Multidetector-CT (MDCT) with polyethylene glycol (PEG) solution versus multidetector-CT enteroclysis in small bowel disease

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Purpose

The radiological evaluation of the small bowel includes conventional modalities, such as oral barium studies and barium enema with methylcellulose, and imaging studies targeted to evaluate the intestinal wall and to identify extraluminal pathological patterns, such as sonography, CT and MRI.

An adequate visceral distension is the primary requirement of CT imaging of the small bowel. There are different modalities of administration and different types of contrast agents used to obtain the distension of the small bowel loops [1]. The small bowel can be opacified with positive contrast agents (1-2% barium sulphate suspension, 2-3% water-soluble iodinated solution) or with negative contrast agents (oral water, oral oil emulsions, Polyethylene Glycol solution [PEG], suspension of 0.1% barium sulphate [Volumen], Mucofalk or methylcellulose by naso-duodenal tube) [1-3].

Oral contrast agents have the disadvantage of an inadequate non-uniform distension of all small bowel loops, particularly of jejunal loops; the problem is overcome at the cost of higher invasiveness, time and costs with CT-enteroclysis. In CT-enteroclysis (CT-E) negative or positive contrast material is infused through a naso-jejunal tube and contiguous axial images are obtained after total opacification of the small intestine. This technique has a unique theoretical advantage in its ability to simultaneously show intraluminal, mural and extraintestinal complications of small bowel Crohn's disease, combining the advantages of CT and barium enteroclysis with methylcellulose into one technique [4]. The most important limitations of the CT-enteroclysis are the increased radiation dose and the increased time (almost 1 hour from intubation to exam CT).

The aim of the present study is to evaluate multidetector CT (MDCT) with Polyethylene Glycol solution (PEG-CT) as alternative technique to MDCT-enteroclysis (CT-E) in patients with suspected small bowel disease.

Methods and Materials

We prospectively evaluated 145 consecutive patients (65 men and 80 women; age range 18-85 years, mean 48 years), known or suspected to have small bowel disease, that underwent abdominal 16-row MDCT (Light Speed Pro 16, GE Medical Systems, Milwaukee, USA).

The selection criteria were: diarrhoea (> 3 bouts/die), abdominal pain or bleeding pertinent to small bowel, histological data suspected or positive for Crohn's disease, endoscopy or radiological exams positive for small bowel disease. Exclusion criteria included pregnancy, renal insufficiency, documented reaction to iodinated contrast material, previous intestinal resection.
All patients gave oral informed consent for the procedure. CT-Enteroclysis was proposed to all patients. Patients who refused the naso-jejunal tube or patients in which intubation failed, underwent PEG-CT.

Before examination, all patients underwent an intestinal preparation according to the following plan: two days before, a light diet free of fruit and vegetables; the day before, 150 mg of a mixture in equal parts of sennosides A and B with a cup of sugared tea at 8:00 a.m.; at 1:00 p.m. a semi-liquid diet; at 5:00 p.m., 15 gr of magnesium sulphate in three-quarters of a glass of lukewarm water followed by the consumption of 3 litres of water during the following 4-5 hours; at 9:00 p.m., a cup of hot soup; fasting from 9:00 p.m.

**Technique**

70 patients, enrolled in CT-enteroclysis, underwent fluoroscopically placement of a 12-16-F naso-jejunal tube, then they were brought into the CT room. Contrast material (1500-2500 mL of 0.5% methylcellulose) was hand infused, using 60 ml/syringes. We aimed to have a constant and continuous injection, approximately 4 syringes per minute. An anticholinergic compound (N-butyl-joscine bromide) was administered iv to avoid spasms, to obtain homogeneous small bowel distension and to reduce patient abdominal discomfort. We administered 10 mg when the patient complained about abdominal discomfort and 10 mg just before a CT scan.

