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Sources of false positives in computer-assisted CT colonography

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Abstract

The application of computer-aided detection (CAD) is expected to improve reader sensitivity and to reduce inter-observer variance in computed tomographic (CT) colonography. However, current CAD systems display a large number of false-positive (FP) detections. The reviewing of a large number of FP CAD detections increases interpretation time, and it may also reduce the specificity and/or sensitivity of a computer-assisted reader. Therefore, it is important to be aware of the patterns and pitfalls of FP CAD detections. This pictorial essay reviews common sources of FP CAD detections that have been observed in the literature and in our experiments in computer-assisted CT colonography. Also the recommended computer-assisted reading technique is described.

Key words: Computed tomographic colonography—Computer-aided detection—False-positives—Image interpretation—Colorectal neoplasms

Abbreviations

CT	Computed tomographic
2D	Two-dimensional
3D	Three-dimensional
CAD	Computer-aided detection
FP	False-positive
ICV	Ileocecal valve
EC	Electronic cleansing

Computed tomographic (CT) colonography is a minimally invasive technique for detecting colorectal lesions by use of virtual two-dimensional (2D) and three-dimensional (3D) visualizations of abdominal CT scans [1]. Multi-center trials have demonstrated that CT colonography has a per-patient sensitivity of approximately 90–94% and a specificity of 85–96% in the detection of large (≥10 mm in diameter) colonoscopy-confirmed adenomas and cancers, when it is performed with state-of-the-art methods and experienced readers [2–5]. For smaller lesions (6–9 and <6 mm in diameter), the reported detection sensitivities have been somewhat lower and more variable [6].

It is expected that the application of computer-aided detection (CAD) could be used to overcome the problems of variable detection sensitivity and high inter-observer variance in CT colonography [7]. CAD can be defined as a diagnosis made by a physician who is supported by the output of a fully automated quantitative image analysis scheme [8]. In CT colonography, CAD systems are used to indicate image patterns that are similar to those of colorectal lesions. To date, several CAD systems have been reported to be able to detect retrospectively visible colorectal lesions in CT colonography at a high-detection sensitivity, and pilot observer studies have indicated that CAD indeed has the potential of increasing the detection sensitivity and reducing the inter-observer variance of human readers, especially with inexperienced readers [7].

However, current CAD systems for CT colonography display a much larger number of false-positive (FP) detections than do human readers. Unaided experienced readers report in the order of less than 0.1 FP detections per patient on average, whereas CAD systems display at least 2–10 FP detections per patient on average. The interpretation of FP CAD detections increases interpretation time, and it may also reduce detection specificity [9]. There is also evidence that, under some unfavorable circumstances, having to review a large number of FP CAD detections could be detrimental to the detection sensitivity of a computer-assisted reader [10, 11]. To date, CT colonography studies have investigated the effect of FP CAD detections on reader performance only with CAD systems that display large numbers of FP detections [12, 13].

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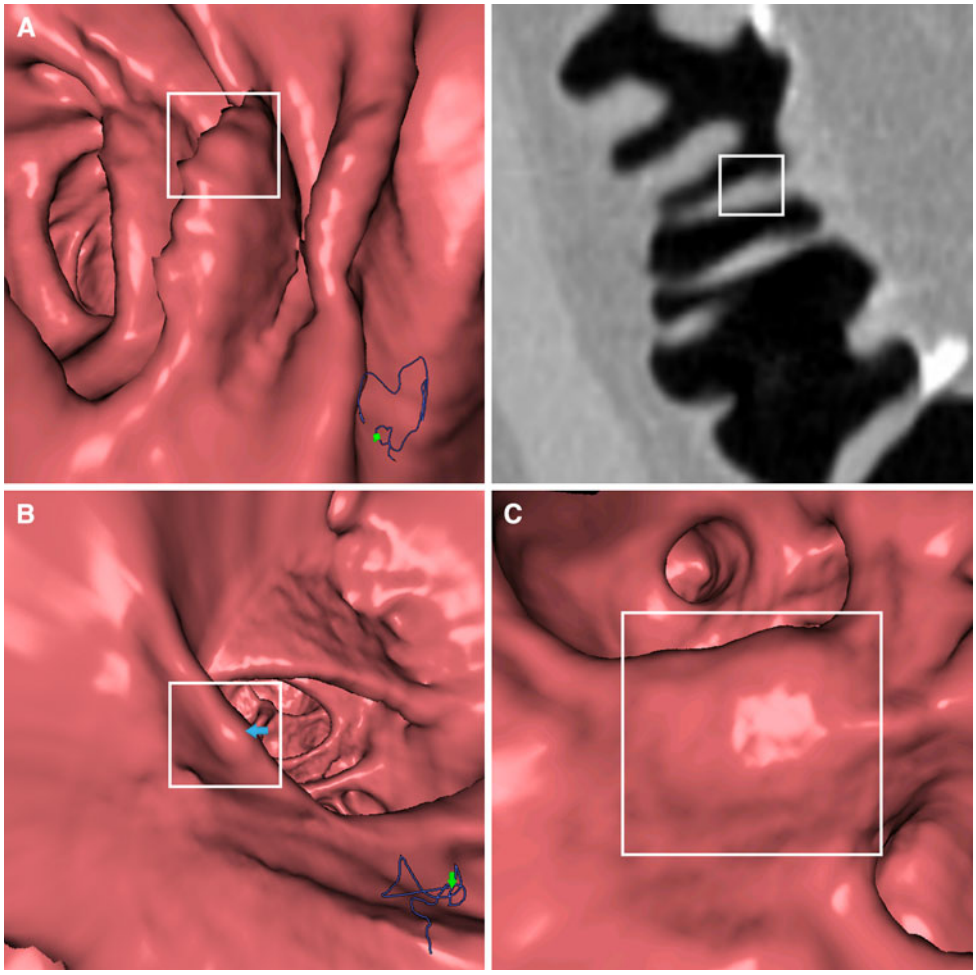

Fig. 1. FP CAD detections (location indicated by *squares*) due to normal folds. **A** 3D (*left*) and 2D (*right*) view of the CAD detection of a thickened fold. The similar appearance of the nearby folds suggests that this is a normal fold. **B** Detection of a nodular fold. **C** A detection of converging normal folds.

Understanding the patterns and pitfalls of FP CAD detections is important for maximizing the potential benefit in reader sensitivity without detrimental effect on reader performance. This pictorial essay discusses common sources of FPs that have been observed in the literature and in our experiments with computer-assisted CT colonography. Also the recommended computer-assisted reading technique is described.

Common sources of FP CAD detections

The types of FPs that are detected by CAD systems are similar to those encountered by radiologists. Most of these detections are easy to differentiate from true lesions by the application of the usual interpretation guidelines of unaided CT colonography [14, 15]. Studies have indicated that only about 10–20% of FP CAD detections are challenging to dismiss [7].

