Abstract
Diagnostic imaging plays a key role in the diagnosis and management of inflammatory bowel disease (IBD). However due to the relapsing nature of IBD, there is growing concern that IBD patients may be exposed to potentially harmful cumulative levels of ionising radiation in their lifetime, increasing malignant potential in a population already at risk. In this review we explore the proportion of IBD patients exposed to high cumulative radiation doses, the risk factors associated with higher radiation exposures, and we compare conventional diagnostic imaging with newer radiation-free imaging techniques used in the evaluation of patients with IBD. While computed tomography (CT) performs well as an imaging modality for IBD, the effective radiation dose is considerably higher than other abdominal imaging modalities. It is increasingly recognised that CT imaging remains responsible for the majority of diagnostic medical radiation to which IBD patients are exposed. Magnetic resonance imaging (MRI) and small intestine contrast enhanced ultrasonography (SICUS) have now emerged as suitable radiation-free alternatives to CT imaging, with comparable diagnostic accuracy. The routine use of MRI and SICUS for the clinical evaluation of patients with known or suspected small bowel Crohn’s disease is to be encouraged wherever possible. More provision is needed for out-of-hours radiation-free imaging modalities to reduce the need for CT.

Key words: Diagnostic medical radiation; Inflammatory bowel disease; Small bowel follow-through; Computerised tomography; Nuclear medicine; Magnetic resonance enterography; Small intestine contrast-enhanced ultrasonography

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Due to the chronic and relapsing nature of inflammatory bowel disease (IBD), patients are at risk of exposure to potentially harmful cumulative radiation...
doses in their lifetime. Computed tomography (CT) imaging remains responsible for the majority of this radiation exposure. As well as new reduced radiation CT imaging techniques, radiation-free alternatives magnetic resonance imaging and small intestine contrast enhanced ultrasonography have emerged, offering comparable diagnostic accuracy. In this review we explore the proportion of IBD patients exposed to high cumulative radiation doses, the factors associated with higher radiation exposures, and we compare conventional imaging with newer radiation-free imaging techniques for the evaluation of patients with IBD.

INTRODUCTION

Inflammatory bowel disease (IBD), consisting of ulcerative colitis (UC) and Crohn’s disease (CD), is a chronic relapsing-remitting inflammatory disorder of the gastrointestinal tract. The prevalence of IBD is increasing worldwide, with 2.2 million and 1.4 million people affected in Europe and United States respectively.

Diagnostic imaging is required to aid the diagnosis of IBD, assess disease extent and severity, detect complications including extra-intestinal manifestations, and monitor response to treatment. Due to the relapsing nature of IBD, multiple imaging studies are often required. Despite this, in clinical practice cumulative exposure to radiation is not routinely monitored.

Patients with IBD have an increased lifetime risk of developing colorectal and small intestinal cancers, irrespective of diagnostic radiation exposure. There is growing concern that repeated X-ray based imaging may additionally expose this typically young cohort of patients to harmful cumulative levels of ionising radiation, further increasing their lifetime cancer risk.

In this article we review the proportion of IBD patients exposed to potentially harmful cumulative radiation doses and the risk factors associated with higher radiation exposures. We explore and compare conventional diagnostic imaging and newer radiation-free imaging techniques for the evaluation of patients with IBD.

RADIATION EXPOSURE AND CANCER RISK

Extensive study of the atomic bomb survivors from Hiroshima and Nagasaki has formed the basis for quantitative estimates of radiation-induced cancer risk. In this large cohort of survivors, the rates of solid cancer deaths were positively associated with higher radiation doses and younger age of exposure. In a 2012 study of the atomic bomb survivors, the relative risk of solid cancers increased by 29% per decade decrease in the initial age of radiation exposure. Younger people appear to be inherently more radiosensitive, and have more remaining life-years during which a cancer may develop.

It is estimated that diagnostic medical radiation (DMR) exposure may be responsible for up to 2% of cancers worldwide. Younger patients and females appear to have the greatest radiation-induced cancer risk. Epidemiological data suggests that ionising radiation levels as low as 50 millisieverts (mSv) have been implicated in the development of solid tumours. Potentially harmful radiation exposure is, therefore, commonly defined as cumulative effective dose (CED) > 50 mSV; the equivalent of five computed tomography (CT) abdominal-pelvis scans. A reference table comparing radiation exposure doses of common diagnostic gastrointestinal imaging techniques is included in Table 1.

| Imaging procedure | Average effective dose (mSv) | Time period for equivalent effective dose from natural background radiation |
|-------------------|-----------------------------|-----------------------------------------------------------------------|
| Multiphase CT abdomen and pelvis | 31 | 10.3 yr |
| PET/CT | 25 | 8.3 yr |
| CT Abdomen and Pelvis | 10 | 3.3 yr |
| CT Colonography | 10 | 3.3 yr |
| CT Abdomen | 8 | 2.7 yr |
| Barium Enema | 8 | 2.7 yr |
| Small bowel follow-through | 5 | 1.7 yr |
| X-ray abdomen | 0.7 | 2.8 mo |

1Based on the assumption of an average effective dose of 3 mSv per year from natural background radiation. CT: Computed tomography; PET: Positron emission tomography.

CUMULATIVE RADIATION EXPOSURE IN IBD PATIENTS

Several published studies have attempted to quantify the proportion of IBD patients exposed to potentially harmful cumulative levels of ionising radiation (summarised in Table 2). Desmond et al first evaluated DMR exposure in 354 patients with CD in a single tertiary centre in Ireland. CT imaging accounted for 77.2% of the total DMR exposure. The mean CED was 36.1 mSv and exceeded 75 mSv in 15.5% of patients. More recently, a meta-analysis by Chatu et al...
Table 2  Quantification of the cumulative effective dose of diagnostic radiation received by IBD patients, and factors associated with high cumulative radiation exposure (cumulative effective dose > 50 mSv); adapted from Chatu et al[12] with permission

| Study               | Number of patients (n) | Country             | Design                                                                 | Patient population | Outcome CED ≥ 50 mSv | Mean/Median CED (mSv) | Factors associated with high radiation exposure |
|---------------------|------------------------|---------------------|------------------------------------------------------------------------|--------------------|----------------------|------------------------|------------------------------------------------|
| Newnham et al[59], 2007 | 100 (62 CD, 37 UC, 1 indeterminate colitis) | Australia          | Retrospective study, single tertiary centre, patients recruited consecutively from clinic | Adult (16-84 yr) 11/100 (11%) 9 CD, 2 UC | Median CED 10 mSv | Assessed: age, gender, disease, disease duration, previous surgery, immunomodulator use, referral source Significant: none |
| Desmond et al[11], 2008 | 354 CD                  | Ireland            | Retrospective study, single tertiary centre, patients recruited from IBD database July 1992-June 2007 | Adult and paediatric (8.6-78.3 yr) CED ≥ 75 mSv in 55/354 patients (15.5%) | Mean CED 36.1 mSv | Assessed: age, gender, smoking, FH, disease distribution, disease behaviour, medication, surgical history Significant: age < 17 at diagnosis, upper GI tract disease, penetrating disease, requirement for IV steroids, infliximab use, multiple surgeries |
| Peloquin et al[18], 2008 | 215 (103 CD, 112 UC)    | United States      | Retrospective study, population based inception cohort diagnosed between 1991 to 2001 from Olmsted County | Adult and paediatric (1.2-91.4 yr) N/A | N/A | Median CED CD: 26.6 mSv UC: 10.5 mSv |
| Levi et al[60], 2009  | 324 (199 CD, 125 UC)    | Israel             | Retrospective study, single tertiary centre, patients diagnosed Jan 1999-Dec 2006, recruited from IBD database | Adult and paediatric ≤ 17 yr (18) > 18 yr (306) 23/324 (7.1%) | Mean CED CD: 21.1 mSv UC: 15.1 mSv | Assessed: age, surgery, diagnosis, medical therapy, disease duration, gender Significant: CD, surgery, prednisolone use, disease duration, first year of disease, age |
| Palmer et al[61], 2009 | 1593 (965 CD, 628 UC)   | United States      | Retrospective study, population based cohort recruited from insurance claims database Jan 2003-December 2004 | Paediatric (2-18 yr) N/A (34% CD, 23% UC exposed to moderate radiation - at least 1 CT or 3 fluoroscopic procedures) | N/A | N/A |
| Kroecker et al[62], 2011 | 553 (371 CD, 182 UC)    | Canada             | Retrospective study, single tertiary centre, patients diagnosed 2003-2008, recruited from IBD database | Adult and paediatric (15-84 yr) 28/553 (5%) 27 CD, 1 UC | Mean CED CD: 14.3 mSv UC: 5.9 mSv | Assessed: age at diagnosis, gender, disease distribution, previous surgery Significant: prevalent surgery Assessed in CD cohort: gender, disease behaviour, previous surgery, disease duration, elevated platelet count at diagnosis Significant: previous surgery, elevated platelet count at diagnosis |
| Fuchs et al[63], 2011  | 257 (171 CD, 86 UC)     | United States      | Retrospective study Paediatric (< 18 yr) 15/257 (5.8%) 14 CD, 1 UC | Mean CED CD: 20.5 mSv UC: 11.7 mSv Median CED CD: 15.6 mSv UC: 7.2 mSv |
| Sauer et al[64], 2011  | 117 (86 CD, 31 UC)      | United States      | Retrospective study, single tertiary centre, patients reviewed Jan-May 2008 | Paediatric (2-18 yr) 6/117 (5%) 6 CD | Median CED CD: 20.5 mSv UC: 11.7 mSv Median CED CD: 15.6 mSv UC: 7.2 mSv |