At the end of the infusion of the methylcellulose, the patients underwent multidetector 16-row CT, using the following scanning parameters: collimation (mm) 1.25, table speed (mm/rot): 13.75; pitch 1.375; rotation time: 0.6 sec, 120 KVP, 500 MAs. Unenhanced and contrast-enhanced CT was performed with the patient in the supine position from the diaphragm to the perineum during a single breath-hold. A further 200-250 mL of methylcellulose was given after the unenhanced scans in the case of inadequate small bowel distension. Contrast-enhanced CT images were acquired 40 seconds after i.v. injection of 130-150 mL contrast agent at a rate of 3 mL/sec (Ultravist 370, Schering AG, Berlin, Germany). Image 2D processing was performed with a computer workstation (Advantage Windows, GE Medical Systems, Milwaukee, USA). We also performed MIP-reconstructions.

75 patients enrolled in PEG-CT obtained small bowel distension with oral administration of 1.5-2.0 L of iso-osmotic polyethylene glycol solution (PEG) (Isocolan, Giuliani S.P.A.) administered in equal doses of 100 ml starting 45 minutes before the CT exam. We administered 10 mg of the anticholinergic compound (N-butyl-joscine bromide-Buscopan) when the patient complained about abdominal discomfort and 10 mg just before the CT scan. A further 200-250 mL of PEG was given after the unenhanced scans in the case of inadequate small bowel distension. CT parameters were the same of the CT-enteroclysis.

**Analysis of images**
Two gastrointestinal radiologists reviewed all images in consensus. The results of CT were classified as: normal, Crohn's disease, other disease.

In CT after iodinated contrast medium injection, the normal wall of the distended loop (normal parietal thickness < 3 mm) shows a linear and homogeneous hyperdense appearance between endoluminal low-density solution and extraparietal hypodensity of the peritoneal fat.

The CT criteria for the diagnosis of small bowel disease was the parietal thickening. In particular we analysed density (H.U.), grade (mm) and symmetry of the parietal thickening, and presence of associate extraluminal anomalies to perform a differential diagnosis between several small bowel diseases (tumours, inflammatory disease, others).

The CT criteria for the diagnosis of small bowel Crohn's disease was the parietal thickening (> 3 mm) in association with at least one extraparietal inflammatory involvement. In patients with Crohn's disease we have also considered: diameter of small bowel lumen; presence of stenosis; presence, site and number of abnormal altered bowel segments; degree of mural thickening; mural enhancement; presence of target sign (alternating rings of high and low density); presence of comb sign (hypervascularity of the involved mesentery); presence of perienteric stranding (loss of the normal sharp interface between the bowel wall and mesentery); presence of fibrofatty proliferation (increased attenuation value of mesenteric fat to 20-60 H.U.); presence of fistulas; presence of sinus tract (linear extension from small bowel loop into an exoenteric inflammatory process); lymphadenopathy (diameter > 1 cm); presence of abscesses; other signs.

We have also looked for small bowel distension and evaluated the difference between the two CT techniques. The distension of each small bowel segment (proximal jejunum, distal jejunum, proximal ileum, distal ileum, last ileal loop) was classified in a four-point scale (0= absent, 1= incomplete, 2= partial, 3= complete).

The comparable statistic evaluations were carried out by $\chi^2$ testing (Yates corrected). A value of p< 0.05 is considered statistically significant.

**Results**

The different degrees of distension of the loops (classified with a four-point scale) are summarised in the Tables 1 and 2. In patients studied by PEG-CT we found a complete distension of the proximal jejunal loops in 30/75 (40%) patients, distal jejunal loops in 45/75 (60%) patients, proximal ileum in 58/75 (77.5%) patients, distal ileum in 64/75 (85.5%) patients and last ileal loop in 60/75 (80%) patients (table 1) on page . In patients studied by CT-enteroclysis we found a complete distension of proximal jejunal loops in 54/70 (77%) patients, distal jejunal loops in 59/70 (84.5%) patients, proximal
ileum in 62/70 (88.5%) patients, distal ileum in 64/70 (91%) patients and last ileal loop in 63/70 (90%) patients (table 2).

