Protocol details

1.1 ***PROTOCOL TITLE:*** What is the scope for low field MRI to replace cone beam computed tomography in dentistry?

1.2 Names (titles), roles and contact details of:

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1.3 Protocol details

Version number: 1.0
Final/draft: Final
Date: 14/03/2025

2 Signature Page

The Chief Investigator and the R&D (sponsor office) have discussed this protocol. The investigators agree to perform the investigations and to abide by this protocol

Chief investigator

[Insert name of CI]

Signature Date

Sponsor Representative

R&D to Add
GSTFT

Signature Date

This Protocol template is intended for use with UK sites only.

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3 List of Abbreviations and Definitions

AE	Adverse Event
AR	Adverse Reaction
ASR	Annual Safety Report
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
EC	European Commission
GAfREC	Governance Arrangements for NHS Research Ethics Committees
ICF	Informed Consent Form
ISRCTN	International Standard Randomised Controlled Trial Number
MA	Marketing Authorisation
MS	Member State
Main REC	Main Research Ethics Committee
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
Participant	An individual who takes part in a clinical trial
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedure
SSA	Site Specific Assessment
TMG	Trial Management Group
TSC	Trial Steering Committee

4 Summary/Synopsis

Title	What is the scope for low field MRI to replace cone beam computed tomography in dentistry?
Protocol Short Title/Acronym	DDMRI
Protocol Version number and Date	V1.0 14/03/2025
Study Phase if not mentioned in title	Prospective cohort study
Is the study a Pilot?	Yes
IRAS Number	304665
REC Reference	TBC
Sponsor Reference	EDGE 166436
Study Duration	24 months
Methodology	Feasibility investigation of a new imaging modality
Sponsor name	Guy's and St-Thomas' Foundation Trust and King's College London
Chief Investigator	Dr. Saoirse O'Toole
Funder Name	N/A
Medical condition or disease under investigation	Orofacial Pathologies
Purpose of research study	To optimise imaging parameters and assess diagnostic value of MRI in orofacial conditions
Primary objective	To determine the diagnostic accuracy of MRI compared to standard of care
Secondary objective (s)	To optimise imaging parameters and assess health resource use
Number of Subjects/Patients	50
Trial Design	Comparative effectiveness trial
Endpoints	Software parameters and applications assessed for delivery of standard of care
Main Inclusion Criteria	Patients requiring imaging of an orofacial pathology
Statistical Methodology and Analysis	This is a feasibility study. Initial qualitative assessments of diagnostic accuracy will be made. We will then use simple descriptives assessing the number of patients who were eligible to use the radiation free imaging modality (MRI) and those that required further conventional radiography. Health resource use will also be documented and compared using simple descriptives as part of this pilot investigation.

Introduction

Magnetic Resonance Imaging (MRI) has emerged as a powerful diagnostic tool that offers numerous advantages over conventional radiography techniques. Unlike traditional X-ray or computed tomography (CT) scans, MRI utilizes a magnetic field and radio waves to generate detailed and high-resolution images of the body's internal structures. This non-invasive imaging modality provides a wealth of benefits, including superior soft tissue visualization, multiplanar imaging capabilities, and the absence of ionizing radiation. Furthermore, MRI enables the detection and characterization of a wide range of pathologies with exceptional accuracy, leading to improved diagnostic capabilities and better patient outcomes.

To date, the use of MRI in dentistry has been limited. This is due to several reasons

1. Cost: MRI machines are expensive to purchase, operate, and maintain. The high cost associated with MRI equipment and procedures makes it less feasible for routine dental imaging, where other more cost-effective imaging modalities like conventional 2D X-rays and Cone Beam Computed Tomography (CBCT) are available.
2. Accessibility: MRI machines are larger and require more space compared to dental radiographic equipment.
3. Time: MRI scans can take longer to perform compared to other imaging modalities. The longer scan times associated with MRI have, to-date, been impractical in a dental setting.
4. Hard tissue focus: MRI imaging is typically suited for examining soft tissues, such as muscles, ligaments, and organs. In dental applications, the primary focus is on the teeth and jawbones, which can be easily visualized with conventional X-rays or CBCT. Typical MRI machines have not provided the same level of detail and resolution for dental structures as these other modalities.

