Study Title: Proning pillows for Intensive Care Unit (ICU): Comparison of chest and pelvis interface pressure distributions between a novel proning pillow system and standard pillows in healthy subjects

Internal Reference No: SP0857

Ethics Ref: N/A

IRAS ID: 304653

Version No: 2.0

Date: 11th January 2022

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the **Liverpool University Hospitals NHS Foundation Trust** SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of Liverpool University Hospitals NHS Foundation Trust

Signature: Date:
.....
......./...../.....

Name (please print):

.....

Position:
.....

Chief Investigator:

Signature: Date:
.....

Name: (please print):Dr Tristan Payne

.....

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Committees	N/A

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host (s), regulatory authorities, and members of the Research Ethics Committee.

TABLE OF CONTENTS

1. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

2. SYNOPSIS

The study will compare the pressure distribution between novel proning pillows and standard pillows used in the ICU. NHS staff will be recruited and will be asked to lie on each pillow for a short period of time. The pressure distribution will be measured using a pressure mat placed between the subject and pillow.

Study Title	Proning pillows for Intensive Care Unit (ICU): Comparison of chest and pelvis interface pressure distributions between a novel proning pillow system and standard pillows in healthy subjects
Internal ref. no.	SP0857
Type of study	Interventional
Trial Design	Cross-sectional comparative study
Trial Participants	NHS staff
Planned Sample Size	50
Follow-up duration	N/A
Planned Trial Period	1 year
Primary Objective	To evaluate any differences in chest and pelvis interface pressures between novel proning pillows and standard pillows used in ICU.
Secondary Objectives	N/A
Primary Endpoint	Peak interface pressure differences between the two pillows
Secondary Endpoints	N/A
Device Name	Prone Pillow System
Manufacturer Name	Putnam Health Co Ltd (Devon, UK)
Principle intended use	The proning system has been specifically designed and shaped to work together to assist with the positioning of proned patients to aid even distribution pressure reducing the number of pressure points and enable positioning in the neutral position to reduce the need for frequent repositioning and therefore need for trained manpower, which in significant shortage due to the surge in COVID patients on 'Critical Care.
Length of time use the device has been in use.	Device has been in use since January 2021

3. ABBREVIATIONS

AE	Adverse event
ADE	Adverse Device Effect
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
CT	Clinical Trials
CTA	Clinical Trials Authorisation
GCP	Good Clinical Practice
GP	General Practitioner
ICF	Informed Consent Form
ICH	International Conference of Harmonisation
LUHFT	Liverpool University Hospitals NHS Foundation Trust
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NRES	National Research Ethics Service (previously known as COREC)
PI	Principal Investigator
PIL	Participant/ Patient Information Leaflet
R&I	R&I Department
REC	Research Ethics Committee
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SIL	Subject Information Leaflet (see PIL)
SOP	Standard Operating Procedure
TMF	Trial Master File
USADE	Unanticipated Serious Adverse Device Effect

4. BACKGROUND AND RATIONALE

During the COVID-19 pandemic, intensive care units (ICUs) across the country have been inundated with increasing numbers of COVID patients. Hypoxic patients in ICU require mechanical ventilation and this can be improved by proning these patients to improve oxygenation and prevent ventilator-induced lung injury (Guerin et al, 2013). Standard practice is to use standard hospital pillows to support the pelvis and chest of the patient while they are proned. These pillows do not provide much support to the patients and often need to be adjusted due to the patient 'sinking' into them. Prolonged pronation also leads to pressure sores in these anatomical locations which burden the Trust financially and also cause distress to patients.

A new proning pillow system was developed by Dr Sashika Selladurai and manufactured for the ICU in Aintree hospital which is made from polyurethane memory foam designed to relieve pressure on the patients and prevent pressure sores that often occur during prolonged proning. The pillow system is also designed to withstand the load of heavier patients and reduce the risk of 'sinking' into the pillows when proned for long periods of time.