Haustral folds

Haustral folds are the most common source of FP CAD detections in cathartically prepared CT colonography. Some of these detections are easy to dismiss, whereas others require careful workup. Pilot observer studies have indicated that FP CAD detections due to folds are also a leading cause of potentially CAD-induced FPs of computer-assisted readers [9, 12].

Detections of simple normal haustral folds are easy to dismiss. Such FP CAD detections are usually caused by image artifacts, such as partial-volume distortion of thin folds or pseudo-enhancement effects due to adjacent positive-contrast tagging [16].

Detections of thickened folds can provide challenging interpretation pitfalls. In general, if the nearby folds in the segment have similar appearance to the detected fold, the CAD detection may be dismissed as a FP (Fig. 1A). Such CAD detections could be caused by suboptimal colon distension or sigmoid muscular hypertrophy. However, if the detected fold looks very different from the nearby folds, it could represent a non-polypoid lesion or an infiltrative carcinoma [17].

Also detections of nodular folds can be challenging to dismiss, because they can imitate polyps or non-polypoid lesions on a fold (Fig. 1B). Sometimes such image patterns are caused by movement or reconstruction

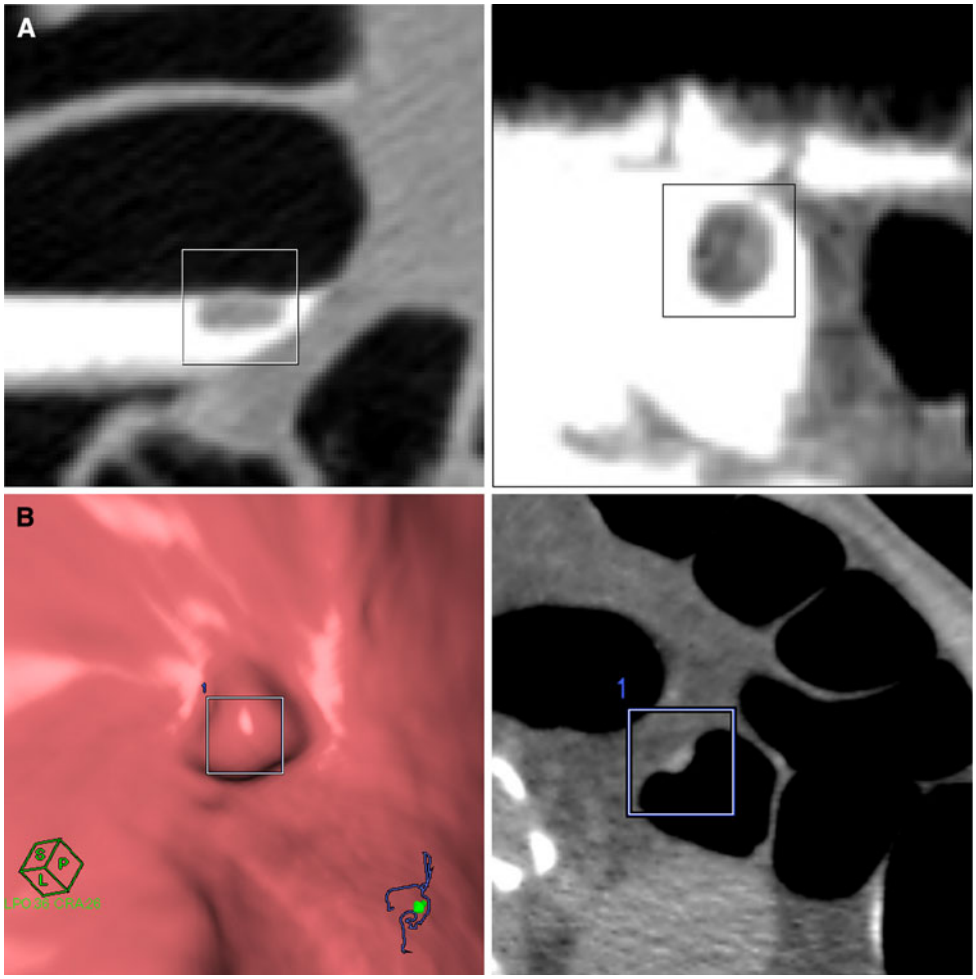

Fig. 2. FP CAD detections due to stool. **A** Untagged stool imitating a soft-tissue lesion in a lung-tissue window level setting (*left*). The internal density variation that can be seen by adjusting the soft-tissue window level setting (*right*) suggests that the detected lesion is likely to be stool. **B** *Left*: 3D view of a CAD detection of poorly tagged stool. In 2D view (*right*), the low tagging level causes the lesion to imitate the density of a polyp, necessitating further workup.

artifacts. Confident differentiation may require reconciliation between 2D and 3D views [18].

It is also relatively common for CAD to detect convergences of two or more normal folds (Fig. 1C). Such patterns should be reconciled in 2D and 3D views with correlation to other scan views (supine, prone, decubitus) to confirm that the image pattern is not caused by a non-polypoid lesion [19].

Untagged or poorly tagged stool

Untagged or poorly tagged stool and feces are the second most common source of FP CAD detections in cathartically prepared CT colonography and the most common source of FP CAD detections in non-cathartically prepared CT colonography. They are also a significant source of FP detections of computer-assisted readers [9, 12].

Many FP CAD detections due to stool can be identified based upon their internal mottle texture pattern or irregular angulated contour. A review in 2D view with an optimal soft-tissue window level setting (Fig. 2A) or in 3D view with a translucency or color map tool [15] may reveal internal diffuse gas or internal positive-contrast tagging. Tagged stool is indicated generally by the enhancement of internal density (Fig. 3A), but one should be careful in not dismissing CAD detections of true lesions that may have been coated by a layer of tagging [20] (Fig. 3B). Also, some of the detected stool may not be clearly tagged and can imitate polyps in their internal density (Fig. 2B), thereby requiring a more detailed analysis. Large pieces of stool may also be indicated by their low CT attenuation (<−200 Hounsfield units).

Most CAD systems do not check for the mobility of a detected lesion between the different scan views of a patient. Therefore, the reader should check if the CAD detection demonstrates significant longitudinal movement or circumferential movement to the dependent side between scan views (Fig. 4). However, one should confirm that such observed positional movement is not caused by the circumferential rotation or contraction of the colon between scans, or by movement of the head of a pedunculated lesion [21, 22].

