REAL-TIME HEAD POSITION STABILIZATION OF HEALTHY VOLUNTEERS

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Study Summary

Title	*Real-Time Head Stabilization of Healthy Volunteers*
Short Title	*Head Stabilization- Volunteers*
IRB Number	*843058*
Protocol Number	*Not applicable*
Methodology	*Observational*
Study Duration	*24 months*
Study Center(s)	*Single-center*
Objectives	• *Development of an advanced motion control system.* • *Design and construction of a clinical robotic stereotactic radiosurgery system (SRS) using real-time 3D image tracking.* • *Validation of the SRS.*
Number of Subjects	*20 subjects*
Main Inclusion and Exclusion Criteria	*Healthy individuals will be recruited to this study.*
Intervention	*Head motion data collection using motion-detection cameras.*
Statistical Methodology	*The endpoint is purely quantitative in nature and will be determined by analyzing the real-time 6D target motion during the SRS procedure.*

Data and Safety Monitoring Plan	*The Principal Investigator will be responsible for the data quality management and the ongoing safety of subjects.*

Background and Study Rationale

This study will be conducted in full accordance with all applicable University of Pennsylvania Research Policies and Procedures and all applicable Federal and state laws and regulations including as applicable include the following regulations as they apply 45 CFR 46, 21 CFR Parts 50, 54, 56 All episodes of noncompliance will be documented.

1 Introduction

This is a single-center observational study in which we aim to collect real-time head motion in healthy volunteers. This data is a first step in developing an advanced motion control system for head stabilization in patients undergoing whole brain radiation therapy.

1.1 Background and Relevant Literature

Stereotactic radiosurgery (SRS) is a therapy modality used for the treatment of brain disorders with precise radiation dose placement[1], [2]. To achieve the 1-2 mm precision for intracranial SRS, a metal head ring is rigidly fixated to the patient's skull using screws under local anesthesia, and then bolted on the treatment couch [3]. The discomfort, inconvenience, and invasive nature associated with the frame preparation have been identified as the main cause of poor patient compliance and poor clinical efficiencies when SRS is medically indicated[4]. For certain patients, with extreme cranial anatomy or prior surgical bone flaps, ring placement is not possible. In addition, the frame prohibits cases when a hypo-fractionated scheduled is desired leading to the use of techniques with far less accuracy. For clinics, with tight patient LINAC scheduling, or high patient to LINAC volumes, frame based SRS scheduling can prove to be problematic due to the necessity of performing the CT scan, planning, setup, and treatment on the same day. Recent research, aimed at eliminating the ring placement, has so far resulted in implementations of frameless SRS with less accuracy than frame based SRS[5], [6]. Removal of the head ring allows room for small intrinsic head motions to occur. No radiotherapy delivery device has yet been developed to correct for such deviations.

2 Study Objectives

The goal of our research is to develop a next generation frameless SRS approach where such small intrinsic head motions are continuously cancelled/corrected throughout SRS treatment. Similar to a noise cancellation headset, where outside noise is sampled, shifted in phase by 180o, and then added to the incoming sound for cancellation, the proposed method will sample head motion using real-time 6D optical tracking, calculate its inverse, and add it to incoming head motion using a robotic 6DOF head stage for cancellation of patient head motion. This approach has the potential to be less invasive than current frameless SRS techniques while still achieving accuracies better or equal to traditional frame based SRS.

2.1 Primary Objective

This particular study aims to passively monitor the real-time head motions of healthy volunteers positioned to simulate whole brain radiation therapy. Such real-time head motion data is necessary in order to understand the type (amplitude/frequency) of motion that the robotic stage will be expected to compensate for and will play an important role in the overall modeling and designing process of the robotic prototype.

3 Investigational Plan

3.1 General Design

The study will consist of cancelling the head motions of 20 volunteers lying in a comfortable supine position. The volunteer population will consist of healthy individuals including individuals associated with The University of Pennsylvania.

