STUDY PROTOCOL

A magnetic resonance imaging study of the changes in the angle between the tracheal and laryngeal axes in the sniffing, neutral and head extended positions.

1. INTRODUCTION

1.1 Background

The traditional method of tracheal intubation requires the insertion of a laryngoscope with the left hand into the oral cavity to displace the tongue and directly visualise the glottis.

The "sniffing the morning air" (or "sniffing") position has been traditionally used for tracheal intubation using direct laryngoscopy. This comprises of flexion of the lower cervical spine, extension at the atlanto-occiptal joint and a horizontal level between the tragus of the ear and sternum (Brindley, et al. 2010). The theoretical purpose of this position is to improve the glottic visualisation by aligning the oral, pharyngeal and tracheal axes (Figure 1, B).

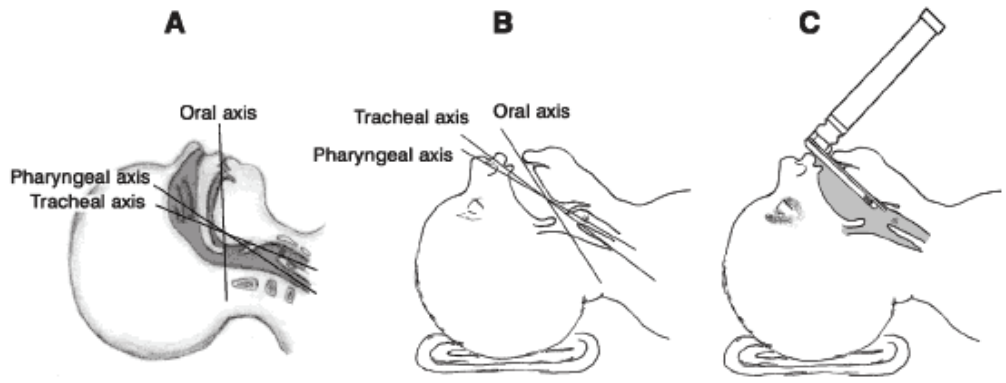

Figure 1. Traditional head and neck position for tracheal intubation

A. Normal head position showing 3 axes in supine position.
B. Sniffing the morning air position with occiput raised showing alignment of 3 axes.
C. Direct laryngoscopy in the sniffing position.

In recent years with the advancement of technology, videolaryngoscopy has become popular and many centres are now using only videolaryngoscopes for tracheal intubation. Visualisation occurs "indirectly" through fibreoptic or digital channels. Most videolaryngoscopes use two types of blades. The Macintosh type for normal airway and hyper-angulated blade for difficult airway.

Hyperangulated blades such as the Glidescope LoPro (Verathon Inc, Bothwell, WA, USA) (Figure 2 B), McGrath Series 5 X blade (Medtronic, Minneapolis, MN, USA) and Storz C-Mac D-blade (Karl Storz Endoscoke, Tuttlingen, Germany) are more curved than the traditional standard geometry (Mcintosh blades – Figure 2 A) used with direct laryngoscopy and are thought to improve glottis visualisation without significant change in head position. However, visualisation of glottis is one of the three steps involved in videolaryngoscopy assisted tracheal intubation. The other two steps include aligning the tube with the glottic inlet and advancing the tube through the glottis into the trachea.