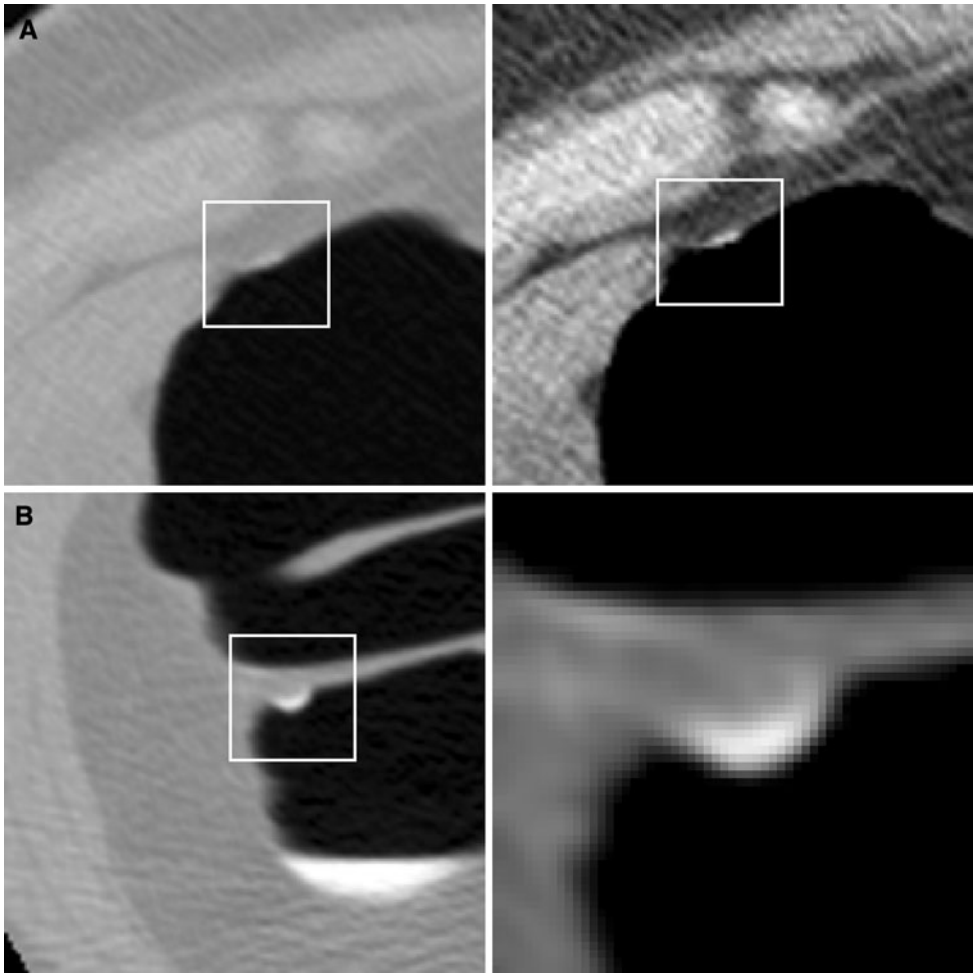

Fig. 3. **A** Tagged stool is often indicated by the enhancement of its internal density. Isolated thin layers of tagging (*left*) may need to be resolved carefully by use of a soft-tissue window level adjustment (*right*). **B** An interpretation pitfall: CAD detections of clearly tagged regions should be checked carefully for underlying true lesions. Here, the tagging is adhering to an underlying 10-mm sessile adenoma.

Ileocecal valves

Ileocecal valve (ICV) is a frequent source of FP CAD detections, although the number of such detections is necessarily limited per patient. Because of its characteristic image pattern and location near the cecum, FP CAD detections due to ICVs are relatively easy to dismiss (Fig. 5A). However, they do present some important interpretation pitfalls. First, one should be familiar with the wide variation of the shape and density of normal ICVs [23, 24] in order to not to call CAD detections of some normal ICVs erroneously as true lesions (Fig. 5B). Second, polyps can grow on ICVs, and therefore some CAD detections on an ICV may indeed represent true lesions (Fig. 5C). Third, some large polypoid or flat carcinomas can imitate the shape and density of an ICV in the ascending colon. Therefore, when reviewing CAD detections on what appears to be the ICV, one should always confirm the location and extent of the true ICV and not overlook potential nearby lesions.

Electronic cleansing and tagging artifacts

Application of orally administered positive-contrast tagging is highly recommended in CT colonography (1) to reveal lesions that may be covered by tagged fluid and (2) to differentiate residual stool and feces from true lesions. However, tagging presents significant technical challenges to CAD algorithms in CT colonography [25], and therefore it presents a potential source of FP CAD detections. Fortunately, most of these CAD detections are easy to dismiss.

It is often assumed that electronic cleansing (EC) can be used to subtract tagged materials from CT colonography data before the application of CAD. This approach has the problem that EC algorithms tend to produce a large number of small residual subtraction artifacts [26] that are detected as abnormal image patterns by CAD systems [7] (Fig. 6). Therefore, the application of EC with CAD may be limited to the detection of large and conspicuous lesions and/or to cathartic bowel preparations with clearly tagged fluid.

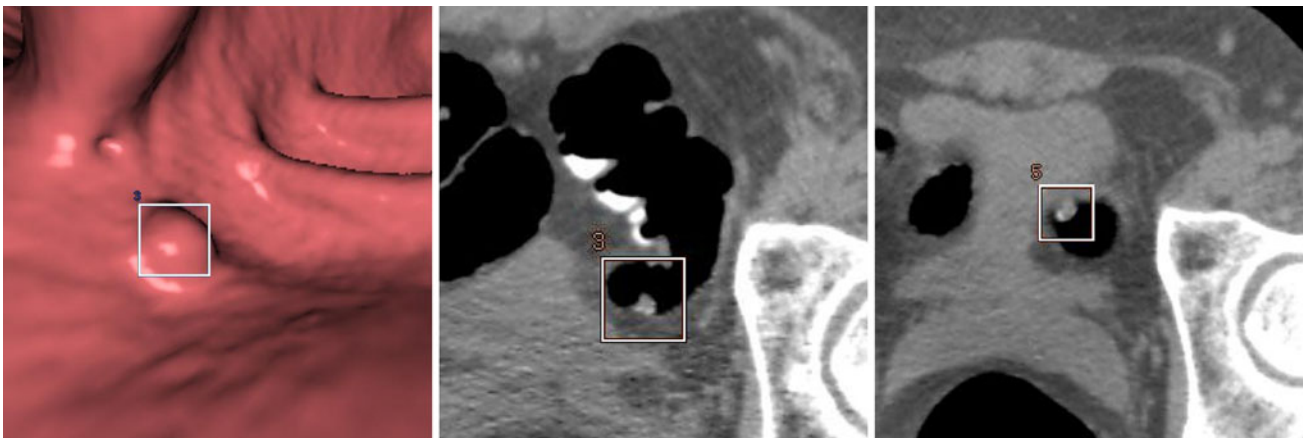

Fig. 4. A FP CAD detection due to poorly tagged stool. In 3D view (*left*), the stool imitates a round polyp. Correlation of the detection in supine and prone scan views (*middle and right*) reveals positional movement to the dependent side.