Zakeri N et al. Imaging and radiation exposure in IBD
evaluated six studies including a total of 1704 IBD patients. It reported a pooled estimate of 8.4% of IBD patients receiving high dose radiation exposure (CED > 50 mSv). More patients with CD (11.1%) were exposed to high cumulative radiation doses (CED > 50 mSv) than patients with UC (2%) \(^{[12]}\).

Similar trends have been found in studies following this meta-analysis. A 2015 retrospective review of 325 IBD patients in Chile, reported 19.5% of patients with CD and 2.4% of patients with UC, to be exposed to CED > 50 mSv\(^{[13]}\). A recent United Kingdom retrospective study of 415 patients with IBD referred from primary care, reported a median total CED of 7.2 mSv in CD patients and 2.8 mSv in UC patients, with 8% of IBD patients overall exposed to CED > 50 mSv. Kaplan Meier analysis projected a probability

| Publication | Year | Patients | Country | Study Design | Cohort | Radiation Exposed | CED Median | CED Range | Significant Factors |
|-------------|------|----------|---------|--------------|--------|------------------|------------|------------|-------------------|
| Huang et al\(^{[6]}\), 2011 | 2011 | 105 (63 CD, 32 UC, 12 indeterminate colitis) | United States | Single tertiary paediatric centre, patients identified from medical records | Paediatric cohort (11 mo-18 yr) | 6/105 (6%) | Mean CED 15 mSv | | Assessed: surgery, disease type, disease location, racioethic background, anti TNF agents, use of immunomodulators, hospital admissions, age at diagnosis

Significant: CD, small bowel involvement, black ethnicity, number of hospital admissions, previous surgery, anti TNF alpha use |

| Butcher et al\(^{[7]}\), 2012 | 2012 | 280 | United Kingdom | Retrospective study, Single tertiary centre, consecutive patients attending IBD clinic | Adult cohort | 6.3% CD | Mean CED 10.17 mSv | Median CED 4.12 mSv | Assessed: smoking status, disease duration, previous surgery |

Significant: For CD - longer disease duration, ileocolonic disease, upper GI tract involvement, surgery, hospitalisation, 5-ASA use, steroids, immunomodulator use |

| Jung et al\(^{[8]}\), 2013 | 2013 | 2199 (777 CD, 1422 UC) | South Korea | Retrospective study, multicentre conducted at 13 university hospitals in South Korea, patients diagnosed July 1987-Jan 2012 included | Adult cohort (Mean age: CD 29.2 yr; UC 42.2 yr) | 34.7% CD, 8.4% UC | Mean CED CD: 53.6 mSv; UC: 16.4 mSv | | Assessed: gender, age at diagnosis, disease duration, disease extent, surgery, hospitalisation, 5-ASA use, steroids, immunomodulator use |

Significant: For CD - longer disease duration, ileocolonic disease, upper GI tract involvement, surgery, hospitalisation, steroids

For UC - surgery, hospitalisation, infliximab use |

| Chaturvedi et al\(^{[9]}\), 2013 | 2013 | 415 (217 CD, 198 UC) | United Kingdom | Retrospective study, single tertiary centre, patients consecutively recruited from clinic Jan 2011- June 2011 | Adult cohort (Mean age: CD 30.8 yr; UC 36.9 yr) | 32/415 (8%); 29 CD, 3 UC | Median CED CD: 7.2 mSv; UC: 2.8 mSv | | Assessed: gender, age at diagnosis, disease type, steroid use within 3 mo diagnosis, use of immunomodulators or biologics, extraintestinal features, IBD related surgery

Significant: males, IBD related surgery |

| Estay et al\(^{[10]}\), 2015 | 2015 | 325 (82 CD, 243 UC) | Chile | Retrospective study, patients recruited from IBD Registry 2011-2013 | Adult cohort (16-86 yr) | 22/325 (6.8%); CD 16 (19.5%); UC 6 (2.5%) | Mean CED CD: 11.97 mSv; UC: 5.92 mSv | | Assessed in CD cohort only: age at diagnosis, disease duration, disease location, disease behaviour, perianal disease, surgery, hospitalisation, medications

Significant: longer disease duration, ileal involvement, strictureting disease, treatment with steroids and biological agents, CD related hospitalisation or surgery |

UC: Ulcerative colitis; CD: Crohn’s disease; IBD: Inflammatory bowel disease; CED: Cumulative effective dose; mSv: Milisieverts of radiation; ED: Emergency department; FH: Family history.
of exposure to CED > 50 mSv of 6% and 14% at 10 years and 15 years from IBD diagnosis respectively (Figure 1)\cite{14}.

Concerningly, a retrospective study of IBD patients in South Korea, conducted across 13 university hospitals, reported even higher proportions of patients exposed to potentially harmful radiation levels. 34.7% of patients with CD and 8.4% of patients with UC were exposed to CED > 50 mSv\cite{15}. CT imaging accounted for the vast majority of this radiation exposure (81.6% of the total CED in CD vs 71.2% in UC)\cite{15}, indicating that overuse of CT imaging remains a concern worldwide, and may reflect limited availability or lack of awareness of preferable imaging modalities.

Despite the high proportion of IBD patients exposed to high radiation doses, cumulative radiation exposures are not routinely recorded in clinical practice. The creation of IBD radiation diaries has been proposed to log total radiation exposures\cite{16}, and improve recognition among physicians where a patient has previously been exposed to ionising radiation.

**FACTORS ASSOCIATED WITH INCREASED RADIATION EXPOSURE IN IBD PATIENTS**

Risk factors for high radiation exposure in IBD patients have been widely studied\cite{11,15,17}. In a cohort of 354 adult and paediatric patients with CD, Desmond et al\cite{11} identified that patients diagnosed under the age of 17, patients with upper gastrointestinal (GI) disease, penetrating disease, multiple surgeries, or those that required intravenous steroids or infliximab, were at greater risk of receiving high cumulative radiation exposure. Following this, a 2012 meta-analysis of five studies evaluating risk factors in 2627 IBD patients, found a significant association with only previous IBD related surgery and corticosteroid use. The pooled adjusted odds ratios were 5.4 and 2.4, respectively\cite{16}.

Across studies, patients with CD consistently appear to receive higher cumulative radiation exposures than patients with UC, possibly due to a greater likelihood of extraluminal complications commonly examined by CT. After adjusting for time since symptom onset, a retrospective study by Peloquin et al\cite{18} (2008) found patients with CD to be exposed to 2.46 times more diagnostic radiation than patients with UC (median CED 26.6 mSv in CD vs 10.5 mSv in UC).

A summary of outcomes from studies investigating predictive factors for high radiation exposure in IBD patients is provided in Table 2. While there are discrepancies regarding the significance of some associations, the majority of the risk factors described are surrogate markers of disease activity and severity. It is therefore apparent that patients with more severe disease, who are more likely to receive corticosteroids and require surgery, undergo more diagnostic imaging including greater use of CT imaging, to guide further management.

