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Citation for published version (APA):

Theelen, A., Martens, J., Bosmans, G., Houben, R., Jager, J. J., Rutten, I., Lambin, P., Minken, A. W., & Baumert, B. G. (2012). Relocatable fixation systems in intracranial stereotactic radiotherapy Accuracy of serial CT scans and patient acceptance in a randomized design. *Strahlentherapie Und onkologie*, 188(1), 84-90. <https://doi.org/10.1007/s00066-011-0018-7>

Document status and date:

Published: 01/01/2012

DOI:

[10.1007/s00066-011-0018-7](https://doi.org/10.1007/s00066-011-0018-7)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

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Strahlenther Onkol 2012 · 188:84–90
 DOI 10.1007/s00066-011-0018-7
 Received: 7 April 2011
 Accepted: 28 June 2011
 Published online: 24 December 2011
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A. Theelen¹ · J. Martens¹ · G. Bosmans¹ · R. Houben¹ · J.J. Jager¹ · I. Rutten¹ · P. Lambin¹ · A.W. Minken^{1,2} · B.G. Baumert¹

¹ Department of Radiation-Oncology (MAASTRO), GROW (School for Oncology & Developmental Biology), Maastricht University Medical Centre (MUMC), Maastricht

² Department of Medical Physics, Radiotherapeutic Institute RISO, Deventer

Relocatable fixation systems in intracranial stereotactic radiotherapy

Accuracy of serial CT scans and patient acceptance in a randomized design

Stereotactic conformal radiotherapy (SCRT) combines the precision of stereotactically guided tumour localization and the radiobiological advantages of fractionation [9, 26]. The main indications for stereotactic radiotherapy are benign tumours which do not infiltrate into surrounding tissue and, thus, do not need an added margin in the form of a clinical target volume (CTV) [3, 12], whereas for malignant tumours in case of reirradiation or dose escalation, the dose is given to the tumour with a small restricted CTV margin only [4, 11]. Thus, the addition of margins takes into account only daily treatment inaccuracy and delineation accuracy.

Patient set-up and daily repositioning for SCRT is usually checked by an electronic portal-imaging device (EPID) [1, 12, 24] which is also performed for radiosurgery [29]. Another way of assessing isocentre repositioning accuracy is serial computer tomography (CT) at regular intervals [17, 21, 22, 25, 30, 31].

This study aimed at providing a quantitative evaluation of the accuracy of different fixation methods. Repositioning accuracy was evaluated in a randomized manner patient-dependent but independent of the fixation systems with the main endpoint being accurate reproducibility evaluated by repeated CT scans. Secondary endpoints were whether it would be

possible to detect interfractional tumour motion as well as the evaluation of patients' acceptance for the different fixation systems.

Methods

The study was approved by the local ethics committee according to the Dutch legislation. Written informed consent was obtained from all patients.

A total of 16 patients with meningioma ($n=6$), acoustic neuroma ($n=3$), pituitary adenoma ($n=4$) and astrocytoma ($n=1$) were included. For 14 of 16 patients, CT data sets and 151 repeated measurements

were evaluable (69, 39 and 43 scans for fixations S, A and B, respectively).

Study design

A prospective study was used to evaluate the sequence of fixation measurements in a randomized manner (■ Fig. 1). Sixteen consecutive patients with a primary brain tumour undergoing SCRT for 6 weeks were selected. Daily treatment was performed for all patients with the standard fixation; the other fixations were evaluated only. The standard fixation was evaluated by weekly CT scans (6 CTs); the other systems in parallel by weekly scans with

