CT Colonography: Is It There Yet?
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“I think we need to discuss this wine appreciation course you are taking”
Introduction

CT colonography (CTC) - a.k.a. CT colonoscopy, virtual colonoscopy, etc.

First conceived of by Dr. David Vining at Wake Forest University, more than a decade ago

Initial clinical development at the Mayo Clinic (Amy Hara & C. Daniel Johnson, Radiology 1996)

Subsequent development/refinement over the next several years by radiologists at Stanford (Beaulieu, Jeffrey, & Napel), UCSF (Yee), NYU (Macari), Boston University (Barish & Ferrucci), U of Chicago (Dachman), U of Wisconsin (Pickhardt) & other U.S. & non-U.S. centers (Halligan & Taylor – UK)

Introduction

CTC is as an alternative imaging test to screening colonoscopy for polyps/colon CA

Advantages and disadvantages of CTC c/w conventional colonoscopy (CC) remain similar since the initial development of CTC

Advantages: No sedation, decreased risk of perforation; no long wait c/w for CC at many centers/practices; potentially higher rate of patient acceptance & compliance with follow-up

Disadvantages: Purely a diagnostic test, cannot remove/biopsy lesions; ionizing radiation; somewhat time consuming to do and interpret; as of summer 2007, reimbursable for limited indications only, in most of the U.S.
Introduction

- **CTC entails:**
  - bowel preparation prior to exam
  - insufflation of the colon with room air or CO$_2$
    (less cramping with the latter; more readily absorbed) via rectal tube
  - "scout" digital radiograph
  - supine and prone CT acquisitions; re-insufflate colon between acquisitions as needed
  - interpretation of both sets of CT data, including colonic and extra-colonic findings
  - report generated by MD with recommendations as appropriate

Hardware & Software Development

- Initial reports used single-slice helical CT scanners
- Continued advancement of CT technology over the past decade – now 16 to 64+ multi-detector/multi-channel
- Routine use of thin-slice acquisitions (1 mm or thinner) – “isotropic voxels”
- Permits rapid reconstruction to high-quality multiplanar (coronal/sagittal) and 3D reformations (“fly throughs”, i.e., volumetric renderings)
Hardware & Software Development

- Use of current CT technology/techniques reduces or eliminates motion artifacts, volume averaging artifacts (with more accurate characterization of polyps versus retained stool, e.g.), and stair-step artifacts.
- Advanced workstations permit synchronization of 2D and 3D data sets, more automated functions, & computed-assisted diagnosis (CAD).
- Halligan S et al. (Gastroenterology 2006): CAD significantly improved accuracy for inexperienced readers, but could not substitute for adequate training.

59-year-old – 5 mm polyp on screening CTC
Bowel Preparation

- **Bowel preparation** - remains the biggest patient impediment to both CTC and CC - for initial screening and follow-up
- At present, cannot effectively just “tag” all the stool with oral contrast, and then electronically “subtract” the high density stool
- Most centers use a preparation protocol similar to that for a barium enema (oral sodium phosphate or magnesium citrate; clear liquid diet the day before; +/- enema), with some modifications (particularly a high density stool tagging agent, to tag residual stool)
- Prep for CC - OK, but often more residual fluid
- Preparation kits are commercially available specifically for CTC

Technical Aspects - Consensus

- **There is consensus amongst radiologists on the following aspects of CTC:**
  1) **BOTH supine and prone acquisitions are mandatory** (although this doubles the radiation dose), for:
    - mobilization of colonic fluid which may hide polyps
    - differentiation of stool versus polyps
  2) **Radiation dose can be substantially reduced** (with low mAs - e.g., 50, and 120 kVp or less) without compromising diagnostic quality - high intrinsic contrast of gas-filled lumen compared with the colonic wall
Technical Aspects - Consensus

- potential cancer risks from CTC are small compared with the potential benefits (Brenner DJ et al. Gastroenterology 2005)

3) **The data set must be reviewed for both colonic and extra-colonic findings**

- need to review at least one and ideally both data sets using bone “windows” & abdominal “windows”
- incidental extra-colonic findings are relatively common & may be problematic for the radiologist/patient
- they are occasionally of substantial importance (e.g., renal cancer, AAA) & may generate additional testing (and potential patient anxiety)

3) (Continued) **Multiple reports on extracolonic findings:**

- Hara AK et al. (Radiology 2000): 264 patients, 30 (11%) with highly important extra-colonic findings; added average $28 to workup
- Similar findings in a larger series from the same group (Gluecker TM et al. Gastroenterology 2003)
- Yee J et al. (Radiology 2005): 500 male patients, 315 (63%) with extra-colonic findings, 45 (9%) with clinically important findings
Technical Aspects - Consensus

