

Annual Review of Biomedical Engineering
**Frontiers of Medical Robotics:
 From Concept to Systems to
 Clinical Translation**

Jocelyne Troccaz,^{1,*} Giulio Dagnino,^{2,*}
 and Guang-Zhong Yang²

¹Université Grenoble Alpes, CNRS, Grenoble INP, TIMC-IMAG, F-38000 Grenoble, France;
 email: Jocelyne.Troccaz@univ-grenoble-alpes.fr

²The Hamlyn Centre for Robotic Surgery, Imperial College London, London SW7 2AZ,
 United Kingdom; email: g.dagnino@imperial.ac.uk, g.z.yang@imperial.ac.uk

Annu. Rev. Biomed. Eng. 2019. 21:193–218

First published as a Review in Advance on
 March 1, 2019

The *Annual Review of Biomedical Engineering* is
 online at bioeng.annualreviews.org

<https://doi.org/10.1146/annurev-bioeng-060418-052502>

Copyright © 2019 by Annual Reviews.
 All rights reserved

*These authors contributed equally to this article

Keywords

medical robotics, surgical robots, minimally invasive surgery, MIS,
 computer-assisted medical intervention, human–robot interaction, clinical
 translation

Abstract

Medical robotics is poised to transform all aspects of medicine—from surgical intervention to targeted therapy, rehabilitation, and hospital automation. A key area is the development of robots for minimally invasive interventions. This review provides a detailed analysis of the evolution of interventional robots and discusses how the integration of imaging, sensing, and robotics can influence the patient care pathway toward precision intervention and patient-specific treatment. It outlines how closer coupling of perception, decision, and action can lead to enhanced dexterity, greater precision, and reduced invasiveness. It provides a critical analysis of some of the key interventional robot platforms developed over the years and their relative merit and intrinsic limitations. The review also presents a future outlook for robotic interventions and emerging trends in making them easier to use, lightweight, ergonomic, and intelligent, and thus smarter, safer, and more accessible for clinical use.

**ANNUAL
REVIEWS CONNECT**

www.annualreviews.org

- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

Contents

1. INTRODUCTION	194
2. ADVANCES IN MEDICAL ROBOTICS	197
2.1. Neurosurgery and Ear, Nose, and Throat Surgery	199
2.2. Orthopedics	200
2.3. Minimally Invasive Surgery: Laparoscopy and Endoluminal Intervention	201
3. OPEN CHALLENGES AND THE FUTURE OF MEDICAL ROBOTICS	205
4. CONCLUSIONS	209

1. INTRODUCTION

Earlier diagnosis, improved efficiency, and delivery of therapeutic measures in combination with advances in surgical techniques have brought improved prognosis and functional outcome to patients, prolonging life and continuously extending the boundary of survival. As a result, the role of clinicians has undoubtedly become more demanding, requiring the handling of much multimodal, multidimensional, multiscale, interventional, metabolic, and system-level information beyond anatomical details. Early diagnosis also means smaller target lesions, requiring not only minimally invasive access but also precision intervention that challenges the perceptual and sensory capabilities of the surgeons, in many cases requiring superhuman dexterity, vision, reasoning, and decision making. In this regard, medical robotics has a significant role to play in directing the future of surgery toward precision intervention and targeted therapy.

This general evolution of medical techniques and instrumentation began long ago: The first endoscope, developed by Bozzini, was used in urology in 1806. In 1890, Zernov, a Russian professor of anatomy, inspired by geographic systems of coordinates, invented the encephalometer, the ancestor of modern stereotactic frames that is used for precise, noninvasive localization of brain structures. However, this evolution accelerated in the twentieth century thanks to discoveries in basic sciences and technical revolutions in electronics, computer science, and robotics. Eighty years after the discovery of X-rays (1895) by Roentgen, it became possible to capture internal anatomy as three-dimensional (3D) data and to manipulate it virtually. Advances toward the actual planning and guidance of interventions also occurred rapidly. As an example, Kall et al. (1) describe an image-based and computer-controlled system for neurosurgery developed at the Mayo Clinic. Kelly et al. (2) reported extensive clinical data (1,000 patients in two centers). A new domain at the forefront of medicine and information sciences emerged: computer-assisted medical intervention.

The initial goal of computer-assisted intervention was to assist medical practitioners in executing efficient and safe diagnostic or therapeutic actions. These actions should be as uninvasive as possible, and their quality should be quantifiable. Moreover, computer-assisted intervention systems and devices must demonstrate added clinical value, and their use must respect ethics and regulations. The clinical objectives gave rise to a classical perception–decision–action loop (Figure 1).

Here, perception relates to the acquisition of patient data and information related to the procedure in progress (e.g., position of a surgical instrument or of a prosthesis, force in a joint, or deformation of an organ). This phase may require the development of specific sensors, processing of data from these sensors, and structural information [e.g., the shape of a particular anatomical structure from a volume of data from computed tomography (CT) or magnetic resonance imaging (MRI) or the characterization of the aggressive nature of cancer from histological data]. A crucial

Computer-assisted medical intervention:

provides the clinician with tools to use quantitatively multimodal data to plan, simulate, and efficiently execute minimally invasive diagnostic or therapeutic interventions



Figure 1

Perception–decision–action loop. The goal of robotics and computer assistance is to provide as much information and support to the clinical team as possible to produce the best possible treatment. The acquisition and processing of patient-specific data (e.g., computed tomography, magnetic resonance images) are crucial to preplan the procedure and support the clinicians in developing the optimal strategy. The effective fusion of preoperative planning with intraoperative real-time imaging, sensing, and robotic assistance is necessary to support the clinician in delivering the best possible treatment and producing cost-effective outcomes.

step is the fusion of patient-specific data with general medical knowledge (e.g., a phase of a surgical process, an anatomical atlas, a biomechanical model of a joint, the average shape of an organ and its major modes of deformation). Very often, the clinician mentally and qualitatively performs this data fusion step. A major goal of computer-assisted intervention is to merge all the available information into a single, quantitative model. For example, in order to make prostate cancer diagnosis more reliable, one can merge preoperative MRI of the prostate, for which the target lesion has been identified by appropriate classification methods (3), with intraoperative ultrasound, for example, to guide a biopsy needle to this area (4). The digital representation incorporating this information also serves as a basis for decision making. This may involve planning the optimal procedure in a given clinical context—for example, determining the radiation plan for delivering a prescribed dose to a tumor of a specific shape while limiting the maximum dose to organs at risk in radiotherapy. When the optimal strategy is difficult to express mathematically, procedure simulation may be used for preplanning. This process requires patient-specific models of living tissues (5) and the ability to simulate interactions between instruments and organs (6). Both issues are very challenging. In practice, when target organs move or are modified by the intervention, intraoperative information may have to be acquired and processed in real time in order to update or replan a strategy accordingly, so that guiding systems can execute the planned action onto the patient.

Another goal of computer-assisted intervention concerns the training and education of clinicians. Computerized simulation makes intensive training of technical skills possible since the intervention can take place virtually on modeled patients. Training also concerns the process workflow.

Active robot: system that autonomously executes a preplanned procedure

Passive robot: unactuated and manually driven system

Semi-active robot: system with constrained (e.g., cooperated) motion; constraints may be produced by specific hardware or may be programmable

Teleoperated robot: tool held by a robot and remotely controlled by a human

Access to massive quantities of data (on patients, pathologies, and traces of medical interventions) and the rebirth of artificial intelligence (AI) could enable automatic extraction of relevant information and knowledge, contributing to better decision making and intervention guidance (7, 8).

With the introduction of robotics, computer-assisted intervention uses the robot as both an input and an output medium. The robot is a unique device that is able to sense the physical world, to modify it, and to interact with humans while being computer controlled and, therefore, in close connection to data models and the physical world. However, the clinical constraints can be strong. Tasks are complex and unique—each patient is different—and take place in a nonstructured environment. Workspace is limited and must be shared with humans; safety (electrical, mechanical, biological, etc.) and reliability are mandatory; and additional constraints may arise from application-specific requirements (e.g., being MRI compatible and free of ferromagnetic materials). Finally, regulations applying to medical devices have to be conformed to at all times.

This review reports on interventional robots assisting a clinician for diagnostic or therapeutic interventions. It focuses on robotic systems and publications that represent key advances in medical robotics and identify open challenges and research directions. This review includes, when possible, systems that have proceeded to commercialization, highlighting their clinical impact and innovation (**Figure 2**). The taxonomy used in this article focuses on interaction between the user and the robotic system regarding tool motion, as follows:

- Active robots are those that autonomously execute a preplanned motion.
- Passive robots are unactuated and manually driven.
- Semi-active (e.g., cooperated) robots employ constrained motion.
- Teleoperated robots involve a tool held by the robot and remotely controlled by the human.

