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Flat polyps of the colon: accuracy of detection by CT colonography and histologic significance

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Abstract

There is controversy regarding the prevalence, clinical importance, and appropriate screening methods for nonpolypoid (flat and depressed) polyps in the colon. Investigators in Japan have reported higher prevalence of nonpolypoid adenomas in the general population and there have been several reports of higher incidence of high-grade dysplasia in flat adenomas in these Eastern studies. Historically, many Western gastroenterologists have been skeptical of these findings and there have been conflicting studies regarding the prevalence of flat adenomas and incidence of high-grade dysplasia in these lesions. Multiple reasons have been postulated for this apparent difference. Therefore further research into this topic is needed to clarify these issues. In this article we will review the controversy related to the definitions and clinical importance of nonpolypoid neoplasms in the colon, demonstrate the appearance of these unique lesions at CT colonography (CTC) and discuss the accuracy of CTC.

Key words: CT colonography—Colon—Abnormalities—Colon cancer—Flat adenomas—Colon polyps—Colonoscopy

Definition

The initial description of flat adenomas was published by Muto in 1985 [1]. The term "flat" was used to describe elevations less than 1 cm in diameter with a slightly elevated, flat, or depressed surface whose thickness does not exceed twice that of healthy mucosa. The depressed type lesions are felt to be at the greatest risk for having the highest invasive risk into the submucosa or high-grade dysplasia [2–9]. Definitions of flat lesions have been described both histologically and endoscopically.

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Histologic definitions

Several histologic definitions of flat adenomas have been used. The most widely accepted is a nonpolypoid adenoma with a height no more than twice that of the adjoining mucosa. A second definition includes lateral or radial extension of the dysplastic epithelium in the superficial mucosa without vertical extension into the crypt bases. A third definition is an adenoma with a thickness of ≤1.3 mm [1, 8, 10, 11].

Flat depressed and flat elevated lesions have also been differentiated histologically as the dysplastic tissue does not protrude above the mucosal surface in flat depressed lesions, while the dysplastic tissue is no more than twice the thickness of the mucosa in flat elevated lesions [10].

Histologic assessment is needed to classify polyps by the above criteria. However, this is not applicable to colonoscopy or CTC. Therefore macroscopic criteria have also been developed.

Macroscopic definitions

Macroscopic criteria have included a mucosal elevation with a flat or slightly rounded surface and a height of less than half the greatest diameter of the lesion [3, 6, 11]. Most flat lesions have been reported to be less than 2–3 mm in elevation and only very broad lesions 5 mm high [6, 12]. Others have indicated the majority of flat adenomas are ≤1.3 mm in height [13]. They are usually <1 cm in greatest diameter and occasionally will have a central red colored depression associated with the flat top identified endoscopically [10, 14]. Therefore, some authors have recommended that a height of 3 mm should be the limit for defining flat adenomas [15]. However since many of the published studies have used the criteria of a height of less than half the greatest diameter of the lesion, several of these reported lesions may be greater than 3 mm in height.

Because of the various methods in reporting flat lesions, there is a need for a more universal classification [16]. One of these is the Paris classification where colo-

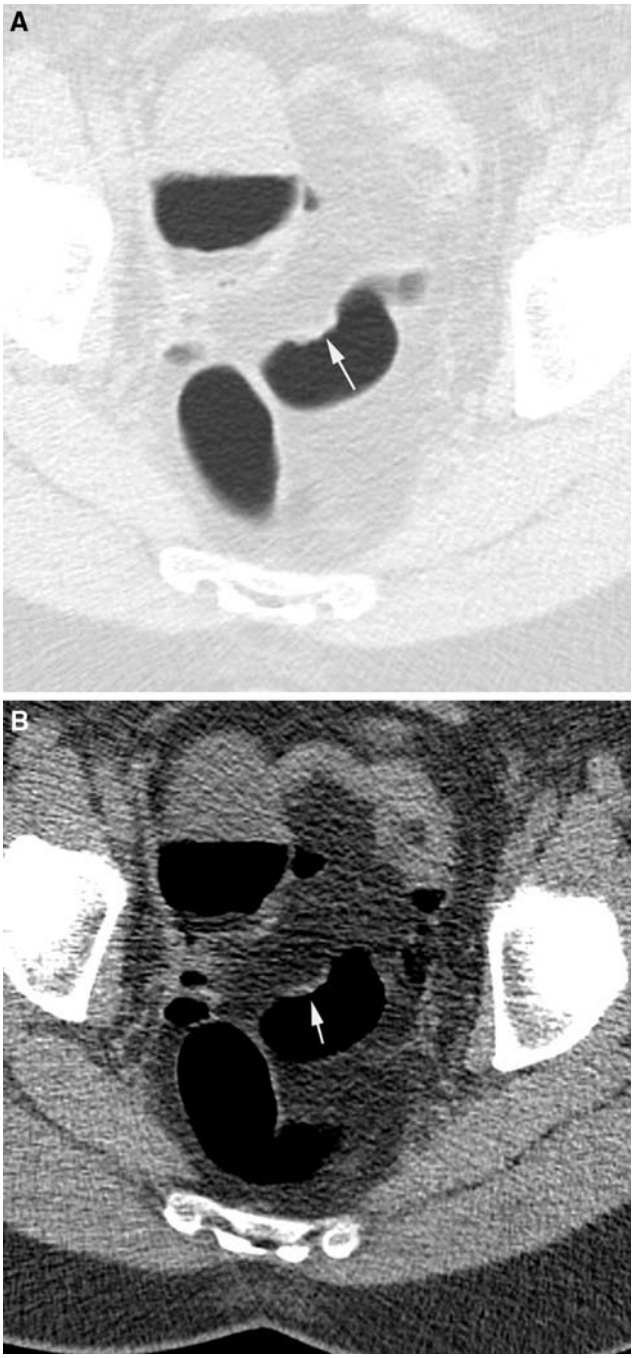

Fig. 1. Unenhanced CTC. (**A**) axial lung and (**B**) soft tissue windows show a 1 cm flat adenoma (*arrow*) in the sigmoid colon located between the folds. A focal bulge into the colon lumen is a key for detection.

rectal neoplasm can be classified into polypoid and nonpolypoid types. The polypoid type consists of the pedunculated and sessile morphology. The nonpolypoid type consists of slightly elevated (IIa), completely flat (IIb), and slightly depressed (IIc) lesions. Many times slightly elevated lesions are classified as flat lesions because completely flat lesions are very rare [16]. The height of the lesion should be compared to the closed cusp of a biopsy forceps that measures 2.5 mm in size. Lesions protruding above this are classified as sessile while those located below are considered flat [16].

Prevalence

Because of the lack of standardization in reporting and variation in techniques utilized the reported prevalence of flat adenomas is highly variable. Some have postulated the variations in prevalence and associations with high-grade dysplasia may be secondary due to a variety of reasons including: endoscopic reporting, endoscopic technique, pathologic reporting, differences in patient groups, and perhaps differences in the disease process secondary to genetic or environmental factors [17, 18].

Flat adenomas have been extensively reported in Japan since originally described by Muto in 1985 with prevalence rates varying from 13% to 48% [2, 12, 17–21].

Initially these lesions were thought to be rare in Western countries; however, there have been recent reports from the United Kingdom, Sweden, Canada, and the United States that have shown these lesions do exist in Western countries [3, 4, 6, 9, 22–26]. Moreover, there has been a wide range (7–55%) in prevalence reported.

The prevalence of polyps limited to only flat (IIb) and slightly depressed (IIc) is much lower and varies between 1.2% and 3% in the Western institutions compared to 2–3% in Japan [18].

The reported location of flat adenomas has also varied with some reporting a preponderance for the right hemicolon [3, 4] while others have reported that they are more likely discovered in the transverse, descending, and sigmoid [13].

Significance

The clinical significance of flat adenomas is that they may be more pathologically advanced with higher incidence of high-grade dysplasia or carcinomas despite their relatively small size. They also may be more difficult to detect given their small size and unique morphology. The incidence of high-grade dysplasia appears to be the greatest in the flat depressed subtype. In addition investigators have proposed that these lesions may be a source of de novo carcinomas that develop in the absence of any precursor adenomatous polyps [5, 7, 27].

