

La colon-TAC: accurata, ma applicabile come screening di massa?

Daniele Regge

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VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR
Gruppo
Italiano
Screening
ColoRettale

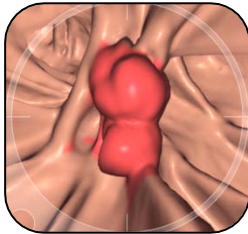
ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

Timeline

- 2001 the idea... (CTC as a screening test). Radiologist idea!
- 2002 software development. Computer scientists.

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform

New test



Software development

Clinical validation

Timeline

- 2001 the idea... (CTC as a screening test). Radiologist idea!
- 2002 software development. Computer scientists.
- 2004 the first trial... Many radiologists....

Clinical validation (IMPACT trial)

Diagnostic Accuracy of Computed Tomographic Colonography for the Detection of Advanced Neoplasia in Individuals at Increased Risk of Colorectal Cancer

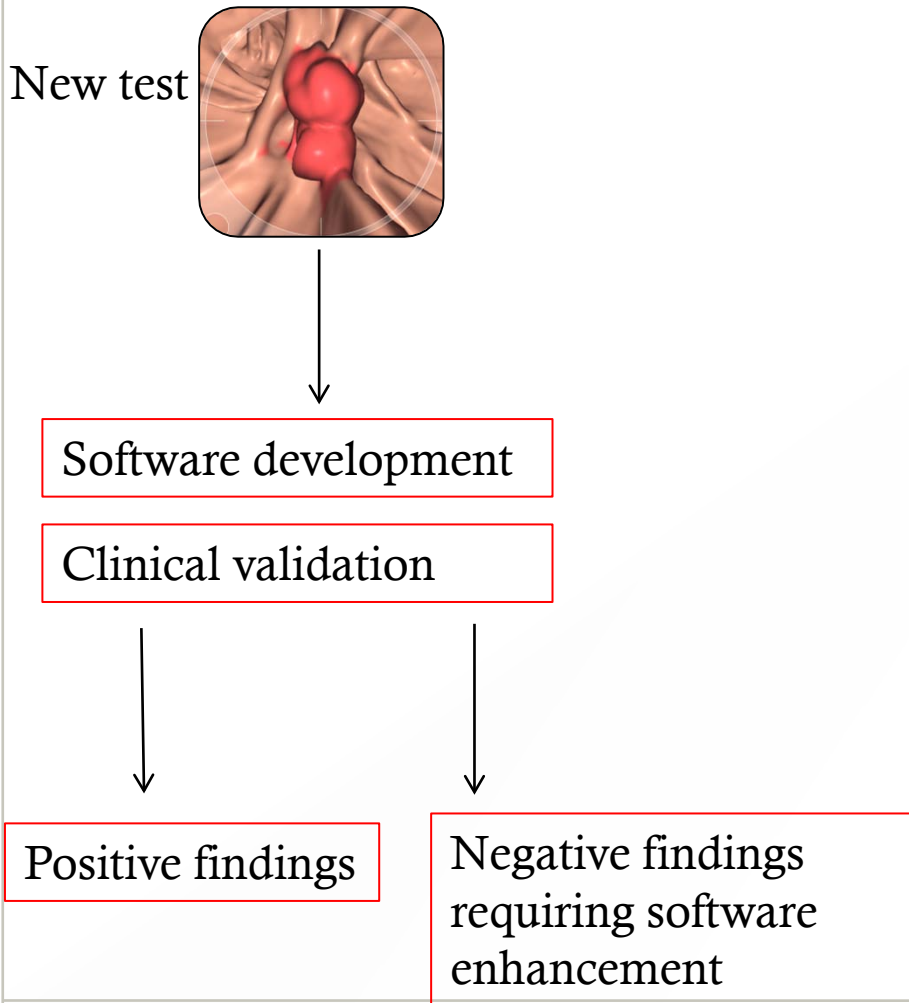
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 Andrea Laghi, MD
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 Carlo Senore, MD
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 JAMA. 20

Table 6. Per-Polyp Analysis of the Sensitivity of CT Colonography for the Detection of Advanced Adenoma and Cancer^a

| | Size | | |
|-----------------------------|------------------|------------------|------------------|
| | ≥6 mm | ≥10 mm | 6-9 mm |
| Advanced adenoma | | | |
| Sensitivity, % (95% CI) | 72.0 (65.0-78.2) | 80.3 (72.2-87.0) | 56.7 (44.0-68.8) |
| Detected lesions | 136 | 98 | 38 |
| No. of lesions | 189 | 122 | 67 |
| Carcinoma | | | |
| Sensitivity, % (95% CI) | 95.5 (84.5-99.4) | 95.1 (83.5-99.4) | 100 (36.8-100) |
| Detected lesions | 42 ^b | 39 ^b | 3 |
| No. of lesions | 44 | 41 | 3 |
| All advanced lesions | | | |
| Sensitivity, % (95% CI) | 76.4 (70.3-81.6) | 84.1 (77.3-89.1) | 58.6 (46.2-70.0) |
| Detected lesions | 178 | 137 | 41 |
| No. of lesions | 233 | 163 | 70 |

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform



| Measure | Result | |
|---------------------------------------|--------|--------|
| Sensitivity (≥ 10 mm lesions-%) | 85 | Green |
| PPV (≥ 6 mm-%) | 50 | Yellow |
| Sensitivity (6-9 mm lesions-%) | 60 | Red |
| Reporting time (min) | 20 | Red |



Double reading unfeasible

Timeline

- 2001 the idea... (CTC as a screening test). Radiologist idea!
- 2002 software development. Computer scientists.
- 2004 the first trial... Many radiologists....
- 2006 CAD development and validation.... Computer scientists and many radiologists...

Computer Aided Detection

i CAD-COLON COMPUTER AIDED DETECTION

im3D MEDICAL IMAGING LAB

PATIENT
NOME E COGNOME: GRILL IUGNE SUSANNA
ID: GRILL IUGNE SUSANNA
DATA ESAME: 2007-03-23
ORF. ESAME: 12-05:27

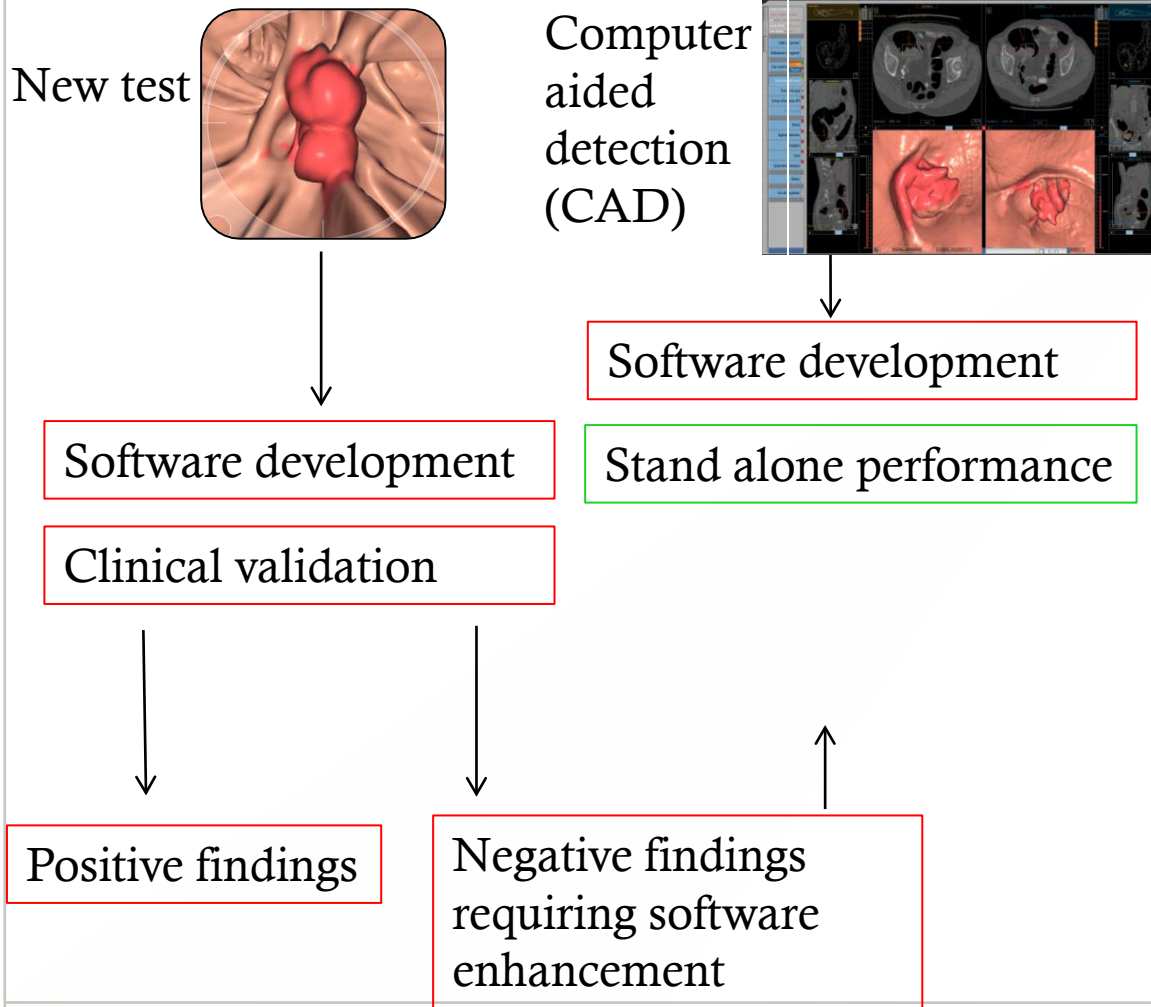
REPORT
Sceita del paziente
Ordinamento dei segmenti
Zone sospette: **CAD** / Manuali
Sottrazione elettronica
Finestra dei grigi
Lettura attenuazione ROI
Piani di taglio
Misura
Aggiungi marcatura
Fotografia
Zoom
Spostamento immagine
Referto
Esci dal programma

