

# World Journal of *Gastrointestinal Endoscopy*

*World J Gastrointest Endosc* 2021 March 16; 13(3): 72-96



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**INDEXING/ABSTRACTING**

The WJGE is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, China National Knowledge Infrastructure (CNKI), and Superstar Journals Database.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Li-Li Wang, Production Department Director: Yun-Xiaojuan Wu, Editorial Office Director: Jia-Ping Yan.

**NAME OF JOURNAL**

*World Journal of Gastrointestinal Endoscopy*

**ISSN**

ISSN 1948-5190 (online)

**LAUNCH DATE**

October 15, 2009

**FREQUENCY**

Monthly

**EDITORS-IN-CHIEF**

Anastasios Koulaouzidis, Sang Chul Lee, Bing Hu

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/1948-5190/editorialboard.htm>

**PUBLICATION DATE**

March 16, 2021

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## Computed tomography colonography and radiation risk: How low can we go?

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**Author contributions:** Popic J made contributions to the conception and design of the study, involved in drafting and revising the manuscript critically; Tipuric S, Balen I and Mrzljak A were involved in collecting data, drafting and writing the manuscript. All authors read and approved the final manuscript.

**Conflict-of-interest statement:** The authors declare no conflict of interest.

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**Manuscript source:** Invited

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### Abstract

Computed tomography colonography (CTC) has become a key examination in detecting colonic polyps and colorectal carcinoma (CRC). It is particularly useful after incomplete optical colonoscopy (OC) for patients with sedation risks and patients anxious about the risks or potential discomfort associated with OC. CTC's main advantages compared with OC are its non-invasive nature, better patient compliance, and the ability to assess the extracolonic disease. Despite these advantages, ionizing radiation remains the most significant burden of CTC. This opinion review comprehensively addresses the radiation risk of CTC, incorporating imaging technology refinements such as automatic tube current modulation, filtered back projections, lowering the tube voltage, and iterative reconstructions as tools for optimizing low and ultra-low dose protocols of CTC. Future perspectives arise from integrating artificial intelligence in computed tomography machines for the screening of CRC.

**Key Words:** Computed tomography colonography; Colorectal cancer; Radiation risk; Image quality; Image noise; Iterative reconstruction

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manuscript

**Specialty type:** Gastroenterology and hepatology**Country/Territory of origin:** Croatia**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**Received:** January 8, 2021**Peer-review started:** January 8, 2021**First decision:** January 23, 2021**Revised:** January 23, 2021**Accepted:** February 18, 2021**Article in press:** February 18, 2021**Published online:** March 16, 2021**P-Reviewer:** O'Shea A, Ricci ZJ, Sun X**S-Editor:** Zhang H**L-Editor:** A**P-Editor:** Wang LL

**Core Tip:** Computed tomography colonography (CTC) is an important imaging technique with significant advantages over optical colonoscopy in terms of less invasiveness, better compliance, and assessment of extracolonic structures. Ionizing radiation is the most significant burden of this technique. This opinion review comprehensively addresses the radiation risk in CTC with imaging technology refinements that should be used to lower radiation doses.

**Citation:** Popic J, Tipuric S, Balen I, Mrzljak A. Computed tomography colonography and radiation risk: How low can we go? *World J Gastrointest Endosc* 2021; 13(3): 72-81

**URL:** <https://www.wjgnet.com/1948-5190/full/v13/i3/72.htm>

**DOI:** <https://dx.doi.org/10.4253/wjge.v13.i3.72>

## INTRODUCTION

Computed tomography colonography (CTC), also referred to as a virtual colonoscopy (VC), was introduced in 1994 by Vining *et al*<sup>[1]</sup>. They were the first to describe this modified computed tomography (CT) examination of the large intestine as a diagnostic test for colorectal carcinoma (CRC) and polyps<sup>[2]</sup>. Since then, CTC has become an examination of crucial importance in imaging polyps and potential CRC in patients not amenable to optical colonoscopy (OC). CTC has advantages over OC because of its less invasive nature, better patient compliance, and the ability to detect extracolonic disease<sup>[3]</sup>. Hence, CTC is an accepted screening test for CRC and is growing in its utilization. We have to be aware that no CTC findings allow us to distinguish adenomas from non-neoplastic polypoid lesions such as hyperplastic or inflammatory polyps, making the histological study necessary in all instances. One of the drawbacks of CTC is usually missed flat lesions such as a flat polyp. Images that can be misinterpreted and can mimic polyps include untagged stool, partially distended haustra, or focally thickened folds<sup>[4]</sup>.

