Digestive Endoscopy

Experimental assessment of a novel robotically-driven endoscopic capsule compared to traditional colonoscopy

Alberto Arezzo [a,*], Arianna Menciassi [b], Pietro Valdastri [c], Gastone Ciuti [b], Gioia Lucarini [b], Marco Salerno [b], Christian Di Natali [c], Mauro Verra [a], Paolo Dario [b], Mario Morino [a]

[a] Department of Surgical Sciences, University of Torino, Italy
[b] The BioRobotics Institute, Scuola Superiore Sant'Anna, Pisa, Italy
[c] STORM Lab, Vanderbilt University, Nashville, TN, USA

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ABSTRACT

Background: Despite colonoscopy represents the conventional diagnostic tool for colorectal pathology, its undeniable discomfort reduces compliance to screening programmes.
Aims: To evaluate feasibility and accuracy of a novel robotically-driven magnetic capsule for colonoscopy as compared to the traditional technique.
Methods: Eleven experts and eleven trainees performed complete colonoscopy by robotic magnetic capsule and by conventional colonoscope in a phantom ex vivo model (artificially clean swine bowel). Feasibility, overall accuracy to detect installed pins, procedure elapsed time and intuitiveness were measured for both techniques in both operator groups.
Results: Complete colonoscopy was feasible in all cases with both techniques. Overall 544/672 pins (80.9%) were detected by experimental capsule procedure, while 591/689 pins (85.8%) were detected within conventional colonoscopy procedure ($P=$ns), thus establishing non-inferiority. With the experimental capsule procedure, experts detected 74.2% of pins vs. 87.6% detected by trainees ($P<0.0001$). Overall time to complete colon inspection by robotic capsule was significantly higher than by conventional colonoscopy (556 ± 188 s vs. 194 ± 158 s, respectively; $P=0.0001$).
Conclusion: With the limitations represented by an ex vivo setting (artificially clean swine bowel and the absence of peristalsis), colonoscopy by this novel robotically-driven capsule resulted feasible and showed adequate accuracy compared to conventional colonoscopy.

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1. Introduction

Colorectal cancer (CRC) is a major cause of mortality of the general population in the Western world [1]. Although identification and removal of precancerous adenomatous polyps during colonoscopy has been demonstrated to be highly effective in preventing CRC [2–4], the application of CRC screening is low, especially when compared with the high rate of attendance for other screening programmes [5,6]. Various reasons have been suggested to explain the disappointing compliance of the population to CRC screening programmes, including lack of symptoms, fear of detecting a tumour, difficulty in bowel preparation and even lack of knowledge or awareness of the benefits of regular colorectal screening [7]. Nevertheless, there is no doubt that the major obstacle is represented by the embarrassment and discomfort

that many patients believe accompanies the procedure. Although introduction of better sedation (including use of Propofol) seems to somewhat improve patient acceptance of colonoscopy [8], colonoscopy under sedation remains limited in many countries due to economical and organization issue.

At the same time, a high-quality colonoscopy is necessary to provide all the benefits of endoscopic screening. In various studies, conventional colonoscopy seems to have a 5% polyp miss rate for polyps greater than 1 cm, which rises up to 25% for polyps smaller than 5 mm. Even the rates of missed cancers are reported as high as 6% in the right and transverse colon and 2% in the descending colon, sigmoid and rectum [9]. Known factors that influence the quality of colonoscopy in terms of polyp detection are withdrawal time, adequacy of bowel preparation and thorough inspection behind every intestinal fold [10,11].

In the recent past, availability of technologies enabled the development of wireless capsule endoscopy (WCE), which entails the ingestion of a miniaturized camera that navigates passively along the gastrointestinal tract by means of peristalsis, enabling inspection of the digestive system without discomfort or need for sedation

[12,13]. A significant example for capsule colonic inspection is represented by the PillCam COLON 2 (CCE-2) [12]. Recently a European, prospective, multicenter trial including eight European sites, but a limited number of cases, was published [14]. In this paper CCE-2 was able to detect 88% of polyps at least 10 mm in size was 88% (95% CI 76–99%) compared to conventional colonoscopy. Nevertheless concerns about the necessity to rely on passive peristaltic movement persist.

