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## Full length article

## Pilot study of endoscopic retrograde 3-dimensional – computed tomography enteroclysis for the assessment of Crohn's disease

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## ABSTRACT

**Purpose:** Endoscopic retrograde ileography (ERIG) is developed in our institute and applied clinically for the diagnosis and assessment of the Crohn's disease activity. We have further improved the technique using 3-dimensional – computed tomography enteroclysis (3D-CTE) and conducted a retrospective study to determine the feasibility and the diagnostic value of endoscopic retrograde 3D-CTE (ER 3D-CTE) in Crohn's disease patients in a state of remission.

**Methods:** Thirteen Crohn's patients were included in this pilot study. CTE was performed after the infusion of air or CO<sub>2</sub> through the balloon tube following conventional colonoscopy. The primary endpoint of this study was to assess the safety of this method. Secondly, the specific findings of Crohn's disease and length of the visualized small intestine were assessed.

**Results:** The procedures were completed without any adverse events. Gas passed through the small intestine and enterographic images were obtained in 10 out of 13 cases, but, in the remaining patients, insertion of the balloon tubes into the terminal ileum failed. Various features specific to Crohn's disease were visualized using ER 3D-CTE. A cobble stone appearance or hammock-like malformation was specific and effective for diagnosing Crohn's disease and the features of anastomosis after the surgical operations were also well described. Therefore, this technique may be useful after surgery.

**Conclusion:** In this study, ER 3D-CTE was performed safely in Crohn's disease patients and may be used for the diagnosis and follow-up of this disease.

### 1. Introduction

Imaging techniques in Crohn's disease patients are indispensable for the proper management of the disease [1]. Crohn's disease is an inflammatory bowel disease characterized by pathophysiological changes in the whole gastrointestinal tract, in which the terminal ileum is frequently affected by ulceration, stenosis, and/or perforation. The colonoscopic direct evaluation of the small intestine is limited to the last ileal loop due to practical reasons. Therefore, many endoscopic methods have been developed, including balloon enteroscopy and capsule endoscopy, which enable the clinician to observe the small intestine [2,3]. Capsule endoscopy is useful for the observation of true mucosal color and the detection of minute mucosal lesions, such as ulcerations or aphthous lesions, but not for the submucosal inflammation observed in cases of Crohn's disease [2]. Since enteroscopy is an

invasive method, a scope is used when the therapy is changed [4]. Meta-analyses have shown similar diagnostic yields for the above methods, and many reviews have assessed the limitations and complications of these techniques [5,6].

In the present study, we developed a novel imaging technique using the combined endoscopic technique and computed tomography (CT). In a previous report, an endoscopic retrograde ileography (ERIG) method is developed to assess the terminal ileum following conventional colonoscopy [7]. We then applied CT with an image analysis software program to improve the visualization and obtain 3-dimensional images. A pilot study was subsequently conducted to determine the feasibility and safety of the method and the diagnostic value of the method was explored.

**Abbreviations:** ER 3D-CTE, endoscopic retrograde 3-dimensional; ERIG, endoscopic retrograde ileography

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**Table 1**  
Characteristics of the patients.

|                        |       |
|------------------------|-------|
| age (y)                |       |
| median                 | 34    |
| range                  | 21–53 |
| gender (n)             |       |
| male                   | 11    |
| female                 | 2     |
| disease type (n)       |       |
| ileitis                | 6     |
| ileo-colitis           | 6     |
| colitis                | 1     |
| current therapy (n)    |       |
| anti-TNF               | 6     |
| anti-TNF, IM           | 6     |
| IM                     | 1     |
| previous-operation (n) | 6     |
| ileoectomy             | 2     |
| ileo-colectomy         | 2     |
| ileo-cecal resection   | 2     |

