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The Impact of Body Composition on Setup Errors in Patients Undergoing Radiotherapy with Thermoplastic Mask Immobilization: A Single-Center Prospective Cohort Study

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TITLE PAGE

Title:

The Impact of Body Composition on Setup Errors in Patients Undergoing Radiotherapy with Thermoplastic Mask Immobilization: A Single-Center Prospective Cohort Study Protocol (BODY-SET Study)

Running title: Body Composition and Setup Errors in Radiotherapy

INTRODUCTION

Background

Radiotherapy is a cornerstone of cancer treatment, with approximately 50-70% of patients requiring radiotherapy during their disease course. Accurate patient positioning is essential for ensuring adequate target volume coverage while sparing organs at risk. Thermoplastic masks are among the most commonly used immobilization devices; however, setup reproducibility varies considerably among patients. Previous studies have demonstrated that patients with higher body mass index (BMI) exhibit significantly greater setup errors, yet the underlying mechanisms remain poorly understood.

BMI as a predictor—and its limitations

Previous studies have demonstrated that patients with BMI ⩾24 kg/m² exhibit significantly greater setup errors across multiple directions (X, Y, Z axes) in breast, cervical, and thoracic cancers compared with normal-weight patients. In breast cancer, Wan et al. found that BMI ⩾24 kg/m² significantly affected Z-axis (anterior-posterior) setup errors. In cervical cancer, studies have shown that BMI influences the choice of immobilization device—thermoplastic masks are preferred for overweight patients while vacuum cushions are more suitable for normal-weight patients. In thoracic tumors, patients with BMI ⩾24 kg/m² had significantly greater setup errors and higher heart and lung radiation doses compared with normal-weight patients.

However, BMI is a crude anthropometric measure that cannot distinguish between fat and muscle mass—two tissue types with fundamentally different mechanical properties that may affect mask fit and positional reproducibility. Subcutaneous fat affects mask-skin interface compliance, whereas visceral fat may influence intra-abdominal organ mobility. The differential effects of these tissue types on immobilization quality remain unexplored.

The role of body composition

Bioelectrical impedance analysis (BIA) provides a non-invasive, convenient method for

measuring body composition parameters, including skeletal muscle mass (SMM), body fat percentage (BFP), phase angle (PhA), and fat-free mass (FFM). Phase angle, in particular, reflects cell membrane integrity and cellular mass, and has been validated as a sensitive marker of muscle quality and nutritional status in cancer patients. BIA has been successfully used to monitor body composition changes in head and neck cancer patients during radiotherapy, with measurements typically performed at baseline, mid-treatment, and post-treatment. However, the value of BIA-derived body composition parameters in predicting radiotherapy setup errors has not been systematically explored.

Dynamic changes during radiotherapy

Furthermore, radiotherapy-induced weight loss is common, but the underlying tissue loss—muscle versus fat—may differentially affect immobilization over the treatment course. In cervical cancer patients, changes in BMI during radiotherapy have been shown to correlate positively with setup errors. When body weight change exceeds 10%, setup errors increase significantly, suggesting the need for mask re- fabrication. However, no study has examined the temporal relationship between body composition changes (as opposed to simple weight change) and setup error evolution during radiotherapy.

Study rationale and objectives

This protocol describes the BODY-SET study, a prospective cohort study designed to: (1) investigate the association between baseline body composition parameters and setup errors in patients immobilized with thermoplastic masks; (2) analyze the relationship between body composition changes during radiotherapy and setup error evolution; and (3) identify threshold values for body composition changes that trigger clinically significant increases in setup errors.

METHODS AND ANALYSIS

Study design

This is a single-center, prospective observational cohort study conducted at the Department of Radiation Oncology, Shijiazhuang People's Hospital, China. This study has been approved by the Research Ethics Committee of Shijiazhuang People‘s Hospital (approval number: 2026(119), approval date: June 23, 2026).