The aim of the study is to compare the performance of the new proning pillow system with standard pillows, particularly in relation to the risk of pressure sores, by evaluating differences in chest and pelvis interface pressures between the two pillow types. This will be done by having healthy NHS staff lie on the pillows in the prone position for a short period of time while recording the pressure distribution on the pillows using pressure mats placed between them and the pillows. This will help understand the relative risk of pressure sores developing when the new pillow system is used. It is hypothesised that the new pillow system does not increase the risk of pressure sores developing.

The new proning pillow system is a Class 1 CE marked medical device. The proning pillow system consists of a chest pillow and a pelvis pillow made from memory foam designed to reduce contact pressures and peak interface pressures in patients and allow patients to be placed in neutral position for ventilation.

This research is to be submitted in fulfilment of an academic qualification, a Masters of Science in Clinical Sciences (Clinical Engineering). The student will be doing this project under supervision. The student will recruit participants, take informed consent and take measurements.

5. OBJECTIVES

5.1 Primary Objective

To evaluate any differences in chest and pelvis interface pressures between novel proning pillows and standard pillows used in ICU.

5.2 Secondary Objectives

None

6. CROSS-SECTIONAL COMPARATIVE DESIGN

6.1 Summary of Study Design

Each participant will use both the Proning Pillow System and standard pillows. Each participant will only visit once with no further follow-up periods.

6.2 Primary and Secondary Endpoints/Outcome Measures

The primary outcome measure is the peak interface pressure, as measured by the pressure mat, for both types of pillows.

6.3 Study Participants

6.3.1 Overall Description of Study Participants

Healthy participants working for the NHS.

6.3.2 Inclusion Criteria

- Work for Liverpool University Hospital NHS Foundation Trust
- Participant is willing and able to give informed consent for participation in the study.
- Agree to have weight, height, chest and waist measurements taken
- Agree to the study protocol
- Aged 18 years or above.

6.3.3 Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- Presentation of skin lesions
- Absence of any limb
- Female participant who is pregnant

- Have a lower back problem
- Pain or injury in shoulders or arms
- History of conditions that would make it difficult to lie prone, such as pressure injury or surgery within six months leading up to the study
- Any conditions that significantly affect movement and sensation such as diabetes or mobility limitations

6.4 Study Procedures

6.4.1 Screening and Eligibility Assessment

Staff from the Clinical Engineering Department at the Royal Liverpool University Hospital as well as staff from other departments such as the ICU in Aintree Hospital will be sent an email regarding the study and asked to participate. Staff must be over 18 years of age, and must agree to have their height, weight, chest and waist measured. The email will consist of a description of what the study is about. Interested participants will then be asked if they have any conditions mentioned in the exclusion criteria (Section 0). If they do, they will be excluded.

6.4.2 Informed Consent

The participant must personally sign and date the latest approved version of the informed consent form before any study specific procedures are performed.
Written and verbal versions of the participant information and Informed consent will be presented to the participants detailing no less than: the exact nature of the study; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participants if requested. The original signed

form will be retained at the study site.

6.4.3 Baseline Assessments

Height, weight, gender.

6.4.4 Randomisation and Codebreaking

All participants will lie on both sets of pillows. The only randomisation will be the order of pillows that participants will be asked to lie on.

6.4.5 Subsequent assessments

Once informed consent has been taken, each participant will have their height, weight, waist and chest size measured and recorded, along with their gender. Participants will be asked to remove any belts or large objects that may interfere with the study. The following will then be repeated 3 times for each set of pillows: Each participant will be given instructions and be asked to lie down on the pillows (adjusting the position of the pillows to suit their height if necessary). The participant will then be given a short period of time (~1 minute) to get comfortable. The pressure mat data recording will then start, and the co-investigator will press down on the pressure mat at the approximate location of anatomical landmarks. The participant will continue to lie on the pillow for approximately 3 further minutes to allow pressure measurements to be taken. The participant will be asked to stand up and will be given a short rest period (~30 seconds) before being asked to reposition themselves back on the pillows and get comfortable.

