CT Colonography and CRC screening: an update

Andrea Laghi M.D.
Dept of Radiological Sciences, Oncology and Pathology
“Sapienza”, University of Rome
Polo Pontino – Latina
andrea.laghi@uniroma1.it
SCREENING

POPULATION

OPPORTUNISTIC
SCREENING

POPULATION

OPPORTUNISTIC
CTC in 2015

- The best radiological test for colon imaging
- Patient-friendly and safe
- Completely replacing BE
- Complimentary to CS
20th anniversary of CT Colonography

Presented by DJ Vining at ARRS meeting in 1994

1997: SINGLE-SLICE CTC
2014: MULTISLICE CTC
European society of gastrointestinal and abdominal radiology (ESGAR): Consensus statement on CT colonography

The second ESGAR consensus statement on CT colonography

Emanuele Neri · Steve Halligan · Mikael Hellström · Philippe Lefere · Thomas Mang · Daniele Regge · Jaap Stoker · Stuart Taylor · Andrea Laghi · ESGAR CT Colonography Working Group
1. Bowel prep
2. Colon distention
3. CT scanning
4. Image reviewing
TECHNIQUE: BOWEL PREP

Laxative-free

Low-fiber diet

Reduced prep

1L PEG
4 tablets bysacodil

Iopamidol
Diatrizoate meglumine

80mL + 80mL

90mL
REDUCE PREP/LAXATIVE-FREE

- Partial cleansing (due to osmolarity)
- Iodine-tagged residual fluids and stools
1) Identification of “submerged” lesions
2) Characterization of tiny polyps
TECHNIQUE

- No SEDATION
- Colon distention (room air/CO₂)
- Two 10s scans
- Overall time, 15 min
COMPUTED ASSISTED DIAGNOSIS

- Software for automatic detection of polyp candidates

2nd read CAD is recommended because it increases sensitivity for polyp detection without an unacceptable decrease in specificity.

- Reduce perceptual errors (≈50%)
- Reduce interobserver variability
Clinical indications for computed tomographic colonography: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) Guideline

Cristiano Spada, Jaap Stoker, Onofre Alarcón, Federico Barbaro, Davide Bellini, Michael Brethauer, Margriet C. De Haan, Jean-Marc Dumonceau, Monika Ferlitsch, Steve Halligan, Emma Helbren, Mikael Hellstrom, Ernst J. Kuipers, Philippe Lefere, Thomas Mang, Emanuele Neri, Lucio Petruzziello, Andrew Plumb, Daniele Regge, Stuart A. Taylor, Cesare Hassan, Andrea Laghi

Authors

Institutions

Institutions are listed at the end of article.
ESGE/ESGAR do not recommend CTC as a primary test for population screening or in subjects with a first-degree positive family history (EL: Moderate; RG: Weak)
EFFICACY
ACCEPTABILITY
SAFETY
COST-EFFECTIVENESS
LOGISTICS
CTC AND POPULATION CRC SCREENING

- EFFICACY
- ACCEPTABILITY
- SAFETY
- COST-EFFECTIVENESS
- LOGISTICS
### CTC: THE EVIDENCES

<table>
<thead>
<tr>
<th>RCT</th>
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- **CTC = CS for CRC and >10 mm polyps**
- **CTC < CS for 6-9 mm polyps**
- **CTC << CS for <6 mm polyps**
### CTC: THE EVIDENCES

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- **CTC > FS** (only left colon)
- **CTC >> FOBT** (cancer only)
CTC AND POPULATION CRC SCREENING

• EFFICACY
• ACCEPTABILITY
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CTC AND POPULATION CRC SCREENING

- Exam ACCEPTABILITY influences subjects adherence to screening

FOBT adherence: ITALY

<table>
<thead>
<tr>
<th>Region</th>
<th>Adherence</th>
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<tbody>
<tr>
<td>Nord</td>
<td>50.9</td>
</tr>
<tr>
<td>Centro</td>
<td>49.9</td>
</tr>
<tr>
<td>Sud-Isole</td>
<td>38.6</td>
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Data courtesy of dr Carlo Senore, CPO, Piedmont, Italy
CTC AND POPULATION
CRC SCREENING

2009

9%
CTC AND POPULATION
CRC SCREENING

EFFICACY

ADHERENCE

EFFICIENCY
(CRC prevention rate)
COLONOSCOPY

76% × 9% = 7%

CT COLONOGRAPHY

62% × 34% = 21%
Participation and yield of colonoscopy versus non-cathartic CT colonography in population-based screening for colorectal cancer: a randomised controlled trial