On the other hand, OC is often associated with anxiety, fear, and discomfort compared to CTC, and carries a risk of being incomplete, especially in elderly patients<sup>[5]</sup>. Despite these advantages of CTC, ionizing radiation is the most significant burden of this technique (Table 1). However, imaging technology refinements, favorable cost analyses, and the impact of extracolonic findings make this method a suitable alternative to OC for CRC screening<sup>[3]</sup>.

## CTC FOLLOWING INCOMPLETE OPTICAL COLONOSCOPY

One of the unanimously accepted CTC indications is to complete a colonic workup after an incomplete OC. Some 10% of colonoscopies cannot be completed for different causes: Neoplastic stenosis, diverticulosis, adhesions, loops, or redundant colon<sup>[6-9]</sup>. A study revealed that 4.3% of neoplasms were missed by incomplete colonoscopy and were found in additional imaging studies<sup>[6]</sup>. Moreover, the proximal colon study is particularly important in neoplastic stenosis, as the percentage of synchronous cancer is high (4%-5%)<sup>[10]</sup>. In some patients, OC can be technically challenging, with the inability to achieve cecal intubation, resulting in inadequate visualization of the entire colon, hence a potential risk of undetected colon cancer and polyps<sup>[11,12]</sup>. Except radiology practices with an active screening program, incomplete OC examinations likely account for the vast majority of CTC requests<sup>[13]</sup>. Factors previously shown to contribute to the risk of incomplete OC include; increasing patient age, low body mass index, female gender, history of prior abdominal and pelvic surgeries, presence of severe diverticular disease, poor bowel preparation, the experience of the endoscopist, tumorous obstruction of the entire lumen and anesthesia-related complications<sup>[7]</sup>.

There are two primary strategies regarding the timing of CTC following incomplete OC. The first and most common is same-day CTC utilizing the prior OC prep, often supplemented with oral contrast after recovery from OC<sup>[14]</sup>. This is often the more convenient option for the patient as they do not have to undergo further bowel preparation (assuming bowel prep for OC was adequate) and return on a separate day. CTC is usually performed 2-3 h later. Another option is to have the patient return for CTC at a later date utilizing a standard CTC bowel regimen with an osmotic

**Table 1 Advantages and limitations of computed tomography colonography**

Advantage	Limitation
Minimally invasive procedure	Exclusively diagnostic method
Safe procedure	Ionizing radiation
No need for sedation	Fecal residue simulate pathology
Short examination time	Laxative residue simulate pathology
Assess to extracolonic disease	Flat lesions
Three dimensional view	
View of the entire colonic surface	
Access to post-obstructed bowel	
"Second look"	

cathartic and dual agent tagging protocol. CTC should be delayed if an endoscopic resection has been performed during OC<sup>[15]</sup>.

## SCREENING FOR CRC

Most population-based screening programs for CRC target the age range from 50 to 74 years old and include indirect screening, such as fecal occult blood testing or direct visualization with flexible sigmoidoscopy or OC<sup>[16]</sup>. The most common is the stool test-based screening [guaiac fecal occult blood test (FOBT) or fecal immunochemical test (FIT)] due to its low cost, availability, safety, and easy transport (*via post*). If positive, FOBT and FIT are usually followed by OC to confirm neoplasia or suspect polyps<sup>[5]</sup>.

Since CTC has become an available alternative option to OC, more patients choose CTC as a more desirable option. In a multicenter survey of 1417 individuals, 68% chose CTC over OC due to its less invasive nature, and 47% chose CTC to avoid the risks associated with OC<sup>[17]</sup>. Another Dutch study showed that 93% of patients would choose another CTC after the initial one<sup>[18]</sup>.