Distension of the proximal and distal jejunum was found to be significantly better (tab 3) in patients studied with E-CT than those studied with PEG-CT (fig 1), as confirmed by the $\chi^2$ test with Yates correction ($p<0.05$: statistically significant difference). No significantly difference (tab 3) was present for others sites ($p>0.05$).

A further 200-250 mL of methylcellulose or PEG was given after the unenhanced scans for the inadequate small bowel distension in 20/145 (14%) patients (5 studied by CT-E and 15 studied by PEG-CT).

In total, Crohn disease was diagnosed in 64 patients (34 with CT-enteroclysis and 30 with PEG-CT). In these patients the pathological loops showed wall thickening ranging between 4 and 12 mm (mean 7 mm), loop diameter ranging between 12 and 31 mm (mean 23 mm), luminal diameter between 2 and 19 mm (mean 9 mm), longitudinal extent between 10 cm and 32 cm (mean 15 cm). Unenhanced CT depicted density values of involved segments ranging between 20 and 57 H.U. and the degree of their contrast enhancement ranged between 75 and 208 H.U. Distal ileum and last ileal loop were the most frequently involved sites; we found only one jejunal localisation. A target sign was observed in 57 patients (fig 2), perienteric stranding in 18 patients, comb sign in 24 patients (fig 3, fig 4) on page. Other signs were fibrofatty proliferation in 14 patients, stenosis in 26 patients and fistulas in 12 (fig 5) on page. In 4 patients abscesses were present (fig 6), characterized by partially encapsuled fluid collection.

Other diseases were: neoplasms in 16 patients (6 with lymphoma non Hodgkin, 3 with carcinoid, 2 with Peutz-Jeghers syndrome, 2 with adenocarcinoma, 2 with lymphoma, 1 with metastasis from melanoma) (fig 7, 8) on page and adhesions in 6 patients. In all 16 patients with neoplasms the diagnosis were confirmed by surgery.

Ileoscopy was performed in 35 patients; a mean time between MDCT and ileoscopy was 10 days. Barium enema with methylcellulose was performed in 50 patients and small bowel follow-through in 60 patients; a mean time between MDCT and barium studies was 7 days. In total, we found 6 false negative CT cases (3 with PEG-CT and 3 with CT-enteroclysis) due to early Crohn disease (erosions and/or ulcers) and 2 false positive CT cases (only of the PEG-CT) due to suboptimal distension of the loops. The values of sensitivity, specificity and diagnostic accuracy were respectively 94, 100 and 96% with CT-E, and 93, 94 and 93% with PEG-CT (tab 4).
**Fig.** CT-E coronal image (A) shows better distension of the jejunal loops (J) than PEG-CT coronal image (B).
Fig.: PEG-CT shows thickening of some ileal loops with target sign and narrowing of the lumen (arrows).
PEG-CT (coronal image) shows thickening of the last ileal loop and the distal ileum (white arrows); in particular target sign and so-called comb sign (black arrows) are clearly seen.
**Fig.**: CT-E (MIP reconstruction) shows clearly the comb sign (white arrows) associated to the thickening of the last ileal loop (black arrow).
Fig.: CT-E shows some fistulas (arrows) between two distal ileal loops.
**Fig.** CT-E shows a small oval fluid-density mass delimited by a hyperdense wall (arrow) referring to abscess.
Fig.: PEG-CT shows a polyp (arrow) in the last ileal loop of a patient with Peutz-Jeghers Syndrome.
**Fig.**: CT-E shows a large parietal mass (arrow) with ulceration. Surgical report: adenocarcinoma.
Table 1. Degree of small bowel loop's distension in PEG-CT (total patients n=75)

