**FULL STUDY TITLE**

Can diffusion-weighted MRI replace exploratory laparoscopy in the assessment of peritoneal carcinomatosis from ovarian cancer?

**DESCRIPTION OF THE PROJECT**

This a phase IV clinical trial to assess whether diffusion weighted MRI can accurately predict the extent of abdominal metastasis in patients with metastatic ovarian cancer. We will be using a scoring tool called the Peritoneal Cancer Index (PCI) to quantify the amount of carcinomatosis present in the peritoneal cavity. We aim to correlate the PCI as assessed by an experienced radiologist with the PCI scored by a gynecological oncologist at diagnostic laparoscopy.

Our research question is, can diffusion-weighted MRI replace exploratory laparoscopy in the assessment of peritoneal carcinomatosis from ovarian cancer?

Research will be conducted in accordance with the following legislation and guidance:

• National Health and Medical Research Council (NHMRC) Act 1992 including

National Statement on Ethical Conduct in Human Research (NHMRC) 2007

Australian Code for the Responsible Conduct of Research (NHMRC) 2007

Guidelines and Publications

• Royal Australian New Zealand College of Radiologists (RANZCR)

Standards of Practice (V10 2014)

Code of Ethics (V1 2015)

• Australian Medical Association (AMA)

Good Medical Practice: A Code of Conduct for Doctors in Australia (March 2014)

• Health and Medical Research Unit (HMRU) – Queensland Health

Research Management Policy (QH-POL-013:2015)

• Catholic Health Australia – Mater Hospital Brisbane

Code of Ethical Standards for Catholic Health and Aged Care Services in Australia (2001)

• Australian Health Practitioner Regulation Agency (AHPRA)

**STUDY INVESTIGATOR(S)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Name** | **Phone** | **Email** | **Institution** | **Study Role (e.g. PI)** |
| Sinead Barry | 0467970951 | sineadcbarry@gmail.com | Mater Hospital | Lead investigator |
| Luke Danaher |  | Dr.luke.danaher@gmail.com | Mater Hospital | Co-investigator |
| Lewis Perrin |  | Lewisperrin21@gmail.com | Mater Hospital | Principle Investigator |
| Rino Olivotto |  | Rino.olivotto@mater.org.au | Mater Hospital | Principle Investigator |
| Naven Chetty |  | navenchetty@icloud.com | Mater Hospital | Co-investigator |
| Nisha Jagasia |  | nishajagasia@gmail.com | Mater Hospital | Co-investigator |

1. **INTRODUCTION AND RATIONALE**

Ovarian cancer is associated with the highest mortality of all gynecologic cancers in the western world. The majority of patients receive a diagnosis of advanced disease that has spread beyond the ovaries to the peritoneal surface. The most effective treatment for advanced disease involves a maximum effort to reduce the tumor burden through surgery followed by six cycles of intravenous chemotherapy with carboplatin and paclitaxel. Alternatively, interval cytoreductive surgery is performed after three cycles of chemotherapy. The majority of patients (80%) will have persistent disease or will develop recurrent disease.

Anatomic imaging of peritoneal disease from advanced ovarian cancer patients is routinely performed with computed tomography with good per patient sensitivity (92%) but poorer per-lesion sensitivity (as little at 20%) depending on the site of the lesion and its size. The reason for this is that small implants invaginated in the peritoneal reflections or coating the serosal surfaces of the intestine are often masked by the similarity in attenuation or signal intensity of the adjacent structures.

Pre-operative identification of foci of peritoneal dissemination is important to determine the patients’ eligibility for primary cytoreduction or neo-adjuvant chemotherapy, in the post-operative setting the ability to detect 5mm deposits carries prognostic information and at the time of recurrence it could help plan secondary cytoreduction.

The shortcomings of CT which involves issues with contrast between normal tissue and tumour can be overcome by diffusion weighted (DW) imaging. This modality is being used increasingly in oncology and does not require extra hardware or excessively prolonged scanning times. It can be incorporated into existing MR protocols. The combined interpretation of conventional MR with diffusion weighted MR has increased accuracy in detecting more sites of involvement .The addition of apparent diffusion coefficient (ADC) values shows promise as a biomarker for tumour grade and response to treatment in other gynaecological cancers ([1](#_ENREF_1)).

