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WISER-M: Developing software to measure bone disease on imaging for patients with multiple myeloma

Submission date 12/07/2024	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 09/10/2024	**Overall study status** Ongoing	
Last Edited 09/10/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

In multiple myeloma, NICE recommends whole-body MRI for diagnostic staging. However, a survey showed that only 10% of NHS sites use whole-body MRI, despite it being more accurate and being more cost effective. There are a number of reasons for this including a lack of expertise to perform this type of scan and interpret the images, and a lack of software for whole-body MRI analysis. Where used, whole-body MRI scans are reviewed visually by radiologists, who will then produce a text-based report. This is limited because there can be variation in image interpretation by different radiologists, review time can be long and qualitative descriptions (such as small vs. large volume) can be imprecise. Through previous NIHR funding, together with a commercial partner, a CE-labelled software for identification and quantitation of bone disease has been developed for use in patients with metastatic prostate cancer. This software may also have a role in detecting and measuring bone disease in patients with suspected myeloma, requiring development and validation of a myeloma-specific software algorithm. The WISER-M study involves the retrospective collection of whole-body MR scans and limited patient data, previously acquired as part of routine care and available via electronic patient records. It has two main objectives:

1. to develop and internally validate a myeloma-specific algorithm with optimal diagnostic performance to detect and measure bone disease on whole-body MRI in patients with active focal disease associated with multiple myeloma via a single-centre retrospective study (Training /Internal Validation cohort, n=100 cases)
2. to externally validate the diagnostic performance of the algorithm as measured by its per-lesion sensitivity to detect focal lesions in newly diagnosed myeloma cases via multi-centre retrospective study (External Validation cohort, n=60 cases).

WISER-M also includes a sub-study to evaluate clinical usability to provide preliminary evidence to inform future trials
testing a validated myeloma-specific algorithm.

Who can participate?

This study is for patients with confirmed multiple myeloma who underwent a WBMRI scan as standard of care during their diagnostic (Training/Internal Validation & External Validation

Cohorts) and/or treatment (Training/Internal Validation Cohort only) pathway, within the preceding 8 years.

What does the study involve?
WISER-M is limited to retrospective collection of routinely acquired scans and data available within electronic patient records. The WISER-M study team will receive de-identified data only. Local NHS site teams will be responsible for pseudo-anonymisation of WBMRI and patient data prior to transfer to the central image repository and study database, respectively. Eligible patients will be identified via electronic patient records by the site team, and each patient identified will be assigned a unique Study ID.

What are the possible benefits and risks of participating?
None

Where is the study run from?
The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU), Sutton (UK)

When is the study starting and how long is it expected to run for?
October 2023 to March 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
315705

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 57925, NIHR202161, IRAS 315705

Study information

Scientific Title
Development and validation of an algorithm to detect and measure bone disease on whole-body MRI in patients with multiple myeloma

Acronym
WISER-M

Study objectives
Objectives:
1. To develop and internally validate a myeloma-specific algorithm with optimal diagnostic performance to detect and measure bone disease on whole-body MRI in patients with active focal disease associated with multiple myeloma via a single-centre retrospective study (Training /Internal Validation cohort, n=100 cases)
2. To externally validate the diagnostic performance of the algorithm as measured by its per-lesion sensitivity to detect focal lesions in newly diagnosed myeloma cases via a multi-centre retrospective study (External Validation cohort, n=60 cases).
WISER-M also includes a sub-study to evaluate clinical usability to provide preliminary evidence to inform future trials testing a validated myeloma-specific algorithm

Ethics approval required
Ethics approval required

Ethics approval(s)

Approved 24/06/2024, West of Scotland REC 5, West of Scotland Research Ethics Service (Ward 11, Dykebar Hospital Grahamston Road, Paisley, PA2 7DE, United Kingdom; +44 141 314 0213; WoSREC5@ggc.scot.nhs.uk), ref: 24/WS/0076

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied
Multiple myeloma

Interventions
WISER-M is a multi-centre, multi-cohort retrospective study involving collection and analyses of routinely acquired whole-body MRI scans and clinical diagnostic and clinical outcome data in patients with myeloma to develop and validate an algorithm for automated detection and measurement of bone disease on whole-body MRI, including:

A. Single-centre retrospective study (Training/Internal Validation cohort): Retrospective collection and analysis of whole-body MRI scans and limited diagnostic clinical, laboratory and pathology data from a single UK site for training of a whole-body MRI algorithm for detecting and measuring bone disease in patients with active focal disease associated with myeloma – Royal Marsden Hospital (n=100)

B. Multi-centre retrospective study (External Validation cohort): Retrospective collection and analysis of whole-body MRI scans from up to 6 UK sites excluding Royal Marsden Hospital for validation of the whole-body MRI algorithm for detecting and measuring bone disease in patients with newly diagnosed myeloma (n=60)

C. Clinical Usability Sub-study: clinical review of up to 20 case studies from the Training Cohort to evaluate clinical usability of the software. This will provide preliminary evidence to inform design of future real-world testing of a validated myeloma-specific algorithm.