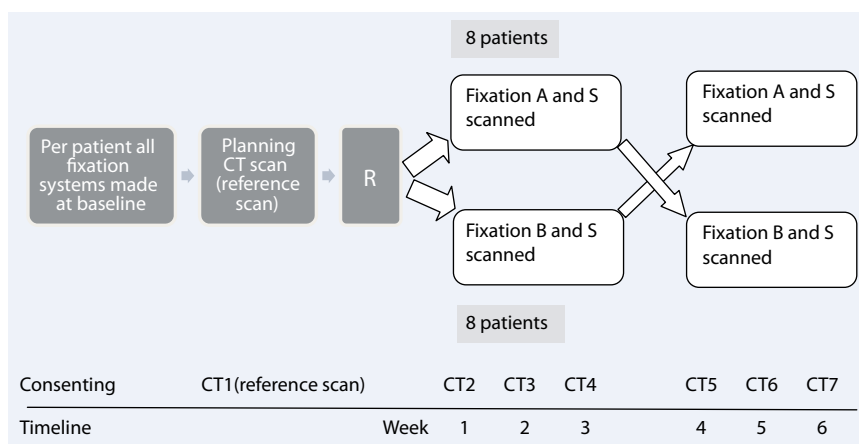


Fig. 1 ▲ Study design with randomization schedule for sequence of measurements. R randomize



Fig. 2 ▲ Fixation systems: the standard fixation S consisting of thermoplastic mask with bite-block (a). The custom-made dental fixation, bite-block (b). Fixation B consisting of a custom-made neck and head support (PUR) and a bite-block (c)

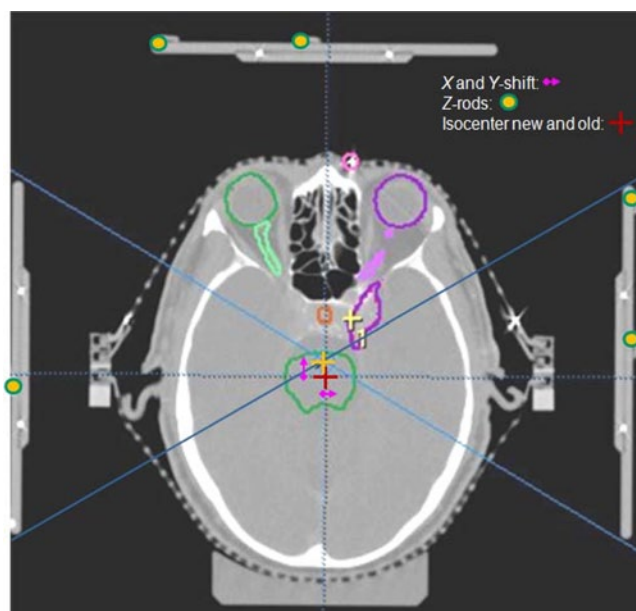


Fig. 3 ◀ Reconstruction of the new isocentre (yellow) in relation to the reference CT scan (original isocentre in red) by defining the coordination system of the co-registered data set. Measurement of shifts in x and y direction (arrows). Shifts in z direction are measured by defining the rods in the localizer box (green rings)

a cross-over design: 3 scans with one fixation, 3 weeks with another (■ Fig. 1) with each patient being its own control. Each patient's opinion about the fixation system was evaluated by a questionnaire.

Patient immobilization

Fixation systems evaluated were the BrainLAB® thermoplastic mask (BrainLAB®, Munich, Germany), with (standard fixation S) and without a (A) custom made bite-block and a homemade neck support using poly-urethane (PUR) with bite-block based on the BrainLAB® frame (B)(■ Fig. 2). The neck support was chosen to be investigated under the hypothesis that it would provide better neck support and skull base fixation and reduce cervical movement.

Measurements and CT scanning

Weekly CT scans were taken using exactly the same protocol parameters as used for the first planning CT scan (i.e. field-of-view, slice thickness of 2 mm, stereotactic localizer) but without contrast. In the last week, the CT scan was performed with intravenous contrast to make the tumour visible. All CT images were co-registered with the reference planning CT (image fusion software from BrainLAB®, BRAINSCAN, version 5.3.1). The isocentre was made visible with small lead markers (integrated into the mask material) placed during the first fraction in the position of the orthogonal and ceiling lasers. The majority of the tumours, and therefore the isocentre, were located in the skull base ($n=12$), the other 2 were located in the frontal and temporal fossa.