## 2. Material and methods

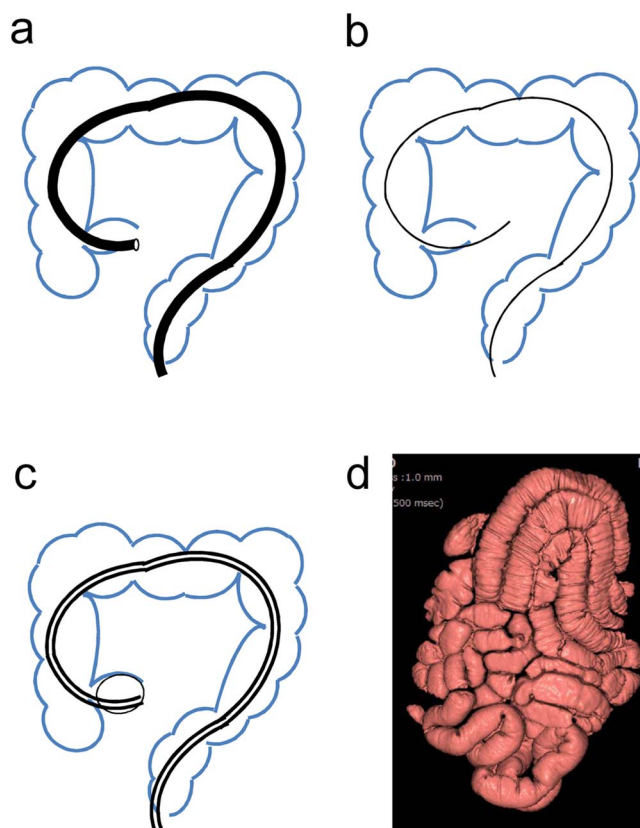
One aim of this study was to determine the feasibility and safety of the procedure for ER 3D-CTE. Another endpoints were to investigate the success rate of the procedure and to examine the obtained images.

### 2.1. Patients

This retrospective study included 13 Crohn's disease patients who underwent colonoscopy followed by CT enteroclysis from July 2011 to July 2013. The characteristics of the patients are shown in Table 1. All cases were treated with surgical operation and/or by appropriate reagents, including tumor necrosis factor antibodies or immunomodulators. The clinical activity was in a state of remission in all cases assessed, and patients in an active disease state were excluded from this pilot study. Informed consent was obtained from each patient, and the present study was approved by the institutional review board (No. 15020).

### 2.2. Technical procedure

Endoscopic retrograde 3-dimensional – computed tomography enteroclysis (ER 3D-CTE) is a hybrid technique that combines endoscopic retrograde ileography and CT enteroclysis (Fig. 1). The detailed procedure of ileography developed in our institute is described in a previous report [7]. Briefly, 1000–2000 ml of polyethylene glycol solution was administered orally until emptying the contents of the colon for bowel preparation, colonoscopy was performed with PCF-260AI or CF-SV (Olympus Corporation, Tokyo, Japan) by two experienced endoscopists (H.T. and T.I.), without sedation. Colonoscopy was replaced with a double-lumen silicone balloon tube (Create Medic Co. Ltd., Yokohama, Japan) with a wire-guided technique. Following air inflation of the balloon to anchor in the terminal ileum, air or CO<sub>2</sub> was injected through the tubes into the small intestine, as a negative contrast medium. Air was infused with manual injection using a 50 ml syringe, or CO<sub>2</sub> was continuously injected under the positive pressure with an automated CO<sub>2</sub> injector (ProtoCO<sub>2</sub>L, Eidia Corporation, Ibaragi, Japan). This CO<sub>2</sub> injector was available January 2012 in our institute, and used for the patients thereafter. The injected volume was checked with radioscopy to achieve adequate dilation of the small bowel (Table 2), and the patients were transferred to CT.



**Fig. 1.** The procedure of ER 3D-CTE. (a) Colonoscopy was performed and the scope was inserted into the terminal ileum. (b) A guide wire was inserted through the scope. (c) A double-lumen silicone balloon tube was replaced with a wire-guided technique. (d) Following injection of the air or CO<sub>2</sub>, 3D-CTE images were reconstructed.

### 2.3. Image analysis

CT was performed with a multidetector CT scanner (Aquilion 32, TOSHIBA Medical Systems Corporation, Tochigi, Japan) in both the prone and supine positions patient. The dose length product (DLP) was extracted from the scanner dose report. The images were visualized on the Synapse Vincent software package (Fuji Film Medical corporation, Tokyo, Japan), which possess volume-rendering capabilities. 3D image reconstruction produces both enterographic images and endoscopic images. The length of the visualized small bowel was measured with an image analysis conducted by the software program. Ten of the 13 patients underwent ERIG following CT scanning.

