PROTOCOL TITLE:
Utility of diffusion-weighted MR imaging in guiding selective percutaneous drainage of postoperative intra-abdominal abscesses after colorectal resection

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FUNDING:
Internal: Department of Radiology Magnetic Resonance Imaging Research Center (MRIRC) specifically for 20 hours of cost-free MRI scans at the MRIRC

SPONSOR:
PI (internal)

TYPE OF RESEARCH:
Prospective cohort

INTERVENTION:
Diffusion-weighted magnetic resonance scan (DW-MRI)

MANUFACTURER OF INTERVENTION:
N/A

IND OR IDE #:
N/A

NAME OF PERSON WHO HOLDS IND OR IDE:
N/A

PROTOCOL VERSION:
1.2

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STUDY SUMMARY

TITLE	Utility of diffusion-weighted MR imaging in guiding selective percutaneous drainage of postoperative intra-abdominal abscesses after colorectal resection
SHORT TITLE	MRI for post-operative abscess
PROTOCOL NUMBER	
PHASE	N/A
METHODOLOGY	Prospective cohort
STUDY DURATION	12-15 months (2016-2017)
STUDY CENTER(S)	Single-Center (UCMC)
OBJECTIVES	***Objective 1***. To devise a limited DW-MRI protocol for evaluation of post-operative intra-abdominal collections ***Objective 2***. To compare and determine best DW-MRI metrics for differentiation of sterile and infected intra-abdominal fluid collections in the post-operative setting. ***Objective 3.*** To construct a protocol using diffusion-weighted MR imaging to guide selective percutaneous drainage of post-operative intra-abdominal abscesses after colorectal resection, and prevent drainage of sterile collections.
NUMBER OF SUBJECTS	20 (anticipated)
DIAGNOSIS AND MAIN INCLUSION CRITERIA	Adult patients who have undergone a colon or rectal resection at UCM and have developed a CT-proven abdominopelvic fluid collection > 3 cm in average diameter, for which the surgeon determines percutaneous drainage is indicated, will be eligible for inclusion in the study.
STUDY PRODUCT, DOSE, ROUTE, REGIMEN	**DW-MRI acquisition:** Each exam will be limited to the collection that was already detected and localized by CT. Each exam will include a breath-hold T2-SSFSE, T1-w GRE and DWI sequence. Total scanner

	time per patient is expected to be under 30 minutes.
DURATION OF ADMINISTRATION	N/A
REFERENCE THERAPY	N/A
STATISTICAL METHODOLOGY	Sensitivity and specificity of each review session for each radiologist will be calculated. McNemar's test will be used for multiple comparisons of sensitivity of different review sessions. Confidence score of each review session will be compared using Wilcoxon-signed rank test. Two-tailed Student's *t* test will be used for comparison of ADC values. Simple κ coefficients will be used to assess interobserver agreement for confidence score and ADC measurements. An ROC curve will be constructed for ADC values, and area under the curve measured the overall ability of ADC in differentiation of abscess from non-infected collections.

LIST OF ABBREVIATIONS

ADC	Apparent diffusion coefficient
CT	Computed tomography
DWI	Diffusion-weighted Imaging
DW-MRI	Diffusion-weighted magnetic resonance image
GRE	Gradient echo
IAA	Intra-abdominal abscess
IV	Intravenous
kHz	Kilohertz
MRI	Magnetic resonance image
MRIRC	MRI research center
NEX	Number of excitations
PO	Per oral
ROI	Region of Interest
SENSE	Sensitivity encoding
SSFSE	Single shot fast spin echo
TE	Echo time
TR	Repetition Time
UCMC	University of Chicago Medical Center
UC	University of Chicago

1. INTRODUCTION

A. BACKGROUND AND RATIONALE

Describe the following in detail:

a) **Background—** Intra-abdominal abscesses are a known complication after colon and rectal resection. Percutaneous drainage, as compared to surgical drainage, has been a mark of great progress in the management of post-operative intra-abdominal abscesses. However, increased use of cross sectional imaging with computed tomography (CT) as well as improved resolution of these images had led to identification of fluid collections of unclear clinical significance (Sarkissian). Both clinical and radiologic assessment is necessary to objectively determine who will require drainage. Percutaneous drainage is not without risk, and these interventions can prolong hospital stay, result in further imaging, increase need for homecare, and cause patient discomfort. Within the subset of patients who ultimately undergo percutaneous aspiration and drainage, there is a subset with smaller abscesses who would have resolved spontaneously, and a subset who are found to have sterile collections, both representing unique overtreatment groups. Current radiologic criteria felt to be selective for abscesses (i.e. rim-enhancement on CT) results in aspiration of sterile collections in up to 40% of cases (Sarkissian).