This review is not intended to provide an exhaustive taxonomy of research publications; instead, we refer the readers to existing reviews on medical robotics (9–26). In addition, we do

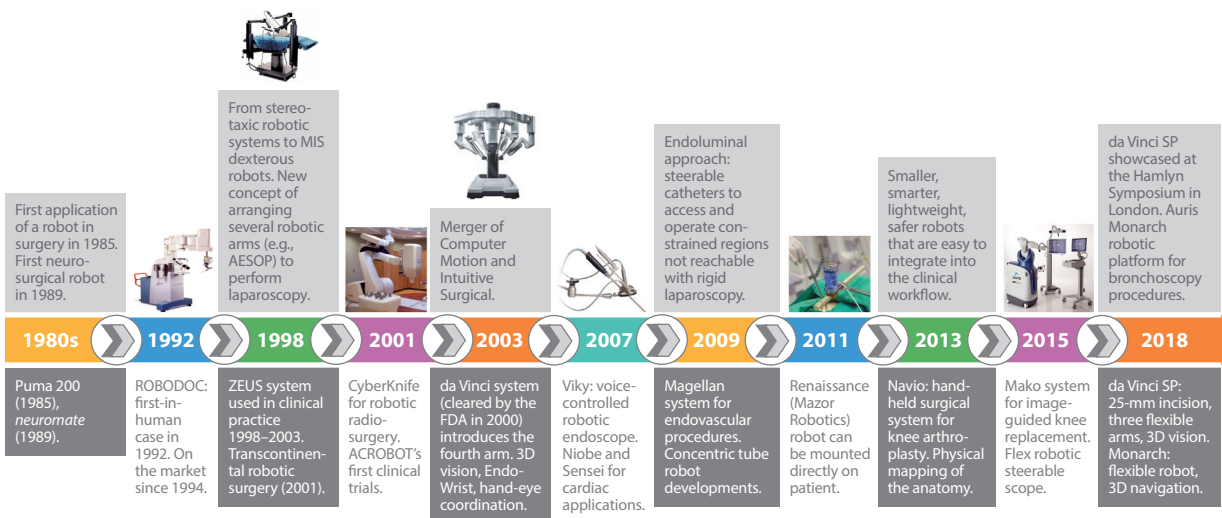


Figure 2

Timeline of medical robotics showing key milestones in medical robotics and computer-assisted intervention. Only commercial surgical platforms are depicted. Abbreviations: 3D, three-dimensional; FDA, Food and Drug Administration; MIS, minimally invasive surgery; SP, single port. Images are adapted with permission as follows: ROBODOC, Reference 130; ZEUS/AESOP, Reference 20; CyberKnife, Wikimedia Commons (CC BY 2.0); da Vinci, Intuitive Surgical Inc., © 2018; Viky, Endocontrol, © 2018; Mazor Robotics Renaissance, Mazor Robotics; Mako, Reference 131.

not cover robots that assist patients, disabled persons, or the elderly; robots used for lifting/transportation of loads in the hospital; or robots for pharmacy and biological sample analyses.

2. ADVANCES IN MEDICAL ROBOTICS

This section provides an overview of the evolution of medical robots, as well as integration of imaging, sensing, and robotics for improved human–robot interaction. From one generation of robotic systems to the next, perception, decision, and action become more and more intertwined, resulting in improved dexterity and precision and reduced invasiveness, access trauma, and tissue damage. Representative examples are shown in **Figure 3** and summarized in **Table 1**.

Surgical robots were originally developed to address the clinical demand for greater accuracy in manipulation and visualization, overcoming the ergonomic challenge of conventional minimally



Figure 3

Examples of surgical robot specializations. Abbreviation: ENT, ear, nose, and throat. Images are adapted with permission as follows: *neuromate*, Renishaw, © 2018; CyberKnife, Wikimedia Commons (CC BY 2.0); μ RALP Surgical System, Mattos et al. (μ RALP Consortium; <https://www.microralp.edu>); da Vinci, Intuitive Surgical Inc., © 2018; ZEUS/AESOP, Reference 20; i-Snake, Reference 26; Mako, Reference 131; ROBODOC, Reference 130; Navio, Reference 131; Micro-IGES, Reference 88; Magellan and Niobe, Reference 24. Figure inspired by Reference 26.

Table 1 Examples of commercially available medical robots

Robotic platform	Company	Clinical application	Vision	Sensing	Level of autonomy/ interaction	Reference
<i>neuromate</i>	Renishaw	Neurosurgery	3D	No	Semi-active (parallel)	30
ROBODOC	Curexo Technology	Orthopedics	3D	Force	Active	123
Acrobot	Stryker	Orthopedics	3D	Force	Semi-active (parallel)	41
Navio	Smith & Nephew	Orthopedics	Infrared guidance	No	Semi-active (serial)	47
Mako	Stryker	Orthopedics	3D	Force	Semi-active (parallel)	46
Renaissance	Mazor Robotics	Spine surgery	3D	No	Semi-active (parallel)	51
CyberKnife	Accuray Inc.	Radiation therapy	3D	No	Active	31
ZEUS/AESOP	Computer Motion Inc.	Laparoscopy	2D	No	Teleoperated	78
da Vinci	Intuitive Surgical Inc.	Laparoscopy	3D	No	Teleoperated	80
Viky	Endocontrol Medical	Laparoscopy	2D	No	Voice controlled or visual servo	75
Niobe	Stereotaxis	Vascular surgery	3D	No	Teleoperated	93
Sensei	Hansen Medical (now Auris)	Vascular surgery	3D	Force	Teleoperated	91
Magellan	Hansen Medical (now Auris)	Vascular surgery	2D	No	Teleoperated	92
Flex Robotic Scope	Medrobotics	Endoluminal surgery	2D	Force	Teleoperated	84

invasive approaches (see the sidebar titled Robot-Assisted Minimally Invasive Surgery). The first generation of surgical robots was applied, unsurprisingly, to stereotaxic neurosurgery and orthopedics, as both deal with rigid and well-defined structures. This simplifies registration between the robotic system and the patient's anatomy, which can be easily maintained throughout the whole procedure, enabling real-time intraoperative navigation, tracking, and vision-based closed-loop control of the robot.

ROBOT-ASSISTED MINIMALLY INVASIVE SURGERY

Technological advances in the 1980s led minimally invasive surgery (MIS) to become an established approach across several surgical techniques; the first laparoscopic procedure took place in 1985 (20, 26). Despite their advantages over traditional open surgery (e.g., faster patient recovery, reduced trauma and hospitalization costs), MIS procedures are ergonomically difficult to perform due to the use of rigid instruments, limited sensory feedback, misalignment of visuomotor axes, and the need for high dexterity. In response to these limitations, robotics and computer assistance have been integrated into the clinical workflow to provide augmentation of surgical skills in terms of enhanced dexterity, sensing, and image guidance (20). The introduction of these technologies gave rise to two innovative robotics platforms: ZEUS (Computer Motion, Sunnyvale, CA; now Intuitive Surgical) and da Vinci (Intuitive Surgical, Sunnyvale, CA). Thereafter, integration of robotic technologies into clinical practice intensified, resulting in flexible microrobots that are able to further minimize surgical trauma by accessing the anatomy through single incisions and natural orifices. Robotic MIS is evolving toward the development of smaller, smarter, safer, and more cost-effective platforms able to operate at the cellular level through miniaturized devices. Stronger collaboration between academia and commercial organizations will be required to facilitate the development, clinical translation, and economic sustainability of novel robotics technology (25).

2.1. Neurosurgery and Ear, Nose, and Throat Surgery

The performance of neurosurgery is intricately connected to 3D imaging and requires both high accuracy and minimally invasive access. A robotic arm could be a natural extension of the surgeon's hand, to be connected with planning software and imaging data. In the first application of an anthropomorphic robotic arm in neurosurgery, conducted by Kwoh et al. (27), an industrial robotic manipulator (PUMA 200; Unimation, Danbury, CT) was used to position a mechanical guide used by the surgeon to introduce a needle and perform a brain biopsy. On April 11, 1985, the robotic system was successfully tested on a patient.

Since then, the use of a modified industrial robot in neurosurgery (28, 29), first tested on patients in March 1989 and used for several years, evolved into one of the first neurosurgical robots to be approved by the Food and Drug Administration (FDA) in the United States and to receive Conformité Européenne (CE) marking in Europe: the *neuromate* (available from Renishaw, New Mills, UK). The *neuromate* system is a semi-active, five-DOF (degrees of freedom), image-guided robot that allows precise and accurate positioning of a tool holder along preplanned trajectories to perform a broad range of neurosurgical procedures such as electrode implantation, neuroendoscopy, and biopsy. The robot's software supports the registration of intraoperative images (ultrasound, X-ray) with preoperative 3D images (CT, MRI) (29). The robotic arm automatically positions the surgical tool holder on the basis of preoperative planning and intraoperative registration. The *neuromate* system can also operate in a frameless mode, wherein an implantable base is mounted onto the patient and is used to map CT and MRI localization markers to the patient's coordinates (10). The system achieved submillimeter accuracy (0.86 mm) in the frame-based configuration and millimeter accuracy (1.95 mm) in the frameless configuration (30). The *neuromate* system is widely used worldwide, with tens of thousands of patient cases (10).

CyberKnife (Accuray Inc., Sunnyvale, CA) is another example of a commercially available and widely used frameless robot. It is a minimally invasive radiosurgical robotic system employed for the treatment of cranial and spinal tumors (as well as prostate, lung, liver, and pancreas cancers) using linear accelerators. CyberKnife contains integrated imaging systems that can automatically detect and compensate for motion, allowing for frameless treatment (31). CyberKnife tracks and autonomously adapts to tumor or patient movement during treatment to deliver a maximum dose of radiation directly to the tumor while preserving healthy organs and tissues. For organs that move with respiration, CyberKnife synchronizes its motion to the target anatomy on the basis of a learned model and multimodal sensing. This system is recognized as a standard radiation oncology technology, with more than 100,000 patients treated worldwide (32).

Recent technological advances in surgical visualization and miniaturization methodologies have contributed to the application of robotics to skull base and ear, nose, and throat (ENT) microsurgical procedures, which typically require submillimeter accuracy and reliable visuotactile feedback (33). Research at the ARTORG Center for Biomedical Engineering Research in Switzerland by Weber et al. (34) resulted in an image-guided, sensor-controlled, robotic system for cochlear implantation. This system, consisting of a five-DOF serial manipulator, preplanning software, intraoperative real-time image guidance, and in situ assessment of tissue properties, was developed along with a specific surgical protocol, and clinical trials commenced with the first-in-human case in 2016.

The μ RALP surgical system, developed by Mattos and colleagues (35–37), redesigned the surgical setup for the microsurgical treatment of laryngeal lesions by providing the ENT surgeon with assistive robotic teleoperation, real-time in situ pathology detection, intelligent cognitive system, augmented reality, and improved ergonomics. The system was tested in preclinical trials on cadavers in 2015 and is undergoing further technical developments, paving the way toward clinical trials.