In order to overcome these problems and limitations, technical improvements to conventional colonoscopes and new devices are being developed ranging from simple diagnostic cameras to complete and autonomous diagnostic and therapeutic robotic platforms [15–24], which aim to achieve a higher quality colonic exploration with reduced invasiveness. In this framework, magnetic active locomotion represents the most promising solution [25]. Recently Olympus Endoscopy (Tokyo, Japan) and Siemens Healthcare (Erlangen, Germany) joined their effort to produce a modified endoscopic capsule endoscope controlled by magnetic guidance, for the upper gastrointestinal tract [26].

In this paper, the authors present a robotically-driven colonoscopic capsule platform, which was tested in an ex vivo setting and compared to conventional colonoscopy to verify feasibility and accuracy of the proposed technology and related technique.

2. Materials and methods

2.1. Robotic platform overview and control architecture

The robotic platform used in the study (Fig. 1) includes a 6 degrees of freedom (DoF) robotic arm (Fig. 1b – RV-6SB, Mitsubishi Electric, Tokyo, Japan) with a 7th custom-DoF at the end-effector for increasing the robot dexterity to complete the endoscopic procedure (Fig. 2). The external permanent magnet (EPM) consists of a NdFeB cylindrical-shaped 1.38 T magnet fixed to the robotic arm end-effector. A human–machine interface (HMI), including an intuitive 6 DoF control peripheral (Phantom Omni, Sensable, USA) (Fig. 1c), acts as an active high-level control core. The robotic arm is used to hold, move, and orient the EPM, that establishes a magnetic link with the endoscopic capsule equipped with an internal permanent magnet (IPM). The IPM is composed by 3 NdFeB cylindrical-shaped 1.48 T magnets. A proper dimensioning of the EPM-IPMs magnetic link was addressed in order to achieve effective magnetic interaction with the capsule at an operative distance of 150 mm [27]. The user imposes robotic arm motion through the input device, which interacts with a real-time motion control system driving the robotic arm. The input device is a positional sensing compact haptic device with force feedback. The control peripheral returns translational and rotational motion commands as the difference of the joystick current position respect to a centre-zero point. These data are processed by the robotic arm as increments to be added to the actual end-effector absolute position for the execution of the next motion command.

The magnetic driven component of the platform consists of a wired endoscopic capsule (Fig. 1a) measuring 13.5 mm × 29.5 mm and embedding a wired charge-coupled device (CCD) camera (KARL STORZ GmbH and Co. KG, Tuttlingen, Germany) and 6 white light emitting diodes (NESW007BT, Nichia Chemical Europe GmbH, Nuremberg, Germany). The camera has a 550 × 582 pixel resolution and a field of view of 120°. The image stream is displayed on a dedicated video screen (Fig. 1d). Images are used not only for diagnosis, but also as feedback to manoeuvre the capsule along the colon lumen. The capsule also embeds a triaxial magnetic sensor (Hall Effect Sensor CY-P15A, Chen Yang Technologies GmbH and Co. KG) used to monitor the magnetic link magnitude, to prevent the risk to lose it, by means of a purposely developed data processing algorithm returning an acoustic alarm signal. In the current prototype, a 2 mm large soft cable, covered by a hydrophilic sheath, provides energy and allows data transmission.