Several studies from Eastern countries have reported higher incidence of high-grade dysplasia occurring in flat adenomas [1, 5, 8, 27]. Mitooka et al. found that the rate of severe atypia for diminutive (< 5 mm) flat depressed lesion was 17.9% vs. 1.3% for diminutive polypoid adenomas [8]. Adachi et al. reported that 12% of flat adenomas had severe atypia. Depressed lesions had a 22% rate of severe atypia compared to 9% without depression [5]. Suzuki et al. found that 10% of carcinomas demonstrated flat configuration and varied between

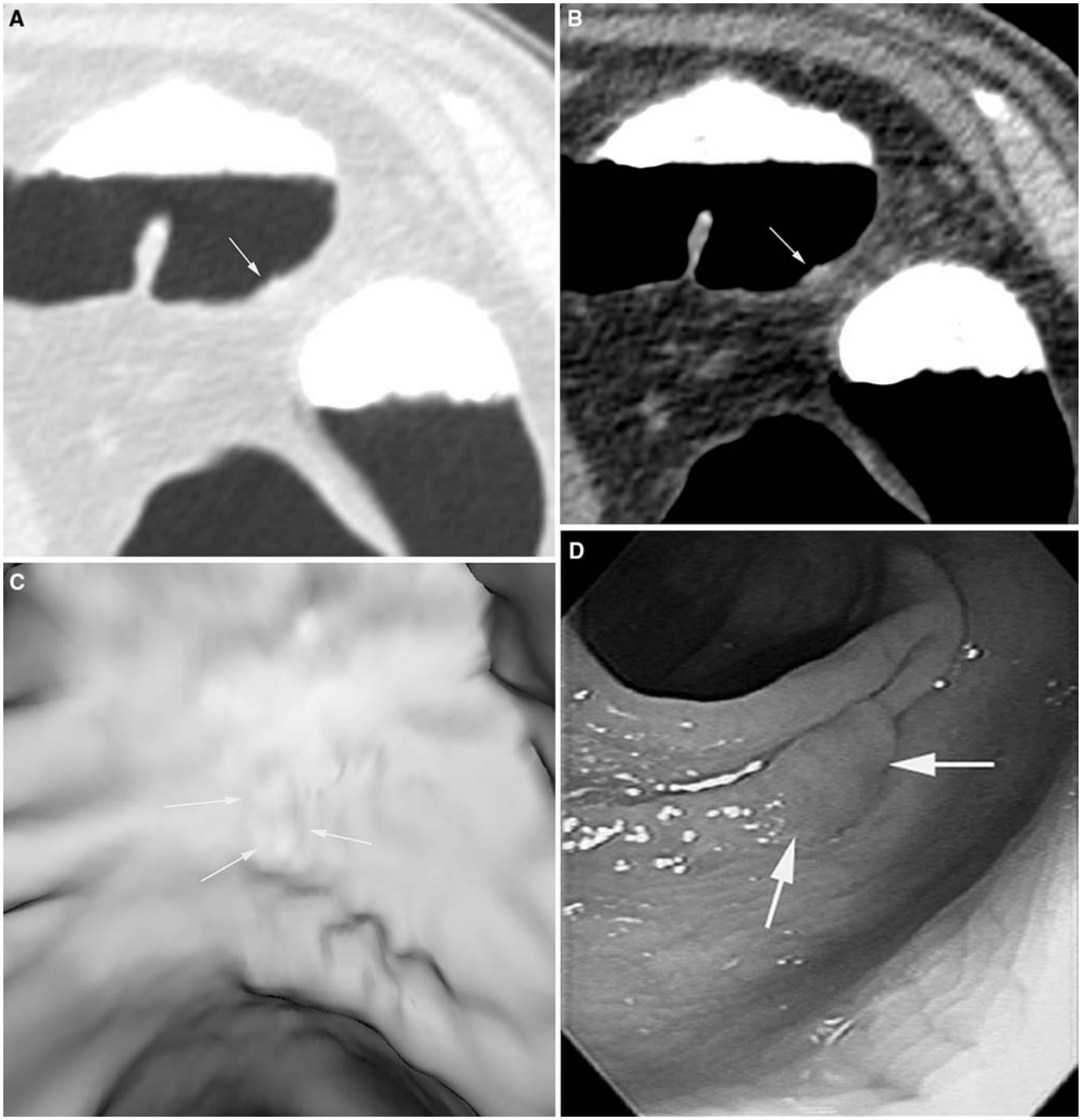

Fig. 2. Unenhanced CTC with tagging. (**A**) axial lung, (**B**) soft tissue, (**C**) 3D endoluminal, and (**D**) conventional colonoscopy show a 7 mm flat adenoma with 2 mm elevation in the transverse colon (*arrow*). In this example the polyp is more conspicuous on the soft tissue than lung window settings due to focal bowel wall thickening. Note the surrounding irregularity on the 3D endoluminal view secondary to residual tagged stool. 2D images need to be viewed with both lung and soft tissue windows.

8 and 15 mm in size (mean 11 mm) [28]. Kudo et al. reported that 10.9% of invasive carcinomas were flat and had invasion of the submucosa even though the size was < 10 mm.

Some Western studies also have shown higher incidence of high-grade dysplasia in flat adenomas. In one study it was found that flat lesions were 10 times more likely to contain severe dysplasia than polypoid lesions (41% vs. 4%). All of the flat polyps were less than or equal to 1 cm [26]. In another study high-grade dysplasia was seen in 18% of flat depressed lesions in contrast to 7.3% of protruding adenomas [9].

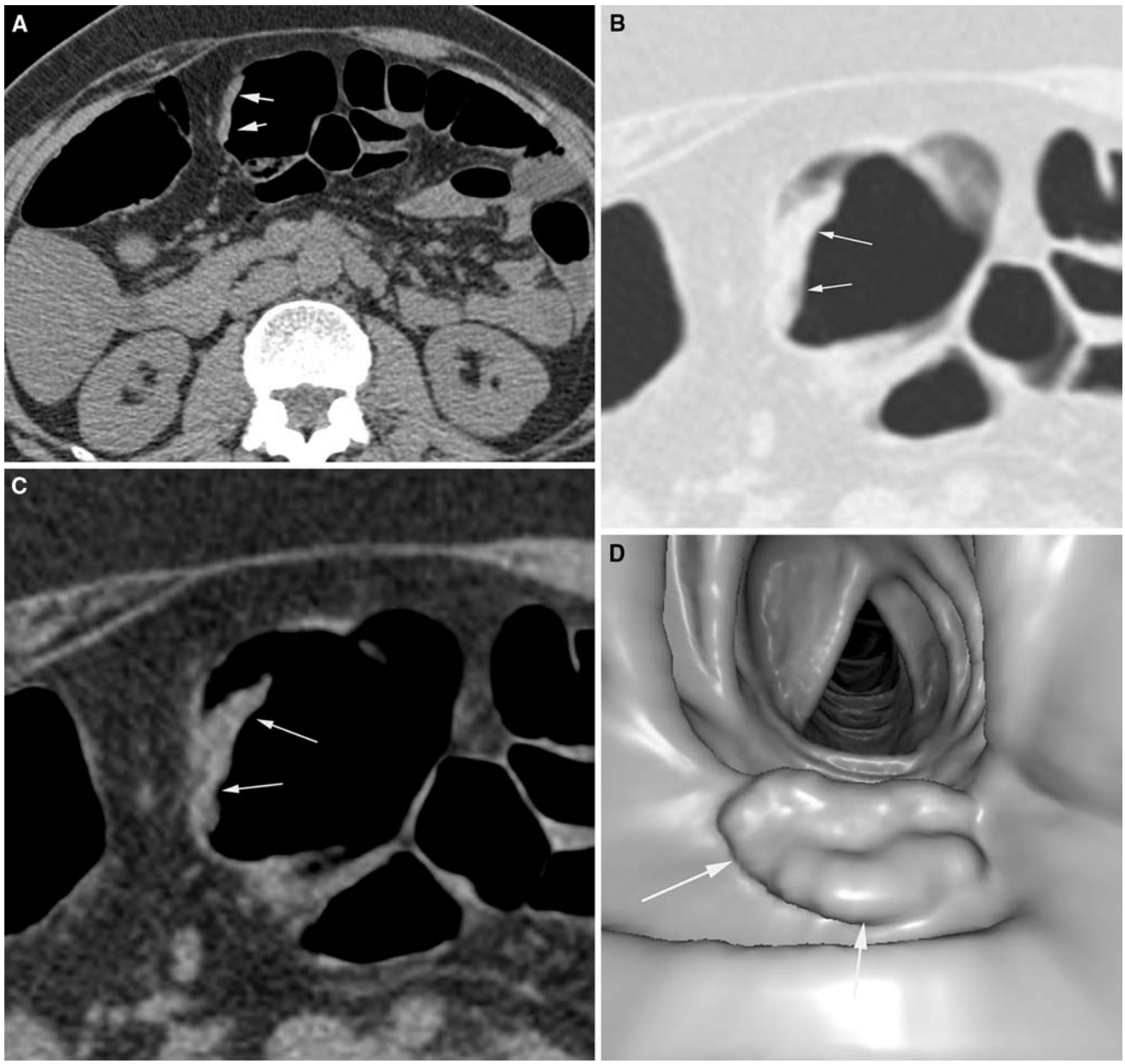

Fig. 3. Unenhanced CTC. (**A**) axial soft tissue, (**B**) oblique axial lung, (**C**) oblique axial soft tissue windows, and (**D**) 3D endoluminal view show a 3 cm flat adenoma with 4 mm elevation in the transverse colon (*arrow*). The polyp is well seen on all images. Adherent stool is usually not as homogeneous in attenuation. Stool tagging can be helpful in discriminating adherent stool from flat polyps.