The lead markers and localizer rods were delineated on each CT scan. In order to define the position of the localizer box (the coordination system) and reconstruct the isocentre of the repeat CT scan, the centre of the localizer box was defined as shown in ■ Fig. 3. The isocentric shift was defined as the length of the vector of the deviations in three orthogonal directions. After reconstruction of the isocentre position of the repeat scan, shifts in x and y directions were measured (■ Fig. 3). Translations in the z direction were measured by the use of the delin-

eated rods and by the use of the formula $(225/150) \times z$ (cm) – 85.5 for each rod, where z was defined as the mean of distances (left, right, ventral) between the localizer box positions. Hereafter, the location of lead markers in relation to the reconstructed isocentre was measured in order to define potential shifts.

Calculation of rotational shift

The calculation of the rotational shift was based on the rotation matrix (R) of Ezzell et al. [8]:

$$R = \begin{bmatrix} \cos(\beta)\cos(\gamma) \\ -\cos(\beta)\sin(\gamma) \\ \sin(\beta) \\ \sin(\alpha)\sin(\beta)\cos(\gamma) + \cos(\alpha)\sin(\gamma) \\ -\sin(\alpha)\sin(\beta)\sin(\gamma) + \cos(\alpha)\cos(\gamma) \\ -\sin(\alpha)\cos(\beta) \\ -\cos(\alpha)\sin(\beta)\cos(\gamma) + \sin(\alpha)\sin(\gamma) \\ \cos(\alpha)\sin(\beta)\sin(\gamma) + \sin(\alpha)\cos(\gamma) \\ \cos(\alpha)\cos(\beta) \end{bmatrix} \quad (1)$$

$$SetI_{Rot} = R \times SetI$$

The reconstructed coordinates of the markers from CT scans are used to calculate the rotational angles of the x (α), y (β) and z (γ) axes. A search through the angles α , β and γ to find the best-fit combination gives the rotation between the CT scans. The program utilizes user-selected search parameters to find the corresponding rotation matrix R . The optimum angle was defined with an angle variation of -3° to 3° in steps of 0.1° . This range represents realistic patient rotations.

Patient's acceptance

At the start and the end of the treatment patients filled in a questionnaire evaluating criteria of comfort, claustrophobic aspects and pain according to the different fixation systems as well as patients' preference for a fixation method.

Electronic portal imaging (EPI)

For the EPI procedure, exported digitally reconstructed radiographs (DRR) were used as reference images. Reference DRRs and EPIS are fused using TheraviewNT software (V2.4., Cablon Medical BV, The Netherlands) to measure deviations. EPIS

Strahlenther Onkol 2012 · 188:84–90 DOI 10.1007/s00066-011-0018-7
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Relocatable fixation systems in intracranial stereotactic radiotherapy. Accuracy of serial CT scans and patient acceptance in a randomized design

Abstract

Purpose. The goal was to provide a quantitative evaluation of the accuracy of three different fixation systems for stereotactic radiotherapy and to evaluate patients' acceptance for all fixations.

Methods. A total of 16 consecutive patients with brain tumours undergoing fractionated stereotactic radiotherapy (SCRT) were enrolled after informed consent (Clinical trials.gov: NCT00181350). Fixation systems evaluated were the BrainLAB® mask, with and without custom made bite-block (fixations S and A) and a homemade neck support with bite-block (fixation B) based on the BrainLAB® frame. The sequence of measurements was evaluated in a randomized manner with a cross-over design and patients' acceptance by a questionnaire.

Results. The mean three-dimensional (3D) displacement and standard deviations were 1.16 ± 0.68 mm for fixation S, 1.92 ± 1.28 and 1.70 ± 0.83 mm for fixations A and B, respectively. There was a significant improvement of

the overall alignment (3D vector) when using the standard fixation instead of fixation A or B in the craniocaudal direction ($p=0.037$). Rotational deviations were significantly less for the standard fixation S in relation to fixations A ($p=0.005$) and B ($p=0.03$). EPI imaging with off-line correction further improved reproducibility. Five out of 8 patients preferred the neck support with the bite-block.

Conclusion. The mask fixation system in conjunction with a bite-block is the most accurate fixation for SCRT reducing craniocaudal and rotational movements. Patients favoured the more comfortable but less accurate neck support. To optimize the accuracy of SCRT, additional regular portal imaging is warranted.