b) **Disease and current understanding of disease—** Percutaneous drainage of intra-abdominal abscesses occurring as a complication of colon and rectal resection has been a major advance in the management of surgical patients. Proper patient selection is critical for safe and effective management in this population. Almost ¾ of patients undergoing CT scan after colorectal resection due to clinical suspicion of intrabdominal process will have at least one fluid collection identified. These collections can represent a spectrum of clinical entities and there is not a consensus on the most effective management of these collections or even the definition of abscess. Currently, reliance on radiologic criteria in isolation can lead to overuse of interventional procedures. For example, 40% of rim-enhancing collections are sterile on aspiration. The surgeons' clinical suspicion for abscess and radiologic proximity to an anastomosis are the only criteria that are useful in predicting abscess versus sterile collection (Sarkissian). A further consideration is the natural history of these abscesses. Studies in the diverticulitis literature have demonstrated that abscesses less than 3 cm in greatest dimension are successfully managed with antibiotics alone, while abscesses greater than 6.5 cm are likely to require intervention. However, this leaves a great number of abscesses between 3 cm and 6.5 cm that fall into uncertain grounds (Oto, Kumar). In contrast to diverticulitis, where it can be reasonably inferred that an associated abdominopelvic collection is indeed and abscess, management of fluid collections identified post-operatively

and determination of who will benefit from drainage is less clear. A novel radiologic technique with high discrimination between sterile and infected collection would be of great clinical utility in the post-operative management of fluid collections after colorectal resection.

c) **Past research and/or preclinical data**—Oto *et. al.* have identified a novel method using diffusion weighted magnetic resonance imaging (DW-MRI) of abdominopelvic collections that can perfectly discriminate abscesses from ascites with a threshold apparent diffusion coefficient (ADC) of 2.0 x 10^{-3} mm^2/s ([i]). It is important to note this study *did not* include collections identified in the post-operative setting; it is unclear whether inflammatory fluid or presence of blood may diminish this discrimination. If the discriminatory capacity is *not* diminished, then clearly DW-MRI has great potential within the diagnosis and treatment of post-operative abscess formation in colon and rectal resection.

d) **Rationale for conducting this research**— Further investigation is required in order to determine whether DW-MRI is applicable in the evaluation of post-operative collections, and whether utilization of DW-MRI can enhance application of percutaneous drainage and prevent unnecessary drainage. DW-MRI is well established in the identification and management of brain abscesses. Oto *et. al.* have already demonstrated the utility of DW-MRI in discriminating abdominopelvic abscess from ascites. They compared ADC values of abscess and non-infected ascites in 58 patients. Compared to T2-weighted images alone, addition of DW-MRI images allowed for nearly 100% detection of abscesses. Further, a cutoff ADC value of 2.0 x 10^{-3} mm^2/s allows for perfect discrimination between abscess and non-infected ascites (Oto), thereby increasing the abscess detection rate (**Fig. 1** (Fig . 7 from Oto *et. al.)*) and potentially minimizing unnecessary percutaneous aspiration or drainage.

e) **Dose rationale and risks/benefits (as applicable) –** Not applicable

f) **Rationale for research design and population—** The novelty of the proposed research project is that it seeks to broaden applicability of a proven but rarely used method, DW-MRI, to discriminate sterile or benign from infected abdominopelvic fluid collections, in order to enhance the utilization of percutaneous drainage in the post-operative setting after colorectal resection (Oto). Ability to streamline a limited MRI protocol to efficiently obtain diffusion weighted imaging of the abdominal cavity will be key to applying this methodology into daily practice. Secondly, it is not known whether DW-MRI can effectively discriminate specifically *post-operative* sterile collections from abscesses. This is one of the primary aims of this pilot study and will be used to generate hypothesis for a full-scale study.