2.2. Experimental setting

In order to verify the feasibility of a complete colon inspection and the accuracy compared to conventional colonoscopy, an ex vivo experimental protocol was defined including a statistical analysis of relevant control parameters (video 1). The proposed task consisted in exploring ex vivo swine large bowel tracts of animals weighing approximately 80 kg. Bowel tissue was composed of straight and curved paths inserted in a human abdominal phantom (Limbs & Things Ltd., Bristol, UK) (Fig. 2) and arranged to mimic human anatomical angles and alignments as well as mesenteric attachments of the entire colon tract, from the rectum to the cecum (850 mm in length); an anal sphincter was also simulated. In order to simulate anatomical stability and hide the tissue arrangement from the operator's view, a foam rubber layer (10 mm in thickness) was interposed between the bowel and a Plexiglas plate, used to reproduce abdominal wall constraint. A fixed constant endoluminal pressure of 1 mmHg was maintained by an endoscopic insufflator (Surgiflator-40, W.O.M. Word of Medicine AG, Germany) connected to a Foley catheter placed transanally. Several 3 mm coloured pins were placed along the colon on the internal surface and their number and position were randomly changed in each trial. For each setting, the user, unaware about the total number of pins to be identified, had first to navigate the capsule through the colon, starting from the rectum and reaching the cecum, identifying and asserting each visualized pin. The same procedure was repeated through a conventional colonoscope. In the case of capsule control, the user took advantage of the magnetic field sensors for the knowledge about the magnetic link strength. Time to complete each test was recorded from the introduction of the scope or capsule to the achievement of the cecum. Twenty-two actors participated to the study: 11 experts, defined as endoscopists with over 5 years' experience and over 1000 colonoscopies performed, and 11 trainees, chosen among residents of the School of Surgery and the School of Gastroenterology of the local University, at their first experience with flexible endoscopy. All the trials were observed by an assistant who recorded the observed target sequence. Before each session, a theoretical briefing on the capsule platform and practical training of 5 min were organized. Medical doctors involved in the tests had no previous experience with the proposed platform. At the end of the test, each user compiled a questionnaire including an evaluation in a scale from 1 (worst) to 5 (best) on how intuitive were the overall control of the robotic platform using the Phantom Omni control peripheral and the overall control with the conventional endoscopic tool in the proposed tasks.

2.3. Statistical analysis

The primary goal of the study was to test the accuracy of the proposed technique. The primary hypothesis was to test in a pilot study the non-inferiority of the proposed technique in terms of accuracy in detecting pins (simulating human polyps). We planned a study of independent cases (capsule endoscopy) and controls (conventional endoscopy). Prior data indicated that the polyp detectability rate by conventional endoscopy is 85%. If the true detectability rate for capsule endoscopy would be 80%, we would need to study at least 632 pins per group to be able to reject the hypothesis that the detectability rates for capsule endoscopy is inferior to conventional endoscopy with probability (power) 80%. The Type I error probability associated with this test of this null hypothesis is 5%. The sample size determined would allow us to detect a non-inferiority margin difference between the group rates of 11.3%. The non-inferiority
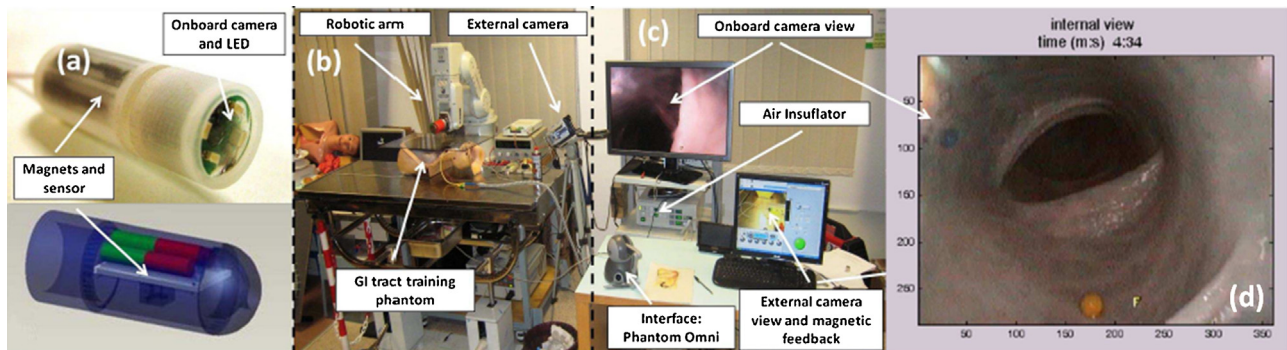
Fig. 1. Robotic platform overview and control architecture: (a) wired endoscopic capsule embedding a complete vision system and a magnetic module for proper coupling with the external permanent magnet (EPM), (b) 6 degrees of freedom (DoF) anthropomorphic robotic arm (RV-3SB, Mitsubishi Electric, Tokyo, Japan), with a 7th custom-made DoF at the end-effector to widen the workspace, connected to an EPM, (c) an intuitive 6 DoF control haptic peripheral (Phantom Omni, Sensable, USA) with force feedback to hold, move, and orient the EPM, and (d) image stream is transmitted to the robotic platform and displayed on a dedicated video screen, where coloured pins are visible.

hypothesis was assessed by constructing the upper limit of a 95% confidence interval for the difference in detectability rates (conventional endoscopy minus capsule endoscopy). Pins were assigned randomly in a number between 28 and 34 to each single test, stratified per groups (capsule and conventional endoscopy, experts and trainees).