The peritoneal cancer index (PCI) is the most widely validated and precise quantitative prognostic indicator for peritoneal carcinomatosis ([2-4](#_ENREF_2)). For patients undergoing cytoreductive surgery (CRS), the PCI is one factor associated with determining whether a complete surgical cytoreduction can be achieved ([5](#_ENREF_5)).

MR imaging provides considerable advantages for imaging patients with peritoneal tumor. Its inherently superior contrast resolution compared to CT allows MRI to more accurately depict small peritoneal tumors that are often missed on other imaging tests. Combining different contrast mechanisms including diffusion-weighted (DW) MRI and gadolinium-enhanced MRI provides a powerful tool for preoperative and surveillance imaging in patients being considered for CRS.

Preoperative MRI and CT of the abdomen and pelvis play an integral role in determining the extent of peritoneal and visceral disease in patients being considered for CRS for appendiceal, ovarian, colorectal, primary peritoneal, gastric, mesothelioma and other rare types of gastrointestinal disease involving the peritoneum ([6-13](#_ENREF_6)). Careful patient selection based on preoperative imaging may prevent unnecessary surgeries in patients whose tumors are too extensive and cannot be adequately cytoreduced. Following CRS surveillance imaging combined with serial tumor markers are routinely used to detect recurrent tumor ([14](#_ENREF_14)).

Currently our diagnostic work up involves a preliminary diagnosis of ovarian cancer based on tumour markers, clinical history, CT findings and exploratory laparoscopy. At the time of exploratory laparoscopy patients are assessed as suitable for primary cytoreduction or not. If a patient is not suitable for primary cytoreduction, they receive three cycles of neo-adjuvant chemotherapy and after repeat Ca125 and a CT scan they have a further exploratory laparoscopy to plan cytoreduction. This process for some patients involves 3 general anaesthetics (GA), 2 for planning purposes and a third for cytoreduction. It is our hope that DW MRI can replace the need for exploratory laparoscopy by accurately assessing the PCI.

As a result of multiple GA’s, patients run the risk of infection, bleeding, DVT, hospital acquired infections at a time when they need to stay well. Also, many of our patients have to travel long distances at great upset to themselves and their families and at great cost to the health service in order to undergo the exploratory procedures. We feel that it would provide a significant reduction to patient risk and reduce the personal burden of treatment on our patients if laparoscopic assessment could be replaced with an MRI scan.

**Comparison with other imaging modalities**

While CT is limited to assessing attenuation of X-rays, MR imaging uses multiple sequences to improve its sensitivity for depicting small peritoneal tumors. Initial experience confirmed that peritoneal tumors show marked enhancement on images obtained 5 min after administration of gadolinium contrast material ([15](#_ENREF_15)). The increased conspicuity of these enhancing peritoneal tumors improved detection of small and microscopic tumors that are often missed on CT scans([16](#_ENREF_16), [17](#_ENREF_17)). The addition of diffusion imaging to the MRI tool chest further improves peritoneal tumor depiction. Diffusion-weighted (DW) MR images assess microscopic movement of water protons ([18](#_ENREF_18), [19](#_ENREF_19)). Most tumors restrict water diffusion causing them to appear as high signal areas on diffusion images. In our experience the combination of diffusion weighted imaging (DWI) and delayed gadolinium-enhanced MR imaging is most accurate for detecting peritoneal tumors ([20](#_ENREF_20), [21](#_ENREF_21)).

Multidetector contrast enhanced CT is commonly used for preoperative imaging in patients undergoing surgical cytoreduction but is very limited in its ability to depict small peritoneal tumors. Coakley et al. ([16](#_ENREF_16)) noted sensitivity of helical CT for peritoneal tumors < than 1cm was only 25-50% compared with 85-95% for all tumors. Low et al. ([17](#_ENREF_17)) reported the sensitivity of gadolinium enhanced MR images for depicting peritoneal tumors at < than 1 cm was 85-90% compared to 22-33% for CT. The average sensitivity of MR for depicting peritoneal tumors of all sizes was 84% compared with 54% for CT. Klumpp et al. reported similar results with gadolinium-enhanced MRI demonstrating an 87% segment sensitivity and 88% accuracy for depicting peritoneal tumors compared to surgical findings ([11](#_ENREF_11)).

