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# CT Colonography: External Clinical Validation of an Algorithm for Computer-assisted Prone and Supine Registration<sup>1</sup>

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## Purpose:

To perform external validation of a computer-assisted registration algorithm for prone and supine computed tomographic (CT) colonography and to compare the results with those of an existing centerline method.

## Materials and Methods:

All contributing centers had institutional review board approval; participants provided informed consent. A validation sample of CT colonographic examinations of 51 patients with 68 polyps (6–55 mm) was selected from a publicly available, HIPAA compliant, anonymized archive. No patients were excluded because of poor preparation or inadequate distension. Corresponding prone and supine polyp coordinates were recorded, and endoluminal surfaces were registered automatically by using a computer algorithm. Two observers independently scored three-dimensional endoluminal polyp registration success. Results were compared with those obtained by using the normalized distance along the colonic centerline (NDACC) method. Pairwise Wilcoxon signed rank tests were used to compare gross registration error and McNemar tests were used to compare polyp conspicuity.

## Results:

Registration was possible in all 51 patients, and 136 paired polyp coordinates were generated (68 polyps) to test the algorithm. Overall mean three-dimensional polyp registration error (mean  $\pm$  standard deviation, 19.9 mm  $\pm$  20.4) was significantly less than that for the NDACC method (mean, 27.4 mm  $\pm$  15.1;  $P = .001$ ). Accuracy was unaffected by colonic segment ( $P = .76$ ) or luminal collapse ( $P = .066$ ). During endoluminal review by two observers (272 matching tasks, 68 polyps, prone to supine and supine to prone coordinates), 223 (82%) polyp matches were visible (120° field of view) compared with just 129 (47%) when the NDACC method was used ( $P < .001$ ). By using multiplanar visualization, 48 (70%) polyps were visible after scrolling  $\pm$  15 mm in any multiplanar axis compared with 16 (24%) for NDACC ( $P < .001$ ).

## Conclusion:

Computer-assisted registration is more accurate than the NDACC method for mapping the endoluminal surface and matching the location of polyps in corresponding prone and supine CT colonographic acquisitions.

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interpretation of CT colonographic studies is difficult and time consuming, even for experienced readers (1) and perceptual error accounts for most missed lesions (2). Retained residue or anatomic structures can simulate polyps, and luminal collapse may also impair visualization. To overcome this, prone and supine images are acquired routinely (3,4); the redistribution of gas and residue reveals abnormalities that were previously inconspicuous. Moreover, potential polyps identified in one acquisition dataset are more likely true-positive if present in a corresponding position in the opposing dataset; unlike residue, mural polyps remain relatively fixed (5). Therefore, matching corresponding endoluminal locations in prone and supine acquisitions is central to

### Advances in Knowledge

- A two-step registration algorithm comprising haustral fold-based initialization followed by nonrigid registration of cylindrical colonic representations provided clinically useful matching of the endoluminal surface between acquisitions, with a mean  $\pm$  standard deviation polyp registration error of  $19.9 \text{ mm} \pm 20.4$ .
- By using an endoluminal display, our method generated 223 of 272 (82%) successful polyp matches according to predefined criteria; likewise, by using a multiplanar approach, 48 of 68 (70%) polyp-matching tasks were successful.
- Our algorithm compared favorably with the normalized distance along the colonic centerline method, which produced a greater mean polyp registration error of  $27.4 \text{ mm} \pm 15.1$ ;  $P = .001$ ; moreover, observer-graded polyp conspicuity was significantly lower when the normalized distance along the colonic centerline method was used, with 129 (47%) successful polyp matches at endoluminal ( $P < .001$ ) and 16 (24%) at multiplanar review ( $P < .001$ ).

competent interpretation (6). Unfortunately, the colon undergoes considerable deformation during repositioning (7), which complicates matching, prolongs interpretation, and induces error.

By using software algorithms, investigators have attempted to provide corresponding endoluminal locations between prone and supine acquisitions (8–16) by registering equivalent distances along the colonic centerline (8–11,13,14,17). However, these methods can only provide a one-dimensional endoluminal location from which to search rather than specify a discrete three-dimensional (3D) point on the mural surface. Nevertheless, centerline registration is reasonably accurate for matching endoluminal locations (8–11,13,14,17), and is incorporated in some vendor workstations (18). Fluid residue and luminal collapse affect the accuracy of centerline algorithms (9), yet patient selection criteria are often reported incompletely in research studies (8,9,14–17). Restricting validation to patients with optimal CT colonographic datasets does not represent the reality of clinical practice, where approximately 50% of patients are poorly prepared (19). Also, to enhance generalizability of results, validation should include data from centers that have not contributed to algorithm development (external validation) (20,21).

