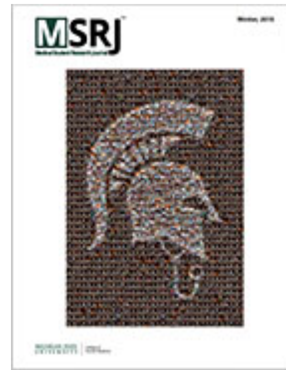
Accepted Manuscript



Systematic review of the accuracy of magnetic resonance imaging in the diagnosis of acute appendicitis in children: comparison with computed tomography

Whitt, Benjamin

DOI: 10.15404/msrj/07.2017.0001

Reference: MSRJ

To appear in: *Medical Student Research Journal*

Received Date: 29 September 2016

Revised Date: 21 March 2017

Accepted Date: 1 July 2017

Please cite this article as: Whitt, Benjamin. Systematic review of the accuracy of magnetic resonance imaging in the diagnosis of acute appendicitis in children: comparison with computed tomography, *Medical Student Research Journal* (2015), 4(3), 54-58.

Systematic review of the accuracy of magnetic resonance imaging in the diagnosis of acute appendicitis in children: comparison with computed tomography

Benjamin Whitt

Saba University School of Medicine

USA

Corresponding author:
Benjamin Whitt
27 Jackson Road, Suite 301
Devens, MA 01434
Btwhitt22@gmail.com

Short Title:
Key Phrases: Appendicitis; Diagnostic Imaging; Sensitivity; Specificity; Children

Word Count: 4378
Figure Count: 1
Table Count: 2

The author does not have anything to disclose.

Title: Systematic review of the accuracy of magnetic resonance imaging in the diagnosis of acute appendicitis in children: comparison with computed tomography

Abstract

OBJECTIVE: Computed tomography (CT) has emerged as the gold standard test for the evaluation of suspected appendicitis in pediatric patients. It has been shown to have excellent accuracy and to decrease negative appendectomy rates. However, CT scans expose patients to ionizing radiation, which is of especially high concern in children. Magnetic resonance imaging (MRI) is a potential alternative that could be used to evaluate children while eliminating exposure to radiation. This systematic review tests the hypothesis that the sensitivity and specificity of MRI are not inferior to that of CT in the evaluation of suspected appendicitis in children.

METHODS: A search of the Medline database was conducted to identify articles that used MRI to evaluate children with suspected appendicitis. Articles that focused on pediatric subjects and reported sensitivity and specificity of MRI in these subjects were included. Data for the calculation of sensitivity, specificity, and 95% confidence intervals for each were extracted from each study included. Pooled data for sensitivity and specificity of MRI were calculated and tested for significance compared to sensitivity and specificity of CT using Fisher's exact test.

RESULTS: Nine studies were found to be relevant to the question posed by this systematic review and met the inclusion criteria. The pooled sensitivity and specificity of MRI for the diagnosis of appendicitis were 0.96 (95% CI: 0.94-0.98) and 0.97 (95% CI: 0.96-0.98) as opposed to values of 0.94 (95% CI: 0.92-0.97) and 0.95 (95% CI: 0.94-0.97) for CT. The difference between MRI and CT was not statistically significant for sensitivity ($p=0.11$) or specificity ($p=0.06$) in the evaluation of suspected appendicitis in children.

CONCLUSIONS: In children with suspected appendicitis, the sensitivity and specificity of MRI are comparable to those of CT in terms of sensitivity and specificity. MRI is a viable choice for imaging in these patients and limits exposure to radiation.

Introduction

Appendicitis is the most common indication for emergent abdominal surgery in patients under 18 years old, with more than 70,000 such patients diagnosed with appendicitis each year in the United States.[1-2] A missed or delayed diagnosis often results in perforation of the appendix and deterioration of the patient's condition. On the other hand, a false diagnosis of acute appendicitis can lead to unnecessary surgical interventions. In a study of 475,651 appendectomy cases in the United States between 1998 and 2007, the negative appendectomy rate was found to be 11.83%.[3] As an attempt to minimize the incidence of such adverse events and as a result of the high level of variation in signs of appendicitis in pediatric patients, the vast majority of children undergo preoperative imaging prior to appendectomy.[4] The use of diagnostic cross-sectional imaging in the evaluation of patients with suspected acute appendicitis has increased dramatically over past decades, especially the use of computed tomography (CT), which has emerged as the current gold standard test. The widespread use of CT in the diagnosis of appendicitis is largely due to its being widely available and relatively simple to operate compared to other cross-sectional imaging modalities such as magnetic resonance imaging (MRI).[5] The high sensitivity and specificity of CT in diagnosing appendicitis is well documented in both children and adults, and its use in preoperative situations has been found to be correlated with a significant decrease in the negative appendectomy rate.[6-8] The largest meta-analysis to date on the accuracy of CT in the diagnosis of acute appendicitis analyzed 26 studies including 9356 children, concluding that CT has sensitivity of 0.94 (95% CI: 0.92-0.97) and specificity of

0.95 (95% CI: 0.94-0.97) for evaluation of pediatric patients.[9] However, a single abdominal CT scan exposes patients to as much ionizing radiation as over 50 conventional x-rays of the abdomen. Several studies have found that people that underwent CT as children have a significantly elevated risk of malignancy later in life.[10-12] Furthermore, the intravenous contrast agent commonly administered during CT is associated with a small but significant risk of allergic reactions and/or nephropathy.[13-14] As a result, more institutions are utilizing ultrasonography for the diagnosis of appendicitis, and it has become the first line diagnostic modality in pregnant and pediatric patients in most facilities. Ultrasonography is almost universally available, uses no ionizing radiation, and has lower associated costs, but it is operator dependent, resulting in highly variable sensitivity findings.[9, 15-17] As a result, CT remains the most commonly used preoperative imaging modality in children undergoing appendectomy.[4] A strategy involving the use of ultrasonography as the first line test for acute appendicitis and CT for use only in cases with indeterminate ultrasound has recently been recommended, and has been shown to be highly accurate.[18-19]