Food and Drug Administration

(FDA): US federal agency that regulates (among other things) the medical devices market

Conformité Européenne (CE) marking:

indicates that a medical device available in Europe fulfills certain requirements

Degrees of freedom (DOF): the number of DOF defines the motion capabilities of a robot (i.e., number of independent displacements)

Ear, nose, and throat (ENT) surgery:

surgical specialty dealing with conditions of head and neck structures (also known as otolaryngology)

2.2. Orthopedics

Orthopedic robotic systems evolved similarly—and in parallel—to neurosurgical systems. The first commercially available surgical robot for orthopedics was ROBODOC (Curexo Technology, Fremont, CA), developed in 1986 by Taylor and colleagues (38, 39) at IBM with the objective of improving the results of permanent fixation in total hip replacement. ROBODOC was clinically evaluated through animal trials and the first-in-human case in 1992 (40). The system was commercialized by Integrated Surgical Systems (Sacramento, CA) in 1994 and tested in Europe. ROBODOC was based on the integration of a modified SCARA (selective compliance assembly robot arm) and patient-specific CT data. A CT scan of the patient's anatomy was acquired and used to develop a surgical plan to precisely mill a cavity in the femur to receive the replacement implant. Transferring the plan to the clinical situation was based on fiducials (pins implanted in the bone before the CT, visible in planning data and palpated by the robot before the surgery). The system was fully autonomous during milling, with the surgeon supervising the execution of the surgical plan and intervening with modifications if needed. As a safety feature, ROBODOC mounted a six-axis force/torque sensor, which introduced the concept of force sensing into robotic surgery (40). The TSolution One surgical system (Think Surgical, Fremont, CA), an evolution of ROBODOC, is used to perform total hip and knee arthroplasty.

Acrobot, developed at Imperial College London by Davies and colleagues (41), was a competing system for total knee replacement. Similarly to ROBODOC, a CT scan of the patient was acquired and used to generate a surgical plan. However, Acrobot did not execute the surgical procedure autonomously but rather operated synergistically with the surgeon. It was a semi-active system that introduced a new concept wherein the surgeon actively cooperates with the robot to perform the surgery. This interaction mode is also described as hands-on, comanipulation, or synergistic; it was initially proposed by several groups for better control of the tool and for safety (42). The planning software generated constraints or virtual fixtures (43, 44): active constraints for Acrobot (41) or passive ones for other systems such as PADyC (passive arm with dynamic constraints) (45). The constraints are transferred to the robotic system to guide the surgeon in the milling operations, ensuring that the robot operates only in predefined, allowable areas. Acrobot incorporated a six-DOF force/torque sensor whose feedback was used in the active constraint control of the robot.

The Mako system (Stryker, Kalamazoo, MI) is another semi-active robotic system used for knee replacement that shares many features with Acrobot. Mako uses preoperative CT scans to build a model of the patient's knee to preoperatively plan the surgery. After image registration, the surgeon intraoperatively views the 3D model of the knee in a screen while manipulating the burr. The system provides both auditory and haptic feedback, limiting the workspace of the burr. So-called no-fly areas are generated by the system to avoid burring the bone outside the predefined areas (46).

The growing need for more specific clinical, technical, and safety requirements gradually led the field to move away from industrial manipulators toward the design of dedicated robotic systems. Greater demand for custom-designed, smaller, and clinically usable robotic systems that can be easily integrated within the surgical workflow resulted in the development of smaller-scale frameless systems such as the Navio Surgical System (47, 48), the Praxiteles/OMNIBotics (49, 50), and the Mazor Robotics Renaissance (51–53).

The Navio (Smith & Nephew, London, UK) is a handheld robotized drill for knee arthroplasty. Unlike Acrobot and Mako, Navio does not rely on preoperative CT scans, as the system continuously tracks both the patient anatomy and the handheld robotic device through the use of an infrared camera and optical tools (47). A 3D model of the knee is generated through a physical map of the anatomy created by passing the tracked optical probe over it. The Navio does

not provide haptic constraints but rather works with a speed/exposure control safeguard applied through the handheld robotized tool, which allows the resection of surgeon-identified bone layers (48). According to the concept of serial-parallel comanipulation (54), in parallel comanipulators the forces of the operator are added to those exerted by the robotic system to produce movement, whereas in serial comanipulators the speeds and DOF are added. Therefore, according to this definition, Acrobot and Mako are parallel comanipulators (the user and robot work together to move the tool), while Navio is a serial comanipulator (the user holds and moves the robot, which moves the tool).

The OMNIBotics (OMNI life science, Raynham, MA) and Mazor Robotics Renaissance (Mazor Robotics, Caesarea, Israel) systems are semi-active surgical robots that can be mounted directly onto a patient to perform knee and spine surgery, respectively. These systems operate according to an idea introduced by Gonzalez et al. (55) and Vilchis et al. (56) and clinically evaluated by Martinelli et al. (57) involving placing the robot directly onto a patient so as to follow their motion and to facilitate integration in the operating room. OMNIBotics enables the surgeon to accurately prepare knee surfaces from intraoperative information in total knee arthroplasty. Mazor Robotics Renaissance guides the surgeon to place tools and implants in the patient's spine on the basis of preoperative CT planning. The precision of the robotic guidance has been demonstrated to be high (58). The Mazor system is available in 250 centers worldwide; as of 2018, more than 29,000 surgical cases using this robot have been performed. Mazor Robotics Renaissance received CE marking and FDA approval in 2011 (59).

To date, most orthopedic surgical systems have been developed for joint replacement. However, in the last few decades, robotic surgical systems with 3D image guidance have been proposed to improve fracture surgeries as well (60–66). Research conducted by Dogramadzi and colleagues (67–69) toward improving minimally invasive fracture surgery resulted in the RAFS (robot-assisted fracture surgery) surgical system. RAFS is an active robotic system that performs percutaneous reduction of knee fractures based on preoperative planning. The surgeon interacts with CT-generated 3D bone models to virtually reduce the fracture in the computer preoperatively. In the operating room, the preoperative planning is registered with the patient and the robot performs the physical reduction under the supervision of the surgeon, who can intervene for modification if needed. RAFS provides real-time intraoperative 3D navigation by tracking both the patient anatomy and the robotic manipulators. It also implements six-DOF force sensing for safety. RAFS was successfully tested on cadavers in 2016 (69) and is undergoing further developments toward first-in-human trials (70).

As mentioned above, the successful introduction of robotics in neurosurgery, skull and ENT surgeries, and orthopedics surgery is possible thanks to the rigid nature of bones, enabling simple and consistent image registration between the robotic system and the anatomy and hence the possibility of preplanning robot trajectories. However, this possibility could not be readily translated into minimally invasive interventions involving soft tissue manipulation for several reasons, including the difficulty of tracking deformable anatomy and a lack of force feedback, 3D vision, and surgical dexterity. These limitations became the focus of the next generation of surgical robots, which are based on synergic collaboration between the robot and the surgeon (teleoperation), integration of different imaging modalities, and increased dexterity in manipulating soft tissue in a restricted operational workspace.

Robot-assisted fracture surgery (RAFS): technique aiming to restore bone anatomy (anatomical reduction) after trauma in a minimally invasive way

2.3. Minimally Invasive Surgery: Laparoscopy and Endoluminal Intervention

Robotic devices in this category were initially camera endoscope manipulators built to eliminate the need for human camera assistants. The first robotic system designed for this kind of

Minimally invasive surgery (MIS):

a surgical technique that limits the size of incision, typically associated with faster recovery and less pain

application was the AESOP (Automated Endoscopic System for Optimal Positioning), developed by Computer Motion. AESOP is a voice-controlled robot arm system that mimics the form and function of a human arm, holding and moving the camera endoscope to different positions (71). In 1994, AESOP became the first FDA-approved robotic system used in a surgery. Since then, more than 500 units have been used worldwide to treat more than 100,000 patients. Other original examples of telerobotic systems for endoscopic camera control are the system developed by Taylor et al. (72) and the head-controlled EndoAssist created by Finlay & Ornstein (73). Research by Berkelman et al. (74) on lightweight endoscope robots paved the way to Viky (Endo-control Medical, La Tronche, France), a robotic system for laparoscopy. Viky is a robotic endoscope that holds and positions the camera through a surgeon's voice control or visual servoing on instrument position (75). This autoclavable system is mounted on the operating table and is compatible with all types of commercially available endoscopes and trocars. After its first-in-human test in 2007, Viky received CE marking and FDA approval, and more than 150 units exist worldwide.

The first surgical robots for minimally invasive surgery (MIS) applications started to appear in the early 1990s. PROBOT, created by Davies and colleagues (76), is an example of a soft-tissue robotic surgeon. Designed for prostatectomy and first tested on a human in 1991 (76), PROBOT was an adapted version of the PUMA 560 industrial robot (with eight DOF). The adaptation involved the addition of a safety frame to limit the workspace of the arm. Initially manually controlled by the surgeon, PROBOT evolved into an active system able to perform a preoperative plan autonomously under the surgeon's supervision (77).

The concept of arranging several robotic arms (AESOP) to perform laparoscopic surgery and moving the surgeon from the table to the operating console resulted in the ZEUS platform, developed by Computer Motion (78). Following animal testing in 1996, the ZEUS system was used in clinical practice between 1998 and 2003 to perform minimally invasive cardiac surgery, including coronary artery bypass, and it was employed in the famous transatlantic robot-assisted cholecystectomy performed by Marescaux et al. (79) (with the surgeons in New York and the patient in Strasbourg, France). The main features of the ZEUS system include the ability of the robotic arm to mimic surgeon gestures, motion scaling, and hand tremor filtering to improve surgical accuracy. The ZEUS system was withdrawn from the market in 2003 in favor of the da Vinci system following the merger of Computer Motion and Intuitive Surgical.