**DIAGNOSTIC IMAGING MODALITIES IN IBD**

**Small bowel follow-through**

A 2011 survey revealed small bowel follow-through (SBFT) to be the most frequently performed investigation in the United Kingdom for the assessment of small bowel CD\cite{21}. CT was predominantly performed for suspected extra-luminal complications or obstruction\cite{19}. SBFT and small bowel enteroclysis (SBE) have, for many years, been the routine first-line imaging modalities to evaluate small bowel involvement in patients with suspected or confirmed CD. Both SBFT and SBE have similar sensitivities (85%-95%) and specificities (89%-94%) for detecting radiological features of CD\cite{20}. SBFT is usually preferred for patient tolerance, since nasal or oral intubation is not required. However, these techniques both employ ionising radiation and appear to have lower diagnostic accuracy compared to newer cross-sectional imaging modalities\cite{21,22}.

In a 2005 United States study, SBFT had a lower diagnostic yield for mild to moderate CD compared to CT enterography, video capsule endoscopy and ileoscopy\cite{21}. A 2009 Korean study of 30 patients with CD, found a significantly lower sensitivity of SBFT for the detection of extra-enteric complications ($P < 0.01$), although no significant difference in the detection of active terminal ileitis, compared to CT and magnetic resonance enterography (MRE)\cite{22}. Barium based studies may still have a role to play in the evaluation of small bowel CD, but are increasingly being replaced by alternative imaging modalities such as CT, MRE and small bowel ultrasound.

**CT**

In the United States, CT has largely superseded...
SBFT as the preferred first-line imaging modality for CD. Between 2002 and 2007, there was a reported 840% increase in the use of CT enterography in IBD patients in Minnesota, United States[6]. Similarly, a 310% increase in use of abdominal CT imaging was reported in a United Kingdom study of IBD patients between 1990 and 2010[14]. CT imaging offers the advantages of widespread availability, rapid acquisition of images, high sensitivity and specificity for the detection of intramural and extra-intestinal disease, as well as being well tolerated by patients[4]. The effective radiation dose is, however, considerably higher than other abdominal imaging modalities (Table 1)[6,10]. The United States National Research Council estimates that one out of every 1000 patients undergoing a 10 mSv CT scan will develop a radiation-induced cancer in their lifetime[23].

Conventional CT abdominal-pelvis imaging is typically used for the detection of extra-intestinal complications of IBD, such as abscesses, fistula, bowel obstruction or perforation. It may have a limited role in the assessment of colonic disease activity. A small study by Patel et al[26] of 23 patients with UC (2012), identified positive correlation of contrast-enhanced CT features (bowel wall thickening, mucosal hyper-enhancement and mural stratification), compared with clinical assessment (P < 0.05) and colonoscopy (P < 0.0001) in evaluating UC disease severity. However, only increasing bowel wall thickness on CT correlated with histological disease severity[24].

Conventional CT is limited in its assessment of small bowel inflammation due to artefact produced from collapsed bowel loops. CT enterography (CTE) is a newer imaging technique, combining high resolution CT scanning with multiplanar reconstructions after administration of an oral and parenteral contrast which acts to promote bowel loop distension. This improves visualisation of the small bowel mucosa, enabling more accurate assessment of small bowel disease activity[25]. High correlation has been shown between quantitative measures of bowel wall thickness and terminal ileal mural attenuation at CTE compared with ileocolonoscopy and histological analysis in active CD[26]. Furthermore, CTE may be a useful adjunct to ileocolonoscopy. In a 2012 study of 153 patients with CD in the United States, CTE detected active small bowel disease in 36 of the 67 patients (54%) with normal ileoscopy appearances. The negative ileoscopy results were largely due to disease "skipping" of the terminal ileum, or confinement to intramural or mesenteric distal ileum. CTE also detected extracolonic CD in 26% of patients[7].

Data for the benefit of CTE in assessing colonic disease is limited. A small study analysing CTE in 35 patients with inflammatory colitis, identified a sensitivity of 93% and specificity of 91% for the detection of moderate to severe disease in well-distended colons. However, there was a tendency for CTE to underestimate the full extent and severity of colonic disease[28].

CT colonography (CTC) is an emerging imaging technique developed for colonic evaluation. While colonoscopy remains standard practice for the assessment of colonic disease, CTC may offer advantages where colonoscopy is incomplete or contra-indicated. The majority of data comparing CTC and colonoscopy has been obtained from studies detecting colorectal cancer[25]. Only a few studies have investigated the efficacy of CTC in IBD, hence its role is not clearly defined. A small German prospective study of 21 IBD patients suggested sensitivities of 63.6% and 100% for the identification of acute and chronic IBD by CTC, with a specificity of 75% and 100% respectively[29]. CTC requires full bowel preparation, as well as air or carbon dioxide insufflation for colonic distension, and therefore is not always well tolerated. There have been reported cases of CTC-induced bowel perforation as well. Although the perforation rate is low, at around 0.04%, CTC is generally avoided in the acute phase of IBD[30].

Unfortunately while CT performs very well as an imaging modality there is an emerging recognition that it is responsible for the majority of the total radiation dose to which IBD patients are exposed[41-13,15]. Indeed in a recent study from Chile, abdominal-pelvic CT and CT enteroclysis accounted for 93.6% of the total CED exposure[13]. Excessive use of CT imaging in IBD patients presenting to the emergency department (ED) has also raised concern. In a study from the United States, no significant findings were observed in 32.8% of CT imaging studies carried out in IBD patients in the ED[31]. Preliminary algorithms to avoid inappropriate use of CT imaging in IBD patients presenting to the ED have been proposed and require validation[31,32].

Reduced radiation dose CT

Due to concerns regarding high radiation exposure from CT imaging, recent developments in technology have paved the way for strategies to reduce the radiation dose associated with CT imaging, without compromising diagnostic imaging quality. These techniques include tube current (mA) modulation, lowering tube potential modulation (kV), and minimising the number of dynamic CT phases[33]. Multiphase CT abdomen and pelvis imaging exposes a patient to around 31 mSv, equivalent to over three times the radiation dose of standard CT abdominal-pelvis imaging[9]. Single-phase CTE is in most cases believed to be sufficient to evaluate small bowel CD[33]. Reduced radiation CT techniques may help to lessen cumulative radiation exposures and bridge the gap in situations where radiation-free imaging is not widely available.

Nuclear medicine imaging

Technetium-99-m hexamethyl-propyleneamine oxime (99mTc-HMPAO) labeled white blood cell scintigraphy is an imaging technique that employs radioactive isotopes
to detect active inflammation. It may be used in IBD to assess disease activity, but due to limited availability and high cost, it is not routinely performed. 99mTc-HMPAO white cell scintigraphy can visualise the entire GI tract and emits a lower radiation dose than CT (2-4 mSv). Reported uses include evaluating responses to treatment and differentiating between disease relapse and fibrotic tissue post surgery. It also has a role in assessing disease extent in acute severe colitis, where colonoscopy is usually contra-indicated. A United Kingdom study by Subramanian et al. of 135 patients with UC, noted substantial correlation (k = 0.7) between 99mTc-HMPAO white cell scintigraphy and histological assessment of the proximal extent of disease involvement in patients with UC. Scintigraphy performed better than colonoscopy (P = 0.02) in assessing patients with more extensive colitis, while colonoscopy predicted disease extent more accurately in patients with limited colitis (P = 0.002).

Positron emission tomography (PET) is a non-invasive nuclear imaging technique that provides three-dimensional, quantitative imaging. It is primarily used for tumour staging, though preliminary data has shown it may have some value in the diagnosis of IBD. PET imaging is expensive and its availability is limited to certain centres. Data on the potential role of Fluorine-18-Fluorodeoxyglucose/PET (18F-FDG/PET) and PET/CT in IBD is limited and requires further review. Routine use of PET/CT for IBD assessment is unlikely due to the high doses of radiation involved (table 1).

RADIATION-FREE DIAGNOSTIC IMAGING MODALITIES

In view of the concerns over cumulative radiation exposure in IBD patients, alternative radiation-free imaging strategies have emerged as a focus of interest, and are increasingly being favoured in clinical practice. Studies comparing the diagnostic accuracies for radiation-free imaging vs conventional imaging modalities in small bowel CD are summarised in Table 3.