## 3. Results

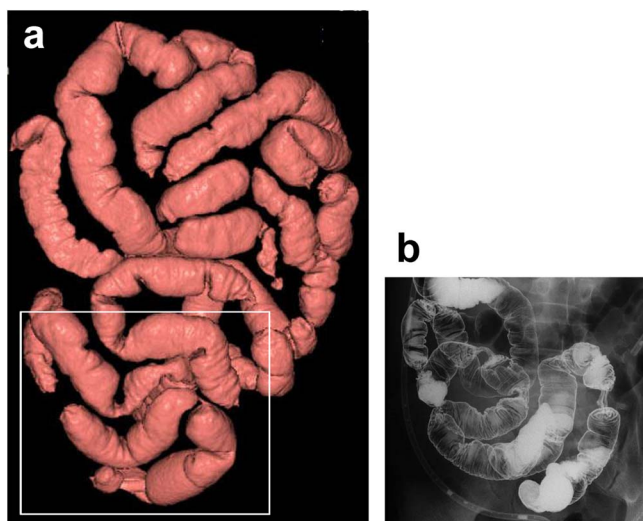
During enteroclysis, air or CO<sub>2</sub> was injected into the small bowel as a negative contrast medium in 8 and 5 cases, respectively (Table 2). No complications occurred during the procedure. Air was injected manually with a syringe just before CTE, and CO<sub>2</sub> was continuously infused with the apparatus, which automatically measured the volume, ranging from 300 to 3000 ml. When the procedures were successfully completed, image reconstruction produced both enterographic images and endoscopic images (Fig. 2a and See Supplementary Video S1 in the online version at DOI: <http://dx.doi.org/10.1016/j.ejro.2017.04.003>). The established DLP ranged from 240.6 to 387.5 mGy\*cm (Table 2).

Ten cases were successfully evaluated with ER 3D-CTE; however, 3 cases (cases 3, 10, and 13) were not completed because of dislocation of the balloon tubes from the terminal ileum to colon during the injection of contrast medium into the small intestine (Fig. 3). ER 3D-CTE effectively demonstrated the surgical anastomosis in 3 cases. Typical images of Crohn's disease, including a cobble stone appearance or

**Table 2**  
Technical parameters, observed findings and length of the small intestinal images visualized in this study.

| case | contrast media | volume (ml) | dose length product (mGy*cm) | major findings          | length of the image (cm) |       | length of ERIG image (cm) |
|------|----------------|-------------|------------------------------|-------------------------|--------------------------|-------|---------------------------|
|      |                |             |                              |                         | supine                   | prone |                           |
| 1    | air            | n.m.        | 363.5                        | no significant finding  | 126                      | 227   | 100                       |
| 2    | air            | n.m.        | 268.0                        | cobble stone appearance | –                        | 204   | 30                        |
| 3    | air            | n.m.        | 370.6                        | n.d.                    | –                        | –     | –                         |
| 4    | air            | n.m.        | 240.6                        | no significant finding  | 103                      | 360   | 50                        |
| 5    | air            | n.m.        | 387.5                        | anastomosis             | 153                      | 199   | 60                        |
| 6    | air            | n.m.        | 275.1                        | no significant finding  | 124                      | 121   | 50                        |
| 7    | air            | n.m.        | 244.9                        | no significant finding  | 147                      | 130   | 80                        |
| 8    | air            | n.m.        | 333.4                        | anastomosis             | –                        | 165   | 55                        |
| 9    | CO2            | 1600        | n.r.                         | pouch                   | 120                      | 109   | 60                        |
| 10   | CO2            | 1800        | 286.2                        | n.d.                    | –                        | –     | –                         |
| 11   | CO2            | 3000        | n.r.                         | hammock malformation    | 84                       | 121   | 60                        |
| 12   | CO2            | 1400        | 328.0                        | no significant finding  | 302                      | 405   | 95                        |
| 13   | CO2            | 300         | n.r.                         | n.d.                    | –                        | –     | –                         |

n.m., not measured; n.r., not recorded; n.d., not demonstrated; ERIG, endoscopic retrograde ileography.