The CRC screening potential of CTC has been investigated in three European randomized trials: COCOS study in the Netherlands (CTC *vs* OC)<sup>[19]</sup>, SAVE<sup>[20]</sup>, and PROTEUS<sup>[21]</sup> studies in Italy.

The SAVE study compared reduced preparation and full-preparation CTC, FIT, and OC, while the PROTEUS study compared CTC *vs* sigmoidoscopy. The participation rates, positivity rate, and CTC detection rates were similar amongst the studies. The participation rate for screening CTC was higher than that for an OC, with a slightly lower detection rate, but with comparable yield per invitee. The participation rate for screening CTC was much lower than that for FIT, but its detection rate was three-fold that of one FIT round. CTC and sigmoidoscopy showed similar participation and detection rate. These results encourage CTC implementation in screening programs for CRC<sup>[22]</sup>.

## RADIATION INDUCED RISKS

CTC's main disadvantage is ionizing radiation, especially since CTC has been considered a CRC screening tool. Radiation dose significantly determines CT image quality, its diagnostic accuracy, and clinical utility. Strategies for lowering radiation dose are utilized to maintain and improve image quality. The dose should only be reduced if one can preserve the diagnostic image quality for the specific pathology. It is essential to understand the relation between image quality and radiation dose to optimize the radiation dose in CTC<sup>[23]</sup>.

CTC dose is lower than the conventional CT examination, about one half of the dose, because of high natural contrast between the soft tissue of the colonic wall, luminal gas, and tagged fecal residue and fluids<sup>[6]</sup>.

To give the proper insight, it is meaningful to compare the doses of different diagnostic procedures with the chest X-ray dose or years of exposure to natural background radiation, ranging from 1 to 3 mSv/year, depending on the geographical



region. Thus, mammography has a dose of 0.13 mSv, which corresponds to 6 chest X-rays or 14 days of background radiation. An average abdominal CT has 5-25 mSv, which corresponds to 250-1250 chest X-rays or 2-11.5 years of background radiation, depending on the number of phases that have to be scanned to confirm the suspect diagnosis<sup>[24]</sup> (Table 2).

During the last few decades, physicists, radiologists, and technologists have studied CT technology to find ways to reduce radiation doses for specific "diagnosis-related" CT examinations. Currently, we have well-established "diagnosis-related" protocols such as "low-dose" kidney stone dedicated protocol, "low-dose" lung cancer screening protocol, *etc.*

Dose reduction can be achieved in two ways. Firstly it is crucial to appropriately target image quality for a specific diagnostic test, not demanding lower noise or higher spatial resolution than necessary. For instance, in a high-contrast setting, as in the detection of colon polyps from a background of air and contrast-tagged stool<sup>[25,26]</sup>, it allows high noise level and relatively low radiation dose without sacrificing the diagnostic confidence. Detection and characterization of low-contrast lesions present in CT imaging of hepatobiliary and brain pathology require a relatively low noise level and higher radiation dose. Consensus agreement on image quality requirements exists in guidelines and standards<sup>[27]</sup>, but precise quantitative requirements exist only for several examinations<sup>[28]</sup>.

There are many ways to adjust scanning parameters in order to lower the dose. One way to reduce the dose is to change the technical exposure parameters of scanning: The tube current or the voltage depending on the tissue density and contrast, scanning region, and the patients' body shape and size<sup>[29]</sup>.

Modern CT equipment can automatically modulate the X-ray tube current after obtaining a scanned region's initial topogram, known as automatic tube current modulation (ATCM). ATCM adjusts the X-ray tube current (mAs) according to the size and the attenuation of the examined body part. It has been recommended to use ATCM for CTC<sup>[5,20,21]</sup>.