In a multi-institutional study Esquivel et al found that the preoperative CT PCI score underestimated the extent of carcinomatosis in 33% of patients([22](#_ENREF_22)) . The poor sensitivity of CT for detecting small peritoneal tumors limits its accuracy in determining a patient’s preoperative PCI score ([22](#_ENREF_22), [23](#_ENREF_23)). There is also growing concern regarding the cumulative radiation exposure that patients receive from repeated CT scans ([24](#_ENREF_24), [25](#_ENREF_25)). The use of PETCT has been explored in patients with peritoneal carcinomatosis with improved results compared to CT alone ([21-23](#_ENREF_21), [25](#_ENREF_25), [26](#_ENREF_26)). Our experience indicates that subtle small volume peritoneal tumors are not well depicted on PET.

### Diffusion-weighted (DW) MR imaging

Diffusion is a physical property that describes the microscopic random movement of molecules in response to thermal energy([18](#_ENREF_18)) . Also known as Brownian motion, diffusion may be affected by the biophysical properties of tissues such as cell organization and density, microstructure and microcirculation. DW imaging utilizes pulse sequences and techniques that are sensitive to very small-scale motion of water protons at the microscopic level. Single shot echo planar imaging (EPI) DW imaging is utilized to provide very rapid imaging sensitive to subtle small-scale alternations in diffusion. Areas of restricted water diffusion are displayed as areas of high signal intensity ([9](#_ENREF_9), [27-33](#_ENREF_27)).

Oncologic applications of DW imaging take advantage of restricted diffusion shown by most tumors ([18](#_ENREF_18), [19](#_ENREF_19)). The higher cellularity of solid tumors and their increase in cell membranes per unit volume results in restriction of water movement and corresponding high signal intensity on DW images. Abdominal DW imaging can be performed on commercially available high field MR systems.

The sensitivity of the DW imaging sequence to water motion can be varied by changing the b-value which depends on the amplitude and the timing of the paired bipolar diffusion sensitizing gradients ([23](#_ENREF_23)). One typically acquires at least two b-values of 0 s/mm2 combined with a second intermediate to a high b-value of 400 to 1,000 s/mm2. Acquiring additional b-values will improve the accuracy of the quantitative data obtained from DW imaging. Higher b-values result in more diffusion weighting with better background suppression, at the expense of reduced signal and increasing artifacts([18](#_ENREF_18), [19](#_ENREF_19)) . At our institution we typically use b-value 0 s/mm2 combined with intermediate b-values of 500 s/mm2. For anatomic DW imaging these intermediate b-values achieve reasonable diffusion weighting while maintaining good image quality. Fat suppression is implemented to improve the contrast to background ratio on the DW images.

### Gadolinium-enhanced MR imaging

Peritoneal tumors enhance with intravenous gadolinium increasing their conspicuity so that very small tumors are depicted easily ([14](#_ENREF_14), [15](#_ENREF_15)). Peritoneal tumors enhance slowly so that they may not be visible on early arterial phase images but are best depicted on the final set of images obtained at about 5 minutes following gadolinium administration. For this reason the final set of axial 2D SGE is most important to achieve perfect breath-holding. If the patient is breathing small peritoneal tumors will be masked. These final set of images should be repeated if there is any motion artifact.

To depict small tumors a reasonably high in-plane resolution must be balanced against the requirements for times short enough to allow for breath hold imaging. Our current post contrast imaging is performed with 3D FSGPR images obtained an in plane resolution of 320×256. The delayed axial 2D SGE images are obtained with an interpolated resolution of 512×256. In our experience peritoneal tumors often present as sheets of tumor cells lining the peritoneal surfaces rather than as solitary discrete small tumor nodules. In this setting high contrast resolution is probably more essential to distinguish thin sheets of tumor from normal anatomic structures. Increasing the in plane resolution, while maintaining the same breath hold time, can be achieved by using a higher bandwidth and or acceleration factor.