A 2008 meta-analysis by Horsthuis et al. comparing magnetic resonance imaging (MRI), ultrasonography (US), scintigraphy and CT across 33 studies, showed high per-patient sensitivity for the diagnosis of IBD with no significant differences between imaging modalities. Mean sensitivity estimates were 93%, 90%, 88% and 84% for MRI, US, white cell scintigraphy and CT respectively. Per-patient specificity was also high and comparable across imaging modalities: 93%, 96%, 85% and 95% for MRI, US, scintigraphy and CT respectively. The only significant difference was a lower specificity for scintigraphy compared to US (P = 0.009). Mean per-bowel-segment sensitivity estimates were lower across all imaging modalities (70%, 74%, 77% and 68% for MRI, US, scintigraphy and CT respectively). Per-bowel-segment analysis showed CT to be significantly less sensitive and specific compared to MRI (P = 0.037) and scintigraphy (P = 0.006). More recently, a 2011 systematic review by Panés et al. also compared US, MRI and CT for the assessment of disease location and extension in CD. Overall, US had superior diagnostic accuracy for the detection of disease localised to the terminal ileum and colon, while MRI performed better than US for the detection of CD lesions in the jejunum and proximal ileum. CT and MRI demonstrated similar diagnostic accuracy for the assessment of CD extension and activity.

MRE

MRE is a non-invasive technique used to obtain cross-sectional imaging of the small bowel without exposure to diagnostic medical radiation. MRE provides superior soft tissue contrast resolution compared to CTE, allowing detailed visualisation of inflammatory and fibrotic bowel wall. A 2011 Italian prospective study by Fiorino et al. compared MRE and CTE in 44 patients with ileocolonic CD. They found comparable accuracy between MRE and CTE in localising CD, assessing bowel wall thickening, bowel wall enhancement and enterocutaneous fistula. However, MRE was superior to CTE in detecting strictures (P = 0.04) and ileal wall enhancement (P = 0.02). A 2014 meta-analysis by Qiu et al. of 290 CD patients across six studies, found no significant difference between the diagnostic accuracy of MRE and CTE in detecting active small bowel CD and its complications including fistula, stenosis and abscess formation.

Given its proven diagnostic accuracy, updated guidelines by the European Crohn’s and Colitis Organisation and the European Society of Gastrointestinal and Abdominal Radiology, advocate increased routine usage of MRI for the assessment of small bowel CD, to reduce radiation exposure in this cohort of patients.

Recently, diagnostic indices from MRE have been developed to attempt to quantify disease severity. The magnetic resonance index of activity score has demonstrated a significant correlation with the CD endoscopic index of severity. In perianal CD, MRI remains the preferred imaging modality, permitting accurate diagnosis and staging of perianal fistula. Drawbacks of MR imaging, however, include higher procedure costs, lengthy acquisition times and limited availability, particularly out of routine working hours.

The efficacy of MR Colonography (MRC) for the evaluation of colonic disease activity in IBD is less well defined. A 2005 study comparing MRC using contrast gadolinium enemas, to standard colonoscopy in 22 patients with suspected or known IBD revealed disappointing results, with a per-segment sensitivity of 58.8% and 31.6% for identifying colonic inflammation in UC and CD respectively. Other studies have
Table 3  Comparison of diagnostic accuracies of radiation-free imaging (ultrasonography/magnetic resonance imaging) vs conventional ionising radiation imaging for the evaluation of small bowel Crohn’s disease

| Study                  | Country     | Number of patients (n) | Design                          | Imaging compared                                                                 | Study findings                                                                                                                                                                                                 |
|------------------------|-------------|------------------------|--------------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Low et al[66], 2000    | United States  | 26 CD                  | Prospective study,            | Contrast enhanced MR with single phase CT using findings from surgery, barium studies, endoscopic and histological findings as reference standard | Side-by-side comparison: MR imaging superior than helical CT in depiction of normal bowel wall, mural thickening or enhancement and overall GI tract evaluation                                                                                           |
|                        |             |                        |                               |                                                                                  | MR images showed 55 (85%) and 52 (80%) of 65 abnormal bowel segments for the two observers, compared with helical CT which showed 39 (60%) and 43 (65%) of bowel segments affected by CD (P < 0.001, P < 0.05)                                             |
| Maconi et al[67], 2003 | Italy       | 128 CD                 | Single centre Prospective study, consecutive CD patients who underwent surgery immediately after diagnostic work-up | US, barium studies, CT to detect internal fistulae and intra-abdominal abscesses compared to intraoperative findings | Detecting internal fistula: comparable diagnostic accuracy of US (85.2%) and barium X-ray (84.8%) studies                                                                                                   |
|                        |             |                        |                               |                                                                                  | Sensitivity US (71.4%), X-ray (69.6%), Specificity US (95.8%), X-ray (95.8%)                                                                                                                               |
|                        |             |                        |                               |                                                                                  | Detection of abscesses: US (90.9%), CT (86.4%) Overall diagnostic accuracy higher with CT than US (91.8% vs 86.9%) due to false positives with US                                                                 |
| Parente et al[49], 2004 | Italy       | 102 CD                 | Prospective study, consecutive patients with proven CD by BE and ileocolonoscopy enrolled from IBD clinic Dec 2002-July 2003 Adult cohort (≥ 18 yr) | Conventional US vs oral contrast enhanced US, compared to BE and ileocolonoscopy as gold standard | Per segment analysis: Superior diagnostic accuracy of contrast US in detecting small bowel CD. Sensitivity: conventional US 91.4%, contrast US 96.1%                                                                 |
|                        |             |                        |                               |                                                                                  | Good correlation of disease extent measurements with BE: US (r = 0.83), contrast US (r = 0.94)                                                                                                                  |
|                        |             |                        |                               |                                                                                  | Higher sensitivity and specificity with contrast US in detecting ≥ 1 small bowel strictures: Sensitivity: US (74%), contrast US (88.8%) Specificity: US (93.3%), contrast US (97.3%)˚ US and contrast US more accurate in detecting internal fistulas than BE, but no significant difference in diagnostic accuracy between US and contrast US: US (80%), contrast US (86%), BE (67%) |
|                        |             |                        |                               |                                                                                  | Significantly improved interobserver variability between sonographers with contrast US for detecting bowel wall thickness and disease location                                                                 |
| Calabrese et al[55], 2005 | Italy       | 28 CD                  | Prospective study, consecutive patients recruited from IBD clinic Adult cohort (age range 21-60 yr) | SICUS (performed by a sonologist of 1 yr experience) vs TUS (performed by an experienced sonologist of 10 yr experience), compared to SBE as gold standard | Sensitivity for detection of small bowel lesions: 96% TUS, 100% SICUS Greater correlation of extension of lesions between SICUS and SBE (r = 0.88) vs TUS and SBE (r = 0.64) |
|                        |             |                        |                               |                                                                                  | Sensitivity for detection of ≥ 1 stricture: 76% TUS, 94% SICUS Sensitivity and specificity for assessing prestenotic dilatation: 50% and 100% for TUS, 100% and 90% for SICUS                                                                 |
| Horsthuis et al[40], 2007 | Amsterdam | 1735 (sample size 15-440) | Meta-analysis of 33 prospective studies published between Jan 1993- Feb 2006 Adult and paediatric cohort (age range 2-86 yr) | US, MRI, scintigraphy, CT US evaluated in 11 studies, MRI in 11, scintigraphy in 9 and CT in 7 studies | Per-patient analysis: Significantly lower specificity for scintigraphy vs US. No significant difference between mean sensitivities for diagnosis of IBD Sensitivities: 89.7% US, 93% MRI, 87.8% scintigraphy, 84.3% CT Specificities: 95.6% US, 92.8% MR, 84.5% scintigraphy, 95.1% CT |
|                        |             |                        |                               |                                                                                  | Per bowel segment analysis: Significantly lower sensitivity and specificity for CT compared to scintigraphy and MRI. Sensitivities: 73.5% US, 70.4% MRI, 77.3% scintigraphy, 67.4% CT Specificities: 92.9% US, 94% MRI, 90.3% scintigraphy, 90.2% CT |

