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CoRIPS Research Award - £9,958.00

Comparison of Double Inversion Recovery Magnetic Resonance imaging (DIR-MRI) and Dynamic contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) in Detection of Prostate Cancer: A Pilot Study

Abstract

Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI) is well established for detecting prostate cancer. However, it requires a gadolinium contrast agent, which has serious potential risks for patients. Double Inversion Recovery Magnetic Resonance Imaging (DIR-MRI) simultaneously nullifies the signals from two different tissues; therefore a tumour may be distinguished from the background normal tissue. DIR-MRI is currently used for imaging the brain. DIR-MRI does not use a contrast agent, meaning there is less risk to patients and the scans are cheaper and quicker. To enable us assess whether there is equivalence between DIR-MRI and DCE-MRI in the detection of prostate cancer, we wish to gather pilot data from DIR-MRI and DCE-MRI of the prostate, to inform a sample size calculation for a fully powered equivalence trial.

Aims and Objectives

This pilot study will aim to gather data from DIR-MRI and DCE-MRI of the prostate, to inform a sample size calculation for a subsequent, fully powered equivalence trial. At present DIR-MRI has not been used to detect prostate cancer and therefore, in order to calculate what sample size is necessary for a fully powered equivalence trial, pilot data must be collected.

Primary Research questions

Is DIR-MRI equivalent to DCE-MRI in the detection of prostate cancer: A pilot study to determine sample size?

Secondary Research question

Does the addition of DIR-MRI improve accuracy of cancer diagnosis?

Methodology: Quantitative pilot study comparing DCE-MRI with DIR-MRI for equivalence, in detection of Prostate Cancer.

i) Sampling:

All patients referred for an MRI scan for prostate cancer, who meet the inclusion criteria, will be offered the opportunity to take part in this pilot study. Patients will be offered the non-invasive DIR-MRI, in addition to standard care.

ii) Recruitment process:

Department staff will identify potential study participants. It is usual practice for a radiographer or radiologist to review a referral and subsequently issue an appointment. At this point, eligible patients will also receive a Patient Information Sheet (PIS) and invitation letter for the study. A staff with Good Clinical Practice Training will consent willing patients into the study.

Inclusion criteria:

Eligible participants will be patients referred for mpMRI of the prostate, with the suspicion of prostate cancer prior to prostate biopsy. Such patients have been referred as a result of

- Raised Prostate Specific Antigen (PSA)
- A suspicious digital rectal examination
- PET scan showing focal increased tracer uptake in the prostate

Exclusion criteria:

- Patients who are not safe to undergo an MRI scan
- Patients who have undergone a prostate biopsy in the previous 10 weeks
- Patients who decline to consent.

iii) Data Collection

Participants will have a DIR–MRI of the prostate before the DCE-MRI.
DICOM images will be reviewed on the PACS system by an experienced Consultant Radiologist. He will be shadowed by a novice reporter to identify a Region of Interest (ROI) within a suspected cancer and within a normal looking prostate using a freehand technique. The potential cancer lesions in the prostate in each of the sequence will then be quantified using a lesion to normal background prostate signal ratio (LNR).

iv) Data analysis and interpretation

We want to demonstrate statistical equivalence difference between LNR on DIR-MRI and DCE-MRI. In addition, we will use exploratory analysis to consider the accuracy of cancer diagnosis using the standard combination of images with DCE-MRI and DIR-MRI which will be compared with biopsy results

g) Potential Impact of the study

Currently, DIR-MRI has not been used in the detection prostate cancer. This pilot study will provide the necessary data to calculate a sample size for a subsequent study which will assess whether there is equivalence between DIR-MRI and DCE-MRI in the detection of prostate cancer.

This research will add to the understanding of DIR-MRI and particularly how best to perform it for the most useful images of the prostate. In doing so we are hoping to introduce, a reliable non-contrast means of accurately distinguishing between normal and abnormal prostate, between types of abnormality within the prostate and possibly between indolent and aggressive cancer. This being so, we aim to follow this small pilot study with a larger study demonstrating the value of DIR-MRI.

Eventually this could mean a cost and time saving if DIR-MRI replaces DCE-MRI in mpMRI of the prostate. Moreover, patients who cannot have the contrast agent or decline the administration of contrast can have their prostate accurately evaluated, reducing associated contrast risks such as kidney disease, and biopsies of the prostate can be targeted better, reducing the chance of missing significant disease. Furthermore, as repeat biopsy is used in some follow up pathways for prostate cancer if mpMRI is advanced further it might replace the more invasive biopsy as the follow up technique of choice.

h) Dissemination strategy

The research findings will be disseminated through a feedback PPI group meeting. In addition, the research will be written up for publication in peer reviewed journals including Radiography journal. Research findings will also be shared through health conferences and seminars, such as the United Kingdom Radiology Congress (UKRC) and the Annual Scientific Meeting of the Royal College of Radiologists.