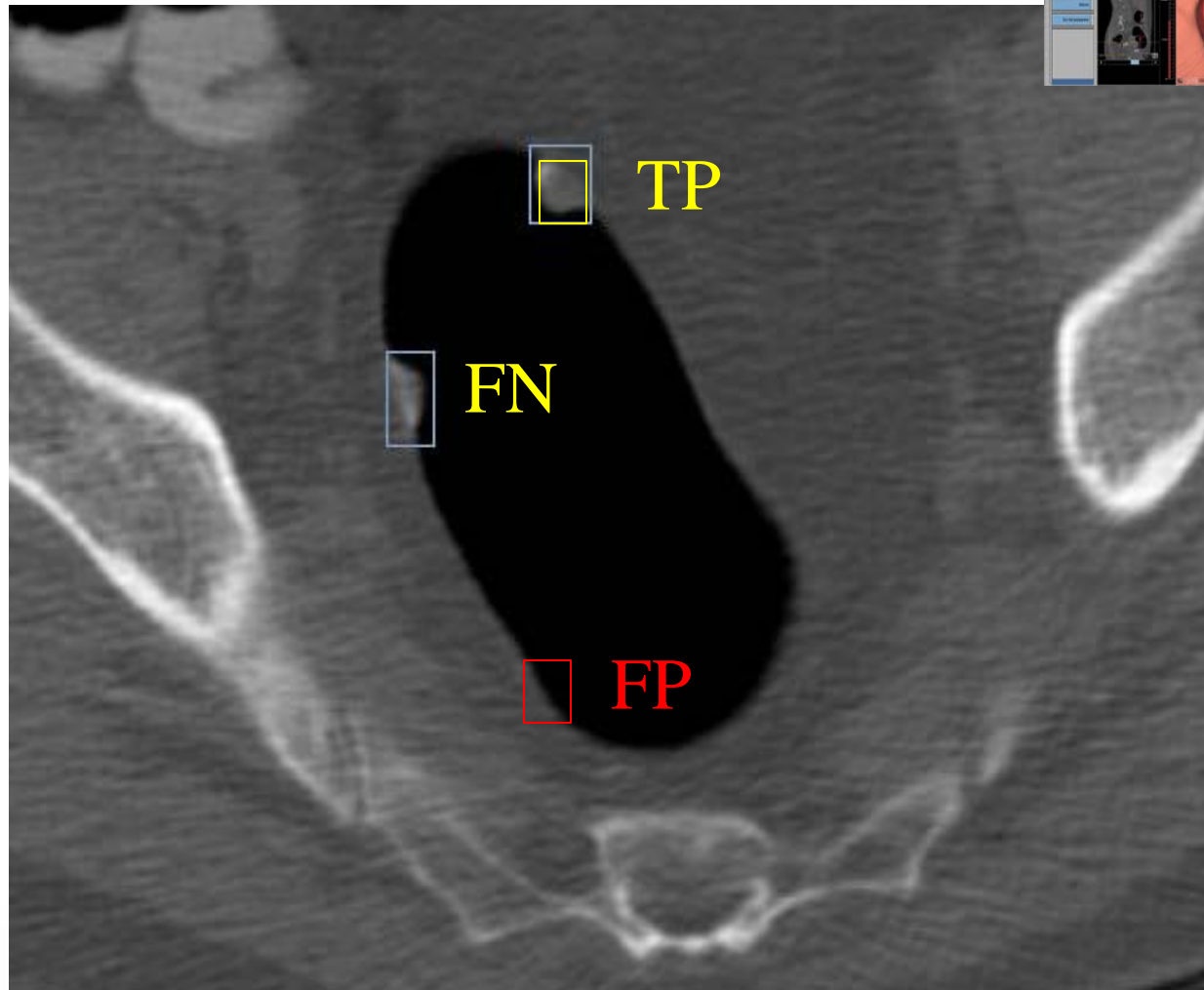
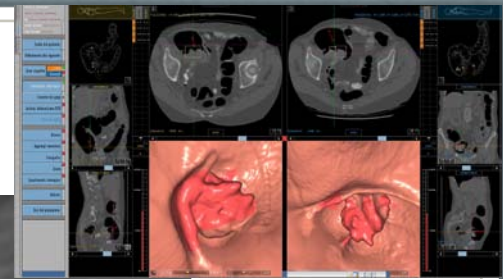
PRONE
ASSIALE: Posizione: x=194 y=93 z=265 mm
CORONALE: Densita': -856 Hu
SAGITTALE: Densita': -856 Hu

ASSIALE
ASSIALE: Posizione: x=109 y=140 z=279 mm
CORONALE: Densita': 148 Hu
SAGITTALE: Densita': 148 Hu

SUPINE
CORONALE
SAGITTALE

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform





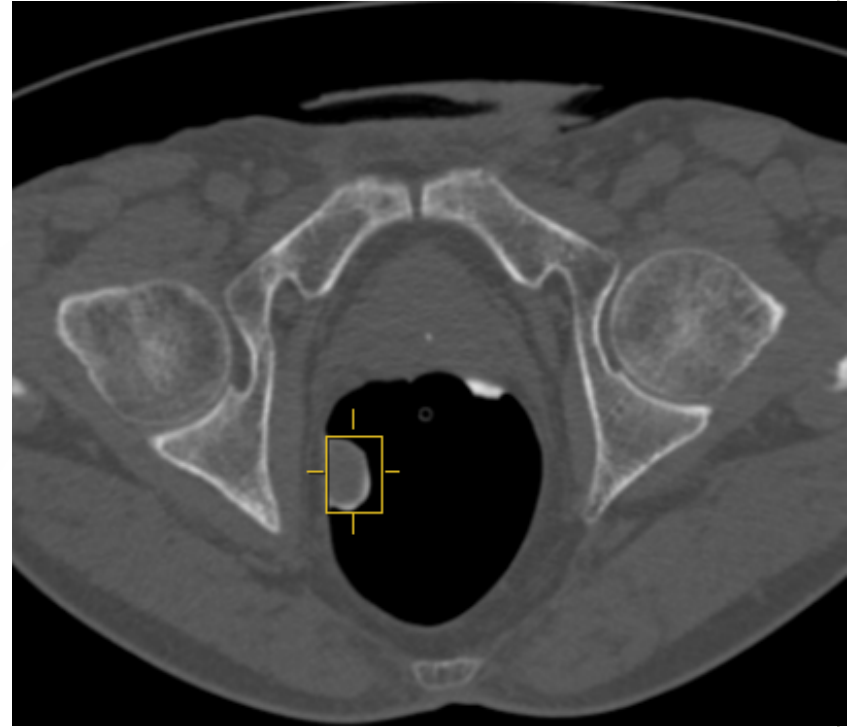
Stand-alone CAD performance

| | Number of patients (Number of polyps) | Sensitivity per polyp \geq 10 mm (%) | FPs per patient | Fecal tagging |
|--|--|---|-----------------|---------------|
| Yoshida, Radiographics 2002 | 71 (35) | 21/23 (91) | 2 | No |
| Mani, JCAT 2004 | 41 (69) | 10/12 (83) | ND | No |
| Bogoni, Br J of Radiology 2005 | 62 (39) | 10/10 (100) | 8 | No |
| Summers, Gastroenterology 2005 | 792 (173) | 25/28 (89.3) | 7.9 – 2.1 | Yes |
| Halligan, Clin Radiol 2006 | 25 (57) | 9/10 (90) | ND | Yes |
| Taylor, AJR 2006 | 25 (32) | 11/12 (92) | 13 | No |
| Taylor, Radiology 2006 | 20 (43) | 9/9 (100) | ND | Yes |
| Halligan, Gastroenterology 2006 | 167 (142) | 17/19 (89.5) | 11.6 | No |
| Taylor, Radiology 2007 | 25 (69) | 18/19 (95) | 19 | No |
| Mang, Eur Radiology 2007 | 52 (55) | 24/25 (96) | 1.7 | No |
| Petrick, Radiology 2008 | 60 (24) | 5/5 (100) | ND | Yes |
| Summers, AJR 2008 | 104 (86) | 43/47 (91.5) | 9.6 | Yes |
| Regge Radology 2013 | 618 (256) | 230/256 (90%) | 14 | Yes |