For newly diagnosed cases included in (A) and (B) the following clinical, laboratory and pathology data routinely acquired during the patient's diagnostic and treatment pathway, and available within electronic patient records, will be collected:
1. Date of confirmed diagnosis of myeloma

2. Laboratory markers of disease burden (blood and urinary tumour markers, bone marrow biopsy)
3. Molecular subtype and other molecular characteristics if available
4. Patient management recommendations including treatment and follow-up schedule following confirmed diagnosis and prior to start of treatment pathway
5. Clinical outcome data including serological response to treatment, assessment of minimal residual disease if performed locally, and survival status if known

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Per-lesion sensitivity of the software to identify focal lesions, compared to a “gold standard” reading provided by a central expert radiologist. Per-lesion sensitivity of the software is defined as the proportion of lesions identified as active focal lesions by the software amongst the total of true focal lesions as defined by the central expert radiologist. This will be reported for each cohort

Secondary outcome measures
1. Per-lesion positive predictive value (precision) of the software to identify focal lesions, compared to a “gold standard” (ground truth) reading provided by a central expert radiologist. Per lesion positive predictive value of the software is defined as the proportion of true focal lesions, as determined by the central expert radiologist, amongst all lesions identified as active focal lesions by the software. This will be reported for each cohort
2. Overall disease burden as measured by the total diffuse disease volume (TDV) and apparent diffuse coefficient (ADC) metrics. Overall disease burden will be measured by the total diffuse disease volume (TDV) and apparent diffuse coefficient (ADC) metrics. Quantitative analysis of the diffusion-weighted MRI parameters will be performed for each cohort. Existing software will calculate ADCs using an iterative weighted linear least-square approach. Code for the fitting algorithm will be integrated as a plugin into the OsiriX radiological viewing platform. The region of interest (ROI) will be segmented semi-automatically using highest b-value (b750s/mm2) with reference to T2- weighted images. The ROI will be then transferred to the corresponding ADC map at each timepoint, and first-order histogram measures will be derived from the enclosed ADC voxel values, including mean, median, variance, skewness, kurtosis, and selected percentiles (dwMRI parameters). This will be reported for each cohort
3. Degree of perceived overall helpfulness as measured on a 4-point Likert scale (1=not helpful at all, 4=extremely helpful) (Clinical Usability Sub-Study)

Overall study start date
01/10/2023

Completion date
31/03/2026

Eligibility

Key inclusion criteria

Patients with a confirmed diagnosis of multiple myeloma who underwent a whole-body MRI scan as standard of care during their diagnostic (Training/Internal Validation & External Validation Cohorts) and/or treatment (Training/Internal Validation Cohort only) pathway, within the preceding 8 years, fulfilling all of the following:
1. WBMRI scan acquisition protocol included axial-diffusion-weighted MRI with at least 2 b-values
2. WBMRI scan acquisition protocol included axial Dixon T1-weighted MRI
3. WBMRI scan showed at least two radiographically active focal lesions defined as high signal on diffusion-weighted imaging, low ADC values (500-10000s/mm²) and low relative fact fraction (< 20%)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 160; UK Sample Size: 160

Key exclusion criteria
Inadequate whole-body MRI image quality

Date of first enrolment
01/10/2024

Date of final enrolment
30/09/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road
London
United Kingdom
SW3 6JJ

Sponsor information

Organisation
Institute of Cancer Research

Sponsor details
Royal Cancer Hospital
123 Old Brompton Road
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+44 2071535165
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Sponsor type
Hospital/treatment centre

Website
http://www.icr.ac.uk/

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF)

Results and Publications

Publication and dissemination plan
Planned publication in a peer-reviewed journal

Intention to publish date
31/03/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Wiser-icrctsu@icr.ac.uk and via a standard proforma describing the nature of the proposed research and extent of data requirements. Data recipients are required to enter a formal data sharing agreement that describes the conditions for release and requirements for

data transfer, storage, archiving, publication, and intellectual property. Requests are reviewed by the Trial Management Group (TMG) in terms of scientific merit and ethical considerations including patient consent. Data sharing is undertaken if proposed projects have a sound scientific or patient benefit rationale as agreed by the TMG and approved by the Independent Advisory Group (IAG) as required. Restrictions relating to patient confidentiality and consent will be limited by aggregating and anonymising identifiable patient data. Additionally, all indirect identifiers that could lead to deductive disclosures will be removed. Generally, data access requests will be considered only after publication of the principal analysis of the primary endpoint.

IPD sharing plan summary

Available on request