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Replacement of a surgical procedure called transurethral resection of bladder tumour with a painless imaging procedure called magnetic resonance imaging in patients with muscle invasive bladder cancer

Submission date
03/11/2016

Recruitment status
No longer recruiting

Registration date
14/11/2016

Overall study status
Completed

Last Edited
29/04/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 12/07/2019:
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-to-improve-the-diagnosis-of-bladder-cancer-bladderpath-study

Previous plain English summary:
Background and study aims
Bladder cancer treatment and outcomes have not changed significantly in 30 years. Standard treatment involves flexible cystoscopy, where the bladder is inspected by inserting a small cystoscope (tube) through the urethra (the tube through which urine passes). If a bladder tumour is seen, the tumour is removed under general anaesthetic using a larger, rigid cystoscope – this is called transurethral resection of bladder tumour (TURBT). The removed tumour is assessed to decide if it is confined to the bladder lining (non-muscle-invasive bladder cancer – NMIBC) or invading bladder muscle (muscle-invasive bladder cancer – MIBC). For NMIBC, the procedure should successfully remove all tumour; nonetheless further drug treatment into the bladder is usually given to reduce the risk of the tumour coming back (recurrence). For MIBC, removal is generally incomplete and further treatment is required. This may involve cystectomy (to remove the bladder) or radiotherapy with or without chemotherapy. A major concern with the current treatment pathway is that TURBT delays the definitive treatment - in the UK the typical delay is over 100 days. TURBT may also actively spread tumour into tissues around the bladder or into the bloodstream. The prolonged pathway and potentially unnecessary TURBT may contribute to the poor outcomes seen with bladder cancer – around 50% of patients die of the disease within 5 years. The ideal pathway would therefore separate NMIBC from MIBC early, with treatment tailored more appropriately and rapidly according to disease stage. The aim of this study is to test a modified pathway in which flexible cystoscopy plus biopsy (tissue sample) is used as the first assessment. The very small biopsy obtainable by this procedure is enough to confirm the presence of cancer and also the grade of tumour (high or low). Most muscle-invasive

tumours are high grade. Non-muscle invasive tumours may be high or low grade. The urologist can also assess the overall appearance of the tumour. Combining these factors, patients can be divided into probable NMIBC and possible MIBC. Probable NMIBC (around 50% of the total) would continue with the current standard treatment. Those with possible muscle-invasion would undergo an MRI scan to be further separated into MIBC and NMIBC. Patients with no evidence of muscle-invasion would undergo standard TURBT. Patients with evidence of muscle-invasion undergo definitive treatment, avoiding TURBT and reducing delay.

Who can participate?
Patients aged 18 or over suspected of having bladder cancer

What does the study involve?
Participants are randomly allocated to one of two groups. One group is treated according to the current standard treatment pathway - TURBT to remove most/all of the tumour, followed by chemotherapy, radiotherapy or cystectomy for patients with MIBC. The other group is treated according to the new accelerated pathway - an MRI scan to distinguish NMIBC from MIBC, then the patients with NMIBC undergo TURBT, while the patients with MIBC undergo chemotherapy, radiotherapy or cystectomy. The time taken to receive definitive treatment (chemotherapy, radiotherapy or cystectomy) and the relapse rates after 2 years are measured in both groups.

What are the possible benefits and risks of participating?
There may be no immediate benefit from taking part in this study. However, the information obtained from this study may result in changes in the future diagnosis, treatment, and follow-up of patients with bladder cancer. These changes may also benefit the participants. No method of assessing tumours for treatment is 100% accurate. There is thus a risk of either over- or under-treatment with both pathways. For the standard pathway these risks are well known and are principally that the initial TURBT wrongly assesses the tumour as not invading muscle in the bladder, leading to under-treatment. Up to 30% of patients who are thought to have non-muscle invasive disease actually turn out to have disease invading muscle and therefore are initially undertreated. When TURBT is carried out on patients with muscle-invasive disease there is also a risk that the procedure itself may spread cancer cells elsewhere in the bladder and elsewhere in the body. The new accelerated pathway relies on the MRI scan to determine whether the tumour is invading the bladder muscle. If the scan wrongly identifies the tumour as muscle invasive, it is possible that the patient may be overtreated. This is the main risk of participating in this study. This is most likely to occur in cases of NMIBC that are large and aggressive looking. Since nobody has previously carried out a study like this before, it is not known how often overtreatment will occur but it is predicted to occur in fewer than 1 in 20 of patients diagnosed with bladder cancer. If the scan wrongly assesses a muscle-invasive tumour as not invading muscle, the patient will have a TURBT. Since this is what happens in the standard pathway anyway, so the patient will have had an additional unnecessary scan but no additional treatment.