Secondary objectives of the study were the time to complete the procedure, expressed in seconds, and the intuitiveness of the robotic platform and of the conventional endoscope expressed in a scale from 1 to 5. Fisher's exact test for categorical variables and Wilcoxon test for continuous ones were used. All reported P-values were obtained by the two-sided exact method, at the conventional 5% significance level. Data were analysed by SPSS 20.0.0 (IBM, USA) and R Project 2.14.1 (University of Auckland, Auckland, New Zealand) statistics software.

3. Results

Complete colonoscopy was feasible in all cases with both techniques. Overall, expert and trainee results for accuracy in target detection are summarized in Table 1. Pins detected divided by groups are represented in Table 2. A total of 672 pins could be identified in the capsule group and 689 in the conventional colonoscopy group. Of these, 544 (80.9%) were detected in the capsule group and 591 (85.8%) in the conventional colonoscopy group. Difference between conventional and capsule colonoscopy on detectability rates was 4.8% (95% CI, 0.9–8.8%); the upper 95% confidence boundary for the difference (8.8%) is lower than the non-inferiority

margin of 10.3%. As a subgroup analysis, we investigated differences between different expertise and different technologies. Among experts, 248 of 334 pins (74.2%) were detected in the capsule group as compared to 286 of 341 pins (83.9%) in the conventional colonoscopy group ($P = 0.002$). Among trainees, 296 of 338 pins (87.6%) were detected in the capsule group compared to 305 of 348 pins (87.6%) in the conventional colonoscopy group ($P = 1.00$). Consequently, in the capsule group experts detected 74.2% of pins as compared to 87.6% detected by trainees ($P < 0.0001$) while in the conventional colonoscopy group experts detected 83.9% of pins as compared to 87.6% detected by trainees ($P = 0.16$). Interestingly, experts in the conventional colonoscopy group detected 83.9% of pins as compared to 87.6% detected by trainees in the capsule group ($P = 0.17$).

Overall mean time to complete colon inspection by magnetic capsule was 556 ± 188 s vs. 194 ± 158 s for conventional colonoscopy ($P = 0.0001$); in the experts' group mean time to complete colon inspection was 578 ± 216 s by magnetic capsule vs. 77 ± 34 s for conventional colonoscopy ($P < 0.0001$); in the trainees' group 535 ± 163 s vs. 311 ± 145 s, respectively ($P = 0.0028$). No relationship between duration of the procedure and number of pins identified was observed. The intuitiveness of the robotic platform and that of the conventional endoscope was evaluated according to the judgement of the users. The mean overall intuitiveness score was 3.95 ± 0.90 (median 4, range 2–5) for both groups. Among experts, intuitiveness of the robotic capsule was judged 3.72 ± 0.90 (median 4, range 2–5), while conventional colonoscopy 4.36 ± 0.67 (median 4, range 3–5) ($P = 0.07$). Among trainees, intuitiveness of
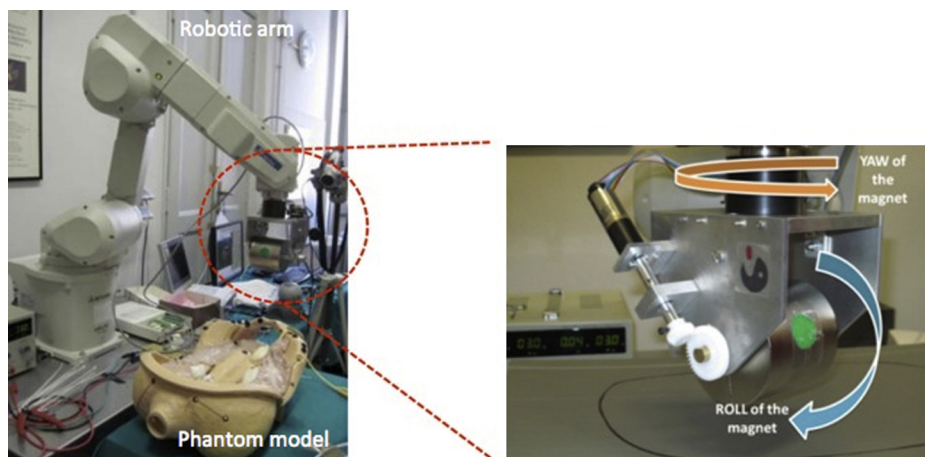

Fig. 2. A 7th custom-made DoF is added at the end-effector to widen the workspace and allow the capsule to turn >180°, in order to reach the cecum.