However, recent developments have led to the development of a dental-specific coil for use with a low field strength (0.55 Tesla) MRI scanner, without the use of exogenous contrast agents. This has resulted in high diagnostic quality soft and hard tissue images and reduced imaging time.

As this imaging modality has rarely been used before in dentistry, the aim of this study is to investigate its use for dental imaging, refining parameters and assessing the diagnostic quality of dental scans taken using MRI and the specific dental coil. We will be getting a CE marked coil and present its documents. We will use the coil in the manner it is certified for to run standard Siemens protocols on selected patients under a stated ethics. The aim is to get exploratory data so we can better understand how to optimise clinical examinations in the future.

5 Trial objectives and purpose

The overall aim of this feasibility project is to optimise MRI parameters for dental use (i.e., dental-dedicated MRI)and assess the diagnostic quality of dental scans taken using MRI.

The objectives are to assess if MRI imaging has altered the diagnosis, retrospectively analyse the numbers of patients which can be diagnosed effectively using this radiation free imaging modality and document health resource use to inform a full health technology assessment trial.

The primary objective is to assess the feasibility of providing MRI scanning to dental patients and the resultant benefit. As such we will examine the percentage of patients whose diagnosis was altered as a result of additional MRI scanning.

The secondary objectives are to assess:

1. The percentage of patients who would have been able to complete their diagnosis with an MRI scan alone

2. Percentage of eligible patients who agreed to have an MRI scan

3. Percentage of patients who completed the MRI scan

4. Clinician rated diagnostic acceptability

5. Patient acceptability of the imaging modality (as determined by VAS scale)

6. Documentation of Health resource use including intervention costs

6 Study design & Flowchart

6.1 Study Design

This will be a single-centre, tertiary care based, interdisciplinary prospective cohort study. Patients requiring orofacial imaging, provided their treating clinician would see significant value in obtaining an MRI image, will be invited to take a dental-dedicated MRI scan in addition to conventional dental radiography. The diagnostic value of the MRI scan will be graded by the treating clinician. Separately a member of the research team will grade the scan quality and diagnostic value and also provide a diagnostic report relating to the data collected. Data will be collected on age, gender, ethnicity, medical condition etc and the number of patients who could be effectively diagnosed using dental-dedicated MRI alone, versus those who needed an additional scan modality such as a Cone Beam CT or conventional CT will be documented.

Primary outcome: Percentage of patients whose diagnosis/care changed as a result of the additional dental MRI imaging compared to the total number of patients imaged using conventional radiography.

Secondary outcomes

We will also record:

1. Whether the diagnosis could have been obtained using dental-dedicated MRI alone
2. Differences in scanning time
3. Differences in radiation exposure
4. Health resources used
5. Patient visual analog scale when they use both modalities

6.2 Flowchart

	Initial Consultation	Visit 1: MRI scan	Visit 2: Reassessment
Eligibility checked by treating clinician and research dentist	x		
Conventional Radiography obtained (3-5 min)	x		
Patient Information sheet given (1 min)	x		
Consent for additional screening procedures (5 min)	x		
MRI Scan (10-20 min)		x	
Patient VAS questionnaire (<1 min)	x	x	
Treating clinician assesses report and diagnostic value of MRI			x
Advises patient of diagnosis (5-10min)			x
Document Health Resource Use	x	x	x

7 Subject selection

This will be a single-centre, tertiary care based, interdisciplinary prospective cohort study. Participants will be recruited from King's Health Partners Dental Service. Potential participants will be identified by the direct care team at their consultation in clinic. Patients (or their carers/guardians) referred for investigation of an orofacial pathology which may have a soft tissue pathological component will be informed by their direct care team that they or their child may be eligible to be imaged using a novel, radiation-free imaging modality and asked if they would like to speak to a research dentist or nurse about participation.