The real-time head monitoring will be performed using either an optical camera 3D surface imager (AlignRT, VisionRT, UK) or IR marker camera (Polaris, NDI, Canada) that is either mounted to the ceiling or supported on a tripod. Both cameras are FDA approved medical devices that are routinely used in our clinic. Similar to a video camera, real-time head position monitoring by the camera will be performed passively and will not interfere with the volunteer. Using the real-time head position data provided by the camera, a motion stage placed under the head support will slowly move in order to cancel out small motions in order to maintain a stationary head position.

3.2 Study Endpoints

3.2.1 Primary Study Endpoint

The primary endpoint is collection of head motion data to be used in developing head stabilization methods in brain radiation patients.

4 Study Population and Duration of Participation

The volunteer population will consist of healthy individuals. Subjects will be recruited by the PI and his research team. We do not plan to use any internet, radio, newspaper etc. advertisements for this study. Subjects will undergo a one-time motion detection session.

4.1 Duration of Study Participation

Subjects will be considered “on study” from consent through completion of the head stabilization session; there is no follow-up involved.

4.2 Total Number of Subjects and Sites

This is a single-institution study for which we aim to accrue 20 subjects.

4.3 Inclusion Criteria

Inclusion criteria are:

- Subjects 18 and older
- Subjects must be able to read and understand English
- Participants must sign the informed consent form

4.4 Exclusion Criteria

Any subjects not meeting the above inclusion criteria will not be considered for this study.

4.5 Subject Recruitment

Subjects will be recruited from staff, faculty, and students of the University of Pennsylvania.

4.6 Vulnerable Populations

Children, pregnant women, fetuses, neonates, or prisoners are not included in this research study.

5 Study Procedures

5.1 *Screening*

Subjects will be recruited by the study team via face-to-face interactions and word-of-mouth. A member of the study team will thoroughly explain the study to each subject, reviewing all the elements of the consent form with them. Subjects will have ample opportunity to review the consent form and have their questions answered to their satisfaction. All interactions will take place in a private consultation room within the Department of Radiation Oncology. We anticipate that all subjects will self-identify to the study team so staff, students, and faculty of the University of Pennsylvania will face no undue pressure to participate. Once a subject is deemed eligible, a head motion session will be scheduled at their convenience.

5.2 Study Intervention

The AlignRT system consists of three units attached to the ceiling where one unit is located at each lateral side of the patient treatment table and one at the center above the foot of the table. Each unit contains two cameras, which take pictures at slightly different perspectives, allowing for image depth reconstruction (3D surface image). Analysis and comparison of these 3D surface images as taken during the course of treatment can allow extraction of patient motions during treatment.

The Polaris infrared (IR) camera consists of a single unit either attached to the ceiling or mounted on a tripod. Each unit contains two cameras, which take pictures of IR markers attached to the volunteers head at slightly different perspectives, allowing for triangulation of the marker positions and thus determination of head position.

As both the AlignRT and Polaris devices use optical camera monitoring, it is non-invasive and will not physically touch or interfere with the volunteer. Both systems are routinely used in the clinic for assuring that patients are correctly positioned on the treatment table. The research proposed here does not deviate from the FDA approved operation of the AlignRT or Polaris in anyway.

The volunteer head support (Freedom Pursuit Robotic Platform, CDR Systems, Canada) consists of a stage that can both move and rotate along the volunteers superior-inferior (SI), anterior-posterior (AP), and left-right (LR) directions using electric motors. The motions produced by the stage are in the millimeter range.

The volunteer will be requested to lie down in a relaxed supine position with their head supported on top of the stage. The AlignRT or Polaris camera system will be initialized and made to track the real-time motions of the volunteer's head. Real-time head motion tracking will proceed for approximately 15 – 30 minutes with either the motion compensation stage turned on or off. All volunteer head motion will be logged for later analysis.

5.3 Subject Withdrawal

Subjects may choose to withdraw at any time with no consequence. Any withdrawals will be replaced in order to have 20 evaluable subjects.

5.3.1 Data Collection and Follow-up for Withdrawn Subjects

Subjects undergo a one-time head motion detection session, there is no follow-up once the session is completed or once subjects withdraw.