3) (Continued)
- Rajapaksa RC, Macari M, et al. (J Clin Gastroenterol 2004): 250 patients; 136 extra-colonic findings, 17 (12.5%) highly significant - of which 14 proved to be new
- Khan KY et al. (Br J Surg 2007): 225 patients (all symptomatic/high risk) - 37% of 73 patients with colonic tumors had extra-colonic findings; 53% of those who did not have colonic tumors on CTC had extra-colonic findings

44-year-old man with blood in stool
77-year-old woman with failed CC & negative CTC

59-year-old woman with findings consistent with ovarian CA
Technical Aspects - Controversies

1) Is stool tagging (with oral high density contrast agents) routinely necessary?
- currently our center is not using this, but other centers are using it routinely; may improve accuracy (Pickhardt PJ et al. NEJM 2003)

2) What is the utility of IV contrast for CTC?
- may improve yield for polyp identification, and improved staging if malignancy is present
- adds expense, effort, & some risk
- I would use only in selected non-screening situations (e.g. patient with lower GI bleeding who cannot undergo CC, with a high index of suspicion for frank malignancy)

69-year-old man with anemia and probable lesion on barium enema
Technical Aspects - Controversies

3) **What is the best interpretation approach, for accuracy and speed?**

- **primary “2D”** (cine axial image review, supplemented by multiplanar imaging and “fly throughs” as needed) **versus primary “3D”** (rely primarily on fly-through interpretation)

- varies depending on the authors/center; opinions are quite heated re. one versus the other

- my bias is primary 2D; 3D requires review of 4 separate passes (antegrade/retroflexion for supine + prone images)
Technical Aspects - Controversies

- regardless of primary 2D vs. 3D approach, there is a learning curve
- 4) How should polyps be measured?
  - on what sequence(s) should they be measured? should only the longest dimension (with or without the stalk) be reported?
  - role for volumetric analysis? (evolving with workstations/CAD)
- 5) Should “diminutive” polyps be reported, and should they trigger CC?
  - some authorities advocate not mentioning them in the CTC report (Pickhardt PJ et al. Cancer 2007; ACR 2005 guidelines); others believe smaller polyps/potential polyps should trigger CC – “leave no polyp behind” (Rex D Am J Gastro 2005)

74-year-old woman with incomplete colonoscopy

[Image of CT scans showing polyps]
Technical Aspects - Controversies

6) **Is there a role for spasmolytics?**

- Studies initially suggested no role for either glucagon or butyl scopolamine (Buscopan)
- Did not improve colonic distension or diagnostic accuracy (Yee J et al. AJR 1999; Bruzzi JF et al. Eur Radiol 2004)
- A more recent publication noted improved colonic distension (in supine position) with butyl scopolamine and to a lesser extent with glucagon (Rogalla P et al. Radiology 2005)
- Some authorities give glucagon to make the examination more comfortable - but adds some cost, and relaxes the ileocecal valve (Dachman AH Radiology 2006)

University of Wisconsin Practice Model

- **CTC and CC clinics run simultaneously**
- Patients are initially counseled/consented regarding potentially having both procedures
- CTC examinations are interpreted immediately after performance; if positive, patients go directly to CC for further evaluation/biopsy
- Patients with incomplete CC go directly to CTC for complete colonic evaluation
- Advantages of only one bowel preparation, definitive diagnosis and therapy the same day
U. of Wisconsin Practice Model

- Both services complement each other and should lead to increased referrals for both radiologists & gastroenterologists or surgeons performing CC; GI physicians can focus on therapeutic CC
- Series of 1110 adults underwent screening CTC (Pickhardt PJ et al. Radiology 2005):
  - Large polyps (10 mm +) found in 43 (3.9%)
  - Medium polyps (6-9 mm) found in 77 (6.9%)
  - 31 patients with medium-sized polyps chose CC, 46 chose follow-up CTC in the future
  - 71 patients underwent CC, with concordant lesions found in 65; 92% PPV
  - 86% of CC performed the same day at CTC

78-year-old woman with anemia and incomplete initial CC

- Sigmoid colon is redundant
- 9 mm cecal polyp at CTC
- Polyp confirmed on 2nd CC
77-year-old woman with incomplete CC