Table 1
Results for accuracy in target detection for experimental robotic capsule and conventional colonoscopy.

	Overall		Experts		Trainees	
	Robotic capsule	Conventional colonoscopy	Robotic capsule	Conventional colonoscopy	Robotic capsule	Conventional colonoscopy
n	22	22	11	11	11	11
Mean accuracy ± SD	80.9 ± 11.0%	85.8 ± 9.9%	74.2 ± 6.7%	83.9 ± 11.1%	87.6 ± 9.4%	87.6 ± 8.5%
Minimum for single tester	54%	65%	54%	65%	79%	69%
Maximum for single tester	92%	100%	92%	96%	93%	100%
Percentiles						
25th	70%	77%	65%	76%	85%	81%
50th (median)	85%	87%	71%	85%	88%	88%
75th	89%	94%	85%	92%	92%	96%

SD = standard deviation.

Table 2
Targets detected with experimental robotic capsule and conventional colonoscopy.

	Overall		Experts		Trainees	
	Robotic capsule	Conventional colonoscopy	Robotic capsule	Conventional colonoscopy	Robotic capsule	Conventional colonoscopy
Modelled polyps	672	689	334	341	338	348
Modelled polyps detected	544	591	248	286	296	305
Detection rate	80.9%	85.8%	74.2%[*]/[**]	83.9%	87.6%[*]	87.6%[**]

[*] P = 0.002.
[**] P < 0.0001.

the robotic capsule was judged 4.18 ± 0.87 (median 4, range 3–5), while conventional colonoscopy 3.55 ± 0.93 (median 3, range 2–5) (P = 0.11).

4. Discussion

Capsule endoscopy has fascinated both physicians and patients from its introduction in 2000, but since then only indications for small-bowel diagnostics have been established [28–30]. From the very beginning, attempts were made to extend indications such as oesophageal diagnostics [31], though use of oesophageal capsule endoscopy in clinical routine [32,33] is still lacking. Similarly the colon capsule, now in its second generation, has been preliminary demonstrated a sensitivity for detecting colonic lesions of at least 6 mm of about 85%, but a specificity of less than 70%, compared with the use of conventional colonoscopy [14,34].

After we introduced the concept of robotic capsule endoscopy, based on the combined use of an external robotically driven permanent magnetic field and on-board IPMs [35], we proceeded in the technical development and technology refinement. In [35] the authors demonstrated that magnetic based locomotion for capsule endoscopy is more precise if the external magnet is moved by a robotic arm rather than by hand. But no comparative studies have been performed with conventional colonoscopy until now. The main goal was to justify the use of a robot for this platform. The technology presented there improved in several aspects, the more relevant consisting of a further DoF that allows major dexterity; the robotic arm end-effector and consequently the capsule can turn >180°, in order to easily reach the cecum (Fig. 2).

In the present study we focused on the feasibility of a human colon inspection in an ex vivo model. The limits of the present experimental settings are underlined by the ability of trainees with no experience to complete colonoscopy in 100% of the cases. Nevertheless, with the potential limits of an artificially cleaned bowel and no peristalsis, and the use of a standard colonoscope as control (although more flexible endoscopes are available today for screening), results were promising. If confirmed in a human setting, this novel technology might represent an important step towards a better screening and diagnostic tool to replace flexible endoscopy. Despite the current experimental setting was not designed to prove

it, the system characteristics allow us to suppose an increased tolerability of the procedure, which should make of little importance the even significantly increased time of performance.