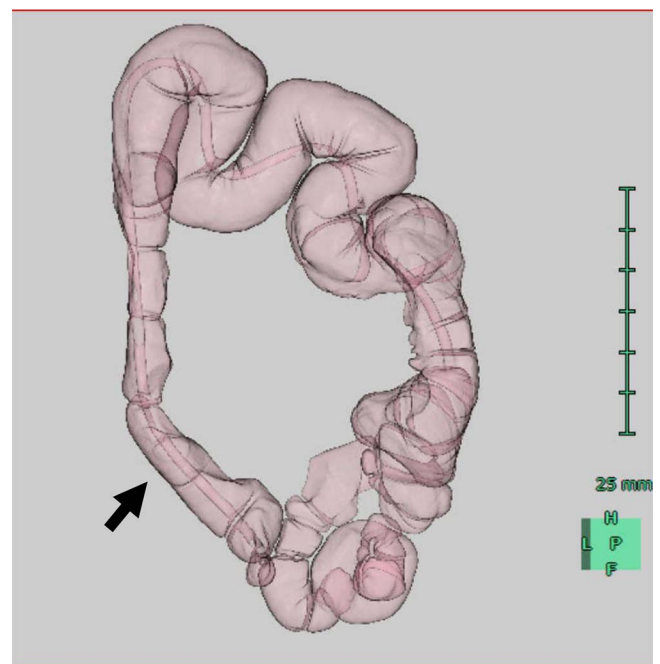
**Fig. 2.** ER 3D-CTE image and ERIG. (a) Enterographic image of case 1 reconstructed by Synapse Vincent software. White square indicate the area covered by ERIG. (b) ERIG image depicts ileal loop in the small intestine. The length of the loop is 100 cm.

hammock-like malformation, were clearly depicted (Figs. 4 a and 5 a and b). These findings were appropriate on 3D images and confirmed visually on the endoscopic images (Fig. 4b and c), in addition to ERIG (Figs. 4 d and 5 c). Original axial view showed wall thickness in the distended small bowel (Fig. 5d).

The length of the small bowel constructed with ER 3D-CTE was measured in the software package (Table 2). More than 100 cm of the ileum was appreciated in 10 cases, in which whole small bowel images were constructed in 2 cases. While, the length on ERIG was up to 100 cm.

#### 4. Discussion

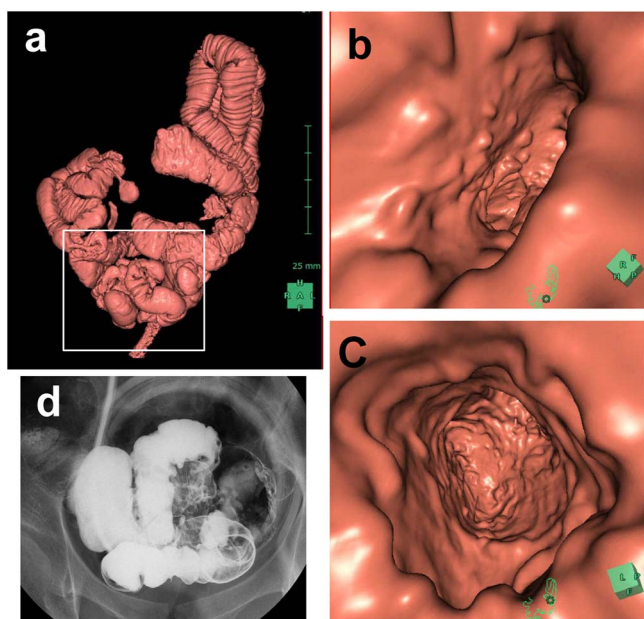
This pilot study was performed to investigate the feasibility of applying ER 3D-CTE, in which the ERIG technique and 3D-CT are combined, in the clinical setting. ERIG is useful for obtaining precise diagnostic ileographic images in patients with Crohn's disease [7]. In ER 3D-CTE, a 3D reconstructed image is further created after obtaining CT images of the air/CO<sub>2</sub>-inflated small intestine. The procedure was performed safely without any complications, as well as ERIG, in a small number of examinations. Developments in CT imaging have enabled clinicians to use harmless contrast materials, such as air and CO<sub>2</sub> [8]. Gas passed thorough the small intestine in 10 of 13 cases in the present study. A commercially available software program allowed us to



