Details online

Methodological description:

Patient inclusion: Volunteers aged 41-70.

Patient exclusion: Patients with known gastrointestinal pathology or contra-indication for iodine ingestion.

IRB/registration:
Human study: Multi-centre prospective observational case series (within the R&D framework of Good clinical practice). All studies were approved by the local IRB ethics committees. All patients signed an informed consent form.
Swine study: Animal care, facilities and activities were approved and monitored according to ISO9001 standards for quality and service and were approved by the animal ethics committee.

Main outcomes:
Feasibility, safety, and visualization of a novel prep-less X-ray imaging capsule for colon screening.

Study approach:

Device and technique:

The capsule (Check-Cap, Mount Carmel, Israel) is 34 mm long and 11.5 mm in diameter, weighing 12 grams (Supplementary Figure 1).

Swine pilot study: One swine weighing 70 kg was studied. The capsule was placed surgically under general anesthesia in the terminal ileum. This was necessary due to slow motility of the porcine gastrointestinal tract. Silicone beads (5 measuring 10 mm, 5 measuring 5 mm) were surgically implanted in the non-prepped colon to simulate human polyps. Swine was then allowed to recuperate and roam freely. Contrast agent (25 ml twice daily, mixed with milk) was added during meals. Capsule traveled autonomously and was expelled naturally while data was collected. The capsule provided reconstructed images of the porcine colon and had sufficient resolution to detect 4/5 10-mm- as well as 5mm-polyps (Supplementary Figure 2). Animal health was maintained throughout the studies according to the Ministry of Health regulations. The colon was subsequently excised to correlate capsule findings with actual polyps.
Human studies:
Dummy capsule study:
Capsules were retrieved by the participants at the end of the procedure and inspected for any leakage or damage. The first phase of the study was conducted in Hamburg-Eppendorf University Hospital with capsules identical in shape, dimensions and specific gravity to the scanning capsules albeit somewhat lighter (9 vs. 12 grams). In the second phase, conducted at Rambam Health Care Campus, capsules were also of identical weight.
Scanning capsule study:
The capsule traveled through the GI tract until expulsion. During the study, a lightweight external recording unit was strapped to the waist while normal daily routine was maintained. Subjects swallowed standard iodine-based contrast agent (Telebrix Gastro, Guerbet, France), 50–70 ml daily in total, together with their usual diet, until the capsule was eliminated. Capsules were retrieved by the participants at the end of the procedure and inspected for any leakage or damage. Total transit time was calculated.

The capsule positioning system was programmed to activate the capsule to scan only when forward movement of the capsule in the colon was detected. At all other times the capsule remained in standby mode without emission. Data were transferred to the recorder at the end of each scan for image reconstruction. Real-time position and capsule data were available to technicians that monitored the patient on line**.** Colon transit time was calculated.

Total patient's exposure to radiation was calculated based on actual measured capsule-emitted photons.

The study was conducted at the Tel Aviv Medical Center and Laniado Hospital.

Details of results

Endoscopy details

Pilot studies: Colon reconstructions from synthetic phantoms, bovine cadaver and swine showed spatial resolution of 2–3 mm in colon diameter measurements. In experiments performed in a phantom silicone colon, the system is currently optimized to image 10 mm polyps with 100% sensitivity and specificity. Clear luminal and polyp images were also seen in the cadaveric bovine model (data not shown).

Human study:

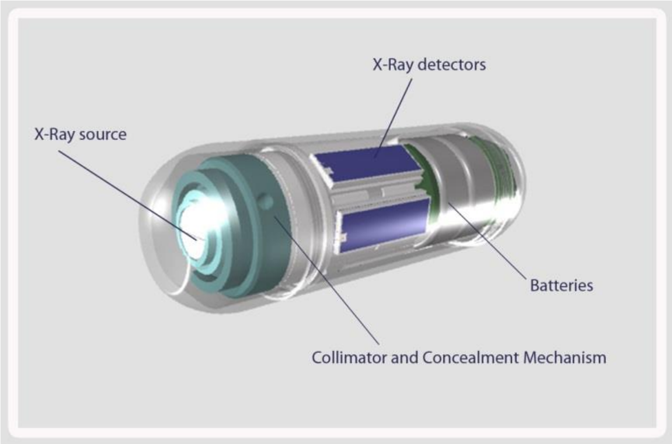
Preliminary safety study: 75 dummy capsules were swallowed: 61 and 14 in the first and second phases, respectively. All capsules were eliminated naturally and uneventfully.