Where is the study run from?
1. University Hospitals Birmingham NHS Foundation Trust (UK)
2. University Hospitals Coventry & Warwickshire NHS Trust (UK)
3. Sheffield Teaching Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2016 to November 2024

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
Mrs Ana Hughes
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Study website
https://www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/Bladder-Path/index.aspx

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
HTA 14/08/60

Study information

Scientific Title
Image-directed redesign of bladder cancer treatment pathways: a randomised controlled trial

Acronym
BladderPath

Study objectives
The purpose of the BladderPath trial is to evaluate a new pathway that would largely eliminate transurethral resection of bladder tumour (TURBT) from the initial management of muscle

invasive bladder cancer (MIBC) patients. This allows more expeditious treatments for both MIBC (by eliminating delays) and NMIBC (by reducing demand for TURBT). The approach integrates flexible cystoscopy, urine cytology, biopsy and detailed imaging to confirm the diagnosis and stage of disease. Appropriate definitive radical therapy can then be rapidly commenced. This is paradigm-shifting in the context of bladder cancer but is standard practice in virtually every other solid tumour setting (e.g. prostate, breast, lung, etc.). Although TURBT is considered a standard part of care for NMIBC, for MIBC it is less obviously essential, particularly for patients undergoing subsequent radical surgery. This study will test the utility of TURBT as a component of care for MIBC in a randomised fashion.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/140860

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/12/2017, London Bridge Research Ethics Committee (REC) (Skipton House, 80 London Road, London, SE1 6LH; +44 (0)20 7104 8222; nrescommittee.london-londonbridge@nhs.net), ref: 17/LO/1819

Study design
Open-label Phase II/III randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Available on trial website

Health condition(s) or problem(s) studied
Bladder cancer

Interventions
There are three overlapping stages:
1. Feasibility stage: the anticipated duration is 1 year in three centres; 150 patients
2. Intermediate stage: the estimated sample size for this stage is event-driven and requires at least 20 MIBC patients to have definitive treatment across both treatment arms
3. Final clinical stage: the anticipated duration is 30 months in 15 regional referral centres. The estimated sample size for this stage is event-driven (380 progression events; or approximately 950 patients with bladder cancer) - updated 26/07/2022: NOT DONE (recruitment closed after the Feasibility/Intermediate stages)

Patients are randomly assigned to either the standard treatment pathway or the image guided pathway (intervention), as described below:

Pathway 1: Standard investigation and initial treatment pathway
Currently, patients with both early bladder cancer confined to the inner lining of the bladder (non-muscle-invasive bladder cancer (NMIBC)) and more advanced bladder cancer growing into the deeper muscle layers in the bladder wall (muscle-invasive bladder cancer (MIBC)) receive the same initial treatment. A transurethral resection of bladder tumour (TURBT) is performed which involves the removal of most, or all, of the tumour, which is taken away in small pieces. For patients with muscle-invasive disease, it is usually not possible to remove all tumour in this way without severely damaging the bladder muscle with a risk of leaving a hole in the bladder wall. For patients with bladder cancer confined to the inner lining of the bladder this treatment is very often effective in removing the entire cancer. However, for patients with MIBC this procedure does not usually remove all of the cancer and further treatment will be necessary to eradicate the cancer. There are a number of options that are used and these include chemotherapy, radiotherapy or surgery to remove the bladder completely.

Pathway 2: Image-guided pathway – trial intervention arm
Patients have a multi-parametric MRI scan rather than the TURBT. Previous small studies have shown that this scan can distinguish tumours that are confined to the lining (NMIBC) from those that are invading muscle (MIBC). If the scan suggests that the patient has NMIBC, they will be booked for a TURBT as this is the main treatment for this condition. If on the other hand, the scan suggests that the patient has a muscle invasive tumour, they will be booked directly for treatment (chemotherapy, radiotherapy or surgery), without having a TURBT first. The aim is to reduce the time it takes for MIBC patients to receive these other essential and effective treatments. This reduced delay may improve the success of these treatments. This will be one of the main outcome measures of the trial.

The protocol is available to view at the trial website (added 19/06/2019).

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Feasibility stage: the proportion of possible MIBC patients randomised to pathway 2 who correctly follow the pathway protocol, measured after 150 patients have been entered into the study and completed pathway 2
2. Intermediate stage: the time to definitive treatment (TTDT) for all possible MIBC patients
3. Final clinical stage: clinical progression-free survival (CPFS), assessed after 2 years follow-up - updated 26/07/2022: NOT DONE (recruitment closed after the Feasibility/Intermediate stages)

Secondary outcome measures
Feasibility stage:
Measured after 150 patients have been entered into the study and completed pathway 2:
1. Overall proportion of patients who correctly follow protocol
2. Recruitment and retention rates at each study site
3. Counts of each definitive treatment

Intermediate stage:
1. TTDT for all patients
2. TTDT for probable NMIBC patients

3. Proportion of all patients who correctly follow pathway protocol
4. Recruitment and retention rates at each study site

