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μRALP and beyond: Micro-technologies and systems for robot-assisted endoscopic laser microsurgery

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19 **Keywords: laser microsurgery, micro-robot, flexible robotic endoscope, surgeon-robot**
20 **interface, cancer imaging, augmented reality, computer-assisted surgery, cognitive surgical**
21 **system.**

22

Abstract

24 Transoral laser microsurgery is the current gold standard technique for the treatment of diseases in
25 delicate structures such as the larynx. However, the operations require large surgical expertise and
26 dexterity, and face significant limitations imposed by available technology, such as the requirement
27 for direct line of sight to the surgical site, restricted access, and relatively long operative distances. All
28 of these factors can severely affect surgical quality, which is critical to the patient's survival and post-
29 treatment quality of life. To change this status quo, the European project μRALP proposed a complete
30 redesign of the surgical setup through the development of micro-technologies and systems for robot-
31 assisted endoscopic laser microsurgery. This paper reviews the achievements and key contributions of
32 this project, whose primary target application was phonosurgery, i.e., the challenging surgical
33 treatment of vocal cords. The paper starts by presenting μRALP's motivations and rationale, which
34 leads to the introduction of robotics as an enabling technology for improved surgical site accessibility,
35 visualization and management. Then, the goals and achievements of the different research areas that

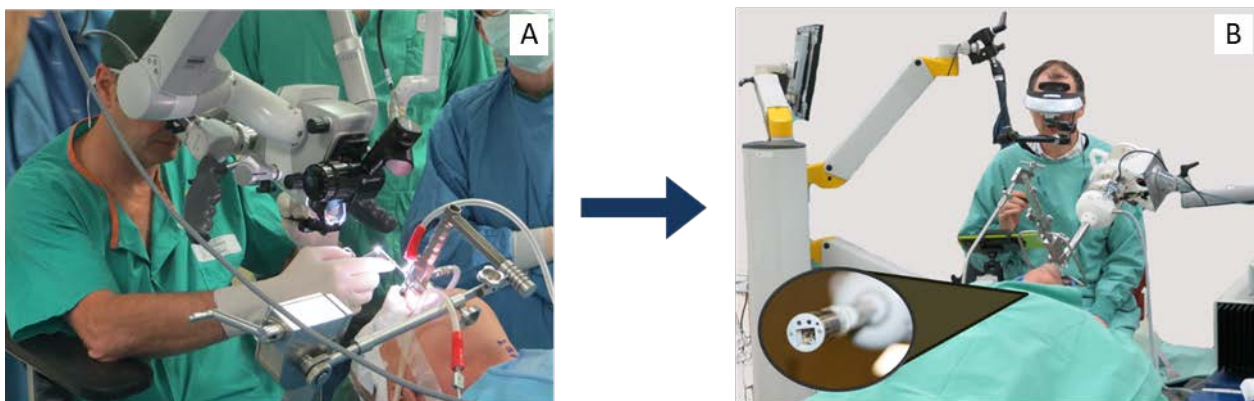
36 composed the project are presented, including an overview of results achieved beyond and
37 independently of μRALP. This includes research in micro-robotic laser steering, flexible robotic
38 endoscopes, augmented imaging, assistive surgeon-robot interfaces, and cognitive surgical systems.
39 Innovations in each of these areas are shown to provide sizable progress towards more precise, safer
40 and higher quality transoral laser microsurgies. Yet, major impact is really expected from the full
41 integration of such individual contributions into a complete clinical surgical robotic system, as
42 illustrated in the end of this paper with a description of preliminary cadaver trials conducted with the
43 integrated μRALP system. Overall, the contribution of this paper lays in outlining the current state of
44 the art and open challenges in the area of robot-assisted endoscopic laser microsurgery, which has
45 important clinical applications even beyond transoral operations.

46

47 **1 Introduction**

48 Lasers form an increasingly common tool for precision treatment of pathological conditions on delicate
49 and vital human organs. One example is transoral laser microsurgery (TOLMS), which involves the
50 use of a surgical laser and challenging surgical techniques for treating abnormalities in the glottis and
51 supraglottic regions (Steiner and Ambrosch, 2000).

52 TOLMS is the current gold-standard technique for phonosurgeries, i.e., the surgical treatment of
53 the vocal cords (Rubinstein and Armstrong, 2011). These are delicate operations that require high
54 surgical precision. However, they are currently performed with very limited technological support, so
55 large surgical dexterity and expertise is needed. The consequence is that the quality of such surgeries
56 relies completely on the dexterity and capabilities of the operating surgeon, who must control the
57 surgical tools with micrometric precision to both eradicate the disease and minimize damage to healthy
58 tissue. If not performed well, phonosurgery can have a large impact on the quality of life of the
59 patient, as it can affect both phonation and deglutition (Presutti, 2010).



60 Fig. 1. μRALP achievement: complete redesign of the traditional free-beam laser phonomicrosurgery surgical setup (A) to enhance
61 surgical safety, accuracy and quality through a novel endoscopic robot-assisted laser phonomicrosurgery system (B).

62

63 Performing TLM currently requires the use of a laryngoscope to provide both visualization and access
64 to the surgical site, which is located deep down the throat of the patients. The laryngoscope is basically
65 a metal tube that is inserted through the mouth of the patient to provide this required operative channel.
66 It allows the use of an external microscope and specialistic surgical tools. As Fig. 1 shows, the surgeon
67 operates through the laryngoscope while using a microscope, a laser micromanipulator and long
68 microsurgical forceps.

69 The ergonomics of the current TLM setup is also sub-optimal, complicating the achievement of high
70 precision surgical tasks. In addition, other difficulties include the fact that the laser beam is controlled
71 manually from the outside the patient's body, from a comparatively large range from the surgical site
72 (typically 400mm). This results in a stringent requirement for direct line-of-sight for laser control,
73 imposing limits on the types of patients that can benefit from this state of the art treatment due to their
74 specific anatomy [Peretti et al. 2016]. Furthermore, the long operating range causes laser aiming
75 accuracy and consistency problems, increasing the need for extensive surgeon training.

76 Considering this context, the European project μRALP proposed a complete redesign of the TLM
77 surgical setup and pursued the development of a new flexible endoscopic system for robot-assisted
78 laser phonomicrosurgery. The result was the creation of an advanced micro-surgical robotic system
79 through research on novel robotic endoscopes and precision micro-robotic end effectors, which
80 allowed relocating the imaging sensors and the laser actuator closer to the surgical site. In addition,
81 research in real-time cancer imaging, surgeon-robot interfaces, cognitive controllers, augmented-
82 reality and assistive teleoperation contributed to improve the surgical site visualization, the
83 controllability of the surgical tools, and the precision of the operations.

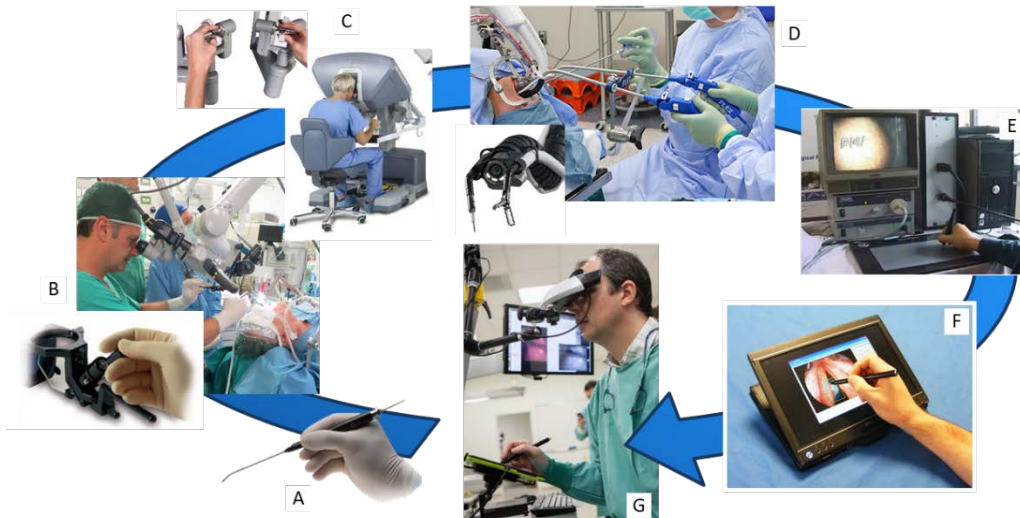
84 μRALP was a three-year project executed in the period between 2011 and 2015. It involved five
85 European institutions, three engineering institutions and two hospitals. The project was coordinated
86 by the Italian Institute of Technology (IIT, Genoa, Italy) and included the University of Franche-Comté
87 (UFC, Besançon, France), the Leibniz University (LUH, Hannover, Germany), the University Hospital
88 of Besançon (UHB, Besançon, France) and the University of Genova (UNIGE, Genoa, Italy).