B. OBJECTIVES

a) **Hypothesis-** DW-MRI is effective in discriminating sterile from benign abdominopelvic collections in the post-operative setting after colon or rectal resection with a high degree of discrimination using a defined apparent diffusion coefficient threshold.

b) Describe in detail the study objectives, including primary and secondary

a. *Objective 1.* To devise a limited abdominal diffusion-weighed imaging protocol for evaluation of intra-abdominal collections in the post-operative setting.
b. *Objective 2.* To identify the DW-MRI characteristics of infected and sterile intra-abdominal fluid collections in the post-operative setting after colon and rectal resection, and compare and determine best DW-MRI metrics for their differentiation.
c. *Objective 3.* To construct and demonstrate safety and feasibility of a protocol using diffusion-weighted MR imaging to guide selective percutaneous drainage of post-operative intra-abdominal abscesses after colorectal resection, and prevent drainage of sterile collections

2. STUDY DESIGN

Describe the following in detail:

a) **Type of study & characteristics of this type of research:** Prospective cohort
b) **Duration of study:** 12-14 months
c) **Schedule of events:**
    a. *Clinical schedule*: Adult patients who have undergone a colon or rectal resection at the University of Chicago Medicine and have developed a CT-proven abdominopelvic fluid collection > 3 cm in average diameter, whom the surgeon has determined using traditional clinical and radiologic factors to be a candidate for percutaneous drainage, will be eligible for inclusion in the study. (**Fig. 2**) These patients will undergo DW-MRI (see Objective 1), and then be taken directly to the interventional radiology suite for drainage. Fluid will be sent for culture and gram stain. In addition, the interventional radiology team will qualify the fluid in their notation as purulent, turbid/murky, serous, serosanguinous, sanguinous, bilious, or feculent. In the event a patient otherwise meets criteria but the surgeon has determined that percutaneous drainage is not indicated, they will not be eligible for inclusion in the study. If, due to nonresolution or worsening clinical status, the surgeon later decides that percutaneous drainage is appropriate, that patient will only then become eligible for the study.
    b. *MRI acquisition:* MR imaging will be performed on a 3-T (Ingenia, Philips Healthcare) MR scanner with eight-channel-phased array body coil. MR imaging protocol will consist of axial and coronal T2-weighted single-shot fast spin echo sequences (TR, infinite; TE, 90 ms; matrix = 256 × 256; slice thickness = 6 mm; gap = 0 mm), an axial diffusion-weighted single-shot echo-planar sequence (free breathing with respiratory gating, TR/TE = 3,000–10,000/70–80, *b* factors 0, 100, 500, 800, 1200 mm^2/s, field of view = 32–50 cm, receiver bandwidth = 64 kHz, four signals acquired, section thickness = 5 mm, section interval = 7 mm, and acquisition time = 4–6 min) and a T1-weighted three-dimensional gradient echo with fat suppression sequence (TR/TE = 4.2–4.6/2.0–2.3 ms, flip angle = 12–20°, matrix = 320 × 192,

field of view = 30–38 cm, receiver bandwidth = 64 kHz, a parallel imaging reduction factor of 2, one signal acquired, section thickness = 5 mm, section interval = 2.5 mm) . These images will be obtained through the known location of the abscess based on previous CT examination. The total duration of MR scan time will be 25 minutes or under. We will optimize our protocol by scanning two volunteers and test different SENSE, TR/TE and NEX parameters for an optimum protocol.

d) **Summary of sequence and duration of all study periods**: The project duration is estimated at one year. Based on the pilot data, the investigators will commit to submitting a full grant application within 3 months of completing the pilot data project.
   a. *Month 1 – 9: Patient accrual*: The Section of Colon and Rectal Surgery is committed to recruiting twenty (20) patients within this timeframe who have undergone colon or rectal resection including appendectomy and who through usual clinical processes have undergone cross-sectional imaging in the from of CT, with a discrete abdominopelvic abscess >3 cm in average diameter identified. The patients will then be put through the pilot protocol as above (see Objective 3 and **Fig. 2**).
   b. *Month 10-12: Data analysis and assessment*:
      i. Objective 1: The protocol will be validated for efficacy and cost, with the primary endpoint being ability to report an ADC value for a collection identified on prior CT through use of the DW-MRI protocol.
      ii. Objective 2: DW-MRI readings will be analyzed and ADC values will be compared and validated in an attempt to report a threshold ADC that reliably discriminates sterile and infected post-operative fluid collections.
      iii. Objective 3: Determine the effect size from utilization of DW-MRI (defined as a change in management decision to pursue drainage or hold on drainage)
      iv. Global Assessment: Determine whether the outcome measures are appropriate, reliable, and feasible. Finalize eligibility criteria for a larger study. Generate hypothesis and determine sample size calculation for larger study.
   c. The investigator team will meet at 2-month intervals for a research in progress meeting to discuss accrual logistics and problem areas in order to fine tune the study protocol, and identify key parameters that will require adjustment prior to submission of a full grant application.