MRI is another viable modality for imaging the abdomen in pediatric patients, but it currently plays only a minor role in the evaluation of patients with suspected acute appendicitis. This is largely due to high associated costs, limited availability, and the high level of operator expertise required. Additionally, MRI requires patients to lie still for extended periods of time, which may be of particular concern when evaluating small children. MRI already has an established role in imaging of pregnant women with suspected acute appendicitis and inconclusive ultrasound findings, but the American College of Radiology continues to list MRI as less appropriate than CT for the evaluation of both children and non-pregnant adults with suspected acute appendicitis, citing a lack of evidence of the diagnostic accuracy of MRI in the general population.[20] However, MRI is beginning to emerge as an alternative modality for the evaluation of patients with abdominopelvic pain, particularly as it becomes more readily available in the emergency setting and more rapid imaging sequences are developed.[21] MRI could be a particularly attractive option in evaluation of pediatric patients with suspected appendicitis as it does not involve exposure to ionizing radiation. Recent small-scale studies on the accuracy of MRI in the diagnosis of acute appendicitis show sensitivity and specificity similar to that of CT, but many of these studies cite a need for larger-scale research to confirm these results.[22] If MRI were found to have comparable accuracy to that of CT in pediatric patients, clinicians could avoid exposing children to damaging ionizing radiation, as well as prevent the development of radiation-induced malignancies without sacrificing diagnostic efficacy. The purpose of this review is to research the relevant literature on the accuracy of MRI in diagnosing acute appendicitis in children in order to analyze the hypothesis that the accuracy of MRI in the diagnosis of acute appendicitis in pediatric patients is not inferior to that of CT.

Methods

For this review, a search of the Medline database for literature regarding the accuracy of MRI in the evaluation of suspected appendicitis in children was conducted using the "advanced search" feature and the medical subject headings (MeSH) database. Only studies published within the past 10 years were included in this review. To be included, studies had to focus on pediatric patients under age 18 and include sensitivity and specificity values for MRI and 95% confidence intervals for each, or else provide sufficient data to permit the calculation of these values. Studies that included pregnant patients were excluded. One study that duplicated data by basing multiple data points on each MR image by including multiple interpretations was also excluded.

Each study considered for inclusion in this review was analyzed for quality and content. Several elements were evaluated when reviewing an article for quality and likelihood of bias. This included methods for subject selection, particularly how potential subjects were chosen for further imaging. Another important element that was evaluated was the heterogeneity of imaging protocols used in each study, including the MRI sequences used and whether gadolinium-based contrast was used. Some other considerations were the reference standard and index test used, completeness of subject follow-up, and protocols for radiographic diagnosis of appendicitis. For reference, each study in this review was also assigned an evidence level of 1-4 based on study design, with level 1 being of highest value. Randomized controlled trials were considered level 1. Non-randomized controlled trials were considered level 2. Observational studies with controls were considered level 3, while observational studies without controls were considered level 4.

Sensitivity and specificity for MRI in the evaluation of suspected appendicitis in each study was calculated, along with 95% confidence intervals for both. An evidence table and forest plot were constructed containing the results of each study included in this review. In order to compare the sensitivity and specificity of MRI to that of CT in the diagnosis of acute appendicitis, the MRI data from all included studies were pooled and compared to sensitivity and specificity results from the largest meta-analysis on the accuracy of CT in diagnosing acute appendicitis to date[9]. A test for significance was conducted using Fisher's exact test. An analysis was also carried out using Fisher's exact test to compare sensitivity and specificity of MRI in studies in which MRI was used only after an indeterminate ultrasound versus in studies in which MRI was used as the primary imaging modality. In both analyses a two-tailed p value of <0.05 indicated significance.

Results

A preliminary search for "appendicitis/diagnosis" [MeSH] OR "appendicitis/radiography" [MeSH] returned 8335 results. Adding the term "child" [MeSH] to the search narrowed the results to 2624 articles. The addition of the term "magnetic resonance imaging" [MeSH] further narrowed the results down to 37 articles. Exclusion of all studies published more than 10 years ago decreased the number of results to 30. These 30 articles were closely evaluated by the author to determine their level of relevance to the hypothesis tested in this review, as well as for whether or not the inclusion and exclusion criteria were met. 9 studies were found to meet all requirements and be relevant to the hypothesis tested by this review. Among these, three are prospective studies, six are retrospective studies, and one is a comparative study. Two studies directly compare the accuracy of MRI to that of CT in diagnosing appendicitis in children, while the other eight report sensitivity and specificity of only MRI. Between them, the ten studies included in this review analyzed 1524 pediatric patients.[23-32]

Evaluation of use of MRI following indeterminate ultrasound results

Dillman, Gadepalli, and Sroufe et al.[23] conducted a retrospective analysis of the charts of 161 pediatric patients who underwent MRI or CT for suspected appendicitis after an indeterminate ultrasound. Of these, 103 subjects underwent MRI and 58 underwent CT. Sensitivity and specificity of MRI and CT in the diagnosis of appendicitis in the study sample were calculated, and the Fisher exact test was used to compare these values for MRI versus CT, with $p<0.05$ indicating significance. MRI correctly identified 17/18 subjects with confirmed appendicitis (Sensitivity=0.944; 95% CI: 0.727-0.999) and 85/85 of the remaining subjects who did not have appendicitis (Specificity=1.00; 95% CI: 0.958-1.00). CT correctly identified 11/11 patients with confirmed appendicitis (Sensitivity=1.00; 95% CI: 0.715-1.00) and 46/47 of subjects without appendicitis (Specificity=0.979; 95% CI: 0.887-1.00. Using the Fisher exact test, the difference between the sensitivities (p=1.00) and specificities (p=0.36) showed no statistically significant difference.[23]