Similarly to ZEUS, the first application of da Vinci was in cardiac surgery, and it is now used in a wide variety of surgical procedures, such as cholecystectomy, fundoplication, colorectal surgery, and radical prostatectomy—currently its primary application (80, 81). By 2017, more than 4,500 da Vinci systems had been sold worldwide, and more than 800,000 procedures were performed in 2017 alone (with an estimated growth rate of 15% per year) (see <https://isrg.gcs-web.com/>). da Vinci offers an immersive surgeon console that allows the surgeon to grasp the master controls below the display, thus restoring hand-eye coordination. The 3D endoscope provides the surgeon with stereo vision, restoring the sense of depth that is missing in traditional laparoscopy. A full range of EndoWrist instruments (for clamping, dissecting, suturing, manipulating, etc.) with seven DOF allow the surgeon to interact with the anatomy with the wrist articulation, which is otherwise impossible in standard laparoscopy. Despite these advantages, da Vinci does not provide haptic feedback.

The crucial aspect of providing haptic feedback in laparoscopy, together with reducing the bulkiness of the surgical robots while further minimizing patient trauma, remains an open challenge for both industry and academia (82). Miniaturized flexible robots represent a promising technology that could improve MIS through transluminal and/or endoluminal procedures (20).

CardioArm (Medrobotics, Raynham, MA) (83) is an example of a flexible robot that can perform minimally invasive heart and throat surgery. The robot consists of serially connected rigid cylindrical links connected by three cables and articulated by spherical joints. The user specifies the inputs for the distal tip of the robot through a joystick, and the other links follow its location (in a follow-the-leader mechanism). Visualization is provided by an embedded fiberscope.

Flex Robotic System, another technology developed and commercialized by Medrobotics, is the first robotic surgical platform based on a steerable and shapeable robotics scope that provides scar-free access in otolaryngology and colorectal procedures. The highly articulated multilinked scope can be steered through a single access point along nonlinear, tortuous anatomy that is hard or impossible to reach and visualize with traditional straight scopes. When the anatomy of interest is reached, the robotic scope becomes rigid and serves as a stable platform from which flexible instruments are deployed, visualized, and manipulated. Flex Robotic System embeds a two-dimensional (2D) high-definition camera that provides anatomy visualization on an external screen. After first-in-patient trials in 2014, Flex Robotic System received CE marking in the same year and FDA approval in 2015 (84).

Another snake-like system, the i-Snake developed by Yang and colleagues (85), uses modular universal joints with embedded micromotors and tendons as well as internal channels to deploy an endoscopic camera and instruments. The i-Snake allows exploration of a large area of the anatomy through NOTES (natural orifice transluminal endoscopic surgery) without requiring laparoscopic-style external manipulation, and it has full retroflexion capabilities (86). Endoluminal lesions of the gastrointestinal (GI), respiratory, or nasopharyngeal tract are accessible through minimally invasive means. However, even lesions close to the external orifice remain challenging to excise completely due to a lack of effective instrumentation, leading to significant operator dependency and risks of hemorrhage and perforation. To address these issues, Yang and colleagues (87, 88) at the Hamlyn Centre in London have developed the Micro-IGES (Microscopic Image Guided Endoluminal Surgery) robotic system, which allows endoluminal tasks to be performed with a significantly improved degree of precision and accuracy through integrated sensing, probe-based microscopic imaging, and robotically assisted intraoperative guidance. The platform has been tested in clinical trials and is in the process of being commercialized.

The platforms described above can reach several anatomical regions in the abdomen or in the chest. However, due to their large diameter they cannot operate in constrained regions, such as vessels, or inside the heart, kidneys, or brain. For these reasons, flexible robots have been further miniaturized, generating steerable catheters and concentric tube robots with diameters of a few millimeters. Catheters are commonly used in endovascular (EV) interventions to navigate the vasculature, reach the anatomy of interest, and perform the clinical procedure. Stenting, cardiac ablation, embolization, and device delivery are examples of EV procedures (89). However, maneuvering of catheters to reach target areas of the vasculature is challenging, and unintentional yet frequent contact between wires or catheters and the vessel wall can have catastrophic consequences for the patient (90). There is increasing interest in robotic steerable-catheter technology, the benefits of which include improved precision and stability, reduced radiation doses, improved patient comfort, and access to difficult-to-reach and tortuous anatomy (24). Different steering solutions have been investigated in both industry and academia; these include tendon-driven, electromagnetic, and smart materials and hydraulic drives. For a review of these systems, see References 24 and 89.

Commercially available robotic platforms are used in both electrophysiological (EP) and EV applications. Hansen Medical (acquired by Auris Health Inc., Redwood City, CA) developed two major robotic platforms for both EP (Sensei X2) (91) and EV (Magellan) procedures (92). These platforms are teleoperated, are arranged in a master/slave configuration, and use steerable

(tendon-driven) catheters remotely controlled by buttons and a joystick. The Sensei X2 incorporates a distal tip force system (IntelliSense), which provides a visual display of forces and tactile feedback through the vibration of the motion controller. The Magellan system does not provide any force feedback. While the Magellan system relies on 2D fluoroscopic imaging for guidance, the Sensei X2 enables integration of 3D guidance through the compatible EnSite Precision (St. Jude Medical, Saint Paul, MN) or CARTO3 (Biosense Webster, Brussels, Belgium) 3D mapping system.

Niobe (Stereotaxis, St. Louis, MO) is another teleoperated commercial platform used in EP applications (93). Niobe uses a magnetic field created by two permanent magnets to control the orientation of custom-designed EP catheters and guidewires through the mouse or joystick at the control station. Advancement and retraction of such catheters and guidewires are performed through mechanical motor drivers. 3D navigation is provided through the integration of the CARTO3 system. Advantages of Niobe include soft and consistent contact due to the lower stiffness of the catheters in comparison to tendon-driven catheters. The intraoperative use of 3D images based on preoperative data helps reduce X-ray exposure for both the patient and the surgical staff, as continuous intraoperative fluoroscopy is no longer needed for guidance. Furthermore, given that the control station is outside the operating room, the surgeon is completely outside the X-ray fluoroscopy field.

Artis Zeego (Siemens Healthineers, Erlangen, Germany) and Discovery (GE Healthcare, Chicago, IL) are other commercially available robotic systems that allows image guidance during procedures such as interventional angiography. Both systems can operate as real-time 2D fluoroscopy and as rapid 3D fluoroscopy CT-like imaging systems (94), providing uninterrupted, unobstructed access to the surgical area and full flexibility to patient positioning. The Discovery system provides advanced image guidance for EV procedures, enabling 3D image fusion and navigation through advanced software solutions (i.e., ASSIST software) for aneurysm repairs and aortic valve replacement.

Other robotic systems include the Amigo (Catheter Robotics Inc., Ledgewood, NJ) and Aeon Phocus (Aeon Scientific, Schlieren, Switzerland) systems. The CorPath GRX (Corindus Vascular Robotics, Waltham, MA) and the R-One (Robocath, Rouen, France) are used in EV applications. Readers are referred to References 24 and 89 for a comprehensive review.

As mentioned above, the flexibility of steerable catheters allows them to navigate long and intricate paths. However, their inability to apply high forces is a main limitation. Concentric tube robots provide the required flexibility to navigate tortuous anatomy while providing higher stiffness than that of steerable catheter robots. Concentric tube robots consist of nested sets of pre-curved elastic tubes that bend and deform when they are translated and rotated with respect to one another (21). In 2005 and 2006, this technology attracted extensive attention from the surgical robotics community due to research by Sears & Dupont (95), Webster (96), and Furusho et al. (97). Since then, concentric tube robots have evolved in terms of design (98), control (99), sensing (100), and image guidance (101) to enable teleoperated surgery. This technology has been proposed for use in a number of surgical applications (21); cardiac and endonasal applications have been extensively studied by Dupont and colleagues (102) and Webster and colleagues (103), respectively. Concentric tube robots are being investigated by many research groups (21), although the ability to achieve path-following navigation may present a major hurdle for certain intraluminal clinical applications.

The Monarch platform (Auris Health Inc.) integrates flexible robots and enhanced 3D imaging and sensing to perform lung cancer surgery through an endoluminal approach. The Monarch platform is intended for both diagnostic and therapeutic bronchoscopy and had its first-in-human use in April 2018, shortly after receiving FDA approval; it is expected to become commercially

available in the near future (see <https://www.aurishealth.com/home.html>). Similarly, the SPORT system (Titan Medical Inc., Toronto, Canada), which has been used on patients since 2017 (104), provides a competing alternative to da Vinci SP (see <https://www.intuitivesurgical.com/sp/>) for single-port laparoscopic surgery.

Although flexible robots are promising for the future of MIS, newer enabling technologies are paving the way toward the next generation of surgical robots. Wireless capsule endoscopes and microrobots promise enhanced diagnostic and therapeutic capabilities as well as potentially unlimited intracorporeal navigation (23). Wireless capsule endoscopes were introduced in 2000 (105) as an alternative to traditional endoscopy of the GI tract. Capsule endoscopes are external biocompatible devices (typically 11 mm in diameter and 26 mm in length) that contain a vision module, a control and communication unit, and an energy source (23). Once swallowed, the capsules are moved through the GI tract via peristalsis (in approximately 8–10 h) so as to perform diagnosis through image acquisition (106). The first capsule endoscope, PillCam (Given Imaging, Yokneam Illit, Israel), became commercially available in 2001. Since then, several other devices have been launched (see Reference 23 for a comprehensive review).