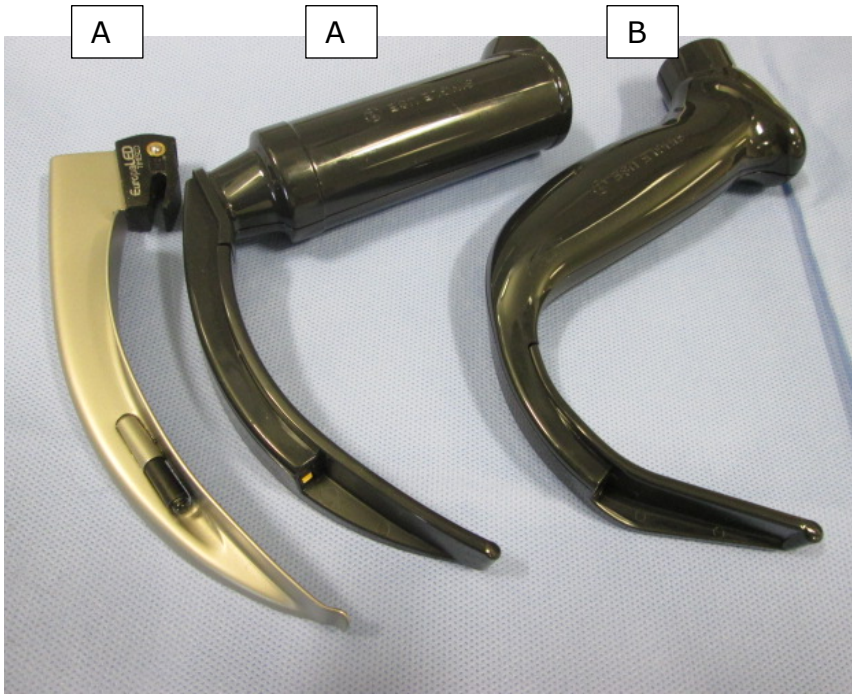

Figure 2. Geometrical comparison of blade types, A: Macintosh (Mac) blades and B: hyper angulated blade

One of the main drawbacks in videolaryngoscopy is that despite good view of glottis on the screen, it can be difficult to successfully advance the tracheal tube into the trachea. Anterior impingement of the tracheal tube at the sub-glottic region is a recognised problem with hyperangulated and channelled videolaryngoscopes (Levitan 2011). VL directs the pre-formed tracheal tube anteriorly but the trachea descends posteriorly into the thorax creating an acute angle impeding passage of the tube (Levitan, et al. 2011). This is demonstrated in figure 3. This can result in difficult intubation or a failed intubation. Manoeuvres such as tube rotation and rotation of bougie (Mendonca, et al. 2018) can rectify this problem to some extent.

Aziz, et al. (2016) found that laryngoscopy was more difficult with hyper-angulated blades in the "sniffing" position compared to neutral position

contradictory to traditional laryngoscopy teaching. Intermediary positions between "sniffing" and supine should be studied as these may balance the needs of maintaining sufficient mouth opening and not hindering angles affecting the axial alignment (Levitan, et al. 2011). Both studies recommend the benefits of a ramped position as it does reduce the time to desaturation and reduces aspiration risk compared to supine neutral positions and should be considered when using hyperangulated blades. Mendonca, et al. (2018) studied neutral and sniffing position with no difference in success rate in tracheal intubation between two positions.

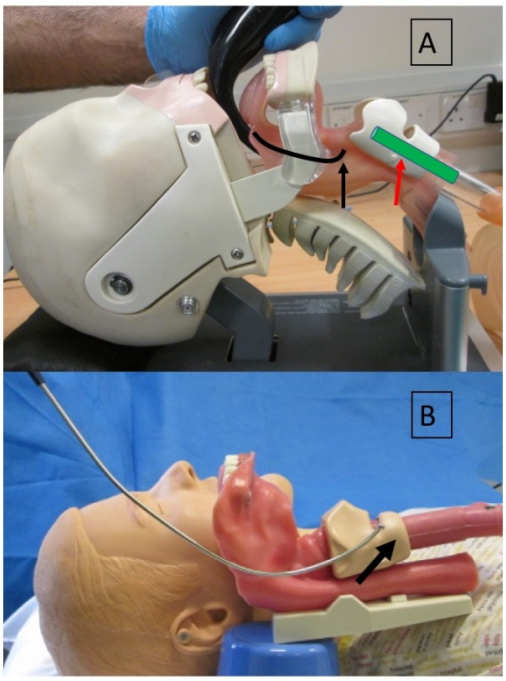

Figure 3. A) Acute angle produced by the trajectory of the tube (black arrow) and the trachea (green tube – marked by red arrow). B) Preformed acute angle stylet directing the tube anteriorly leading to anterior impingement.