Thieme, Leeuwenburgh, and Valdehueza et al.[24] prospectively studied a cohort of 104 consecutive pediatric patients with clinically suspected appendicitis, all of whom underwent abdominal ultrasound followed by MRI. This study evaluated three diagnostic strategies: ultrasound alone, ultrasound followed by MRI if the result is equivocal, and MRI alone. Sensitivity and specificity were calculated for each strategy. The authors used the McNemar test statistic to compare each method, with $p<0.05$ indicating significance. Ultrasound alone correctly identified 44/58 patients with appendicitis (Sensitivity=0.76; 95% CI: 0.63-0.85) and 41 of 46 patients without appendicitis (Specificity=0.89; 95% CI: 0.76-0.96). The conditional MRI strategy correctly identified 58/58 patients with appendicitis (Sensitivity=1.0; 95% CI: 0.92-1.0) and 37/46 patients without appendicitis (Specificity=0.80; 95% CI: 0.66-0.90). MRI alone correctly identified 58/58 patients with appendicitis (Sensitivity=1.0; 95% CI: 0.92-1.0) and 41/46 patients without appendicitis (Specificity=0.89; 95% CI: 0.76-0.96). The sensitivities of conditional MRI and MRI alone were found to be significantly higher than that of ultrasound alone ($p<0.001$), while there was no significant difference in specificity between any of the three strategies (p=0.13 for ultrasound alone, 0.13 for conditional MRI, 1.00 for MRI alone).[24]

Herliczek, Swenson, and Mayo-Smith[25] conducted a retrospective analysis of a cohort of 60 consecutive pediatric patients that underwent MRI for suspected appendicitis following an inconclusive ultrasound. The accuracy of MRI in this context was evaluated by calculating sensitivity and specificity for MRI in the diagnosis of acute appendicitis in the sample after an inconclusive ultrasound examination. Two MRI readers correctly identified 10/10 subjects with confirmed appendicitis (Sensitivity=1.00; 95% CI: 0.69-1.00) and 48/50 of those without appendicitis (Specificity=0.96; 95% CI: 0.86-1.00).[25]

A retrospective analysis conducted by Rosines, Chow, and Lampl et al.[26] evaluated 49 pediatric patients that underwent MRI for suspected acute appendicitis following an indeterminate ultrasound. MRI both with and without contrast was used for each patient. MR images were interpreted by a team of five radiologists, who came to a consensus on each image. Accuracy of MRI was evaluated by calculating the sensitivity and specificity for MRI in the diagnosis of acute appendicitis in this sample after indeterminate ultrasound. MRI correctly identified 15/16 subjects with appendicitis (Sensitivity=0.94; 95% CI: 0.70-1.00) and 33/33 of those without appendicitis (Specificity=1.00; 95% CI: 0.89-1.00).[26]

Studies that evaluate use of MRI alone

Kulaylat, Moore, and Engbrecht et al.[27] retrospectively analyzed a cohort of 655 pediatric patients that underwent imaging for suspected appendicitis. 510 of these subjects were evaluated by MRI, and images were evaluated independently by three reviewers. Sensitivity and specificity of MRI were calculated to assess diagnostic accuracy. MRI correctly identified 122/126 subjects with confirmed appendicitis (Sensitivity=0.968; 95% CI: 0.921-0.991) and 374/384 of those without appendicitis (Specificity=0.974; 95% CI: 0.953-0.987).[27]

Moore, Gustas, and Choudhary et al.[28] completed a retrospective study analyzing the accuracy of MRI 208 pediatric patients with suspected acute appendicitis. MR images were interpreted by one of six pediatric radiologists, and values for sensitivity and specificity of MRI were calculated. MRI correctly identified 40/41 subjects with confirmed appendicitis (Sensitivity=0.976; 95% CI: 0.871-0.999) and 162/167 subjects without appendicitis (Specificity=0.970; 95% CI: 0.932-0.990).[28]

Orth, Guillerman, Zhang, Masand, and Bisset[29] conducted a prospective study of 81 pediatric patients that were to undergo an ultrasound examination for suspected acute appendicitis and underwent MRI. 453 subjects met the inclusion criteria for the study but consent could not be obtained for 372 of these. The remaining 81 subjects included by the authors underwent both abdominal ultrasound and MRI. Accuracy of MRI was evaluated by calculating its sensitivity and specificity in this sample. These values were calculated twice: once with equivocal results designated as positive, and once with equivocal cases designated as negative. MRI correctly identified 28/30 subjects with confirmed appendicitis (Sensitivity=0.933; 95% CI: 0.779-0.992), and 50/51 subjects without appendicitis (Specificity=0.980; 95% CI: 0.896-1.00). None of the MR studies were found to be equivocal for acute appendicitis.[29]