Each time the scanning parameters are changed, it influences the image's quality, namely spatial and/or contrast resolution, which are important for detecting specific pathologies. Spatial resolution relates to sharp boundaries of the tissues, organs, or structures, while contrast resolution involves the difference in contrast of various tissues (*e.g.*, normal or pathologically altered). Low dose protocols have a higher image noise due to altered (lower) electrical conditions. Spatial or contrast resolution is sacrificed, and the radiologist has to get the same information from granulated images. Therefore, it is important to balance the dose by adjusting electrical conditions and maintaining image quality. The image quality needs to be good enough to distinguish pathologic lesions from normal structures. Thus, it is crucial to find a delicate balance between the lowest dose and acceptable image quality, making it possible for a radiologist to discern pathologic structures<sup>[5]</sup>. This is also referred to as the As Low As Reasonably Achievable principle, well established in the area of radiation protection<sup>[23]</sup>. In addition to altering exposure parameters, software options have been developed to make less image noise by keeping the tube current as low as possible. These software reconstructions techniques are Sinogram-Affirmed Iterative Reconstruction (SAFIRE) and a conventional filtered back projection. These techniques allowed the use of even lower doses of radiation than the conventional low dose (LD) protocol named ultra-low dose (ULD) with maintained image quality<sup>[5,24,30]</sup>. In 2018, a study evaluating the ULD protocol's diagnostic value in detecting polyps<sup>[31]</sup> showed that the ULD protocol lowers the effective dose up to 63.2% compared to LD protocol (0.98 mSv for ULD and 2.69 mSv for LD). Image noise measurements with ULD were slightly lower (28.6) than with LD (29.8) ( $P = 0.09$ ). Image quality was not different between 2D and 3D with either ULD and LD. A special 3D software option must be used to navigate the large bowel and when interpreting CTC to help detect intraluminal lesions. In contrast, the 2D option is the routine CT examination technique. Polyp detection was also comparable, with no significant difference in detection rate and polyp measurement for LD and ULD protocols<sup>[30]</sup>. Therefore if iterative reconstruction methods (the software option in almost all modern CT scanners) were included during the scanning, there was no significant image quality degradation with ULD-CTC compared with LD-CTC.

Advantages of specific computer software for CTC interpretation, which enables dynamic viewing of two-dimensional axial images, multi-planar reformats, and three-dimensional renderings, require radiologists' interactive training. The radiologist can use either 2D axial images or 3D renderings for CTC's primary interpretation, with the alternate method reserved for problem-solving specific questions related to a potential lesion. 3D reading is an additional software option that enhances polyp detection and

**Table 2 Comparison of different ionizing radiation doses for different examinations**

Examination	Ionizing radiation dose [mSv]
X-ray lung	0, 1
X-ray abdomen	1
Barium enema fluoroscopy exam	9
CT abdomen and pelvis (w/o contrast)	10
CTC (2 series)	20
CTC ultra low-dose protocol	2

CT: Computed tomography; CTC: Computed tomography colonography.

decreases the interpretation time without increasing the patient dose (Figure 1).

Skilled usage of these techniques acquired by comprehensive training correlate with polyp detection sensitivity<sup>[31]</sup>. Primary 2D interpretation is rendered from magnified colonic axial images gained in supine and prone positions. Compared to primary 3D interpretation, it shortens the assessment time of lesion density and homogeneity.

Sessile polyps have round or ovoid morphology and are of soft tissue density. They remain fixed in location on the colon wall in both the supine and prone images. The stool can be differentiated from polyps since it is typically mixed density and shifts location when the patient changes position. Pedunculated polyps can shift in location when the patient moves from supine to prone positions, but the stalk is typically easily identified on 2D and 3D images. Multiplanar reformats and 3D images are useful for evaluating lesion morphology and confirming polyps<sup>[32]</sup>.

In addition to widely used techniques of lowering radiation dose such as automatic tube dose modulation (automatic adjustment after the initial topogram), lowering the tube current, and applying iterative reconstruction (IR), lowering tube voltage can be useful. This option is rarely used for routine CT scanning because it impairs X-ray penetration through the scanned region. However, during the CTC, the bowel has a high contrast due to intraluminal gas; therefore, high voltage is not needed. If there is an option for IR, we can lower the voltage and turn on IR. The iterative reconstruction software option will fix the image noise which arises from the lower voltage<sup>[29]</sup>.

The data suggest that low tube voltage with IR results in a 27 % radiation reduction while maintaining the image quality and detection (100kVp vs 80kVp)<sup>[33]</sup>. In addition, new IR such as SAFIRE could lower the voltage even more<sup>[30]</sup>.