Following this the participant will be given a period of time to recover while the pillows are changed to either standard hospital pillows or the novel proning pillows (the order will be randomized). They will then be asked to lie down again, get comfortable and have pressure measurements taken in the same way as before.

No follow-up assessments will take place.

6.5 Definition of End of Trial

Refer to section 15.

6.6 Discontinuation/ Withdrawal of Participants from Study Treatment

Each participant has the right to withdraw study at any time. In addition, the investigator may discontinue a participant from the study at any time if the investigator considers it necessary for any reason including:

- Non-compliant with the established protocol by moving excessively during the testing
- Ineligibility (either arising during the study or retrospective having been overlooked at screening)
- Significant protocol deviation
- Significant non-compliance with study requirements
- An adverse event which requires discontinuation of the study medication or results in inability to continue to comply with study procedures
- Consent withdrawn

Withdrawn participants will be replaced.

The reason for withdrawal will be recorded in the CRF.
If the participant is withdrawn due to an adverse event, the investigator will arrange for follow-up visits or telephone calls until the adverse event has resolved or stabilised.

6.7 Source Data

CRF entries will be considered source data if the CRF is the site of the original recording (e.g., there is no other written or electronic record of data). In this study the CRF will be used as the source document for weight, height, waist and chest size, and gender.

All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant code, not by name.

7. TREATMENT OFSTUDY PARTICIPANTS

7.1 Description of Study Intervention(s)

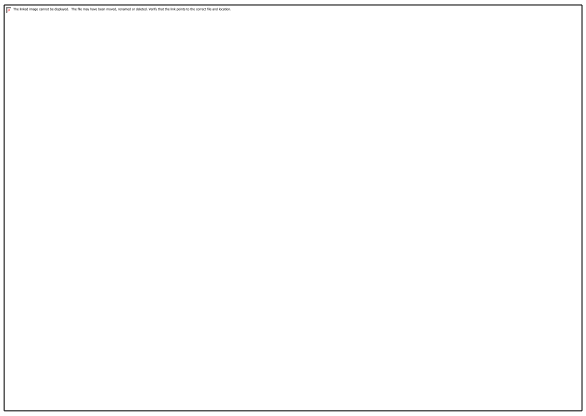
The standard pillows used in the ICU were the Sleepsia Bamboo Pillows, 508mm x 660.4mm x 127mm. Each pillow would be placed under the pelvis and chest.

The novel Proning Pillow System is a CE marked device manufactured by Putnam Health Co Ltd (Eastern wood Road, Langage Industrial Estate, Plympton, Devon, England, PL7 5ET) that includes two separate pillows for the chest and pelvis:

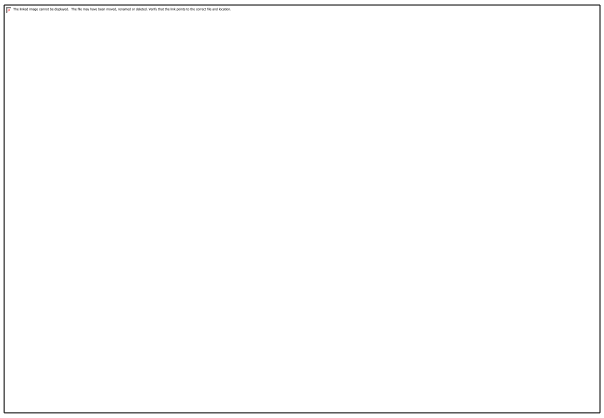
Ortho Solutions chest pillow 800 x 300 x 180 mm

Ortho Solutions Pelvic pillow 700 x 300 x 180 mm

Chest pillow



Pelvic pillow



In each case, a pressure mat (BoditTrak Pro standard, CE 0413) will be placed on each pillow (chest and pelvis). The participant will lie on top of the pillows. The pressure mat will be connected to a laptop which will capture the data using the BodiTrak Pro software.