Hurlstone et al. found high-grade dysplasia in 44.6% of flat adenomas >8 mm in diameter compared to 17% in sessile or pedunculated. However only 10% of flat adenomas <8 mm had high-grade dysplasia [3].

In a study performed in the United States, Saitoh et al. found that flat and depressed lesions were more likely to be adenomatous than polypoid (82% vs. 67%) and contained more invasive cancer (4.5% vs. 0%). The average sizes of the flat and depressed advanced lesions were 10.75 $\pm$ 2.7 mm vs. 20 $\pm$ 2.9 mm for the polypoid lesions [25].

While some Western studies have shown higher incidence of high-grade dysplasia compared to polypoid lesions, other have not. Despite a high prevalence of flat adenomas (55%), Jaramillo et al. found no adenocarcinomas in lesions <1 cm in size. In addition the rate of high-grade dysplasia or cancer was lower than in pedunculated or sessile polyps. However, there was increased high-grade dysplasia in flat lesion with a central depression [4]. Remacken et al. found that lesions smaller than 10 mm in diameter whether flat or polypoid are unlikely to contain early cancer. The risks

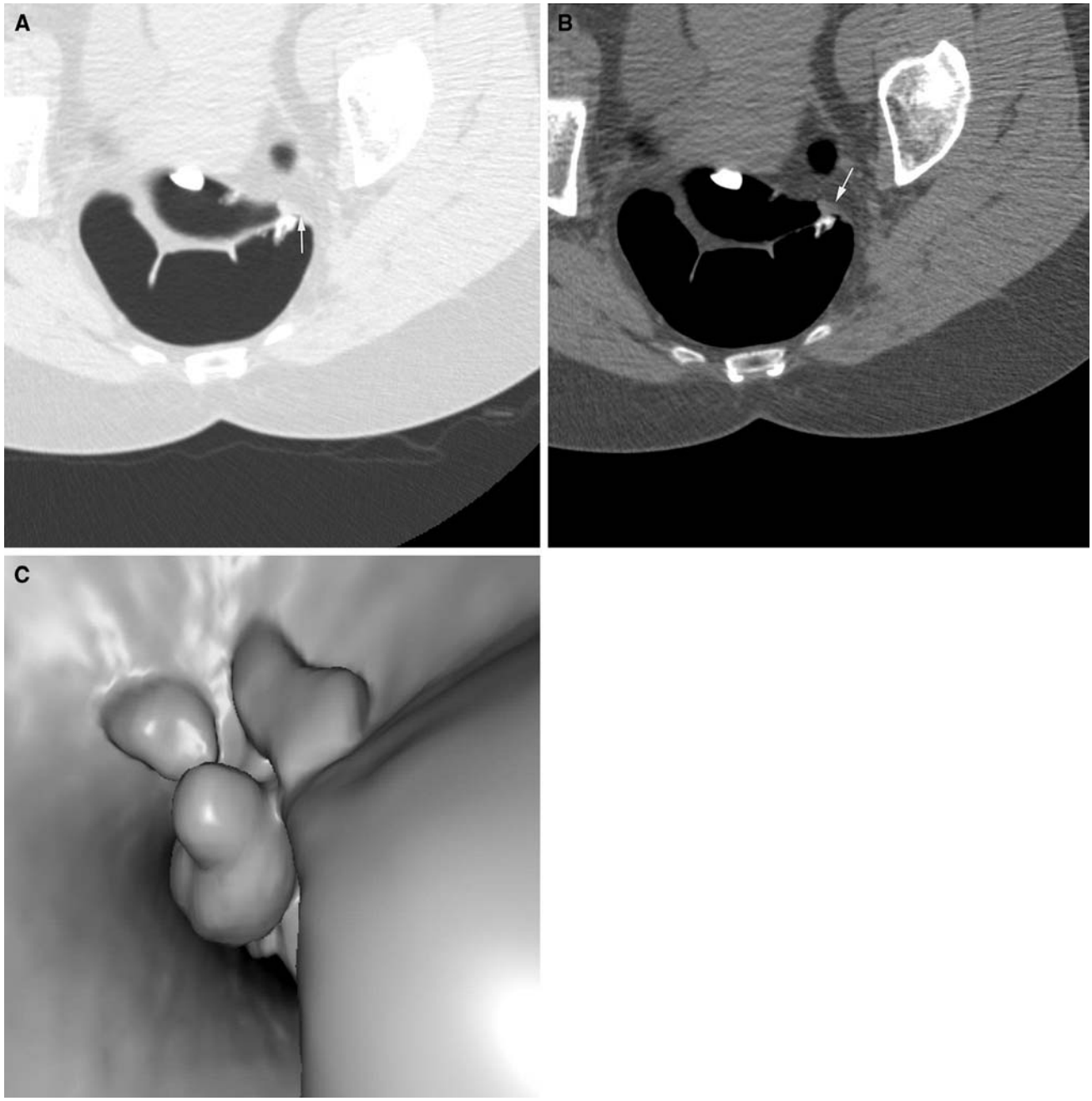

Fig. 4. Unenhanced CTC with oral stool tagging. (**A**) axial lung, (**B**) soft tissue windows and (**C**) 3D endoluminal view of a 2 cm flat adenoma with 5 mm elevation in the sigmoid colon (*arrow*). Note the polyp is covered by barium tagged stool and obscured on the 3D endoluminal view. It is important to assess the bowel wall beneath residual stool tagging.

were 4% in small (<10 mm) flat lesions, 6% in small polyps, 16% in large (≥10 mm) polyps, 29% in large flat lesions, and 75% in all depressed lesions. The average size of the depressed lesions was 9 mm [6]. Between 1980 and 1990 patients were recruited for the National Polyp Study in the United States. At the time of colonoscopy polyps were only described as sessile or pedunculated. The term flat was not used then. Obrien et al. retrospectively reclassified 933 sessile polyps into flat or sessile based on the adenoma thickness criteria discussed previously. Twenty-seven percent of the sessile polyps were reclassified as flat and were no more likely to exhibit high-grade dysplasia than sessile or pedunculated adenomas. The mean size was 0.5 cm for flat adenomas and 0.98 cm for sessile adenomas. High-grade dysplasia occurred in 1.3% of flat adenomas compared to 7.4% of sessile adenomas. In this study larger flat lesions would have been classified as sessile polyps which might have been included in other publications [11].