We have developed software that registers prone and supine endoluminal surfaces. The initialization step (22) compares patterns of neighboring haustral folds to establish landmark-based correspondence, and 3D spatial correspondence is achieved by mapping the endoluminal surfaces to cylindrical representations followed by nonrigid registration (23). Although technical feasibility with optimized cases has

been demonstrated (22,23), clinical validation of examinations of patients that are more representative of common practice situations is required. We aimed to perform external validation of a computer-assisted registration algorithm for prone and supine CT colonography and to compare this to an existing centerline method (24).

### Materials and Methods

All centers had local institutional review board approval and contributed anonymized cases to protect patient privacy according to Health Insurance Portability and Accountability Act regulations. All participants provided signed informed consent. The authors' local research ethics committee approved the study. S.H., S.A.T., J.R.M., and G.G.S. were previously research consultants for or employees of Medicsight (Hammersmith, London, England), who provided software implementation guidance to H.R.R., T.E.H., and D.J.H. during prior algorithm development and provided reading software for our study. D.J.B. and E.H. had control of data inclusion and had no prior or current affiliation with Medicsight.

### Patient Characteristics and Selection

Patient data were obtained from the National CT Colonography Trial of the

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#### Abbreviations:

ACRIN = American College of Radiology Imaging Network

NDACC = normalized distance along the colonic centerline

3D = three-dimensional

#### Author contributions:

Guarantor of integrity of entire study, S.H.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, D.J.B., S.H., H.R.R., T.E.H., S.A.T., D.J.H.; clinical studies, D.J.B., G.G.S.; experimental studies, D.J.B., H.R.R., T.E.H., E.H., G.G.S., J.M., M.H., D.J.H.; statistical analysis, D.J.B., S.H., H.R.R., D.J.H.; and manuscript editing, D.J.B., S.H., H.R.R., T.E.H., G.G.S., J.R.M., S.P., S.A.T., D.J.H.

Conflicts of interest are listed at the end of this article.

American College of Radiology Imaging Network (ACRIN, 6664) (25) by searching the National Biomedical Imaging Archive (<https://imaging.nci.nih.gov/ncia/>) of the National Cancer Institute. These data had not been used to develop our registration algorithm. The trial protocol was described previously (<http://www.acrin.org/TabID/151/Default.aspx>). Asymptomatic adults ( $n = 2604$ ) scheduled for colonoscopy were recruited from 15 centers in the United States (25). All patients underwent CT colonography after catharsis, carbon dioxide insufflation, and fecal tagging followed by same-day colonoscopy. The archive comprises 825 CT examinations randomly selected from the trial (CT colonography collection at the Cancer Imaging Archive: <http://cancerimagingarchive.net/>). Of these, 35 had at least one polyp greater than or equal to 10 mm. A further 68 had one or more polyps that measured 6–9 mm (one case appears twice in the online archive). Reference data (diameter, segment, axial section) were available for 62 patients (29 in which the largest polyp measured 10 mm or more and 33 in which the largest polyp measured 6–9 mm) (<https://wiki.cancerimagingarchive.net/x/DQE2>).

Datasets were downloaded and transferred to a CT colonographic workstation (MedicRead 3.0; MedicSight). For each study, a radiologist (D.J.B., with experience of more than 500 endoscopically validated CT colonographic cases), recorded a subjective impression of distension and residue (Table E1 [online]) to assess generalizability of our sample with the scoring system used for the ACRIN CT colonography database (19). Patients were considered poorly prepared if one or more colonic segments were filled with residual fluid by greater than 50%, and collapsed if one or more regions of complete luminal occlusion were present in either acquisition (26). D.J.B. used the external reference data to locate polyps in datasets from prone and supine acquisitions, first navigating to the segmental location and then to the axial locations provided on an