Bayraktutan, Oral, and Kantarci et al.[30] conducted a prospective study of 47 consecutive pediatric patients with clinically diagnosed acute appendicitis or an appendix that could not be visualized on ultrasonography. 31 patients underwent abdominal ultrasound, and 45 underwent MRI. Two subjects did not undergo MRI due to claustrophobia. All 45 patients that underwent MRI underwent both diffusion-weighted and conventional MRI. Images were interpreted in three stages. First, the diagnosis was made based on diffusion-weighted MR images only. Second, the diagnosis was made based on conventional MR images only. And third, the diagnosis was made by reviewing both simultaneously. Sensitivity and specificity were determined for each of the three diagnostic approaches, and the McNemar test was used to determine any significant differences between the three. Results were considered significant with a two-tailed $P< 0.05$. 36 out of 45 patients were found to have acute appendicitis. The diagnostic strategy in which both diffusion-weighted and conventional MR images were utilized simultaneously correctly identified 33 of these (Sensitivity=0.92; 95% CI: 0.78-0.98) as well as all nine of the patients that did not have appendicitis (Specificity=1.00; 95% CI: 0.66-1.00). Using the McNemar test, the combined strategy of using both diffusion-weighted and conventional MRI simultaneously was found to have statistically higher sensitivity and accuracy than either diffusion-weighted or conventional MRI alone ($p<0.05$). No significant difference was found between sensitivity and accuracy of the diffusion-weighted MRI alone and conventional MRI alone strategies.[30]

Koning, Naheedy, and Kruk[31] conducted a retrospective review of 364 consecutive pediatric patients undergoing gadolinium-enhanced MRI for suspected MRI. Images were interpreted by any of nine pediatric radiologists, who were not blinded to previous imaging and clinical findings. Pathologic findings served as the reference standard in patients who underwent surgery, while documentation of the alternate diagnosis was used in those that did not. Several patients that did not undergo surgery were imaged using CT in addition to MRI. For these patients, CT was used as the reference standard. To assess diagnostic performance of MRI, sensitivity and specificity values were calculated. MRI correctly identified 127/132 subjects with confirmed appendicitis (Sensitivity=0.962; 95% CI: 0.914-0.984) and 222/232 subjects without appendicitis (Specificity=0.957; 95% CI: 0.923-0.976).[31]

Comparison of MRI following indeterminate ultrasound versus as the primary imaging modality

A subgroup analysis of results from subjects that underwent MRI after indeterminate ultrasound versus those that underwent MRI as the primary modality showed that MRI following indeterminate ultrasound correctly identified 100/102 subjects with confirmed appendicitis and 203/217 subjects without appendicitis. MRI alone correctly identified 350/365 subjects with confirmed appendicitis and 817/843 subjects without appendicitis. An analysis using Fisher's exact test revealed no significant difference between sensitivity ($p=0.39$) and specificity ($p=0.10$) of MRI following indeterminate ultrasound versus as the primary imaging modality.

Pooled Data and Comparison to CT

Among the 1524 subjects from the nine studies included in this review, 467 were found to have acute appendicitis by the reference standard used in each respective study.[24-32] MRI correctly identified 450 of these patients as positive for appendicitis (Sensitivity=0.96; 95% CI: 0.94-0.98). Of the remaining 1057 patients that did not have appendicitis, MRI correctly identified 1024 as negative for appendicitis (Specificity=0.97; 95% CI: 0.96-0.98). The largest meta-analysis conducted to date on the accuracy of CT in the diagnosis of children with suspected appendicitis found that CT has sensitivity of 0.94 (95% CI: 0.92-0.97) and specificity of 0.95 (0.94-0.97).[9] Using Fisher's exact test, it was found that there is no significant difference between sensitivity (p=0.11) and specificity (p=0.06) of MRI versus CT for diagnosing acute appendicitis in pediatric patients. A summary of the sensitivity and specificity of MRI in the included studies can be seen in figure 1 and table 1 below.

The nine studies included in this review are not without their limitations. Four studies were limited by small sample size and by being single institution studies. In two studies, the reference standard was not independent of imaging results, as the expert panel had access to previous imaging and/or clinical findings. The study by Orth et al. suffered from non-response bias, as 170 of 453 potential subjects refused consent. Two studies used MRI with gadolinium-based contrast, while the others used only non-contrast MRI. In three studies, MR images were read by any of multiple radiologists. This would introduce more bias into the studies than in those in which multiple readers come to a consensus on each image.