7.1 Subject inclusion criteria

1. Patients aged 3 or over with suspected orofacial pathology involving a soft tissue component or healthy volunteers
2. The patient is willing to undergo an MRI investigation
3. Patient or their carer/guardian is able to provide informed consent to the study

7.2 Subject exclusion criteria

1. Patient or their carer is unable to show Gillick competency for consent.
2. The patient has pronounced claustrophobia.

3. The patient has a pacemaker or implanted defibrillator.
4. The patient has history of metal shrapnel injuries to the eyes or MRI incompatible metallic inclusions or implants/ large tattoos.
5. The patient has non-removable piercings.
6. Pregnant patients, or patients who suspect they could be pregnant

7. The patient has participated in other research studies within the previous 30 days.

8 Study procedures

8.1 Subject recruitment

Initial Consultation

Participants will be recruited from Guy's and St Thomas's Hospital dental services. Potential participants will be identified by the direct care team before or at their consultation visit in clinic by assessing their follow up status or referral letter. Patients or the guardian/carers of patients who require dental imaging of an orofacial pathology with a possible soft tissue pathological component will be informed by the direct care team that they may be eligible to be imaged using a novel radiation-free dental MRI scan in addition to conventional radiography.

Interested participants will then be asked additional questions about claustrophobia, previous implant history and piercings. Most dental implants are non ferromagnetic – making them perfectly safe to enter an MRI scanner, as are orthodontic brackets, but their stability should be checked prior to the scan. Eligibility of all screened participants will be assessed according to the inclusion and exclusion criteria. They or their parents will then be provided with a patient information sheet and given a minimum of 24 hours to make their decision.

8.2 Imaging Procedures

Visit 1

If participants agree to take part in the study, they will be given a separate appointment at the Advanced MRI centre at St Thomas's Hospital. Full written informed consent will be obtained by the research nurse or dentist and, participants will undergo a brief screening by the MRI radiographer to ensure that they have no implants or piercings in place. They will then undergo a dental-dedicated MRI scan, which does not include the use of exougenous contrast agents. This will be directly uploaded onto the patient's permanent medical file via the current cloud-based, secure Patient Archiving and Communicating System (PACS) called Epic. A VAS questionnaire of Magnetic Resonance Imaging and conventional radiographic imaging acceptability will be given to the patient. An oral maxillofacial radiologist will review the scan and make a report in conjunction with a neuroradiologist/head and neck radiologist if required.

Visit 2

At their follow up consultation, the treating clinician will have access to the dental-dedicated MRI and report. It will then assess if the diagnosis has changed in the light of the MRI report. Pathologies visible on the dental-dedicated MRI will be compared to pathologies visible on the conventional radiography. Clinicians will then be given a clinician Likert questionnaire.

8.3 Masking & other measures taken to avoid bias

8.3.1 Masking

An independent oral maxillofacial radiologist will review the dental-dedicated MRI scan and inspect if the scan was of sufficient diagnostic value independent of the conventional radiography. In the case of a disagreement between the clinician and oral maxillofacial radiologist, a third clinician or oral maxillofacial radiologist will be invited to give a third opinion.

8.4 Patient and Clinician Acceptability

VAS scores of imaging modality accepatability from patients will be compared

Clinician likert scores of MRI accepatability will be recorded.

8.5 Health Economics

During this feasibility phase, we will collect simple descriptives on health resource use on an excel spreadsheet.

8.6 End of Study Definition

The end of study is defined as when the diagnostic quality of the dental MRI machine/scans has been assessed, a signal of clinical efficacy has been obtained and health economic resource use has been documented to enable power calculations for a definitive health technology assessment.