**Table 1****Patient and Polyp Selection Criteria**

Patient and Polyp Selection Criteria	Polyp Size		Total
	6–9 mm	$\geq 10$ mm	
Patients available	68	35	103
Patient exclusion criteria			
External reference data missing or inconsistent	35	6	41
Incomplete CT colonographic dataset	2	1	3
Patients included	26	25	51
Additional polyps			
In patients whose largest polyp was 6–9 mm	11	3	14
In patients whose largest polyp was $\geq 10$ mm	0	3	3
Polyp exclusion criteria			
Concealed by untagged residue	3	2	5
Concealed by luminal collapse	2	1	3
Polyps included	37	31	68

accompanying database spreadsheet. If no polyp was present, the search was repeated after subtraction of the axial location from the total number of axial sections (to account for inconsistencies in axial numbering between vendor platforms). Patients were selected if one or more matched polyp of 6 mm or larger was clearly demonstrated in both acquisitions (Table 1). Three patients were excluded because of incomplete CT data. Five patients were excluded in whom the polyp was completely obscured by untagged fluid or luminal collapse, to ensure reproducible polyp coordinates. However, no patients were excluded on the basis of poor preparation alone; the proportion of poorly prepared and underdistended patients is shown in Table 2. When patients had multiple polyps, each polyp was subjected to the same criteria; thus, a further three polyps greater than or equal to 10 mm and 14 polyps of 6–9 mm were included. Hence, the validation sample was 51 patients with 68 polyps (31  $\geq 10$  mm; 37, 6–9 mm) (Table E2 [online]). Per-polyp segmental location is shown in Table 3.

**Recording 3D Polyp Locations**

For each polyp, 3D endoluminal location was recorded by using a segmentation tool for medical images (ITK-SNAP; [www.itksnap.org](http://www.itksnap.org)) (27). D.J.B.

manually circumscribed each polyp on both acquisitions, providing corresponding prone and supine endoluminal surface coordinates to test the algorithm.

**Algorithm Development and Implementation**

Technical details of the algorithms have been described in detail previously (22,23). After development by using a separate training dataset (28), the algorithm was locked. No development occurred during the present study; no ACRIN data were used for development.

In-house 3D endoluminal visualization software designed by T.E.H. and H.R.R. was used to test the algorithm. The software displays 120° 3D endoluminal colonography and, by means of mouse clicking a location in one dataset, automatically updates the opposing endoluminal view to point directly at the corresponding location generated by either our algorithm or the normalized distance along the colonic centerline (NDACC) method (24). The reference standard polyp locations were confirmed by overlaying colored masks (derived by using the procedure outlined above) onto the endoluminal surface. In practice, a registration prompt (Fig 1) indicated the corresponding voxel location; however, this was deactivated for the comparison of the algorithm with the centerline-based method, to minimize bias.

**Table 2****Summary of Algorithm and NDACC Registration Errors**

Variable	Algorithm Registration Error (mm)			NDACC Registration Error (mm)		
	Mean*	Median	P Value	Mean*	Median	P Value
Luminal collapse status			.066			.073
At least one luminal collapse (n = 37)	21.8 ± 19.5	17 (1.2–85.8)		30.2 ± 16.3	25.5 (5.5–92.0)	
No luminal collapse (n = 31)	17.7 ± 21.6	8.2 (1.0–76.9)		24.1 ± 13.1	20.7 (4.1–65.0)	
Colonic residue status			.060			.537
Excess colonic residue† (n = 38)	23.4 ± 21.3	19.2 (1.0–85.8)		29.4 ± 18.0	24.3 (4.1–92.0)	
Low colonic residue (n = 30)	15.5 ± 18.7	8.4 (1.1–76.9)		24.9 ± 10.2	23.2 (11.0–65.0)	
Overall gross registration error (n = 68)	19.9 ± 20.4	12.3 (1.0–85.8)		27.4 ± 15.1	23.5 (4.1–92.0)	.001‡

Note.—Unless otherwise indicated, data in parentheses are the range.

\* Data are mean ± standard deviation.

† Excess colonic residue defined as greater than 50% luminal fluid in one or more colonic segments.

‡ Algorithm registration error is significantly smaller than that of NDACC.

**Table 3****Per-Segment Distribution of Polyps and Mean Registration Error**

Segment	Total Polyps ≥ 6 mm		Mean Gross Registration Error	
	ACRIN Study Sample	Validation Sample	Algorithm*	NDACC†
Rectum	90 (16)	14 (21)	19.2	24.3
Sigmoid	147 (27)	15 (22)	22.2	30.8
Descending	58 (11)	11 (16)	18.1	31.0
Transverse	95 (17)	7 (10)	25.5	32.7
Ascending	97 (18)	13 (19)	21.7	25.9
Cecum	60 (11)	8 (12)	11.7	19.1
Total	547	68	19.9	27.4‡

Note.—Unless otherwise indicated, data are number of polyps, with percentage in parentheses.

\* Data are 3D error/mm. No significant change in algorithm 3D registration error due to polyp position per colonic segment ( $P = .76$ , Kruskal-Wallis statistic).

† Data are 3D error/mm. NDACC 3D error is calculated as the smallest vector from a centerline point perpendicular to the true polyp location.