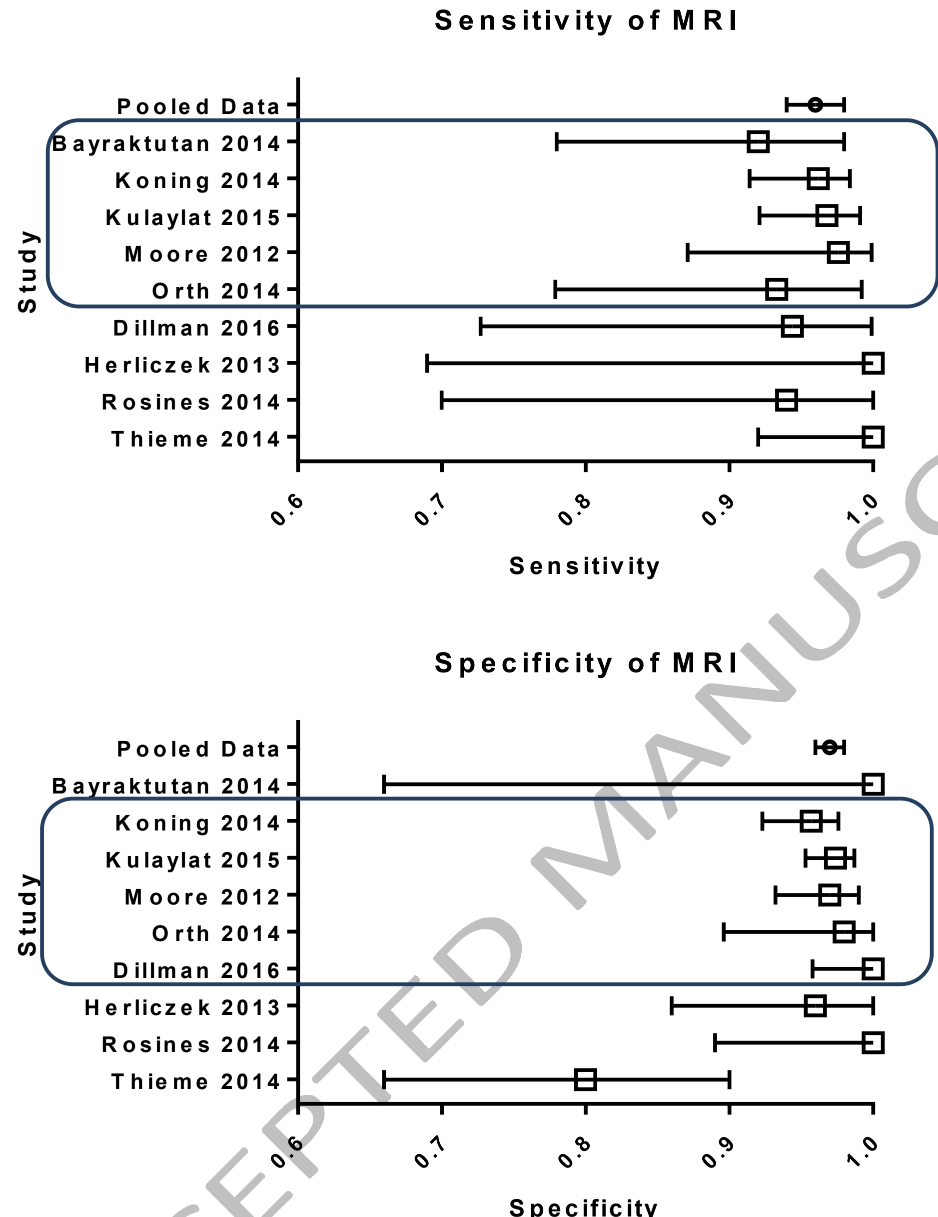


Figure 1. Forest plots summarizing sensitivity and specificity of MRI in the included studies. Studies contained within the boxes studied the use of MRI alone, while those outside the boxes studied the use of MRI after indeterminate ultrasound.

	TP	FN	FP	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bayraktutan 2014	33	0	3	9	0.92 [0.78, 0.98]	1.00 [0.66, 1.00]
Koning 2014	127	10	5	222	0.96 [0.91, 0.99]	0.96 [0.92, 0.98]
Kulaylat 2015	122	10	4	374	0.97 [0.92, 0.99]	0.97 [0.95, 0.99]
Moore 2012	40	5	1	162	0.98 [0.87, 1.00]	0.97 [0.93, 0.99]
Orth 2014	28	1	2	50	0.93 [0.78, 0.99]	0.98 [0.90, 1.00]
Dillman 2016	17	0	1	85	0.94 [0.73, 1.00]	1.00 [0.96, 1.00]
Herliczek 2013	10	2	0	48	1.00 [0.69, 1.00]	0.96 [0.86, 1.00]
Rosines 2014	15	3	1	33	0.94 [0.70, 1.00]	0.92 [0.78, 0.98]
Thieme 2014	58	9	0	37	1.00 [0.94, 1.00]	0.80 [0.66, 0.91]
Pooled Data	**450**	**40**	**17**	**1020**	**0.96 [0.94, 0.98]**	**0.96 [0.95, 0.97]**

Table 1. Summary of sensitivity and specificity in the included studies.

Discussion

At the conclusion of this review, it was found that the sensitivity and specificity of MRI for the diagnosis of acute appendicitis in pediatric patients are comparable to the sensitivity and specificity of CT. This is true both if MRI is used as a standalone modality, as well as if it is used only after an indeterminate ultrasound examination. This confirms the hypothesis set at the beginning of this review. Given the amount of radiation exposure associated with CT, discussions should be had about whether CT might be over-utilized in the evaluation of suspected appendicitis, especially in pediatric patients who are more susceptible to the effects of radiation. While there are many factors to consider when choosing an imaging modality, it is clear that MRI is a valid choice in the evaluation of suspected appendicitis, and deserves serious consideration.

There are, however, many questions still to be answered about the use of MRI in the evaluation of suspected acute appendicitis in children. For example, although MRI may have comparable sensitivity and specificity to CT, MRI is still associated with higher costs. On the other hand, two recent studies in the Netherlands on utilization of MRI in the evaluation of adults with suspected appendicitis have found a protocol utilizing MRI rather than CT actually resulted in a net savings for their respective institutions.[32-33] Further study is needed to determine the cost-effectiveness of MRI for diagnosis of appendicitis on a broader scale. Some other disadvantages to MRI are the general lack of availability in the emergency setting, slower speed of imaging than CT, and that claustrophobic patients and young children may not be able to tolerate remaining perfectly still for imaging. Hopefully as knowledge about the utility of MRI in emergency situations grows, its availability will increase as well, making its utilization more feasible on a larger scale. As the development of ultra-fast MRI sequences progresses, it is also our hope that it will become easier for claustrophobic and very young patients to tolerate MRI without need for sedation.