<table>
<thead>
<tr>
<th></th>
<th>0 Absent N° patients (%)</th>
<th>1 Incomplete N° patients (%)</th>
<th>2 Partial N° patients (%)</th>
<th>3 Complete N° patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PJ</td>
<td>10 (13.5)</td>
<td>15 (20)</td>
<td>20 (26.5)</td>
<td>30 (40)</td>
</tr>
<tr>
<td>DJ</td>
<td>5 (6.5)</td>
<td>10 (13.5)</td>
<td>15 (20)</td>
<td>45 (60)</td>
</tr>
<tr>
<td>PI</td>
<td>2 (2.5)</td>
<td>5 (6.5)</td>
<td>10 (13.5)</td>
<td>58 (77.5)</td>
</tr>
<tr>
<td>DI</td>
<td>2 (2.5)</td>
<td>4 (5.5)</td>
<td>5 (6.5)</td>
<td>64 (85.5)</td>
</tr>
<tr>
<td>LIL</td>
<td>1 (1.5)</td>
<td>5 (6.5)</td>
<td>9 (12)</td>
<td>60 (80)</td>
</tr>
</tbody>
</table>

PJ: proximal jejunum; DJ: distal jejunum; PI: proximal ileum; DI: distal ileum; LIL: last ileal loop

Fig.: Degree of small bowel loop's distension in PEG-CT (total patients n=75)
<table>
<thead>
<tr>
<th></th>
<th>0 Absent N° patients (%)</th>
<th>1 Incomplete N° patients (%)</th>
<th>2 Partial N° patients (%)</th>
<th>3 Complete N° patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PJ</td>
<td>3 (4)</td>
<td>4 (6)</td>
<td>9 (13)</td>
<td>54 (77)</td>
</tr>
<tr>
<td>DJ</td>
<td>3 (4)</td>
<td>3 (4)</td>
<td>5 (7.5)</td>
<td>59 (84.5)</td>
</tr>
<tr>
<td>PI</td>
<td>1 (1.5)</td>
<td>3 (4)</td>
<td>4 (6)</td>
<td>62 (88.5)</td>
</tr>
<tr>
<td>DI</td>
<td>0 (0)</td>
<td>2 (3)</td>
<td>4 (6)</td>
<td>64 (91)</td>
</tr>
<tr>
<td>LIL</td>
<td>2 (3)</td>
<td>2 (3)</td>
<td>3 (4)</td>
<td>63 (90)</td>
</tr>
</tbody>
</table>

PJ: proximal jejunum; DJ: distal jejunum; PI: proximal ileum; DI: distal ileum; LIL: last ileal loop

**Fig.:** Degree of small bowel loop's in CT-E (total patients n=70)
**Tab 3: Statistical analysis of the distension between CT-E and PEG-CT**

<table>
<thead>
<tr>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>proximal jejunum</td>
<td>0.0000*</td>
</tr>
<tr>
<td>distal jejunum</td>
<td>0.0022*</td>
</tr>
<tr>
<td>proximal ileum</td>
<td>0.1164</td>
</tr>
<tr>
<td>distal ileum</td>
<td>0.3779</td>
</tr>
<tr>
<td>last ileal loop</td>
<td>0.1483</td>
</tr>
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</table>

*p<0.05: statistically significant difference

**Fig.:** Statistical analysis of the distension between CT-E and PEG-CT
**Tab 4: sensitivity, specificity and diagnostic accuracy of PEG-CT and E-CT**

<table>
<thead>
<tr>
<th></th>
<th>E-CT (70 pt)</th>
<th>PEG-CT (75 pt)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive false cases (PF)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Negative false cases (NF)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Negative true cases (NT)</td>
<td>20</td>
<td>31</td>
</tr>
<tr>
<td>Positive true cases (PT)</td>
<td>34 Crohn disease, 9 (\text{neoplasms, 4 adhesion})</td>
<td>30 Crohn, 7 neoplasms, 2 (\text{adhesions})</td>
</tr>
<tr>
<td>Sensitivity (PT/PT+NF)</td>
<td>94%</td>
<td>93%</td>
</tr>
<tr>
<td>Specificity (NT/NT+PF)</td>
<td>100%</td>
<td>94%</td>
</tr>
<tr>
<td>Accuracy (PT+NT/total)</td>
<td>96%</td>
<td>93%</td>
</tr>
</tbody>
</table>

**Fig.:** sensitivity, specificity and diagnostic accuracy of PEG-CT and E-CT
Conclusion

The recent development of faster machines, the rapid increase of the spatial resolution with the introduction of multidetector CT and better multiplanar reconstructions have modified the approach to the small bowel diagnostic imaging [5, 6], so CT has became one of the most important techniques to evaluate patients with suspected or known small bowel disease.