7.2 Maintenance and storage of device

The pillows, bed and pressure mat will be wiped clean with disinfectant wipes (approved by the Infection Prevention and Control Team) between participants. The pillows will be stored in Aintree hospital.

7.3 Concomitant Medication (if applicable)

N/A

8. SAFETY REPORTING

Definitions for DD, AE, ADE, SAE and SADE are in Section 19.

8.1 Reporting of AE

All AEs occurring during the study observed by the investigator or reported by the participant, whether or not attributed to the device under investigation, will be reported, without undue delay, to the Chief Investigator and LUHFT R&D and recorded on the hospital incident reporting system, in the source data (medical notes) and the CRF. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

8.2 Reporting of DDs/SAEs/SADEs/USADEs

All SAEs, SADEs, and USADEs will be reported to the sponsor/legal representative, Chief Investigator and LUHFT R&D **immediately**; regardless of relationship to the device. DDs that might have led to an SAE if suitable action had not been taken, intervention had not been made or if circumstances had been less fortunate are similarly reported. All SAEs, SADEs and USADEs will be recorded on the hospital incident reporting system, in the source data (medical notes) and the CRF.

Reports of related and unexpected SAEs should be submitted to the Research Ethics Committee (REC)within 15 days of the Chief Investigator becoming aware of the event, using the SAE report form for non-CTIMPs published on the HRA website[1].

All reporting to LUHFT R&D should be by email to RGT@rlbuht.nhs.uk giving as much information about the incident as possible, and should be signed by the PI or Co-investigator. The LUHFT SADE reporting form should be used for LUHFT sponsored studies.

[1] https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/, accessed 16/Aug/2021

The LUHFT R&D Department will undertake an initial review of the information and ensure it is reviewed by LUHFT. Events will be followed up until resolution, any appropriate further information will be sent by the research team in a timely manner.

Reporting to the MHRA will be done in liaison with the Chief Investigator.

8.3: Annual Reports

In addition to the above reporting the Chief Investigator will submit once a year, throughout the trial, or on request a progress/safety report to the REC and R&D.

9. STATISTICS

9.1 Description of Statistical Methods

A model-based approach will be used to test the hypothesis. This approach considers complexities such as repeated measurements, unbalanced observations and determination of the magnitude of effects. The model incorporates the measured peak pressure for each participant at each anatomic location (chest and pelvis) and the two different pillow systems (new and standard).

9.2 The Number of Participants

Based on the complexity of the model used to test the experimental hypotheses, and the fact that the sample size should be of the order of 10 times the number of parameters estimated by the model [Harrell], we estimate a sample size of 50 is required.

9.3 The Level of Statistical Significance and Model Validation

Considering the small sample size and the complexity of the model, a significance level of 0.01 will be considered for rejection of the null hypotheses of no difference between peak pressures, with the aim to control the false discovery rate [Harrell]. However, since it is generally recognised that statistical significance alone doesn't necessarily provide a realistic picture of the underlying processes generating the data [Harrell], other measures of quality of the statistical inference will be reported, namely approximate confidence intervals, Akaike Information Criterion, and analysis of residuals.

9.4 Procedure for Accounting for Missing, Unused, and Spurious Data.

The chosen statistical methods can be applied even with unbalanced observations (i.e. outcomes need not be observed for all possible combinations of the experimental factors pillow and position) [Pinheiro]. Due to the nature of the experimental design and the type of

measurements involved, no missing, unused, or spurious data are expected.

9.6 Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviation(s) from the original statistical will be described and justified in protocol and/or in the final report, as appropriate.

9.7 Inclusion in Analysis

All eligible participants

10. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

11. QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures.

Regular monitoring will be performed according to ICH GCP. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents. Following written standard operating procedures, the monitors will verify that the clinical trial is conducted and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

12. ETHICS

12.1 Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

12.2 ICH Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice R2

12.3 Approvals

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to the Health Research Authority. Local approvals will be sought from participating NHS organisations and the sponsor.