Another concern that remains in regards to the feasibility of using MRI in the evaluation of suspected appendicitis is the relative lack of research on inter-reviewer reliability and the effect of reader experience or inexperience on accuracy. A 2014 study in the Netherlands assessed inter-reviewer reliability between MR experts and non-experts in 223 cases of suspected appendicitis in adults that were evaluated using MRI. The study found that although experts showed higher accuracy in reading MR images in patients with suspected appendicitis, experts and non-experts agreed 89% of the time, indicating a good inter-reviewer reliability (kappa=0.78).[34] These results are promising, but more research is still needed to confirm these results as well as to establish inter-reviewer reliability in diagnosing suspected appendicitis in the pediatric population.

It is important to recognize that this review does have some general limitations. First, the reference standard used to determine final diagnoses was not independent of the result of the MRI evaluations. Patients with positive findings for appendicitis underwent surgery, and surgical pathologic findings served as the reference standard, while the reference standard for patients with negative findings for appendicitis was clinical follow-up. Another limitation is the variation of inclusion and exclusion criteria amongst the studies included in this review. Some authors chose to use MRI to image only those patients with an inconclusive ultrasound, while others imaged all patients that were to undergo imaging for suspected acute appendicitis. A third limitation is that these studies used differing MRI protocols. Different sequences were used in each study, and two of the nine studies used contrast-enhanced MRI while the others did not. The MRI sequences used in each study are summarized in Table 2. A last potential limitation is publication bias. Results that show high sensitivity and specificity for MRI in the diagnosis of acute appendicitis are more likely to be submitted for publishing. This could have significantly inflated the results for accuracy of MRI.

First Author	Field Strength	T1 GRE	T1 TSE	T2 TSE	T2 SSFSE	DWI	STIR	bSSFP	T1 w/ contrast	bSSFP contrast
Bayraktutan	1.5 T		✓	✓*		✓				
Dillman	1.5& 3T				✓*					
Herliczek	1.5& 3T			✓	✓		✓	✓		
Koning	1.5 T				✓	✓		✓	✓	
Kulaylat	1.5& 3T			✓						
Moore	1.5 T				✓*					
Orth	1.5 T	✓		✓*		✓				
Rosines	1.5 T	✓			✓					✓*
Thieme	1.5 T				✓	✓		✓*		

Table 2: Summary of MRI protocols used in the included studies
*-indicates that fat suppression was used in this sequence
GRE=gradient-recalled echo; TSE=turbo-spin echo; SSFSE=single shot fast-spin echo
STIR=short inversion time inversion recovery; bSSFP=balanced steady state free precession
DWI=diffusion-weighted imaging; SPAIR=spectral adiabatic inversion recovery

Despite these limitations, the conclusions of this review remain valid. Although MRI protocol differed between the studies included in this review, this likely to be the case in different clinical centers that may choose to implement MRI in the evaluation of suspected appendicitis in children. The inclusion of studies that used MRI only after indeterminate ultrasound and as the primary modality is a potential concern, but an analysis of the sensitivity and specificity in these two scenarios revealed no statistically significant difference. The difference in the reference standard used depending on imaging results is also certainly more similar to actual clinical scenarios, as unnecessary surgical interventions should always be avoided. Although a publication bias cannot be completely ruled out, a search of the

ClinicalTrials.gov database returned only one result for the search terms "MRI" and "appendicitis".

Conclusion

In conclusion, MR imaging has demonstrated sensitivity and specificity equal to that of the current gold standard test (CT) in the evaluation of pediatric patients with suspected acute appendicitis. MRI is an attractive option in this scenario as it does not require exposure to large amounts of ionizing radiation, which children are more susceptible to. Although more research is needed to determine the cost-effectiveness and feasibility of implementing MRI on a large scale, it is clear that clinicians can make the decision to use MRI without sacrificing diagnostic accuracy.

References

1. Guthery, S.L., Hutchings, C., Dean, J.M., & Hoff, C. (2004). National estimates of hospital utilization by children with gastrointestinal disorders: analysis of the 1997 kids' inpatient database. *The Journal of Pediatrics*, 144(5), 589-94. http://dx.doi.org/10.1016/j.peds.2004.02.029

2. Addiss, D.G., Shaffer, N., Fowler, B.S., & Tauxe, R.V. (1990). The epidemiology of appendicitis and appendectomy in the United States. *American Journal of Epidemiology*, 132 (5), 910-25.

3. Seetahal, S.A., Bolorunduro, O.B., & Sookdeo, T.C. et al. (2011). Negative appendectomy: a 10-year review of a nationally representative sample. *American Journal of Surgery*, 201(4), 433-7. http://dx.doi.org/10.1016/j.amjsurg.2010.10.009

4. Saito, J.M., Yan, Y., Evashwick, T.W., Warner, B.W., & Tarr, P.I. (2013). Use and accuracy of diagnostic imaging by hospital type in pediatric appendicitis. *Pediatrics*, 131(1), 37-44. http://dx.doi.org/10.1542/peds.2012-1665

5. Fahimi, J., Herring, A., Harries, A., Gonzales, R., & Alter, H. (2012). Computed tomography use among children presenting to emergency departments with abdominal pain. *Pediatrics*, 130(5), 1069-75. http://dx.doi.org/10.1542/peds.2012-0739

6. Hernanz-Schulman, M. (2010). CT and US in the diagnosis of appendicitis: an argument for CT. *Radiology*, 255(1), 3-7. http://dx.doi.org/10.1148/radiol.2553201003

7. Raja, A.S., Wright, C., & Sodickson, A.D. et al. (2010). Negative appendectomy rates in the era of CT: an 18-year perspective. *Radiology*, 256(2), 460-65. http://dx.doi.org/10.1148/radiol.10091570

8. Charfi, S., Sellami, A., Affes, A., Yaich, K., Mzali, R., & Boudawara, T.S. (2014). Histopathological findings in appendectomy specimens: a study of 24,697 cases. *International Journal of Colorectal Disease*, 29(8), 1009-12. http://dx.doi.org/10.1007/s00384-014-1934-7