Esther M Stoop*, Margriet C de Haan*, Thomas R de Wijkerslooth, Patrick M Bossuyt, Marjolein van Ballegooijen, C Yung Nio, Marc J van de Vijver, Katharina Biermann, Maarten Thomeer, Monique E van Leerdam, Paul Fockens, Jaap Stoker, Ernst J Kuipers, Evelien Dekker

www.thelancet.com/oncology  Published online November 15, 2011  DOI:10.1016/S1470-2045(11)70283-2
Protéus trial
RCT: FS vs CS

- **CTC:** 30.4%
- **FS:** 27.0%
- Male uptake of CTC higher than FS (OR, 1.6; 95% CI: 1.1-2.3; P=0.01)

Regge D et al, data presented at ECR 2015
• “Unfair” comparison between a well-established test and a “new-comer” in a region where population-based CRC screening using FS works

Segnan N et al, SCORE trial, JNCI 2011

Regge D et al, data presented at ECR 2015
• Further “marketing” of CTC (PCP; public opinion)

• Among CTC invitees, the following key groups were more likely to uptake screening:
  - male (ORs, 2.4; 95% CI: 1.4-4.1)
  - retired (ORs, 2.10; 95% CI: 1.2-2.7)
  - those asking general practitioner for counseling (ORs, 2.6; 95% CI: 1.3-5.4)
  - those having friends/relatives with CRC (ORs, 4.1; 95% CI: 1.6-10.9)
  - those who have read information material (ORs, 7.3; 95% CI: 2.6-19.2)
PROTEUS TRIAL: OPEN ISSUES

• Unexplained higher adherence in males

• Participation rate in males is **HIGHER** (opposite to FS trial)
  • Why?
  • Are males more scared of an endoscope?
  • Or are they simply more interested in technological innovations?

Regge D et al, data presented at ECR 2015
• Bowel preparation and level of embarrassment in favor of FS
Patient’s experience

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<tr>
<th>Bowel preparation side effects</th>
<th>FS</th>
<th>CTC</th>
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<tr>
<td>None/very mild</td>
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<td>171</td>
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<td>80.3%</td>
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<td>Mild</td>
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<td>22</td>
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<td>12.4%</td>
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</tr>
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<td>Moderate / severe</td>
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**1. Preparation needs to be improved**

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<th>Level of pain *</th>
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**19 vs 27%**

*1=none, 5=very high

** OR (TCT vs FS): 2.77; 95%CI:1.52-5.01

*** OR (TCT vs FS): 0.59; 95%CI:0.37-0.91
## Patient’s experience

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### Level of anxiety *

11. CT room setup is probably not adequate for screening

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### Level of Embarassment *

** OR (TCT vs FS): 2.77; 95%CI:1.52-5.01

0.59; 95%CI:0.37-0.91

16 vs 26%
CTC AND POPULATION CRC SCREENING

- EFFICACY
- ACCEPTABILITY
- SAFETY
- COST-EFFECTIVENESS
- LOGISTICS
SAFETY

• Radiation exposure
• Complications (perforations)
• Current recommendations
  • Reasonably low-dose exam
  • Total effective dose: ≈ 5 mSv

2nd ESGAR Consensus Statement on CTC

• Benefits clearly outweigh radiation risks

Risk/benefit: 1:24 / 1:35

Berrington de Gonzalez, AJR, 2010
• New technology (ITERATIVE algorithm)
• Dose exposure lower than natural background

Annual radiation background  ≈2.5-3.0 mSv
CTC (iterative recon)        ≈1.5 mSv
RADIATION EXPOSURE

• Carcinogenic risk of low-dose radiation exposure is neither demonstrated nor scientifically demonstrable.

• Beyond LNT, other theories do exist.

Radiation Dose-Response Models

There is substantial and convincing scientific evidence for health risks following high-dose exposures. However, below 5–10 rem (which includes occupational and environmental exposures), risks of health effects are either too small to be observed or are nonexistent.
Some facts

Among airline cabin crew in Europe, there was no increase in mortality that could be attributed to cosmic radiation or other occupational exposures to any substantial extent.
Iterative Reconstruction: CTC

**ASIR 50%**
- $kV = 100$
- $mAs = 25$
- $mSv = 0.75$

**FBP**
- $kV = 120$
- $mAs = 50$
- $mSv = 2.32$
Meta-analysis >100,000 patients

CTC, 0.02% vs CS, 0.03%

- CS data are underestimated
- Surgical rate: CTC, 0.008% (1:12,500)  
  CS, 100%
- NO CTC-related deaths
CTC AND POPULATION
CRC SCREENING

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### COST/EFFECTIVENESS OF CTC