How to use CAD



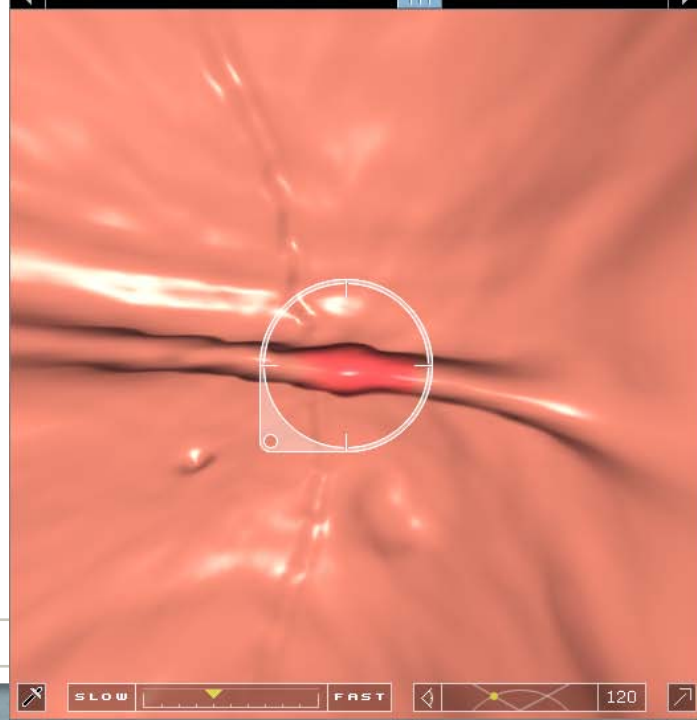
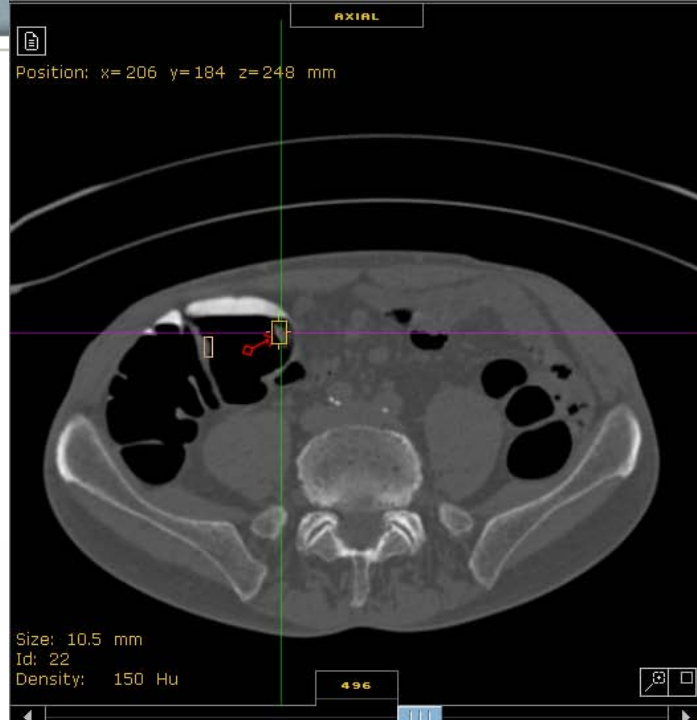
?



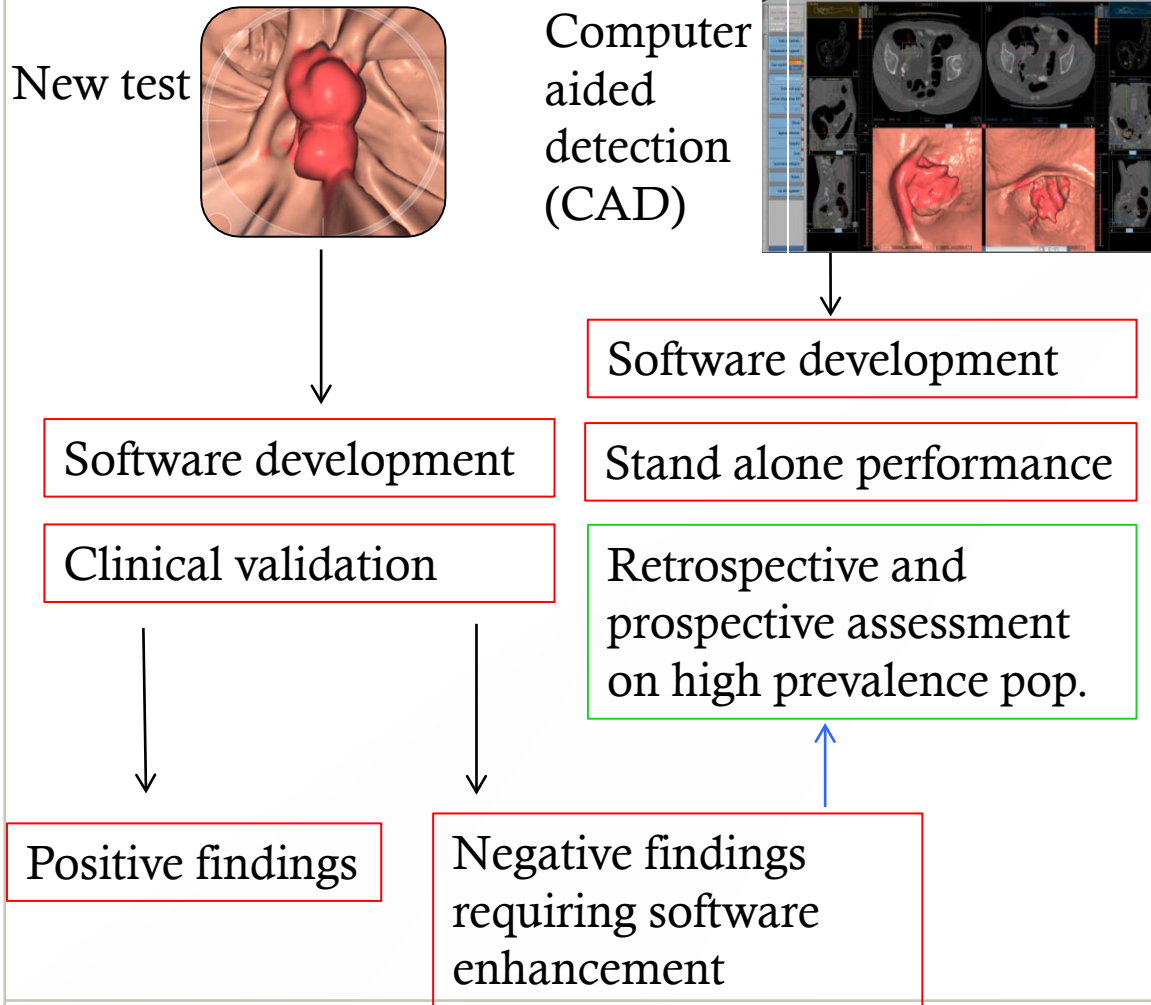
2° Reader



| TYPE | DISTANCE | DIAMETER |
|------|----------|----------|
| P | 5.4 | 23.0 |
| C | 27.6 | 7.9 |
| C | 45.7 | 3.0 |
| C | 102 | 5.0 |
| C | 130 | 8.6 |
| C | 155 | 8.0 |
| C | 155 | 3.3 |
| C | 160 | 10.5 |
| C | 161 | 9.9 |
| C | 162 | 11.2 |



A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform



Efficacy of Computer-aided Detection as a Second Reader for 6–9-mm Lesions at CT Colonography: Multicenter Prospective Trial¹

Purpose:

To assess the effect of computer-aided detection (CAD) as a second reader on the sensitivity and specificity of computed tomographic (CT) colonography in detecting 6–9-mm colorectal cancer (CRC) lesions.

**Materials and
Methods:**

Individuals with clinical indications for colonoscopy—either for symptoms or as part of participating in a surveillance

Table 2**Per-Patient CT Colonography Performance according to Reading Modality and Lesion Size**

| Parameter and Lesion Size (mm) | Unassisted Reading | CAD-assisted Reading | PValue |
|--------------------------------|-----------------------------|-----------------------------|---------------|
| Sensitivity | | | |
| ≥6 | 130/154 (84.4) [77.7, 89.8] | 136/154 (88.3) [82.2, 92.9] | .016 |
| 6–9 | 34/52 (65.4) [50.9, 78.0] | 40/52 (76.9) [63.2, 87.5] | .016 |
| ≥10 | 96/102 (94.1) [87.6, 97.8] | 96/102 (94.1) [87.6, 97.8] | Not estimable |
| Specificity for lesions ≥ 6 mm | 426/464 (91.8) [88.9, 94.1] | 422/464 (90.9) [88.0, 93.4] | .063 |

Note.—Sensitivities and specificities for lesion detection are expressed as number of lesions/total number of lesions, with percentages in parentheses and corresponding 95% CIs in brackets. Nonadenomatous lesions were included.