9 Assessment of Safety

All adverse events (AEs) will be recorded from when the participant was first enrolled in the study. AEs will be classified according to severity and whether related to the study intervention. The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amended Regulations 2006 gives the following definitions:

- Adverse Event (AE): Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

- Serious adverse Event (SAE): Any adverse event that:
  - results in death;

- is life-threatening;
- required hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability or incapacity;
- consists of a congenital anomaly or birth defect.

• Important Medical Events (IME) & Pregnancy: Events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the participant or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious. Although not a serious adverse event, any unplanned pregnancy will also be reported via the SAE reporting system.

All SAEs will be reported immediately by the Chief Investigator (and no later than 24hrs) to the GSTT R&D office (Sponsor).

9.1 Ethics Reporting

Reports of related and unexpected SAEs will be submitted to the Main REC within 15 days of the chief investigator becoming aware of the event, using the NRES template. The form will be completed in typescript and signed by the chief investigator. The main REC will acknowledge receipt of safety reports within 30 days. A copy of the SAE notification and acknowledgement receipt will be sent to the R&D Directorate.

9.2 Trial Management Group

There is an inter-disciplinary research team of clinical academics consisting of dentists, oral surgeons, oral and maxillofacial radiologists and neurologist. If any safety concerns become apparent there will be an emergency meeting set up for optimal care or changes to the protocol. The chief investigator is responsible for trial oversight.

9.3 Ethics & Regulatory Approvals

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (1996), the principles of GCP and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework and the Medicines for Human Use (Clinical Trial) Regulations 2004, as amended in 2006 and any subsequent amendments.

This protocol and related documents (PIS, ICF and MRI report template) will be submitted for review to Research Ethics Committee (REC) under the HRA.

10 Compliance and withdrawal

10.1 Subject compliance

Compliance with the dental MRI scan will be assessed by recording the number of patients who were booked in for a scan versus the number of patients who did not complete the scan.
If the patient is unable to comply with the device, conventional radiography will be performed.

10.2 Withdrawal / dropout of subjects

Participants will be free to withdraw at any stage of their assessment journey with no impact to their clinical care. If a patient withdraws, drops out or loses capacity to consent/assent, data that has been deidentified will be retained for analysis. Data will be analysed per protocol. If a patient withdraws prior to receiving the MRI scan, they will return to standard of care and another participant will be recruited.

10.3 Protocol Compliance

All non-compliances with the protocol will be documented. As this is a feasibility study any deviations from the protocol will be discussed with our PPI group and research team and will inform definitive care protocols.

