

DOES CT COLONOGRAPHY (CTC) HAVE A ROLE IN COLON CANCER SCREENING?



**DANIEL SWERDLOW M.D.
ASSISTANT PROFESSOR OF RADIOLOGY
GEORGETOWN UNIVERSITY HOSPITAL**

Will Virtual Colonoscopy (CT Colonography) Replace Optical Colonoscopy (OC) For The Screening Of Colorectal Cancer?

NO!



Congratulations, you're going to be on the first episode of TLC's "Extreme Colonoscopies".

GOALS/OUTLINE

- **Review of recent major validation literature**
- **Hot topics in CTC**
- **Examine large scale feasibility modeling**
- **Where does CTC go from here?**

DEATH OF THE BARIUM ENEMA

- **At least three recent publications have detailed the superiority of CTC and OC over the double contrast barium enema for polyp detection**

RECENT BIG PUBLICATIONS

- **Kim DH, Pickhardt P, et al CT Colonography For the Detection Of Advanced Neoplasia. NEJM 2007; 357:1403**
- **ACRIN Trial NEJM 2008; 359:1207**
- **Munich Trial Gut 2009;58:241**
- **JAMA Flat Lesion Study 2008;299(9):1027**
- **ACS Updated Recommendations**

KIM et al NEJM 2007

- 3120 CTC vs. 3163 OC, 1-2 polyps 6-9 mm at CTC offered OC or follow up in 1-3 years. Polyps ≥ 10 mm at CTC referred to OC
- 246 CTC patients referred for OC (7.9%)
- 123/561 vs. 121/2434 Adv. adenomas/polypectomy
- 3.2% vs. 3.4% Incidence advanced adenoma/patient
- 14 vs. 4 Invasive cancers
- 0 vs. 7 Perforations

KIM et al NEJM 2007

- Concluded similar detection rates for both groups supporting CTC for screening
- The similar detection rate was despite more than 4 fold fewer polypectomies in the CTC arm
- 2,006 polypectomies for polyps ≤ 5 mm in the OC arm: 4 advanced adenomas, 0 cancers

KIM SURVEILLANCE GROUP

- 246/3120 (7.9%) Pt. referred to OC
- 158 Pt. with 193 polyps are being followed
- 54 Pt. have returned-70 polyps
- 67 Polyps stable or decreased
- 3 Polyps grew at least 1 mm
- All 3 resected- all tubular adenoma

GRASER et al (MUNICH) TRIAL

- Compared CTC, OC, Flex Sig, FIT And FOBT
- Stool samples, same day CTC and OC, with segmental unblinding in 307 avg. risk adults
- 221 Adenomas In 307 patients
- Sensitivities: OC 100%, CTC 96.7%, FS 83.3%, FIT 32%, FOBT 20% (No increase For FIT + FOBT)
- Concluded CTC is viable for screening & flex sig preferred if patient is unwilling to prep

Graser A, et al *GUT* 2009;58:241**GRASER et al PER POLYP SENSITIVITY**

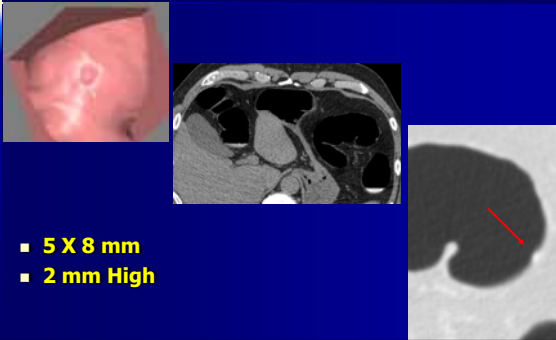
# of adenomas N=221	SMALL ≤ 5 mm	MEDIUM 6-9mm	LARGE ≥ 10 mm
CTC	59.2% 84/147	90.2% 37/41	93.9% 31/33
OC	94.6% 139/147	92.7% 38/41	100.0% 33/33

JAMA FLAT LESION

- 1,819 California vets over 12 cons. months
- 9.35% Incidence (5.84% screen, 15.44% surveillance, 6.01% symptomatic)
- Flat or depressed lesions had higher risk of carcinoma and at a smaller size than polypoid adenomas
- Utilized an exchange program with Japan and an indigo-carmine dye spray not commonly performed in the U.S.