e) **Discuss randomization processes and use of controls or placebos, as applicable:** Not applicable

f) Primary and secondary endpoints:
   a. Primary output measures are ADC threshold to discriminate sterile from infected post-operative fluid collections

g) **Primary safety endpoints (must be measurable):** Not applicable

h) **Rationale for study design**: The results of this pilot trial will form the basis of the R21 grant that our team is planning to submit in 2018. The data will help us to identify potential limitations of DWI in differentiation of abscess from non-infected collections allow us to determine the appropriate cohort size for the NIH grant. Based on the correlation with DWI and clinical data, we will explore and suggest novel acquisition and analysis methods for quantitative DWI. Each exam will be limited to the collection that was already detected and localized by CT. Each exam will include a breath-hold T2-SSFSE, T1-w GRE and DWI sequence. Total scanner time per patient is expected to be under 30 minutes.

3. SUBJECT SELECTION AND WITHDRAWAL

a) **Number of subjects:** 20
b) **Gender of subjects:** Any (goal is consecutive recruitment)
c) **Age of subjects:** Adult
d) **Racial and Ethnic Origin:** Any (goal is consecutive recruitment)
e) **Inclusion Criteria**:
    i. Adult (18 years or older) patients able to participate in the consent process
    ii. Have undergone colon or rectal resection within 30 days
    iii. CT-proven abdominopelvic fluid collection > 3 cm in average diameter
    iv. Surgeon has determined patient is clinically stable for unaccompanied transport to the MRIRC for image acquisition
f) Exclusion Criteria:
    i. Contraindication to MRI (eg. Implant or other medical device)
    ii. Pregnant women, prisoners, and cognitively impaired persons
    iii. Claustrophobia preventing MRI acquisition
    iv. Not clinically stable to be transported unaccompanied to the MRIRC for image acquisition
    v. MRI acquisition will delay percutaneous drainage
g) **Vulnerable Subjects/Subject Capacity to provide consent:** Otherwise eligible subjects must retain capacity to consent to DW-MRI in order to be considered for the study.
h) **Location where research is to be conducted (building, floor, clinic/suite number):** CUMC and the MRIRC
i) **Describe how subject's primary treating physician will be notified of, and if appropriate, involved in the proposed research:** All UCMC surgical faculty who perform colon or rectal resection will be briefed on the study details. The surgeon study team will not have direct involvement in DW-MRI acquisition and image analysis. The radiology study team will not have direct involvement in clinical care or clinical decision-making.
j) **As applicable, the coordination of any interdepartmental faculty, and where necessary, the inclusion of those faculty as participants**: All UCMC surgical faculty who perform colon or rectal resection will be briefed on the study details. The surgeon study team will not have direct involvement in DW-MRI acquisition

and image analysis. The radiology study team will not have direct involvement in clinical care or clinical decision-making.

k) **Method of subject identification and recruitment.** Adult patients who have undergone a colon or rectal resection at the University of Chicago Medicine within 30 days and have developed a CT-proven abdominopelvic fluid collection > 3 cm in average diameter, for which the surgeon determines based on best clinical practice that percutaneous drainage is indicated, will be eligible for inclusion in the study. These patients will be reasonably on the colon and rectal surgery census, the surgical oncology patient census, or the resident acute care surgery census or in any of these complimentary ambulatory settings. In the event a patient otherwise meets criteria but the surgeon has determined that percutaneous drainage is not indicated, they will not be eligible for inclusion in the study. If, due to nonresolution or worsening clinical status, the surgeon later decides that percutaneous drainage is appropriate, that patient will only then become eligible for the study.

l) **Describe plans for remuneration to subject, as applicable***:* N/A

m) Informed consent process
Click here for an Informed Consent Checklist template

n) **Waiver of consent/waiver of authorization (as applicable):** N/A

o) **Method of withdrawing subjects following completion of study**: N/A – single point intervention (DW-MRI acquisition)

p) **Method of withdrawing subjects before completion (i.e., early termination):**

i. In the event that a subject consents for the study and only after this discloses extreme claustrophobia or metal implant which would preclude them from DW-MRI, this will be considered a screening failure and these patients will not be included on any analysis.