Study setting and timeline

- Enrollment period: July 1, 2026 to June 30, 2027
- Data collection: July 1, 2026 to December 31, 2027

- Data analysis: January to March 2028

Participants

Inclusion criteria:

1. Pathologically confirmed malignancy
2. Age ⩾18 years
3. Receiving radical or adjuvant intensity-modulated radiotherapy (IMRT) with planned ⩾25 fractions
4. Immobilized with thermoplastic mask
5. ECOG Performance Status 0-2
6. Willing and able to provide written informed consent

Exclusion criteria:

1. Metal implants (pacemaker, artificial joints) affecting BIA measurements
2. Severe edema or ascites
3. Inability to cooperate with immobilization or CBCT scanning
4. Radiotherapy interruption >5 fractions
5. Pregnancy or lactation

Sample size calculation

Based on previous literature, assuming a difference of 1.2 mm (SD 1.8 mm) in setup error between high and low muscle mass groups, with $\alpha=0.05$ (two-sided) and $\beta=0.20$, 36 patients per group are required. Accounting for stratification by disease site (head and neck, thorax, abdomen/pelvis; approximately 40 patients each) and 20% attrition, the target sample size is 120-150 patients.

Study procedures

Baseline assessment (T0, within 1 week before radiotherapy simulation):

- Demographic and clinical data collection (age, sex, height, weight, tumor type, stage, ECOG PS)
- BIA body composition measurement (SMM, BFP, PhA, FFM) using multi-frequency bioelectrical impedance analyzer, performed in the morning before treatment, fasting, after bladder emptying

- CT simulation and thermoplastic mask fabrication according to departmental standard protocol
- L3 vertebral level skeletal muscle and fat area measurement (for validation)

During radiotherapy:

- Daily setup with thermoplastic mask
- CBCT: 3 times in week 1, then weekly
- Six-degree-of-freedom setup errors recorded (Tx, Ty, Tz, Rx, Ry, Rz)
- BIA reassessment at fraction 20 (±2 fractions), maintaining same measurement conditions as T0

Post-radiotherapy:

- Data cleaning and database lock
- Statistical analysis

Outcome measures

Primary outcome:

- Six-degree-of-freedom setup errors (Tx, Ty, Tz, Rx, Ry, Rz) measured by CBCT with gray-value registration

Secondary outcomes:

- Three-dimensional vector error = $\sqrt{(Tx^2+Ty^2+Tz^2)}$
- Changes in body composition parameters (ΔSMM, ΔBFP, ΔPhA, ΔFFM) from T0 to T1
- Correlation between body composition changes and setup error evolution
- ROC-derived threshold values for body composition changes predicting significant setup error increases (>2 mm)

Data collection and management

Data will be collected using standardized case report forms. Double data entry with verification will be performed. Data will be stored in an encrypted electronic database with regular backups. All data will be de-identified using study numbers. Data will be stored for 5 years after study completion.

Statistical analysis

- Descriptive statistics for body composition parameters and setup errors
- Group comparisons: independent t-test or Mann-Whitney U test
- Correlation: Spearman's rank correlation
- Multivariable analysis: multiple linear regression (dependent variable: setup errors; independent variables: SMM, BFP, PhA, BMI, age, disease site)
- Longitudinal analysis: generalized estimating equations (GEE) for repeated CBCT measurements
- Threshold analysis: ROC curves to identify optimal cut-off values
- Significance level: $\alpha=0.05$ (two-sided)
- Software: SPSS 26.0 and R 4.2

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Part 1: Study Introduction

1. Why is this study being done?

Radiotherapy is an important treatment for cancer. Accurate patient positioning is critical for ensuring that radiation is precisely delivered to the tumor. Thermoplastic masks are commonly used for immobilization. We have observed that positioning reproducibility varies among patients with different body types, and body mass index (BMI) alone does not fully reflect body composition—some people have more muscle, others more fat—which may affect the fit of the thermoplastic mask.

This study aims to understand whether **body composition parameters (such as muscle mass and body fat percentage) affect radiotherapy setup accuracy**, in order to develop more personalized immobilization strategies for patients with different body types in the future.