Keywords

Stereotactic intracranial radiotherapy · Brain tumours · Bite-block · Serial CT · Reproducibility

Reproduzierbarkeit von Fixationssystemen in der intrakraniellen stereotaktischen Radiotherapie. Genauigkeit durch serielle CT-Scans und Patientenakzeptanz im randomisierten Design

Zusammenfassung

Ziel. Untersuchung zur Lagerungsgenauigkeit von drei verschiedenen Fixationssystemen für die intrakranielle stereotaktische Radiotherapie und die Patientenakzeptanz der verschiedenen Maskensysteme.

Methoden. 16 konsekutive Patienten mit Hirntumoren, bei denen eine stereotaktische Radiotherapie geplant war, wurden nach schriftlicher Zustimmung prospektiv in die Studie eingeschlossen (Clinical trials.gov: NCT00181350). Untersuchte Fixationssysteme waren das Maskensystem von BrainLAB® mit und ohne Oberkieferbissplatte (Fixationen S und A) und eine in unserem Haus angefertigte Nackenstütze mit Bissplatte (Fixation B) auf der Basis des BrainLAB®-Rahmens (Fig. 2). Die Reihenfolge der Messungen wurde mit Hilfe eines Cross-Over-Designs (Fig. 1) randomisiert. Die Patientenakzeptanz wurde mit einem Fragebogen evaluiert.

Ergebnisse. Die mittleren dreidimensionalen (3-D) Verschiebungen und Standardabweichungen waren $1,16 \pm 0,68$ mm für die Standardfixation S, $1,92 \pm 1,28$ mm und $1,70 \pm 0,83$ mm für die Fixationen A und B. Es ergab sich eine si-

gnifikante Verbesserung des 3-D-Vektors mit der Standardfixation im Vergleich zu den Fixationen A und B in kraniokaudaler Richtung ($p=0,037$; Tab. 1). Rotationsabweichungen traten signifikant weniger bei der Standardfixation S auf im Vergleich zu A ($p=0,005$) und B ($p=0,03$). Elektronische Portfilm-Bildgebung mit „Off-line“-Korrektur verbesserte die Reproduzierbarkeit zusätzlich (Fig. 5). 5 von 8 Patienten bevorzugten die Fixation mit Nackenstütze und Bissplatte.

Schlussfolgerung. Das Maskensystem mit Oberkieferbissplatte erreicht die genaueste Reproduzierbarkeit durch Verringerung der Abweichungen in longitudinaler Richtung und der Rotationen. Patienten bevorzugten die bequemere, aber weniger genaue Fixation mit Nackenstütze. Zusätzliche wiederholte Portfilm-Bildgebung gewährleistet eine weitere Optimierung der Lagerungsgenauigkeit.

Schlüsselwörter

Intrakranielle stereotaktische Radiotherapie · Hirntumoren · Oberkieferbissplatte · Serielle CT · Reproduzierbarkeit

Tab. 1 Translational and rotational displacements of the standard fixation S (mask with bite-block), fixation A (mask without bite-block) and fixation B (neck support PUR with bite-block)