ii. If the subject's clinical status changes after initial screening such that they are no longer safe for transport to the MRIRC for image acquisition, or if it is the case that MRI acquisition will actually delay percutaneous drainage, the subject will be considered a screening failure and will not be included in the analysis.

q) **Method of collecting data and follow-up on subjects who have been withdrawn**: N/A

5. STUDY PROCEDURES

a) Please see patient flow (**Figure 2**) as well as study design.

b) This is a single point intervention (DW-MRI acquisition) within the context of a usual clinical care pathway. The results of the DW-MRI will not be utilized for clinical decision making for the subjects in the study. Primary output measures are ADC threshold to discriminate sterile from infected post-operative fluid collections which may be used to guide a larger prospective study.

c) Labs, diagnostic testing, post-operative visits, and further intervention will be at the discretion of the surgeon based on usual best clinical care and not directly born of the study intervention (i.e. not research related).

d) **Methods and procedures:** See 'MRI acquisition' above under Study Design.

e) **Scales/assessments:** None
f) **Examinations:** None related to this single-point intervention
g) **Questionnaires**: None
h) **Labs to be conducted:** None related to this single-point intervention
i) **Plan for unscheduled visits:** None related to this single-point intervention
j) **Contact between study visits:** None specifically research related. Patients will undergo usual post-operative care.
a) **Future contact regarding research studies:** None specifically research related. Patients will undergo a routing post-operative visit or visits at the discretion of their treating surgeon.

Refer to SCHEMA in Appendix B.

6. STATISTICAL PLAN AND CONSIDERATIONS

For assistance with plans for biostatistics in this research, please visit the Department of Health Studies at www.health.bsd.uchicago.edu.

Discuss the following in detail:

a) **Sample size determination—** Our sample size of twenty (20) patients is justified in that we believe recruitment can be accomplished within 9 months. True pace of recruitment/refusal/crossover will drive the timeline of a future full-scale study, and may influence inclusion/exclusion criteria of the full-scale study.
b) **Power analysis or considerations—** Results of the study (i.e. the calculated ADC threshold) will be used to drive a power analysis for a future larger study to determine if addition of DW-MRI to the care paradigm results in clinically meaningful improvement in care.
c) Statistical methods: **DW-MRI differentiation metrics and abscess characterization**
    - *Qualitative analysis*: The collection will be presented to two separate radiologists who will be blinded to patients' history, laboratory results, findings from other imaging modalities, and final diagnosis. They will independently review the MR images for detection of collections (T2-weighted images together with diffusion-weighted images and ADC maps (T2 + DW-MRI). ADC maps will be generated for each patient using a home grown software. Each radiologist will assign a score from a five-point scale (1 = no abscess; 2 = probably not an abscess; 3 = equivocal; 4 = possible abscess; 5 = definite abscess) based on the level of confidence in the diagnosis for each review session. A score of 4 or 5 will be considered as positive for diagnosis of abscess for each case.
    - *Quantitative analysis*: Following qualitative analysis, the same two radiologists independently will measure ADC of the collections in each patient on ADC maps. Mean and 10th percentile ADC values will be computed by placement of region of interest (ROI) on ADC maps using DW images as guide. Each ROI will be placed in the center of the

collection over the darkest pixels on ADC maps keeping size as large as possible and avoiding the volume averaging from the surrounding tissue. The reference standard for the diagnosis of abscess will be based on the analysis of aspiration fluid from the collection. *Statistical analysis*: For statistical analyses, a software package (SPSS 11.0 for Windows; SPSS Inc., Chicago, IL, USA) will be used. Sensitivity and specificity of each review session for each radiologist will be calculated. McNemar's test will be used for multiple comparisons of sensitivity of different review sessions. Confidence score of each review session will be compared using Wilcoxon-signed rank test. Two-tailed Student's *t* test will be used for comparison of ADC values. A two-tailed *p* value of less than 0.01 will be considered to indicate a statistically significant difference. Simple κ coefficients will be used to assess interobserver agreement for confidence score and ADC measurements. An ROC curve will be constructed for ADC values, and area under the curve measured the overall ability of ADC in differentiation of abscess from non-infected collections.

