec;61 (3):299-308.
- Prisciandaro JI, Frechette CM, Herman MG, Brown PD, Garces YI, Foote RL.
 A methodology to determine margins by EPID measurements of patient setup variation and motion as applied to immobilization devices. Med Phys. 2004 Nov;31(11):2978-88.
- Hong TS, Tome WA, Chappell RJ, Chinaiyan P, Mehta MP, Harari PM.
 The impact of daily setup variation on head-and-neck intensity-modulated radiation therapy. Int J Radiat Oncol Biol Phys. 2005 Mar 1;61(3):779-88.