Using magnetic resonance imaging in awake and healthy patients, Adnet, et al. measured the oral, pharyngeal and tracheal axes using the neutral position, "sniffing" position and simple head extension and found neither position resulted in perfect alignment of the 3 axes. However, they didn't study the effect of position on angle between tracheal and laryngeal axes. The search for further evidence is necessary for VL as there is a paucity of research in with regard to best head and neck position for videolaryngoscopy.

1.2 Proposed study

This study would assess whether differing head and neck positions would improve alignment between upper airway anatomical axes, in particular the tracheal and laryngeal axes and therefore minimise the possibility of anterior impingement.

1.3 Study population

Staff from University Hospitals Coventry & Warwickshire NHS Trust

1.4 Treatment / Intervention (if applicable)

Magnetic resonance imaging (MRI) can safely be used to assess the upper airway anatomy and would allow measurement of the axes described to suggest which head and neck position would provide best anatomical alignment to reduce anterior impingement.

All the MRI scans will be conducted using 3.0 Tesla (Optima 750w, GE Medical, Milwaukee, WI, USA) using the cervical spine section of the coil. T2-weighted images in the sagittal plane will be acquired using a fast recovery fast spin echo (FRFSE) technique with the parameters in Table 1. The scans will take around two and half minutes and a member of the anaesthetic investigator team will be present to facilitate positional changes and maintain consistency.

Acquisition parameters (Table 1):

Repetition time (TR)	2905 ms
Echo time (TE)	107ms
Field of view (FOV)	36 cm
Slice thickness	3 mm
Slice gap	1 mm
ETL	19
Frequency matrix size	352
Phase matrix size	320
Number of excitations (NEX)	3
Receiver band width	41.67 kHz
Scan time	2 min 34 s

MRI scanning will be performed in following 3 head and neck positions:

Neutral position- Participant lying flat on the MRI table, with a vertical gaze, without any pillow (no flexion, no extension of the neck).

Sniffing position is achieved with head resting on Oxford HELP headrest (Alma Medical, London) of 7cm in height to achieve neck flexion by 35° and extension at atlantooccipital joint to achieve face plane extension of 15° (Horton WA 1989)

Extension position: Oxford HELP Base pillow (Alma Medical, London) is placed under the shoulders with head resting off the end and neck in full extension position.

2. RATIONALE

2.1 Aims and hypothesis

To determine which patient positioning significantly improves the alpha (α) angle. It is defined as the angle between the tracheal axis (TA) and laryngeal axis (LA). This can be seen in Figure 4 below.

Other two angles measured would be:

- Beta (β) angle between the laryngeal axes (LA) and pharyngeal axes (LA)
- Delta (δ) angle between pharyngeal axes (PA) and oral axes (OA)