89 The engineering advancements and scientific contributions of μRALP are reviewed in this paper,
90 together with further developments in the area achieved beyond the end of the project. This leads to an
91 outline of the current state of the art and open challenges in the area of robot-assisted endoscopic laser
92 microsurgery.

93

94 **2 μRALP project context and objectives**

95 Back in 2011, a number of clinical devices were already available for laser surgery, including optical
96 scalpels and manual laser micromanipulators commercialized by Deka, KLS Martin, Lumenis,
97 OmniGuide and other companies (see Fig. 2). Now, a decade later, these are still the same devices
98 available commercially for TLM. However, as mentioned above, the control of such devices relies
99 completely on the dexterity and skills of the operating surgeon, who has to go through a long training
100 process to acquire the expertise needed for precision operations such as phonomicrosurgery.
101 Furthermore, ergonomic issues such as sub-optimal surgeon hand support and the need to operate while
102 looking through a microscope, lower the accuracy and aggravate consistency problems that affect these
103 delicate surgeries.



104
105 Fig. 2. User interfaces for laser surgery: (A) Elevate ENT handpiece, an optical scalpel commercialized by OmniGuide Surgical. (B)
106 EasySpot Hybrid, a manual laser micromanipulator by DEKA for surgical microscopes. (C) Intuitive Surgical's da Vinci system and
107 (D) Medrobotics Flex robotic system, both of which can include an optical fiber for laser surgeries. (E) K.U. Leuven's interface for
108 robot-aided laser surgery based on a graphics tablet. (F) IIT's Virtual Scalpel interface based on a tablet PC. (G) μ RALP's Virtual
109 Microscope and tablet-based laser controller.

110 Nonetheless, the recognition that interfaces (and human factors) play a major role in the success and
111 quality of laser surgeries has driven research into augmenting the surgeons' capabilities with new
112 surgical systems such as teleoperated robotic devices. In addition, the creation of hollow core optical
113 fibers capable of transmitting CO₂ laser power has enabled, for example, research into the use of
114 surgical robots, such as the *da Vinci* system (Intuitive Surgical Inc., USA), for laryngeal laser
115 procedures. This possibility was first explored by Solares and Strome (2007), and later by Desai et al.
116 (2008), who have coupled such optical fibers to the *da Vinci's* tool tip and used it for laryngeal
117 surgeries. This idea was successfully demonstrated by both groups, and later corroborated by others
118 using also other robotic systems, such as the Flex robot launched by Medrobotics Corporation (USA)
119 in 2014 (Lang et al. 2017). However, the conclusions of such studies continue to emphasize the need
120 for new robotic technologies to improve access, laser aiming precision, and ablation quality for delicate
121 operations in the glottic region. Current robotic instruments are still too large for deep laryngeal
122 interventions, limiting their effective use to the oral cavity, pharynx and supraglottic regions.

123 By the time the μ RALP project started, research towards new robot-assisted laser surgery systems
124 included the work of Tang et al. (2006) at K.U. Leuven, and Mattos et al. (2011) at the IIT. Their
125 research resulted in the creation of writing-based interfaces for controlling laser aiming in robot-
126 assisted laser surgeries, which demonstrated potential for bringing greatly enhanced precision,
127 controllability, safety, and ergonomics for laser microsurgies. However, similarly to the traditional
128 laser microsurgery setups, both systems were still limited by the need for direct line-of-sight from the
129 outside of the patient to the operative field.

130 Therefore, μ RALP was focused at advancing such state of the art in laser phonomicrosurgeries,
131 specially through the elimination of limitations regarding the access to the surgical site and the need
132 for establishing an operative direct line-of-sight from the outside of the patient's body. For this, the
133 project concept included the creation of a novel teleoperated surgical system based on a micro-robot
134 laser micromanipulator and a custom flexible endoscope, which could bring novel imaging and surgical
135 technologies close to the surgical site. Furthermore, to augment the surgeons' capabilities, the project
136 also aimed at creating a novel ergonomic and information-rich surgeon-machine interface, including
137 augmented visualization, intuitive controllers and assistive cognitive systems. The ultimate goal was

138 to bringing unprecedented levels of accessibility and precision to laser microsurgies to allow
139 operations not previously possible with existing technology.

140 To realize this concept, μRALP focused on accomplishing the following objectives:

- 141 • *Micro-robotic laser micromanipulator*: The engineering of a dexterous micro-robotic end-
142 effector for precise laser power delivery in minimally invasive surgeries. This system should
143 control the surgical laser steering from the immediate vicinity of the surgical site.
- 144 • *Flexible robotic endoscope*: The development of a novel endoscopic system providing the
145 appropriate degrees of freedom for effective access and visualization of all possible
146 phonomicrosurgery sites.
- 147 • *Surgical interface*: The creation of an intuitive and information-rich augmented reality man-
148 machine interface for assisted teleoperation of the robotic system, including real-time surgical
149 guidance based on pre- and intraoperative surgical plans. This goal involved the design of:
 - 150 ○ An assistive teleoperation interface able to achieve the required control system
151 performances and support informed decisions by the surgeon
 - 152 ○ A laser visual servoing system able to demonstrate accurate laser aiming control
 - 153 ○ An augmented reality surgical interface demonstrating accurate preoperative image
154 registration
- 155 • *Cancer tissue visualization*: The study and development of micro-optomechatronic
156 technologies and computer vision methods for intraoperative real-time cancer tissue
157 visualization, to support the intraoperative definition of surgical margins.
- 158 • *Cognitive controller*: The creation of a cognitive system capable of learning and predicting the
159 changing characteristics of the surgical site during laser procedures, to improve laser-tissue
160 interaction quality and safety.

161 To pursue these objectives, μRALP was subdivided into parallel research and technological
162 development work packages, whose results achieved within and beyond the end of the project (also by
163 other research groups) are discussed in the next sections.

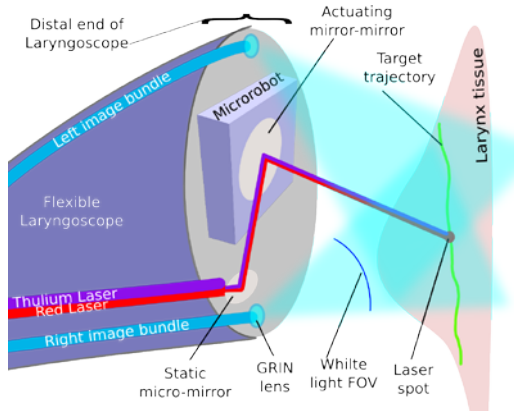
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165 **3 Micro-technologies and systems for robot-assisted endoscopic laser microsurgery**

166 The research leading to the μRALP system demonstrator shown in Fig. 1 included parallel efforts
167 towards the design, development, assessment and integration of its subsystems. Such subsystems
168 focused on the different objectives outlined above, i.e., the creation of: 1) a micro-robotic system to
169 steer the laser beam; 2) a flexible robotic endoscope to bring the imaging sensors and surgical
170 instruments close to the surgical target; 3) optical technologies and computer vision methods for real-
171 time cancer tissue imaging; 4) teleoperation and surgeon-robot interfaces; 5) augmented reality for
172 enhanced surgical awareness and control; and 6) cognitive systems for safety supervision and
173 autonomous operations.

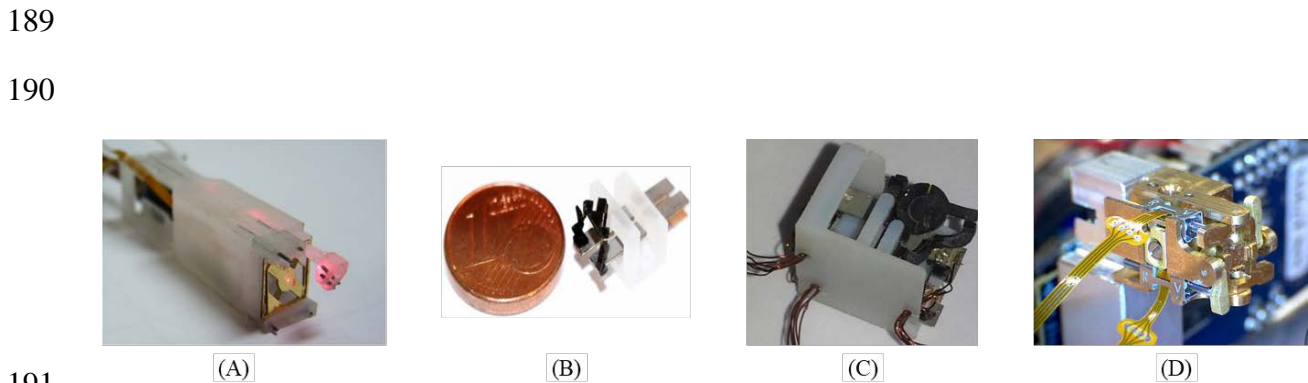
174 **3.1 Micro-robotic laser micromanipulator**

175 The concept driving the design and development of this device is presented in Fig. 3. The goal of the
176 micro-robot is to serve as the end-effector of a new endoscopic system for laser phonosurgeries,
177 allowing accurate laser aiming by providing high resolution motions and fast response times. The
178 micro-robot was also designed to allow teleoperation and automatic control based on visual servoing
179 methods, to enable high-accuracy operations. The design specifications for the creation of the micro-
180 robot included the robot size (diameter ≤ 10 mm), mobility (laser deflection range $\geq 30^\circ$) and laser
181 aiming accuracy (≤ 100 μ m).