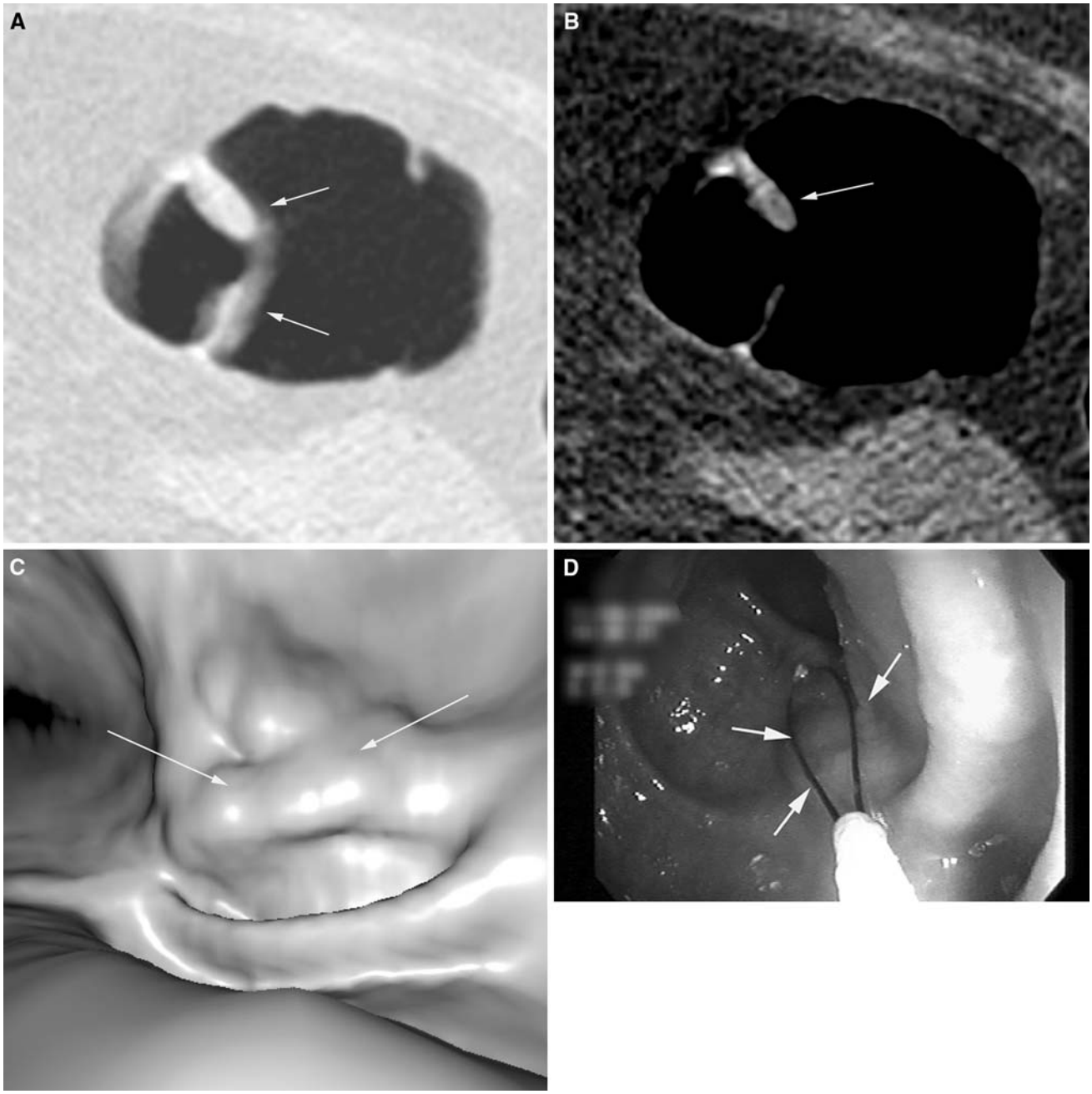

Fig. 5. Unenhanced CTC. (**A**) oblique axial lung, (**B**) soft tissue windows, (**C**) 3D endoluminal view, and (**D**) conventional colonoscopy show a 1.5 cm flat lesion with 3 mm elevation in the transverse colon (*arrow*) located on a fold. In this example the polyp is more conspicuous on the lung than soft tissue windows and is well seen on the 3D endoluminal view. 2D and 3D image displays are complementary.

Some investigators have suggested that the variation in the incidence of high-grade dysplasia in flat lesions between Eastern and Western countries may be secondary to differences in pathologic reporting. In one study the investigators found that high-grade dysplasia may be overreported by Japanese pathologists [18]. In this study there was no significant difference in the frequency of flat lesions between British and Japanese patients; however, Japanese pathologists tended to diagnose higher grades of dysplasia.

There currently is an ongoing multicenter study supported by the American College of Gastroenterology randomizing asymptomatic average-risk patients presenting for screening colonoscopy to either conventional colonoscopy or chromoendoscopy. The neoplasm will be described according to Western and Japanese classifica-

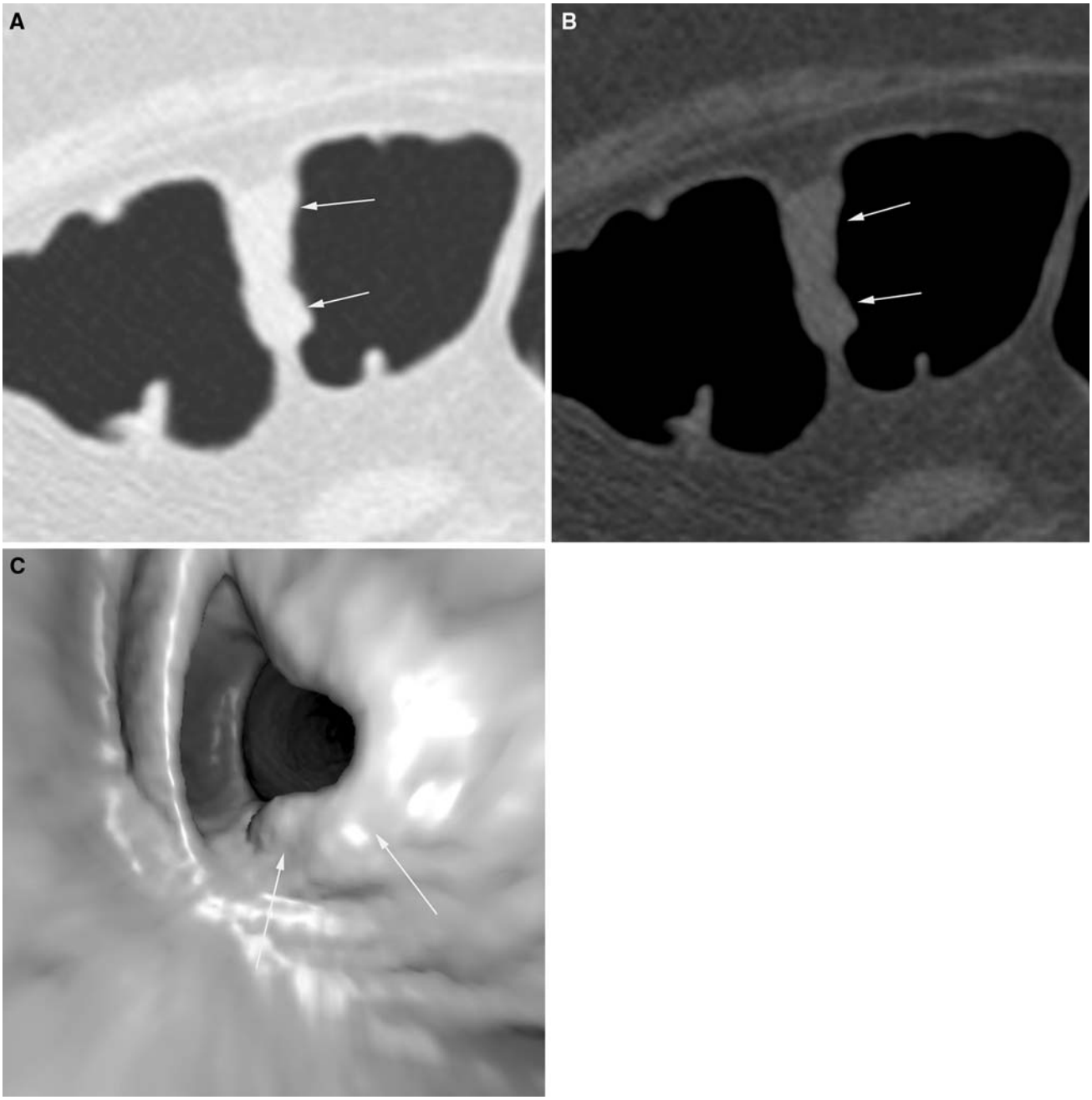

Fig. 6. Unenhanced CTC. (**A**) axial lung, (**B**) soft tissue windows, and (**C**) 3D endoluminal view shows a 1.5 cm flat lesion with 5 mm elevation (*arrow*) on a fold in the transverse colon. Focal fold thickening and surface nodularity are key findings.

tion schemes. This study should provide valuable data on the prevalence of the different types of flat neoplasm in the United States and the incidence of high-grade dysplasia associated with these types.

In summary, the clinical importance of flat adenomas remains unclear. Several studies have shown an increased incidence of high-grade dysplasia in flat (3–20%) and especially depressed lesion compared to the polypoid type [16]. However the natural progression of these lesions is unknown [16] and the size at which there is an increased association with malignancy is controversial given that some investigators have found malignancy only with larger lesions. The percent of flat lesions with submucosal invasive carcinoma has ranged from 0–2.75% to 0–6.7% for depressed types [16].