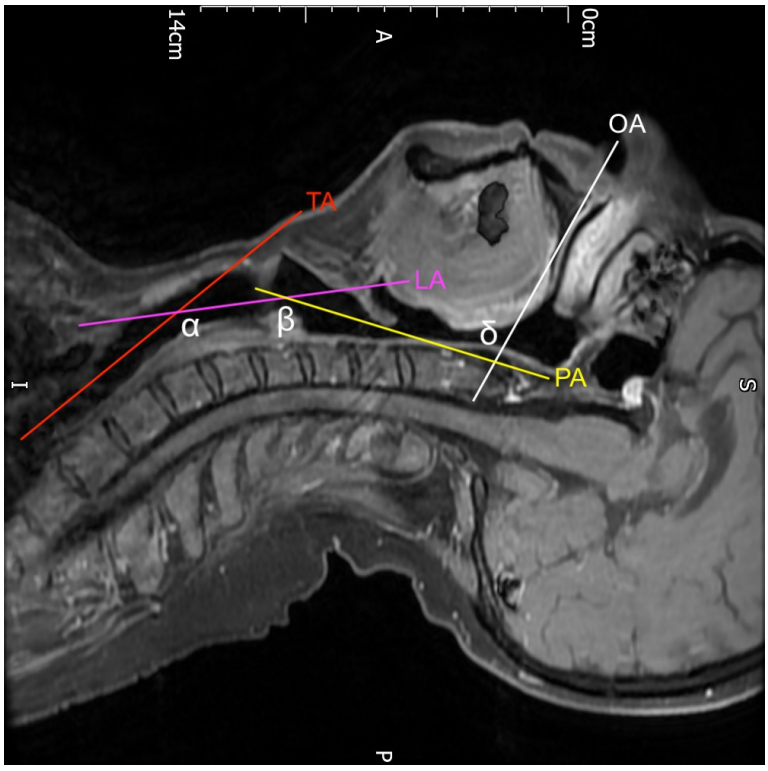

Figure 4. MRI scan showing tracheal, laryngeal axes and pharyngeal axes and corresponding α angle, β angle and δ angle

- The tracheal axis (TA) is defined as a line passing through the centre of intrathoracic part of trachea to the centre of cricoid cartilage.

- The laryngeal axes (LA) is defined as a line passing through the centre of cricoid cartilage to the base of the epiglottis.
- The pharyngeal axis (PA) is defined as a line passing through the anterior portion of the atlas and C2.
- The oral axis (OA) is defined as straight line drawn parallel to the hard palate

2.2 Justification

Videolaryngoscopy (VL) has become a standard of care in anaesthesia and they are included in airway management guidelines. VLs are gradually replacing direct laryngoscopes. For a direct laryngoscopy and tracheal intubation, the sniffing position has been considered as ideal. When this position is transferred to VL, problems such as anterior impingement occur where the tube tip hits the anterior wall of trachea and fails to advance further. Aziz, et al. (2016) found that the "sniffing" position made intubation more difficult than the neutral position. It is therefore critically important to determine what head positions are important to use with VL.

The use of MRI in healthy subjects has been attempted previously to determine the geometrical axes within the oral cavity (Adnet, et al. 2001). These researchers however did not specifically consider the alpha angle we have defined which could reduce anterior impingement with VL. Anterior impingement is an important consideration as it can result in failed intubation and this is clinically important if VL is used as a rescue device in an emergency.

We hypothesise that the position that improves the alpha angle the most would be considered as the ideal position for videolaryngoscopy and tracheal intubation. Due to the widespread and increasing use of videolaryngoscopes, this study would help us to recommend an ideal head and neck position. This will further help to improve the first attempt success rate of tracheal intubation.

2.3 Assessment and management of risk

There are no anticipated risks in undergoing MRI scan. Participants will have to complete the MRI safety checklist and have this reviewed by a radiographer for any risks before they can enter the scanner.

Process if inadvertent abnormality is found: Participants will be asked to consent to any abnormal finding of significance to be reported to their GP

Other considerations:

- Risk of claustrophobia and loud noise can occur during the scan. Ear defenders and an emergency button will be provided as per standard MRI practice.
- Participants will be given the option to withdraw at any stage if they feel that they are not able to tolerating lying down within the MRI Scanner.
- We would also advise participants who are pregnant or who have devices or medical conditions that can be exacerbated by these experiences to not partake.

3. OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary objective

- Measurement alpha (α) angle between the tracheal axis (TA) and laryngeal axes (LA) in three different positions.

The primary objective is to identify which of the three head and neck positions we have identified ("sniffing", extension of neck and neutral position) improves the alpha angle when examined under MRI. We hypothesise the position that most improves the alpha angle would reduce the incidence of anterior impingement with videolaryngoscopy. We hypothesise the position that brings the alpha angle closest to 180° would reduce the incidence of anterior impingement and therefore considered best for tracheal intubation using VL.