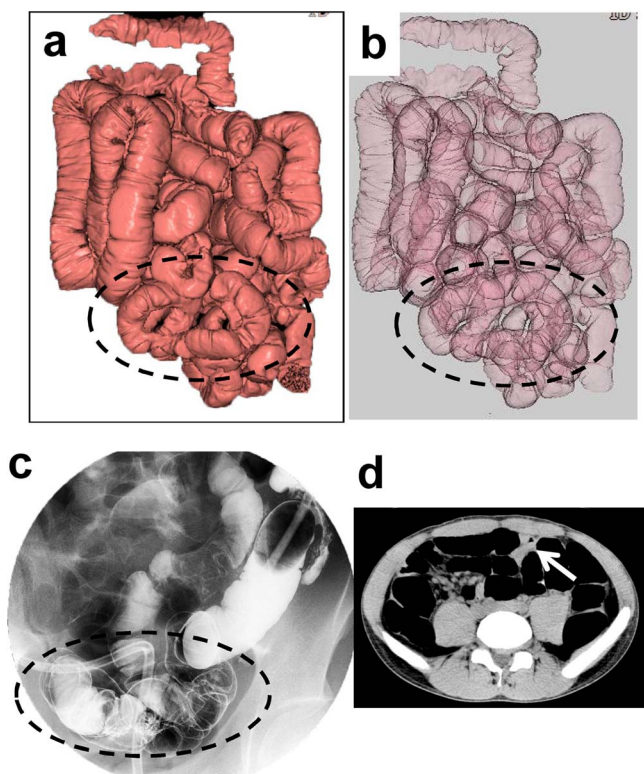
**Fig. 3.** Failure case (case 3 in Table 2). The colonographic view was translucently reconstructed, and the balloon tube was shown in the colon. The balloon was dislocated from the terminal ileum to the ascending colon (arrow).

construct multi-directional views and even virtual enteroscopic images (See Supplementary Video S1 in the online version at DOI: <http://dx.doi.org/10.1016/j.ejro.2017.04.003>).

In recent reviews, many studies were found to have investigated the diagnostic potential of range of imaging techniques in the evaluation of Crohn's disease. These techniques included conventional enteroclysis, ultrasonography, multidetector CT enteroclysis, and MRI enteroclysis [9,10]. Each imaging modality showed high sensitivity and specificity in the diagnosis of Crohn's disease and there were no significant differences in their diagnostic accuracy. MRI with oral contrast medium has been applied to achieve real-time observation [11–13]. Ultrasound is another noninvasive method of assessing the intestines [6,14]. For diagnostic purposes, there is no single gold standard test and the combination of various radiological imaging techniques and endoscopic evaluations are used in the clinical setting [15]. Cross-sectional imaging using CT and MRI is advantageous because it allows the wall thickness to be measured and for extra-intestinal information to be obtained. These imaging modalities are also applicable in patients with active



**Fig. 4.** Cobblestone appearance. (a) A cobblestone appearance was found in some lesions separated by a normal small intestine possessing Kerckring folds. (b and c) The enteroscopic views depicted a cobblestone appearance in which multiple polypoid lesions were observed. (d) ERIG image depicts ileal loop in the small intestine. The length is measured to be 30 cm.



**Fig. 5.** Hammock-like malformation. (a) The distal gut shows a malformation in the inflamed lesion forming so-called ‘hammock-like malformation’. (b) Translucent view improves visualization. (c) ERIG also depicted the malformation in the ileum. Ileal lesions were found on both examinations. The broken circles indicate the same area. (d) Axial scan shows small bowel distention and wall thickness in the inflamed lesion (arrow).

disease and complications, such as fistulas and strictures. The Guidelines of the European Society of Gastrointestinal Endoscopy (ESGE) recommend the use of cross-sectional imaging in evaluating the small bowel of patients with established Crohn’s disease [16]. For patients in

whom cross-sectional imaging of the small intestine is unremarkable or non-diagnostic, small bowel capsule endoscopy is recommended as a subsequent investigation. Endoscopic imaging, such as capsule endoscopy and small bowel endoscopy, is used to observe the surface of the small bowel in detail [3]. Capsule endoscopy was introduced for the direct exploration of the mucosa of the small bowel. Small bowel endoscopy is used to obtain biopsy specimens for pathological examination and for therapies such as balloon dilation for stenotic lesions of Crohn’s disease [17]. The direct observation of the mucosa allows for the evaluation of the disease activity and for a diagnosis to be made at an early stage. However, endoscopy is associated with complications; specifically, the retention of the endoscopic capsule, intestinal perforation, and bleeding. The development of a less invasive modality for diagnostic, evaluative and therapeutic purposes has been expected.