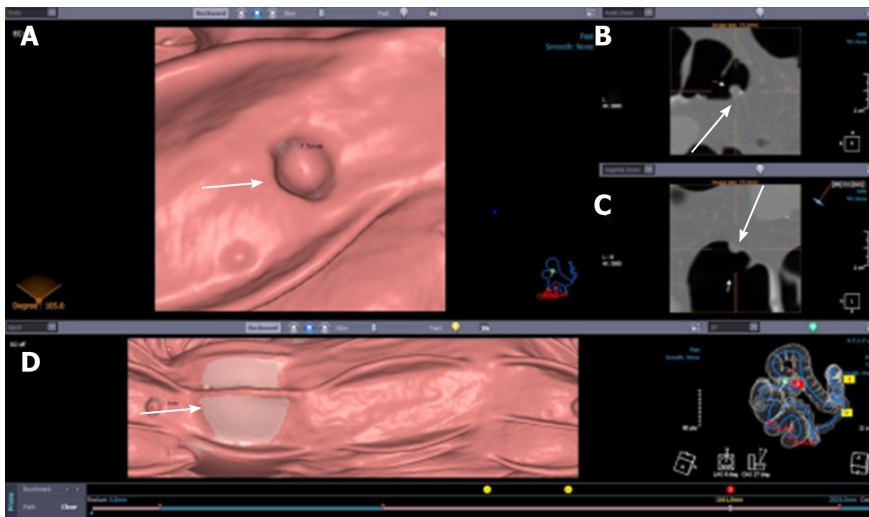
Recent studies show that both hybrid and iterative model reconstruction techniques are suitable for sub-milliSievert ultralow-dose CTC without sacrificing the study's diagnostic performance<sup>[34]</sup>.

Several operational factors typically result in higher doses. Repeated CT scanning, such as multiphase examinations, increases the radiation dose. For example, suppose diagnostic CTC is being performed in a patient with suspected colorectal carcinoma. In that case, intravenous contrast may be necessary, and CT acquisition parameters will typically require higher mAs. If the patient is undergoing CTC as a screening examination, then intravenous contrast is not routinely used.

Patient's height and/or length also influences the radiation dose. Longer scan length results in radiation exposure to a greater anatomic region and hence higher radiation dose. For some reason, for a detailed analysis, radiologist could request thinner images that provide better image resolution and improved visibility of small objects. However, beam intensity needs to be increased to reduce the noise in these thinner images, which concurrently increases the radiation dose<sup>[35]</sup>.

Since the whole abdomen is visible during CTC screening, many abnormalities outside of the colon can be picked up. Several US screening studies collected the data on clinically significant extracolonic findings that required further imaging. The proportion of patients with follow-up CT scans to investigate these findings was in the range of 5-10%<sup>[36,37]</sup>. The most common follow-up scan were; an abdomen CT scan and abdomen/pelvis and chest CT scans. The dose from an abdomen/pelvis CT scan performed with and without contrast is about 20 mSv<sup>[38]</sup>, which will result in a radiation risk that is about twice as high as the risk from CTC. However, as only a small proportion (*e.g.*, 10%) of the screening population will receive these additional scans, it is unlikely that they will increase the average risk to the whole screening population by more than 20%.





**Figure 1** Computed tomography colonography: Two- and three-dimensional view of the polyp (arrows). A: Polyp 3D view; B: Polyp 2D view; C: Polyp 2D view; D: Tagged stool.

The standard American College of Radiology (ACR) CTC protocol<sup>[39-42]</sup> specifies that the patient be scanned in both the supine and prone positions to allow complete evaluation of the colon with the dependent shifting of luminal fluid and complementary distention of non-dependent colonic segments. In a minority of cases, the same colonic segments will be collapsed on the standard positions, necessitating a third series to achieve full diagnostic evaluation. The sigmoid and/or descending colon account for most non-diagnostic segments, necessitating a right lateral decubitus series to complete the examination<sup>[43,44]</sup>.