Optimal fat suppression on the gadolinium-enhanced images will also facilitate depiction of small peritoneal tumors by suppressing the adjacent high signal intensity of mesenteric, retroperitoneal, and abdominal wall fat. One may use chemical selective fat suppression. We currently use sequences that take implement a Dixon fat and water separation technique for more robust fat suppression. These 3D sequences are called Liver Acquisition with Volume Acceleration-eXtended Volume (LAVA FLEX) (General Electric Medical Systems), M-Dixon (Philips Medical), and T1 Dixon (Siemens Medical).

These images typically show more homogeneous fat suppression, sharper anatomic detail, less sensitivity of susceptibility artifact, and slightly better signal to noise ratio. Problems with fat and water swapping have been much improved on the most recent versions of the Dixon sequences ([9](#_ENREF_9)).

### TECHNICAL CONSIDERATIONS

### Patient preparation

The MRI scan may take up to 60 minutes. The patient will change into a gown and a radiographer will discuss the scan and help the patient to fill out a safety form and MRI contrast dye form.

Patients will be informed to wear as little jewellery as possible. They will be given some fluid to drink by the radiographer to help show the stomach and bowel. All patients will have a cannula inserted into a vein in the arm to allow the administration of contrast and other medications. These medications are to slow the movement of the intestines for the duration of the imaging and provide a clearer picture of the bowel. The contrast is standard for this type of imaging.

Patients will be given earplugs and earphones as the MRI scanner is noisy. They will be given a buzzer to alert the radiographer if they need to stop the scan for any reason. They may need to have an enema, however this is decided once the scan has started.

At the end of the scan, the cannula will be removed and they will be allowed to leave after about 15 minutes. The imaging will go to a radiologist for interpretation and the report will be sent to the referring doctor. There is no need to stop any medications or treatments, unless requested by the treating doctor.

**Duration**

The research will take place on a day which must be before surgery. It will be necessary to attend the radiology department at the Mater hospital for the scan.

**Side Effects/Risks**

There are reported cases of allergy to the contrast, although this is very rare (less than 1 in 10,000 for severe reaction).

### Intraluminal contrast material

Water soluble intraluminal contrast material is administered to distend the stomach, small bowel, and colon. Collapsed bowel can mask subtle peritoneal tumors or inflammation involving the bowel serosa, mesentery, or adjacent peritoneum. Alternatively, non-distended segments of small bowel can be mistaken for an abdominal mass. Adequate bowel distention is therefore an essential element in the peritoneal MR imaging protocol that improves the accuracy and confidence on image interpretation ([31](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754308/#r31)).

Water soluble contrast material is administered orally beginning 45 minutes before the start of the MR examination. Water soluble contrast materials are biphasic on MR images producing high intraluminal signal on T2-weighted images and low signal intensity on T1-weighted and gadolinium-enhanced SGE images.

Patients drink 1.0-1.5 liters of oral contrast material of sufficient volume to distend the small bowel and stomach. There are a number of different available oral contrast agents that can be used for MR imaging. While their use for MR imaging is off label they have proven to be safe and effective for bowel distention. These oral contrast agents are predominantly water with some other agents added to decrease absorption of the material through the small bowel wall. Chilling the oral contrast material is also preferred by some patients.

### Intravenous contrast agents

Intravenous gadolinium contrast is administered using a power injector at an injection rate of 2 cc per second. In the past, we have used a double dose of intravenous gadolinium to increase the degree of enhancement of peritoneal tumors and inflammation. We currently use a single dose 0.1 mmol/kg of MultiHance® (gadobenate dimeglumine) (Bracco), which may show greater enhancement of peritoneal tumors due to its higher relaxivity. To our knowledge a comparison of Multihance and other gadolinium chelates for depicting peritoneal disease has not been performed.

### Antiperistaltic agents

A medication should be administered to decrease bowel peristalsis on the gadolinium-enhanced images. The 3D FSPGR and 2D SGE images are sensitive to bowel motion and image quality is improved by administering an antiperistaltic pharmacologic agent. At the time of gadolinium injection, Buscopan® (hyoscine-N-butylbromide), 20mg will be administered intravenously at the start of the examination.

**MR Hardware**

Three T high field strength MR scanner will be used for imaging peritoneal tumors. High performance gradients (50 mT/m, 200 mT/m/sec) are advantageous for high quality DW imaging but are not absolutely essential. Excellent image quality can be achieved on almost any high field MR scanner if one invests some time to optimize protocols and image quality.