Fixation	3D vector (mm)	x (mm) (lateral)	y (mm) (ventro-dorsal)	z (mm) (cranio-caudal)	3D vector (°)	x (°) (lateral)	y (°) (ventro-dorsal)	z (°) (cranio-caudal)
Mean/SD (range)								
S (mask with bite-block)	1.16/0.68 (0.27–2.25)	0.78/1.01 (–2.25–0.60)	0.14/0.37 (–0.30–0.82)	0.18/0.25 (–0.10–0.63)	1.09/0.50 (0.10–2.53)	0.23/0.62 (–1.0–1.50)	0.46/0.88 (–1.40–2.50)	–0.03/0.14 (–0.30–0.30)
B (neck support with bite-block)	1.92/1.28 (0.09–3.68)	1.37/0.97 (–3.0–0.17)	0.12/0.94 (–1.34–2.23)	–0.59/1.19 (–2.99–0.31)	1.35/0.66 (0.10–2.62)	0.79/0.82 (–0.80–2.60)	0.15/0.99 (–1.60–2.30)	–0.05/0.15 (–0.50–0.20)
A (mask without bite-block)	1.70/0.83 (0.60–3.58)	–0.43/1.49 (–3.56–2.54)	0.55/0.96 (–1.83–2.15)	–0.25/0.62 (–0.69–1.48)	1.58/0.83 (0.10–3.17)	0.24/0.79 (–1.10–2.10)	0.96/1.27 (–1.50–3.00)	–0.03/0.14 (–0.20–0.40)
p value	n.s.	n.s.	n.s.	z: p=0.037 B vs. S: p=0.048 B vs. A: n.s.		n.s.	n.s.	n.s.
					S vs. A: p=0.005 B vs. A: n.s. B vs. S: p=0.03			

n.s. not significant, SD standard deviation.

are taken from AP and lateral with standardized anatomic structures defined. An offline SAL protocol is applied with three daily EPIs at treatment start and thereafter weekly [7].

Statistical methods

The null hypothesis was that fixation A is less accurate than fixation B ($H_0: A \leq B$) and the H_1 hypothesis is $B < A$. Because of the small patient sample, nonparametric statistical tests were applied. In a first step a total of 10 patients was estimated which was extended to 16 patients after a first evaluation. The nonparametric Friedman test for repeated measures was used to test whether there were any differences between methods. When statistically significant, pair wise tests were performed to test the hypothesis above. The hypothesis was rejected if $p = 0.05$ (one-sided Wilcoxon signed-rank test).

An overall mean difference of accuracy between fixation systems of > 2 mm between fixations will mean a change of fixation system. Concerning an additional bite block to the BrainLAB® mask an improvement of > 4 mm was aimed at, i.e. for a fixation with the use of bite-block deviations must stay within the range of < 1.2 mm.

Results

Interfraction translational and rotational deviations

The mean overall deviations are shown in **Tab. 1**. The standard fixation had best reproducible accuracy with 1.16 ± 0.68 mm. There was a significant improvement of the overall alignment (3D-vector) in using the standard fixation instead fixations A and B in the cranio-caudal direction ($p = 0.037$, Friedman test) (Tab. 1). Cranio-caudal displacements were significantly less for the standard fixation with 0.18 ± 0.25 mm compared to the neck support with -0.59 ± 1.19 mm ($p = 0.048$, Wilcoxon rank). The rotational deviation is significant less for the standard fixation S in relation to fixation A ($p = 0.005$) and B ($p = 0.03$) (Tab. 1). The largest rotational deviations were seen for fixation B for lateral rotations (x) (0.79° ; range -0.80 to 2.60°).

Deviations over time

The deviations over the 6 weeks of treatment time for the whole population are shown in **Fig. 4**. The smallest deviations are observed for week 4 (CT number 5).

Interfraction tumour motion

No tumour movement could be detected. The reason for this is the fact that tumours studied were often enclosed by or fixed to the bone.

Treatment verification by electronic portal imaging (EPI)

Recent consecutive measurements by EPI revealed necessary corrections for 6 out of 10 patients, whereas 1 patient needed three corrections. Four corrections were necessary after the 10th fraction. Systematic deviations were $\Sigma = 0.6$ (SD of mean) and random $\sigma = 0.8$ (mean SD) with correction and $\Sigma = 1.2$ and $\sigma = 0.8$ without correction, respectively (**Fig. 5**).

Patients' acceptance and preference

There were 16 patients who qualified for the study; 8 returned the questionnaire. Two patients reported pain with the thermoplastic mask and one from the bite-block, 5 out of 8 prefer the neck support with the bite block. One patient preferred the mask for feelings of security.