d) Subject Population(s) for Analysis

- *All-imaged population:* Any subject who underwent DW-MRI in the post-operative setting after identification CT-proven intrabdominal collection > 3 cm in average diameter, whom the surgeon determines based on best clinical practice that percutaneous drainage is indicated.

e) **If any Intent to Treat Analysis will be done on subjects withdrawing before completion or those who remained in the study but withdrew from intervention, please describe in detail:** Not applicable

7. RISKS AND BENEFITS

Describe in detail:

NOTE: Collection of data is through a noninvasive procedure (MRI) routinely employed in clinical practice. Usual risk of MRI as described to patients undergoing this imaging is described below.

a) **Risks associated with study intervention and likelihood of these risks:**

Participation in this study may involve the following risks:

a. *Exposure to magnetic fields:* Apart from its effects on metal objects and implants, there are no known negative effects associated with the magnetic fields used to produce MRI images. Despite the exposure of millions of people to high-intensity magnetic fields in MRI scanners over the last 30 years, there are no confirmed reports of adverse health effects. The radio-frequency energy that is used to excite the MRI signal may in extraordinary circumstances cause heating and burning of tissue. In addition, rapid switching of the gradients may cause transient discomfort. In addition, there is a remote likelihood of tissue damage when rapidly changing magnetic fields are used.

b. *The presence of devices, implants, or other objects containing metal:* Metal objects pose a serious risk to all patients undergoing MRI exams. This includes internally implanted objects such as surgical clips,

biosupport devices (e.g., pacemakers), and artificial joints which contain metal.

c. *Claustrophobia:* Some individuals may experience claustrophobia during the MRI exam due to the limited space available inside the bore of the magnet.
d. *Incidental finding as a result of the study:* It is not anticipated that the DW-MRI will reveal an incidental finding that would *not* have been discovered during the cross sectional CT scan that was obtained during usual best clinical care. Given the CT scan is not the study intervention, incidental finding is not an anticipated risk of the study.
e. *Inadvertent delay in percutaneous drainage:* Delay in percutaneous drainage could result in clinical worsening.

b) **Protection against risks**

a. *Protection against risks related to exposure to magnetic fields:* We will insure that our experimental pulse protocols do not exceed 75% of FDA recommended upper limits for power deposition and gradient slew rates. As a further protection, even if a higher energy pulse programming protocol were to be used in error, the commercial MRI machine that will be used for these studies (a Philips Achieva 1.5 Tesla scanner) is equipped with both software and hardware power limiters that prevent the execution of pulse sequences in excess of FDA limits. The statistical evidence suggests that exposure to excessive RF energy caused by this equipment is, for all practical purposes, impossible -- there have been no reports of significant RF injury in over one hundred thousand clinical MRI exams.
b. *Protection against risks related to presence of metals, devices and other metal containing material:* Participants are questioned carefully before MRI imaging to insure that they do not have metal implants. Prospective study participants who have such implants will be excluded from the study. Patients who have worked in or near machine shops and electronics shops are also excluded from the study. In these work environments metal slivers may become trapped in the eyes, posing a potential hazard if exposed to a strong magnetic field. In addition, metal objects such as heavy key chains that are carried into the scan room can cause serious accidents. Participants will be cautioned to remove all metal objects before entering the scan room. Access to the scan room is carefully controlled to insure that no ferrous metal is inadvertently brought in.
c. *Protection against claustrophobia:* Prospective participants will be counseled about this possibility before the exam. The magnet is equipped with an intercom system enabling study subjects to communicate with the operators at any time during the exam. If they report any discomfort during the MRI examination they will be removed from the magnet immediately.
d. *Breach of confidentiality:* There is a minimal risk that patient confidentiality may be breached. All data is entered in an online database. This database is password protected. Each patient is assigned a unique number, these unique numbers are matched with patient identifiers.

e. *Protection against inadvertent delay in percutaneous drainage:* The study MRI is expected to be obtained during the natural lag-period that is typical after requesting a same-day drainage procedure. In the event the interventional radiology team is immediately available to perform percutaneous drainage, the patient will become ineligible for the study and will not undergo MRI acquisition. The study authors emphasize the importance of not delaying percutaneous drainage as a therapeutic intervention and feel this plan adequately ameliorates any delay in percutaneous drainage,

c) **Potential direct benefits to subject:** There may be no benefit to patients who are enrolled in the study. Direct benefit is low, as the DW-MRI will not be utilized in direct clinical decision-making in the study subjects (decision for or against percutaneous drainage will be based on current best practice which is clinical assessment combined with contrast-enhanced CT).