The frequency for performing a decubitus series at CTC varies considerably according to study indication, practice site, patient age, BMI, and over time. It is critical to note that the CT technologist is primarily responsible for determining the need for a decubitus series—not the radiologist. These results have important implications for clinical practice, including the need for improved training and feedback for CT technologists<sup>[45]</sup>.

Furthermore, practice regarding ancillary imaging before a CTC and after incomplete OC should be discussed as this can also increase radiation dose; for example, some centers perform a scout/topogram or non-contrast CT abdomen following incomplete OC, in order to exclude a perforation; although there is evidence to suggest this is unnecessary.

Perforation is a recognized complication of colonoscopy. Reported perforation rates range from one case in 3115 procedures (0.032%) to one case in 510 procedures (0.196%)<sup>[46-49]</sup>. The short time between incomplete colonoscopy and same-day or next-day CTC may not be adequate to allow some perforations to become clinically apparent. Because of the risk of exacerbating a clinically unsuspected perforation during insufflation at CTC, which can increase sepsis risk, screening for the presence of extraluminal gas before insufflation for CTC may benefit occult perforation among these patients. Colonic perforation after colonoscopy can be clinically occult. Recent studies have shown that some findings justify performing low-dose diagnostic CT before rectal tube insertion and gas insufflation in all patients referred for same-day or next-day CTC after incomplete colonoscopy to minimize the risks associated with exacerbating perforation<sup>[50]</sup>.

## RADIATION DOSE AND CANCER RISK

Effects of radiation and its risk are usually estimations based on the linear extrapolation of the cancer risks associated with ultra-high doses from Hiroshima and Nagasaki atomic bomb survivor studies<sup>[51]</sup>. Still, there is no unambiguous evidence of cancer induction at low dose levels, and the issue remains highly controversial.

In 2016, the Health Physics society published that radiation lower than 100mSv did not impact the human body<sup>[52]</sup>. Assuming that the CTC dose is on average 5mSv, that means that the theoretical cancer risk would be 0.04% in 50-year-old patients and

0.02% in 70-year-old patients after initial screening<sup>[51]</sup>. Keeping in mind that a lifetime risk for developing colon cancer is around 5%, CTC's benefits outweigh its estimated radiation risk. CTC doses are, currently, in many institutions, even lower than 3mSv, the dose which is comparable to annual radiation exposure in some countries such as the United States<sup>[53]</sup>.

Since the age for screening for CRC is above the age of 50, exposure is decreased significantly, and therefore the radiation-related cancer risk is even lower. Since the proportion of dividing human cells decreases with age, this further raises CTC's safety in the older population it mainly serves<sup>[54]</sup>.

It is important to consider the average frequency of each examination in the population and the average radiation dose with each technique to understand the radiation dose of CTC in the context of other ionizing techniques. However, all examination-based techniques (radiography, fluoroscopy, CT, positron emission tomography-CT, scintigraphy, and interventional cardiology) constitute 34 % of the total annual population dose<sup>[53,55]</sup>.

It is important to emphasize that CTC is quite different from the usual CT examination. Inherently high contrast between the air-filled lumen of the colon and the soft-tissue attenuation of the colonic wall allows a relevant dose reduction without loss of diagnostic accuracy<sup>[54]</sup>.

## CONCLUSION

In addition to CTC's high safety profile, slightly better patient compliance, ability to detect extracolonic disease and comparable polyp and cancer detection rate to OC, CTC can be performed with a minimal radiation dose that poses no risk of cancer to the patient.

CTC "good practice" should include individualizing the scanning technique according to the patient's attenuation level and using suitable tube potential selected by advanced automatic exposure control techniques that adjust the tube current. Implementation of iterative reconstruction in everyday clinical practice can bring significant image quality improvement and radiation dose reduction over conventional filtered back-projection-based reconstruction algorithms.

Modern CT equipment allows us to scan CTC at much lower doses ranging from 1 to 5 mSv. These doses are comparable with 1-2 Lung radiograms and are on the annual radiation background level in some countries. Since screening programs mostly include two readers (two experienced radiologists) and "double-blinded" reading, the new perspectives arise from the integration of artificial intelligence in CT machines, which could be used for screening CTC instead of a "second reader".

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