Zakeri N et al. Imaging and radiation exposure in IBD
| Authors | Country | Patients | Study Design | Imaging Techniques | Findings |
|---------|---------|----------|--------------|--------------------|----------|
| Lee et al., 2009 | South Korea | 30 CD | Prospective study, single centre, consecutive patients with known or suspected CD enrolled | Adult cohort (age range 18-44 yr) | No significant difference between CTE, MRE and SBFT for the detection of active terminal ileitis. Sensitivity CTE (89%), MRE (83%), SBFT (67%-72%) and extraenteric complications with ileocolonoscopy as reference standard. Significantly higher sensitivity for MRE (100%) and CTE (100%) compared to SBFT (32% reader 1, 37% reader 2) for the detection of extraenteric complications. |
| Siddiki et al., 2009 | United States | 33 CD | Prospective blinded study, single centre, consecutive patients with suspected active small bowel CD | Adult cohort (age range 20-63 yr) | No significant difference between sensitivity of MRE (90.5%) and CTE (95.2%) in detecting active small bowel CD. In 8 cases (24%) MRE and CTE identified active small bowel inflammation not detected at ileocolonoscopy. MRE significantly lower image quality score than CTE. |
| Ippolito et al., 2009 | Italy | 29 CD | Prospective study, single centre, symptomatic patients with proven CD and suspected relapse, recruited from outpatient clinic | Adult and paediatric cohort (age range 14-70 yr) | Complete agreement between MRE and CTE in classification of disease activity (k = 1). Good level of agreement between MRE and CTE for wall thickening and mucosal hyperenhancement (k = 1), comb (k = 0.9) and halo signs (k = 0.86). CTE superior to MRE in detecting fibrofatty proliferation (P = 0.045). MRE depicted higher number of fistulas than CTE but non-significant (P = 0.085). |
| Schreyer et al., 2010 | Germany | 53 CD | Retrospective study, single centre, patients with advanced CD and acute abdominal pain attending the emergency department | Conventional CT, MRE | No significant difference in image quality between CT and MRE. No significant difference in diagnosis of small bowel inflammation between CT (69.4%) and MRE (71.4%). CT detection of lymph nodes significantly higher than MRE. No significant difference in detection of fistulae (CT n = 25, MRE n = 27) or abscesses (CT n = 52, MRE n = 52). |
| Panés et al., 2011 | Spain | N/A | Systematic review of 68 prospective studies, minimum 15 patients per study | US, CT, MRI for diagnosis of CD, assessment of disease extent and activity, detection of complications | Sensitivity for diagnosis of suspected CD and evaluation of disease activity: US 84%, MRI 93%. Specificity for diagnosis of suspected CD and evaluation of disease activity: US 92%, MRI 90%. CT similar accuracy to MRI for assessment of disease activity and extension. US accuracy lower for disease proximal to terminal ileum. US, CT, MRI all high accuracy for detection of fistulas, abscesses, stenosis. US higher false positive for abscesses. |
| Fiorino et al., 2011 | Italy | 44 CD | Prospective study, single centre, consecutive patients with ileocolonic CD requiring endoscopic or radiological evaluation | Adult cohort (> 18 yr) Mean age 44 yr | CTE and MRE to assess disease activity and complications in ileocolonic CD, using ileocolonoscopy as reference standard. MRE significantly superior to CTE in detecting internal strictures: sensitivity (92% vs 85%), accuracy (95% vs 91%), specificity (90% vs 51%). Overall no significant difference in sensitivity and specificity of MRE and CTE in localising CD in ileal wall thickening, bowel wall enhancement, enterocutaneous fistulas, detection of abdominal nodes, pericolic fat enhancement. Per segment analysis, MRE significantly superior to CTE in detecting ileal wall enhancement, with higher sensitivity (93% vs 81%) and accuracy (88% vs 81%), but lower specificity (72% vs 81%). MRE significantly superior in localising rectal disease, with higher accuracy (93% vs 85%), specificity (100% vs 50.9%) but lower sensitivity (72% vs 81%). |
since produced more promising results. A German study of 23 patients with suspected IBD, comparing MRC using water enemas to colonoscopy findings, identified a sensitivity of 87% and specificity of 100% for detecting colonic inflammatory changes\(^{[47]}\). Recent studies have supported the reliability of diffusion weighted imaging MRC (DWI-MRC) for detecting colonic inflammation in UC, without the need for bowel preparation\(^{[48]}\). Advances in contrast media and DWI-MRI may increase the sensitivity and role of MRC in evaluating colonic inflammation in IBD, particularly in patients intolerant to colonoscopy. However, larger

| Authors          | Country | Study Design | Number | Details                                                                 | Findings                                                                                           |
|------------------|---------|--------------|--------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Jensen et al\(^{[43]}\), 2011 | Denmark | Prospective, multicentre study, patients with symptomatic pre-existing CD requiring small bowel imaging for treatment decisions | 50 CD  | MRE and CTE compared with gold standard of ileoscopy or surgery          | No significant difference between MRE and CTE for detection of small bowel CD                          |
| Chatu et al\(^{[44]}\), 2012   | United Kingdom | Retrospective study, single tertiary centre, all symptomatic patients with known or suspected CD who underwent SICUS retrospectively were reviewed | 143 CD | SICUS compared with SBFT, CT, histological findings from ileocolonoscopy or surgery, and CRP, using final diagnosis as the reference standard | No significant difference for detection of small bowel stenosis. MRE: sensitivity 55%, specificity 92%, CTE: sensitivity 70%, specificity 92% |
| Pallotta et al\(^{[45]}\), 2012 | Italy   | Prospective study, consecutive patients, adult and paediatric CD who underwent resective bowel surgery | 49 CD  | Conventional transabdominal US and SICUS compared to intraoperative and histological findings to assess CD complications | Agreement between SICUS with SBFT \((k = 0.68)\), CT \((k = 0.91)\), histological findings \((k = 0.62)\), CRP \((k = 0.07)\) |
| Qiu et al\(^{[46]}\), 2014      | China   | Systematic review with meta-analysis including six studies, all prospective with enrollment of consecutive CD patients | 290 CD | MRE and CTE in detecting active small bowel CD and complications          | Detect at least one stricture: Sensitivity 97.5%, specificity 100%, \(k = 0.93\)                           |
| Kumar et al\(^{[47]}\), 2015    | United Kingdom | Retrospective study, single tertiary centre. Adult cohort (age 18.8-68.9 yr) | 67 CD  | SICUS and MRE compared to intraoperative findings                        | Detect intra-abdominal abscesses: Sensitivity 100%, specificity 95%, \(k = 0.89\)                         |
| Aloisio et al\(^{[48]}\), 2015  | Italy   | Single tertiary centre for paediatric IBD Paediatric cohort with known or suspected small bowel CD | 25 CD  | MRE, SICUS, CE for diagnosis of small bowel CD                            | No significant difference between MRE and CTE in detecting fistula, stenosis and abscesses.            |

CD: Crohn’s disease; MRE: Magnetic resonance enterography; CT: Computed tomography; CTE: Computerised tomography enterography; SICUS: Small intestine contrast-enhanced ultrasound; CE: Capsule endoscopy; BE: Barium enteroclysis; SBFT: Small bowel follow-through; US: Ultrasoundography; MRE: Magnetic resonance imaging.
Trans-abdominal US and small intestine contrast-enhanced US

Trans-abdominal US has increasingly been favoured as a non-invasive imaging tool useful for the diagnosis of small bowel CD. It has advantages over SBFT in detecting extra-intestinal disease, is more cost effective and better tolerated than MRI, and avoids the radiation exposure of CT imaging. However, conventional trans-abdominal US is often limited by the presence of endoluminal gas and collapsed bowel walls, which may obscure pathology. Administering oral contrast prior to performing US promotes bowel loop distension, improving bowel wall visualisation. As a consequence, small intestine contrast-enhanced US (SICUS) has emerged as a more accurate alternative to conventional US for the diagnosis and monitoring of small bowel CD.

A prospective Italian study by Parente et al. of 102 patients with CD, compared conventional US with SICUS for the diagnosis of CD and its intraluminal complications. Per-segment analysis revealed a superior diagnostic accuracy of SICUS in detecting small bowel CD. Indeed use of an oral anechoic contrast agent resulted in an increase in sensitivity from 91.4% to 96.1%.

SICUS was also more accurate than conventional US in detecting strictures and measuring the extent of small bowel involvement. Both conventional US and SICUS had a higher diagnostic accuracy than SBE in detecting fistulas, using intra-operative findings as the gold standard. More recently, a United Kingdom-based study of 143 patients with suspected or known CD, found SICUS to have a similar diagnostic yield compared to SBFT and CT (k coefficient 0.88 and 0.91 respectively) for the detection of features of small bowel CD in routine clinical practice. The sensitivity and specificity of SICUS for the detection of active small bowel CD was 93% and 99% respectively, with a positive predictive value of 98% and a negative predictive value of 95%. Furthermore, there was substantial agreement between SICUS and histology obtained at ileocolonoscopy or surgery.