d) **If no direct benefit to the subject, describe potential benefit to community, disease population, or science:** If hypothesis is correct and DW-MRI is superior to CT in characterizing abdominopelvic fluid collections, then results of the study may better guide selective percutaneous drainage of post-operative intra-abdominal abscesses after colorectal resection, and prevent drainage of sterile collections. Therefore risks are justified due to the importance of the knowledge that may reasonably be expected to result from the research.

e) **Describe how the benefits in this research justify the potential risks:** Community benefit as stated above and lack of risk to the subject justify this study. As stated above, there is no know risk of magnetic field exposure at this level, patients with stated claustrophobia will be excluded, and usual meticulous screening will be before to ensure participants do not have metal implants.

8. SAFETY AND ADVERSE EVENTS

Discuss the following in detail.

Safety:

a) **Overall risk benefit assessment:** Relative benefit and very low risk profile is justified.

b) **What provisions will be made to protect subject's safety during the course of this study:**

a. *Protection against risks related to exposure to magnetic fields:* We will insure that our experimental pulse protocols do not exceed 75% of FDA recommended upper limits for power deposition and gradient slew rates. As a further protection, even if a higher energy pulse programming protocol were to be used in error, the commercial MRI machine that will be used for these studies (a Philips Achieva 1.5 Tesla scanner) is equipped with both software and hardware power limiters that prevent the execution of pulse sequences in excess of FDA limits. The statistical evidence suggests that exposure to excessive RF energy caused by this equipment is, for all practical purposes, impossible -- there have been no reports of significant RF injury in over one hundred thousand clinical MRI exams.

b. *Protection against risks related to presence of metals, devices and other metal containing material:* Participants are questioned carefully before MRI imaging to insure that they do not have metal implants. Prospective study participants who have such implants will be excluded from the study. Patients who have worked in or near machine shops and electronics shops are also excluded from the study. In these work environments metal slivers may become trapped in the eyes, posing a potential hazard if exposed to a strong magnetic field. In addition, metal objects such as heavy key chains that are carried into the scan room can cause serious accidents. Participants will be cautioned to remove all metal objects before entering the scan room. Access to the scan room is carefully controlled to insure that no ferrous metal is inadvertently brought in.
c. *Protection against claustrophobia:* Prospective participants will be counseled about this possibility before the exam. The magnet is equipped with an intercom system enabling study subjects to communicate with the operators at any time during the exam. If they report any discomfort during the MRI examination they will be removed from the magnet immediately.
d. *Protection against the breach of confidentiality:* Patient identifier will be kept and used only for the purpose of correlating patient data between imaging studies and outcomes. Patient identifier will be removed from data analysis unless it becomes necessary to correlate results of the analysis to other clinical data, which we do not expect. Patient identifier will be removed from all presentations and publications; only data from a group of patients will be reported so that data from any individual patient cannot be identified.
e. *Protection against inadvertent delay in percutaneous drainage:* In the event the interventional radiology team is immediately available to perform percutaneous drainage, the patient will become ineligible for the study and will not undergo MRI acquisition.

c) **Adverse Events:** Not applicable— collection of data is through a noninvasive procedure (MRI) routinely employed in clinical practice.

9. DATA HANDLING AND RECORD KEEPING

Discuss the following in detail:

a) **How will data be collected? Paper? Electronically?** The majority of data will be collected electronically via EHR and entered into an online database. There is a chance minimal paper documents will be generated as well (example, consent form).
b) **Who will provide source documents and CRFs for data collection?** Dr. Hyman and Dr. Cannon will be performing consent, subject to revision if additional investigators or assistants join the study.
c) **Who will manage the data?** The data will be managed by the study investigators and when applicable a statistician who will be compliant with IRB policies and procedures.
d) **Where will data be stored?** Any paper records or data sheets will be maintained in a locked cabinet; electronic data storage will be in an online database and comply will UCMC guidelines.

e) **Who will have access to data?** Only the study investigators will have access to the data. Research assistants who have undergone appropriate CITI training (i.e. a surgical resident) may also have access to the data.
f) **Describe provisions to protect subject's confidentiality (must be in line with HIPAA requirements**)
    a. *labeling of data:* Each DW-MRI will be assigned a unique number which will match with the identifier assigned to the patient.
    b. *identifiers & PHI:* Data will be de-identified. Each patient is assigned a unique number, these unique numbers are matched with patient identifiers in a password protected database. PHI collected may include admission date, procedure date, discharge date. Patient age (year only), sex,

10. STUDY MONITORING, AUDITING AND INSPECTING

All investigator-initiated studies must have a monitoring plan in place.

a) The study investigators will serve as data monitors and assure compliance.