Scanning capsule study: The average total transit time was 73.2 ± 45.4 hours. Colon transit time (once the capsule is propelled out of the caecum) was 8.5 ± 9.1 hours. Total active scanning time was 6-27 minutes. All capsules were retrieved and inspected. There were no reports of capsule malfunction or damage which might have compromised the participants' safety.

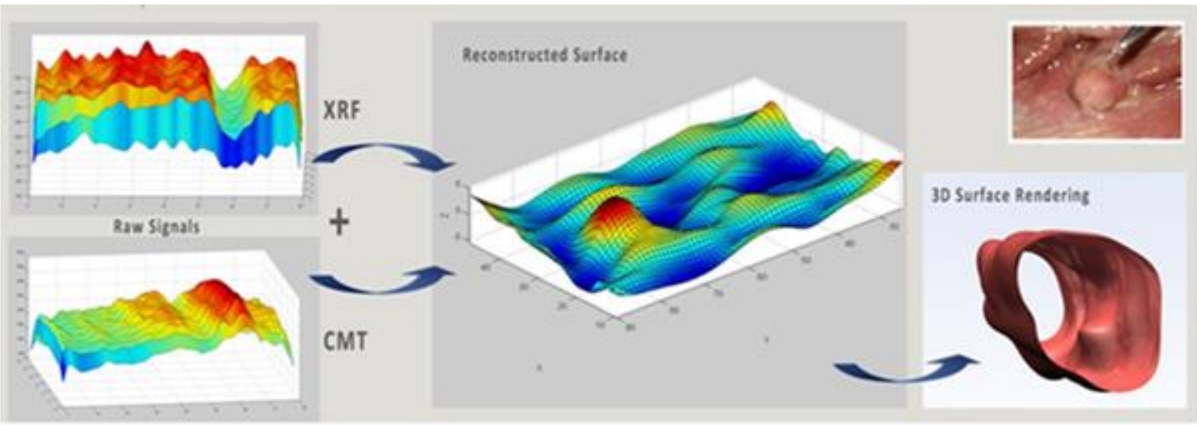
Total patient radiation exposure was 0.03 ± 0.0007 mSv, two orders of magnitude less than the radiation of computerized tomographic colonoscopy.

Image reconstructions allowed 3D views of both the colonic wall and lumen in all participants. The typical contour of different segments (hepatic flexure, triangular shape of the transverse colon) could be demonstrated (Supplementary Figure 3). Colon diameter measurements were estimated to be 18 ±3 mm, similar to dimensions reported in other studies. Additionally, no "haustral rings" were observed during capsule movement, in agreement with their recognized disappearance during colonic contractions (Glocker B et al, Colon Motility Dysfunctions SPIE Medical Imaging. San Diego California, 2007).