Screening techniques

Because flat adenomas especially the nonelevated lesions can be difficult to detect by conventional colonoscopy techniques, investigators in Japan have developed a more sensitive technique, chromoendoscopy. Chromoendoscopy

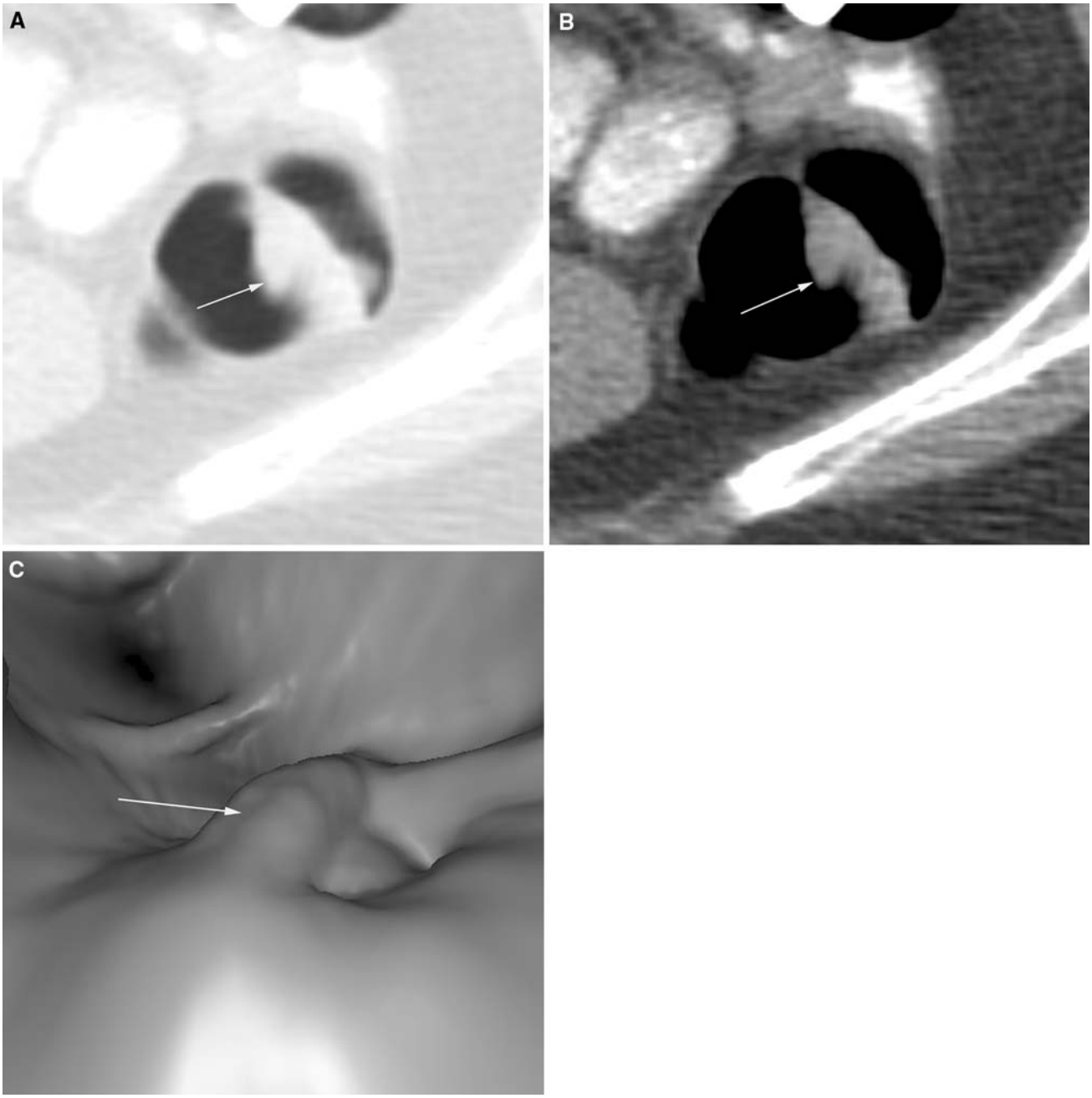

Fig. 7. Unenhanced CTC. (**A**) oblique axial lung, (**B**) soft tissue windows, and (**C**) 3D endoluminal view shows a 1.5 cm flat adenoma with 3 mm elevation on a fold in the descending colon (*arrow*). These lesions can be difficult to discriminate from normal polypoid folds. Optimal distension makes this decision easier.

is a technique in which a dye, most commonly indigo carmine, is sprayed on the mucosal surface of the colon. Spraying the lesion accentuates the contours and margins of the lesion and highlights the pit pattern of the crypts of Lieberkuhn [10]. Magnified views of the colon are then obtained by colonoscopy. This technique has been shown to detect more diminutive adenomas and flat adenomas [3].

Historically chromoendoscopy has not been widely used in the Western hemisphere because many gastroenterologists feel flat adenomas with high-grade dysplasia are rare in these countries. On the other hand some investigators have suggested that not using this technique decreases the ability to detect these lesions and this is one of the reasons why the prevalence in the western countries has been reported as lower. Chromoendoscopy is also technically more difficult with a long learning curve and increased examination time [29].

Because of the perceived technical difficulties other colonoscopy techniques have been developed. One of these is narrow band imaging (NBI). NBI uses optical

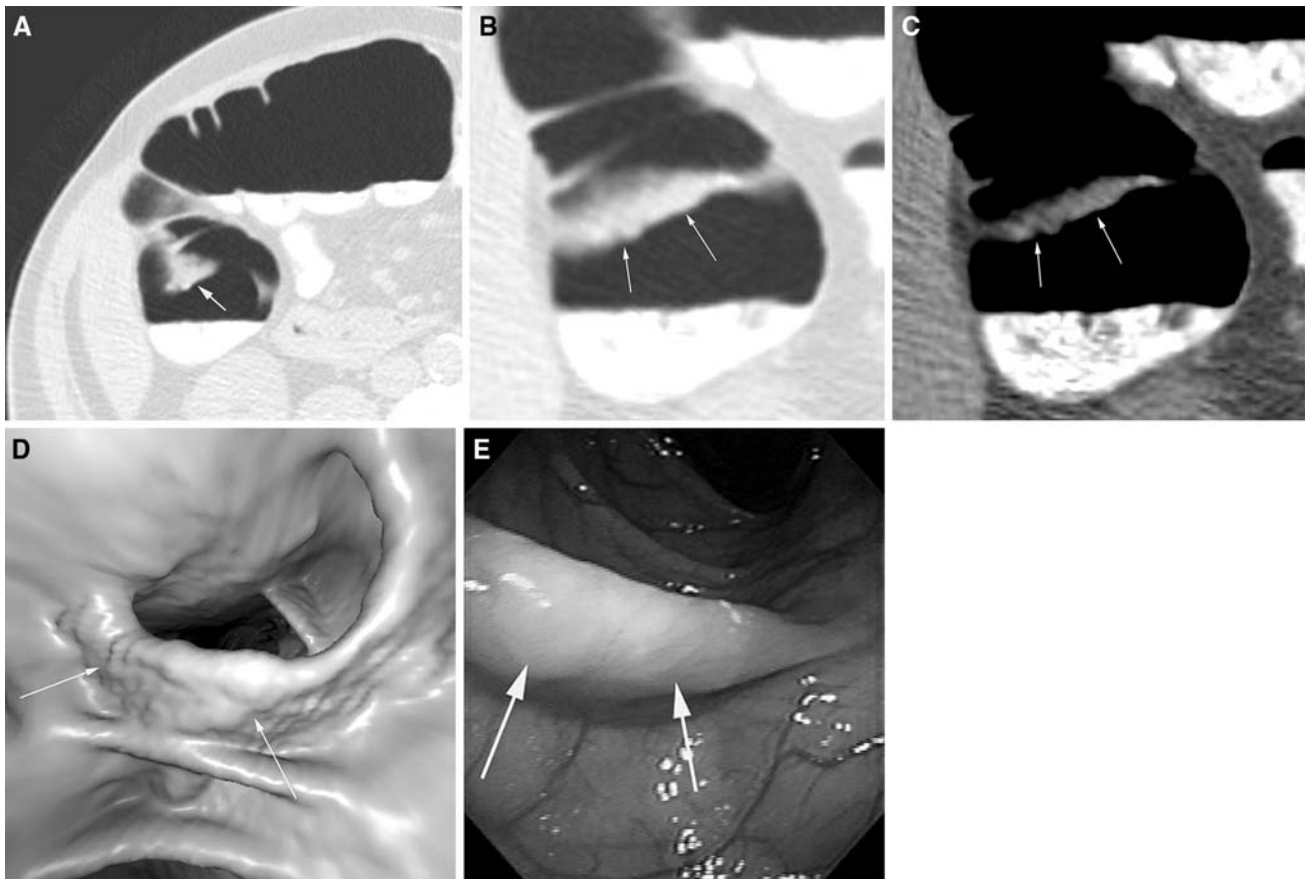

Fig. 8. Unenhanced CTC with oral stool tagging. (**A**) axial lung, (**B**) oblique axial lung, (**C**) oblique axial soft tissue windows, (**D**) 3D endoluminal view, and (**E**) conventional colonoscopy show a 2.3 cm flat adenoma with 3 mm elevation on a fold in the ascending colon (*arrow*). In this case the fold irregularity is subtle on the true axial images but well seen on the 3D endoluminal view. A well-cleansed colon is critical for detection of these lesions, as adherent stool can appear similar.