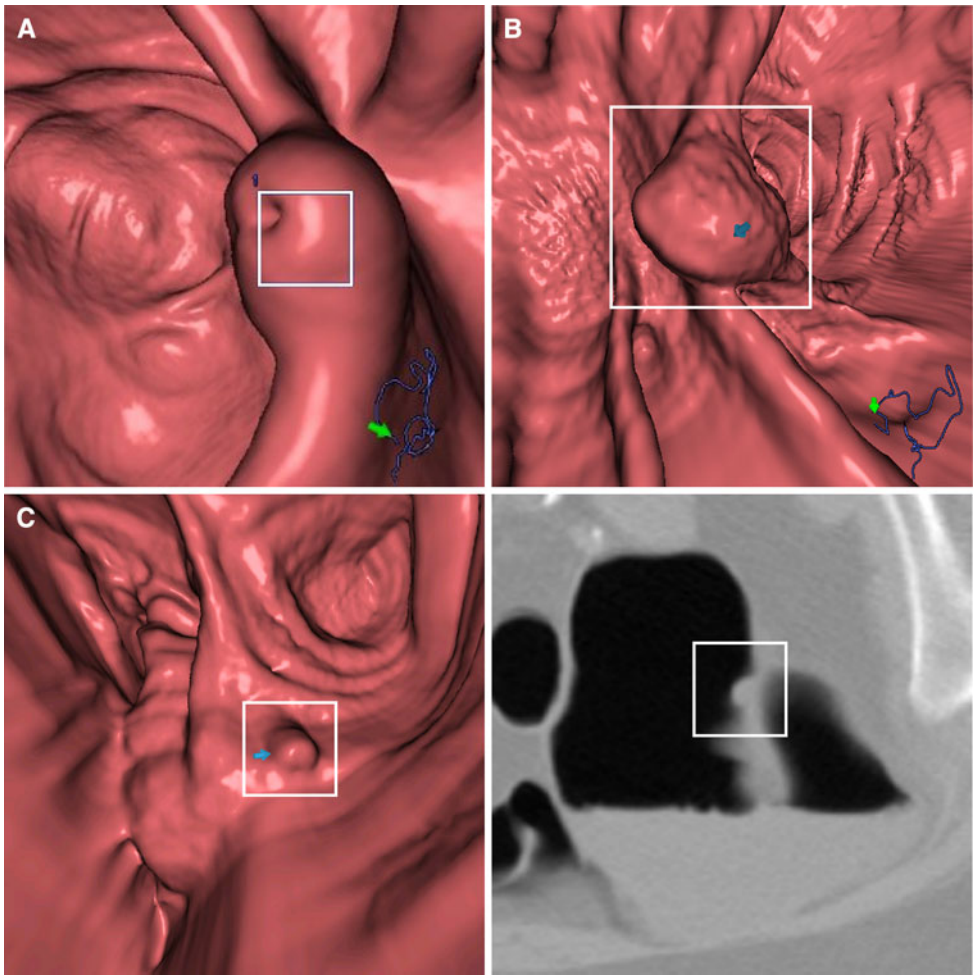

Fig. 5. CAD detections on ileocecal valves. **A** The orifice of a normal ICV. **B** A radiologist misinterpreted this CAD detection of a normal dilated ileocecal valve as a true lesion. **C** An interpretation pitfall: 3D (*left*) and 2D (*right*) views of a 6-mm polyp on an ileocecal valve. A radiologist misinterpreted this CAD detection as a FP.

Some CAD systems can analyze positive-contrast tagged CT colonography data directly without the use of EC [7]. The application of some of these methods is limited to cathartic CT colonography where residual materials appear mostly as fluid [27], whereas others are also applicable to non-cathartic CT colonography where residual materials can appear in solid forms [25, 28]. Nevertheless, such CAD systems may still display FP detections due to some types of partial-volume tagging artifacts (Fig. 7) [28].

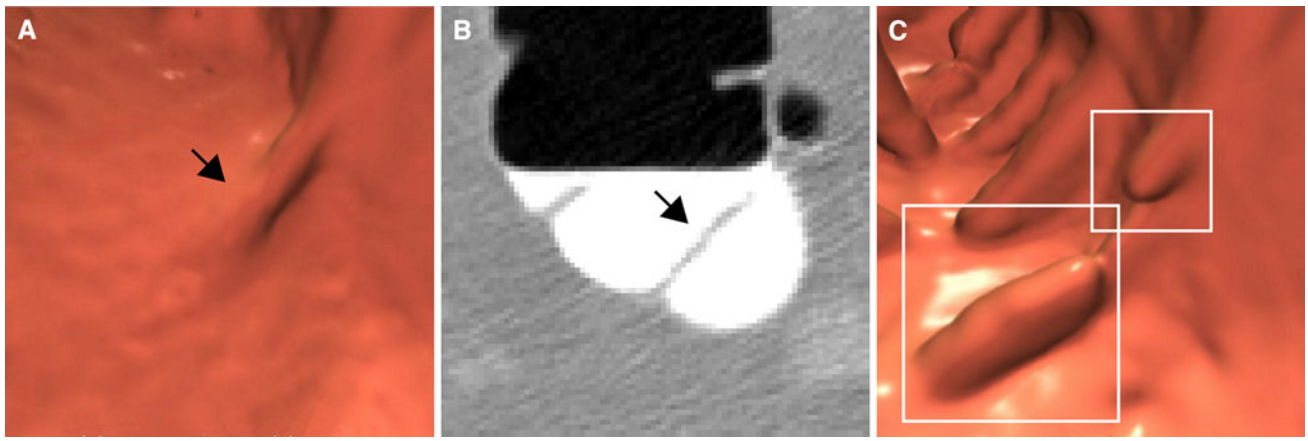

Fig. 6. An example of FP CAD detections due to residual artifacts of electronic cleansing. **A**, **B** Before electronic cleansing, a haustral fold (*arrow*) is submerged partially in tagged fluid. **C** After electronic cleansing, the fold has been partially removed. The residuals of the fold were detected as FPs by a CAD scheme that was applied to the electronically cleansed data.