We thus consider that ER 3D-CTE could be a useful technique in patients that with a history of undergoing surgical operations and it could be used to identify the postoperative recurrence of Crohn’s disease. Because endoscopic methods are sometimes difficult to apply due to the presence of stenosis or dilatation after undergoing surgery such as ileocectomy [17]. ER 3D-CTE may supplement imaging methods and endoscopic observation and for detailed information about the ileum to be obtained, especially in patients undergoing surgery. The advantages of the ER 3D-CTE is that the 3D reconstruction of enterographic, cross-sectional, and enteroscopic images, using an analytical software program will yield information on the patient’s status [18]. In the present study, once the injection of air or CO<sub>2</sub> into the small intestine was successful, CT scanning was performed and 3D images were obtained in enterographic and endoscopic views. The multiple views constructed by the software represented great advances in the visualization of the small bowel, because the complex loops of the small intestine overlap in enterography. The images obtained by ER 3D-CTE, which depict detailed mucosal lesions in the distal ileum, provided wider and longer coverage of the small intestine in comparison to ERIG (Table 2). ER 3D-CTE was capable of obtaining a great deal of information from leading colonoscopy and the analysis of reconstructed images. The luminal surface of the colon and terminal ileum were observed via colonoscopy. Enteroclysis with a CT analysis allowed us to determine the wall thickness and provided extra-intestinal information as well as the luminal surface. If iodinated contrast medium had been used with this procedure, then the enhancement of the mucosa and wall could thus have been evaluated simultaneously. Further improvements are expected in ER 3D-CTE concerning the distention of the small bowel and also in the mathematical model for evaluation, due to the continuous advancement in CT colonography imaging.

However, the present study was associated with a limitation in that it was technically difficult to perform, as it was necessary for the preceding colonoscopy to reach the terminal ileum, for the balloon tube to be inserted into the terminal ileum and for negative contrast medium to be infused through the tube. The preparation for colonoscopy is not acceptable for all Crohn’s disease patients, who have active inflammatory bowel disease as the ingestion of 1000–2000 ml of polyethylene glycol solution may lead to a deterioration in disease activity. Thus, in the present pilot study, we applied this technique to Crohn’s disease patients who were in remission. Given that some cases show adhesion after surgery, stenosis or intestinal deformation. The application of these endoscopic techniques may be limited in patients with active Crohn’s diseases or in the postoperative setting [15]. A second limitation associated with this study is the lack of any mucosal color that is normally observed with other endoscopic techniques, such as capsule endoscopy.

The exposure young Crohn’s disease patients to radiation, which may increase the risk of developing cancer [16], is an important consideration in ER 3D-CTE. Our results in ER 3D-CTE have indicated low values for DLP. Because of the need for frequent re-evaluation, the use of a radiation-free imaging modality is preferable. We must therefore give the matter careful consideration in order to avoid irradiation in

CT scanning. Low-dose CT would allow young patients to undergo multiple examinations.

## 5. Conclusion

In summary, we performed a pilot study of ER 3D-CTE in order to assess Crohn's disease. In this study, ER 3D-CTE was performed safely and 3D reconstruction images were obtained. Since various features specific to Crohn's disease were visualized, ER 3D-CTE may therefore be useful for the diagnosis and follow-up of this disease.

## Contribution

Study concepts: Hiroki Tanabe, Takahiro Ito.

Study design: Hiroki Tanabe.

Data acquisition: Takahiro Ito, Yuhei Inaba, Kasuyoshi Ando, Yoshiki Nomura, Nobuhiro Ueno, Shin Kashima.

Quality control of data and algorithms: Kentaro Moriichi.

Data analysis and interpretation: Takahiro Ito.

Statistical analysis: N.A.

Manuscript preparation: Hiroki Tanabe.

Manuscript editing: Mikihiro Fujiya.

Manuscript review: Toshikatsu Okumura.

## Ethical approval

Yes.

## Conflicts of interest

None.

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