An external phased array surface coil providing simultaneous coverage of the abdomen and pelvic should be used to improve signal and image quality. Typically this requires a surface coil large enough to provide at least 50 cm in the cranio-caudal direction. Using the large body coil without a phased array surface coil is not an acceptable option.

### MRI peritoneal protocol

#### General principles

Our protocol for peritoneal imaging is optimized for depicting small peritoneal tumors ([21](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754308/#r21),[27](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4754308/" \l "r27)). All images are obtained during suspended respiration to minimize breathing artifact that can obscure subtle peritoneal tumors or inflammation. Faster pulse sequences that facilitate breath hold imaging also decrease the overall examination time which is essential when using intraluminal contrast material to distend to small bowel and colon. Other key elements that improve tumor depiction are fat suppression and high spatial resolution. Fat suppression is utilized for T2-weighted imaging, DWI, and all gadolinium-enhanced images. By suppressing the high signal intensity fat small peritoneal tumors and inflammation become more conspicuous.

**Peritoneal MR imaging protocol**

MR imaging is unique in its ability to show soft tissues using many different types of contrast. By modifying imaging parameters when setting up a scan one can accentuate tumors using T1-weighted, T2-weighted, or diffusion weighted contrast. One can also administer exogenous contrast intravenously to depict tumor enhancement. Each will produce an image that shows the tumor differently. In our experience DW imaging and gadolinium contrast-enhanced images are more useful for showing subtle peritoneal tumors.

## **AIM(S) OF STUDY**

The aim of the study is to compare the radiologically scored PCI with our surgically scored PCI. It is our hope that DW MRI could replace laparoscopy in the work up for ovarian cancer cytoreduction.

## **OBJECTIVE(S)**

### Primary Objective

The primary objective is to assess if MRI scored PCI equates to surgically scored PCI

### Secondary Objective(s)

To identify if personal factors affect the sensitivity of the test (ethnicity, body habitus, age, diabetes, smoking status, neoadjuvant chemotherapy, histology)

To assess the need for an experienced abdominal radiologist versus a junior radiologist in performing accurate scoring

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## **HYPOTHESIS**

PCI assessed radiologically using diffusion weighted MRI can accurately predict surgically scored PCI.

## **STUDY DESIGN**

The only change to standard care is the addition of an MRI scan preoperatively.

Diagram protocol

Diagnosis of ovarian cancer – based on tumour markers, CT scan, clinical history, histology/cytology (standard care)

Review of imaging at radiology conference – clinic review – consent taken for MRI scan

Diffusion weighted MRI

(PCI scored by two radiologists)

Laparoscopy (proceed to cytoreduction or neo-adjuvant chemotherapy)

Neoadjuvant chemotherapy n = cycles

Primary cytoreduction

Record PCI, histology, residual disease

Diffusion weighted MRI (PCI score)

CT, tumour markers, radiology conference review

Laparoscopy +/- proceed to cytoreduction

PCI score, histology, residual disease

This is a prospective interventional study.

## **STUDY SETTING/LOCATION(S)**

This study will be a single-center study at Mater Health Services, Raymond Terrace, South Brisbane 4101.

## **STUDY DURATION**

The protocol will run until we have imaging on 100 patients.

## **STUDY POPULATION**

Seventy five percent of these patients with ovarian cancer are diagnosed with stage III disease. Patients with abdominal metastasis from ovarian cancer will be offered participation.

**Inclusion criteria**

1. Age over 18 years,
2. histological or cytological proven primary epithelial ovarian carcinoma or primary peritoneal cancer (PPSC) or fallopian tube carcinoma
3. FIGO stage III or higher
4. including serous papillary adenocarcinoma, mucinous adenocarcinoma and endometrioid adenocarcinoma.
5. Written informed consent

**Exclusion criteria**

1. Diagnosis other than ovarian cancer,
2. previous abdominal malignancy or Tuberculosis
3. severe claustrophobia

**Sample size calculation**

100 patients (expected recruitment time 18 months)

### Potential for risk, burdens and benefits to participants

MRI scan is associated with minimal risk. There is very low risk of contrast allergy. Minor reactions such as skin irritation can occur at a rate of about 1 in 1000 patients. Severe contract reactions are rare and occur at a rate of less than 1 in 10,000 scans.