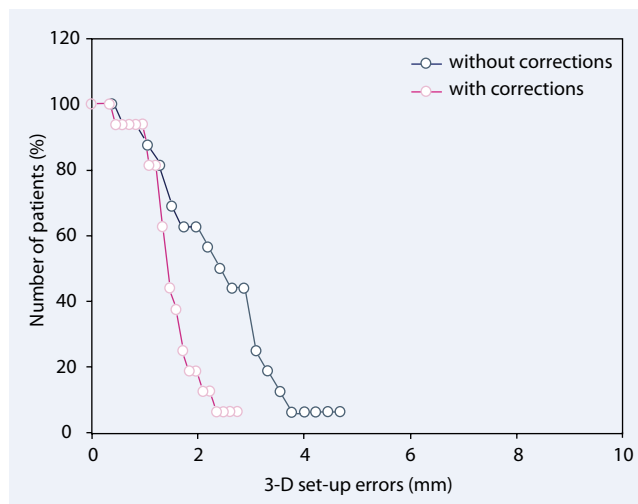
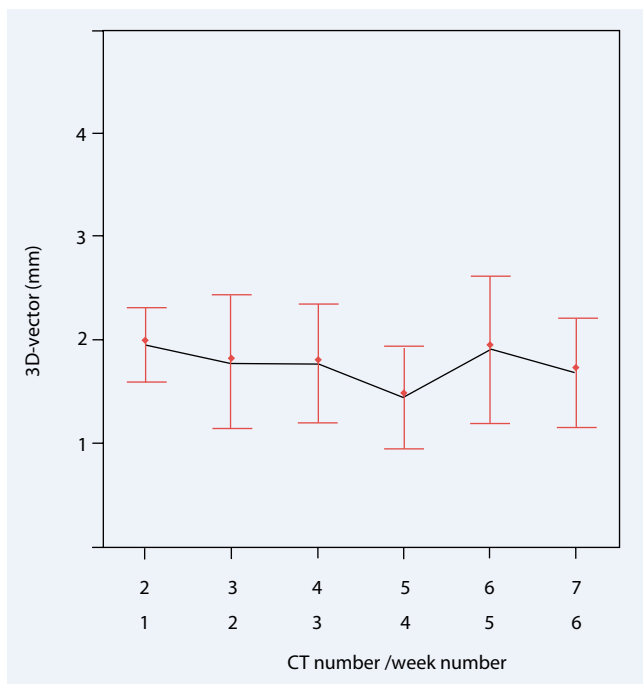


Fig. 5 ▲ Histogram of 3D set-up errors of fractionated stereotactic radiotherapy at MASTROclinic 2010 (115 measurement, 0.6 average number of corrections)

Fig. 4 ◀ Mean 3D-vector deviations for all patients per week (lines represent confidence interval)

Discussion

This study investigated accuracy of different stereotactic fixation systems in a randomized manner. Randomization was applied for definition of sequencing of measurements. There is only one other study published which compared fixation systems for SCRT in a randomized manner [6]. Patients were randomized for treatment between the Gill–Thomas–Cosman frame and the thermoplastic mask without a dental fixation. This is different from our study, where we decided not to irradiate patients in one of the other systems as accuracy was unknown at the start of the study. Results of both studies applying randomization are comparable and showed that the additional use of a dental tray improves accuracy.

Different verification methods of reproducibility evaluation with and without dental fixation have been described in the literature with the set-up error for daily repositioning ranging between 2–3 mm for different relocatable masks (■ Tab. 2). Outliers are corrected by portal imaging methods and further improve set-up accuracy [1, 2, 18, 21].

Studies using an additional dental tray found an even higher accuracy of <2 mm (■ Tab. 2). Studies are difficult to compare due to widely varying methods and

endpoints as well as measurement of deviations used. Many studies however found the largest deviation in cranio-caudal direction and deviations were even larger without the use of dental fixation (■ Tab. 2, [1, 5, 17, 28]). Overall, our results are in line with other reports on set-up accuracy for stereotactic radiotherapy (■ Tab. 1). Compared to other groups [17, 23], our results of 1.16 mm mean deviation for the standard fixation are the smallest. Likewise, results are less accurate with deviations of 3.2–3.7 mm if an individual moulded mouth bite is not used [6, 5, 23] and more rotations in the x direction. Other report more rotational deviations in the y direction [6, 5, 15] which we found mainly with the use of the neck support.