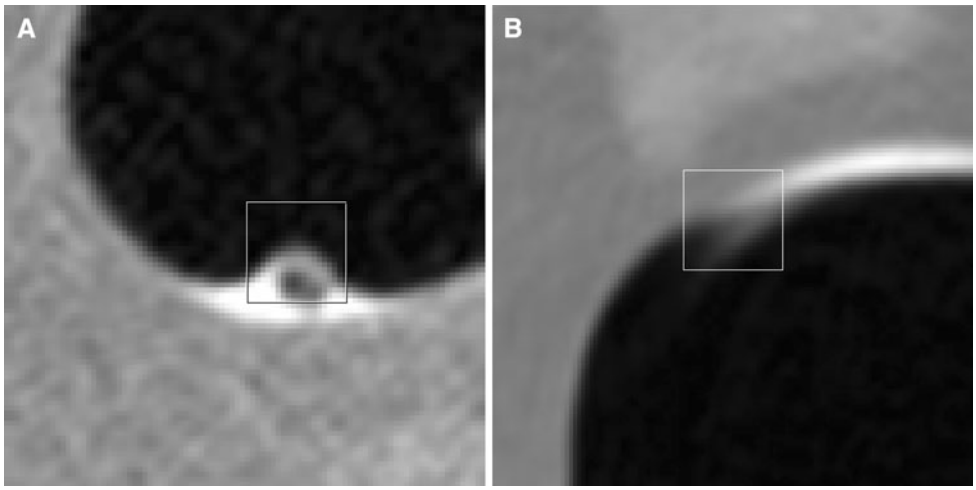

Fig. 7. FP CAD detections due to positive-contrast tagging artifacts in cases where electronic cleansing was not used. **A** A partial-volume artifact imitates a soft-tissue lesion within the material interface between lumen air, tagging, and an air bubble. **B** A partial-volume artifact imitates nonspecific soft tissue at the base of a thin fold next to a tagged region.

Extrinsic compression

Normal structures and organs that are located outside of the colon, such as the liver, aorta, psoas muscle, or adjacent bowel loops, can occasionally cause external compression that imitates the shape of a sessile or flat lesion and may be detected by CAD (Fig. 8). Some of these FP CAD detections can be challenging to dismiss in 3D view and require reconciliation in 2D view [29].

Extra-colonic regions

Most CT colonography workstations rely on semi-automated colon extraction where a radiologist needs to indicate the region of colon in CT data to the computer. On the other hand, standalone CAD systems that attempt to extract the region of colon automatically can erroneously include extra-colonic regions, such as small bowel or stomach, in their extracted colon region. Such extra-colonic regions may occasionally cause FP CAD detections that however are easy to dismiss (Fig. 9). Extra-colonic detections may be largely avoided by limiting the display of CAD detections only to the regions of colon that were indicated manually by the radiologist.

Rectal tubes

FP CAD detections due to rectal tubes are easy to dismiss. Because also automated identification of rectal tubes is a relatively easy task, it is likely that mature CAD systems will display only few FP detections due to rectal tubes. However, when reviewing CAD detections on rectal tubes, one should confirm that the detection was not caused by a true adjacent lesion (Fig. 10).

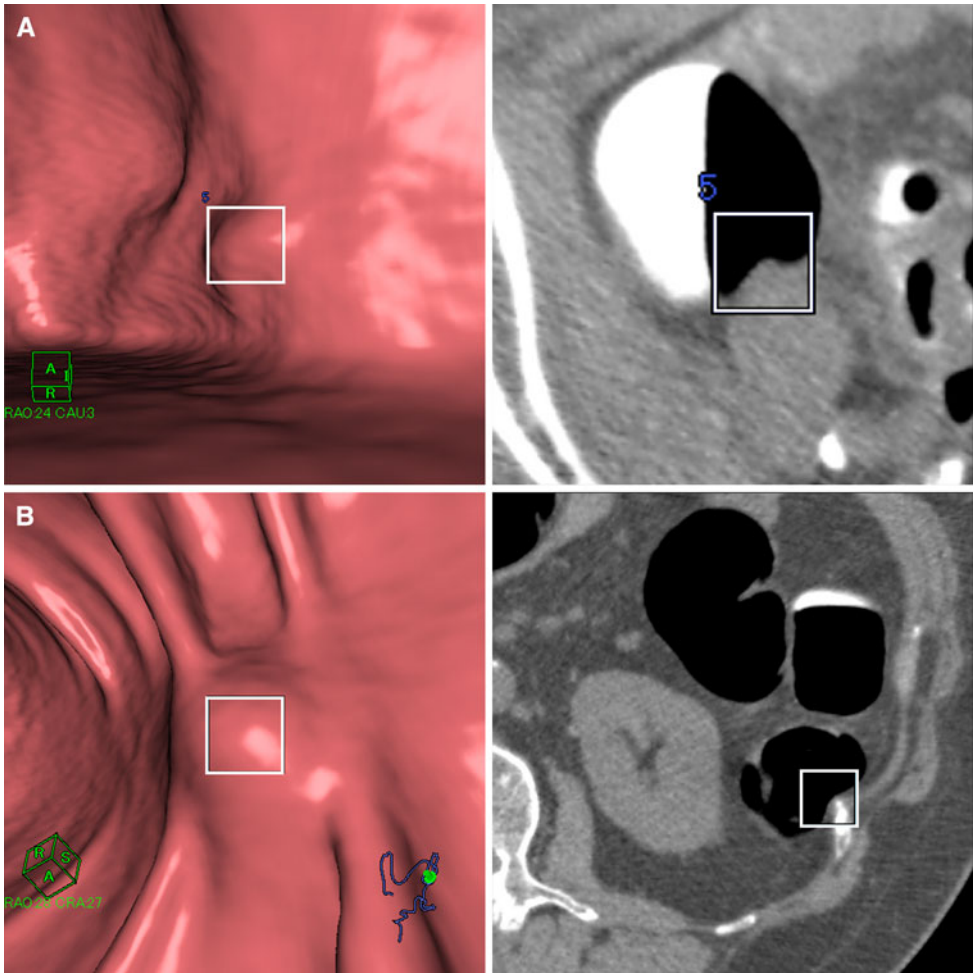

Fig. 8. FP CAD detections due to extrinsic compression, seen in 3D (*left*) and 2D (*right*) views. **A** Muscle. **B** Bone.

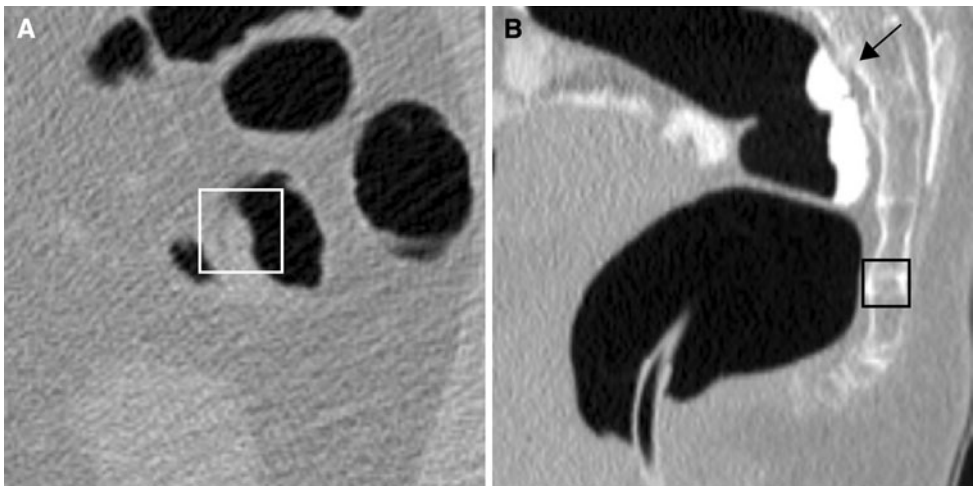

Fig. 9. FP CAD detections of extra-colonic regions. **A** A thickened fold in small bowel. **B** Bone tissue. In this example, the CAD system has included osseous structures incorrectly in the extracted region of the colon because of their similar radiodensity and artificial connection with positive-contrast tagged fluid (*arrow*) in the CT colonography data.