There may be some mild discomfort associated with insertion of the iv cannula and with the rectal enema if it is required. This discomfort is minimal. This is identical to routine practice.

1. **DATA PROTECTION AND STORAGE**

Data will be

Collected by the chief investigator

Recorded in a data collection tool (Microsoft Excel spreadsheet)

This will be password protected, encrypted, and stored behind the Mater Health firewall

Stored for 15 years in accordance with NHMRC guidelines

## **STUDY OUTCOME**

### Primary Outcome(s)

1. To compare surgically score PCI with radiologically scored PCI

### Secondary Outcome(s)

1. To identify if personal factors affect the sensitivity of the test (ethnicity, body habitus, age, comorbidities, chemotherapy, histopathology)
2. To examine the cost effectiveness of replacing surgery with MRI scan?

## **12.** **STUDY PROCEDURES**

Patients will receive standard work-up and standard care for their ovarian cancer. All patients with at least stage 3 disease be offered an MRI as part of their work up.

### Recruitment and consent of participants

All patients who are diagnosed with metastatic ovarian cancer and who can give informed consent will be offered an MRI. We will recruit 140 patients. Consent will be written. All adult participants will be expected to have capacity to consent.

### Withdrawal of participants from a study

Patients can decline involvement in the study and they can withdraw at any time. This will in no way affect the patients care. Data will be retained on all involved patients even if they withdraw. Data collected on study participants up to the time of withdrawal will remain in the study database in order for the study to be scientifically valid.

Patients will be recruited for the study by a senior member of the Gynaecological oncology service

### Randomisation

There will be no randomisation as all patients with abdominal metastasis that meet the inclusion criteria will be offered participation in the study.

### Measurement tools used

The data will be collected to assess the primary and secondary outcomes of the study. The data will be collected from clinic notes, from EMR and from imaging reports. The surgically scored PCI will be recorded in the operation note; the radiologically scored PCI will be recorded by the radiologist on a spreadsheet on the hospital server. The following variables will be collected: age, BMI, Smoking status, co-morbidities, ethnicity, tumour markers, final histology, FIGO stage, tumour grade, chemotherapy regime, chemotherapy effect on the resected specimen, surgically scored PCI score and radiologically scored PCI. We will be using 2 radiologists to assess the reliability between experienced and less experienced radiologists. We will also record the costs involved in doing the exploratory laparoscopy and compare those to the cost of the MRI scan. The MRI image or the radiologically scored PCI will not be available to the surgeon prior to PCI scoring at the laparoscopy.

The data will be collected by me on a spreadsheet stored on the hospital server. All data will be de-identified. From the surgical specimen, we will collect histopathology and tumour grade and chemotherapy effect. This information is standard on all pathology reports.

### Study involvement by participants

Patients will be consented for MRI scan at their clinical workup at Mater Health Services, Raymond Terrace, South Brisbane..

We will not provide any remuneration to patients for their involvement

### Data management and storage

On all study forms, any clinical details and patient data will be identified by a Study Number only. Only the principal investigator and associate investigators will have access to the list of patients registered and their allocated study numbers. All forms will be completed by the Gynaecological Oncologist and radiologist attending to the patient at their enrolment visit, during surgery and at their scan visit. All study forms will be collected by the principal investigator (SB) and stored in locked cabinets within the Department of Gynaecological Oncology. Any electronic data files will be stored on a secure password protected computer in the Gynaecological Oncology office. All electronically stored data will have patients de-identified. Any publication or presentation of results will be such that all patient data is de-identified. Data will be stored for 15 years (as per protocol for clinical trials) and disposed of at the end of the study in a legal manner abiding by Mater Health information Services policy.

* 1. **Data Collection**

Ur number

Age

Body mass index

Ca125

Smoking status

Presence of Diabetes

Received neo-adjuvant chemotherapy- number of cycles

Histopathology at diagnosis

Tumour grade

BRCA status if known

PCI scored at MRI

PCI scored at laparoscopy

Residual disease after cytoreduction

Final histopathology

### Safety considerations/Patient safety

We do not foresee any serious adverse events relating to the MRI scan. Contrast related allergy is rare (0.3%) and can happen at any time in clinical practice and will be managed by the radiographers and radiologists in the usual manner. There are no complications relating to this study that fall outside normal clinical practice. (Biomed Research International 2016).