filters for RGB sequential illumination and narrows the bandwidth of spectral transmittance [30, 31]. By using the blue band which can be combined with HDTV technology there is increased contrast of the superficial colonic surface and the pit pattern. Several studies have shown that this technique may be comparable to chromoendoscopy without the need for dye staining and superior to conventional colonoscopy. NBI may be able to show early mucosal changes such as microcapillaries that may help differentiate hyperplastic polyps from adenomas or early carcinomas [30–34]. NBI can be switched on and off quickly from conventional white light colonoscopy.

CTC appearance

Imaging appearance

As the name implies these lesions typically have a flat appearance at CTC. When these lesions occur between folds, they typically appear as a flat elevation or focal area of wall thickening that protrude into the lumen (Figs. 1–4).

In our experience flat lesions that occur on folds or at the base of folds can be more difficult to detect. When these arise on folds they can lead to the appearance of fold thickening. Lesions that cause irregular fold thickening are more conspicuous than those causing smooth thickening. Higher resolution imaging may aid in identifying this irregularity. Three-dimensional endoluminal views may also be helpful in showing the fold irregularity (Figs. 5–11).

Occasionally flat lesions may arise from a fold and have a short attachment with a large portion of the polyp extending into the lumen. In this setting the polyp may have a ''cigar-like'' appearance [35] (Fig. 12).

In our experience, 2D (soft tissue and lung) and 3D endoluminal views are complementary as some lesions may be more conspicuous on one image display.

Results

There is a paucity of data reporting the results of CTC for detection of flat polyps in the colon. The majority of studies have used a subjective macroscopic classification

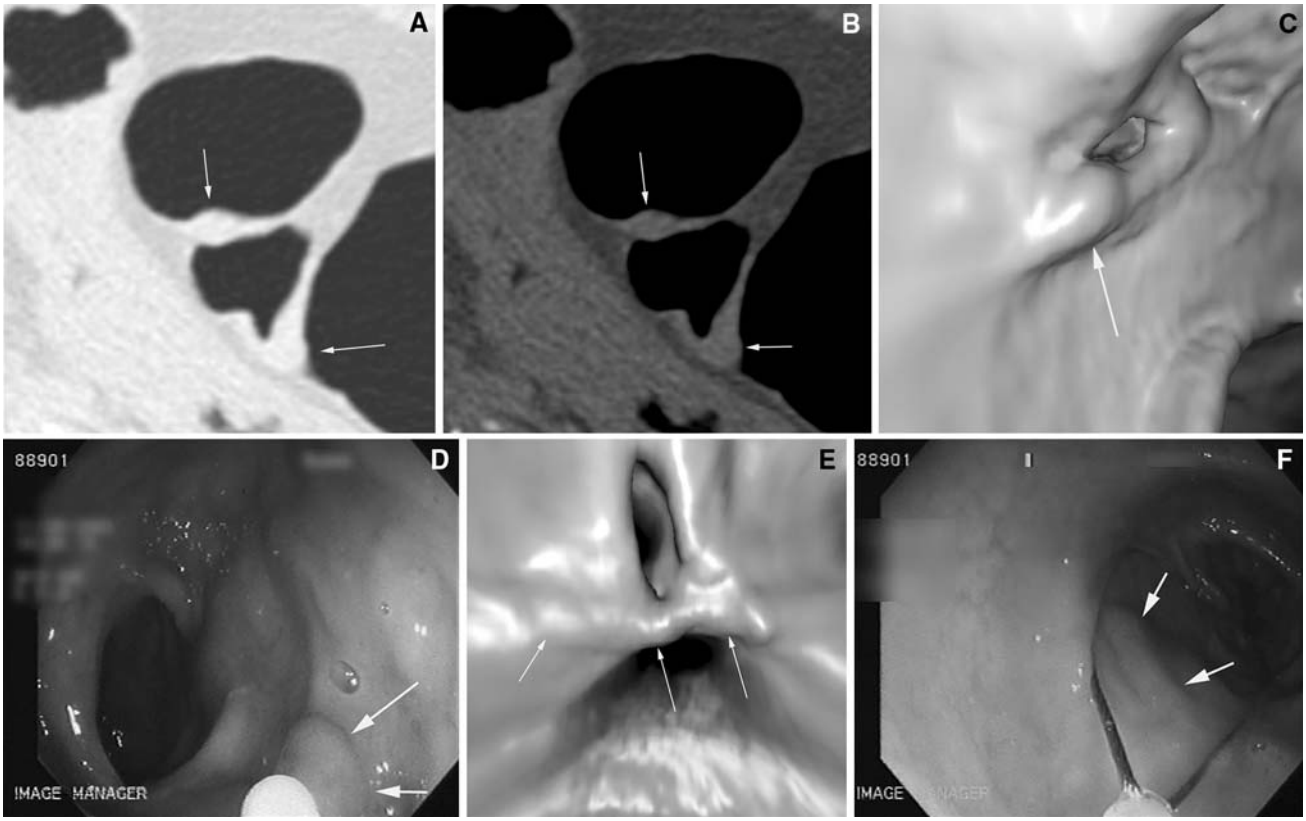

Fig. 9. Unenhanced CTC. (**A**) axial lung and (**B**) soft tissue windows show two flat lesions with 4 and 5 mm elevation in the distal transverse colon (*arrows*). The smaller lesion is seen on the 3D endoluminal view (**C**) and conventional colonoscopy (**D**). The larger lesion is a c-shaped lesion along the base of a fold seen on 3D endoluminal view (**E**) and conventional colonoscopy (**F**). These lesions could be easily mistaken as bulbous folds. These difficult-to-detect lesions require optimal spatial resolution, and a well-cleansed and distended colon.

based on conventional colonoscopy (not high-magnification chromoendoscopy), CTC, or both. It is difficult to compare these studies because of lack of uniformity in distinguishing adenomatous from hyperplastic polyps and in standardized reporting of the height of the polyps. In addition, the lesions that are reported most likely represent lesions that would be classified as superficially elevated.

One of the first reports described the results of a primary 2D interpretation technique in detecting flat lesions from a cohort of two groups of study patients, one a polyp-enriched population and the other a high-risk screening population. Therefore, this was not a true screening population. In this study there was a low prevalence of flat lesions occurring in only 19/547 (3.5%) of patients. Of note the majority of the 22 flat polyps were hyperplastic (n = 14) and only eight were adenomatous. Sensitivity for detection of flat adenomas (≥4 mm) by three reviewers as 100%, 100%, and 13%, respectively. These results were encouraging especially in view of the spatial resolution (5 mm slice thickness), suboptimal bowel distension, and lack of stool and fluid tagging compared to state-of-the-art techniques used today [35].

Pickhardt et al. reported their results from a large screening study of 1233 patients using a primary 3D interpretation approach with stool and fluid tagging. The prevalence of flat lesions in their patient population was 4.2%. Only 29/59 (49.2%) of the flat lesions were adenomatous. CTC detected 24/29 (82.8%) of the flat adenomas ≥6 mm in size. Five flat lesions (8.5%) were missed by conventional colonoscopy [36].

In both the above studies, the sensitivity for all flat lesions including hyperplastic polyps was less than for adenomas alone. This is not surprising given that hyperplastic polyps have been shown to efface or disappear with increasing bowel distension [37, 38]. The most important clinical issue is the detection of adenomas.

