CLINICAL TRIAL PROTOCOL

Intrafractional 6D head movement during stereotactic intracranial radiation therapy with thermoplastic mask fixation

A prospective observational study

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1. Study Summary

Title	Intrafractional 6D head movement during stereotactic intracranial radiation therapy with thermoplastic mask fixation
Study Center	single center Department of Therapeutic Radiology and Oncology Innsbruck
Study Design /Methodology	A prospective observational study
Objectives	to investigate intrafractional head motion during stereotactic intracranial radiation therapy with non invasive thermoplastic mask fixation with repeated X-ray position verification during RT sessions.
Endpoints	3D deviation of head position, rotational and translational deviations. Development of head deviation with time during single RT sessions
Number of Subjects	5
Eligibility Criteria	Male and female patients with a single intracranial solid tumour. Stereotactic radiation therapy with immobilization by non invasive thermoplastic mask.
Study Interventions and Measures	repeated X-ray position verification during RT sessions
Statistical Methodology	calculation of 3D deviation from X, Y, Z translational deviation. Descriptive statistics of 3D, translational and rotational deviation. Analysis of time dependent deviation with Spearman’s correlation. ANOVA Analysis of deviations in 2-minute interval groups.

2. Introduction

2.1. Study Rationale

Invasive head fixation by means of a stereotactic ring for stereotactic intracranial radiation therapy has largely been replaced by non invasive thermoplastic mask fixation. While the deviation between RT sessions can be minimized using modern image guided radiation therapy, the role of intrafractional head movement and its effect on treatment accuracy is still debated. Previous studies have attempted to estimate intrafractional deviation by performing position measurements at the beginning and the end of RT sessions. However, this method is not accurate enough to map patient motions during a treatment session.

2.2. Background and scientific bases

In recent years advances in non-invasive patient immobilization as well as in image-guided radiation therapy (IGRT) have enabled the use of thermoplastic masks and hypofractionated radiotherapy for single brain metastases (1). The use of a rigid, invasive stereotactic head-ring provides reliable and precise immobilization for single fraction radiosurgery. The ring is securely mounted to the skull using pins or screws, thereby achieving a setup inaccuracy of less than 1 mm (2, 3). However, this method suffers from disadvantages such as the need to surgically implant the ring. It also entails the risk of bleeding and infection, possibly accompanied by pain and generally by patient discomfort. Ring implantation, planning and irradiation have to be performed on the same day, which can put a significant burden on clinical and organisational resources. Moreover, this prohibits the use of fractionated RT. The use of non-invasive thermoplastic masks together with image guidance can minimise these limitations and has currently replaced invasive immobilization. (2, 4)

Several studies have shown that image guidance makes set-up and repositioning uncertainty with the non-invasive mask immobilization comparable to that of invasive stereotactic ring application (2, 3, 5, 6). Nevertheless, this method may have less intrafractional accuracy due to the non-rigid construction and indirect immobilization of the skull. This uncertainty can be caused by patient movements during individual radiotherapy sessions. Many studies reported this effect only by means of quantifying pre- and postfractional deviations of the patient's head by either CBCT (cone beam computed tomography) or ExacTrac (2, 3, 7, 8). However, real intrafractional movements cannot be mapped by measuring the position of the head only at the beginning and the end of treatment since this gives no information on possible head movements during the individual irradiation treatments, which last up to 20 minutes each. Larger deviations would need to be accounted for by increasing the PTV margins, thereby exponentially increasing the irradiated volume. Studies have shown that the risk of complications, such as radionecrosis, directly correlates with the size of the irradiated PTV (9, 10).

2.3. Study objectives

The purpose of the present study is to evaluate the precision and reliability of mask fixation of the head during the entire duration of stereotactic RT sessions. In order to assess position accuracy not only at the beginning and the end of the sessions, we repeatedly map deviations of the head position in both translation and rotation, by concomitantly measuring intrafractional movement using the ExacTrac 6D X-Ray Positioning System (Brainlab AG, Munich, Germany). From the obtained data we evaluate the need to adjust safety margins around the gross tumor volume (GTV) whenever the investigated thermoplastic mask is used instead of invasive ring fixation.

3. Study design and Methods

3.1. General study design

This is a prospective observational study investigating patient motion during radiation therapy sessions of patients treated with stereotactic radiation therapy.