9. Doria, A.S., Moineddin, R., & Kellenberger, C.J. et al. (2006). US or CT for Diagnosis of Appendicitis in Children and Adults? A Meta-Analysis. *Radiology*, 241(1), 83-94. http://dx.doi.org/10.1148/radiol.2411050913

10. Brenner, D.J. & Hall, E.J. (2007). Computed tomography—an increasing source of radiation exposure. *New England Journal of Medicine*, 357(22), 2277-84. http://dx.doi.org/10.1056/NEJMra072149

11. Mathews, J.D., Forsythe, A.V., & Brady, Z. et al. (2013). Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. *BMJ*, 346. http://dx.doi.org/10.1136/bmj.f2360

12. Pearce, M.S., Salotti, J.A., & Little, M.P. et al. (2012). Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. *Lancet*, 380(9840), 499-505. http://dx.doi.org/10.1016/S0140-6736(12)60815-0

13. Nash, K., Hafeez, A., & Hou, S. (2002). Hospital-acquired renal insufficiency. *American Journal of Kidney Diseases*, 39(5), 930-36. http://dx.doi.org/10.1053/ajkd.2002.32766

14. Laroche, D., Aimone-Gastin, I., & Dubois, F. et al. (1998). Mechanisms of severe, immediate reactions to iodinated contrast material. *Radiology*, 209(1), 183-90. http://dx.doi.org/10.1148/radiology.209.1.9769830

15. Cogley, J.R., O'Connor, S.C., Houshyar, R., & Al Dulaimy, K. (2012). Emergent pediatric US: what every radiologist should know. *Radiographics*, 32(3), 651-65. http://dx.doi.org/10.1148/rg.323115111

16. van Randen, A., Bipat, S., Zwinderman, A.H., Ubbink, D.T., Stoker, J., & Boermeester, M.A. (2008). Acute appendicitis: meta-analysis of diagnostic performance of CT and graded compression US related to prevalence of disease. *Radiology*, 249(1), 97-106. http://dx.doi.org/10.1148/radiol.2483071652

17. Lowe, L.H., Penney, M.W., & Stein, S.M. et al. (2001). Unenhanced limited CT of the abdomen in the diagnosis of appendicitis in children: comparison with sonography. *American Journal of Roentgenology*, 176(1), 31-35. http://dx.doi.org/10.2214/ajr.176.1.1760031

18. Krishnamoorthi, R., Ramarajan, N., & Wang, N.E. et al. (2011). Effectiveness of a staged US and CT protocol for the diagnosis of pediatric appendicitis: reducing radiation exposure in the age of ALARA. *Radiology*, 259(1), 231-39. http://dx.doi.org/10.1148/radiol.10100984

19. Poletti, P.A., Platon, A., & De Perrot, T. et al. (2011). Acute appendicitis: prospective evaluation of a diagnostic algorithm integrating ultrasound and low-dose CT to reduce the need of standard CT. *European Radiology*, 21(12), 2558-66. http://dx.doi.org/10.1007/s00330-011-2212-5

20. Rosen, M.P., Ding, A., & Blake, M.A. et al. (2011). ACR Appropriateness Criteria® right lower quadrant pain—suspected appendicitis. *Journal of the American College of Radiology*, 8(11), 749-55. http://dx.doi.org/10.1016/j.jacr.2011.07.010

21. Pedrosa, I. & Rofsky, N.M. (2003). MR imaging in abdominal emergencies. *Radiologic*

Clinics of North America, 41(6), 1243-73.

22. Barger Jr, R.L. & Nandalur, K.R. (2010). Diagnostic performance of magnetic resonance imaging in the detection of appendicitis in adults: a meta-analysis. *Academic Radiology*, 17(10), 1211-16. http://dx.doi.org/10.1016/j.acra.2010.05.003

23. Dillman, J.R., Gadepalli, S., & Sroufe, N.S. et al. (2016). Equivocal Pediatric Appendicitis: Unenhanced MR Imaging Protocol for Nonsedated Children-A Clinical Effectiveness Study. *Radiology*, 279(1), 216-25. http://dx.doi.org/10.1148/radiol.2015150941

24. Thieme, M.E., Leeuwenburgh, M.M., & Valdehueza, Z.D. et al. (2014). Diagnostic accuracy and patient acceptance of MRI in children with suspected appendicitis. *European Radiology*, 24(3), 630-37. http://dx.doi.org/10.1007/s00330-013-3044-2

25. Herliczek, T.W., Swenson, D.W., & Mayo-Smith, W.W. (2013). Utility of MRI after inconclusive ultrasound in pediatric patients with suspected appendicitis: retrospective review of 60 consecutive patients. *American Journal of Roentgenology*, 200(5), 969-73. http://dx.doi.org/10.2214/AJR.12.10078

26. Rosines, L.A., Chow, D.S., & Lampl, B.S. et al. (2014) Value of gadolinium-enhanced MRI in detection of acute appendicitis in children and adolescents. *American Journal of Roentgenology*, 203(5), 543-48. http://dx.doi.org/10.2214/AJR.13.12093

27. Kulaylat, A.N., Moore, M.M., & Engbrecht, B.W. et al. (2015). An implemented MRI program to eliminate radiation from the evaluation of pediatric appendicitis. *Journal of Pediatric Surgery*, 50(8), 1359-63. http://dx.doi.org/10.1016/j.jpedsurg.2014.12.012