11 Data

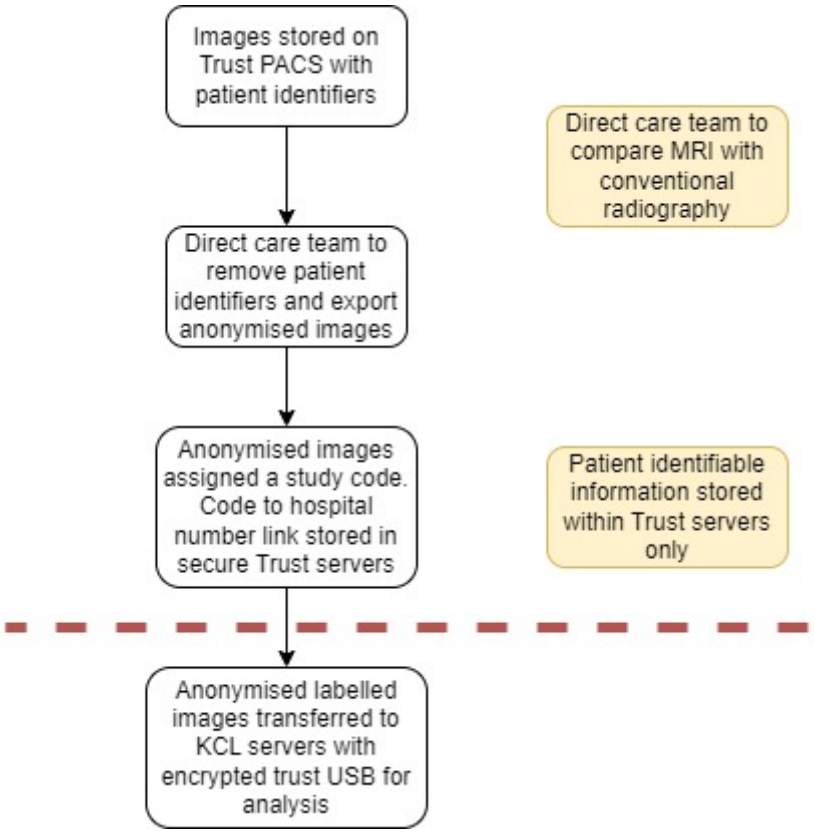
11.1 Data to be collected

Data Collection Table					
Variable	Source of data	Collection time point(s)	Who will collect data	Validity of tool	Form data will take
Primary Outcome					
Percentage of patients whose diagnosis/care changed as a result of their dental MRI scan	Documenting numbers of those whose diagnosis based upon conventional radiography changed after reviewing the dental MRI scan compared to the total number receiving the MRI scan	At patient's conventional radiography appointment and at patient's follow up visit	The research team	Simple demographics	Numeric
Secondary Outcomes					
Percentage of patients who would have been able to complete their diagnosis with a dental MRI scan alone	Documenting numbers of those where the diagnostic value provided by the MRI was sufficient	At patient's follow up visit	The research team	Simple demographics	Numeric

	without the need for conventional radiography				
Percentage of eligible patients who agreed to have an dental MRI scan	Documenting numbers of those meeting the elligibily criteria versus those who agreed to have an MRI scan	After screening has taken place	The research team	Simple demographics	Numeric
Percentage of patients who completed the dental MRI scan	Documenting numbers of those who were scanned and those who completed the scan	After the patients who were recruited to the trial complete the second gastroenterology assessment appointment	The research team	Simple demographics	Numeric
Patient acceptability of the imaging modality (as determined by VAS scale	Patient VAS scale	After each scan was taken	The research team	Simple descriptives	Numeric
Documentation of Health resource use including intervention costs	Documentation of resources used to include average appointment times and attending health care practitioners	Throughout trial	Research team	N/A	N/A

11.2 Data handling and record keeping

The actual medical scan and report will be uploaded onto the patients medical file and stored within the trust PACS following their standard protocols. SSL-encrypted data transmission over NHS e-mail when communicating with NHS practices will be employed. All data surrounding the trial will be entered into a secure password protected online excel sheet by a clinical research dentist. Clinical scan data used for analysis will be pseudoanonymised. Scans will have all identifiers removed and a participant ID assigned so that no combination of variables will allow an individual to be directly or indirectly identified. A codesheet linking participant ID with their consent form will be held in a locked filing cabinet in the PI's locked office. This will not be shared with KCL. An overview of the data flow is shown below



All data storage will be follow this anonymisation protocol and data will be backed up onto a secure RAID server with restricted access. De-identified data will be published and then the clinical trials data will be stored for 25 years by the King's Health Partners Clinical Trials Office and all data will be protected in adherence to the Data Protection Act 2024. The chief investigator and trial team will ensure the quality of the data.

12 Statistical considerations

This is a feasibility study. Simple descriptives statistics will be done by Dr. Saoirse O'Toole. Baseline characteristics will be summarized for all participants. The percentage of participants whose diagnosis altered as a result of the dental MRI scan, the percentage of participants where diagnosis could have

been made based upon the MRI scan alone will be reported as descriptives. Participants' uptake of and adherence to imaging modalities, as well patient and clinician acceptability will be summarized and presented as percentages.

Correlation studies assessing differences between dental MRI and conventional radiography for osteomyelitis in the extremities have high levels of agreement [1]. Using these as part of a power calculation meant that small sample sizes (n=7 at 90% power and alpha of 5%). This is a cohort study to determine under what circumstances an MRI scan can be used for complete diagnosis of the patient, ultimately leading to a full health technology assessment, sample size calculations based upon level of agreements are of limited use.