### Data monitoring

Data monitoring

A chart will be produced to track the following

**Weekly**

Number MRI scans booked for the week (in advance)

Completed consent forms

Adverse outcomes reviewed

Identify any missing variables

**Monthly**

Interim review of adverse outcome rates

Exclusion rates

Other technical issues reviewed

Feedback will be sought from all investigators to identify recruitment, patient exclusion, technical, and safety issues

The trial will be discontinued if

Unacceptable complication rate

Serious adverse outcomes as a result of the trial

A statistically significant treatment benefit is identified placing the patients at unacceptable risk

## 3 monthly

Identification of early trends

**6 monthly**

Projected trial completion date based on number or participants

Interim analysis of primary and secondary outcome measures

## **SAMPLE SIZE AND DATA ANALYSIS**

### Sample size and statistical power

A sample size of 140 as calculated with a confidence level of 95% .

We used the sample size recommended by Bland(2004) based on the Bland Altman method (Bland +Altman 1986) This guideline is not based on a formal powering process as the Bland-Altman approach is not inferential. Bland 2004 recommends a sample of at least 100 patients for the Bland –Altman approach.

We employed both the ICC (Intra class correlation) and the Bland Altman approach to gauge both inter-method and inter-rater (within MRI) agreement. The ICC was used as it provides a single measure of agreement with a 95% CI. Whereas Bland and Altman was used because it is much more informative about the specific causes of lack of agreement (bias, noise, spectrum bias, spectrum noise) Bland and Altman is also much more intuitive.

### Data analysis plan

Descriptive statistics will be described as means and standard deviations. Correlation analysis will be performed on parametric and non parametric data using pearsons and spearmans tests. Paired t tests will be used to compare scores between observers. Multivariate analysis will be used to assess predictors of PCI. We will consult a statistician at the time of analysis. Paired t testing will be used to compare PCI in both groups.

## **ETHICAL CONSIDERATIONS**

This research protocol considers

Relevant professional, ethical, and institutional requirements

Technical quality assurance

Potential risks and benefits

Safeguarding the interests of patients enrolled in the trial

Voluntary consent and withdrawal

A Patient Information and Consent Form (PICF) has been produced

## **DISSEMINATION OF RESULTS AND PUBLICATIONs**

**Presentation**

It is anticipated that interim and final results will be presented at Medical meetings in the gynaecological oncology department

National conferences

International conferences

It is anticipated that the chief investigator will present the findings

Other members of the research team will be invited to present findings where appropriate

**Publication**

Interim and final results will be published in

International scientific literature

National scientific literature

Hospital bulletins

Departmental newsletters

**Authorship**

The chief investigator will publish data in accordance with ICMJE guidelines

All relevant authors will be included in publication

Key stakeholders will be acknowledged

**Policy**

Should a significant safety benefit exist in relation to the study group, the relevant patient safety

units will be informed at Mater Hospital Brisbane – Clinical Safety and Quality Unit

Policy change will then be reviewed at this level and within the respective medical departments

## **OUTCOMES AND SIGNIFICANCE**

There is an emerging body of evidence which suggests that DW MRI can accurately assess peritoneal carcinomatosis. This study is designed to answer this question both in the settling of primary surgery and in the setting of neo-adjuvant chemotherapy. If DW MRI proves to be accurate in predicting PCI, it could replace the need for laparoscopy in the ovarian cancer work –up. This would significantly reduce costs, significantly reduced the burden on the patient and streamline care for patients who live far away from their specialist centre. It has the potential to change local, national and international practice.

## **BUDGET**

Funding for the MRI scans is being sought from the Mater Research Foundation

## 

## **GLOSSARY OF ABBREVIATIONS**

DW Diffusion weighted

CRS Cytoreductive surgery

PCI Peritoneal cancer Index

MRI Magnetic resonance imaging

CT Computed Tomography

## GA General anaesthesia

PICF Patient Information and Consent Form

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