2. Who will be invited to participate?

Patients with pathologically confirmed malignancies receiving radical or adjuvant radiotherapy with thermoplastic mask immobilization at the Department of Radiation Oncology, Shijiazhuang People's Hospital, aged ⩾18 years, with planned radiotherapy course of ⩾25 fractions.

3. How many people will participate?

This study plans to enroll **120-150** participants.

4. What does the study involve?

If you agree to participate, you will need to:

- **Before radiotherapy (1 time)**: We will perform a body composition measurement using bioelectrical impedance analysis (BIA). You will stand on the device for about 2-3 minutes—it is non-invasive, painless, and radiation-free.
- **During radiotherapy**: You will receive radiotherapy according to the standard protocol. The daily cone-beam computed tomography (CBCT) scans performed before each treatment are part of our routine practice; we will record the scan

results for research purposes.

- **Around fraction 20 (1 time)**: We will repeat the body composition measurement to understand how your body composition changes during radiotherapy.

Other than the two additional body composition measurements, this study does not add any extra examinations, blood draws, or radiation exposure.

5. How long will this study last?

From enrollment to the end of radiotherapy, approximately 4-6 weeks.

6. What are the risks of participating?

This is an observational study with no additional interventions. BIA is non-invasive, painless, and radiation-free. CBCT is a routine radiotherapy procedure and does not add extra radiation exposure. **There are no anticipated risks** associated with this study.

7. What are the benefits of participating?

You will not receive direct therapeutic benefit from participating. However, your participation will help us understand the impact of body composition on radiotherapy setup accuracy, providing scientific evidence for improving radiotherapy techniques in the future.

8. Is participation mandatory?

Your participation is entirely voluntary. If you choose not to participate, it will not affect your current or future medical care. Even if you agree to participate, you may withdraw at any time without penalty or loss of benefits.

9. What about costs and compensation?

The BIA body composition measurements are provided free of charge. This study does not provide travel or compensation for lost wages.

10. Will I be paid for participating?

No.

11. What if I am injured as a result of the study?

This is an observational study with no anticipated risks of injury.

12. Will my information be kept confidential?

If you decide to participate, your personal information will be kept confidential. Your

data will be identified by a study code rather than your name. All research staff will protect your identity. Your records will be securely stored and accessible only to research team members. Results will be published in aggregate form without identifiable information.

Additionally, as required by U.S. law, a description of this study will be available at **www.clinicaltrials.gov**. This website will not include information that can identify you. At most, it will include a summary of the results.

13. Who should I contact if I have questions?

For questions about the study, contact **Dr. Chaoxing Liu** at **+86-17603119780**.

For questions about your rights as a research participant, contact the **Research Ethics Committee of Shijiazhuang People's Hospital** at **+86-311-69089455** or **sjzsrmyykjc@163.com**.

Part 2: Signature Page

Investigator's Statement

"I have informed the participant about the background, purpose, procedures, risks, and benefits of this study. I have given him/her sufficient time to read the consent form, discuss it with others, and ask questions. I have informed the participant that they may contact Dr. Chaoxing Liu for study-related questions and the Research Ethics Committee for questions about their rights. I have informed the participant that participation is voluntary and they may withdraw at any time. I have informed the participant that they will receive a copy of this signed consent form."

Investigator Signature: _____ **Date**: _____

Participant's Statement

"I have been informed about the background, purpose, procedures, risks, and benefits of this study. I have had sufficient time and opportunity to ask questions, and I am satisfied with the answers. I have been informed of who to contact if I have questions, concerns, or suggestions. I have read this consent form and agree to participate. I understand that I may withdraw from the study at any time without any reason. I have been informed that I will receive a copy of this signed consent form."

Participant Signature: _____ **Date**: _____

(If the participant lacks decision-making capacity:)

Legally Authorized Representative Signature: _____ **Date**: _____

Relationship to Participant: _____