<table>
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<tr>
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<th>Follow-up Interval</th>
<th>Sensitivity for Cancer, Specificity</th>
<th>Test Costs</th>
<th>Dominant vs.</th>
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<td>Hassan, 2007 (44)</td>
<td>10 years, all findings</td>
<td>95, 86</td>
<td>97 FSIG, COL</td>
<td>CS</td>
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<td>Ladabaum, 2004 (53)</td>
<td>10 years, all findings</td>
<td>95, 85</td>
<td>1,037 COL</td>
<td>36,300</td>
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<td>Pickhardt, 2007 (19)</td>
<td>10 years, findings 6+ mm</td>
<td>95, 86</td>
<td>555 FSIG, COL</td>
<td>CS</td>
</tr>
<tr>
<td>Sonnenberg, 2000 (54)</td>
<td>10 years, all findings</td>
<td>80, 95</td>
<td>741 COL</td>
<td>17,800</td>
</tr>
<tr>
<td>Vijan, 2007 (23)</td>
<td>5 years, all findings</td>
<td>91, 91</td>
<td>707 gFOBT, COL, FSIG, FSIG + gFOBT</td>
<td>10,300–21,800</td>
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<tr>
<td>Zauber, 2009 (MISCAN) (22)</td>
<td>5 years, findings 6+ mm</td>
<td>84–92, 80–88</td>
<td>522 gFOBT, SENSA, COL, FSIG, FIT, FSIG + gFOBT</td>
<td>9,500–10,200</td>
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<td>1,900–2,100</td>
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CTC dominated by CC, FSIG + gFOBT
Dutch costs of CT-screening were substantially lower than the cost assumptions that were used in published cost-effectiveness analyses on CTC screening.

Average costs per participant: €169.40
CTC AND POPULATION
CRC SCREENING

• EFFICACY
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• LOGISTICS
Projected impact of colorectal cancer screening with computerized tomographic colonography on current radiological capacity in Europe

C. HASSAN*, A. LAGHI†, P. J. PICKHARDT‡,§, D. H. KIM‡, A. ZULLO*, F. IAFRATE† & S. MORINI*

28,760,130 European population (30% compliance)

3,482 available CT units

START-UP PERIOD
6.6 CTC/CT unit/day

STEADY STATE
4.3 CTC/CT unit/day
That's all Folks!
ESGE/ESGAR strongly recommend CTC in the case of positive FOBT/FIT with incomplete or unfeasible CS within organized population screening programs. (RG: Strong; EL: Low).

Se for >6 mm polyps is 89%
Sp is lower, 75%
“CTC is a good alternative if CS is undesirable”

Plumb AA et al. Eur Radiol 2014
CTC: integration into FOBT-based CRC screening programs

- Patients with +FOBT/FIT refusing CS

Data courtesy of dr Carlo Senore, CPO, Piedmont, Italy

SCREENING

POPULATION

• EFFICACY
• SAFETY

OPPORTUNISTIC
ESGE/ESGAR …suggest (CTC) as a CRC screening test on an individual basis providing the screenes are adequately informed about test characteristics, benefits and risks. (EL: Moderate ; RG: Weak )
Colon and rectal cancer

Beginning at age 50, both men and women at average risk for developing colorectal cancer should use one of the screening tests below. The tests that are designed to find both early cancer and polyps are preferred if these tests are available to you and you are willing to have one of these more invasive tests. Talk to your doctor about which test is best for you.

Tests that find polyps and cancer

- flexible sigmoidoscopy every 5 years*
- colonoscopy every 10 years
- double contrast barium enema every 5 years*
- CT colonography (virtual colonoscopy) every 5 years*

Tests that mainly find cancer

- fecal occult blood test (FOBT) every year*,**,
- fecal immunochemical test (FIT) every year*
- stool DNA test (sDNA), interval uncertain*
President Obama Gets Virtual Colonoscopy (CT Colonography) Coverage to Seniors

Medicare Should Cover Screening CT Colonography for Older Americans Who Want It WASHINGTON, March /PRNewswire-USNewswire/ -- President Obama, in his first routine physical exam as commander in chief, received a CT colonography (CTC), commonly known as a virtual colonoscopy, to screen him for colorectal cancer. However, Obama Administration officials at the Centers for Medicare and Medicaid Services (CMS) previously denied coverage of the same exam for seniors enrolled in Medicare, cutting off access for many an exam proven to increase compliance with nationally accepted colon cancer...
CONCLUSIONS

- **CTC CANNOT** be proposed as a *population screening* test today
  - Recommendations from EU are for FOBT/FIT
  - Missing data on cost/effectiveness
  - Shortage of radiologists and equipments??

- **CTC CAN** be integrated in a *population screening* programme based on FOBT/FIT
  - To replace BE in pts with +FOBT/FIT and incomplete CC
  - To investigate pts with +FOBT/FIT who refuse CC
CONCLUSIONS

- CTC is effective, acceptable and safe as an **opportunistic** screening test
  - asymptomatic, average-risk subjects; starting @ age 50; time interval, 5 yrs