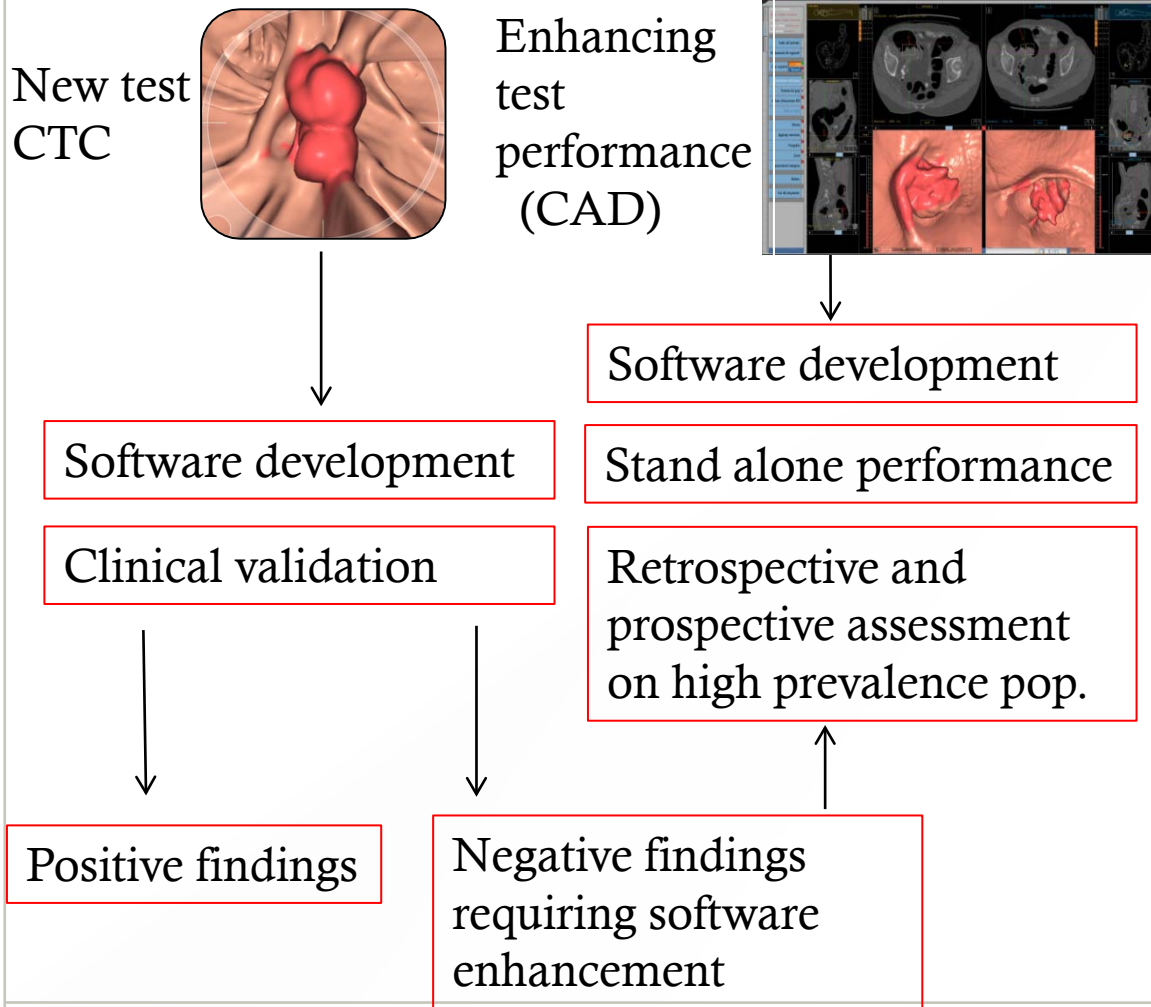
Per-lesion sensitivity / Reporting time

| Trial | Sensitivity (≥6 mm) | Sensitivity (≥10 mm) | Sensitivity (6-9 mm) | Reading time (min) |
|------------------------------|---------------------|----------------------|----------------------|--------------------|
| IMPACT | 136/189 (72%) | 98/122 (80%) | 38/67 (57%) | 18 |
| CAD - IMPACT unassited | 89/120 (74%) | 52/57 (91%) | 37/63 (59%) | 5.8 |
| CAD - IMPACT assisted | 96/120 (80%) | 53/57 (93%) | 43/63 (68%) | Additional 1.5 |

↓
+ 9 %

↓
-10.5 min

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform

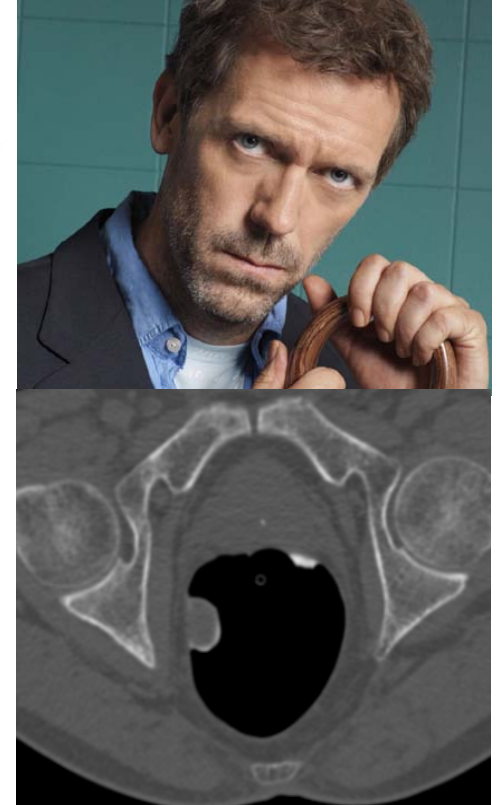
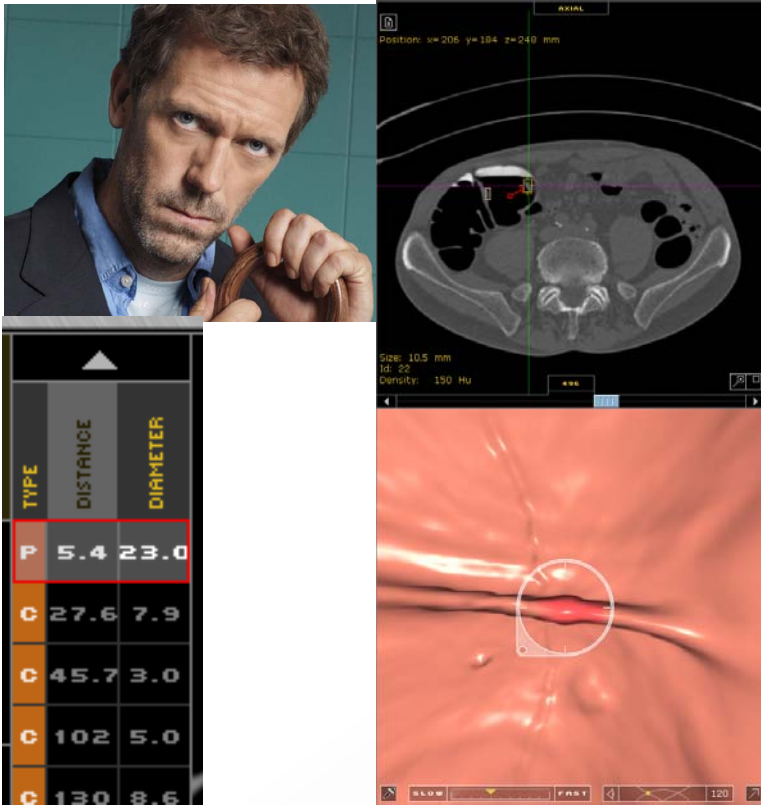


| Measure | Result | |
|---------------------------------------|--------|--|
| Sensitivity (≥ 10 mm lesions-%) | 94 | |
| PPV (≥ 6 mm-%) | 76 | |
| Sensitivity (6-9 mm lesions-%) | 77 | |
| Reporting time (min) | >7 | |

Timeline

- 2001 the idea... (CTC as a screening test). Radiologist idea!
- 2002 software development. Computer scientists.
- 2004 the first trial... Many radiologists....
- 2006 CAD development and validation.... Computer scientists and many radiologists...
- 2008 CTC primary test for screening Radiologists, computer scientists, epidemiologists and gastroenterologists (one in particular..)