182
183 Fig. 3. Schematic view of micro-robotic laser micromanipulator concept.

184
185 During μ RALP, four solutions were proposed for the micro-robotic laser micromanipulator. These are
186 presented in Fig. 4 and included a hybrid piezoelectric compliant mechanism (Rabenorosa et al.,
187 2014), two different piezoelectric smart composite microstructures (Lescano, 2015), and a solution
188 based on conventional clockwork technology (HorloBot).



191
192 Fig. 4. Micro-robotic laser micromanipulators developed during μ RALP: (A) Squipabot; (B) PIBOT, (C) Micro Agile-Eye, (D)
193 HorloBot.

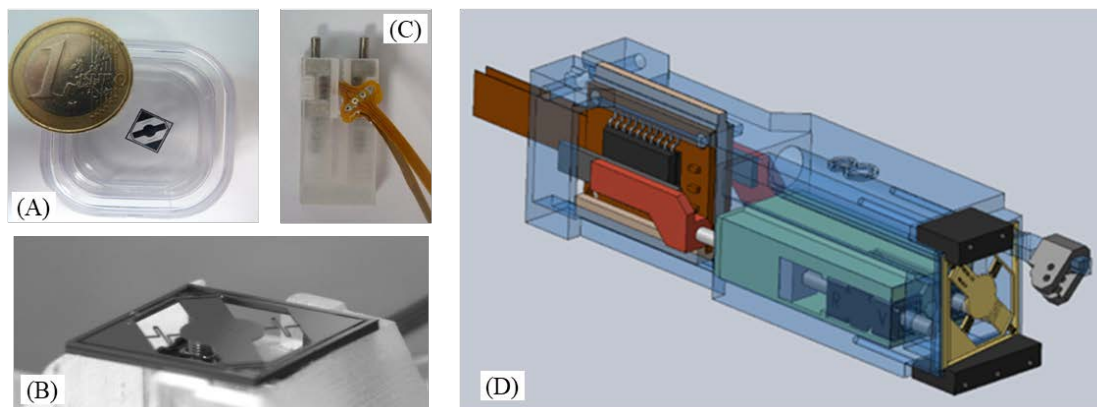
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195 The PiBot and the Micro Agile-Eye piezoelectric smart composite microstructure robots were proposed
196 to satisfy the stringent system requirements by combining the following principles:

- 197 • The use of piezoelectric cantilevers allows the achievement of very high positioning resolution
198 (submicrometric).
- 199 • The use of several piezoelectric actuators and the lever principle can amplify displacements.

- 200
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- A parallel kinematic structure allows high miniaturization of the structure while maintaining the range of displacements and of velocities offered by the piezoelectric actuators.
 - The use of a 5R (for micro Agile-Eye) and 2 RUS (for the PiBot) parallel kinematic structures allows transforming linear displacements into angular displacements for laser scanning with conservation of the high velocity capability.
 - The use of smart composites microstructures (SCM) fabrication process can allow microfabrication of the whole piezoelectric microrobot with minimized complexity. The principle consists in machining first the structure in planar form, then folding this in order to obtain the 3D structure.

209 The HorloBot micro-robot was developed based on conventional clockwork solutions. Developments
210 here involved undergraduate students at Lycée E. Faure in Morteau and resulted in the creation of a
211 working prototype using linear micromotors.

212 The Squipabot was the micromechatronic laser micromanipulator finally integrated in the μ RALP
213 endoscope. This device was selected for its simple fabrication and assembly methods, and for its higher
214 technology readiness level (TRL) for integration with the other μ RALP systems. The Squipabot is
215 based on the use of conventional mechanisms and MEMS technology. More precisely, it is a
216 combination of a compliant micro-fabricated silicon structure (deformable mirror) with innovative
217 linear micromotors, used to actuate the two decoupled and high range (up to 45°) tilting stages with
218 high accuracy (Renevier et al., 2017). Details of this micro-robot are shown in Fig. 5.



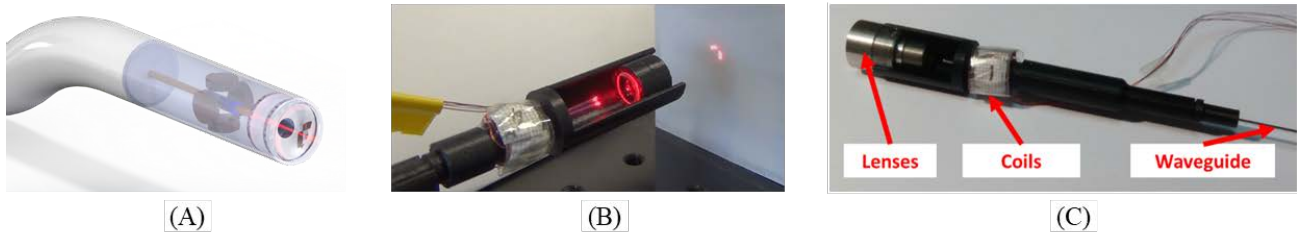
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220 Fig. 5. Details of μ RALP's Squipabot micro-robotic laser micromanipulator: (A) and (B) the deformable micromirror (MEMS). (C) the
221 linear piezoelectric microstages. (D) CAD model of the assembled microrobot.

222 The Squipabot featured integrated high-resolution magnetic position sensors to determine, in real-time,
223 the position of the linear stages and, consequently, the position of the beam deflection micro-mirror.
224 All components (linear micromotors, MEMS mirror, sensors, laser fiber, fixed mirror, electrical wires)
225 were assembled and packaged in a 3D printed housing. The entire integrated micro-robot (depicted in
226 Fig. 4) measured 9 mm x 11 mm x 42 mm. It successfully satisfied the performance requirements by
227 demonstrating closed-loop trajectory following root-mean-square (RMS) errors in the order of 80 μ m,
228 laser deflection velocity up to 95 °/s, and control loop frequency up to 40 Hz.

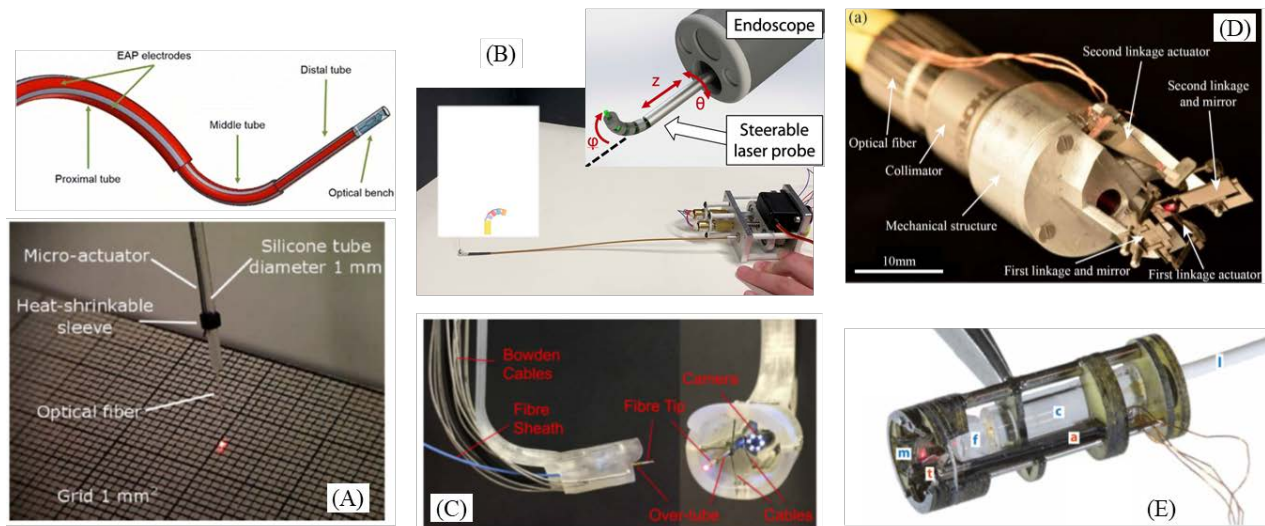
229 Beyond the end of μ RALP, project partners continued the research towards higher TRL and alternative
230 technological solutions for the micro-robotic laser micromanipulator. These efforts resulted, for
231 example, in the creation of a magnetically actuated laser scanner for endoscopic microsurgery
232 (Acemoglu et al., 2019), which demonstrated open-loop accuracy below 1.4 mrad (90 μ m at 30 mm
233 working distance) for scanning frequencies up to 15 Hz. This device, depicted in Fig. 6, is based on

234 the creation of a local magnetic field to bend a cantilevered laser fiber in a controllable fashion. It was
235 originally based on the use of a standard silicon optical fiber with 300 μm core diameter, but was
236 subsequently enhanced to use a waveguide for CO₂ lasers. This allowed demonstrating higher quality
237 tissue ablations when compared to the bare waveguides currently in clinical use, enabling both
238 reduced carbonization levels and narrower ablation craters (Acemoglu and Mattos, 2018). The concept
239 of this device was later extended to allow closed-loop control of the scanning fiber, demonstrating
240 promising results towards a system with higher robustness and accuracy (Mohammadbagherpoor et al.
241 2019).