3.2. Study population

5 patients treated with intracranial stereotactic radiation therapy for single primary tumours at the Department of Therapeutic Radiology and Oncology Innsbruck.

3.2.1. Inclusion criteria

- Males and females ages ≥ 18
- Single intracranial primary tumour or metastasis
- conventional or hypofractionated stereotactic radiation therapy
- position verification with ExacTrac 6D X-Ray Positioning System
- Karnovski performance scale 80 or higher

3.2.2. Exclusion criteria

- Position verification with ExacTrac 6D X-Ray Positioning System not possible if the masks frame overlaps the orthogonal KV X-ray images used for position measurement.

3.3. Study procedures

3.3.1. Date range of the study

Enrolment of patients between November 2014 and September 2015

3.3.2. Procedures

To detect intrafractional motion during treatment delivery, the ExacTrac in-room based monitoring system (Brainlab AG, Munich, Germany) is used (11, 12). It is employed in this study to repeatedly record 3D deviations of the target isocenter for both translation and rotation, during a single RT session.

Following thermoplastic mask molding, contrast-enhanced treatment planning CT is performed. CT scans are also used for image registration to reference ExacTrac recordings and CBCT-guided patient positioning at the beginning of each treatment session. Calculated 6D shifts are checked and, if indicated, translational and rotational deviations from reference positions are computed and corrected by adjusting the treatment couch (equipped with the HexaPod evo RT system, Elekta AB, Stockholm, Sweden) until translational deviation in each direction are < 1.0 mm and rotational errors are < 1.0°.

The first ExacTrac measurement is taken before treatment start at a rotatable baseplate position of 0°. This initial ExacTrac recording is used as a reference point for comparison with the subsequent intrafractional measurements made during irradiation (N = 3 to 10). Patient positions are not corrected during a treatment session.

ExacTrac measurements are taken simultaneously with arc irradiations (five per RT session) at gantry angles of 0°, 90°, 180° or 270° with a tolerance range of +/- 10°. For shaped beam application, ExacTrac recordings are taken immediately after each field application (five to eight per fraction). A final pair of ExacTrac images at a reset baseplate position of 0° are acquired at the end of each treatment session.

4. Data management

4.1.1. Data sources

Patient head position data is extracted from the ExacTrac 6D X-Ray Positioning System.

4.1.2. Data collection and variable abstraction

The following parameters are extracted, saved in a database and analysed:

- baseplate position [°]
- elapsed time since treatment start
- X axis translation
- Y axis translation
- Z axis translation

- X axis rotation
- Y axis rotation
- Z axis rotation
- 3D deviation is calculated from X-, Y- and Z-translation

4.1.3. Data capture methods and storage

All data collected is be saved databases using Microsoft Excel and IBM SPSS Statistics. The files are be stored encrypted on our department's file servers. Patient identifiers are stored in a separate file. All data and records generated throughout the course of the study are kept confidential. Only the study investigators have access to the data. In case of publication of the studies results patients personal information will be kept confidential.

5. Statistical analysis

Translations in the x (medial-lateral), y (superior-inferior) and z (anterior-posterior) directions as well as rotations around the x (transversal), y (longitudinal) and z (sagittal) axes are analysed. The resulting 3DV is calculated as follows:

$$3DV = \sqrt{x^2 + y^2 + z^2}$$

IBM SPSS Statistics 22 (IBM Cooperation, Armonk, NY, USA) is used for statistical analysis To evaluate the correlation between the time elapsed since the first measurement in each treatment session and the 3DV, Spearman's rank correlation coefficient is calculated. An analysis of variance (ANOVA) is used to analyse this correlation further. A p value of < 0.05 is deemed to be significant.

6. Ethical considerations

The study is conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments.There is no risk involved for the participating patients. All parameters and measurements required for the study are routinely collected as part of the treatment. All patient data is kept confidential and the rights and welfare of the enrolled patients is not adversely affected. Every patient is informed about the analysis of data collected over the course of the treatment. Written informed consent for this analysis is obtained. While there is no direct benefit for the patients participating in the study, results from the study will help improve treatment for future patients treated in our department. Information about the accuracy of treatment and the extent of patient motion during treatment sessions is vital in order to determine the necessary safety margins used in treatment planning. If patient motion is found to significantly exceed 1 mm an additional safety margin will be implemented.

7. Literature

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8. Signatures

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