CAD first reader



Fast unassisted read

Reviewing CT Colonography: Preliminary Assessment of a Double-Read Paradigm That Uses Computer-aided Detection as the First Reader¹

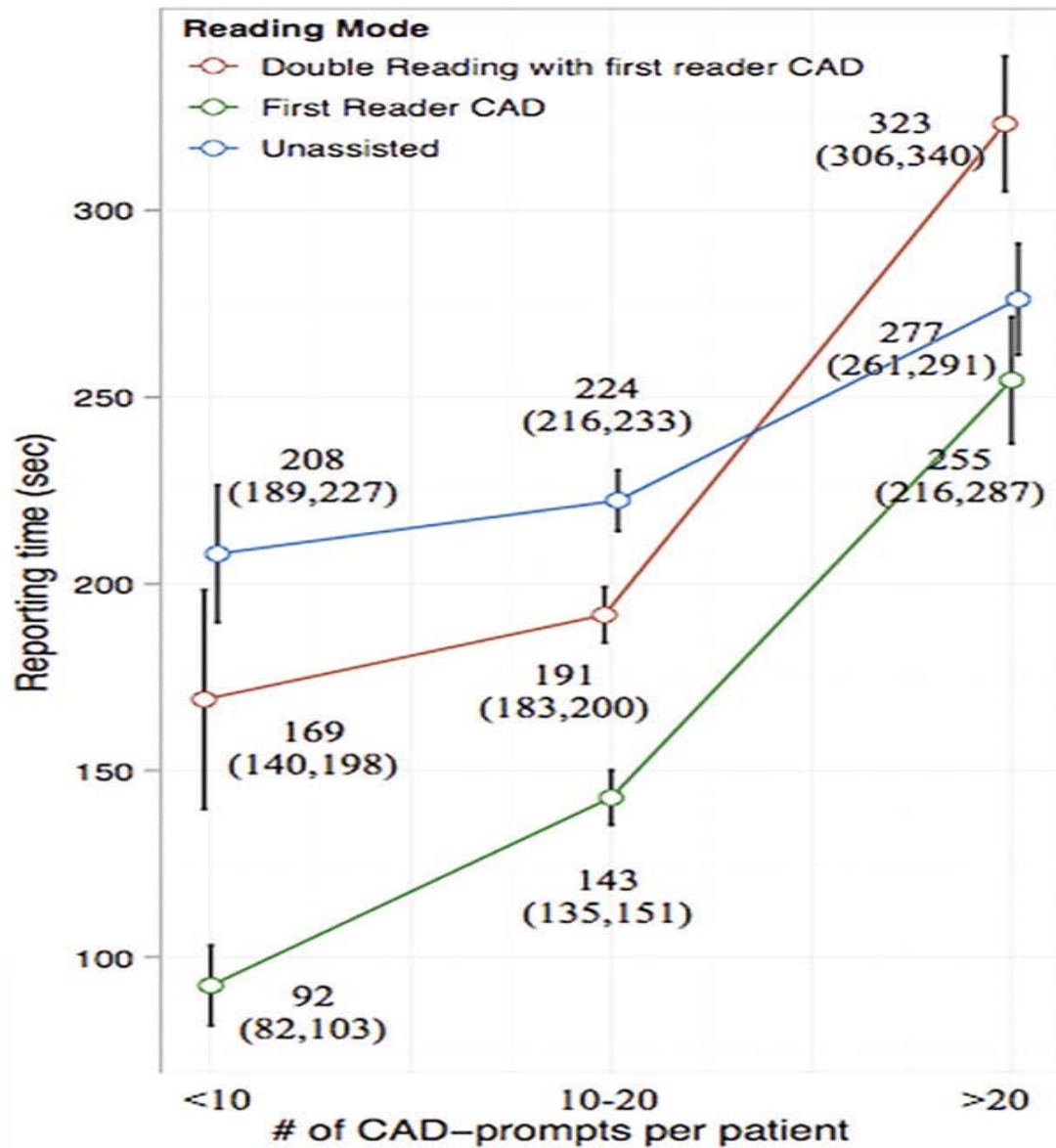
Gabriella Iussich, MD
Loredana Correale, PhD
Carlo Senore, MD
Nereo Segnan, MD
Andrea Laghi, MD
Franco Iafrate, MD
Delia Campanella, MD
Emanuele Neri, MD
Francesca Cerri, MD
Cesare Hassan
Daniele Regge, MD

Purpose:

To compare diagnostic performance and time efficiency of double-reading first-reader computer-aided detection (CAD) (DR FR CAD) followed by radiologist interpretation with that of an unassisted read using segmentally unblinded colonoscopy as reference standard.

Materials and Methods:

The local ethical committee approved this study. Written consent to use examinations was obtained from patients. Three experienced radiologists searched for polyps 6 mm or larger in 155 computed tomographic (CT) colonographic studies (57 containing 10 masses and 79 polyps ≥ 6 mm). Reading was randomized to either unassisted read or DR FR CAD. Data sets were reread 6 weeks later using the opposite paradigm. DR FR CAD consists of evaluation of CAD prompts, followed by fast two-dimensional review for mass detection. CAD sensitivity was calculated. Readers'



Lesion detection, per-patient

Double Reading Paradigms

| | CAD Second Reader | | CAD First Reader | |
|-----------------|-----------------------|-----------------------|-----------------------|-----------------------|
| | Unassisted reading | Radiologist + CAD | CAD | CAD + Radiologist |
| Sensitivity (%) | 80 (74/93) (70,87) | 86 (80/93) (77,92) | 85 (79/93) (75,91) | 89 (83/93) (81,95) |
| Specificity (%) | 92 (82/93) (82,97) | 90 (80/89) (82,95) | 93 (83/93) (86,97) | 91 (81/93) (83,96) |
| PPV (%) | 91 (74/81) (83,96) | 90 (80/89) (82,95) | 92 (78/84) (85,97) | 91 (83/91) (83,96) |
| AUC | 0.86 ± 0.04 | 0.90 ± 0.03 | 0.92 ± 0.02 | 0.94 ± 0.02 |

The difference in sensitivity between SR and DR with FR CAD was not statistically significant (P=0.5)
 Compared to the Unassisted reading, CAD increased sensitivity for both reading paradigm (P=0.03)
 For both CAD reading modes, the AUCs increased with CAD (P=0.02)

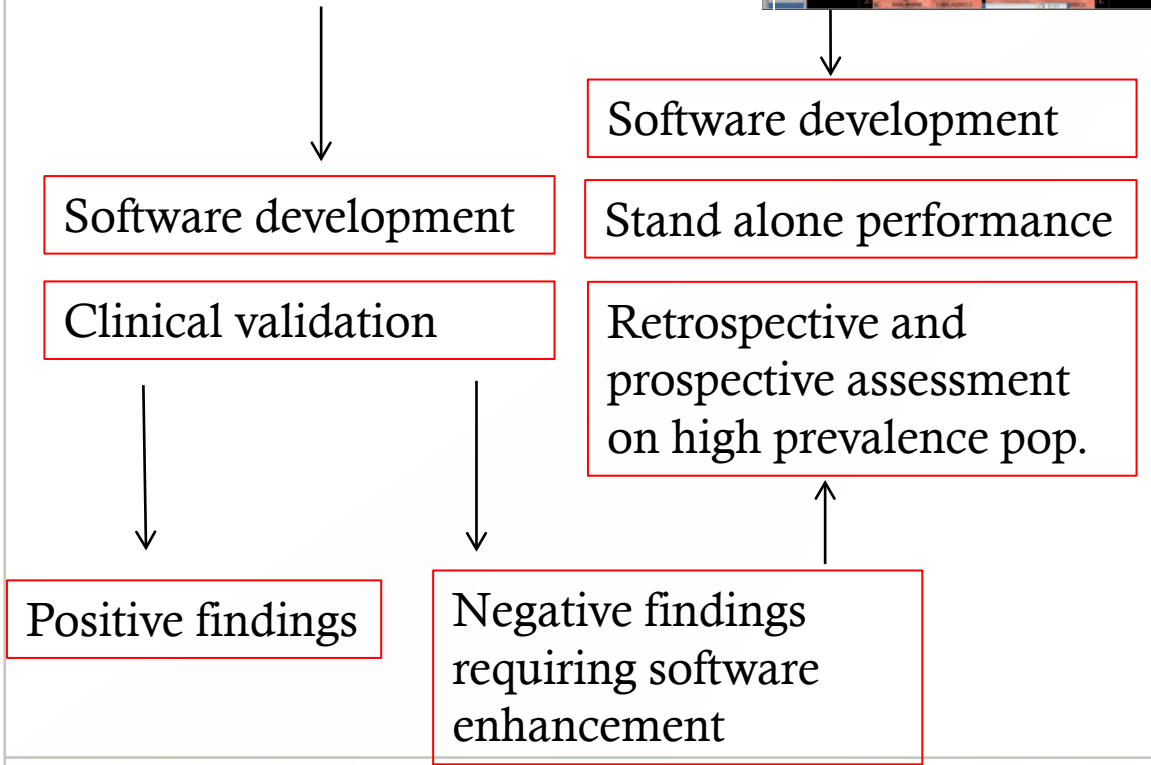
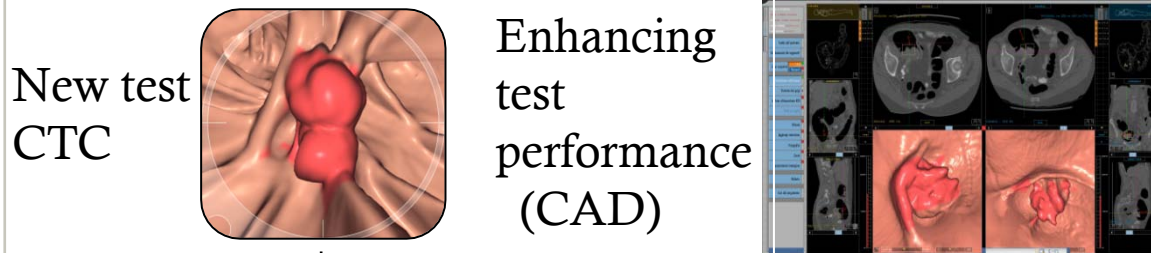
Reading time