Final clinical stage - updated 26/07/2022: NOT DONE (recruitment closed after the Feasibility /Intermediate stages):
1. Cost-effectiveness of each pathway; for the health economics analysis questionnaire EQ-5DL is completed at baseline, 3, 6, 9, 12, 18 and 24 months
2. Quality of life, measured using the EORTC-QLQ-BLM30 questionnaire at baseline, 3, 6, 9, 12, 18 and 24 months
Assessed at 2 years follow-up:
3. The proportion of patients who correctly follow pathway protocol
4. TTDT for all possible MIBC patients
5. TTDT for all probable NMIBC patients
6. TTDT for all MIBC patients
7. TTDT for all NMIBC patients
8. Time to correct treatment
9. Time to each treatment type
10. Time to recurrence, progression or metastatic disease
11. Number of recurrences; progressions and incidence of metastatic disease
12. Number of each type of treatment(s) received
13. Accuracy of MRI/TURBT by comparison with histological confirmed diagnoses
14. Overall and disease specific survival
15. Number of unnecessary radical cystectomies
16. Number of SAEs

Overall study start date
20/01/2016

Completion date
30/11/2024

Eligibility

Key inclusion criteria
1. Provision of written informed consent
2. ≥18 years of age
3. Patients attending haematuria clinic for the investigation of symptoms suspicious of bladder cancer (initial consent process)
4. Patients given a diagnosis of suspected bladder cancer and requiring a TURBT based on visual cystoscopic examination of the bladder (confirmatory consent process, post cystoscopy)
Note: as the study does not involve additional drug therapy or ionising radiation, there are no restrictions on women of childbearing potential

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
950

Total final enrolment
143

Key exclusion criteria
1. Patients unable or unwilling to undergo MRI. Criteria include but is not exclusive of the presence of foreign bodies or pacemakers, claustrophobia, adverse reactions to MRI contrast media and eGFR of less than 40 ml/min/1.73m2
2. Patients who are pregnant or breastfeeding
3. Previous diagnosis of bladder cancer
4. Previous entry into the present trial
5. Patients not suitable/fit for radical treatment
Note: The study does not include upper age related exclusion criteria

Date of first enrolment
01/03/2017

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
University Hospitals Coventry & Warwickshire NHS Trust
Walsgrave General Hospital
Clifford Bridge Road

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United Kingdom
CV2 2DX

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
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Study participating centre
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Sam Lane
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Study participating centre
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PL6 8DH

Study participating centre
Arrowe Park Hospital
Arrowe Park Road
Upton
Birkenhead
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CH49 5PE

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Morriston
Cwmrhydyceirw

Swansea
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SA6 6NL

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
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M13 9WL

Study participating centre
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

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Royal Oldham Hospital
Rochdale Road
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OL1 2JH

Study participating centre
Nottingham City Hospital
Hucknall Road
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St James's University Hospital
Beckett Street
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United Kingdom
LS9 7TF

Study participating centre
Norfolk & Norwich University Hospital
Colney Lane
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NR4 7UY

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Newcastle Road
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ST4 6QG

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New Cross Hospital
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Study participating centre
The Royal Marsden Hospital (london)
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Sponsor type
University/education

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ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Target meetings for initial presentation of results would be American Society of Clinical Oncology (ASCO), American Urology Association (AUA), European Urology Association (EAU) and European Cancer Conference (ECC). This will ensure results are disseminated to the widest possible international audiences of both oncologists and urologists. The definitive research findings would be published in peer-reviewed medical journals and presented at appropriate medical and patient meetings. The interim results will be published at each of the three stages of the planned trial. The results would also be disseminated via patient forums such as Fight

Bladder Cancer and Action on Bladder Cancer, as well as via websites such as CancerHelp UK (www.cancerhelp.org.uk) and social media outlets. A trial website will also be establish containing materials for both patients and clinical staff, to support the trial.

Intention to publish date
30/12/2024

Individual participant data (IPD) sharing plan
Participant level data will be made available from Prof. Nicholas James (N.D.James@bham.ac.uk) only if approved by the Trial Management Group and signature of a data sharing agreement. All patient trial information will be stored in locked cupboards with limited staff access. The room to which the trial files and patient data are kept should also be locked. All computer files will be password protected and have limited personnel access.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article		01/07/2021	18/10/2021	Yes	No
Protocol file	version 4.0	10/09/2020	06/09/2022	No	No
HRA research summary			26/07/2023	No	No
Results article	feasibility and efficacy of the introducing multiparametric magnetic resonance imaging ahead of transurethral resection of bladder tumour	01/08/2024	10/09/2024	Yes	No
Results article	Randomised comparison of TURBT-staged or mpMRI-staged care	14/01/2025	21/01/2025	Yes	No
Plain English results			29/04/2025	No	Yes