SICUS may also have a role to play in the pre-operative assessment of CD. A prospective study by Pallotta et al. of 49 patients with CD, compared SICUS with intra-operative findings for the detection of small intestinal complications of CD. SICUS demonstrated high sensitivity and specificity for the detection of small bowel strictures (97.5% sensitivity, 100% specificity, k = 0.78), fistulas (96% sensitivity, 90.5% specificity, k = 0.88), and abscesses (100% sensitivity, 95% specificity, k = 0.89). Similarly, Kumar et al. compared SICUS and MRE in routine clinical practice with intra-operative findings in patients with CD requiring surgery. Correlating SICUS and MRE with surgery, there was a high level of agreement in localising strictures (k = 0.75, k = 0.88), fistulae (k = 0.82, 0.79) and abscesses (k = 0.87, 0.77).

SICUS may be particularly well suited to investigating small bowel CD in children, where routine additional challenges include poorer tolerance to ileocolonoscopy (IC) requiring general anaesthetic, difficulty lying still for a time-consuming MRI, and increased sensitivity to ionising radiation. A recent prospective study by Aloi et al. compared MRE, SICUS and video capsule endoscopy in the evaluation of 25 children with suspected or known CD. Overall there was no significant difference among the three imaging modalities for the detection of active small bowel CD. Combining diagnostic imaging improved collective sensitivities, and combining SICUS with the serological marker C-reactive protein increased the specificity for the detection of CD from 89% to 100% in the jejunum, and from 79% to 100% in the distal ileum (P < 0.05).

Preliminary data has suggested a role for power Doppler imaging in enhancing the diagnostic accuracy of conventional US and SICUS. Power Doppler US allows assessment of bowel wall vascularity, which has been shown to correlate well with disease activity in CD. It can also aid in distinguishing between inflammatory and fibrotic stenosis.

Overall, SICUS has emerged as an accurate, well tolerated, radiation-free imaging tool for the assessment of small bowel CD. Limitations include inter-observer variability and difficulty interpreting and comparing images retrospectively given that it is a dynamic procedure. The diagnostic accuracy of SICUS is operator dependent and often thought to be dependent on experience. Although, in a 2005 Italian study SICUS performed by an inexperienced sonographer achieved superior diagnostic accuracy for assessing small bowel CD lesions compared to conventional trans-abdominal US performed by an experienced sonographer. The results of a large multi-centre prospective study comparing MRE with US in CD patients are keenly awaited.

Contrast enhanced ultrasonography

Contrast enhanced ultrasonography (CEUS) is a new technique that involves the administration of an intravenous contrast agent, real-time, during ultrasonography. It allows more accurate evaluation of bowel wall vascularity. Mural hyper-enhancement following contrast in CEUS has been shown to correlate well with bowel inflammation and allows grading of CD activity. CEUS also has the potential additional benefit of better distinguishing between inflammatory and fibro-stenotic lesions, which can be difficult with conventional ultrasound. CEUS does not require oral preparation, therefore it is well tolerated by patients and can be repeatedly performed to monitor disease activity. Limitations include the need for specific software, and increased procedure time.
Current studies suggest a role for CEUS in monitoring treatment response in CD, but further prospective studies are required to quantify how well CEUS correlates with endoscopic changes and SICUS.(57).

CONCLUSION

Increased awareness of the cumulative exposure of IBD patients to diagnostic medical radiation is warranted, particularly given the potential for an increased risk of radiation-induced malignancy in patients exposed at a younger age. Creation of radiation diaries is a useful consideration to log total radiation exposures. MRI and SICUS are alternative, radiation-free imaging modalities, with proven diagnostic accuracy, and should be routinely considered for the diagnosis and evaluation of patients with small bowel CD wherever possible. More provision is needed for out-of-hours radiation-free imaging modalities to reduce the need for CT.

REFERENCES

1. Loftus EV. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 2004; **126**: 1504-1517 [PMID: 15168363 DOI: 10.1053/j.gastro.2004.01.063]

2. Jess T, Gamborg M, Matzen P, Monkholm P, Sorensen TI. Increased risk of intestinal cancer in Crohn's disease: a meta-analysis of population-based cohort studies. *Am J Gastroenterol* 2005; **100**: 2724-2729 [PMID: 16393226 DOI: 10.1111/j.1572-0241.2005.00287.x]

3. Xie J, Itzkowitz SH. Cancer in inflammatory bowel disease. *World J Gastroenterol* 2008; **14**: 378-389 [PMID: 18200660 DOI: 10.3748/wjg.v14.i4.378]

4. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. *N Engl J Med* 2007; **357**: 2277-2284 [PMID: 18046031 DOI: 10.1056/NEJMra072149]

5. Ozasa K, Shimizu Y, Sayama A, Kasagi F, Soda M, Grant EJ, Sakata R, Sugiyama H, Kodama K. Studies of the mortality of atomic bomb survivors, Report 14, 1950-2003: an overview of cancer and noncancer diseases. *Radiat Res* 2012; **177**: 229-243 [PMID: 22171960 DOI: 10.1667/RER2629.1]

6. Flasar M, Patil S. Radiating disparity in IBD. *Dig Dis Sci* 2014; **59**: 504-506 [PMID: 24318801 DOI: 10.1007/s10620-013-2922-4]

7. Smith-Bindman R, Lipson J, Marcus R, Kim KP, Mahesh M, Gould R, Berrington de González A, Miglioretti DL. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med* 2009; **169**: 2078-2086 [PMID: 20008690 DOI: 10.1001/archinternmed.2009.427]

8. Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, Lubin JH, Preston DL, Preston RJ, Puskin JS, Ron E, Sachs RK, Samet JM, Setlow RB, Zaider M. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. *Proc Natl Acad Sci USA* 2003; **100**: 13671-13676 [PMID: 14610281 DOI: 10.1073/pnas.2253592100]

9. Radiological Society of North America (RSNA), American College of Radiology (ACR). RadiologyInfo.org. Radiation dose in X-ray and CT exams. Accessed 2015-04. Available from: URL: http://www.radiologyinfo.org/en/pdf/sby_xray.pdf

10. Mettler FA, Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology* 2008; **248**: 254-263 [PMID: 18566177 DOI: 10.1148/radiol.2481071451]

11. Desmond AN, O’Regan K, Curran C, McWilliams S, Fitzgerald T, Maher MM, Shanahan F. Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. *Gut* 2008; **57**: 1524-1529 [PMID: 18443021 DOI: 10.1136/gut.2008.151415]

12. Chatu S, Subramanian V, Pollok RC. Meta-analysis: diagnostic medical radiation exposure in inflammatory bowel disease. *Aliment Pharmacol Ther* 2012; **35**: 529-539 [PMID: 22293831 DOI: 10.1111/j.1365-2036.2011.04975.x]

13. Estay C, Simian D, Lubascher J, Figueroa C, O'Brien A, Quera R. Ionizing radiation exposure in patients with inflammatory bowel disease: are we overexposing our patients? *J Dig Dis* 2015; **16**: 83-89 [PMID: 25420751 DOI: 10.1111/1751-2890.12121]

14. Chatu S, Poullis A, Holmes R, Greenhalgh R, Pollok RC. Temporal trends in imaging and associated radiation exposure in inflammatory bowel disease. *Int J Clin Pract* 2013; **67**: 1057-1065 [PMID: 24073979 DOI: 10.1111/ijcp.12187]

15. Jung YS, Park DI, Kim ER, Kim YH, Lee CK, Lee SH, Kim JH, Chan Huh K, Jung SA, Yoon SM, Song HJ, Boo SJ, Kang HJ, Kim YS, Lee KM, Shin JE. Quantifying exposure to diagnostic radiation and factors associated with exposure to high levels of radiation in Korean patients with inflammatory bowel disease. *Inflamm Bowel Dis* 2013; **19**: 1852-1857 [PMID: 23702806 DOI: 10.1097/MIB.0b013e31828c444]

16. Herfarth H, Palmer L. Risk of radiation and choice of imaging. *Dig Dis* 2009; **27**: 278-284 [PMID: 19786752 DOI: 10.1159/000228561]

17. Butcher RO, Nixon E, Sapundzieski M, Filobbos R, Limdi JK. Radiation exposure in patients with inflammatory bowel disease: primum non nocere? * scand J Gastroenterol* 2012; **47**: 1192-1199 [PMID: 22827741]