- 8 and 5 mm right colonic polyps identified on CTC; more easily seen on prone images (motion on supine images)
- Repeat CC confirmed CTC findings
74-year-old woman with incomplete CC due to hernia

- 9 mm sigmoid polyp was initially seen at CC but not removed
- CTC revealed another 1 cm cecal polyp + several diminutive right colonic polyps
Numerous accuracy studies - initially on symptomatic/high risk patients - then on asymptomatic people/a mixture of the two

Most studies have same conclusions: for polyps $\geq 1$ cm, sensitivity/accuracy is around 90%

Meta-analysis of 33 articles on CTC; included 6400 patients (Mulhall BP et al. Ann Intern Med 2005):
- 85% sensitivity & 97% specificity for polyps 10+ mm; sensitivity varied study-to-study and observer-to-observer

Very high accuracy in the military study (Pickhardt PJ et al. NEJM 2003); improved c/w the reports of Cotton (JAMA 2004) and Rockey (Lancet 2005)
**Accuracy of CTC**

- Lower accuracy for 6-9 mm, flat polyps; lowest accuracy for 5 mm or smaller polyps
- Almost all studies have used CC as the reference standard - more recently with segmental “unblinding” during CC, following CTC
- **But a single CC is operator dependent and not a perfect reference standard**
  - Barclay RL et al. (NEJM 2006): 12 experienced gastroenterologists performed CC on 7,882 patients
  - - large differences - up to 10-fold - in rates of adenoma detection amongst the 12
  - - slower procedure time correlated with higher discovery rates

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**Accuracy of CTC**

- Iannaccone R et al. (Radiology 2005): 88 patients, initial CTC, then CC (diagnostic only) completely blinded to CTC findings
  - then 2\textsuperscript{nd} CC within 2 weeks as reference standard, with awareness by the endoscopist of initial CC and CTC findings
  - - CTC correctly depicted 6 of 16 polyps which were not seen at initial CC (including two 8 mm polyps and one 14 mm polyp) & all 11 polyps 10 mm or larger
  - - sensitivities for patients with polyps 6 mm or larger - 84% for CTC and 90% for CC; specificities of 82% and 100%
CTC – CC concordance (case courtesy Dr. Christopher Beaulieu, Stanford University)

Colonic Findings & Pitfalls

  - haustal folds (multiplanar images/cine review invaluable for distinguishing from polyps, supplemented by 3D views)
  - stool (mobile; gas bubbles within it on thin sections/lung windows)
  - ileocecal valve – contains fat
  - colonic lipoma
  - catheter tip
  - hemorrhoids
  - prior surgical/biopsy sites
  - inverted appendiceal stump
Ileocecal valve

Colonic Findings & Pitfalls

- Polyps:
  - soft-tissue density
  - if not hidden by fluid, generally persist on prone & supine views; confirm on multiplanar & 3D views as needed
  - cannot reliably predict histology on CTC (hyperplastic, adenomatous, hamartomous, etc.)
  - correctly identifying polyps can occasionally be difficult, even for experienced interpreters

- Masses:
  - unless clearly fat-containing, almost all need further evaluation/biopsy
Polyp hidden on supine images (case courtesy Dr. Christopher Beaulieu, Stanford University)

Retained stool (top) and lipoma (bottom) (courtesy Dr. Christopher Beaulieu, Stanford University)
Pitfalls

- Interpretation can only be as good as the bowel preparation & degree of distension (Park SH et al. Radiology 2005; Gluecker TM et al. AJR 2004)
- Stool may not necessarily have gas within it
- Substantial minority of polyps, particularly if pedunculated, may move from a dorsal to ventral position or vice versa when a patient’s position is changed – potentially simulating stool (Laks S, Macari M, et al. Radiology 2004)
- Cecum in particular can move between prone and supine acquisitions, leading to false-negative diagnoses (Chen JC & Dachman AH, AJR 2006)
- Polyps hiding on/around folds; blind spots on 3D

Pseudopolyps (Courtesy Dr. Christopher Beaulieu, Stanford University)

- Top row - all retained stool
- Bottom row - all prominent folds
Pitfalls

- “Flat” (height < ½ width) polyps are notoriously difficult to diagnose on CTC (and CC)
- Fortunately these are very uncommon
- Fidler JL et al. (Abdom Imaging 2002): 547 patients underwent CTC & CC; found 22 flat polyps (4%)
- Pickhardt PJ et al. (AJR 2004): 59 flat polyps in 52 patients, out of 1,233 patients (also 4%) whom had CTC + CC
- 17 found at both, 17 at CC only, 25 at CTC only
- Only 4 proven flat polyps were 10+ mm
- Park SH et al. (AJR 2006): fewer than 50% of 18 flat polyps could be identified on CTC