One of the main limitations of capsule endoscopes is their lack of active controllability, which prohibits arbitrary movement of the camera (e.g., closer to a suspicious lesion). Other drawbacks include the lack of tissue interaction (e.g., biopsy collection) and the limited field of view (which may result in, e.g., false-negative diagnosis). Several research groups have studied the actuation for capsule active locomotion, proposing both onboard and external locomotion techniques. Bioinspired onboard legged locomotion and wormlike locomotion systems were proposed by Dario and colleagues (107) and Kim and colleagues (108), respectively. The main drawbacks of this actuation are the high power consumption, short functionality time, and poor controllability (23). External locomotion approaches using magnetic steering have been attempted to address these issues. In such approaches, a large magnetic field is created near (but outside) the patient, by either electromagnet(s) or permanent magnet(s) (23), to manipulate the capsule inside the patient, thus removing the need for onboard actuation. Similar to the Niobe system for catheter steering, described above, Dario and colleagues (109, 110) used a six-DOF industrial robot to hold and manipulate a large permanent magnet outside the patient to actuate the endoscopic capsule. Olympus and Siemens jointly developed a technique for generating an external magnetic field using an MRI scanner (111). Recent research by Abbott and colleagues (112) demonstrated for the first time that a single rotating magnet can be used to simultaneously localize and actuate a screw-type capsule. Capsule endoscopes can also perform biopsies through different sampling techniques, such as the thermosensitive tissue-cutting razor developed by Cho and colleagues (113) or the magnetic-field-actuated blades proposed by Valdastrì and colleagues (114). Abbott and colleagues (112) also demonstrated that screw-type capsules can penetrate soft tissue, paving the way toward newer sampling techniques.

3. OPEN CHALLENGES AND THE FUTURE OF MEDICAL ROBOTICS

The examples reported above show how medical robots evolved over the last three decades. This evolution began with large-scale, commercially available industrial manipulators used to improve the positioning accuracy of surgical instruments such as *neuromate* or ROBODOC, and became smaller, smarter, and custom designed for specific clinical applications. Medical robots such as CardioArm and the Flex robotic systems can now be mounted directly on the patient's body or can even be handheld (115, 116) and are able to operate precisely in a limited workspace with minimal damage to soft tissue. Thanks to recent advances in microrobotics, robots can also be implanted directly inside the patient or swallowed to effect intracorporeal interventions and/or

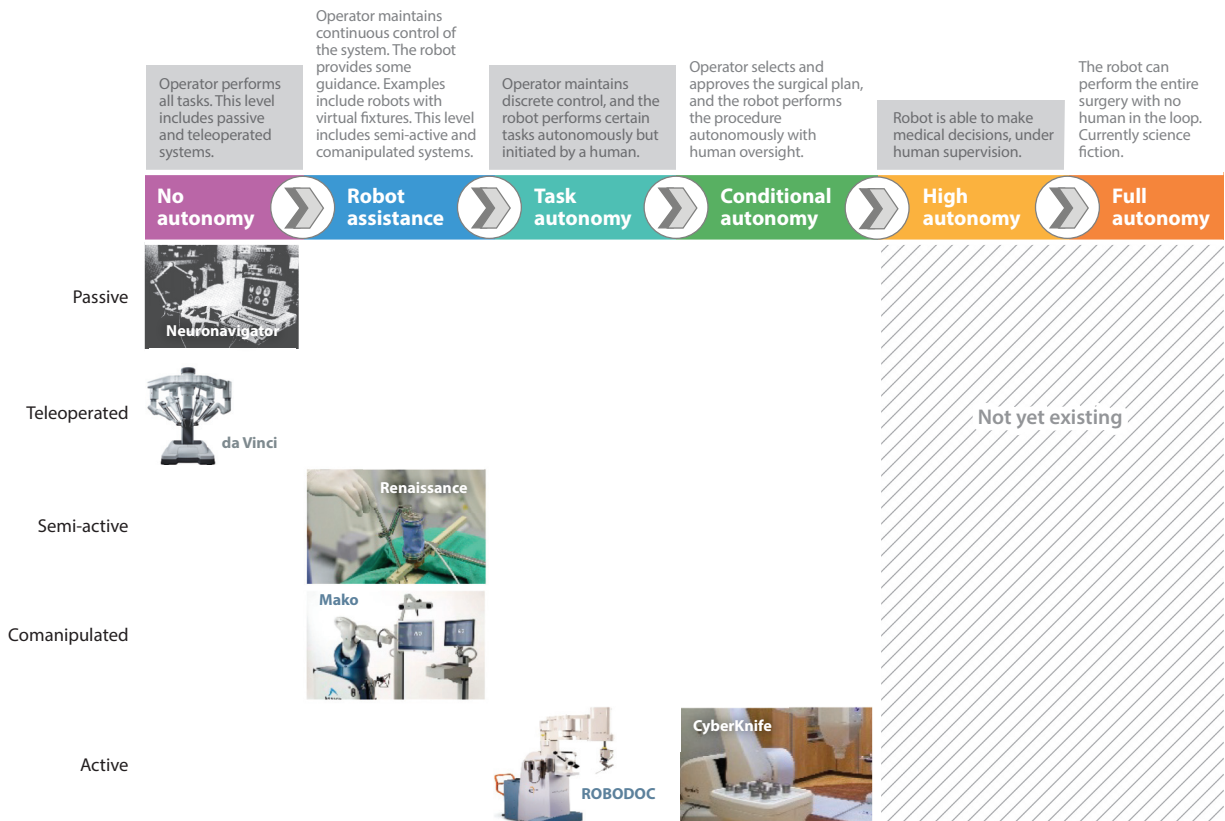


Figure 4

Different levels of human–robot interaction and autonomy mapped to medical robots. Levels of human–robot interactions are described in Reference 132; decision levels are described in Reference 122. Images are adapted with permission as follows: Neuronavigator, Reference 145; da Vinci, Intuitive Surgical Inc., © 2018; Mazor Robotics Renaissance, Mazor Robotics; Mako, Reference 131; ROBODOC, Reference 130; CyberKnife, Wikimedia Commons.

detect pathologies, as shown in pioneering research by Dario and colleagues (107) and Abbott and colleagues (112). Recent advances in the design, fabrication, and operation of micro- and nanorobots have greatly enhanced their power, function, and versatility, pushing the boundaries of this research area toward the development of problem-oriented medical devices for specific diagnostic or therapeutic functions (117). Research results from other domains such as biology, electrochemistry, and so forth can also provide innovative solutions, such as biofuel cells to supply electrical power to implanted devices (118) using natural substrates present in the living body.

The evolution of surgical robots encompasses not only size and architecture but also cooperative interaction with the surgical team and safety measures (Figure 4). The implementation of a suitable human–robot interface and specific control strategies is paramount for the safety and optimal outcome of the surgery. Initially, medical robots were used as passive tool holders [as in the case of Neuronavigator (145)], and eventually, they became able to adapt in real time preprogrammed plans to the intraoperative position of a target [as in the case of CyberKnife (32)]. Future surgical robotic systems will be better able to cooperate with surgeons, providing them not only

with superhuman dexterity but also with integrated real-time intraoperative image guidance, sensing, and decision making. Sight and sense information will allow the surgeon to close the control loop of the system and synergistically operate with the robot. As a result, the standard master/slave configuration (wherein the slave manipulator inside the patient replicates the movements of the surgeon's hands as the master) could be further improved through the use of real-time imaging and sensing in the control architecture.

This implementation of the perception–decision–action loop architecture along with surgical robotic assistance will guarantee the best possible treatment in terms of surgical success and safety. Physicians will cooperate with robotic systems such that they will complement each other, with a minimal footprint in the operating or radiology room and maximum integration with the clinical workflow. Thus, future interventional systems need to be simple—despite their intrinsic complexity—as well as easy to use, lightweight, ergonomic, and intelligent. They will enhance the medical or surgical workflow by providing as much information and support as possible to the clinical team intraoperatively and in real time. To this end, MRI-compatible surgical robots (119) will allow the use of real-time functional 3D imaging in the operating room to provide an unprecedented level of surgical navigation and superhuman dexterity. Also, future surgical systems will interact with the pathology at a cellular level by providing *in situ*, *in vivo* cellular imaging for real-time diagnosis and tissue identification (e.g., optical biopsy). The incorporation of such imaging in microrobots will allow not only the detection of pathologies but also targeted treatment, for example, by delivering drugs in a localized area so as to preserve healthy tissue.

Further improvements to medical robotics will require the development of new technologies through joint efforts by engineers, clinicians, physicists, chemists, and biologists. Yang et al. (120) have identified grand challenges in medical robotics that will enable technical advances to have a significant impact on health care. A primary challenge may be the development of surgical systems with an increased level of autonomy—for example, systems that can autonomously recognize the relevant anatomy and perform surgical tasks appropriately. For instance, EV interventions involve navigating a catheter through the vasculature to perform a surgical task. Learning algorithms can be used to automate certain steps of the EV task while the surgeon takes control of others, utilizing a shared surgical control platform with increased technical performance and safety (121, 122). Another grand challenge is the realization of micro- and nanorobots to perform targeted diagnosis and therapy, as outlined above. Although some technology of this type has already been developed (18), a great deal of research is still needed in terms of design, biocompatibility, autonomy, tracking, and control (120).

Another significant challenge for researchers in robot-assisted intervention—both in academia and in industry—is the process of moving a medical device prototype from the lab to the clinic. In order to ensure the safety and effectiveness of new medical devices, the prototypes must obtain regulatory approval. Regulatory bodies such as the FDA aim to ensure that new medical devices are properly designed and not harmful to patients. In general, this process consists of (a) developing a clinical prototype, resulting in a first-in-human study; (b) evaluating the prototype through clinical trials; (c) obtaining regulatory approval; and (d) adopting the device (see the sidebar titled Medical Robotics and Health Economics).