Interpretation Time

| Reading Paradigm | Phase 1 | Phase II | TOT |
|--|--------------|--------------|--------------|
| Double reading CAD Second Reader | 318 ± 27 sec | 177 ± 20 sec | 495 ± 38 sec |
| Double reading CAD First Reader | 276 ± 20 sec | 108 ± 8 sec | 384 ± 22 sec |

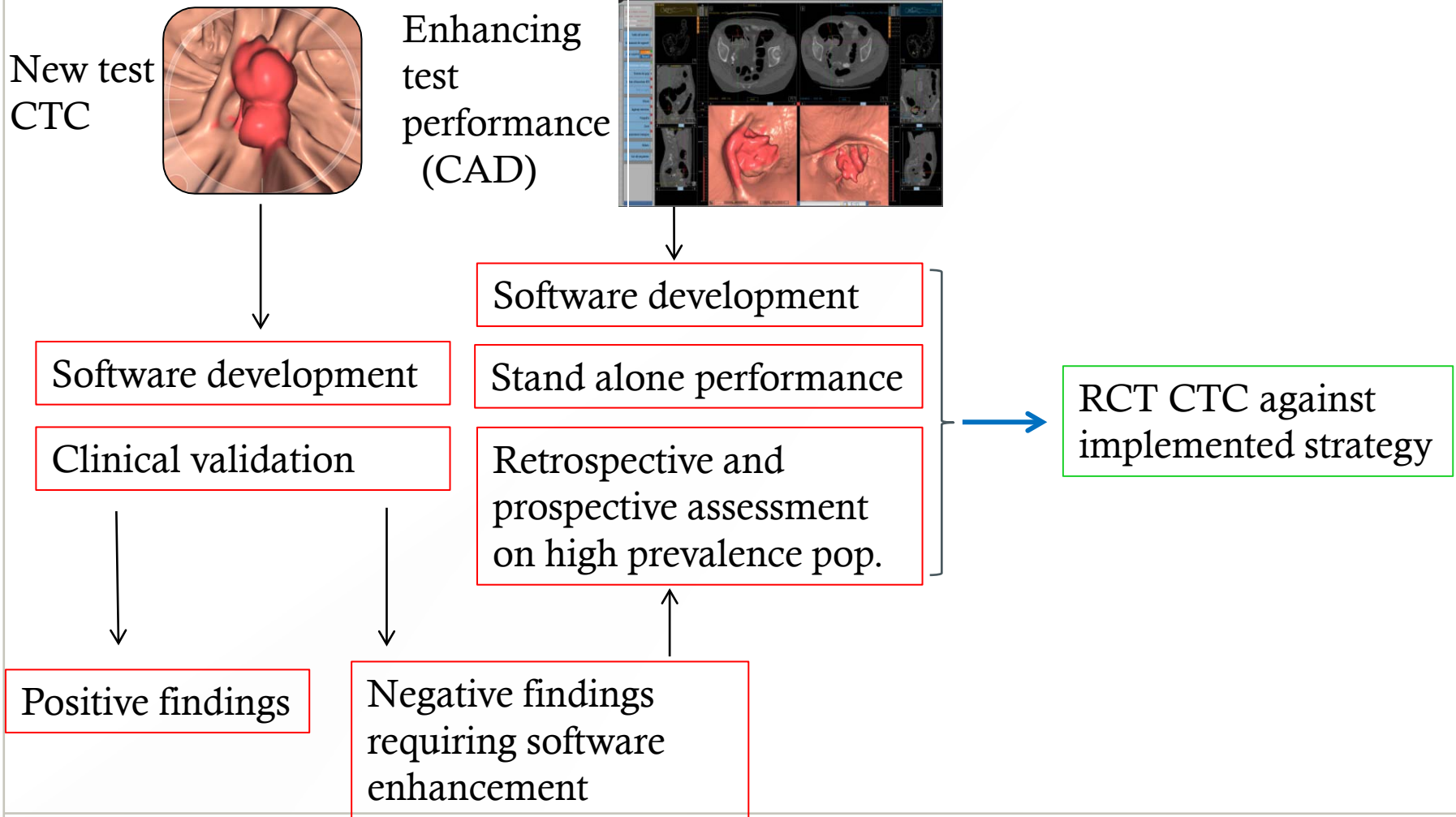
Double reading CAD FR reporting time was significantly shorter than double reader CAD SR (p=0.001)

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform

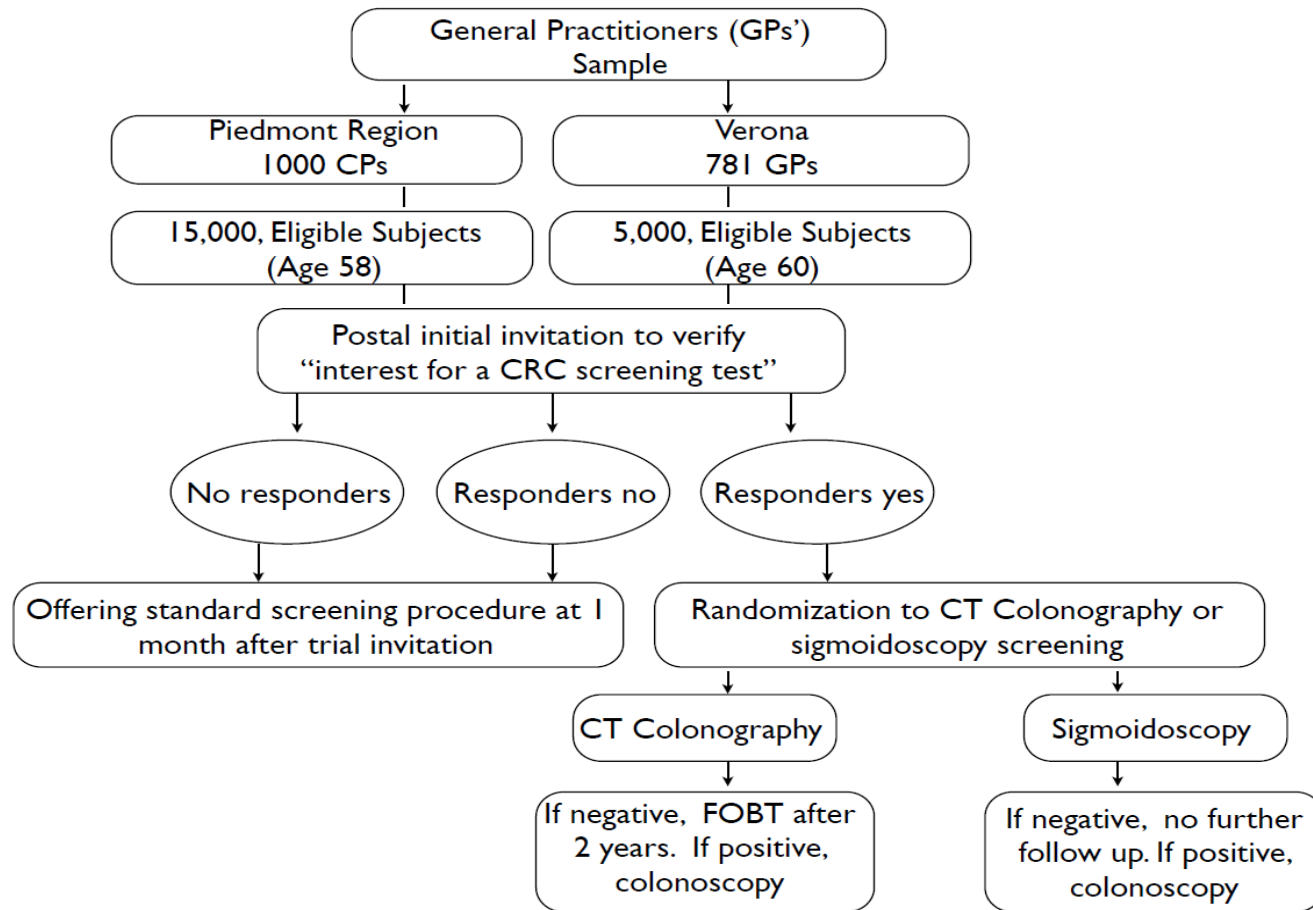


| Measure | Result | |
|---------------------------------------|--------|--|
| Sensitivity (≥ 10 mm lesions-%) | 94 | |
| PPV (≥ 6 mm lesions-%) | 76 | |
| Sensitivity (6-9 mm lesions-%) | 77 | |
| Reporting time (min) | 6 | |