3.2 Secondary objectives

The other two angle measurements include

Beta (β) angle between laryngeal (LA) and pharyngeal axes (PA). This is the alignment between line passing through the voice box and pharynx (on the MRI image line passes through the top part of second cervical vertebra)

Delta (δ) angle between pharyngeal axes (PA) and oral axes (OA). This is the alignment between pharyngeal axis and the line passing parallel to the palate.

The MRI reports will be interpreted by a Consultant Radiologist.

3.3 Primary endpoint/outcome

The alpha (α) angle in degrees.

3.4 Secondary endpoints/outcomes

The Beta (β) angle and Delta (δ) angle in degrees

4. STUDY DESIGN

Controlled trial without randomisation

5. STUDY SETTING

Single centre study at University Hospitals Coventry and Warwickshire NHS Trust

6. ELIGIBILITY CRITERIA

6.1 Inclusion criteria

- Able to provide consent
- Volunteers, UHCW staff, aged > 18 years
- Medically able and willing undertake MRI scanning.

- Should pass the MRI safety check list to enter the MRI suite. All participants will complete an MR safety questionnaire immediately prior to their MR scan

6.1 Exclusion criteria

- Unable to provide consent
- Not willing to have MRI scan or unable to undergo MRI scanning and restricted neck movements. For MRI safety reasons all participants with a cardiac pacemaker or other electronic implants will be excluded from the study.

7. TRIAL PROCEDURES

Screening

Step 1 – Convenience sampling used to recruit participants (UHCW Staff) by the investigators. Inclusion and exclusion criteria will be discussed. Aim to recruit 2 participants every week. We anticipate this phase will take 10 -12 weeks.

Baseline

Step 2- Information leaflet provided and study outcomes discussed. MRI safety questionnaire also reviewed by the potential participant. Any reasons that would preclude positioning in an MRI machine will also be recorded.

Participants will be allowed to enough time to read and understand the participant information. The procedure for any abnormal findings will be discussed in consent and in the participant information sheet.

Step 3 – For participants who would like to volunteer, consent form signed. Any queries clarified. Baseline demographic and airway assessment recorded. This data will be stored securely within the research locker located in the Anaesthetic department, UHCW.

Pre-booked MRI slot in the future is allocated to the participant.

Step 4 - Participants will be reminded about MRI slot 1 day prior to scan

MRI Suite

Step 4 – Participants attend MRI Suite, UHCW Radiology department at specified time. MRI Safety questionnaire reviewed again and completed for Radiology department. Any remaining questions answered by anaesthetic investigators and/or radiographer.

Step 5 – MRI Conduct. Anticipate each scan will take 2.5 minutes (total 7.5 minutes for 3 scans), with re-positioning in the middle by one of the Anaesthetic investigators. Including questions and filling out questionnaire anticipate this will take 30 minutes per participant in total.

There is capacity to scan 2 participants per week on per pre-booked MRI slot and therefore this phase will take at the minimum 10 to 12 weeks.

Participant involvement ends with MRI scan in the final head and neck position.

Review
Step 6 – This sequence will produce three sagittal MRI images per participant. These images will have their personal data removed and will be pseudo-anonymised (tokenization) after the images have been reviewed for any abnormal findings and the angles will be measured by the Consultant Radiologist.

Step 7 – Tokenized results analysed by Anaesthetic investigator team

Step 8 – Further anonymised data will be analysed by the statistician and anticipate this will take another 6 -8 weeks.

7.1 Recruitment
Staff members of University Hospitals Coventry and Warwickshire NHS Trust (UHCW) will be invited to participate as volunteers in this study. This will be sampled conveniently, and the inclusion and exclusion criteria will be checked. They will then review the MRI safety check list for eligibility to undergo MRU scan. Written informed consent will be obtained from the participants.

7.1.1 Screening
Participants will be provided information regarding preparation for an MRI and questions related to this will be answered by the lead radiographer.