During the development of new medical devices (**Figure 5**), effective communication between the technical and clinical parties is essential. It is crucial for engineers to ask clinicians what is required at each stage of development. While clinicians may initially have certain ideas about what the device should look like and/or what it should do, technical barriers can prevent exact implementation. Continuous clinical input and feedback are essential during this developmental process. Another major challenge is the testing of new devices in patients. While testing

MEDICAL ROBOTICS AND HEALTH ECONOMICS

One challenge that innovation in medical robotics faces is the effect of the uptake of new technologies on health care economics. The cost-effectiveness of medical robotics has been discussed in several reports, mostly with regard to the da Vinci system (126–129). Studies indicate that the costs associated with medical robots should be further reduced to facilitate their uptake; however, scientific research on cost-effectiveness has been limited due to the lack of data availability, which is mostly related to earlier generations of robotic systems. To gain better insight into the impact of medical robots on the health care system, we should wait until more systems have been adopted and more data become available. Furthermore, early adoption is more expensive, so we expect that the area of medical robotics and its health economics will change appreciably in the near future, when costs will decrease as more devices become available and more competitors enter the market (25).

may start on phantoms or animals, patient evidence is critical for any device to achieve clinical uptake.

In terms of regulatory issues, different pathways can be followed before approval, depending on the nature of the device. For example, FDA premarket notification 510(k) must be followed “if the device is substantially equivalent to a predicate device and does not necessarily require clinical

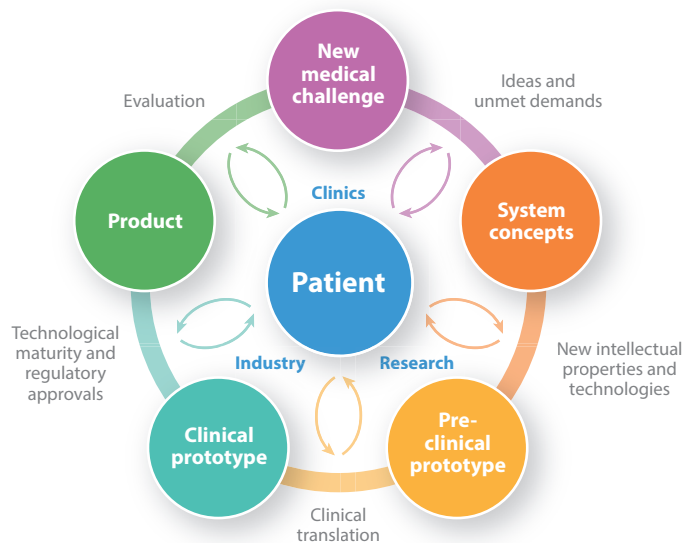


Figure 5

Clinical innovation cycle. To solve a new clinical challenge, as specified by clinicians (e.g., automating seed placement in prostate brachytherapy), the development team first provides ideas, concepts, and methods underlying the solution to be solved. Researchers may patent these concepts or methods. A preclinical prototype [e.g., the PROSPER robot (133)] is developed and tested, for instance, on anatomical parts, allowing researchers to foresee the medical service to be demonstrated (134). A clinical prototype is then developed (135) in compliance with regulatory and ethical requirements and is tested on patients in the first evaluation of the medical service. Preproducts or products enable evaluation of the medical service provided by the system to be finalized. Routine use of the system may generate new medical challenges. Each stage of this process involves close collaboration among medical, research, and industrial teams.

data.” Premarket approval is the appropriate regulatory pathway if the device is “not substantially equivalent” to a predicate device and requires reasonable evidence of safety and effectiveness. Another regulatory pathway is humanitarian device exemption, for devices intended for use in patients with rare diseases or conditions. In general, the pathway for lower-risk devices is usually less rigorous than for high-risk devices, allowing for their more rapid approval.

Similar to devices marketed in the United States, medical devices commercialized in Europe must receive CE marking by demonstrating compliance with the applicable essential requirements. This process includes the clinical investigation of the device, consisting of the assessment of clinical data to demonstrate safety and performance.

Such clinical studies must consider cost-effectiveness and evidence of improving outcomes and competition by different solutions. The clinical added value of the device may concern better efficiency (better functional outcome, longer survival, etc.), lower rates of adverse effects (blood loss, radiation of healthy organs, etc.), or organizational aspects (number of people involved, duration of the procedure, duration of recovery, etc.). Typical clinical studies may take years to perform, and the outcome of improvement may not always be clear. The story of ROBODOC (123) clearly illustrates this challenging issue. In this example, more precise milling of a bone, which is quite easy to evaluate, does not mean that the prosthesis will last longer or be more stable than with conventional surgery. This functional evaluation is much longer term. As such, the duration and cost of studies often discourage many commercial companies from investing in health care technologies but rather suggest focusing only on fast-growing consumer markets. Coupled with the complex procurement processes, adopting new technologies in clinical practice is often challenging.

A study conducted by Marcus et al. (124) investigated the translation of new devices from the laboratory to first-in-human studies between 1993 and 2000. This study showed that clinical rather than industry collaboration was the most important predictor of success; devices developed with clinical collaboration were more than six times more likely to lead to a first-in-human study than those without. A more recent study by the same research group (125) examined the regulatory clearance and/or approval of new medical devices between 2000 and 2004. In contrast to the earlier results, this study showed that the likelihood of a device obtaining regulatory approval was higher if developed by industry alone. The likelihood decreased if it was developed jointly by industry and academia and was lowest if developed by academia alone. This incongruity is likely the result of the varying role of clinical and industry collaboration through the device development pathway; early clinical studies may be more reliant on clinicians, and later regulatory approval more reliant on industry. Also, the findings suggest that industrial interests are the main drivers of regulatory approval for specific devices.

4. CONCLUSIONS

In the past 30 years, the field of surgical robotics has evolved from a research niche into commercial reality with accelerating clinical uptake. According to a recent analysis (136), the medical robot market is evaluated at US\$5.7 billion (2017), approximately one-eighth of the industrial robot market (evaluated at US\$42 billion in the same year). However, driven by the increasing usage of robotics systems in health care, it is expected to grow by more than 20% by 2025—a much faster growth than the industrial robots market (estimated ~10%). The increasing availability of robotics systems such as the ones reported above has led to wide adoption of robotic devices. For example, approximately 750,000 surgical robotics procedures were performed in the United States in 2016, with greater adoption in urology and gynecology. More specifically, robot-assisted radical prostatectomy was performed in approximately 85% of these cases (14% traditional laparoscopic,

1% open) and robot-assisted hysterectomy in 34% (16% traditional laparoscopic, 36% open, 14% vaginal) (137).

Medical robotics is intrinsically cross-disciplinary, involving many key engineering disciplines: image and signal processing, computer vision, data fusion, modeling and simulation, and human-machine interfaces. New collaborations between academia and industry need to be created to facilitate the adoption and clinical translation of medical devices with a realistic social-economic impact. Moreover, there is a lack of reliable cost-benefit analyses with respect to improved postoperative outcome that needs to be addressed. While the literature on this topic is growing (138–143), there is still a need for high-quality comparative studies in this area. The use of robotic platforms in health care “requires demonstrating the superior clinical benefit of these devices while considering the full set of costs for these systems” (144, p. 836). Activity-based costing studies (141) fail to capture all costs throughout the total cycle of care (e.g., cost of complications and cost of additional care required) and undervalue procedures that have fewer postsurgical complications while overvaluing procedures that have lower upfront investment costs (i.e., focusing only on upfront costs, ignoring long-term costs). Time-driven activity-based costing studies (142) provide a more accurate comparison of costing between procedures by capturing all costs throughout the cycle of care—including upfront investments, surgical costs, and postsurgical costs.

This review has shown that the technology to improve many medical and surgical procedures already exists, but further technological and engineering advances are needed to develop the next generation of computer-assisted intervention platforms. Current robotic platforms provide the clinical team with increased dexterity and precision but generally are still too bulky and not well integrated with the clinical workflow, especially with real-time intraoperative imaging. This represents one of the major limitations that needs to be addressed in order for these platforms to be of clinical value. In parallel with the general paradigm shift toward early detection and intervention in medicine, we envision that in the near future surgical robots will become smaller, smarter, and more cost-effective, and thus more clinically relevant. Microrobots will be able to autonomously interact directly with the pathology at the cellular level to perform diagnosis and deliver therapy simultaneously. With the rise of smarter robotic platforms, surgical procedures will become more and more patient specific: Surgical systems, as depicted in **Figure 2**, are now entering a new era influenced by the rebirth of AI and access to big data. The access to huge amounts of information regarding patient health underpins improved patient-specific diagnoses and therapeutic decisions. Surgical robotics represents an ideal opportunity to make AI successful. The evolution from robotic tools into robotic assistants has already begun and will require us to rethink the patient-clinician relationship, so as to make robots available and accessible to all.

SUMMARY POINTS

1. Medical robotics, be it used for surgical intervention, targeted therapy, rehabilitation, or hospital automation, is one of the fastest-growing sectors in the health care industry.
2. The integration of robotics and computer assistance into the clinical workflow could improve current medical procedures by providing as much information and support to the surgical team as possible to produce better outcomes.
3. In the last 30 years, medical robotics has evolved to become a major area of innovation, research, and development.
4. Medical robots, initially based on bulky, commercially available industrial manipulators, are now smaller, smarter, and custom-designed devices for specific clinical applications.

5. Recent advances in microrobotics, imaging, and sensing have led to the innovation and improvement of medical robots that are able to cooperate with the clinician.
6. The implementation of the perception–decision–action loop architecture, along with surgical robotic assistance, improves treatments in terms of increased clinical outcome and safety.

FUTURE ISSUES

1. It is envisioned that medical robots will become smaller, smarter, and more cost-effective, and thus more clinically relevant.
2. A primary challenge will be the development of medical robots with greater autonomy—for example, robots that can autonomously recognize the relevant anatomy and appropriately perform clinical tasks (e.g., delivery of a therapy).
3. Future surgical systems (e.g., micro- and nanorobots) will be able to interact with the pathology at the cellular level by providing in situ, in vivo, real-time diagnosis and treatment.
4. Greater interaction with other disciplines such as biology, bioengineering, biochemistry, and so forth will be necessary to improve the biocompatibility and usability of implanted devices.
5. New collaborations between academia and industry will be necessary to facilitate the adoption and clinical translation of medical devices with a realistic social-economic impact.
6. The lack of a standardized framework for medical robot benchmarking presents a major challenge to overcoming translational barriers. There is a need to identify appropriate and clinical comparators to obtain a fair cost-effectiveness analysis of medical robots.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that may be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

The authors acknowledge grant support from the Wellcome Trust (Translational Partnership for Robotic Surgery), the UK Engineering and Physical Sciences Research Council (EP/N024877/1 and EP/P012779/1), and the French Agence Nationale de la Recherche (Investissements d'Avenir program, Labex CAMI, ANR-11-LABX-0004).