28. Moore, M.M., Gustas, C.N., & Choudhary, A.K. et al. (2012). MRI for clinically suspected pediatric appendicitis: an implemented program. *Pediatric Radiology*, 42(9), 1056-63. http://dx.doi.org/10.1007/s00247-012-2412-4

29. Orth, R.C., Guillerman, R.P., Zhang, W., Masand, P., & Bisset III, G.S. (2014). Prospective comparison of MR imaging and US for the diagnosis of pediatric appendicitis. *Radiology*, 272(1), 233-40. http://dx.doi.org/10.1148/radiol.14132206

30. Bayraktutan, U., Oral, A., & Kantarci, M. et al. (2014). Diagnostic performance of diffusion-weighted MR imaging in detecting acute appendicitis in children: comparison with conventional MRI and surgical findings. *Journal of Magnetic Resonance Imaging*, 39(6), 1518-24. http://dx.doi.org/10.1002/jmri.24316

31. Koning, J.L., Naheedy, J.H., & Kruk, P.G. (2014). Diagnostic performance of contrast-

enhanced MR for acute appendicitis and alternative causes of abdominal pain in children. *Pediatric Radiology*, 44(8), 948-55. http://dx.doi.org/10.1007/s00247-014-2952-x

32. Cobben, L., Groot, I., Kingma, L., Coerkamp, E., Puylaert, J., & Blickman, J. (2009). A simple MRI protocol in patients with clinically suspected appendicitis: results in 138 patients and effect on outcome of appendectomy. *European Radiology*, 19(5), 1175-83. http://dx.doi.org/10.1007/s00330-008-1270-9

33. Heverhagen, J.T., Pfestroff, K., Heverhagen A.E., Klose, K.J., Kessler, K., & Sitter, H. (2012). Diagnostic accuracy of magnetic resonance imaging: a prospective evaluation of patients with suspected appendicitis (diamond). *Journal of Magnetic Resonance Imaging*, 35(3), 617-23. http://dx.doi.org/10.1002/jmri.22854

34. Leeuwenburgh, M.M., Wiarda, B.M., & Jensch, S. et al. (2014). Accuracy and interobserver agreement between MR-non-expert radiologists and MR-experts in reading MRI for suspected appendicitis. *European Journal of Radiology*, 83(1), 103-10. http://dx.doi.org/10.1016/j.ejrad.2013.09.022

APPENDIX—Evidence Table

First Author	Date Published	Study Design	Evidence Level	Study Population	Exposure	
Bayraktutan	June 2014	Prospective Study	2	45 consecutive pediatric patients aged 0-14 presenting to the ED over a 4 month period with diagnosed appendicitis or a non-visualized appendix on ultrasonography	Patients underwent diffusion-weighted and conventional MR imaging. Diagnosis was made using diffusion-weighted and conventional images alone, and then by combining the two images	Th str se (3 0.9 1.0 1.0 se tha or alo
Dillman	April 2016	Retrospective Study	3	161 children that underwent either MRI (n=103) or CT (n=58) for suspected appendicitis after an equivocal ultrasound at a single institution over a two one-year periods	Patients underwent MRI or CT as part of evaluation of suspected appendicitis	M Se (1 0.9 Sp 95 CT Se 95 Sp (4 1.0 No be (p (p CT
Herliczek	May 2013	Retrospective Study	3	60 children aged 7-17 that underwent MRI after an indeterminate ultrasound for suspected appendicitis between Dec. 2009 and Apr. 2012	Patients underwent MRI as part of evaluation for suspected appendicitis	M se (1 1.0 0.9 0.8

Koning	August 2014	Retrospective Study	3	364 consecutive pediatric patients that underwent contrast-enhanced MRI for suspected appendicitis between November 2012 and September 2013.	Patients underwent contrast-enhanced MRI as part of evaluation for suspected appendicitis.	Co ac 0.9 0.9 sp (2 0.9
Kulaylat	August 2015	Retrospective Study	3	510 pediatric patients aged 3-17 that underwent imaging for suspected appendicitis at one institution between July 2011 and Dec. 2013	Patients underwent an MRI examination as part of evaluation for suspected appendicitis	M se (1 0.9 sp (3 0.9 sa
Moore	September 2012	Retrospective Study	3	208 pediatric patients aged 5-17 that were evaluated in the emergency room for suspected appendicitis between March 2010 and March 2011	All patients underwent MRI as the primary imaging modality in the evaluation for suspected appendicitis	M se (4 0.9 0.9 0.9 sa
Orth	July 2014	Prospective Study	2	81 consecutive pediatric patients aged 4-17 that were seen in the ER for suspected appendicitis between June 2012 and May 2013	All patients underwent both ultrasound and MRI of the abdomen as part of the evaluation of suspected appendicitis	M se (2 0.9 0.9 0.8 sa
Rosines	November 2014	Retrospective Study	3	49 pediatric patients that underwent MRI for suspected appendicitis after an indeterminate ultrasound at a single institution	All patients underwent both contrast-enhanced and unenhanced MRI as part of evaluation of suspected appendicitis.	M se (1 1.0 1.0 0.8

Thieme	March 2014	Prospective Study	2	104 consecutive pediatric patients aged 4-18 that presented to the ER with clinically suspected appendicitis between April and December 2009	All patients underwent both ultrasound and MRI of the abdomen as part of evaluation for suspected appendicitis. Three strategies were compared: ultrasound alone, conditional MRI after indeterminate ultrasound, and MRI alone	<u>Co</u> Se CI Sp CI <u>M</u> Se CI Sp CI No wa ser sp str

<u>Evidence levels were determined as follows:</u>
1. Randomized controlled trials
2. Non-randomized controlled trials
3. Observational studies with controls
4. Observational studies without controls