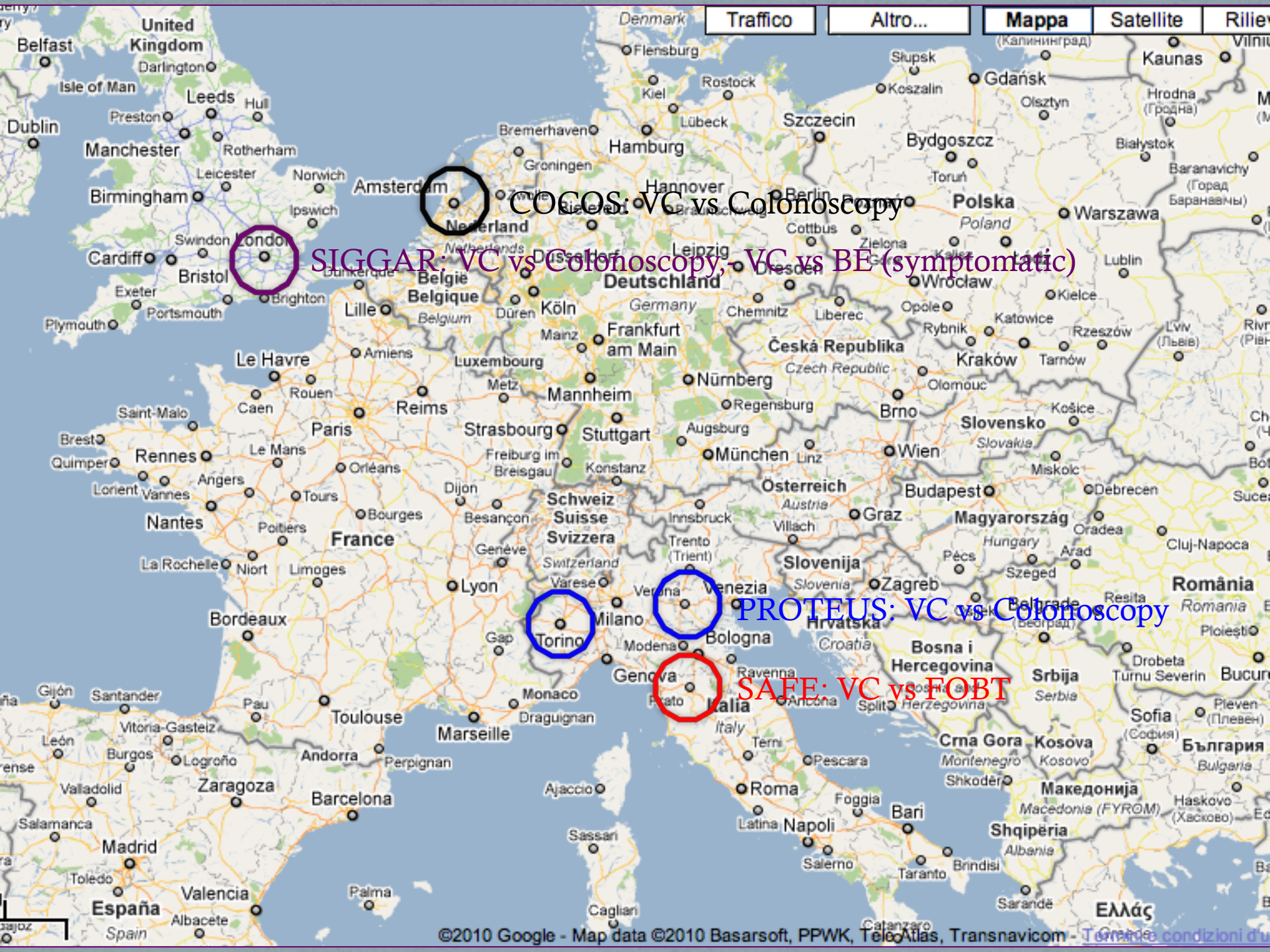
A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform



CTC vs sigmoidoscopy (RCT)







Traffico

Altro...

Mappa

Satellite

Rilievi

Randomized trials endpoints

| Trial name | Study type | Main end points | Referral to colonoscopy (lesion diameter) | Age of invitation (years) |
|-------------------------------------|--|--|--|--|
| <i>COCOS (Amsterdam /Rotterdam)</i> | Randomized controlled trial: OC versus CTC | Participation rate; diagnostic yield | ≥ 10 mm | 50-75 (average 61), not previously invited |
| <i>Protèus (Torino)</i> | Randomized controlled trial: FS versus CTC | Advanced neoplasia detection rate; participation to FS versus CTC | ≥ 6 mm | 58 years, not previously invited |
| <i>SAVE (Firenze)</i> | Randomized controlled trial: FOBT vs CTC versus OC | Advanced adenoma detection /referral rate, CTC versus 3 round FOBT; participation rate to FOBT, CTC and OC | ≥ 6 mm | 55-64 years, not previously invited |

Invitation procedures

| Trial name | End-point | Invitation procedure | Options to respond | Consultations |
|--|--|--|--|---|
| <i>COCOS (Amsterdam/Rotterdam)</i> | participation | Preannouncement, two weeks later invitation (leaflet, reply card), reminder after 4 weeks | Returning card, call centre, e-mail | Yes, by phone (< two weeks), eligibility assessment |
| <i>Protèus (Torino)</i> | participation | Letter (and leaflet) sent by mail, signed by GP to either CTC or FS, reminder after 4 weeks. | Call centre to confirm exam date or change date, eligibility assessment | If requested, by phone |
| <i>Protèus (Torino)</i> | advanced neoplasia detection rate | Letter (and leaflet) sent by mail, signed by GP, with invitation to enter study | Returning card or call center for exam reservation, eligibility assessment | If requested, by phone |
| <i>SAVE (Firenze)</i> | Advanced adenoma detection and participation | Letter (and leaflet) sent by mail, reminder after 3 months | Call centre, e-mail for appointment | Consultation with trained nurse, eligibility assessment |

Main results

| Trial name | End-point | Invitees/tested individuals | Participation rate | Referral to colonoscopy | PPV of CTC | Diagnostic yield for advanced neoplastic ($\geq 10\text{mm}$) |
|--------------------------------|--|-----------------------------|--------------------------------|--|------------------------------------|---|
| COCOS (Amsterdam/Rotterdam) | participation | 8844/ CTC=982 OC=1276 | 34% CTC, 22% colonoscopy | 9% (+ 8% with 6-9mm lesions offered f/u =17%) | 71% (60 TP/84 positives) | 1.5 per 100 invitees for colonoscopy, 2.0 for CTC |
| Protèus (Torino) | advanced neoplasia detection rate | 19662/ 1355 CTC arm | 14% into study | 10% | | |

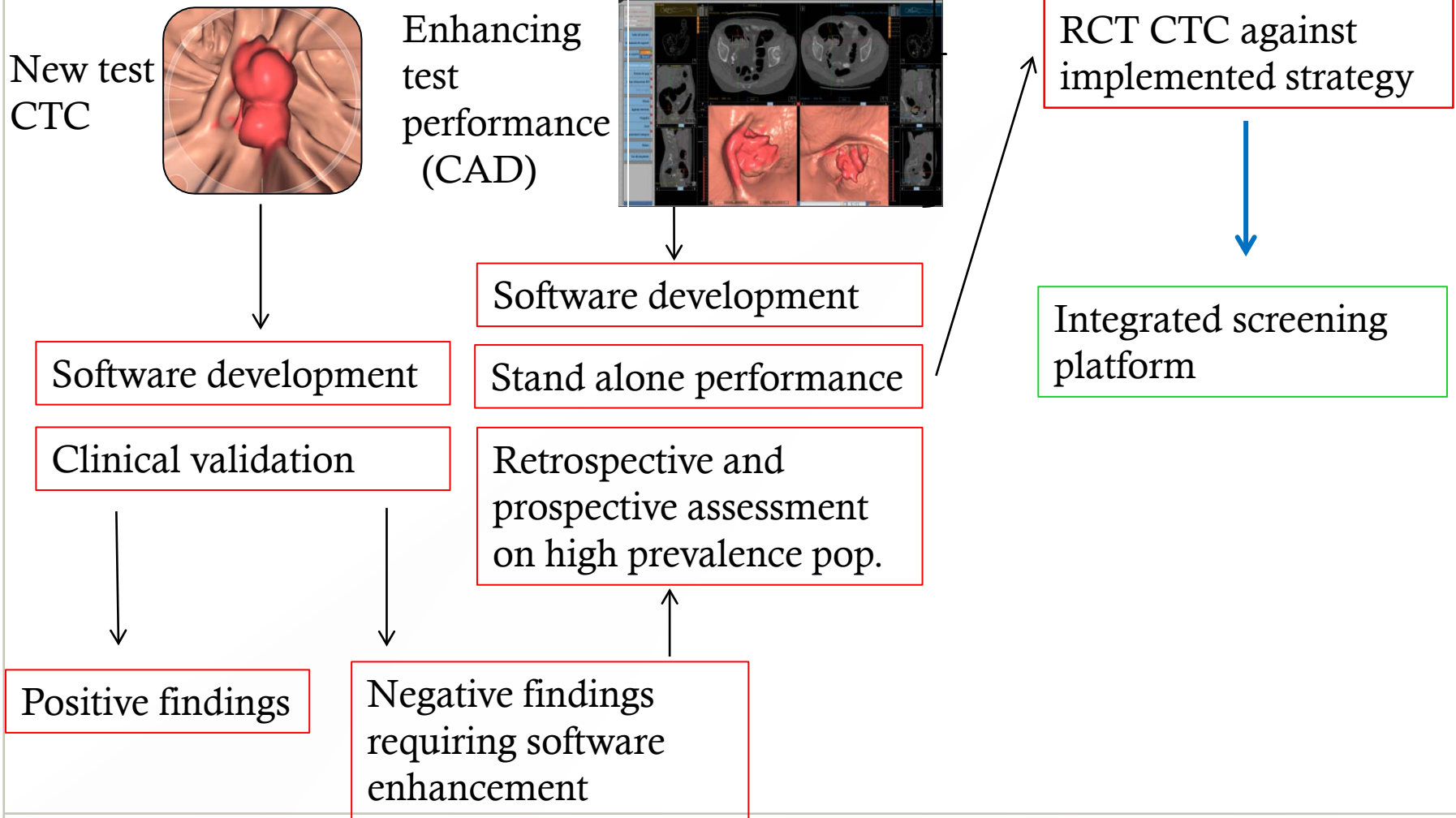
Most advanced lesion (per participant/per invitee)