The use of CT in small bowel disease is aimed at the visualization of the entire organ and adequate distension, the elimination of respiratory and peristaltic motion artefacts, the i.v. administration of contrast agents to evaluate the pattern and extent of wall enhancement. Accurate intestinal cleansing is required as in conventional radiology [1].

Independent of the CT technique used, it is essential to have a fluid-distended loop because mural wall thickening is the hallmark of intestinal disease.

The small bowel can be is most commonly opacified with positive contrast agents: 1-2% barium sulphate suspension or a 2-3% water-soluble iodinated solution allow intestinal loops to be delimited and help verify whether an expansive process is intra or extraluminal but they do not allow, given their high density, accurate evaluation of wall characteristics and they interfere with possible angiography-like 3D reconstructions [7].

Low-density agents are to be preferred because they allow better depiction of wall enhancement between the hypodensity of the intraluminal fluid and the hypodensity of the extraluminal fat and do not interfere with angiography-like 3D reconstructions [8]. Proposed low-density contrast agents are water, air, oil emulsion, 0.1% barium sulphate or PEG for oral use, and methylcellulose or water by naso-jejunal tube [3, 4, 8-16]. Oil emulsions provide lower density values than do water, but because of their taste, patients do not appreciate them, and their high cost limits their routine clinical use. Water is cheap, well-tolerated by patients, allows accurate evaluation of the intestinal wall and its enhancement; however it is absorbed rapidly and tends to stimulate peristalsis, failing to ensure adequate distension of the distal jejunum and the ileum. Air, administered either orally through delayed-release effervescent substances or rectally, for the study of the terminal ileum, has produced satisfactory results in the demonstration of intraluminal and mural diseases. However, the excessive difference between its density (-800 H.U.) and that of the enhanced intestinal wall (+100-135 H.U.) often gives rise to artefacts, which have limited its use.

Recently some authors proposed the oral use of the Mucofalk, that contains fiber from the outer shell seeds podorozhnika Plantago ovata, which retain water in quantities much greater than their weight [17]; using Mucofalk the distension of the small bowel loops were considered optimal only in 55% of the patients, moderate in 26% of the patients and insufficient in 19% of the patients.
On the contrary Maglinte proposed a suspension of 0.1% barium sulphate (Volumen) for oral use [3].

Mazzeo et al proposed [8] the PEG for oral use. The choise of PEG was based on the fact it is a well-known solution in widespread use or the preparation of endoscopic studies. Its main characteristics are an agreeable flavour and lack of toxicity; moreover it has the same density as water but it is not adsorbed in the intestine.

According to literature, we also use PEG solution as hypodense contrast medium for oral use, even if old patients were in difficulties to drink the remarkable amount needed to obtain a good distension of the loops (2 L).

Technique of administration of contrast agents also influences the grade of distension of the loops. The oral dose of contrast agent can be single, double or triple in variable amounts between 600 and 1500 ml, fractionated over 1-2 hours prior to the examination. Gore et al [18] proposed the administration of 1000 ml of contrast medium the evening before the CT exam to obtain also opacification of the colon. Oral administration of 10-20 mg metoclopramide was also proposed to obtain the distension of the last ileal loop [19].