Miscellaneous sources of FPs

There are also various other sources of FP CAD detections that, however, tend to occur less frequently than those listed above. Some of these are easy to dismiss as FPs, whereas others may require careful problem solving.

Anal papillae are a relatively frequent source of FP CAD detections, because they tend to imitate the shape and density of polypoid or non-polypoid lesions (Fig. 11A). Such detections are often easy to identify based upon their location at the anal verge and their

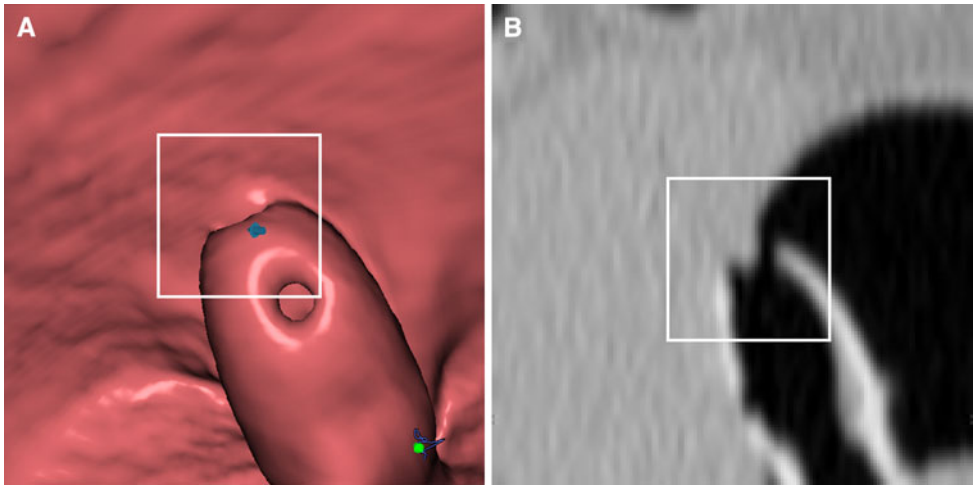

Fig. 10. An interpretation pitfall due to rectal tube: CAD is indicating a 7-mm adenoma that was missed by radiologists during unaided reading. **A** In 3D view, the polyp is hidden by the rectal tube, and therefore the CAD detection could be dismissed incorrectly as a FP detection on the rectal tube. **B** In 2D view, the CAD detection of the polyp is clearly visible.

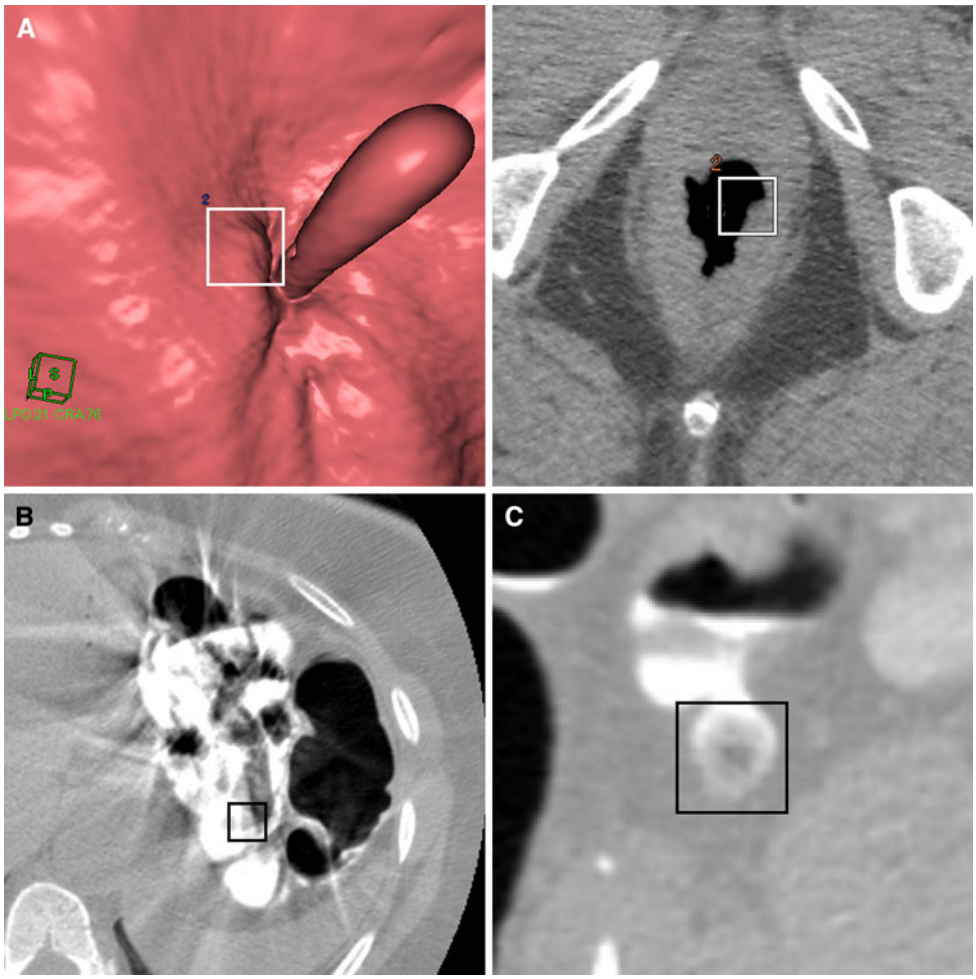

Fig. 11. Miscellaneous sources of FP CAD detections. **A** Anal papilla in 3D and 2D views. **B** Streak artifact caused by high-density tagging. **C** Diverticular fecalith: such CAD detections are easy to dismiss based upon their heterogeneous density and irregular margin.

characteristic pyramidal projection up from the junction between the skin and inside lining of the anus. Some of these detections can also represent internal hemorrhoids or varices. However, one should be especially careful when dismissing CAD detections that appear near but not at the anal verge [15].