The Chief Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

12.4 Participant Confidentiality

The study staff will ensure that the participants' anonymity is maintained. The participants will be identified only by a participants ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by trial staff and authorised personnel. The study will comply with the Data Protection Act 2018 which requires data to be anonymised as soon as it is practical to do so.

12.5 Other Ethical Considerations

N/A

13. DATA HANDLING AND RECORD KEEPING

Data will be processed under the terms of UK data protection law (including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018).

All study data will be entered on a password-protected Microsoft Excel spreadsheet. Once all data has been captured, the spreadsheet will be locked as read-only to protect the integrity of the data.

All pseudonymous data will be stored on a laptop and on the Clinical Engineering LUHFT departmental network.

The participants will be identified by a study specific participants number and/or code in any database. The name and any other identifying detail will NOT be included in any study data electronic file. A copy of the final published results of the study will be sent to the participants should they wish.

14. FINANCING AND INSURANCE

LUHFT ICU will loan a set of pillows for this study. The pressure mats will be supplied by the Posture and Mobility Service in Bryn-y-Neuadd hospital.

NHS bodies are legally liable for the negligent acts and omissions of their employees. If you are harmed whilst taking part in a clinical trial as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. LUHFT, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional circumstances an ex-gratia payment may be offered.

15. END OF STUDY DEFINITION

End of study definition would be when the set of number of participants have been recruited and completed all elements of the study and data has been analysed.

16. PUBLICATION POLICY

Authors will be defined as those who have made:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; **AND**
- Drafting the work or revising it critically for important intellectual content; **AND**
- Final approval of the version to be published; **AND**
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Contributors who have contributed materially to the paper but whose contributions do not justify authorship will be described clearly in acknowledgements

17. ARCHIVING

Following analysis, data will be fully anonymised then stored in electronic format in Clinical Engineering LUHFT departmental network for at least 15 years. The data will be stored for future ethically approved studies. Archiving will be in line with the sponsor's Standard Operating Procedures.

18. REFERENCES

Guérin, C. et al. Prone positioning in severe acute respiratory distress syndrome. N. Engl. J. Med. 368, 2159–2168 (2013).

F. E. Harrell, Jr. Regression Modeling Strategies, 2nd edition. Springer, 2015.

J. C. Pinehiro, D. M. Bates. Mixed-effects Models in S and S-Plus. Springer, 2000.

19. APPENDIX

19.1 Definitions

19.1.1 Device Deficiency (DD)

This is the inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. Device deficiencies include malfunction, use error and inadequate labelling.

19.1.2 Adverse Event (AE):

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

This includes events related to the investigational device or the comparator and events related to the procedures involved (any procedure in the study protocol). For users or other persons, i.e. where the medical occurrence, unintended disease or injury is not in the subject, this definition is restricted to events related to the use of investigational medical devices or comparators.

No potential AEs are identified.

19.1.3: Adverse Device Effect (ADE)

Adverse event related to the use of an investigation medical device. This includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. This includes the comparator if the comparator is a medical device.

All AEs judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the device qualify as ADEs. For guidance on causality assessment, refer to MEDDEV 2.7/3 Clinical Investigations: Serious Adverse Event Reporting Under Directive 90/385/EEC and 93/42/EEC.

19.1.4: Serious Adverse Event (SAE):

SAE is an adverse event that led to any of the following:

- death

- foetal distress, foetal death or congenital abnormality or birth defect including physical or mental impairment.
- serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
    - a life-threatening illness or injury
    - a permanent impairment of a body structure or a body function including chronic diseases
    - in-patient or prolonged hospitalisation
    - medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function

Planned hospitalisation for a pre-existing condition, or a procedure required by the Study Protocol, without serious deterioration in health, is not considered a serious adverse event.