Gluecker et al. characterized the types of lesions missed on a study of 500 asymptomatic high-risk patients using a primary 2D search pattern, 5 mm slice thickness, and no stool or fluid tagging. Out of the 500 patients 77 (15.4%) had a total of 116 polyps 5 mm or larger and 17% of the polyps were flat in morphology. Only 6/10 (60%) of the polyps 1 cm or greater with flat morphology at colonoscopy were detected prospectively and 3/9

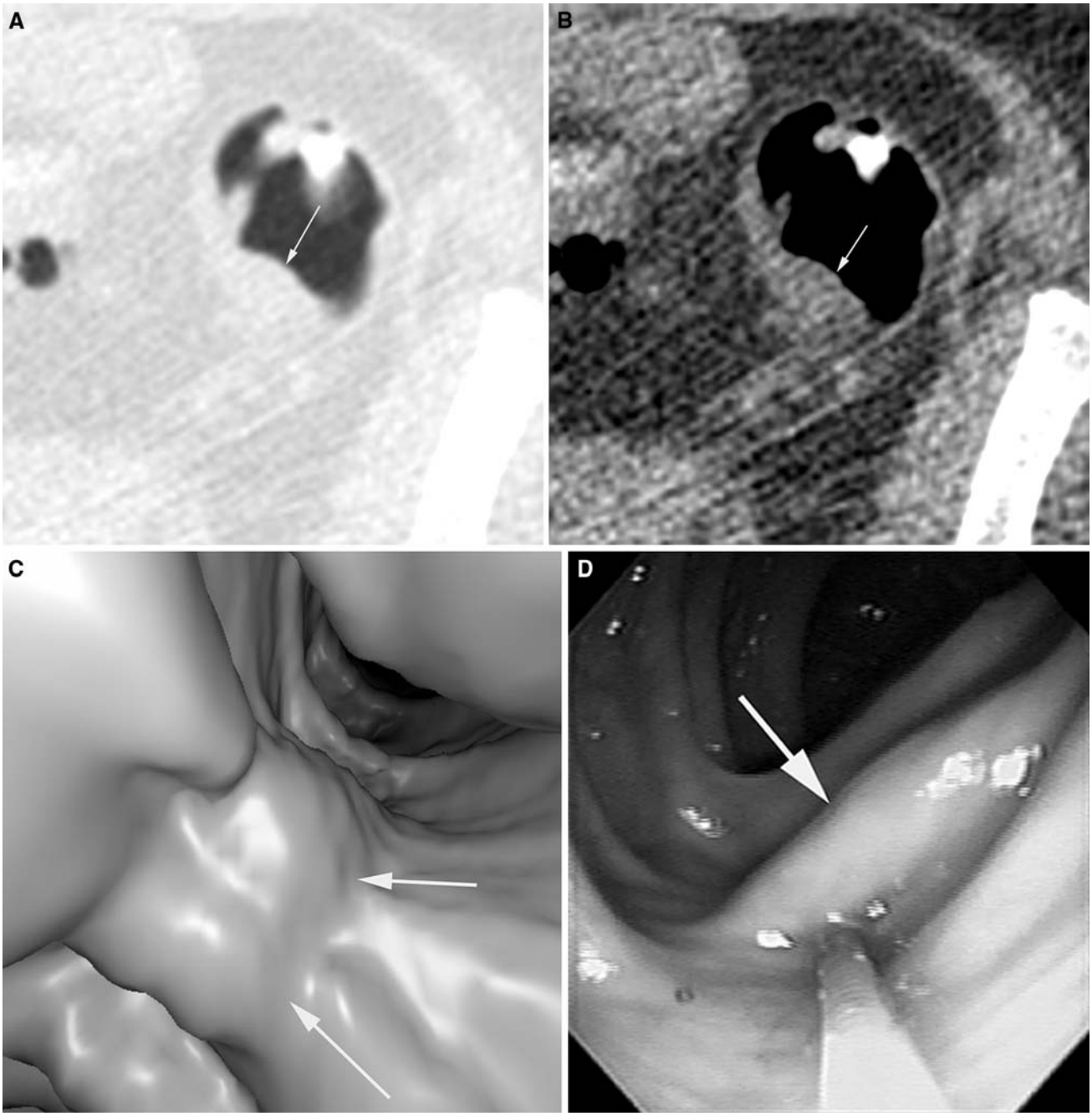

Fig. 10. Unenhanced CTC with oral stool tagging. (**A**) oblique axial lung, (**B**) soft tissue windows, (**C**) 3D endoluminal view, and (**D**) conventional colonoscopy show a flat adenoma (*arrow*) in the sigmoid colon at the base of the confluence of two folds. This lesion is more conspicuous on the soft tissue than lung windows and is well seen on the 3D endoluminal view. The colon is suboptimally distended. Improved distension may have made detection easier.

(30%) of the 5–9 mm flat lesions were seen. Only 25% of the large flat lesions that were missed prospectively could be seen retrospectively. This study did not make any distinction between adenomatous and hyperplastic polyps. The authors concluded that flat lesions were more likely to be missed than sessile or pedunculated. A limitation of this study was the relatively wider slice thickness that limited spatial resolution [39].

Thomeer et al. reported their experience at CTC in detecting flat lesions in a study of 150 patients with various indications using a primary 2D search technique and iodinated contrast for stool and fluid tagging. Five flat lesions were present in the size range 8–25 mm, all with heights not exceeding 2–3 mm. One flat lesion measuring 25 mm × 2 mm in height could not be seen prospectively or retrospectively. Both reviewer saw three

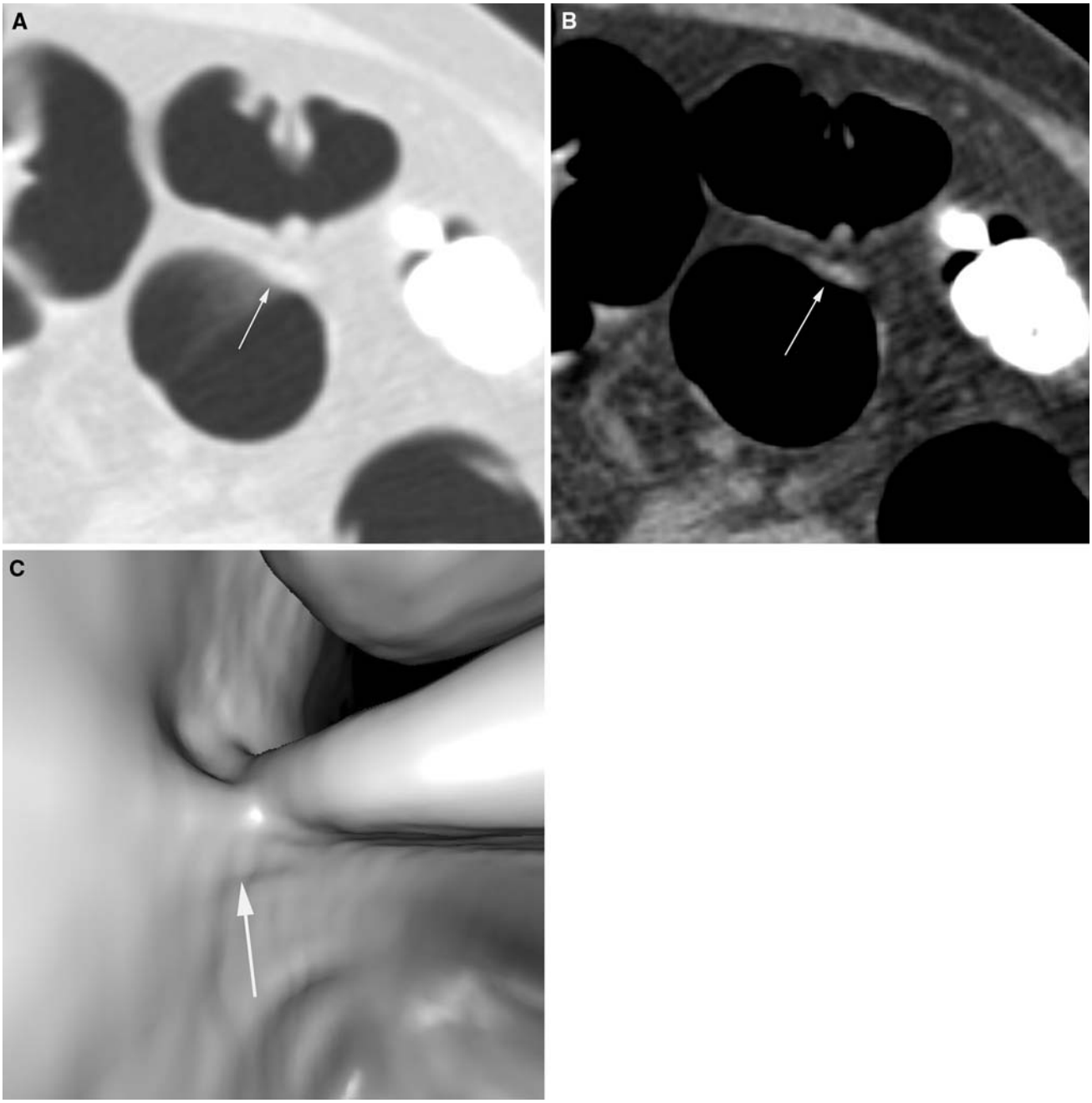

Fig. 11. Unenhanced CTC with oral stool tagging. (**A**) axial lung, (**B**) soft tissue windows, and (**C**) 3D endoluminal view show a small flat adenoma with only 2 mm of width in the sigmoid colon (*arrows*). This lesion is best seen on the soft tissue windows as a focal region of bowel wall thickening and is difficult to see on both the lung and 3D endoluminal views. Note how there is very minimal extension into the lumen and at least half of the lesion is located within the wall.

of the other four flat lesions prospectively. The fourth flat lesion was seen prospectively by one reviewer and retrospectively by the second. Also in this study there was no distinction between adenomas and hyperplastic polyps [40].