High-density objects within the abdomen, such as hip prosthesis or high-density positive-contrast tagging, can cause streak artifacts in the reconstructed CT data that can cause FP CAD detections. Such detections are easy to dismiss in 2D view (Fig. 11B), but one should be careful in not to

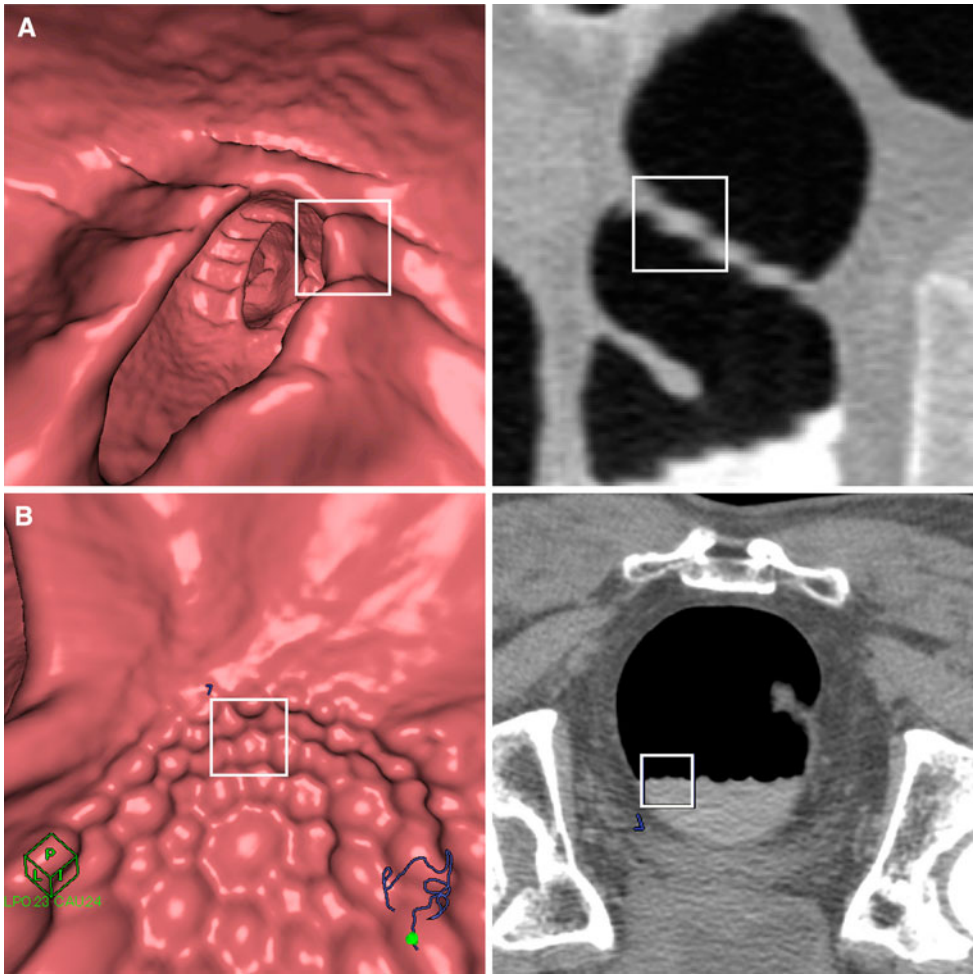

Fig. 12. Miscellaneous sources of FP CAD detections. **A** Motion artifact (distorted fold). **B** Bubbly surface level of (poorly tagged) residual fluid.

dismiss any CAD detections of true lesions in such regions.

When present, diverticular fecaliths [30] that imitate polyps in their shape and density tend to be detected as FPs by CAD systems. Often, such CAD detections are located within diverticula that are submerged in tagging (Fig. 11C).

Movement artifacts, such as peristalsis, can produce malformations of folds and mucosa that tend to be detected as abnormal image patterns by CAD (Fig. 12A). Also CT reconstruction artifacts may produce ripple-like regular distortions of folds and mucosa in a region. Resolving of such CAD detections may require reconciliation between 2D and 3D views and between different scan views.

Some of the FP CAD detections are associated with non-specific coarse surface variation of the colonic mucosa or fluid surface. The surface variation of colonic mucosa can be caused by suboptimal colon distension, non-specific particulate stool, residual EC artifacts, or by low-radiation dose or thick region of the abdomen. The use of polyethylene glycol with bowel preparation tends to produce bubbly fluid surfaces that may be detected by CAD as abnormal patterns (Fig. 12B). Such FP CAD detections are often best identified in 2D view, but one should ensure that the CAD detection of a coarse mucosa does not actually represent a laterally spreading tumor.

Sharp turns or bending of the colon can occasionally produce pseudo-lesions that are detected by CAD. The identification of such flexular pseudo-tumors may require an analysis of the internal density of the CAD detection in 2D view with correlation to another scan view. One should remember not to overlook true polyps in the vicinity.

Inverted diverticula [30] occur less frequently but are often detected by CAD when present in CT colonography data. These can be identified in 2D view with a soft-tissue window level setting based upon the mesenteric fat within their serosal side.

Sources of FPs in CAD algorithms

It is also instructive to review how FP detections are introduced in the detection algorithms of CAD systems. Most CAD systems detect lesions in three basic steps: (1)

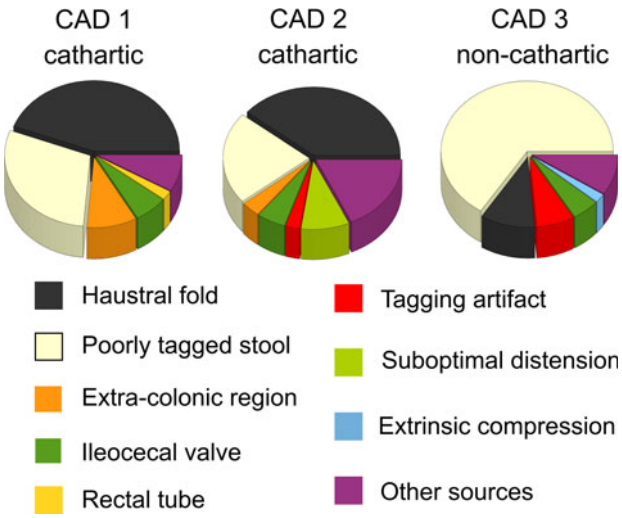

Fig. 13. An example of reported sources of FP detections with three different CAD systems (CAD 1 [44], CAD 2 [13], and CAD 3 [28]). In cathartically prepared CT colonography (CAD 1 and CAD 2), haustral folds are the largest and poorly tagged stool the second largest source of FP CAD detections. In non-cathartic CT colonography (CAD 3), poorly tagged stool are the single largest and haustral folds the second largest source of FP CAD detections.

colon extraction, (2) lesion detection, and (3) FP reduction. The extra-colonic FP CAD detections originate from the colon extraction step, when it includes extra-colonic regions erroneously in the extracted colon region. Next, in an attempt to detect all significant lesions at a nearly 100% sensitivity, the lesion detection step detects not only true lesions but also a huge number of FP detections from the extracted colon region. The final step, FP reduction, attempts to minimize the number of FP detections in CAD output while maximizing the number of true detections, thereby determining the final detection performance of a CAD system that is observed by users.