19.1.5: Serious Adverse Device Effects (SADE):

Adverse device effect that has resulted in any of the consequences of a SAE. This includes device deficiencies that might have led to a SAE if (a) suitable action had not been taken or (b) intervention had not been made or (c) if circumstances had been less fortunate. These are handled under the SAE reporting system.All cases judged by either the reporting medically qualified professional or the sponsor.

19.1.6: Unanticipated Serious Adverse Device Effect (USADE):

Any serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

19.2 Description of Statistical Methods

Suggested statistical approach in more detail.

A model-based approach to hypothesis testing will be applied. This allows incorporation of complexities such as repeated measurements, nested classification factors, unbalanced observations, and determination of the magnitude of effects [Harrell]. The chosen model belongs to the family of linear mixed-effects models [Pinheiro], and it is formulated as follows:

$$\mathbf{y}_{ij} = \mathbf{X}_{ij}\boldsymbol{\beta} + \mathbf{Z}_{i,j}\mathbf{b}_i + \mathbf{Z}_{ij}b_{ij} + \epsilon_{ij}, \quad i = 1, \dots, M, \ j = 1,2$$

$$\mathbf{b}_i \sim N(0, \boldsymbol{\psi}_1), \ b_{ij} \sim N(0, \sigma_2^2), \ \epsilon_{ij} \sim N(0, \sigma^2\mathbf{I})$$

where $\mathbf{y}_{ij}$ is the measured peak pressures for subject i from a sample of size M, at anatomic location j (corresponding to chest and pelvis.) The fixed-effects treatment contrast matrices $\mathbf{X}_{ij}$ encode the experimental factor pillow type (new versus standard). $\mathbf{Z}_{i,j}$ represents the design matrices of the level-1 random effects for subject i on the measurements for anatomic location j within subject i. $\mathbf{Z}_{ij}$ represents the design matrices of the level-2 random effects for anatomic location j within subject i. The normally distributed $\mathbf{b}_i$ are assumed to be independent for different i; and the normally distributed b_{ij} are assumed to be independent for different i or j and to be independent from $\mathbf{b}_i$; finally, the within-group errors ϵ_{ij} (which represent all the variability which is not explained by the model) are assumed to be independent for different i or j and to be independent from the random effects. The parameters to be estimated by the above model are represented by the 2-vector $\boldsymbol{\beta}$, the variance σ_2^2, and the entries of the 2x2 matrix $\boldsymbol{\psi}_1$ (it should be noted that since the latter is a covariance matrix which is forced to be positive definite by construction, only 2 entries need to be estimated.) The total number of parameters is therefore 5.

19.2.1 The Number of Participants

Due to the lack of available information in published sources to determine the effect sizes required for sample size calculation, and due to the complexity of the experimental design, no formal power analysis is possible.

However, a heuristic approach will be applied [Harrell] based on the complexity of the model used to test the experimental hypotheses, namely that the sample size should be of the order of 10 times the number of parameters estimated by the model. With the previous definition of the model complexity, we estimate the sample size to be of the order of $M = 50$.

19.2.2 The Level of Statistical Significance and Model Validation

Considering the small sample size and the complexity of the model, a significance level of 0.01 will be considered for rejection of the null hypotheses of no difference between peak pressures (as represented by parameter β_2), with the aim to control the false discovery rate [Harrell]. However, since it is generally recognised that statistical significance alone doesn't necessarily provide a realistic picture of the underlying processes generating the data [Harrell], other

measures of quality of the statistical inference will be reported, namely approximate confidence intervals, Akaike Information Criterion, and analysis of residuals.

19.2.3 Procedure for Accounting for Missing, Unused, and Spurious Data.

The chosen statistical methods can be applied even with unbalanced observations (i.e. outcomes need not be observed for all possible combinations of the experimental factors pillow and position) [Pinheiro]. Due to the nature of the experimental design and the type of measurements involved, no missing, unused, or spurious data are expected.