Soetikno, R., et al *JAMA* 2008;299:1027

FLAT LESION



- 5 X 8 mm
- 2 mm High

CONTRASTING DATA FROM ROBBINS *et al*

- 5,107 Pt. with 125 flat lesions/106 patients and 602 polyps ≥ 6 mm
- 10 Flat lesions ≥ 30 mm
90% adv. adenomas, 0 cancers
- 92 Flat lesions 6-29mm
25% dysplasia, 5.4% adv. adenomas, 0 malignant
- 363/602 (60%) Polyps dysplasia
- 73/602 (12.1%) Advanced adenomas
- 3/602 (0.5%) Malignant-not significant difference
- 9 Flat lesions missed at CTC: 0 Advanced histology, 2 tubular adenomas

Robbins, J.; Pickhardt, P.; Kim, D. Presented at ARRS April 28, 2009

ACRIN 6664 STUDY

- 15 Centers/2,531 asymptomatic pt. over age 50
- CO₂, stool and fluid tagging
- Glucagon injection
- All readers passed an examination
- 90% Sens. and 86% spec. for adenomas 10 mm or larger

JOHNSON CD, et al. *NEJM* 2008;359:1207

ACRIN RESULTS

- Detected 128 Polyps In 109 pt. ≥ 10 mm (4.3%)
- 7 Cancers ≥ 6 mm
- Scanner or software did not influence results
- 2D as effective as 3D reads (2D 6 minutes less)
- Prevalence lesions ≥ 6 mm low (8.3%)
- Therefore referral for OC will be low

ACRIN RESULTS

- Training is important
- Read 500 studies, or
- Undergo 1.5 days of training including ≥ 50 cases
- Pass a certifying exam, which required detection of 90% of lesions ≥ 10 mm
- Half of readers did not initially pass and required retraining

ACRIN RESULTS

	≥ 5 mm	≥ 6 mm	≥ 7 mm	≥ 8 mm	≥ 9 mm	≥ 10 mm
SENS	65%	78%	84%	87%	90%	90%
SPEC	89%	88%	87%	87%	86%	86%
PPV	45%	40%	35%	31%	25%	23%
NPV	95%	98%	99%	99%	99%	99%

ACS SCREENING GUIDELINES

- Flexible sigmoidoscopy every 5 years
- Optical colonoscopy every 10 years
- Double contrast barium enema every 5 years
- *CT colonography (virtual colonoscopy) every 5 years*

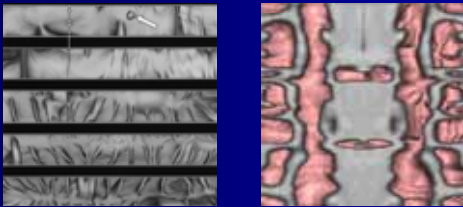
LEVIN B, et al. *Ca Cancer J Clin.* 2008;58.

HOT TOPICS IN CTC

- 2D vs. 3D
- New views
- Reader training
- Decreased/no prep
- Automated measurement
- Computer aided detection
- Extracolonic findings

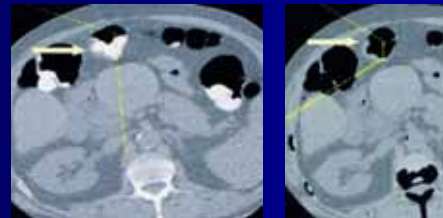
NEW VIEWS

- Filet view AKA virtual dissection view



LOW OR NO PREP

- 5/25 articles in 2008 were on this topic
- Most utilize a combination of stool tagging (barium sulfate) and electronic subtraction



Zalis, M. E. et al. *Radiology* 2003;226:911-917

COMPUTER AIDED DETECTION

- Similar to mammography, works as a second reader to improve sensitivity at the expense of specificity
- Not FDA approved
- Most are currently "sphere" finders: Good at polyps
- Flat lesions more challenging with promising early results

Suzuki, K. et al. 9th International Symposium on Virtual Colonoscopy October, 2008

THE BAD NEWS

- MEDCAC (Medicare Evidence Development & Coverage Advisory Committee) has voted to recommend that CMS not fund CTC at this time as the evidence is "incomplete"
- This, despite evidence presented that OC saves 171 life/years per 1,000 pt. screened and that CTC would offer 168 life/yr
- MEDCAC felt that there would be no increase in screening rates despite evidence presented of a 70% increase in patients screened at U-WI and Bethesda Naval Hospital

<http://www.cms.hhs.gov/mcd/viewmccac>

HOW CTC CAN INCREASE SCREENING

- Allow those unwilling or unable to receive OC to be screened including those medically fragile, anticoagulated or allergic to sedatives or a tortuous colon
- Allow those who lack access to OC to receive screening
- Friedman et al Univ. Of Arizona introduced CTC to 2 remote govt. Indian hospitals with limited OC access and screened 86 patients in 4 months. Images remotely read in Tucson