Interestingly, largest deviations over time are observed in the first 2 weeks which can easily be explained by the fact that patients may be anxious in the beginning and have learned after some time how to deal with the daily fixation and have relaxed. Minniti et al. [21] found during treatment only small differences with no significant difference of the mean deviations in overall patient reproducibility. They reported however not their detailed measurements over time. Peng et al. [23] show that corrections increase in size towards the end of treatment for 1 patient. We have observed necessary corrections

mainly in weeks 3 and 4 (around 15 fractions). The increase of deviations at the end of the treatment course is more difficult to explain, one possible explanation could be a slight deformation of the material after a few weeks of daily use which however has not been reported or measured so far. Another factor is patient's comfort which may be less towards end of treatment in weeks 5 and 6 which is mirrored in the fact that a majority of patients reported in our questionnaire their preference for the open fixation system.

The reason to define and add safety margins to the tumour volume is in order to achieve good coverage of the target volume. An overestimation of the margin would lead to possible toxicity and an underestimation could lead to a geographical miss. The use of the smallest margin consistent with achieving reliable tumour coverage results in the best sparing of the normal tissue. A decrease in cranio-caudal deviations results for example in better sparing of the chiasm for close situated tumours.

Based on the formula of van Herk et al. [27] and the data set presented in this study, we calculated our set-up margin to be 2.38 mm. Based on this and on the report from the working party on geometric uncertainties in radiotherapy [8], we decided to use a margin of 3 mm being sufficient to include 2 SD of 0.7 which cov-

Tab. 2 Literature overview of set-up errors of different stereotactic fixation systems and measurement methods