242
243 Fig. 6. Magnetically actuated laser scanners for endoscopic microsurgery: (A) Concept. (B) Prototype based on a standard silicon
244 optical fiber. (C) Prototype based on a CO₂ laser waveguide.

245
246 Other prototypes proposed beyond μ RALP to steer laser fibers for microsurgery include biocompatible
247 conducting polymer continuum robots (Chikhaoui et al. 2018), tiny flexible steerable instruments to be
248 used through the tool channel of clinical endoscopes (O'Brien et al. 2019), and a cable-driven parallel
249 robotic system for phonosurgery (Zhao et al., 2020). Finally, a millimeter-scale tip/tilt laser scanning
250 system based on a micro-mechatronic structure actuated by piezoelectric beams has been proposed for
251 transoral robotic surgery, demonstrating a field of view of 10 mm x 20 mm and scanning speed up to
252 7 m/s from an 11 mm diameter device (Bothner et al., 2019). This device was subsequently further
253 miniaturized to a diameter of 6 mm and improved to cover a 18 mm x 18 mm workspace (York et al.,
254 2021). Images of such systems are presented in Fig. 7.

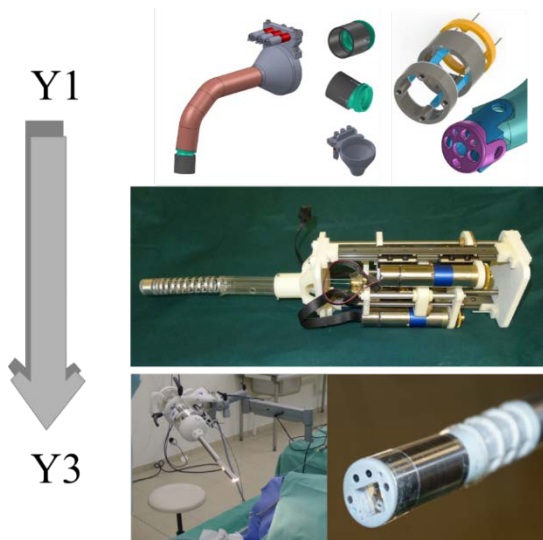


255
256 Fig. 7. Further devices created to steer a surgical laser beams: (A) A biocompatible conducting polymer continuum robot (Chikhaoui et
257 al. 2018). (B) A flexible steerable instrument (O'Brien et al. 2019). (C) A cable-driven parallel robotic system (Zhao et al., 2020). (D) A
258 millimeter-scale tip/tilt laser-steering system (Bothner et al., 2019). (E) Microrobotic laser steering system (York et al., 2021).

259

260 **3.2 Flexible robotic endoscope**

261 The specific objective of this device was to provide a robotic structure to deploy, support, position and
 262 properly orient the imaging and laser steering systems to allow effective laser microsurgery. This
 263 required the creation of a device with the appropriate size, operative channels and degrees of freedom
 264 to access the larynx and all possible surgical sites.



265

266 Fig. 8. Development stages of μRALP's flexible robotic endoscope within the 3-year project.

267

268 The development of this endoscopic system was an iterative process strongly influenced by results of
 269 adjunct research and cadaver trials. As presented in Fig. 8, the design evolved to adapt to demands
 270 identified throughout the μRALP project. The final device consisted of following components: a distal
 271 tip (housing a stereo imaging system, illumination fibers, the Squipabot, and laser focusing optics), one
 272 bendable and extendable continuum segment, one solely bendable continuum segment, a rigid shaft
 273 and an actuation unit (Kundrat et al., 2015).

274 The endoscope's actuation unit provided manual and motorized actuation for the two consecutively
 275 attached continuum segments. Actuation was based on spindle driven carriers, which were attached to
 276 NiTi rods and wires connected to both segments and guided through the rigid shaft. Each segment was
 277 actuated by three rods and wires. Manual actuation was connected to the first segment and allowed for
 278 in-plane bending (1 DoF). Intraoperative positioning of the Squipabot was achieved with the second
 279 continuum segment. The flexible and leak-tight continuum segments were manufactured individually
 280 by silicone casting. The flexible segments were rigidly connected to the distal tip and rigid shaft. Three
 281 motors actuated the spindle-carrier system, enabling bending in two DoF (pan-tilt) and extension of
 282 the segment. Another DoF was achieved by manually rotating the actuation unit inside the customized
 283 interface.

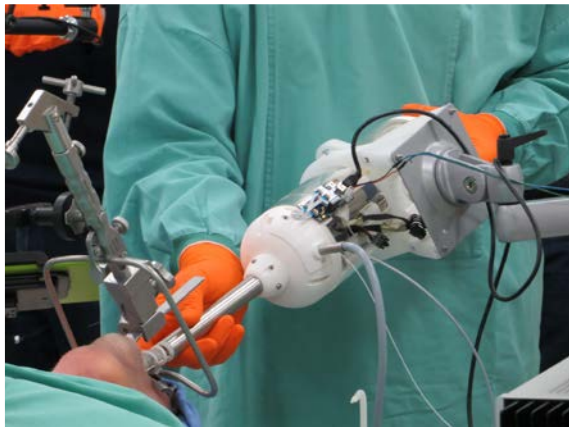
284 Control of the endoscope's actuation system was implemented on a BeagleBone Black embedded
 285 Linux device. A customized extension was designed to connect the motors directly to the RS232
 286 interface and power supply. Customized ROS modules provided low and high level interfacing with

287 the μRALP control framework. Kinematics of the actuated continuum segment were derived
288 considering the novel variable length of segments (Kundrat et al., 2015).

289 As detailed in (Kundrat et al., 2019), direct and inverse kinematics were available, as well as Jacobian
290 formulation for velocity mappings. This enabled control of the endoscope directly from image space
291 based on the stereoscopic imaging information. The adjustment of the distance between the endoscopic
292 tip and the tissue surface was implemented to allow laser focusing and a maximum radiant exposure
293 on the tissue. In this regard, a visual servoing loop was implemented obtaining depth information from
294 stereo triangulation and applying proportional control to adjust the length of the continuum segment to
295 a desired distance from the tissue surface. This feature enabled precise positioning for laser focus
296 adjustments.

297 The endoscope distal tip provided central alignment for the Squipabot. In order to obtain an overlapping
298 workspace, the imaging sensors and illumination light guides were circumferentially aligned and
299 inclined with respect to the laser beam steering micro-robot. Optical fibers and electrical cables were
300 routed within the endoscope in order to be protected during intraoperative handling.

301 The robotic endoscope design also considered different approaches for stabilizing the system with
302 respect to the patient. The decision to use a commercial manually lockable positioning arm was taken
303 after preliminary cadaver experiments, since it demonstrated proper support while being readily
304 available. This support consisted of two parts: a serial kinematics arm and a custom interface to the
305 endoscope unit. The custom interface added two additional degrees of freedom to the supporting
306 system, facilitating intraoperative handling. In addition, the access to the laryngeal anatomy was
307 facilitated by the use of commercial mouth retraction device, allowing improved dexterity for inserting
308 the μRALP endoscope through mouth and oropharynx to finally reach the laryngopharynx (see Fig. 9).