‡ Algorithm total mean registration error significantly smaller than that of NDACC method ( $P = .001$ ).

were defined a priori. Polyps directly marked by the registration prompt by using either display were noted.

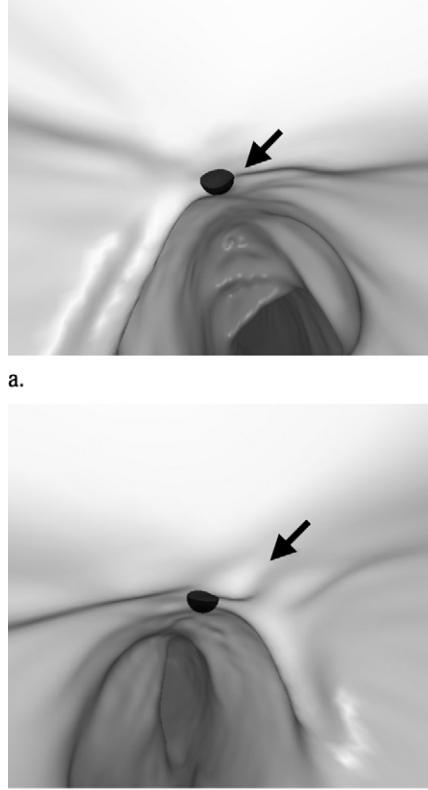
**Testing Algorithm Performance**

Polyp conspicuity after registration was assessed independently by two experienced radiologists (D.J.B. and E.H. with technical assistance from H.R.R., a computer scientist naïve to CT colonographic examination interpretation). H.R.R. loaded data from each patient into the display software, located the polyp by using coordinates obtained as described previously and selected either the matching algorithm or NDACC method according to a randomization table. Observers were unaware which method was being tested (the registration prompt was disabled to prevent unblinding). Having identified the polyp in either the prone or supine dataset (randomly allocated) the endoluminal view was automatically directed to the opposing display by using either the algorithm or NDACC method, depending on the randomization. The observer then attempted to locate the target polyp and graded its conspicuity by using the prespecified score (Table 5). The process was repeated for all polyps, prone to supine and supine to prone by using both registration methods. H.R.R. collated responses, and when the registration algorithm scored a successful result, patients were re-examined with the registration prompt activated to assess its proximity to the polyp.

**Assessment of Clinical Utility**

Scores to estimate potential clinical benefit during multiplanar (Table 3) or primary endoluminal review (Table 4) were developed by S.H. and S.A.T., members of the European Society of Gastrointestinal and Abdominal Radiology CT colonography committee, each with more than 10 years of experience in interpretation of CT colonographic examinations and research. For endoluminal interpretation, we considered registration successful if the polyp was visible in the opposing dataset 120° field of view without need for further

navigation (Fig 2). Matching was partially successful if the polyp became visible after mouse-driven rotation around the endoluminal camera position provided by means of the algorithm (Fig 3). Registration was unsuccessful if any navigation back or forth along the colonic centerline was required to bring the polyp into view (Fig 4). For multiplanar assessment, registration was successful if the polyp was within ±15 mm in any plane and partially successful if the polyp was visible within ±30 mm; greater than 30 mm navigation was considered unsuccessful. These values

**Figure 1**

**Figure 1:** Standard 120° 3D-rendered endoluminal views after automated registration show polyp conspicuity score of 5 (direct hit). **(a)** Registration prompt (black dot) marks and partially obscures 6-mm polyp (arrow) location indicated in supine dataset. **(b)** Prone 3D field of view shows endoluminal coordinates calculated by using algorithm. Registration prompt (black dot) just intersects with base of sessile polyp (arrow).

Multiplanar conspicuity was assessed by using the polyp reference volumes delineated previously. For each polyp, corresponding paired mural coordinates (for our algorithm) or endoluminal locations (for the NDACC method) were calculated. Starting with these point correspondences, the minimum axial, coronal, or sagittal navigation required to locate the polyp in the opposing dataset was determined for both registration methods. Results were scored according to prespecified criteria (Table 4). Polyps with overlapping volumes after registration were examined for registration prompt

**Table 4**

**Polyp Conspicuity Score and Registration Success for Multiplanar Display after Surface Matching Algorithm and NDACC Registration**