Standard operating procedure for patients undertaking an MRI will be followed and led by the radiographer present. At the scan, a member of the anaesthetic investigator team will be present to re-confirm (verbal) consent and facilitate the scan by ensure consistency between positions.

The patient will undergo three MRI scans. At the end of this the participant will be thanked for their involvement. We will state that if they have any questions to contact the research team and if they would like results of the study they can be contacted in the future.

7.1.2 Payment

No payment will be offered for volunteers to this study

7.2 Consent

A written consent will be obtained from all participants. All investigators will be suitably trained to obtain consent as per Good Clinical Practice.

MRI safety questionnaire as per Radiology Information Governance also required.

7.3 Baseline data

Baseline demographic data:

- Age
- Sex

- Ethnicity
- Height
- Weight

Baseline airway assessment data:

- Mallampati score
- Jaw protrusion
- Neck movement
- Thyromental distance
- Sternomental distance

7.4 Long term follow-up assessments

No long-term follow-up is planned for this study.

7.5 End of study definition

This will occur when the 20th patient has their final MRI study performed

8. STATISTICS AND DATA ANALYSIS

8.1 Sample size calculation

Previous studies on volunteers involving radiological imaging recruited 8 , 15 and 42 patients (Adnet. et al, Abramson. et al and Greenland. et al). We aim to recruit 20 volunteers (UHCW staff) to participate in the study.

8.2 Planned recruitment rate

We plan to recruit 10 volunteers every 4 weeks, totally 8 weeks. This will total 20 participants. Recruitment will be undertaken by each of the three Anaesthetic investigators and therefore this is a realistic target due to the relatively small number of participants required.

8.3 Statistical analysis plan

8.3.1 Primary outcome analysis

Data will be analysed using ANOVA or appropriate test and p value less than 0.05 was considered statistically significant

8.3.2 Secondary outcome analysis

Data will be analysed using ANOVA or appropriate test and p value of 0.05 or less will be considered statistically significant

8.4 Subgroup analyses

Subgroup analysis may be possible depending on baseline demographic data.

8.5 Participant population

All participant data will be included in the final analysis if they have attended for the MRI scanning. We will endeavour to ensure this does not occur by reminding participants of scheduled MRI dates and ensuring any concerns are answered fully.

8.6 Procedure(s) to account for missing or spurious data

All data collected from the initial recruitment will be included in the study. Investigators will be trained and be adequately skilled to record the baseline demographic data and the airway assessment data. Participants will be pseudo-anonymised. Any participants who do not attend for the MRI scanning, and therefore will have no MRI images for the study, will not be included in the final analysis.

9. DATA MANAGEMENT

9.1 Data collection tools and source document identification

Data will be collected by the Anaesthetic investigator team. These will be recorded on a case report form (CRF) including the background demographic data. All stored data will comply with Good Clinical Practice guidelines and General Data Protection Regulation (GDPR).

9.2 Data handling and record keeping

All participant data will be handled by the investigator team (MRI radiographer, Consultant Radiologist and Anaesthetic investigator team), and protected on UHCW trust server which is username and password protected.

In terms of the MRI images, these will not be linked to the volunteer's real hospital data. We aim to keep confidentiality by coding each participant (pseudo anonymisation), and each scan (i.e. participant 1, first scan = 1A, second scan = 1B etc).

Hard copies of informed consent will be stored in a locked cabinet within the Anaesthetic department at UHCW. MRI safety questionnaires will be stored as per standard Radiology policy for Information Governance. Personal data will be collected for consent and safety checklists. Access to this data will be by the research team and radiographer to ensure safety check list is correctly completed.

All local investigators will be trained in accordance with the UK Policy Framework for Health and Social Care Research.

9.3 Access to Data

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 - in line with participant consent.

9.4 Archiving

Following the resolution of queries and confirmation of study close-out by the Chief Investigator, all essential documentation will transferred to a third party archiving service, which provides suitable fire and water-resistant facilities. Study files will be archived for a period of 25 years. Access to the study documentation will be restricted to named individuals within the study team with express permission from the Chief Investigator.