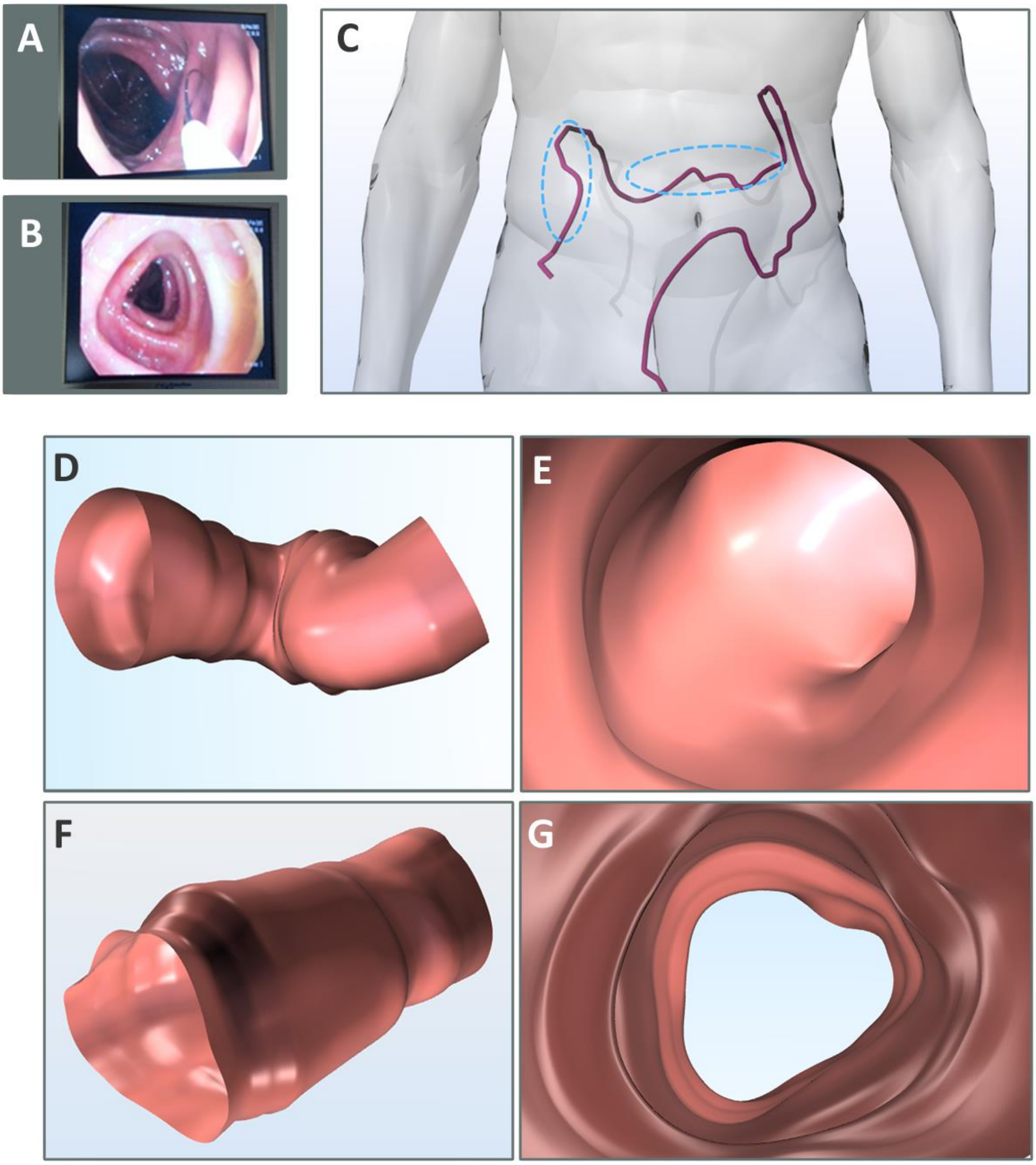
In cases of detected polyps, the contour of the polyp appeared to correspond to its endoscopic appearance (Figures 4a and 4b in main text). Capsule routes were readily demonstrated in all patients, exhibiting significant variability in colon macro-structure (Figures 4a and 4b-Panel B and Supplementary Figure 3C show representative examples).



Supplementary Figure 1. Drawing of the capsule, depicting the X-ray radiation source within a collimator and 6 radiation detectors.



Supplementary Figure 2. **Imaging of swine colon with implanted polyps**. A decrease in x-ray fluorescence (XRF) photon signals and an increase in Compton backscattering (CMT) signals detected by the imaging capsule correspond to the position of an inserted polyp (top right). These two signals are combined in order to form a three dimensional (3D) image (bottom right).



Supplementary Figure 3: Human colon 3D reconstruction. **A+B**. Images taken by an endoscope of (A) ascending colon and (B) transverse colon segments. **C**. A native 3D trace of the colon as measured by the capsule (anteroposterior view). The segments of ascending and transverse colon are marked with vertical and horizontal circles respectively (blue dotted line). **D+E**. The ascending colon segment is reconstructed from the outer surface of the colonic wall (D) as well as from within the lumen (E). **F+G.** The transverse colon segment is reconstructed as in D+E.