Registration Success	PC Score	Definition	Registration Algorithm ( <i>n</i> = 68)	NDACC ( <i>n</i> = 68)
Total SR			48 (71)	16 (24)
SR	5	Polyp visible on opposing MPR after registration without navigation	43 (63)	0 (0)
SR	4	Polyp visible after ±15 mm scrolling in any MPR axis	5 (7)	16 (24)
Total PSR			9 (13)	40 (59)
PSR	3	Polyp not visible within ±15 mm of MPR navigation prompt but visible after ±20 mm	0 (0)	23 (34)
PSR	2	Polyp not within ±20 mm of MPR navigation but visible after ±30 mm	9 (13)	17 (25)
Total USR	1	Polyp not visible despite ±30 mm of navigation on each MPR display	11 (16)	12 (18)

Note.—Data are number of polyps, with percentage in parentheses. MPR = multiplanar reconstruction, PC = polyp conspicuity, PSR = partially successful registration, SR = successful registration, USR = unsuccessful registration.

accuracy. The distance between points on the centerline closest to the polyp apex and algorithm-generated surface correspondence was measured to simulate one-dimensional registration error along the centerline. Finally, the gross 3D registration error was calculated from the vector between the polyp apex and the corresponding mural coordinates (for our algorithm) or the closest position on the centerline (for the NDACC method), following the approach described by Wang et al (14).

#### Statistical Analysis

Polyp location was assumed to be nonparametric; pairwise Wilcoxon signed rank tests were used to compare multiplanar, one-dimensional and Euclidean 3D registration error and multiplanar and 3D polyp conspicuity between registration methods. McNemar testing was used to compare successful conspicuity scores between methods. Subgroup analysis was performed to compare distributions of registration error in patients with different levels of bowel preparation and endoluminal collapse. The segmental distribution of polyps 6 mm or larger in the validation sample was compared with the entire ACRIN CT colonography dataset to investigate generalizability of results. Segmental

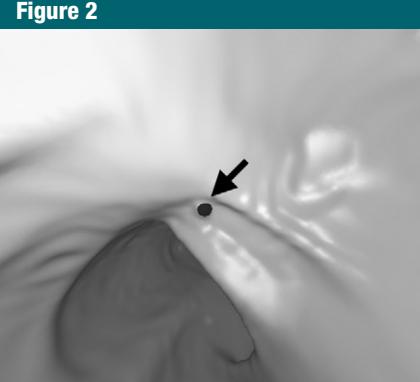
polyp distribution and collapse were compared by using the Kruskal-Wallis test. The Mann-Whitney *U* test was used to compare error distributions in patients with differing methods of colonic cleansing. *P* values less than .05 were considered to indicate a significant difference.

#### Results

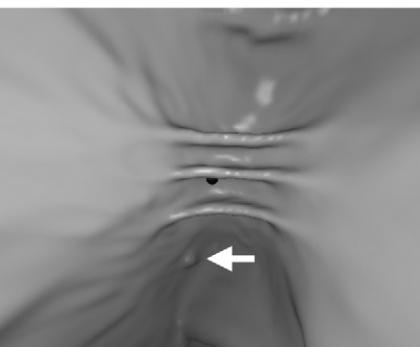
Overall, 51 patients with 68 polyps were included. In 100% of the patients, our algorithm registered the endoluminal surface, providing 136-point correspondences for testing.

#### Validation Sample Characteristics

There was no difference between the segmental distribution of polyps 6 mm or larger in the validation sample (*n* = 68) (Table 3) versus those (*n* = 547) from the entire ACRIN dataset (25) (*n* = 2525) (*P* = .647). By using the criteria proposed by Hara et al (19), 27 (53%) of the patients in the validation trial had excess residual fluid compared with 1313 (52%) of patients in the complete trial dataset. Similarly, 25 (49%) had at least one region of complete luminal collapse (Table E1 [online]) compared with 50 (48%) observed in the total 103 positive patients from the publicly available database.

**Figure 2**

a.

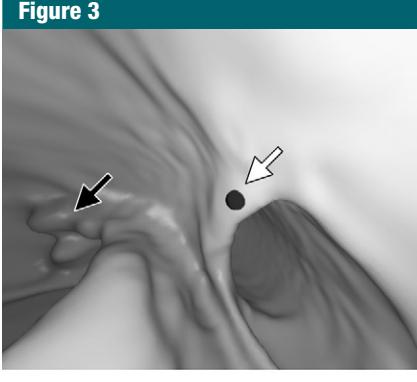


b.