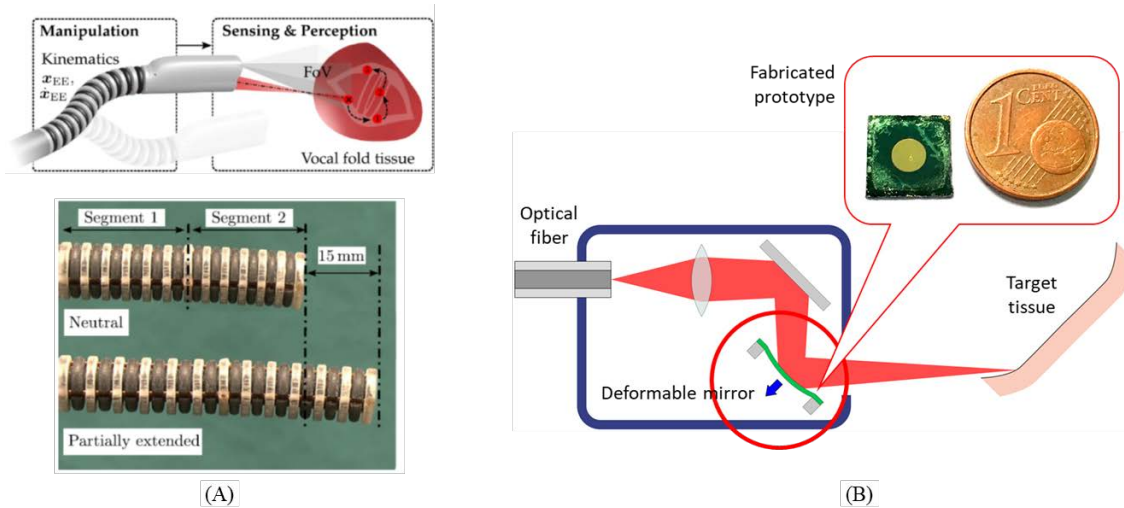


309

310 Fig. 9. Initial rough positioning of μRALP's flexible robotic endoscope was performed manually with the support of a passive lockable
311 holder and a standard mouth retraction device.

312 Beyond the end of μRALP, efforts continued towards the realization of a robotic endoscope with higher
313 TRL. This included the integration of a high power laser into the system and mechanism enhancements
314 for higher robustness and performance. Non-contact soft tissue ablation was demonstrated using a
315 Er:YAG laser (2.94 μm wavelength), delivered using a GeO₂ solid core fiber and appropriate laser
316 focusing optics (Kundrat et al., 2016). Subsequently, a new 5 DOF continuum robotic endoscope
317 composed of two segments with 11 mm outer diameter and a large inner lumen of 5.75 mm was
318 designed and fabricated monolithically. The system featured multiple rigid guidance elements
319 connected to bellow-shaped flexible sections to enable bending, extension, and compression of the

320 structure, which demonstrated bending up to 90° and elongation of up to 80% from its initial length.
321 These capabilities were instrumental to allow the demonstration of assistive and autonomous
322 technologies for laser focus adjustments (Kundrat et al., 2019).



323 (A) (B)
324 Fig. 10. (A) Advanced version of a flexible robotic endoscope for non-contact laser surgery (Kundrat et al., 2019). (B) High power laser
325 auto-focusing system based on a hydraulically actuated MEMS varifocal mirror (Geraldes et al., 2019).

326 The realization that high power laser focusing is critical for the precision and quality of endoscopic
327 laser microsurgeries also lead to parallel research into micro-opto-electromechanical systems
328 (MOEMS) for this purpose. This included the development of a 3 × 4.24 mm hydraulically-actuated
329 MEMS varifocal mirror able to provide laser beam defocusing over 60 diopters. The device proved to
330 be appropriate for use with high power surgical lasers (including CO₂ lasers) and enabled the
331 implementation of an auto-focusing system with focal length ranging from 15 mm to 140 mm (Geraldes
332 et al., 2019).

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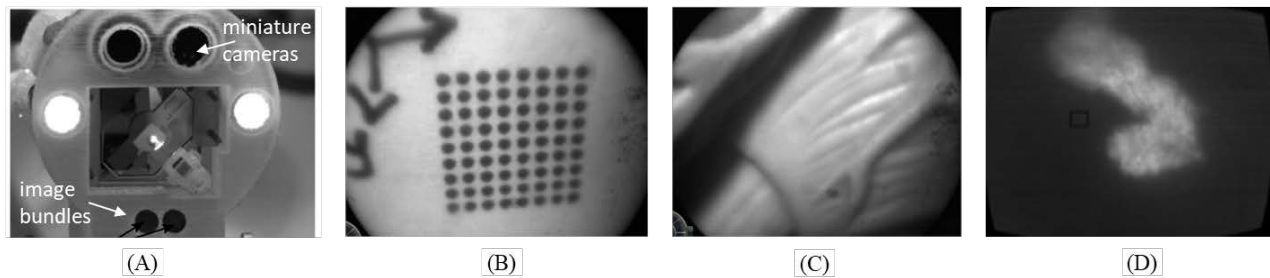
334 3.3 Cancer tissue visualization systems

335 The goal here was to create new technologies to support the detection of tumors and the intraoperative
336 definition of surgical margins. This was pursued through research and development of optical
337 technologies and computer vision methods for enhanced real-time visualization of cancer tissue, which
338 led to the development of a dual imaging system for the acquisition of stereoscopic white-light and
339 fluorescence images.

340 The white-light imaging system was specifically designed for high-speed imaging to enable visual
341 servoing of the laser beam controlled by the Squipabot. It was based on the use of two imaging bundles
342 of 50,000 fibers each, providing monochrome stereo images with a 720×576 pixels resolution at up to
343 1000 frames per second (fps). The system's field of view was 15 mm in diameter at a 25 mm working
344 distance. This corresponded to a pixel resolution of approximately 13 μm/pixel.

345 The fluorescence imaging system was based on the same fiber bundles and an additional fluorescence
346 excitation laser. Optical filters were used outside the endoscope body to select the wavelengths of
347 interest. The system was able acquire 10 fluorescence images per second (10Hz), which were
348 automatically co-registered and with the same 720×576 pixels resolution as the white-light images.

349 The realization of this dual imaging system demonstrated a new hardware for hyperspectral
350 augmented-reality visualization of the surgical field. Figure 11 shows a picture of this system integrated
351 to the μ RALP endoscope tip and sample images acquired with it at 600 fps, which presented
352 satisfactory resolution, contrast and field of view.



353

354 Fig. 11. (A) the μ RALP endoscope tip with integrated dual imaging system. (B) and (C) white-light images acquired at 600fps. (D)
355 Fluorescence image acquired with the same imaging bundle.

356

357 In addition to the development of new hardware for cancer imaging, μ RALP also involved research on
358 computer vision methods for automatic detection and classification of laryngeal tumors based on
359 narrow-band imaging (NBI) endoscopic videos. Around 2011, clinical studies were starting to establish
360 correlations between the characteristics of the laryngeal mucosal microvascular network and different
361 cancer types (Ni et al., 2011). Therefore, the automatic recognition of microvascular patterns was
362 deemed as a promising technology to assist in cancer detection and surgical margins definition.

363 Initial research on this topic focused on detecting and classifying blood vessel patterns based on
364 anisotropic filtering, morphological analysis, and statistical analysis of extracted metrics such as blood
365 vessels' thickness, tortuosity, and density (Barbalata and Mattos, 2016). The method reached an overall
366 classification accuracy of 84.3% during a preliminary assessment, proving the feasibility of the
367 approach. This motivated further research in the area, including the development of machine learning
368 methods for laryngeal tissue classification based on NBI texture analysis (Moccia et al., 2017), which
369 achieved a median recall of 98% on a well-balanced dataset built from endoscopic videos of 33 patients.

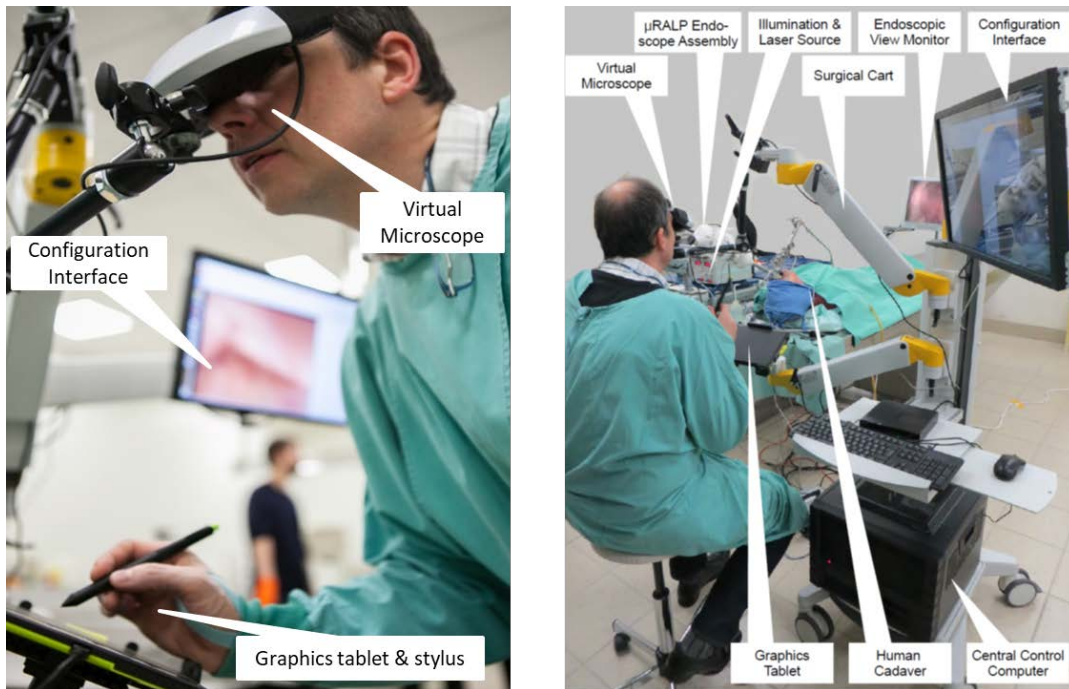
370

371 3.4 Teleoperation and surgeon-robot interfaces

372 The specific goals here were to design and implement the software and hardware infrastructures for
373 the complete integration of the μ RALP system, and to develop novel user interfaces for intuitive,
374 precise, and ergonomic teleoperation of such system.