Friedman, et al Presented at ARRS April 28, 2009

MEDCAC CONCERN ABOUT HARM

- Estimated 1 cancer induced/1000 CTC
- Based on Hiroshima data average age 50
- Focused on lack of data about extracolonic findings and potential harm
- Ignored benefits of extracolonic findings i.e. AAA and non colonic neoplasms which outnumber colon cancers

<http://www.cms.hhs.gov/FACA/downloads/ld45c.pdf>

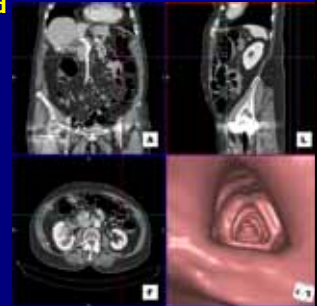
COST EFFECTIVE?

- \$488 was proposed CMS reimbursement
- Not cost effective if screening rates do not exceed 50% (sending OC pt to CTC)
- Would be cost effective if screening rates reached 62.5% (25% more patients screened)
- Ignored cost of new biologic agents for CRC

<http://www.cms.hhs.gov/FACA/downloads/ld45c.pdf>

FOLLOWING KNOWN COLORECTAL CANCER

- For patients in need of surveillance CT for metastases and due for OC
- CTC can be performed with IV contrast to assess solid organs and evaluate the remaining colon



LARGE SCALE FEASIBILITY

- MDCT capacity: Model estimated 1.2-1.6 studies/ct/day at steady state
- Economic impact of working up extracolonic findings (mean cost/pt.):
- Nonsurgical W/U \$31.02
- Surgical W/U \$67.54
- 133/2195 patients 6.1% (inc. 18 w/u not recommended by radiologists)

Pickhardt P, et al *Radiology* 2008;249:151 and Pickhardt P, et al *AJR* 2008; 190:236

WHERE DOES CTC GO FROM HERE?

- CTC has moved "successfully" through the validation stage and into the beginning stages of implementation
- Est. 42 million individuals are unscreened and 20,000 colonoscopists in the U.S.
- CTC would provide a new option for the noncompliant or those otherwise unable to be screened due to medical condition or lack of access

MOVING CTC INTO PRACTICE

- Make sure all physicians and patients understand the decision paradigm following a positive CTC
- Adopt an organized screening program
- Achieve a uniform standard of high quality at all levels of the examination

THE SCREENING PARADIGM

- CTC is inherently different than OC, thus has a different screening strategy
- CTC is noninvasive. A positive test leads to options, reasonable to screen out low risk polyps
- For OC, the added cost and risk of polypectomy is low since the scope is already there
- OC follow up is difficult

THE SCREENING PARADIGM

- Polypectomy for ALL POLYPS ≥ 10 mm or for ≥ 3 POLYPS 6-9 mm
- Polypectomy is offered for all lesions ≥ 6 mm, but 1-2 polyps (6-9mm) MAY BE FOLLOWED
- Polyps ≤ 5 mm are NOT REPORTED

FILTERING AT CTC

- Advanced adenomas are a tiny fraction of all polyps
- Selective polypectomy avoids large numbers of unneeded polypectomies, saving cost and risk
- Kim study showed equivalent numbers of advanced adenomas found despite nearly fivefold fewer polypectomies (561 vs. 2434) and less complications (0 vs. 7) CTC vs. OC

IS SURVEILLANCE SAFE?

- Progression from precursor to cancer takes many years
- Surveillance group (C-rads 2) risk of cancer is 0.1-1.0% which is less than the accepted 2% rate of breast cancer in mammography for the Birads 3 group

POLYP DECISION ANALYSIS

	≤ 5 mm	6-9mm	≥ 10 mm
10 YR. RISK CRC	0.08%	0.7%	15.7%
POLYPECT./ ADV. ADEN.	562	71	2.5
POLYPECT./ CRC	2,352	297	10.7
COST TO REMOVE ALL POLYPS/LFY R.	\$464,407	\$59,015	-\$151

Pickhardt, P, et al AAR 2008; 150:136

A COORDINATED SCREENING TEAM

- The CTC team should be responsible for insuring follow up scheduling and maintaining contact lists
- Review discordant cases regularly to delineate CTC false+ from OC false – and need for follow up
- Data tracking: nondiagnostic exams, advanced neoplasia prevalence rate, OC referral rate, and OC correlation rate
- Maintain reader skill and training
- Adopt a common lexicon (C-rads)
- National data registry

THANK YOU