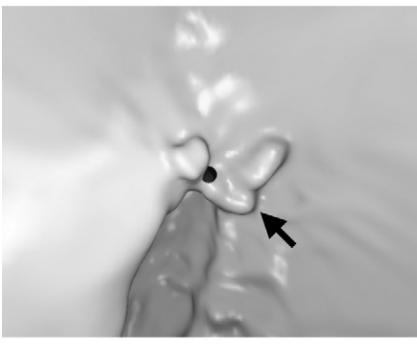
**Figure 2:** Standard 120° 3D-rendered endoluminal views after registration show polyp conspicuity score of 4 (near miss). Polyp is visible without navigation, but prompt does not intersect with polyp. **(a)** Registration prompt (black dot) marks polyp location indicated in prone dataset. Dot partially obscures 6-mm polyp (arrow). **(b)** Supine 3D field of view shows endoluminal coordinates calculated by using algorithm. Registration prompt (black dot) does not indicate polyp (arrow) because of slight (17 mm, 14°) misregistration, but polyp is visible in field of view without navigation. Gross 3D error was 17 mm, but registration was successful according to prespecified criteria.

#### Registration Performance: Gross 3D and One-dimensional Error

Overall mean Euclidean 3D registration error  $\pm$  standard deviation for all 68 polyps was  $19.9 \text{ mm} \pm 20.4$ . In comparison, mean 3D registration error was significantly greater when the NDACC method was used:  $27.4 \text{ mm} \pm 15.1$  ( $P = .001$ ). There was no significant difference in the 3D registration accuracy of the algorithm in the comparison of different colonic segments ( $P = .76$ )

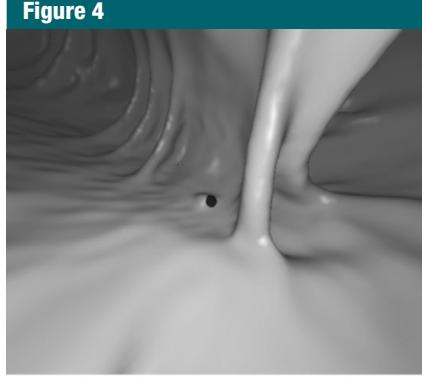
**Figure 3**

a.

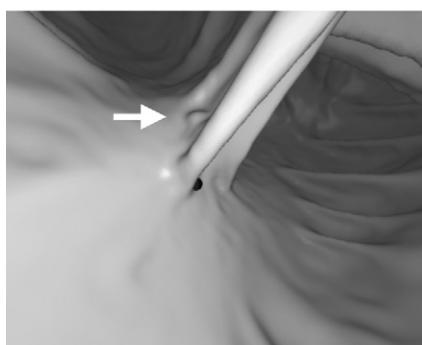


b.

**Figure 3:** Standard 120° 3D-rendered endoluminal views after registration show polyp conspicuity score of 2 or 3 (partially successful). Polyp is visible after rotation but without navigation along lumen. **(a)** Registration prompt (black dot) marks location indicated in prone dataset. Black dot partially obscures 6-mm sessile polyp (white arrow) on fold. Note fecal residue on adjacent fold (black arrow). **(b)** Supine 3D field of view shows endoluminal coordinates calculated by using algorithm, but points toward cluster of fecal residue (black dot, arrow). Actual polyp (not shown) was 22 mm from prompt, requiring 120° rotation but no navigation along lumen to locate. Registration was considered partially successful.

**Figure 4**

a.



b.

**Figure 4:** Standard 120° 3D-rendered endoluminal views after registration show polyp conspicuity score of 1 (unsuccessful registration). Polyp is not visible after rotation; navigation along lumen is required. **(a)** Registration prompt (black dot) marks polyp location indicated in prone dataset. **(b)** Supine 3D field of view shows endoluminal coordinates calculated by using algorithm, but polyp was obscured by fold. Rotation of 360° did not bring polyp into view. Navigation along centerline of 17 mm was required to find polyp (arrow); considered unsuccessful registration. Gross 3D error was only 11 mm; Euclidean error measurements in isolation have limited value for assessment of utility of algorithm in daily practice.

(Table 3). Although no significant difference in registration accuracy was shown between patients with excess residual fluid (23.4 mm;  $n = 38$ ) and those who were well prepared (15.5 mm;  $n = 30$ ) ( $P = .06$ ) or between patients who were well distended (17.7 mm;  $n = 31$ ) and those with luminal collapse (21.8 mm;  $n = 37$ ) ( $P = .066$ ), subgroup sample sizes were small (Table 2). Likewise, although the simulated one-dimensional centerline error was lower for our

method (mean, 17.9 mm) than that with the NDACC method (mean, 21.0 mm), the observed difference was not statistically significant ( $P = .107$ ).