11. FINANCIAL CONSIDERATIONS

a) **Remuneration to subject** - none
b) **Costs to subject** - none

12. ETHICAL CONSIDERATIONS

a) None identified.

13. CONFLICT OF INTEREST

a) **COI on file** – no conflicts identified.

14. PUBLICATION PLAN

Discuss the following in detail:

a) Who expects to publish results from this research? – The PI and study investigators will publish the data in a surgical or radiologic journal.
b) **When are results expected to be submitted for publication? –** Preliminary findings from pilot study expected to be published in 2018.
c) **Who will be involved in the compilation of results for publication?** – The PI and study investigators.

15. REFERENCES

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16. APPENDIXES

A. INFORMED CONSENT FORM
See supporting attachments

B. SCHEDULE OF EVENTS (SCHEMA)
See supporting attachments

C. DATA SAFETY AND MONITORING PLAN
Discuss the following in detail:
The study investigators will serve as data monitors and assure compliance.

D. PATIENT DIARIES
a) N/A

E. FIGURES

a) Figure 1 (Fig . 7 from Oto *et. al.)*:

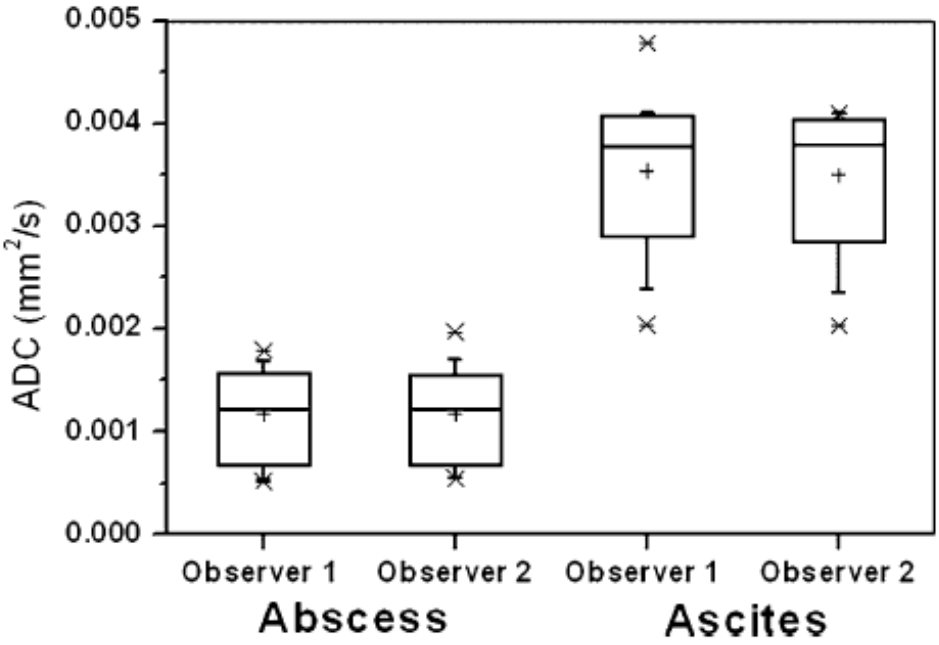

Fig. 7 Comparison of apparent diffusion coefficient (ADC) value between abscesses and ascites. The mean ADC values (+) for abscesses ($1.17\pm0.42\times10^{-3}$ and $1.43\pm1.18\times10^{-3}$ mm²/s for observer 1 and observer 2, respectively) were significantly lower than the mean ADC values (+) for non-infected ascites ($3.57\pm0.68\times10^{-3}$ and $3.42\pm0.67\times10^{-3}$ mm²/s for observer 1 and observer 2, respectively) ($p<0.01$). ADC values of all abscesses were under the set threshold ADC value of 2.00×10^{-3} mm²/s on ROC analysis

b) **Figure 2:** Project Design and Patient Flow