LITERATURE CITED

1. Kall BA, Kelly PJ, Goerss SJ. 1985. Interactive stereotactic surgical system for the removal of intracranial tumors utilizing the CO₂ laser and CT-derived database. *IEEE Trans. Biomed. Eng.* 32:112–16

2. Kelly PJ, Goerss SJ, Kall BA. 1988. Evolution of contemporary instrumentation for computer-assisted stereotactic surgery. *Surg. Neurol.* 30:204–15
3. Niaf E, Rouvière O, Mège-Lechevallier F, Bratan F, Lartzien C. 2012. Computer-aided diagnosis of prostate cancer in the peripheral zone using multiparametric MRI. *Phys. Med. Biol.* 57:3833–51
4. Baumann M, Mozer P, Daanen V, Troccaz J. 2012. Prostate biopsy tracking with deformation estimation. *Med. Image Anal.* 16:562–76
5. Payan Y, ed. 2012. *Soft Tissue Biomechanical Modeling for Computer Assisted Surgery*. Berlin/Heidelberg: Springer
6. Misra S, Ramesh KT, Okamura AM. 2008. Modeling of tool–tissue interactions for computer-based surgical simulation: a literature review. *Presence* 17:463–91
7. Huaulmé A, Voros S, Riffaud L, Forestier G, Moreau-Gaudry A, Jannin P. 2017. Distinguishing surgical behavior by sequential pattern discovery. *J. Biomed. Inform.* 67:34–41
8. Twinanda AP, Shehata S, Mutter D, Marescaux J, de Mathelin M, Padoy N. 2017. EndoNet: a deep architecture for recognition tasks on laparoscopic videos. *IEEE Trans. Med. Imaging* 36:86–97
9. Beasley RA. 2012. Medical robots: current systems and research directions. *J. Robot.* 2012:401613
10. Smith JA, Jivraj J, Wong R, Yang V. 2016. 30 years of neurosurgical robots: review and trends for manipulators and associated navigational systems. *Ann. Biomed. Eng.* 44:836–46
11. Howe RD, Matsuoka Y. 1999. Robotics for surgery. *Annu. Rev. Biomed. Eng.* 1:211–40
12. Dogangil G, Davies BL, Rodriguez y Baena F. 2010. A review of medical robotics for minimally invasive soft tissue surgery. *Proc. Inst. Mech. Eng. H* 224:653–79
13. Davies B. 2000. A review of robotics in surgery. *Proc. Inst. Mech. Eng. H* 214:129–40
14. Taylor RH, Stoianovici D. 2003. Medical robotics in computer-integrated surgery. *IEEE Trans. Robot. Autom.* 19:765–81
15. Camarillo DB, Krummel TM, Salisbury JK. 2004. Robotic technology in surgery: past, present, and future. *Am. J. Surg.* 188(4A Suppl.):2S–15S
16. Rebello KJ. 2004. Applications of MEMS in surgery. *Proc. IEEE* 92:43–55
17. Menciassi A, Quirini M, Dario P. 2007. Microrobotics for future gastrointestinal endoscopy. *Minim. Invasive Ther. Allied Technol.* 16:91–100
18. Nelson BJ, Kaliakatsos IK, Abbott JJ. 2010. Microrobots for minimally invasive medicine. *Annu. Rev. Biomed. Eng.* 12:55–85
19. Ciuti G, Menciassi A, Dario P. 2011. Capsule endoscopy: from current achievements to open challenges. *IEEE Rev. Biomed. Eng.* 4:59–72
20. Vitiello V, Lee SL, Cundy TP, Yang GZ. 2013. Emerging robotic platforms for minimally invasive surgery. *IEEE Rev. Biomed. Eng.* 6:111–26
21. Gilbert HB, Rucker DC, Webster RJ III. 2016. Concentric tube robots: the state of the art and future directions. In *Robotics Research*, ed. M Inaba, P Corke, pp. 253–69. Cham, Switz.: Springer Int.
22. Karas CS, Chiocca EA. 2007. Neurosurgical robotics: a review of brain and spine applications. *J. Robot. Surg.* 1:39–43
23. Valdastri P, Simi M, Webster RJ. 2012. Advanced technologies for gastrointestinal endoscopy. *Annu. Rev. Biomed. Eng.* 14:397–429
24. Rafii-Tari H, Payne CJ, Yang G-Z. 2014. Current and emerging robot-assisted endovascular catheterization technologies: a review. *Ann. Biomed. Eng.* 42:697–715
25. Bergeles C, Vitiello V, Yang G-Z. 2016. *Surgical robotics: the next 25 years. Successes, challenges, and the road ahead*. White pap., UK-RAS, Imp. Coll. London, London, UK
26. Bergeles C, Yang GZ. 2014. From passive tool holders to microsurgeons: safer, smaller, smarter surgical robots. *IEEE Trans. Biomed. Eng.* 61:1565–76
27. Kwoh YS, Hou J, Jonckheere EA, Hayati S. 1988. A robot with improved absolute positioning accuracy for CT guided stereotactic brain surgery. *IEEE Trans. Biomed. Eng.* 35:153–60
28. Benabid AL, Cinquin P, Lavalle S, Le Bas JF, Demongeot J, de Rougemont J. 1987. Computer-driven robot for stereotactic surgery connected to CT scan and magnetic resonance imaging. *Stereotact. Funct. Neurosurg.* 50:153–54

29. Lavallee S, Troccaz J, Gaborit L, Cinquin P, Benabid AL, Hoffmann D. 1992. Image guided operating robot: a clinical application in stereotactic neurosurgery. In *Proceedings of the 1992 IEEE International Conference on Robotics and Automation*, pp. 618–24. Piscataway, NJ: IEEE
30. Li QH, Zamorano L, Pandya A, Perez R, Gong J, Diaz F. 2002. The application accuracy of the NeuroMate robot—a quantitative comparison with frameless and frame-based surgical localization systems. *Comput. Aided Surg.* 7:90–98
31. Schweikard A, Shiomi H, Adler J. 2004. Respiration tracking in radiosurgery. *Med. Phys.* 31:2738–41
32. Bertelsen A, Melo J, Sánchez E, Borro D. 2013. A review of surgical robots for spinal interventions. *Int. J. Med. Robot.* 9:407–22
33. Dahroug B, Tamadazte B, Tavernier L, Weber S, Andreff N. 2018. Review on otological robotic systems: toward micro-robot assisted cholesteatoma surgery. *IEEE Rev. Biomed. Eng.* 11:125–42
34. Weber S, Gavaghan K, Wimmer W, Williamson T, Gerber N, et al. 2017. Instrument flight to the inner ear. *Sci. Robot.* 2:eaa14916
35. Tavernier L, Andreff N, Fujimoto T, Peretti G, Mattos L. 2017. Micro-technologies and systems for robot-assisted laser phonomicrosurgery (μ RALP). In *Robotics and Digital Guidance in ENT-H&N Surgery*, ed. B Lombard, P Céruse, pp. 142–53. Amsterdam: Elsevier
36. Mattos LS, Caldwell DG, Peretti G, Mora F, Guastini L, Cingolani R. 2016. Microsurgery robots: addressing the needs of high-precision surgical interventions. *Swiss Med. Wkly.* 146:w14375
37. Dagnino G, Mattos LS, Caldwell DG. 2015. A vision-based system for fast and accurate laser scanning in robot-assisted phonomicrosurgery. *Int. J. Comput. Assist. Radiol. Surg.* 10:217–29
38. Paul HA, Mittlestadt B, Bargar WL, Musits B, Taylor RH, et al. 1992. A surgical robot for total hip replacement surgery. In *Proceedings of the 1992 IEEE International Conference on Robotics and Automation*, pp. 606–11. Piscataway, NJ: IEEE
39. Taylor RH, Mittlestadt BD, Paul HA, Hanson W, Kazanzides P, et al. 1994. An image-directed robotic system for precise orthopaedic surgery. *IEEE Trans. Robot. Autom.* 10:261–75
40. Paul HA, Bargar WL, Mittlestadt B, Musits B, Taylor RH, et al. 1992. Development of a surgical robot for cementless total hip arthroplasty. *Clin. Orthop. Relat. Res.* 285:57–66
41. Jakopcic M, Harris SJ, Gomes P, Cobb J, Davies BL. 2003. The hands-on orthopaedic robot “Acrobot”: early clinical trials of total knee replacement surgery. *Robot. Autom. IEEE Trans.* 19:902–11
42. Troccaz J, Peshkin M, Davies B. 1998. Guiding systems for computer-assisted surgery: introducing synergistic devices and discussing the different approaches. *Med. Image Anal.* 2:101–19
43. Rosenberg LB. 1993. Virtual fixtures: perceptual tools for telerobotic manipulation. In *Proceedings of IEEE Virtual Reality Annual International Symposium*, pp. 76–82. Piscataway, NJ: IEEE
44. Bowyer SA, Davies BL, Rodríguez y Baena F. 2014. Active constraints/virtual fixtures: a survey. *IEEE Trans. Robot.* 30:138–57
45. Schneider O, Troccaz J. 2001. A six-degree-of-freedom passive arm with dynamic constraints (PADyC) for cardiac surgery application: preliminary experiments. *Comput. Aided Surg.* 6:340–51
46. Lang JE, Mannava S, Floyd AJ, Goddard MS, Smith BP, et al. 2011. Robotic systems in orthopaedic surgery. *Bone Jt. J.* 93B:1296–99
47. Herry Y, Batailler C, Lording T, Servien E, Neyret P, Lustig S. 2017. Improved joint-line restitution in unicompartmental knee arthroplasty using a robotic-assisted surgical technique. *Int. Orthop.* 41:2265–71
48. Lonner JH, Smith JR, Picard F, Hamlin B, Rowe PJ, Riches PE. 2015. High degree of accuracy of a novel image-free handheld robot for unicondylar knee arthroplasty in a cadaveric study. *Clin. Orthop. Relat. Res.* 473:206–12
49. Plaskos C, Cinquin P, Lavallée S, Hodgson AJ. 2005. Praxiteles: a miniature bone-mounted robot for minimal access total knee arthroplasty. *Int. J. Med. Robot. Comput. Assist. Surg.* 1:67–79
50. Koulalis D, O’Loughlin PF, Plaskos C, Kendoff D, Cross MB, Pearle AD. 2011. Sequential versus automated cutting guides in computer-assisted total knee arthroplasty. *Knee* 18:436–42
51. Lieberman IH, Togawa D, Kayanja MM, Reinhardt MK, Friedlander A, et al. 2006. Bone-mounted miniature robotic guidance for pedicle screw and translaminal facet screw placement. Part I. Technical development and a test case result. *Neurosurgery* 59:641–50