18. Peloquin JM, Pardi DS, Sandborn WJ, Fletcher JG, McCollough CH, Schueler BA, Koller JA, Enders FT, Achenbach SJ, Loftus EV. Diagnostic ionizing radiation exposure in a population-based cohort of patients with inflammatory bowel disease. *Am J Gastroenterol* 2008; **103**: 2015-2022 [PMID: 18564113 DOI: 10.1111/j.1572-0241.2008.01920.x]

19. Hafeez R, Greenhalgh R, Rajan J, Bloom S, McCartney S, Halligan S, Taylor SA. Use of small bowel imaging for the diagnosis and staging of Crohn’s disease—a survey of current UK practice. *Br J Radiol* 2011; **84**: 508-517 [PMID: 21081570 DOI: 10.1259/bjr/65972479]

20. Saibeni S, Rondonotti E, Iozzelli A, Spina L, Tontini GE, Cavallaro F, Ciscato C, de Franchis R, Sardaneli F, Vecchi M. Imaging of the small bowel in Crohn’s disease: a review of old and new techniques. *World J Gastroenterol* 2007; **13**: 3279-3287 [PMID: 17650666 DOI: 10.3748/wjg.v13.i24.3279]

21. Hara AK, Leighton JA, Heigh RI, Sharma VK, Silva AC, De Petris G, Hentz JG, Fleischer DE. Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy. *Radiology* 2006; **238**: 128-134 [PMID: 16373764 DOI: 10.1148/ radiol.2381050296]

22. Lee SS, Kim AM, Yang SK, Chung JW, Kim SY, Park SH, Ha HK. Crohn disease of the small bowel: comparison of CT enterography, MR enterography, and small-bowel follow-through, and ileoscopy. *Radiology* 2006; **238**: 128-134 [PMID: 16373764 DOI: 10.1148/radiol.2381050296]

23. Council NR. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2. Washington, DC: The National Academies Press, 2006

24. Patel B, Mottola J, Sahni VA, Cantisani V, Ertuk M, Friedman S, Bellizzi AM, Marcantonio A, Mortele KJ. MDCT assessment of ulcerative colitis: radiologic analysis with clinical, endoscopic, and pathologic correlation. *Abdom Imaging* 2012; **37**: 61-69 [PMID: 21603899 DOI: 10.1007/s00261-011-9751-x]

25. Loghi A. Computed tomography colonography in 2014: an update on technique and indications. *World J Gastroenterol* 2014; **20**: 1685-1686 [PMID: 25492990 DOI: 10.3748/wjg.v20.i45.1685]

26. Bodily KD, Fletcher JG, Solem CA, Johnson CD, Fidler JL, Barlow JM, Brusewitz MR, McCollough CH, Sandborn WJ, Loftus EV, Harnsen WS, Crownhart BS. Crohn Disease: mural attenuation and thickness at contrast-enhanced CT Enterography-
imaging for the diagnosis, assessment of activity and abdominal complications of Crohn’s disease. *Aliment Pharmacol Ther* 2011; 34: 125-145 [PMID: 2161540 DOI: 10.1111/j.1365-2036.2011.04710.x]

42 Amitai MM, Ben-Horin S, Eliakim R, Kopylov U. Magnetic resonance enterography in Crohn’s disease: a guide to common imaging manifestations for the IBD physician. *J Crohns Colitis* 2013; 7: 603-615 [PMID: 23122965 DOI: 10.1016/j.crohns.2012.10.005]

43 Fiorino G, Bonifacio C, Peyrin-Biroulet L, Minuti F, Repici A, Spinelli A, Fries W, Balzarini L, Montorsi M, Malesci A, Danese S. Prospective comparison of computed tomography enterography and magnetic resonance enterography for assessment of disease activity and complications in ileocolonic Crohn’s disease. *Inflamm Bowel Dis* 2011; 17: 1073-1080 [PMID: 21848958 DOI: 10.1002/ibd.21533]

44 Qiu Y, Mao R, Chen BL, Li XH, He Y, Zeng ZR, Li ZP, Chen MH. Systematic review with meta-analysis: magnetic resonance enterography vs. computed tomography enterography for evaluating disease activity in small bowel Crohn’s disease. *Aliment Pharmacol Ther* 2014; 40: 134-146 [PMID: 24912799 DOI: 10.1111/apt.12815]

45 Panes J, Bouchuk V, Reinsch W, Stoker J, Taylor SA, Baumgart DC, Danese S, Halligan S, Marineck B, Matos C, Peyrin-Biroulet L, Rimola J, Rogler G, van Assegh G, Aridzone S, Ba-Salaham A, Bala MI, Bellini D, Biancone L, Castiglione F, Ehehalt R, Grassi R, Kucharzak T, Maccioni F, Maconi G, Magro F, Martin-Comin J, Morana G, Pendsé D, Sebastian S, Signore A, Tolan D, Tieltelk BA, Weihsaupt D, Wiarda B, Laghi A. Imaging techniques for assessment of inflammatory bowel disease: joint ECCO and ESGAR evidence-based consensus guidelines. *J Crohns Colitis* 2013; 7: 556-585 [PMID: 23538097 DOI: 10.1016/j.crohns.2013.02.020]

46 Schreyer AG, Rath HC, Kikinis R, Volland M, Schöllmerich J, Feuerbach S, Rogler G, Seitz J, Herfarth H. Comparison of magnetic resonance imaging colonography with conventional colonoscopy for the assessment of intestinal inflammation in patients with inflammatory bowel disease: a feasibility study. *Gut* 2005; 54: 250-256 [PMID: 15647190 DOI: 10.1136/gut.2003.037390]

47 Ajaj WM, Lauenstein TC, Pelster G, Gerken G, Ruehm SG, Debatin JF, Goehde SC. Magnetic resonance colonography for the detection of inflammatory diseases of the large bowel: quantifying the inflammatory activity. *Gut* 2005; 54: 257-263 [PMID: 15647191 DOI: 10.1136/gut.2003.037085]

48 Oussalah A, Laurent V, Bruot O, Bressenot A, Bigard MA, Régent D, Peyrin-Biroulet L. Diffusion-weighted magnetic resonance without bowel preparation for detecting colonic inflammation in inflammatory bowel disease. *Gut* 2010; 59: 1056-1065 [PMID: 20529570 DOI: 10.1136/gut.2009.197652]

49 Parente F, Greco S, Molteni M, Anderloni A, Sampietro GM, Danelli PG, Bianco R, Gallus S, Bianchi Porro G. Oral contrast enhanced bowel ultrasonography in the assessment of small intestine Crohn’s disease: a prospective comparison with conventional ultrasound, x ray studies, and ileocolonoscopy. *Gut* 2004; 53: 1652-1657 [PMID: 1547988 DOI: 10.1136/gut.2004.031038]

50 Chato S, Pilcher J, Saxena SK, Fry DH, Pollok RC. Diagnostic accuracy of small intestine ultrasonography using an oral contrast agent in Crohn’s disease: comparative study from the UK. *Clin Radiol* 2012; 67: 553-559 [PMID: 22212635 DOI: 10.1111/j.1365-2247.2011.11005.x]

51 Pallotta N, Vincoli G, Montesani C, Chirletti P, Pronio A, Caronna R, Cuccionelli B, Romeo E, Marcheggiano A, Corazzaiai E. Small intestine contrast ultrasonography (SICUS) for the detection of small bowel complications in crohn’s disease: a prospective comparative study versus intraoperative findings. *Inflamm Bowel Dis* 2012; 18: 74-84 [PMID: 21438095 DOI: 10.1002/ibd.21676]

52 Kumar S, Hakim A, Alexakis C, Chhaya V, Tiadas D, Pilcher J, Vilas J, Pollok R. Small intestinal contrast ultrasonography for the detection of small bowel complications in Crohn’s disease: correlation with intraoperative findings and magnetic resonance enterography. *J Gastroenterol Hepatol* 2015; 30: 86-91 [PMID: 25168482 DOI: 10.1111/jgh.12724]

53 Aloj M, Di Nardo G, Romano G, Casciani E, Civitelli F, Oliva S, Viola F, Maccioni F, Gualdi G, Cucchiara S. Magnetic resonance imaging with endoscopic and histologic findings of inflammation. *Radiology* 2006; 238: 505-516 [PMID: 16438815 DOI: 10.1148/radiol.2382041159]

27 Samuel S, Duensing DH, Loftus EV, Becker B, Fletcher JG, Mandrekar JN, Zinsmeister AR, Sandborn WJ. Endoscopic skipping of the distal ileum in Crohn’s disease can lead to negative results from ileocolonoscopy. *Clin Gastroenterol Hepatol* 2012; 10: 1253-1259 [PMID: 22503995 DOI: 10.1016/j.cgh.2012.03.026]