In a small study of 10 patients with 18 flat polyps, Park et al. described their experience at CTC in detecting flat lesions and correlated the detection of polyps to the height of the lesion which was not specifically reported in other studies. The authors' technique included scans performed on 16-MDCT with 1 mm slice thickness, IV contrast administration, and a primary 2D search technique. The authors detected less than 50% of the lesions and determined that lesions must be 2 mm or greater in height and ≥7 mm in diameter before they could be visualized. When evaluating the specific histology of

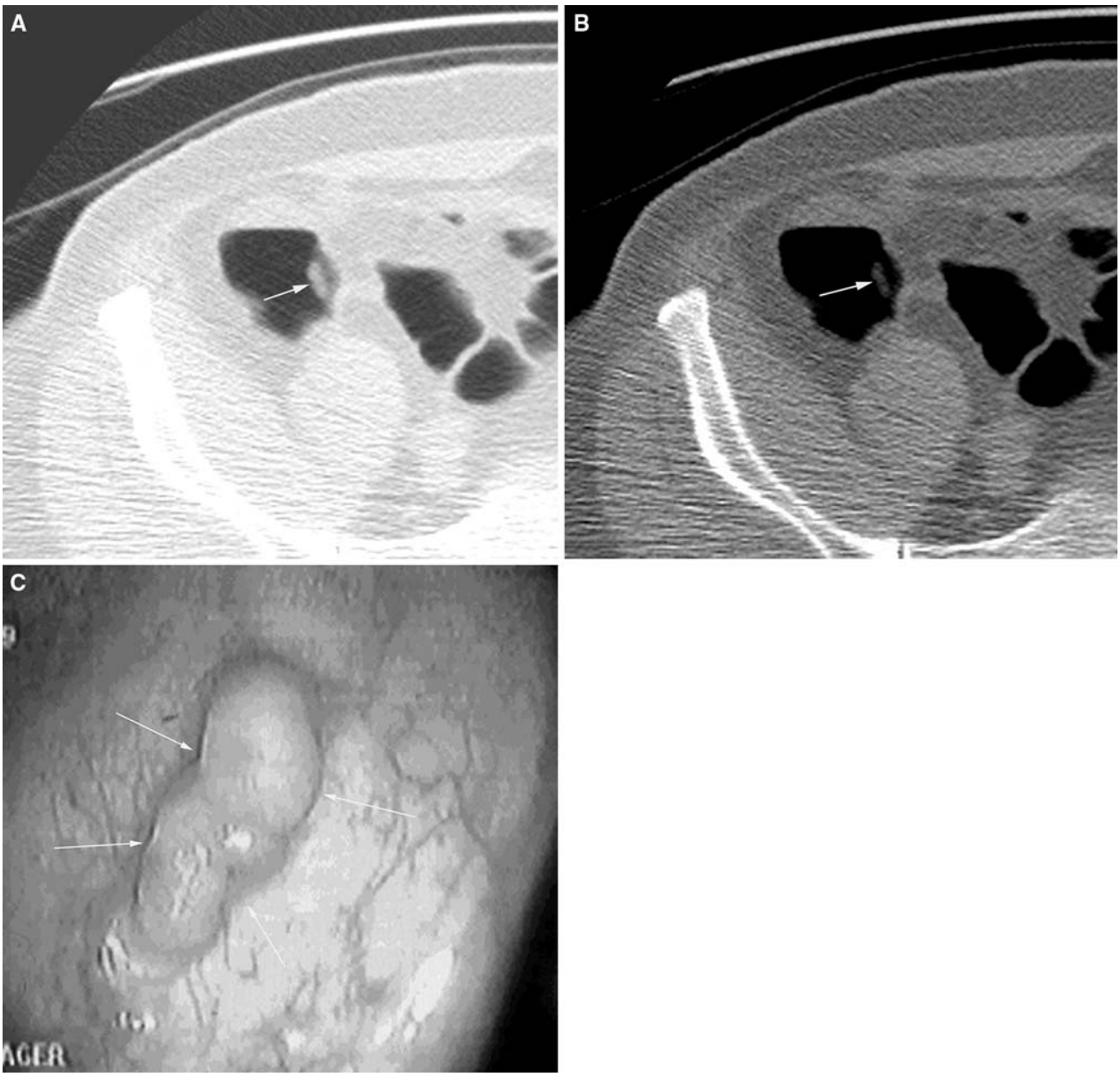

Fig. 12. Unenhanced CTC. (**A**) axial lung, (**B**) soft tissue window, and (**C**) conventional colonoscopy show a 1 cm flat adenoma in the cecum (arrow). Note this has a "cigar-like" appearance.

these lesions, 2/9 adenomas, 2/2 adenocarcinomas, and 0/1 adenocarcinoma in situ were detected. Of the 14 lesions that were missed, one was a hyperplastic polyp and six were in colon segments with excess fluid, poor preparation, or poor distension [41].

In another study these same authors reported that flat lesions may be a main cause of missed lesions at CTC. In a study of 56 patients, three flat lesions were detected at colonoscopy including a 16×3 mm invasive adenocarcinoma, 13×1 mm tubular adenoma with foci of adenocarcinoma, and a 12×3 tubular adenoma. All three of the lesions were missed prospectively; however, two could be seen in retrospect and showed moderate enhancement following IV contrast. These two lesions were felt to be adherent stool on the prospective interpretation. The 13×1 mm lesion could not be seen in retrospect [42].

All these studies emphasize the need for exquisite CTC technique and adequate education in order to recognize these lesions. Stool and fluid tagging or alternatively IV contrast should help in differentiation of flat polyps from adherent stool, and allow visualization in colonic segments where the polyp may be submerged by fluid. Suboptimal colonic distension may

lead to mucosal and fold irregularities that may obscure the detection of flat lesions. When located on folds flat lesions can lead to thickening and irregularity of the fold which can be mimicked by poor colonic distension.

There is uncertainty as to which interpretation technique is superior; however, it is likely that a combination of both 2D and 3D techniques will lead to the greatest sensitivity. 2D interpretation techniques should include both lung and soft tissue or colon window settings to improve conspicuity [35, 41].

In summary, CTC can detect flat adenomas in the colon; however, flat polyps (superficially elevated) can potentially be difficult to detect when there is only 1–2 mm elevation. Suboptimal spatial resolution, colonic cleansing, and distension can also contribute to detection failures. Training is also essential, as these lesions appear different than sessile or pedunculated polyps. For lesions with more mucosal elevation, CTC has been shown to have good sensitivity especially for the adenomatous lesions. Given the controversy and uncertainty of the prevalence of these lesions and the lack of specific diagnostic criteria used in various studies, it is difficult to state what the true sensitivity of CTC is. It will be able to state this with certainty only when there are well-controlled prospective studies using both state-of-the-art colonoscopy and CTC techniques in true screening populations. In addition, better correlation is needed with the lesions classified as truly flat (IIb) or slightly depressed (IIc). Given that colonoscopy requires high-resolution techniques with dye spraying or NBI to detect subtle underlying vascular changes, it is likely that CTC will not be able to detect some of these lesions. One could hypothesize that because depressed lesions may grow more into the colonic wall than protrude into the lumen and may have more dysplasia or even harbor early carcinoma, these lesions may appear as focal areas of soft tissue thickening in the wall. In this scenario, the 2D images may be more useful in identifying these areas of soft tissue thickening in the wall (Fig. 11). However, prospective studies will need to be performed to determine if this theory is correct.

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