In our study we administered 2 L of PEG in equal doses of 100 ml starting 45 minutes before the CT exam. The last two doses were administered just before the CT exam to obtain distension of the proximal jejunum. Because itself PEG is an intestinal transit accelerator, we did not administer any transit accelerator agent (e.g. metoclopramide), but we administered an anticholinergic agent (N-butyl-joscine bromide) to avoid spasms, to obtain homogeneous small bowel distension and to reduce patient abdominal discomfort. In contrast to other authors [15, 20] we preferred to administer the hypotonic agent intravenously in 2 doses: 10 mg was administered when the patient began feeling abdominal pain (generally after receiving of 1.3-1.5 L of the PEG), and another 10 mg was given immediately before starting the CT exam. Following these procedure, the patient was able to drink the total amount of the contrast agent and we obtained a good distension of the small bowel loops; in particular CT showed a complete distension of the proximal jejunal loops in 30/75 (40%) patients, distal jejunal loops in 45/75 (60%) patients, proximal ileum in 58/75 (77.5%) patients, distal ileum in 64/75 (85.5%) patients and last ileal loop in 60/75 (80%) patients.

It is known that a common drawback of oral contrast agents is that they fail to ensure a suitable and uniform distension of all small bowel loops, giving rise to significant problems in differentiating between real wall thickening and inadequate distension or spasm. The problem can be overcome, although with greater invasiveness, time and costs, by using CT-enteroclysis, a method developed in the early 1990s in which variable amounts (2,000-2,750 ml) of low density (methylcellulose or water) or high-density (4%-5% sodium diatrizoate, 1% barium sulphate) contrast material are infused by hand or with a peristaltic pump through a nasojejunal tube before the CT scan with and without IV contrast medium [2-4, 13-16, 21-23]. Manual infusion is limiting because the distension is better when the peristaltic pump is used, even if its use does not always permit to obtain optimal distension
of all the loops. Turetscheck [15], for example, did not recognize a jejunal stenosis due to the unsatisfactory distension and misinterpreted it for a spasm. Wold et al [16] did not use a peristaltic pump to perform CT-enteroclysis and did not find significant difference in the adequacy of luminal distension between peroral water CT enterography and CT-enteroclysis.

As we had no infusion pump, in our study we administered methylcellulose by hand, trying to obtain a constant and continuous injection. CT was performed at the end of the infusion; if the unenhanced scans showed less than optimal distension, we administered an additional dose of methylcellulose (about 200-250 mL). We also used a hypotonic agent to obtain homogenous bowel distension and to reduce abdominal discomfort; as the same in PEG-CT, we administered two doses of 10 mg: the first, administered when the patients felt abdominal pain (usually after the infusion of about 1,5 L of methylcellulose), permitted to tolerate the infusion of the total amount of methylcellulose, the second were administered immediately before the CT scan.

Following these procedure, we obtain a complete distension of proximal jejunal loops in 54/70 (77%) patients, distal jejunal loops in 59/70 (84.5%) patients, proximal ileum in 62/70 (88.5%) patients, distal ileum in 64/70 (91%) patients and last ileal loop in 63/70 (90%) patients.

If we evaluated diagnostic results of both techniques, we found two false positive cases of the PEG-CT due to inadequate distension of the loops and spasms and six false negative cases with both techniques due to early Crohn disease. The quality of the images was better with CT-E than PEG-CT. In fact, distension of the proximal and distal jejunum was found to differ significantly in patients studied with E-CT and those studied with PEG-CT, as confirmed by the $\chi^2$ test with Yates correction ($p<0.05$: statistically significant difference). In other words, distension or the proximal and distal jejunum was significantly better in patients studied with CT-enteroclysis compared with those studied with PEG-CT. No significantly difference was present for others sites ($p>0.05$). Moreover, the most important limitations of the CT-enteroclysis are the increased radiation dose and the time needed for all manoeuvres (almost 1 hour from intubation to exam CT). In our experience the PEG allowed a good evaluation of wall thickness and enhancement as well as complications of Crohn disease. Patients well accepted oral solution after the attempt of intubation with a naso-jejunal tube. Even if it was not possible to obtain an adequate study of the jejunum with CT enterography, the jejunum is rarely affected by Crohn disease.

In conclusion: PEG-CT shows terminal ileum involvement, extraluminal findings and complications of Crohn's disease as well as MD CT-enteroclysis, though CT-enteroclysis gives better bowel distension, especially in the jejunum.