375 Initial efforts focused on a comprehensive assessment of the Virtual Scalpel system involving expert
376 and novices ENT surgeons (Mattos et al., 2014). This system, shown in Fig. 2, allowed the use of a
377 stylus to control the steering and activation of the surgical laser beam directly from a touch-screen
378 monitor, where real-time video of the surgical site was displayed. Results demonstrated the Virtual
379 Scalpel could augment the surgeons' skills by providing a highly intuitive control interface able to
380 eliminate the hand-eye-foot coordination issues that affect the standard laser microsurgery systems
381 used clinically. This translated into significantly enhanced laser aiming accuracy and controllability
382 assessed through a quantitative analysis of trajectory following errors.

383 However, feedback from the surgeons also highlighted the need for stereoscopic visualization of the
384 surgical site for proper depth perception during the delicate laser microsurgeries. Therefore, the Virtual
385 Scalpel system was redesigned to provide such visualization. This led to the development of the
386 Virtual Microscope concept (Deshpande et al., 2014), in which a stereoscopic head-mounted display
387 (HMD) was used to simulate a standard surgical microscope, and a graphics tablet was used as the
388 input device for controlling the laser beam. Results here demonstrated similar performance
389 enhancements as Virtual Scalpel system in terms of laser control accuracy and usability, with the extra
390 benefits of allowing 3D visualization and augmented reality features. Therefore, this was the surgeon
391 interface selected for the μRALP system (Fig. 12).



392

393 Fig. 12. The μRALP teleoperation interface and its components.

394

395 Overall, the final μRALP surgeon interface was composed of the following main elements:

396 • **Input Interface:** A graphics tablet was used for laser aiming control. Buttons on the stylus were
397 used for the definition of intraoperative plans and for system configuration changes.

398 • **Visualization Interface:** The system included three visualization devices:

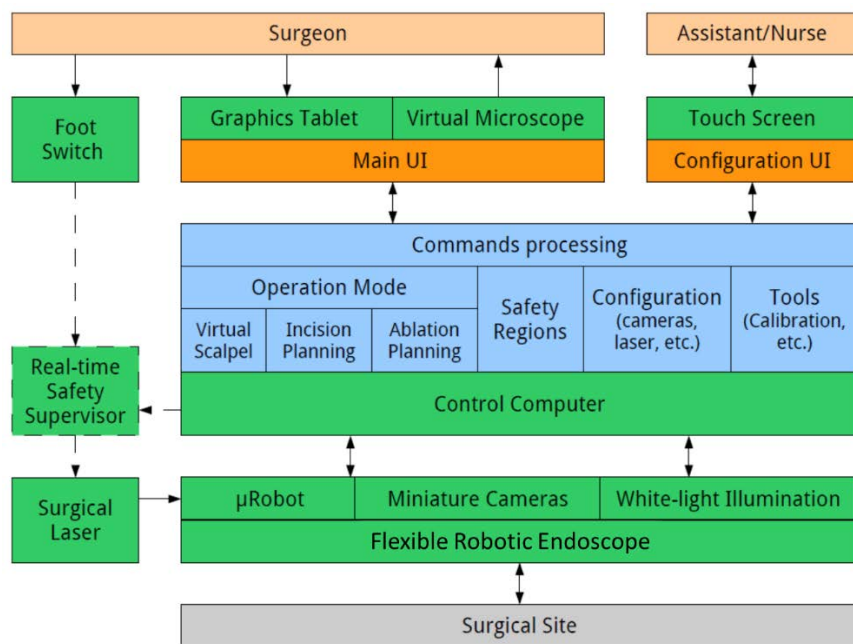
399 ○ **Virtual Microscope:** This component provided real-time stereoscopic visualization of
400 the video streams produced by the endoscope's imaging system. The 3D videos were
401 displayed on a high-definition immersive stereoscopic display fixed to the μRALP
402 surgical cart with an adjustable arm.

403 ○ **Configuration Interface:** A touchscreen monitor was used for system configuration,
404 operating mode selection, alarm messages, and as a supplementary display for surgical
405 site visualization.

406 ○ Endoscopic View Monitor: An additional monitor was used to display the real-time
 407 endoscopic video for the surgical team in the operating room. It also served as a
 408 visualization aid during the manual insertion and rough positioning of the μRALP
 409 endoscope near the surgical site.

410 • Surgical Cart: A cart was used to integrate and organize the different parts of the surgical system
 411 into a single rack-style configuration. It provided housing and support for the system’s control
 412 computer, graphics tablet, virtual microscope, and configuration touchscreen monitor. It was
 413 designed to be easily rolled in and out of operating rooms and reconfigurable to match the
 414 surgeon requirements.

415 Controlling the complete μRALP surgical system from the surgeon interface required full software and
 416 hardware integration and real-time operations. This was implemented following the architecture
 417 presented in Fig. 13. The software components included: Input command processing; Image
 418 acquisition, processing, and display; Visual servoing for closed-loop laser control; Image registration
 419 and 3D reconstruction; Augmented reality processing and display. The hardware components included:
 420 Micro-robotic laser micromanipulator (Squipabot); Robotic endoscope; Illumination; Endoscopic
 421 cameras; Visualization devices.

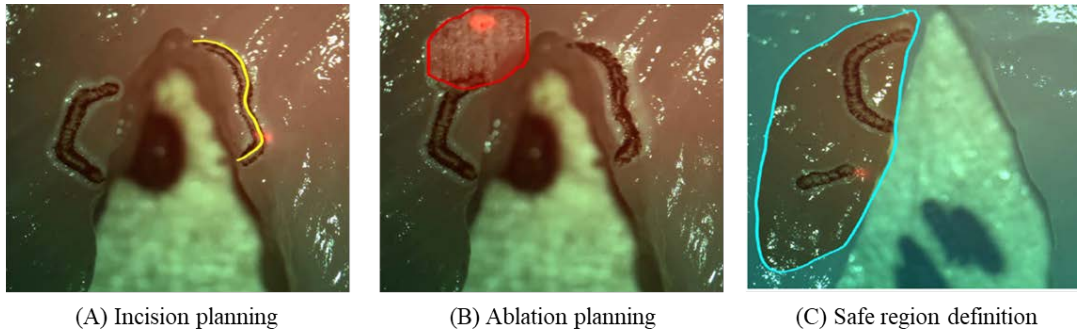


422
 423 Fig. 13. The μRALP surgical system architecture.

424
 425 When using the μRALP system, the surgeon was in full control of the operation. Nonetheless, different
 426 components assisted in the execution of surgical tasks. These provided the following assistive features:

- 427 1. Virtual Scalpel: Real-time laser aiming control using the stylus and tablet interface.
- 428 2. Intraoperative Planning: The stylus could be used to define virtual scan patterns in the surgical
 429 field, allowing the planning of incisions or ablation regions for subsequent automatic execution
 430 (Fig. 14).

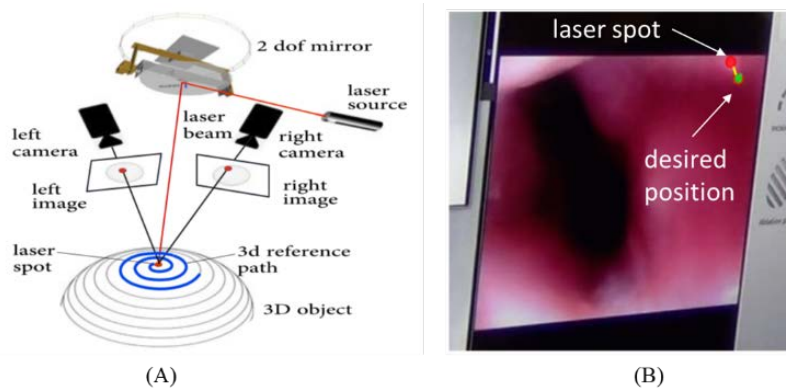
431 3. Predictive Safety: The stylus could also define safe and forbidden virtual regions in the surgical
432 field, which were used as virtual fixtures to automatically enable or disable the high-power
433 surgical laser.



434
435 Fig. 14. Examples of intra-operative planning of incisions paths, ablation patterns, and safety regions based on graphic overlays. The
436 high-power surgical laser was only enabled within the defined safe region.