Author	Fixation system	Patients/ measures (n)	Positioning verification	Results translations (mean, mm)			Results rotations (mean, °)					
				3D-vec- tor+SD	Cranio- caudal(z)	Medio- lateral(x)	Anterior- posterior(y)	Largest deviation(mm)	Cranio- caudal	Medio- lateral	Anterior- posterior	
Kooy 1994 [16]	Relocatable frame + BB	20	Depth helmet	- , +0.4	0.52, +0.09	0.35, +0.06	0.34, +0.09					
Rosenthal 1995 [24]	Mask + BB	10/118	EPID	0.9, +0.4	0.0, +0.5	-0.4, +0.4	0.3, +0.4		0.07, +0.45	0.03, +0.42	-0.14, +0.67	
Hamilton 1996 [12]	Mask + BB	12/104	EPID	1.8, +1.4				z: -4.0				
Wilhner 1997 [30]	Mask	16/22	Serial CT-scans	2.4, +1.3	0.4, +1.5	-0.1, +1.8	0.1, +1.2					
Kortmann 1999 [17]	Mask	20/41	Serial CT-scans	-0.3- 1.2, +1.3-2.0				z: 4.6				
Alheit 2001 [1]	Mask	33/98	Simulator films/EPID	2.1, +1.2	0.8, +1.2	-0.1, +1.1	-0.1, +0.6	z: 3.8, 6.9		0.1, +1.1	-0.2, +1.1	
Kalaparakal 2001 [14]	Relocatable frame + ear plugs	34/305	EPID	1.0, +0.7	1.7, +1.0	1.0, +0.7	0.8, +0.8	z: 3.5,				
Karger 2001 [15]	Mask	4/118	Diagnostic x-rays	1.8, +0.6	0.72	0.48	0.67	y, z	- , +0.70	- , +0.72	- , +0.43	
Lopatta 2003 [19]	Mask + upper jaw support	29/844	Simulator films	-	0.5	0.5	0.6	z				
Kumar 2004 [18]	Relocatable frame + BB	15/149	Depth helmet/EPID	0.7, +0.4	0.3, +0.5	0.1, +0.4	0.0, +0.4	z				
Baumert 2005 [5]	Mask + BB or with upper jaw support Mask only	57/114	Serial CT scans	2.2, +1.1 3.3, +1.8 3.7, +2.8	0.6, +1.8 1.5, +2.6 0.07, +3.1	-0.04, +1.4 0.2, +1.7 -0.5, +3.3	-0.1, +0.8 -0.6, +1.4 -0.7, +1.4	z: 5.1 z: 6.9 z: 3.2	0.1, +0.8 0.2, +0.9 0.2, +1.5	0.2, +0.8 -0.1, +1.5 1.6, +1.7	-0.02, +0.8 0.2, +1.1 -0.6, +0.8	
Van Santvoort 2008 [28]	Mask + BB or with upper jaw support	40	Stereoscopic KV X-ray	1.7, +0.7 2.1, +1.2	-0.47 -0.01	0.58 0.69	0.4 0.46	z: 5.2 z: 8.9	-0.03 0.21	-0.42 -0.41	0.06 0.18	
Ali 2010 [2]	Mask	50	KV-on board imaging	-	-1.0, +1.8	2.0, +2.5	-2.0, +1.2	z				
Peng 2010 [23]	Mask + BB Mask only	25	Cone beam/CT	1.4, +1.2 3.2, +1.5	0.8, +0.6 1.2, +0.7	0.5, +0.4 2.0, +1.6	0.5, +0.4 1.3, +1.0	z				
Minniti 2010 [21]	Mask + upper jaw support	16/456	Serial CT-scans, EPID	0.5, +0.4	0.3, +0.4 0.2, +1.1	0.1, +0.3 0.3, +0.9	0.1, +0.4 -0.2, +1.0	z: 2.7				
Bednarz 2009 [6]	Mask Relocatable frame + BB	69/782	Stereoscopic KV X- ray/depth helmet	3.17, +1.95 2.00, +1.04	0.6, +0.39 0.53, +0.15	0.22, +0.13 -0.23, +0.15	-0.03, +0.16 -0.53, +0.19	z	0.14, +0.2 -0.35, +0.15	-0.13, +0.33 -0.12, +0.11	0.14, +0.19 0.06, +0.09	
This study	Mask + BB Mask only Neck support + BB	14/151	Serial CT scans	1.16, +0.68 1.92, +1.28 1.70, +0.83	0.18, +0.25 -0.25, +0.62 -0.59, +1.19	0.78, +1.01 -0.43, +1.49 1.37, +0.97	0.14, +0.37 0.55, +0.96 0.12, +0.94	z x	-0.03, +0.14 -0.03, +0.14 -0.05, +0.15	0.23, +0.62 0.24, +0.79 0.79, +0.82	0.46, +0.88 0.96, +1.27 0.15, +0.99	

BB bite-block

ers >95% displacements as well as possible inaccuracies of image fusion, volume definition and mechanical errors. Consecutive measurements by EPID using an off-line protocol confirmed reproducibility to be within 3.8 mm without correction and 2.18 mm with correction (3D vector, **■ Fig. 5**). However, the value of 3.8 mm is only a theoretical value as patients are standard treated with a shrinking action level protocol (SAL). EPID imaging improved our set-up from 2.38–2.18 mm.

Conclusion

The fixation system with a mask system in conjunction with a bite-block is the most accurate fixation reducing lateral and cranio-caudal movements. The use of a 3 mm set-up margin in conjunction with an off-line portal imaging correction protocol is feasible and results in a highly daily reproducible set-up. Patients favoured the more comfortable but less accurate neck support in combination with a bite-block; however, most patients reported also no major difficulties in being treated with the standard mask setting.

Corresponding address

Dr. B.G. Baumert

Department of Radiation-Oncology (MAASTRO), GROW (School for Oncology & Developmental Biology), Maastricht University Medical Centre (MUMC)
Dr Tanslaan 12, 6229 Maastricht
The Netherlands
brigitte.baumert@maastro.nl

Acknowledgements. We thank Prof. Martijn Berger of the Department for Methodology and Statistics of the University Maastricht for his support in defining and setting up the study design. We also thank Brigitte Reniers PhD, of the Department of Radiation-Oncology (MAASTRO) for providing us set-up data from EPID measurements of stereotactically treated patients at MAASTRO clinic.

Conflict of interest. The corresponding author states that there are no conflicts of interest.

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