28 Johnson KT, Haras AK, Johnson CD. Evaluation of colitis: usefulness of CT enterography technique. *Emerg Radiol* 2009; 16: 277-282 [PMID: 19214608 DOI: 10.1007/s10140-008-0776-4]

29 Andersen K, Vogt C, Blondin D, Beck A, Heinen W, Aurich V, Häussinger D, Mönner C, Cohnen M. Multi-detector CT-colonography in inflammatory bowel disease: prospective analysis of CT-findings to high-resolution video colonoscopy. *Eur J Radiol* 2006; 58: 140-146 [PMID: 16337356 DOI: 10.1016/j.ejrad.2005.11.004]

30 Bellini D, Rengo M, De Cecco CN, Iafrate F, Hassan A, Lauenstein TC, Pelster G, Gerken G, Ruehm SG, Lauenstein TC, Pelster G, Gerken G, Ruehm SG, Jäger R, Ciccantelli B, Romeo E, Marcheggiano A, Corazziari E. Small intestine contrast ultrasonography (SICUS) for the detection of small bowel complications in Crohn’s disease: a prospective study of postoperative asymptomatic recurrence in Crohn’s disease. *Dig Dis Sci* 1997; 42: 1549-1556 [PMID: 9246062 DOI: 10.1023/A:1018843516651]
enterography, small-intestine contrast US, and capsule endoscopy
to evaluate, the small bowel in pediatric Crohn’s disease: a
prospective, blinded, comparison study. Gastrointest Endosc 2015;
81: 420-427 [PMID: 25115363 DOI: 10.1016/j.gie.2014.07.009]

Drews BH, Barth TF, Härle MM, Akinti AS, Mason RA, Mucchi
R, Thiell R, Pauls S, Klaus J, von Boyen G, Kratzter W. Comparison
of sonographically measured bowel wall vascularity, histology,
and disease activity in Crohn’s disease. Eur Radiol 2019; 19:
1379-1386 [PMID: 19184036 DOI: 10.1007/s00330-008-1290-5]

Calabrese E, La Seta F, Buccellato A, Virdone R, Pallotta
N, Corazzari E, Cottone M. Crohn’s disease: a comparative
prospective study of transabdominal ultrasonography, small
intestine contrast ultrasonography, and small bowel enema. Inflamm
Bowel Dis 2005; 11: 139-145 [PMID: 15677907 DOI: 10.1097/000
54725-200502000-00007]

Taylor S, Mallett S, Bhatnagar G, Bloom S, Gupta A, Halligan
S, Hamlin J, Hart A, Higginson A, Jacobs I, McCartney S, Morris
S, Muirhead N, Murray C, Punwani S, Rodriguez-Justo M, Slater
A, Travis S, Tolan D, Windsor A, Wyle P, Zealley I. METRIC
(MREnterography or ultrasound in Crohn’s disease): a study
protocol for a multicentre, non-randomised, single-arm, prospective
comparison study of magnetic resonance enterography and small
bowel ultrasound compared to a reference standard in those aged
16 and over. BMC Gastroenterol 2014; 14: 142 [PMID: 25110044
DOI: 10.1186/1471-230X-14-142]

Ripollés T, Martínez-Pérez MJ, Blanco E, Delgado F, Vizuete
J, Paredes JM, Vilà J. Contrast-enhanced ultrasound (CEUS) in
Crohn’s disease: technique, image interpretation and clinical
applications. Insights Imaging 2011; 2: 639-652 [PMID: 22347983
DOI: 10.1007/s13244-011-0124-1]

Quià E. Contrast-enhanced ultrasound of the small bowel in
Crohn’s disease. Abdom Imaging 2013; 38: 1005-1013 [PMID:
23728306 DOI: 10.1007/s00261-013-0148-4]

Newham E, Hawkes E, Surender A, James SL, Geczy R, Gibson
PR. Quantifying exposure to diagnostic medical radiation in
patients with inflammatory bowel disease: are we contributing to
malignancy? Aliment Pharmacol Ther 2007; 26: 1019-1024 [PMID:
17877508 DOI: 10.1111/j.1365-2036.2007.03449.x]

Levi Z, Fraser E, Krongrad R, Hazazi R, Benjaminov O, meye-
rovitch J, Tal OB, Choen A, Niv Y, Fraser G. Factors associated with
radiation exposure in patients with inflammatory bowel disease.
Aliment Pharmacol Ther 2009; 30: 1128-1136 [PMID: 19899197]

Palmer I, Herfarth H, Porter CQ, Fordham LA, Sandler RS,
Kappelman MD. Diagnostic ionizing radiation exposure in a
population-based sample of children with inflammatory bowel
diseases. Am J Gastroenterol 2009; 104: 2816-2823 [PMID:
19690524 DOI: 10.1038/ajg.2009.480]

Krocker Kl, Lam S, Birchall I, Fedorak RN. Patients with IBD
are exposed to high levels of ionizing radiation through CT scan
diagnostic imaging: a five-year study. J Clin Gastroenterol 2011; 45:
34-39 [PMID: 20679907 DOI: 10.1097/MCG.0b013e3181ef5d65]

Fuchs Y, Markowitz J, Weinstein T, Kohn N, Choi-Rosen J,
Levine J. Pediatric inflammatory bowel disease and imaging-
related radiation: are we increasing the likelihood of malignancy?
J Pediatr Gastroenterol Nutr 2011; 52: 280-285 [PMID:
21297507 DOI: 10.1097/MPG.0b013e3181f57177]

Sauer CG, Kugathasan S, Martin DR, Applegate KE. Medical
radiation exposure in children with inflammatory bowel disease
estimates high cumulative doses. Inflamm Bowel Dis 2011; 17:
2326-2332 [PMID: 21987300 DOI: 10.1002/ibd.21626]

Huang JS, Tobin A, Harvey L, Nelson TR. Diagnostic medical
radiation in pediatric patients with inflammatory bowel disease.
J Pediatr Gastroenterol Nutr 2011; 53: 502-506 [PMID:
22020539 DOI: 10.1097/MPG.0b013e31820d6b84]

Low RN, Francis IR, Politoske D, Bennett M. Crohn’s disease
evaluation: comparison of contrast-enhanced MR imaging and
single-phase helical CT scanning. J Magn Reson Imaging 2000;
11: 127-135 [PMID: 10713944]

Maconi G, Sampietro GM, Parente F, Pompili G, Russo A,
Cristaldi M, Arborio G, Ardizzone S, Matacena G, Taschieri AM,
Bianchi Porro G. Contrast radiology, computed tomography and
ultrasonography in detecting internal fistulas and intra-abdominal
abscesses in Crohn’s disease: a prospective comparative study. Am
J Gastroenterol 2003; 98: 1545-1555 [PMID: 12873576]

Siddikhi HA, Fidler JL, Fletcher JG, Burton SS, Huprich JE, Hough
DM, Johnson CD, Bruining DH, Loftus EV, Sandborn WJ, Pardi
DS, Mandrekar JN. Prospective comparison of state-of-the-art MR
enterography and CT enterography in small-bowel Crohn’s disease.
AJR Am J Roentgenol 2009; 193: 113-121 [PMID: 19542402 DOI:
10.2214/AJR.08.2007]

Ippolito D, Invernizzi F, Galimberti S, Panelli MR, Sironi S. MR
enterography with polyethylene glycol as oral contrast medium
in the follow-up of patients with Crohn disease: comparison with
CT enterography. Abdom Imaging 2010; 35: 563-570 [PMID:
19582502 DOI: 10.1007/s00261-009-9557-0]

Schreyer AG, Hoftstetter P, Daneschnejad M, Jung EM, Pawlik M,
Friedrich C, Fellner C, Strauch U, Klebl F, Herfarth H, Zorger N.
Comparison of conventional abdominal CT with MR-enterography in
patients with active Crohn’s disease and acute abdominal pain.
Acad Radiol 2010; 17: 352-357 [PMID: 20152727 DOI: 10.1016/
j.acra.2009.10.023]

Jensen MD, Kjeldsen J, Rafaelsen SR, Nathan T. Diagnostic
accuracies of MR enterography and CT enterography in
symptomatic Crohn’s disease. Scand J Gastroenterol 2011; 46:
1449-1457 [PMID: 21905974 DOI: 10.1111/j.1365-2036.2011.6139
47]