#### Comparative Performance: Multiplanar Conspicuity

By using a multiplanar display, we generated 48 (70%) successful matches (Table 4) with the algorithm. Moreover, 43 (63%) polyps were marked directly by the registration prompt. A

**Table 5****Three-dimensional Endoluminal Polyp Conspicuity Score and Registration Success**

Registration Success	PC Score	Definition	Polyps Registered ( <i>n</i> = 68)*					
			Observer 1		Observer 2		Mean†	
			Algorithm	NDACC‡	Algorithm	NDACC‡	Algorithm	NDACC‡
Total SR			113 (83)	53 (39)	110 (81)	76 (56)	82.0	47.4
SR	5	Polyp marked directly by registration prompt	93 (68)	NA	83 (61)	NA	64.7	NA
SR	4	Polyp visible immediately in field of view	20 (15)	53 (39)	27 (20)	76 (56)	17.3	47.4
Total PSR			12 (9)	61 (45)	12 (9)	38 (28)	8.8	36.4
PSR	3	Polyp detected with $\pm$ 90 degrees rotation	9 (7)	40 (29)	10 (7)	27 (20)	7.0	24.7
PSR	2	Polyp visible within 360 degrees rotation	3 (2)	21 (15)	2 (1)	11 (8)	1.8	11.8
Total USR	1	Polyp not visible without navigation along colonic centerline	11 (8)	22 (16)	14 (10)	22 (16)	9.2	16.2

Note.—Unless otherwise indicated, data are numbers, with percentages in parentheses. PSR = partially successful registration, PC = polyp conspicuity, SR = successful registration, USR = unsuccessful registration.

\* Assessed from prone to supine and supine to prone, resulting in 136 individual polyp matching events.

† Data are percentages.

‡ Standard 120 degree field of view used for all endoluminal reconstruction.

further nine (13%) were partially successful, and 11 (16%) polyp-matching tasks were unsuccessful according to our prespecified criteria. When the NDACC method was used, 16 (24%) polyp-matching tasks were successful and 40 (59%) were partially successful, with the result that the NDACC method achieved significantly fewer successful matches than did the algorithm ( $P < .001$ ).

#### Comparative Performance: Observer-graded Endoluminal Polyp Conspicuity

Ease of polyp visualization after registration was assessed from prone to supine and supine to prone in all 51 patients; 68 corresponding polyp pairs generated 136 individual polyp-matching tasks for each observer (272 tasks in total). By using a 3D endoluminal approach (Table 5), the two observers (D.J.B. and E.H.) graded a mean of 82% (113 [83%] and 110 [81%] from 136, for D.J.B. and E.H., respectively) polyp matches as successful, 9% (12 [9%] and 12 [9%]) partially successful, and 9% unsuccessful (11 [8%] and 14 [10%, respectively]). By using the NDACC method, 47% of polyp matches were assessed as successful (53 [39%] and 76 [56%], respectively), 36% (61 [45%] and 38 [28%], respectively) were partially successful,

and 16% (22 [16%] and 22 [16%]) were unsuccessful, with the result that the NDACC method allowed significantly fewer successful registrations ( $P < .001$ ). Moreover, by using the algorithm, 64.8% (93 [68%] and 83 [61%], respectively) of the total polyp matches were marked directly with the registration prompt (interobserver variation was due to borderline cases where the prompt marked the polyp periphery); no such facility is possible when the NDACC method is used.

#### Discussion

Computer-assisted registration for CT colonography is not new; once methods to compute the luminal centerline were developed (29), they were rapidly incorporated into vendor workstations (18) to provide approximate corresponding endoluminal locations between prone and supine acquisitions. However, luminal collapse and residual fluid are encountered regularly in daily practice and impair centerline matching algorithms (9). In an attempt to account for changes in colonic length between prone and supine acquisitions, the endoluminal position can be expressed relative to total centerline length (NDACC), and has been shown to improve upon simple centerline

matching (24,30). Likewise, anatomic reference points (eg, flexures or rectum) can be used to shrink or stretch centerline geometry to improve registration (10,13,14), often with promising results. However, despite correction for colonic torsion by using teniae coli to improve on existing two-dimensional centerline methods (12), Huang et al found a registration error of  $\pm$  61 mm. This may reflect the use of a representative sample (31) with similar selection criteria to those in our study, and their results are likely more generalizable than those of studies restricted to optimally prepared patients (8,9,17). The 3D error of 20.4 mm presented in our study compares favorably to those of Huang et al.