Complications

- Two recent series and several case reports documenting colonic perforation during CTC
- Burling D et al. (Radiology 2006): survey of 50 UK centers, 17,000+ CTC examinations
- 9 perforations (0.08%); 4 asymptomatic and 5 symptomatic, with 1 requiring surgery
- 5 had an identifiable cause, including new diagnosis of UC, new diagnosis of colon CA, & inflation of a rectal stump
- No difference in perforation rates with or without inflated rectal balloon
- 2 perforations with automated insufflation
Complications

- Sosna J et al. (Radiology 2006): survey of 11 Israeli medical centers, 11,800+ CTC examinations
  - 7 cases of perforation (5 sigmoid, 2 rectal; 0.06%); average patient age of 78; 6 men; balloon inflation in 5; 4 required surgery
  - possible contributing factors – left inguinal hernia containing colon (4), severe diverticulosis (3), recent colonic biopsy (2), and obstructive carcinoma (1)
- Risk of perforation from CC between 0.06% and 0.19%, or 1 in 2000-1300 patients; higher if therapeutic colonoscopy

Complications

- Recommendations of Pickhardt PJ (Radiology 2006) and Dachman AH (Radiology 2006):
  - check scout prior to insufflation, for pre-existent perforation
  - use smaller-caliber flexible rectal catheter rather than rigid retention balloon catheter
  - insert rectal tube carefully
  - use patient controlled insufflation/lower pressure automated insufflation
  - if using automated CO₂ pump, turn off pump when moving patient between supine and prone positions (when highest pressure is generated)
  - drain gas slowly via tube to decrease risk of vasovagal reactions
Newer Developments

- Further advancements in workstations, software, integration of 2D and 3D interpretation
- Improvement in CAD programs (vendor and customized)
- Currently not widely used to my knowledge, in contrast to in conjunction with mammography, despite numerous publications
- As with mammography, multiple potential pitfalls of current programs; therefore cannot replace an experienced interpreter
- Automated polyp measurement
- Improvement in subtraction techniques
- Advanced display techniques: “fillet” view

Alternative Imaging

- PET/CTC
- Preliminary reports of fused PET/CTC for more accurate (larger) polyp localization, and for staging of colorectal CA (Quon A et al. J Nucl Med 2006; Veit-Haibach P et al. JAMA 2006)
- Gollub M et al. (AJR 2007): “Excellent image correlation” in 23/27 proven polyps 10+ mm, in 17 patients, using CTC images fused to $^{18}$F-FDG PET
- Adds expense, time, and other challenges
Additional Issues

- In the Mayo Clinic study (Gluecker), 696 patients underwent both CTC and CC:
  - the majority preferred CTC to CC
  - patient willingness to undergo re-screening was significantly greater for CTC compared with CC
  - preparation uncomfortable for 89% & inconvenient for 78%
- Sedative/anamnestic used for CC but not CTC adds bias

Additional Issues

- **Will this translate to improved compliance with follow-up screening examinations?**
- Estimated 80 million people in the US need to be screened, yet only 4 million currently are
- Is CTC more expensive than CC? (Vijan S et al. Am J Gastro 2007)
- Depends on what the reimbursement will be

- **Whom will be performing/interpreting CTC?**
- In my opinion and the opinion of many other body imagers, it takes years of experience to accurately interpret abdominal & pelvic CT - particularly for the extra-colonic findings
Additional Issues

- Ultimately, the perceptions of the public regarding the advantages and disadvantages of CTC and CC will drive utilization.
- Essentially no reports of yield/utility/accuracy of follow-up screening (using CTC and/or CC) at 5 years (or shorter interval) after initial negative CTC/discovery of small polyp(s).
- This is in contrast to mammography and lung cancer screening with CT.
- What will be the future role of thinner scopes, capsular imaging, & DNA probes, for colonic screening - & how will CTC fit in?

Conclusions

- CT colonography is maturing as a viable alternative to conventional colonoscopy.
- As with other aspects of GI medical practice (e.g., complementary roles of imaging and interventions for the pancreas - CT, MR, EUS, ERCP), I believe that CT colonography and conventional colonoscopy are complementary rather than purely competitive examinations: U of Wisconsin practice model.
- In general, from a purely diagnostic standpoint, the answer to “CTC - is it there yet?” is YES, with reimbursement likely to occur soon.
Thank you for your attention!