



## Crohn's disease Activity: Abdominal Computed Tomography Histopathology Correlation



N. Paquet<sup>a</sup>, J.N. Glickman<sup>b,1</sup>, S.M. Erturk<sup>c</sup>, P.R. Ros<sup>d</sup>, J.T. Heverhagen<sup>e</sup>, M.A. Patak<sup>e,f,\*</sup>

<sup>a</sup> Zentrum für Medizinische Radiologie, Röntgeninstitut Cham, Rigistrasse 1, CH-6330 Cham, Switzerland

<sup>b</sup> Department of Pathology, Brigham and Women's Hospital, Boston, MA, United States

<sup>c</sup> Department of Radiology, Sisli Etfal Education and Research Hospital, Etfal Sok Istanbul, 80220 Istanbul, Turkey

<sup>d</sup> Department of Radiology, University Hospitals Case Medical Center/Case Western Reserve University, 11100 Euclid Avenue, Mailstop: BSH 5056, 44106 Cleveland, OH, United States

<sup>e</sup> Department of Radiology, Inselspital Bern, University of Bern, 3010 Bern, Switzerland

<sup>f</sup> Department of Radiology, Hirslanden Clinics Zürich, Witellikerstrasse 40, 8032 Zürich, Switzerland

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### ABSTRACT

**Purpose:** Crohn's disease is a type of inflammatory bowel disease affecting estimated 4 million people worldwide. Therapy stratification of Crohn's disease (CD) is mainly based on the inflammatory activity being assessed by endoscopic biopsy and clinical criteria. Cross-sectional imaging allows for the assessment of structural characteristics of the entire gastrointestinal tract including small bowel loops and may provide potential non-invasive image-based biomarkers for the inflammatory activity of CD. The aim of this study was to explore the predictive value of Computed Tomography-based morphologic patterns for inflammatory activity in CD.

**Material and methods:** 42 patients diagnosed with CD were included in a retrospective study (13 male, 29 female, median age 32 years). Abdominal CT imaging was carried out on symptomatic patients at a single institution 0–10 days prior to endoscopic biopsy or surgery using a protocol optimized for the characterization of structural bowel alterations. Image data were initially reviewed independently by three radiologists and discrepancies were settled in consensus with a focus on mesenteric fat stranding and combing, mesenteric adenopathy, mesenteric abscess, intraperitoneal free fluid, fistula, skip lesions, highest wall thickness and the localization of the affected bowel. The extent of inflammatory activity in the bowel wall was determined subsequently by histological analysis.

**Results:** All intestinal and extraintestinal CT findings except the mesenteric comb sign showed a tendency towards higher extent or prevalence in patients with high histological inflammatory activity score, especially median bowel wall thickness (6.0 mm vs. 3.5 mm), mesenteric abscesses (32% vs. 0%) and mesenteric adenopathy (94% vs. 45%). Spearman rank order correlation coefficient indicated a significant correlation of bowel wall thickness ( $r = 0.40$ ,  $p < 0.05$ ), mesenteric adenopathy ( $r = 0.54$ ,  $p < 0.05$ ), mesenteric abscess ( $r = 0.33$ ,  $p < 0.05$ ) and mesenteric fat stranding ( $r = 0.33$ ,  $p < 0.05$ ) with the histological inflammatory activity score.

**Conclusion:** CT-based biomarkers including wall thickness, mesenteric fat stranding, mesenteric lymphadenopathy and mesenteric abscess positively correlated with the histological inflammatory activity score and therefore provided additional information for therapy stratification in symptomatic patients with CD, particularly as most of these biomarkers are hidden from endoscopy.

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\* Corresponding author at: Radiologie Klinik Hirslanden, Klinik Hirslanden, Witellikerstrasse 40, 8032 Zürich, Switzerland.

E-mail addresses: [n.paquet@gmx.de](mailto:n.paquet@gmx.de) (N. Paquet), [jglickman@miracals.com](mailto:jglickman@miracals.com) (J.N. Glickman), [mehmeterturk@superonline.com](mailto:mehmeterturk@superonline.com) (S.M. Erturk), [Pablo.Ros@uhospitals.org](mailto:Pablo.Ros@uhospitals.org) (P.R. Ros), [johannes.heverhagen@insel.ch](mailto:johannes.heverhagen@insel.ch) (J.T. Heverhagen), [Michael.Patak@hirslanden.ch](mailto:Michael.Patak@hirslanden.ch), [michael@patak.ch](mailto:michael@patak.ch) (M.A. Patak).

<sup>1</sup> Current address: GI Pathology, Miraca Life Sciences, 320 Needham Street, Newton, MA 02464, United States.

**Table 1**  
Summary of patient characteristics.

	Histological inflammatory activity score		
	0–2	3	Overall
n	11	31	42
Male (n)/Female (n)	2/9	11/20	13/29
Age (y)	26 (20–36)	38 (23–65)	32 (20–65)

Data are median and range in brackets.