Centerline studies usually are performed to assess registration accuracy with linear distance measurement (8,9,17), the meaning of which does not transfer readily to clinical practice, where radiologists are looking for abnormalities on the endoluminal surface. De Vries et al (11) attempted to estimate clinical utility by testing endoluminal polyp visibility after registration by using 32 representative datasets from a separate observer study. They found that 70% of polyps were visible after registration by using an unfolded cube visualization (11) but that this

visualization method exposed more of the endoluminal surface than did the conventional 120° virtual colonoscopic field of view used by most workers. We estimated that our algorithm would reveal 91% of polyps by using an unfolded cube. Moreover, indicating a specific location on the endoluminal surface provided the observer with considerably more information than simply a position from which to search; centerline methods inherently cannot indicate a 3D mural location because they operate in one dimension. We found that our algorithm significantly outperformed the NDACC method when both standalone and observer measures were used.

Other algorithms have been developed to provide 3D endoluminal surface correspondence. Suh et al (32) modified a centerline-based rigid registration aided by automated anatomic landmark detection to initialize a voxel-based nonrigid deformation intended to provide true 3D correspondence. They reported a registration error of 13.8 mm ± 6.2 when aligning 24 polyps in 21 patients; however, all of the patients were optimally prepared and distended, and thus, unlikely to be representative. Authors of a subsequent study of four patients with colonic collapse found that the mean error increased to 30.1 mm (13). Moreover, each collapsed segment was matched with a fully distended acquisition to interpolate missing data, a situation uncommon in clinical practice where luminal collapse often occurs in both datasets. Fukano et al (15) attempted surface correspondence by matching haustral folds and reported that 65.1% of large folds matched correctly. When developing our own haustral fold-based initialization (22) we found that colonic torsion between acquisitions induced errors in both registration and reference standard observations. Nevertheless, our method achieved fold-matching accuracy of 83% and 88% with and without local colonic collapse, respectively, regardless of fold morphology (22). Recently, Zeng et al (16) used automated feature detection to create five colonic segments and subsequently mapped each endoluminal surface to a rectangle. They found an

average 3D error of 5.65 mm for 20 paired polyps in optimally distended colons, but they did not present data for collapsed colons.

At the time of writing, all previous attempts at endoluminal surface registration required manual initiation and delineation of fixed colonic landmarks. Our algorithm is more automated; the reader reviews the proposed colonic segmentation, excludes small bowel, and confirms the sequence of colonic segments, defining start and end points, just as when generating a 3D flythrough. We used external validation with patients from hospitals that were not affiliated with the algorithm development to obtain a generalizable estimate of algorithm performance in normal practice. Our study sample closely paralleled the parent ACRIN CT colonography study data with respect to bowel preparation quality and distension, and the registration algorithm outperformed the centerline-based method in these circumstances.

Our study had limitations. Patients were excluded from validation when there was an incomplete external radiologic reference standard or when polyp locations could not be confirmed, despite accounting for inconsistencies in axial section numbering between vendor platforms. Such discrepancies affect the reference standard. However, both the distribution of polyps and the proportion of patients with poor bowel preparation in our sample paralleled those in the ACRIN data (19,25). Although we found no significant difference in registration accuracy when comparing subgroups with varying preparation and distension, sample sizes were small and findings should be interpreted with caution. We excluded patients with absent or incomplete fecal tagging because the algorithm relies on matching surface features and digital cleansing is necessary to achieve this when there is substantial residual fluid. Although alternative displays (eg, filet, unfolded cube, or ultrawide 150° endoluminal view) would have increased successful registrations by our prespecified criteria, a 120° display is standard and widely available. In addition

to prone and supine acquisitions, current implementation guidelines recommend an additional decubitus series in selected patients; registration of decubitus datasets is the subject of future research. The polyp conspicuity scales we developed may not directly reflect utility in normal practice, although we did base the scale on *a priori* discussions of clinical benefit. We plan studies of clinical utility in everyday practice. Although accurate endoluminal registration will facilitate and shorten interpretation time, we did not test this directly or test any effect on sensitivity and specificity, which would require a large number of patients. It is possible that observers who use automated matching could incorrectly reject true-positive polyps if they were incorrectly registered, just as observers who use computer-aided detection may incorrectly reject false-negative polyps (33). Moreover, because computer-aided detection only has regulatory approval for use as a second interpretation (34,35), it is unclear how a registration algorithm such as ours might be regulated.

In summary, we tested a computer-assisted registration algorithm on a representative subset of CT colonographic data from prone and supine acquisitions in a large multicenter trial and found registration accuracy significantly superior to a centerline-based method. The ability to rapidly and automatically match the endoluminal surface location of potential polyps between acquisitions may facilitate CT colonographic interpretation.

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