| | Yield per 100 participants | | | Yield per 100 invitees | | |
|----------------------|----------------------------|-------------------------|---------|------------------------|---------------------------|---------|
| | Colonoscopy (n=1276) | CT colonography (n=982) | p value | Colonoscopy (n=5924) | CT colonography (n= 2920) | p value |
| Colorectal cancer* | 0.5 (7) | 0.5 (5) | 0.91 | 0.1 (7) | 0.2 (5) | 0.50 |
| Advanced adenoma | 8.2 (104) | 5.6 (55) | 0.02 | 1.8 (104) | 1.9 (55) | 0.69 |
| ≥10 mm | 6.3 (80) | 5.4 (53) | 0.30† | 1.4 (80) | 1.8 (53) | 0.11† |
| Non-advanced adenoma | 21.4 (273) | 1.2 (12) | <0.0001 | 4.6 (273) | 0.4 (12) | <0.0001 |
| Serrated adenoma | 2.4 (32) | 0.2 (2) | <0.0001 | 0.5 (32) | 0.1 (2) | 0.001 |
| Hyperplastic polyp | 13.9 (178) | 0.3 (3) | <0.0001 | 3.0 (178) | 0.1 (3) | <0.0001 |
| Advanced neoplasia | 8.7 (111) | 6.1 (60) | 0.02 | 1.9 (111) | 2.1 (60) | 0.56 |
| ≥10 mm | 6.8 (87) | 5.9 (58) | 0.31 | 1.5 (87) | 2.0 (58) | 0.07 |

Numbers in brackets are the actual number of individuals. *All colorectal cancers were 10 mm or larger. †Relative risk for advanced adenomas of 10 mm or more per 100 participants was 1.17 (95% CI 0.82-1.68), relative risk for advanced adenomas of 10 mm or more per 100 invitees was 0.74 (0.52-1.05).

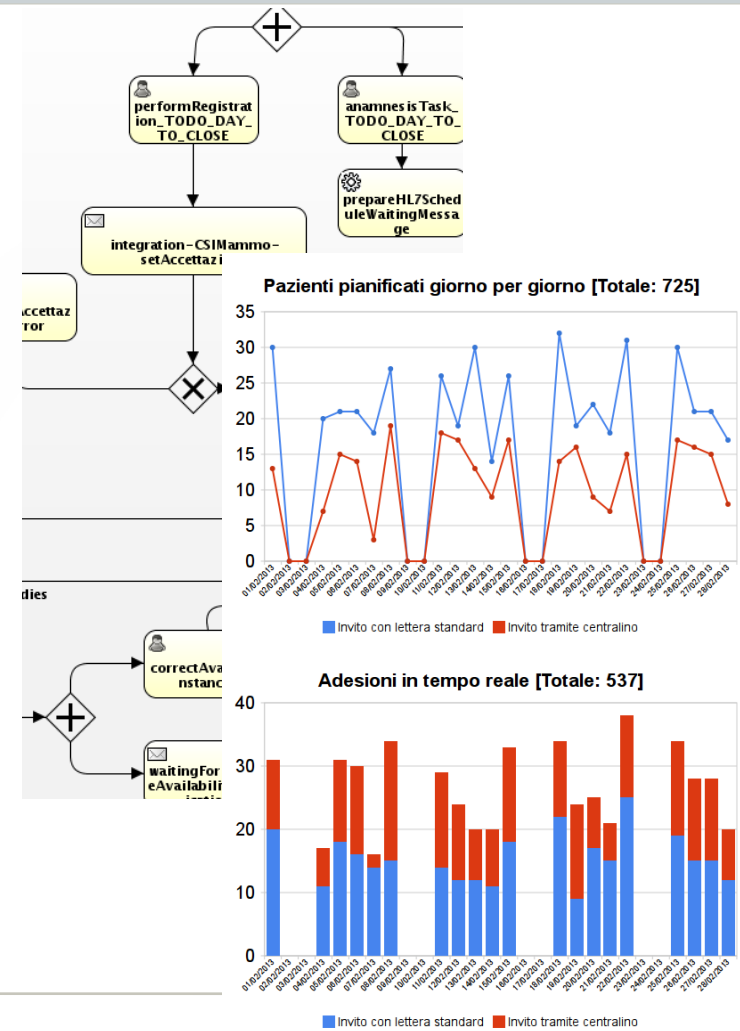
Table 2: Most advanced lesion per participant and per invitee for colonoscopy and CT colonography

A new diagnostic paradigm: a new test - system supporting diagnosis (CAD) - new integrated screening platform



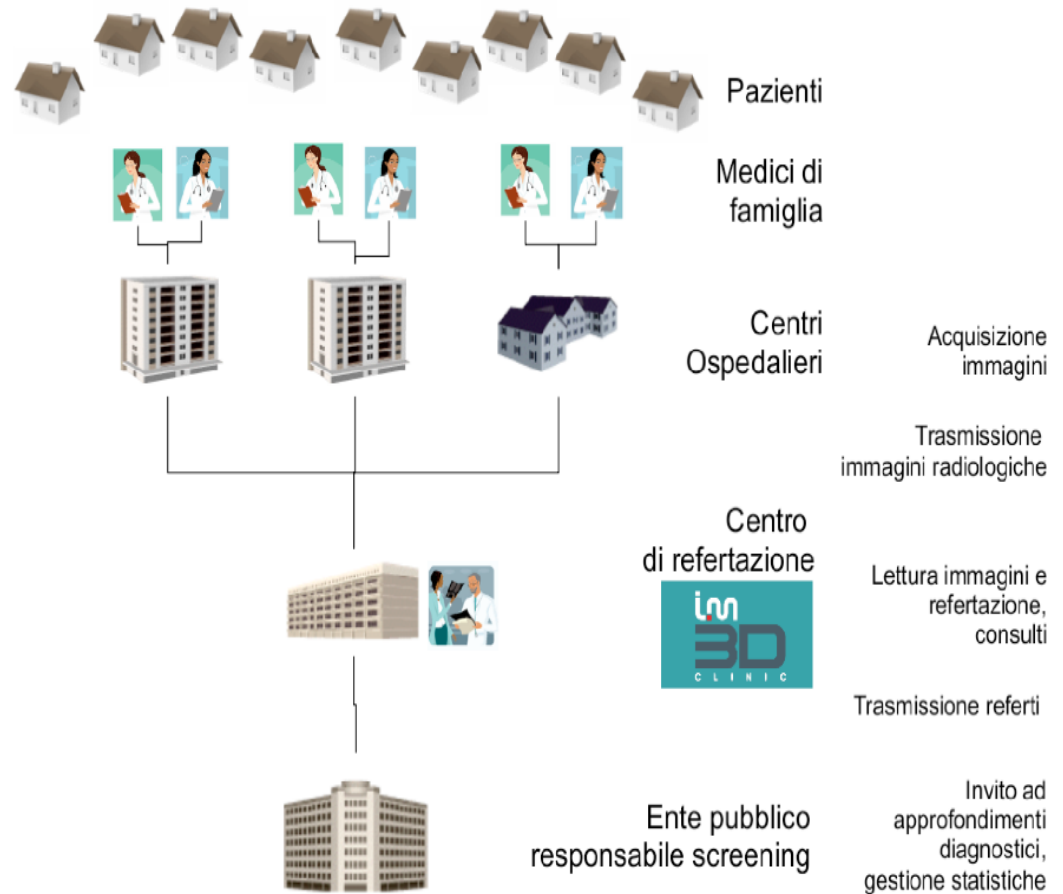
Integrated screening platform

- Fully automated and standardized approach
- Improved workflow
- Real time reporting
- Quality control
- Cost-effectiveness assessment
- Centralizing acquisition of data of scientific relevance



Integrated screening platform

- CTC performed throughout the territory to approach the target subject and thus encourage participation to the screening program
- Centralization of reporting, performed by certified radiologists



ESGE/ESGAR consensus: work in progress

- *CTC is not recommended as a primary test for population screening or in subjects with a first-degree positive family history. However, it may be suggested as a CRC screening test on an individual basis providing the screenees are adequately informed about test characteristics, benefits and risks.*
- *CTC is recommended in the case of positive FOBT/FIT with incomplete or unfeasible colonoscopy within organized population screening programs.*