The reason why time to complete colonoscopy is significantly longer using robotic capsule is due to the setting chosen for the robot and permanent external magnet movement. In order to increase confidence with the novel technology, we limited the excursion of the magnet and consequently the capsule at each movement command; this limit can be overcome with the implementation of a reliable real-time capsule localization [36]. At the same time, as this technology is supposed to cause less discomfort than conventional colonoscopy, we preferred to create conditions to optimize accuracy rate. It is likely to imagine that an increased excursion of movement together with an increased confidence with the technology would reduce the gap with conventional colonoscopy in terms of time to complete the procedure.

The primary hypothesis was to test in a pilot study the non-inferiority of the novel technique in terms of accuracy in detecting pins. The difference in detection rate in the overall groups was in favour of conventional colonoscopy, as expected, but with a difference of only approximately 5%, with an upper 95% confidence boundary of 8.8%. Furthermore the analysis of subgroups produced some interesting results. While there is little surprise that expert endoscopists performed significantly better with a conventional colonoscope, it is quite remarkable that trainees, even with no previous training or specific instruction, were able to perform similarly and successfully in both settings. Even more interesting is the finding that trainees could perform better in the robotic capsule setting than expert endoscopists did in the conventional colonoscopy setting, although this difference was not statistically significant. Therefore, one could conclude that the difference in the detection rate between the two settings depends mainly on the lesser adaptability of the experts to this novel technology, as confirmed both by their accuracy rate and intuitiveness judgement. On the other hand, one could underline the consistently shorter time required by experts to complete the task by conventional endoscopy, which might justify the lower detection rate compared to trainees when using the robotic capsule.

The efforts in the area of magnetic endoscopy by the two main commercial players in capsule endoscopy worldwide, namely

Given Imaging [37] and Olympus [38], further attest to the promise of this approach. Similar attempts of magnetically-driven capsule endoscopy applications have been reported by the group of Swain [37] on a volunteer who received an upper gastrointestinal (GI) investigation. In this case a handheld external magnet was used to manipulate the capsule. Despite the fact that the authors declare an easy handling of the capsule, our previous results in a similar setting demonstrate low accuracy, inferior to a robotic-controlled platform like the one employed in the current study [35]. More recently, a further experience also focusing on upper GI investigation has been reported. In this paper even servo-assisted by a mechanical holder, the endoscopic capsule was controlled around 5 DoF through a magnetic guidance equipment similar to a Magnetic Resonance Imaging (MRI) system, but producing a lower magnetic field [26]. The system proved to obtain good accuracy, but the setting seems to be unnecessarily bulky for the purpose. In this perspective, the combination of the anthropomorphic robotic arm with the addition of conventional units for endoscopy such as a gas insufflator and a camera processor makes the adaptation to current endoscopic environments much more realistic.

While our device proved feasible for the diagnostic evaluation of the lower GI tract, there are limitations to its development. A further reduction in size is desirable; this can be achieved by decreasing the length of the actuation unit in particular, which could be reduced to 20 mm by lodging the IPMs in a different configuration with a more compact package between the internal components, or the IPMs could even be substituted by a magnetic capsule shell. If the image quality and frame rate prove acceptable, a further step should be the integration of a wireless camera. This additional improvement will however raise a significant issue regarding power consumption for imaging acquisition, imaging transmission and illumination. A possible solution for supplying all the intra-capsular subsystems within a reasonable volume may be wireless power induction [39]. Finally, merging information from magnetic and vision sensors would enable automated procedure if used as feedback in the robotic arm control algorithm. A fully automated procedure would minimize the invasiveness and discomfort felt during traditional endoscopic examination with also a potential reduction of time to complete the procedure. Parallel to this development in a different version of the capsule the authors have added a biopsy channel and have tested the system in pigs, by exploiting the same procedure in terms of driving methodology for the capsule [40]. The working channel could be usefully connected to a suction-insufflation pump to be used for irrigation, if bowel preparation and lack of distension should become an issue when transferring the technology to clinical practice.

In conclusion, flexible endoscopy is far from being abandoned even as a simple diagnostic tool. Nevertheless, the results of our study demonstrate that the use of the novel robotically driven capsule for colonoscopy in ex vivo model is feasible. Although the model is still unrealistic, the capsule allowed adequate accuracy, and good acceptance by operators (even higher among inexperienced trainees). Further development should focus on optimizing existing technology into a more ergonomic design to allow in vivo human testing.

Conflict of interest

No conflict of interests or personal funding to declare.

Acknowledgments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dld.2013.01.025.

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