Timetable

Total project	April 2016-April 2017
Set up	April 2016
PPI group meeting	Late April 2016-Early May 2016
Patient recruitment	May 2016-February 2017
Data analysis	February 2017-March 2017
Write up	March 2017
PPI group meeting	Late March 2017- Early April 2017
Submission for publication	April 2017

Background

In the UK, prostate cancer is the commonest of all cancers affecting men and is the second most common cause of death from cancer in men [1]. Every year in the UK, over 10,000 men die from prostate cancer [2, 3]. A significant challenge in prostate cancer management is how to accurately distinguish aggressive from indolent prostate cancer [4-10]. The Gleason scoring system is currently the gold standard measure of prostate cancer aggressiveness [11, 12]. However, it is possible during biopsy to miss foci of aggressive cancer [11-18]. It is documented that in about 30% of men, prostate cancer is upgraded from low grade to high grade disease on the findings of prostatectomy [16]. Hence there is a need for an alternative or adjunct method of detecting and assessing the disease [16, 19].

MRI plays a significant role in the diagnosis and staging of prostate cancer of which DCE-MRI is a major contributor. Many centres perform mpMRI, including anatomic and functional sequences such as T2WI, DWI, Magnetic Resonance Spectroscopic Imaging (MRSI), and DCE-MRI [20]. These techniques have different sensitivities for the detection of prostate cancer and for distinguishing between aggressive and indolent prostate cancer. This approach highlights the fact that no single MRI sequence is sufficient to diagnose prostate cancer and also that each of the components of mpMRI has advantages and limitations. The optimal combination of anatomic and functional magnetic resonance sequences still needs to be established [20]. We postulate that there are other techniques that may be used in mpMRI of the prostate.

DCE-MRI of the prostate provides useful information reliant on the vascular characteristics of normal and pathological prostate tissue. To provide contrast between normal prostate and cancer DCE-MRI relies on neo-angiogenesis in cancers accompanied by increased permeability of the endothelial barrier. These changes in micro vascularity result in earlier, increased enhancement then washout of the intravenous gadolinium containing contrast agent that is seen on T1 weighted images (T1WI) [20]. However, this functional MRI technique has pitfalls [20]. Barentsz et al, in ESUR 2012 [13] state that normal prostate is as well vascularised as abnormal prostate, so a comparison of pre and post gadolinium images is often insufficient to detect prostate cancer.

We have no doubt that this MRI technique plays an important role in prostate cancer diagnosis and management. However, some MRI centres for various reasons, do not apply the technique. Some of the problems, in addition to those mentioned above, may include cost, time, expertise, and variable specificity. To perform a high-quality DCE-MRI examination a good understanding of the technical aspects and limitations of image acquisition and post processing techniques are required [21]. Some patients decline contrast injection for their scan, others have known MRI contrast allergy or renal insufficiency. In the French Radiology Day Conference 2012 the necessity of DCE-MRI was questioned [22]. It is desirable to find a quick and cost effective alternative to this specialized MRI technique to complement other sequences in mpMRI.

DIR-MRI is a T1 relaxation time imaging based technique used to simultaneously nullify the signals from two different tissues when two 180° inversion pulses are applied before a conventional spin-echo acquisition [21]. Several studies have demonstrated the useful application of DIR-MRI in brain imaging, especially multiple sclerosis (MS). In the brain, DIR-MRI sequence attenuates the cerebrospinal fluid (CSF) and also the white matter, therefore attaining a superior definition between grey and white matter [23]. On the other hand, a study by Jeoung et al, 2014 demonstrated the usefulness of DIR-MRI in breast imaging [21]. The application in breast was based on the ability of DIR-MRI to nullify signals from fat and fibro glandular tissue without the need for an intravenous contrast agent. The DIR-MRI sequence is based on T1 relaxation time; therefore a tumour may be distinguished from the background normal tissue by virtue of T1 relaxation time differences [21].

To the best of our knowledge, there is no study that has applied DIR-MRI for evaluating prostate diseases. The application of DIR-MRI in the prostate is simple and may allow cancer detection by nullifying signal from normal tissue around the cancer creating contrast between the cancer and background normal prostate, hence allowing detection without the use of an intravenous contrast agent. Ultimately, we would like to ascertain if DIR-MRI can be used for prostate cancer detection, staging and determination of aggression of the cancer, with as much accuracy as current standard DCE-MRI scan. This pilot study will be the start of this investigation to establish the required sample size for a full equivalence study between DIR-MRI and DCE-MRI.

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