437
438 Accurate automatic execution of surgeon-defined intraoperative plans was pursued through research
439 on novel laser visual servoing methods. This resulted in the development of two methods, called
440 epipolar and trifocal visual servoing. The epipolar method used one of the embedded cameras and
441 Squipabot’s actuated mirror as a virtual camera to implement a weakly calibrated controller able to
442 accurately follow paths in a 3D scene (Andreff et al., 2013). This method was also shown to enable
443 decoupling path following from velocity profile control, offering advantages in terms of laser-tissue
444 interaction control (Seon et al., 2015).

445 The trifocal visual servoing method used the two endoscopic cameras and the actuated mirror (virtual
446 camera) to construct a three-view imaging system and then use the trifocal constraint to design a robust
447 and accurate controller (Andreff and Tamadazte, 2016). This method was shown to simplify the eye-
448 to-hand visual control law of the pan-tilt laser, avoiding the need for a strong Euclidean calibration of
449 the system and for interaction matrix inversions. At the same time, it provided good performance,
450 achieving an RMS error of 1.20 pixels in trajectory tracking tasks during cadaver trials with the μ RALP
451 system.



452
453 Fig. 15. (A) Schematic view of a trifocal laser visual servoing system with two cameras. (B) Intraoperative scene during laser virtual
454 servoing on the vocal cord of a cadaver.

456 Research beyond the end of μ RALP continued the efforts towards fast, accurate and robust laser visual
457 servoing, leading to the development of a new path following method incorporating trifocal constraint
458 (Tamadazte et al., 2018). This method ensures accurate 3D control of laser spot displacements in
459 unknown environments while exhibiting good robustness with respect to the calibration and
460 measurement errors and scene variations. In addition, it allows perfectly decoupling the laser spot
461 velocity from the path shape.

462 Furthermore, continued research towards surgeon interfaces with improved usability, intuitiveness, and
463 laser control performance led to the development of the Haptic Laser Scalpel system (Olivieri et al.,
464 2017). This new control interface brought the sense of haptics to contactless laser surgeries, enriching
465 the surgeon experience and allowing the exploitation of active constraints and guidance techniques to
466 significantly enhance laser control accuracy both in static and dynamic environments. This was realized
467 by exploiting stereoscopic visualization and real-time 3D reconstruction to create a virtual haptic
468 surface representing the real surgical site, which could be explored using a commercial haptic device.
469 This same device was also used to control the steering of the surgical laser beam, allowing the co-
470 location of the haptic feedback and the laser spot seen on the target tissue.



471

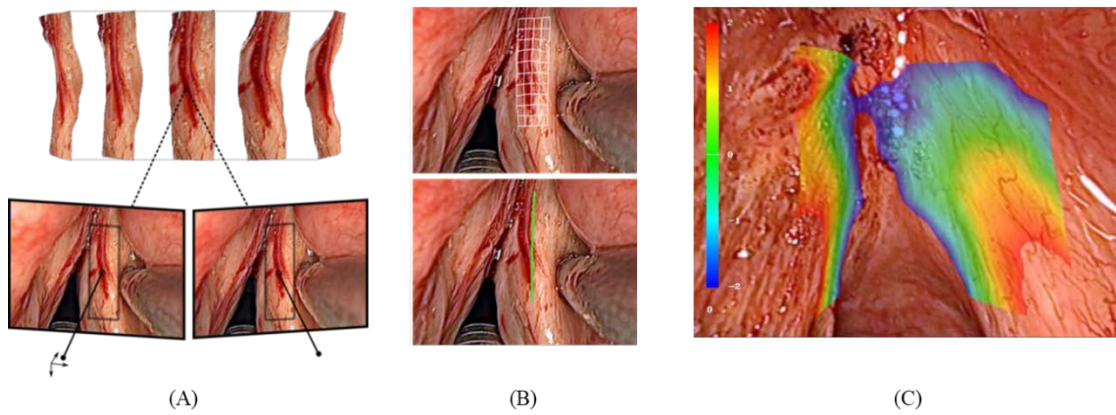
472 Fig. 16. The Haptic Laser Scalpel, developed to bring the sense of haptics to contactless laser surgeries. (A) Surgeon interface. (B) 3D
473 visualization of the surgical site with an augmented reality haptic scalpel avatar.

474

475 3.5 Augmented reality systems

476 The research focus here was on enhancing intraoperative surgical planning and visualization by means
477 of stereoscopic methods. This included the development of methods for planning laser incisions in 3D,
478 for assessing and controlling the laser focus, and for creating image overlays based on information
479 from the tissue surface and from the laser.

480 One of the main achievements in this area regarded real-time intraoperative acquisition of tissue surface
481 information (see Fig. 17). For this, a fast 3D reconstruction method providing sub-pixel accuracy at up
482 to 25 frames per second was developed based on stereo image processing (Schoob et al., 2016). This
483 corresponded to a reconstruction accuracy below 1 mm when using the μ RALP endoscope, which
484 featured a stereo imaging system with working distance between 20 and 30 mm. Furthermore, the
485 method included robust techniques for outlier rejection and for handling radiometric illumination
486 changes, as these naturally occur in the tube-like larynx.



487

488 Fig. 17. Real-time stereoscopic methods for (A) 3D reconstruction, (B) intraoperative incision planning and visualization, and (C) laser
489 focus adjustment.

490

491 Image-based assistance to the surgical workflow was achieved by incorporating the extracted tissue
492 surface information in the definition and visualization of surgical plans. For this, a new method for
493 visual augmentation and three-dimensional feedback was developed. The method included real-time
494 registration of the laser workspace on the live stereoscopic view, enabling accurate registration of laser
495 incision plans with a maximum error of 0.2 mm (Schoob et al., 2016).

496 Tissue surface information was also used to produce a synthetic laser view, which was exploited in the
497 implementation of assistive and automatic laser focusing methods (Schoob et al., 2015). This included
498 an intuitive framework for interactive laser focus positioning, which used color-coded image overlays
499 to highlight regions in the surgical site under proper laser focusing (Schoob et al., 2016b). The system
500 was shown to allow manual positioning of the laser focal plane on the target tissue with an accuracy of
501 0.4 mm within seconds.

502 Research beyond the end of μRALP continued the development and enhancement of these assistive
503 systems for endoscopic laser surgery, introducing extensions able to compensate for tissue motion and
504 tracking inaccuracies such as inconsistent feature matching and drift. The enhanced framework proved
505 to be suitable for online ablation control in laser microsurgery, enabling accurate execution of laser
506 incision paths defined by the surgeon even in the presence of tissue motions and deformations (Schoob
507 et al., 2017). The system demonstrated real-time operation and highly accurate soft tissue tracking
508 performance, providing tracking errors below 0.05 mm and path ablations with RMS error below 0.21
509 mm in dynamic conditions. Subsequently, it was also integrated into the controller of a new robotic
510 endoscope for non-contact endolaryngeal laser surgery, enabling both assistive and autonomous laser
511 focus adjustments (Kundrat et al., 2020).

512

513 **3.6 Cognitive surgical systems**

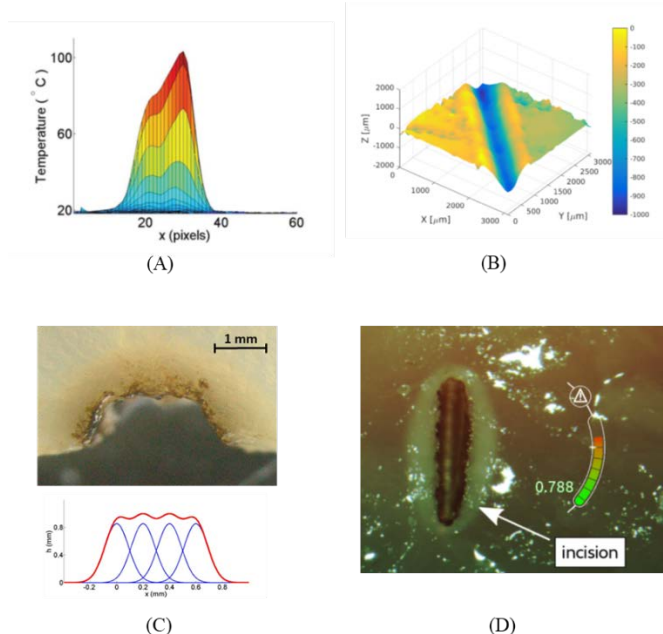
514 The development of cognitive systems within μRALP aimed at providing safety supervision and
515 autonomous operations to further improve the safety, quality, and precision of laser microsurgeries.
516 This led to research towards the modeling and control of laser-tissue interactions, which are critically
517 important in delicate tissue sparing operations such as laser phonosurgery. In fact, after the

518 complete eradication of malignancies, a secondary major clinical goal in this case is the preservation
519 of healthy tissue to maintain key larynx functionalities and enable good post-treatment vocal quality.