## 1. Introduction

Crohn's Disease (CD) is regarded as an unpredictable, relapsing, transmural inflammatory disease potentially affecting any part of the gastrointestinal tract (GI) [1]. It usually involves the large intestine and the distal small bowel causing inflammation, ulcerations, bleeding and ultimately fibrosis and scarring of the GI tract wall [2].

Proper diagnosis of CD is challenging and requires multiple tests. Diagnosis is based on medical history, physical examination, laboratory tests, endoscopy including biopsy and imaging studies. The Montreal classification [3] with age at diagnosis, location, behavior and the CD Activity Index (CDAI) [4] are widely used for disease assessment and therapy stratification. However, these scores are unreliable in differentiating remission and active CD [5]. Currently, endoscopy and biopsy are the gold standard for assessing the inflammatory activity of CD. Nevertheless, diagnosis in the small bowel disease is difficult to achieve, because common endoscopy is limited to the colon and distal small bowel. Furthermore, endoscopic examination including biopsy is not always immediately available and can be stressful for the patient. In contrast, Computed Tomography (CT) imaging is widely available and provides a non-invasive method for the evaluation of the entire GI tract including extraintestinal manifestations and complications of CD, which are not visible by endoscopy. CT and MRI are the imaging modalities of choice to depict the localization and CD severity and provide information on disease activity. Imaging of the morphological characteristics of CD include assessment of mucosal alterations, transmural involvement and extraintestinal manifestations. In this context, CT may provide image-based biomarkers for the inflammatory activity of CD, which could further contribute to effective therapy stratification. Here, we explore the potential value of CT morphologic pattern as predictor of inflammatory activity in CD.

## 2. Material and methods

### 2.1. Patient characteristics

We researched retrospectively the hospital database at a single institution for a period of 5 years. Inclusion criteria were a CT scan performed 0–10 days prior to endoscopic biopsy or surgery and a histopathologically proven diagnosis of CD. Patients with other imaging modalities or with a CT scan but without histopathological correlation were excluded from the study. We included 42 patients diagnosed with CD in our retrospective study (13 male, 29 female, median age 32 years), who underwent abdominal Multidetector Computed Tomography (MDCT) imaging 0–10 days prior to biopsy or surgery. MDCT datasets were acquired at a single institution.

The study entailed patients with acute symptoms and a broad spectrum of inflammatory activity, which was determined by histological analysis of bowel wall tissue specimens. Absence of inflammatory activity (score = 0) was found in 2/42 patients, mild inflammatory activity (score = 1) in 5/42 patients, moderate inflammatory activity (score = 2) in 4/42 patients and high inflammatory activity (score = 3) in 31/42 patients (Table 1). Patients were predominantly female. Median age was 32 years (Table 1). The study was approved by the local Ethics Committee. The work was carried



**Fig. 1.** 33 year old man, axial contrast-enhanced MDCT image of small bowel wall thickening (big arrow) and comb sign (small arrow) involving the distal ileum.

out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). Informed consent was waived.

### 2.2. Histological analysis

The histological evaluation of the inflammatory activity in the bowel wall served as a reference standard. After macroscopic examination, endoscopic and surgical bowel specimens underwent fixation with formalin and standard hematoxylin-eosin safran stain and microscopic analysis. The extent of inflammatory activity was reported by a pathologist with experience in inflammatory bowel disease who was blinded for clinical, biological and radiological data. The standardized evaluation process was based on a semi-quantitative visual 4-point scale of 0 = absence of inflammation, 1 = mild inflammation (neutrophil infiltrate limited to the mucosa), 2 = moderate inflammation (neutrophil infiltrate limited to mucosa and submucosa), and 3 = high inflammation (transmural neutrophil infiltrate affecting the muscularis propria or fistula/abscess of the subserosa) (Fig. 3).

### 2.3. Computed tomography imaging

CT imaging was performed using a 16 row MDCT unit (GE 16 Light Speed CT scanner, General Electric, Milwaukee, WI, USA) using an imaging protocol dedicated to the assessment of structural alterations of the GI tract. Distension of small bowel loops was obtained by administration of approximately 1.0L oral contrast medium (3% Gastrografin solution, meglumine diatrizoate, Bristol-Myers Squibb) over 60 min. Intravenous contrast of 100 mL iopromide (Ultravist 300, 300 mg iodine/mL; Bayer HealthCare Pharmaceuticals Inc, Wayne, NJ) was injected at a rate of 3.0 mL/sec and bolus-tracking with a region of interest in the descending aorta at the level of the first lumbar vertebra was applied to generate enteric phase CT data. Image acquisition started at 35 s after the trigger (trigger threshold level 100HU [Hounsfield Unit]) during breathhold at a mean inspiratory level. Axial and coronal CT images (slice thickness 5.0 mm, reconstruction interval 3.0 mm) were reconstructed and transferred to a picture archiving and communication (PACS) system for image interpretation.

### 2.4. MDCT image evaluation

Image data were independently reviewed by three experienced radiologists who were blinded to clinical or histopathological data. Discrepancies were settled in consensus. The presence or absence of potential CT findings related to CD including mesenteric fat stranding, comb sign (Fig. 1), mesenteric adenopathy, mesenteric abscess,

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