12.1 Data monitoring

The trial manager will be in charge of trial governance, data management and monitoring in addition to a trial administrator who will contact participants, book appointments, file trial documentation. There will be a quarterly group meeting with all investigators, the trial manager and PPI members. All data will be collected according to Good Clinical Practice and will adhere to research governance guidance.

13 Ethical considerations

Ethical approval will be obtained from the HRA. It is highly likely, given that we are offering a radiation free imaging modality, that this will be approved. The participant will be informed that the decision to participate or not participate in the study will not influence any clinical decision or subsequent care. They may withdraw from the study at any stage without affecting care. If a patient requires dental and or medical care during the study period, it will be administered by their treating clinician. Adverse event monitoring will comply with sponsor procedures.

14 Financing and Insurance

The study is co-sponsored by Guys and St Thomas' NHS Foundation Trust (GSTT) and King's College London (KCL). The sponsors will, at all times, maintain adequate insurance in relation to the study. KCL through its' own professional indemnity (Clinical Trials) & no fault compensation and the GSTT having a duty of care to patients via NHS indemnity cover, in respect of any claims arising as a result of negligence by its employees, brought by or on behalf of a study participant.

15 Reporting and dissemination

Results will be presented at national and international conferences in addition to publishing in high impact inter-disciplinary journals. All participants in the research will be directly informed by their clinical care team if the results of the MRI impacted on their diagnosis.

Tables, Figures, References
Appendices
Including (where relevant):
Patient information sheet
Patient consent form

Data collection forms and validation information
Ethics form
Summary of product characteristics
Investigators brochure

Useful reading/websites

Integrated Research Application System (IRAS)
https://www.myresearchproject.org.uk/

Health Research Authority (HRA)
www.hra.nhs.uk

HRA Guidance for Patient Information Sheet and Informed Consent
http://www.hra.nhs.uk/research-community/before-you-apply/participant-information-sheets-and-informed-consent/

CONSORT statement
A set of recommendations for improving the quality of reports of parallel group randomised trials
http://www.consort-statement.org/

ICH Harmonised Tripartite Guidelines for Good Clinical Practice (1996)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

Martin Bland et al, Statistical guide for research grant applications
http://www-users.york.ac.uk/~mb55/guide/guide.htm
Includes detailed information and definitions of many aspects required for a research protocol as well as information about randomisation software and services

Martin Bland, Directory of randomisation software and services
http://www-users.york.ac.uk/~mb55/guide/randsery.htm

Declaration of Helsinki
(http://www.wma.net/en/30publications/10policies/b3/index.html)

Appendix 1 – Information with regards to Safety Reporting in Non-CTIMP Research

	Who	When	How	To Whom
SAE	Chief Investigator	-Report to Sponsor within 24 hours of learning of the event -Report to the MREC within 15 days of learning of the event	SAE Report form for Non-CTIMPs, available from NRES website.	Sponsor and MREC
Urgent Safety Measures	Chief Investigator	Contact the Sponsor and MREC Immediately Within 3 days	By phone Substantial amendment form giving notice in writing setting out the reasons for the urgent safety measures and the plan for future action.	Main REC and Sponsor Main REC with a copy also sent to the sponsor. The MREC will acknowledge this within 30 days of receipt.
Progress Reports	Chief Investigator	Annually (starting 12 months after the date of favourable opinion)	Annual Progress Report Form (non-CTIMPs) available from the NRES website	Main REC
Declaration of the conclusion or early termination of the study	Chief Investigator	Within 90 days (conclusion) Within 15 days (early termination) *The end of study should be defined in the protocol*	End of Study Declaration form available from the NRES website	Main REC with a copy to be sent to the sponsor
Summary of final Report	Chief Investigator	Within one year of conclusion of the Research	No Standard Format However, the following Information should be included:- Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to participants	Main REC with a copy to be sent to the sponsor