520 From a research and technology development perspective, this clinical requirement translates into the
521 need to perform precise and clean laser cuts on the soft laryngeal tissue, avoiding carbonizations and
522 thermal damage to surrounding healthy tissue. In addition, the depth of laser ablations should be
523 properly controlled, to avoid damaging underlying tissue layers.

524 Satisfying these needs requires controlling the laser-tissue interaction process. This was pursued within
525 μRALP not only through laser focus control and laser scanning capabilities as discussed above, but
526 also through the development of cognitive systems to model and control the laser-tissue interactions in
527 real-time. Initially, tissue temperature dynamics under high-power laser irradiation was studied and
528 reliably modeled using nonlinear regression based on Gaussian basis functions (Pardo et al., 2015).
529 This knowledge was then used to generate real-time estimates of the thermal state of soft tissues during
530 laser ablation, proving the approach was suitable to produce feedback for automatic laser incision
531 control (Pardo et al. 2014).

532 Subsequent research focused on the modeling, online estimation and automatic control of the laser
533 incision depth in soft tissues. This resulted in the development of a model able to estimate, in real-time,
534 the depth of laser ablations with RMS error of 0.1 mm for depths ranging up to 1.4 mm (Fichera et al.,
535 2015). This model was then used in a robotic laser microsurgery system to enable both autonomous
536 laser incision depth control along cutting trajectories and autonomous ablation of tissue volumes
537 (Fichera et al., 2015b). Finally, these controllers were extended to allow regulating the laser energy
538 density along the incision path, demonstrating that target depths could be achieved within $\pm 60 \mu\text{m}$ error
539 range (Acemoglu et al., 2017).



540
541 Fig. 18. Results from research on cognitive modeling and control of laser-tissue interactions. (A) Real-time estimate of superficial tissue
542 temperature during high-power laser scanning. (B) Autonomous laser incision depth control along incision paths. (C) Autonomous tissue
543 volume vaporization by laser ablation. (D) Augmented reality gauge for displaying the laser incision depth progression in real-time.

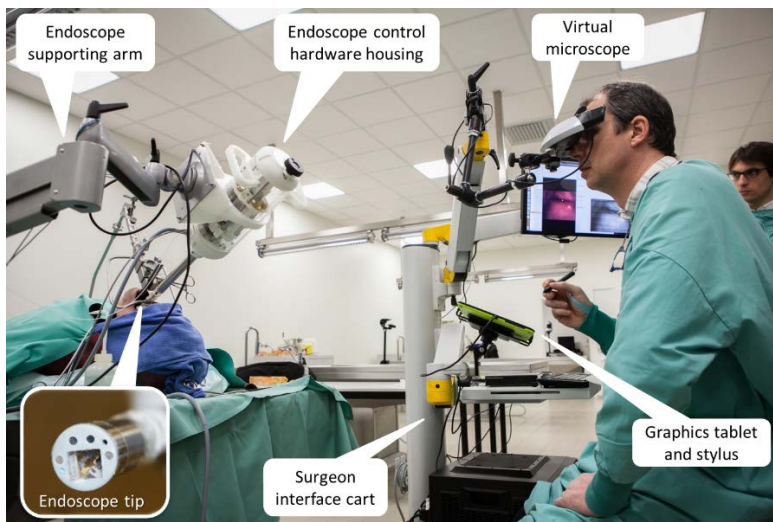
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545 The developed laser-tissue interaction models and controllers were also integrated into μRALP
546 interface to provide assistive functions during surgery. For instance, methods to provide real-time
547 feedback on the laser incision depth to the surgeon were researched. These included the use of an
548 augmented reality gauge to display the incision depth progression (Fichera et al., 2015), and of
549 kinesthetic and vibrotactile haptic feedback to inform the user when a target depth was reached (Fichera
550 et al., 2016). Both systems were shown to significantly enhance the laser incision depth control
551 capabilities of the users during preliminary trials.

552

553 **3.7 μRALP system integration and cadaver trials**

554 After 3 years of intense research work, the μRALP project concluded with the complete integration of
555 the surgical system and tests in human cadavers. The final system consisted of two main parts: The
556 μRALP endoscope and the μRALP teleoperation interface, as depicted in Fig. 19. The cadaver
557 experiments were instrumental for obtaining performance metrics regarding the complete system and
558 all of its sub-components in a realistic surgical scenario. This experience highlighted the benefits of an
559 integrated solution for robot-assisted endoscopic laser microsurgery, with each system component
560 contributing to enhance surgical precision and quality. It also allowed the acquisition of important
561 clinical feedback, which guided the research and development of the technologies beyond the end of
562 the project as detailed above.



563

564 Fig. 19. The integrated μRALP surgical system prototype under evaluation in a human cadaver.

565

566 **4 Conclusion**

567 This paper reviewed the technological advancements and scientific contributions achieved within and
568 beyond μRALP, a collaborative European project that aimed at bringing unprecedented levels of
569 accessibility, precision and quality to endoscopic laser microsurgeries. The range of technologies
570 developed to achieve these goals included flexible robotic endoscopes, micro-mechatronic robotic
571 systems for laser steering, cancer tissue visualization systems, surgeon-robot interfaces, stereoscopic
572 methods for enhanced teleoperation and automatic control, and cognitive surgical systems.
573 Individually, each of these technologies proved to bring incremental levels of improvement towards

574 the project goals. However, major impact is expected to come from their full integration into a complete
575 clinical surgical robotic system, as preliminarily experienced during cadaver trials with the final
576 μRALP prototype.

577 Specifically, the research contributions reviewed in this paper were shown to allow significant
578 advances in:

- 579 • Medical continuum robot design, with the introduction of novel concepts for patient-friendly
580 and surgeon-acceptable continuum robots with large central lumen and adjustable length.
- 581 • Medical micro-mechanisms, with new methodology for designing out-of-plane micro-
582 fabricated mechanisms with high range of motion, and novel devices for high power laser
583 focusing and steering.
- 584 • Surgeon-robot interfaces, with novel methods for intuitive robot control, intraoperative
585 planning, and automatic operations leading to sizable improvements in the precision and safety
586 in laser microsurgeries.
- 587 • Three-dimensional vision and control, with novel solutions for 3D reconstruction of the surgical
588 scene allowing large improvements in surgical robot control, intraoperative planning and in the
589 quality of laser incisions through adaptable laser focusing.
- 590 • Cancer tissue visualization, with a new approach for fiber-based endoscopic hyperspectral
591 imaging and image processing methods for the automatic detection and classification of
592 laryngeal tumors.
- 593 • Cognitive surgical system, with new methods for the modeling and control of laser-tissue
594 interactions enabling autonomous depth control during incisions and volume ablations.

595 At this current point in time, research continues towards improving the TRL of endoscopic laser
596 microsurgery technologies created within and beyond μRALP. This includes further miniaturization of
597 the robotic devices to expand their clinical indications, and the elimination of system limitations such
598 as the lack of endoscopic tissue manipulation capabilities during laser ablation. Nonetheless, it is clear
599 that the technologies reviewed in this paper have the potential to bring many benefits to patients,
600 surgeons, hospitals, and the public healthcare system in general. For example, once they reach clinical
601 use, more patients will qualify for transoral laser microsurgeries and benefit from enhanced surgical
602 precision and quality compared to the current state of the art. Surgeons will benefit from a more
603 intuitive surgical setup and from robotic assistance, which will enable them to better plan and execute
604 delicate interventions. Finally, hospitals will see less complications and revision surgeries, increasing
605 customer satisfaction and, at the same time, contributing to lower healthcare costs.

606 It is also clear that the new knowledge and the new technologies described herein are applicable to a
607 wide range of microsurgery interventions, both laser and otherwise. This expands the impact of the
608 reviewed research beyond the specific application in robot-assisted endoscopic laser microsurgery.

609

610 **5 Data Availability Statement**

611 The laryngeal images dataset used for the development and assessment of cancer detection methods
612 can be found in Zenodo [<https://zenodo.org/record/1003200#.X6LLjVNKhTY>].

613

614 **6 Author Contributions**

615 **The Author Contributions section is mandatory for all articles, including articles by sole authors. If**
616 **an appropriate statement is not provided on submission, a standard one will be inserted during the**
617 **production process. The Author Contributions statement must describe the contributions of individual**
618 **authors referred to by their initials and, in doing so, all authors agree to be accountable for the**
619 **content of the work. Please see [here](#) for full authorship criteria.**

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621 Funding for the μRALP project was provided by the European Union Seventh Framework Programme
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623

624 **8 Supplementary Material**

625 The Supplementary Material for this article can be found online at:
626 <https://www.frontiersin.org/articles/...>

627 **μRALP video**

628

629

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772 **10 Conflict of Interest**

773 The authors declare that the research was conducted in the absence of any commercial or financial
774 relationships that could be construed as a potential conflict of interest.