6 Statistical Plan

The data collected will not be reviewed until the study is closed to accrual. Volunteer head motion data, acquired in Sec. 5, will then be imported into Matlab research software and analyzed in terms of quantifying several basic motion parameters such as mean and maximum positional deviation, velocity of

the motion, and net motion trajectory. These results will be used to quantify the performance of the head positioning stage in maintaining an accurate head position.

6.1 Sample Size and Power Determination

This is a pilot study to collect baseline data, sample size and power calculation is not necessary.

7 Safety and Adverse Events

The head motion detection sessions are non-invasive and do not involve any procedures that would pose risk to any subject nor result in any adverse events. Adverse events are not applicable to this study and will not be tracked.

7.1.1 Data and Safety Monitoring Plan

The Principal Investigator will monitor the study for data integrity and subject safety. As this study involves non-invasive methods to measure head motion, we determine this study to be of minimal risk to participants.

8 Study Administration, Data Handling and Record Keeping

8.1 Confidentiality

All research personnel will be trained to maintain confidentiality and never to discuss study participants or individual research data publicly or in any private setting where they could be overheard.
Name and date of birth will be collected from subjects only to confirm eligibility. All data collected during the head motion detection session will be identified only by subject number. We will not be collecting any PHI.

8.2 Data Collection and Management

All research files and computer databases will be stored in secure locations within the University of Pennsylvania's Department of Radiation Oncology, with access limited to members of the research team. These data files will be maintained for five years after the study is completed and then destroyed and/or erased. Data will not be shared with the study sponsor. Individual data will be reported only in the aggregate.

9 Study Monitoring, Auditing, and Inspecting

9.1 Study Monitoring Plan

The study PI will be responsible for ensuring the ongoing quality and integrity of the research study.

9.2 Risks and Benefits

There are no risks to volunteers as the optical camera tracking process is passive and the type of motions generated by the motion stage are on the order of millimeters. The data generated by this research study are not expected to benefit the subjects personally. The primary benefit of participation in this study would be to contribute to the development of improved SRS methods. The experimental data do not have any clinical use and will be used only for research purposes.

9.3 Informed Consent Process / HIPAA Authorization

All subjects for this study will be provided a consent form describing this study providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the IRB for the study. Potential subjects will review the consent form in detail with the person designated to consent (either PI or CRC) and have the ability to take the consent home for further review. We request waiver of documentation of

consent as this research is minimal risk and involves procedures for which consent is not required outside of the research context. Health information will not be collected, therefore, HIPAA is not applicable,

10 Study Finances

10.1 Funding Source

This study is funded through NIH grant R01-CA227124-02.

10.2 Conflict of Interest

All University of Pennsylvania Investigators will follow the University of Pennsylvania Policy on Conflicts of Interest Related to Research.

10.3 Subject Stipends or Payments

Subjects will not be compensated for participating in this study.

11 Publication Plan

Data acquired from the proposed studies will be analyzed and if significant will be submitted to peer review journals for publication. In all cases all identifying volunteer information will be removed from the data and the data will be completely anonymized.

12. References

[1] R. D. Wiersma, Z. Wen, M. Sadinski, K. Farrey, and K. M. Yenice, “Development of a frameless stereotactic radiosurgery system based on real-time 6D position monitoring and adaptive head motion compensation,” Phys. Med. Biol., vol. 55, no. 2, pp. 389–401, Jan. 2010.
[2] T. Stafinski, G. S. Jhangri, E. Yan, and D. Menon, “Effectiveness of stereotactic radiosurgery alone or in combination with whole brain radiotherapy compared to conventional surgery and/or whole brain radiotherapy for the treatment of one or more brain metastases: a systematic review and meta-analysis,” Cancer Treat. Rev., vol. 32, no. 3, pp. 203–213, May 2006.
[3] M. J. Murphy, “Intrafraction geometric uncertainties in frameless image-guided radiosurgery,” Int. J. Radiat. Oncol. Biol. Phys., vol. 73, no. 5, pp. 1364–1368, Apr. 2009.