The fact that CAD systems are not created equal is often overlooked in clinical trials. Different CAD systems, and sometimes even their different versions, can have quite different detection performance with the same data, or quite different detection performance with different types of data, because of their different design criteria, detection algorithms, and training data [31, 32]. Nevertheless, in cathartically prepared CT colonography, the overall distribution of the sources of FP CAD detections tends to be similar across systems. In contrast, in non-cathartic CT colonography [33, 34], the distribution of FPs, and the CAD performance can be quite different from that of cathartic CT colonography (Fig. 13).

Despite the internal differences between CAD systems, most CAD algorithms also have common design limitations that introduce sources of FP CAD detections and may need to be addressed in future CAD systems to reduce the number of FP CAD detections to an acceptable level. First, most CAD algorithms have been designed to detect local image patterns that are similar to those of colorectal lesions. However, they do not consider the context of these detections. Therefore, human readers can easily dismiss many FP CAD detections simply by considering the context of the detection (Fig. 14).

Second, CAD systems are not able to compare locations between different scans reliably and accurately, and therefore they usually interpret each patient scan as an independent study. In contrast, human readers can dismiss many FP CAD detections by comparing the detected region between the different scans (Fig. 4).

Third, most CAD systems have been designed to detect polypoid lesions in cathartic CT colonography. When such CAD algorithms are used to detect flat polyps or flat lesions [35, 36] or when they are used in non-cathartic CT colonography [28], they can detect much higher numbers of FP detections than what is currently reported for polyp detection in cathartic CT colonography.

Finally, it should be noted that CT colonography involves also various other computer-assisted reading tools than CAD, including different visualization schemes and measurement tools. Such tools can also present potential sources of FP detections in CT colonography. Some 3D visualizations present significant image distortion and may require reconciliation in alternative views [37], and measurement tools may overestimate or underestimate the true size of a measured lesion at the important 6 and 10-mm threshold levels [38, 39].

Recommended use of CAD

The fact that radiologists can occasionally misinterpret FP CAD detections as true lesions while dismissing some true-positive CAD detections erroneously as FPs has been observed in many pilot trials [40–42]. Therefore, appropriate reader training for interpreting CT colonography without and with CAD is necessary.

CAD systems are recommended to be used as "a secondary reader" [7, 43]. That is, each case should be read first without CAD output. Only after completing an unaided primary reading step and having made a diagnosis, one should check the CAD output. The CAD output should not be used as a basis for excluding or including findings of unassisted reading, and the amount of or lack of CAD detections should not be used as a basis for changing the diagnosis. Instead, the CAD output should be considered as a visual aid or "spell checker" to detect lesions that may have been missed or overlooked during the unassisted reading.

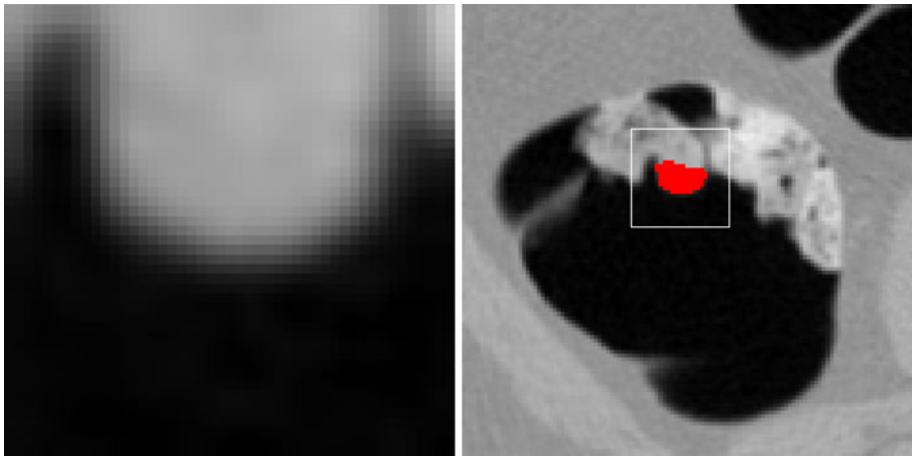

Fig. 14. Many FP CAD detections are caused by the inability of the CAD system to understand the context of the detections. Here, a polyp-like image pattern (*left*) that was detected by a CAD system is actually (*right*) part of the granular surface of poorly tagged feces. *Red color* (or dark gray color in the print version) indicates the region that was extracted by the CAD system as the detected lesion.

Each CAD detection should be reviewed carefully by reconciling its appearance between 2D and 3D views, by analyzing the internal texture in 2D view, and by correlating the location of the detection with alternative scan views. A CAD detection should not be dismissed simply because it does not immediately look like a typical polyp. For example, in cases where the CAD output indicates a clearly tagged region, one should consider if the tagging adheres to an underlying true lesion (Fig. 3B).

Some CAD user interfaces may obscure the internal texture of a detected lesion by painting the detected region (Fig. 14, right image). Such a painting can be very useful in determining what was it precisely that the CAD system detected, but the painting should be turned off for problem-solving in 2D view. Ideally, the internal texture should be reviewed in a scan view where the lesion is surrounded by air rather than by tagging. The display window level setting should be adjusted for optimal visualization of the internal texture of each lesion.

When correlating the location of a CAD detection between scan views, CAD may or may not have detected the lesion in all scans. This should not be considered to indicate that the detected lesion is a true lesion or a FP.

Conclusions

CAD for CT colonography has potential to increase reader sensitivity and to reduce inter-observer variance. However, current CAD systems display at least an order of magnitude larger number of FP detections than do human readers. This increases the interpretation time, and it may also reduce the specificity and/or sensitivity of a computer-assisted reader. The most common sources of FP CAD detections include various types of haustral folds and untagged stool. The differentiation of FP CAD detections from true lesions follows the guidelines of unaided CT colonographic interpretation. The precise number and distribution of FP CAD detections depends on the design of the internal detection algorithms and the training data of the CAD system. Most CAD systems have been designed to detect polypoid lesions in cathartic CT colonography, and they may perform poorly in detecting other types of lesions and/or in non-cathartic CT colonography. Also other computer-assisted interpretation tools in CT colonography introduce potential sources of FP interpretation. To maximize the benefits of CAD while minimizing its potential adverse effects, CAD is recommended to be used only as "a secondary reader" after completing an independent unaided primary reading.

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