10. TRIAL OVERSIGHT

10.1 Role and responsibilities of the Sponsor

UHCW has agreed to act as sponsor for this trial and will undertake the responsibilities of sponsor as defined by the UK Policy Framework for Health and Social Care Research and ICH Good Clinical Practice. An authorised representative of the Sponsor has approved the final version of this protocol with respect to the trial design, conduct, data analysis and interpretation and plans for publication and dissemination of results. As sponsor, UHCW provides indemnity for this trial and, as such, will be responsible for claims for any negligent harm suffered by anyone as a result of participating in this trial. The indemnity is renewed on an annual basis and will continue for the duration of this trial.

10.1.1 Principal Investigators

The Principal Investigator responsibilities include, but are not limited to:

- Ensuring that the trial is conducted as set out in the protocol and supporting documents
- Delegating trial related responsibilities only to suitably trained and qualified personnel and ensuring that those with delegated responsibilities fully understand and agree to the duties being delegated to them;
- Ensuring that CVs and evidence of appropriate training for all Site staff are available in the Trial Site File
- Ensuring that all delegated duties are captured in the study Delegation Log
- Ensuring all Adverse Events are documented and reported promptly to the Trial Manager;
- Accountability for trial treatments at their site;
- Ensuring the trial is conducted in accordance with ICH GCP principles;
- Allowing access to source data for monitoring, audit and inspection;
- Ensuring that all source data is complete and provided to the Trial Manager at regular intervals

11. MONITORING, AUDIT & INSPECTION

The study will be monitored by the Research and Development Department at UHCW as representatives of the Sponsor, UHCW. This is to ensure the study is conducted as per protocol, adhering to Good Clinical Practice and Research Governance.

12. ETHICAL AND REGULATORY CONSIDERATIONS

12.1 Ethical approval and research governance

The study will be conducted in compliance with the principles of the ICH GCP guidelines and in accordance with all applicable regulatory guidance, including, but not limited to, the UK policy framework for health and social care research. Ethical approval for this study will be sought from the Research Ethics Committee combined with Health Research Authority (HRA) approval. No study activities will commence until favourable ethical opinion and HRA approval has been obtained. Progress reports and a final report at the conclusion of the trial will be submitted to the approving REC within the timelines defined by the committee. Confirmation of capacity and capability will be obtained from the R&D department prior to commencement of the study at all participating sites.

12.2 Data protection and patient confidentiality

The study will comply with the current Data Protection regulations and regular checks and monitoring will be undertaken by the Trial Manger to ensure compliance. Participants will be assigned a unique identifier upon enrolment in to the study to allow pseudonymisation of patient-identifiable data. Access to patient identifiable data will be restricted to members of the study co-ordination team who require it for the performance of their role. Electronic data will be stored on password protected encrypted drives and hard copies of study documents will be stored in locked filing cabinets in secure entry-card protected sites.

12.3 Safety reporting

Regarding incidental findings of anomalies on MRI scanning:

During consenting we will ask volunteers to consent for the investigators to be allowed to write to their General Practitioner (GP) if any untoward findings are found incidentally on the reported MRI scans by the Consultant Radiologist. The process will include a copy of the MRI report with a supplementary letter written to the GP asking them to follow-up with the volunteer in regards to their incidental MRI findings.

13. DISSEMINATION POLICY

The results of this study are to be presented locally at the UHCW Department of Anaesthesia Quality Improvement Meeting (QIPS), which is held monthly. This may promote education on altering head positioning when videolaryngoscopy is used.

We will aim to publish the results within an anaesthetic journal for dissemination to a wider audience. As this the first MRI study looking at best head and neck position for videolaryngoscopy, we hope in the future that this study would provide the first step into providing formal guidance for positioning with videolaryngoscopy.

We will aim to publicise the results to the wider public through a plain English, lay summary of findings.

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