52. Togawa D, Kayanja MM, Reinhardt MK, Shoham M, Balter A, et al. 2007. Bone-mounted miniature robotic guidance for pedicle screw and translaminar facet screw placement. Part 2. Evaluation of system accuracy. *Neurosurgery* 60(Suppl. 1):129–39
53. Shoham M, Lieberman IH, Benzel EC, Togawa D, Zehavi E, et al. 2007. Robotic assisted spinal surgery—from concept to clinical practice. *Comput. Aided Surg.* 12:105–15
54. Troccaz J, ed. 2012. *Medical Robotics*. London: ISTE
55. Gonzales AV, Cinquin P, Troccaz J, Guerraz A, Hennion B, et al. 2001. TER: a system for robotic tele-echography. In *Proceedings of the 2001 International Conference on Medical Image Computing and Computer-Assisted Intervention (MICCAI 2001)*, pp. 326–34. Berlin: Springer
56. Vilchis A, Troccaz J, Cinquin P, Masuda K, Pellissier F. 2003. A new robot architecture for tele-echography. *IEEE Trans. Robot. Autom.* 19:922–26
57. Martinelli T, Bosson J-L, Bressollette L, Pellissier F, Boidard E, et al. 2007. Robot-based tele-echography: clinical evaluation of the TER system in abdominal aortic exploration. *J. Ultrasound Med.* 26:1611–16
58. Hu X, Ohnmeiss DD, Lieberman IH. 2013. Robotic-assisted pedicle screw placement: lessons learned from the first 102 patients. *Eur. Spine J.* 22:661–66
59. Fiani B, Quadri SA, Farooqui M, Cathel A, Berman B, et al. 2018. Impact of robot-assisted spine surgery on health care quality and neurosurgical economics: a systemic review. *Neurosurg. Rev.* <https://doi.org/10.1007/s10143-018-0971-z>
60. Buschbaum J, Fremd R, Pohlemann T, Kristen A. 2014. Computer-assisted fracture reduction: a new approach for repositioning femoral fractures and planning reduction paths. *Int. J. Comput. Assist. Radiol. Surg.* 10:149–59
61. Joskowicz L, Milgrom C, Simkin A, Tockus L, Yaniv Z. 1998. FRACAS: a system for computer-aided image-guided long bone fracture surgery. *Comput. Aided Surg.* 3:271–88
62. Warisawa S, Ishizuka T, Mitsuishi M, Sugano N. 2004. Development of a femur fracture reduction robot. In *Proceedings of the 2004 IEEE International Conference on Robotics and Automation*, pp. 3999–4004. Piscataway, NJ: IEEE
63. Westphal R, Winkelbach S, Wahl F, Gösling T, Oszwald M, et al. 2009. Robot-assisted long bone fracture reduction. *Int. J. Robot. Res.* 28:1259–78
64. Tang P, Hu L, Du H, Gong M, Zhang L. 2012. Novel 3D hexapod computer-assisted orthopaedic surgery system for closed diaphyseal fracture reduction. *Int. J. Med. Robot.* 8:17–24
65. Graham AE, Xie SQ, Aw KC, Xu WL, Mukherjee S. 2006. Design of a parallel long bone fracture reduction robot with planning treatment tool. In *Proceedings of the 2006 IEEE/RSJ International Conference on Intelligent Robots and Systems*, pp. 1255–60. Piscataway, NJ: IEEE
66. Wang J, Han W, Lin H. 2013. Femoral fracture reduction with a parallel manipulator robot on a traction table. *Int. J. Med. Robot. Comput. Assist. Surg.* 9:464–71
67. Dagnino G, Georgilas I, Köhler P, Atkins R, Dogramadzi S. 2016. Image-based robotic system for enhanced minimally invasive intra-articular fracture surgeries. In *Proceedings of the 2016 IEEE International Conference on Robotics and Automation*, pp. 696–701. Piscataway, NJ: IEEE
68. Dagnino G, Georgilas I, Köhler P, Morad S, Atkins R, Dogramadzi S. 2016. Navigation system for robot-assisted intra-articular lower-limb fracture surgery. *Int. J. Comput. Assist. Radiol. Surg.* 11:1831–43
69. Dagnino G, Georgilas I, Morad S, Gibbons P, Tarassoli P, et al. 2017. Image-guided surgical robotic system for percutaneous reduction of joint fractures. *Ann. Biomed. Eng.* 45:2648–62
70. Georgilas I, Dagnino G, Tarassoli P, Atkins R, Dogramadzi S. 2018. Robot-assisted fracture surgery: surgical requirements and system design. *Ann. Biomed. Eng.* 46:1637–49
71. Kraft BM, Jäger C, Kraft K, Leibl BJ, Bittner R. 2004. The AESOP robot system in laparoscopic surgery: increased risk or advantage for surgeon and patient? *Surg. Endosc. Interv. Tech.* 18:1216–23
72. Taylor RH, Funda J, Eldridge B, Gomory S, Gruben K, et al. 1995. A telerobotic assistant for laparoscopic surgery. *IEEE Eng. Med. Biol.* 14:279–88
73. Finlay PA, Ornstein MH. 1995. Controlling the movement of a surgical laparoscope. *IEEE Eng. Med. Biol.* 14:289–91

74. Berkelman P, Cinquin P, Boidard E, Troccaz J, Létoublon C, Ayoubi J-M. 2003. Design, control and testing of a novel compact laparoscopic endoscope manipulator. *Proc. Inst. Mech. Eng. I* 217:329–41
75. Voros S, Haber GP, Menudet JF, Long JA, Cinquin P. 2010. Viky robotic scope holder: initial clinical experience and preliminary results using instrument tracking. *IEEE ASME Trans. Mechatron.* 15:879–86
76. Ng WS, Davies BL, Hibberd RD, Timoney AG. 1993. Robotic surgery: a first-hand experience in transurethral resection of the prostate. *IEEE Eng. Med. Biol.* 12:120–25
77. Harris SJ, Arambula-Cosio F, Mei Q, Hibberd RD, Davies BL, et al. 1997. The Probot—an active robot for prostate resection. *Proc. Inst. Mech. Eng. H* 211:317–25
78. Butner SE, Ghodoussi M. 2003. Transforming a surgical robot for human telesurgery. *IEEE Trans. Robot. Autom.* 19:818–24
79. Marescaux J, Leroy J, Gagner M, Rubino F, Mutter D, et al. 2001. Transatlantic robot-assisted telesurgery. *Nature* 413:379–80
80. Guthart GS, Salisbury JK. 2000. The Intuitive telesurgery system: overview and application. In *Proceedings of the 2000 IEEE International Conference on Robotics and Automation*, pp. 618–21. Piscataway, NJ: IEEE
81. Yaxley JW, Coughlin GD, Chambers SK, Occhipinti S, Samaratunga H, et al. 2016. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet* 388:1057–66
82. Pacchierotti C. 2015. *Cutaneous Haptic Feedback in Robotic Teleoperation*. Cham, Switz.: Springer Int.
83. Ota T, Degani A, Schwartzman D, Zubiate B, McGarvey J, et al. 2009. A highly articulated robotic surgical system for minimally invasive surgery. *Ann. Thorac. Surg.* 87:1253–56
84. Lang S, Mattheis S, Hasskamp P, Lawson G, Güldner C, et al. 2017. A European multicenter study evaluating the flex robotic system in transoral robotic surgery. *Laryngoscope* 127:391–95
85. Shang J, Noonan DP, Payne C, Clark J, Sodergren MH, et al. 2011. An articulated universal joint based flexible access robot for minimally invasive surgery. In *Proceedings of the 2011 IEEE International Conference on Robotics and Automation*, pp. 1147–52. Piscataway, NJ: IEEE
86. Newton RC, Noonan DP, Vitiello V, Clark J, Payne CJ, et al. 2012. Robot-assisted transvaginal peritoneoscopy using confocal endomicroscopy: a feasibility study in a porcine model. *Surg. Endosc.* 26:2532–40
87. Di Marco AN, Jeyakumar J, Pratt PJ, Yang G-Z, Darzi AW. 2016. Evaluating a novel 3D stereoscopic visual display for transanal endoscopic surgery: a randomized controlled crossover study. *Ann. Surg.* 263:36–42
88. Shang J, Leibrandt K, Giataganas P, Vitiello V, Seneci CA, et al. 2017. A single-port robotic system for transanal microsurgery—design and validation. *IEEE Robot. Autom. Lett.* 2:1510–17
89. Lee S-L, Constantinescu M, Chi W, Yang G-Z. 2017. *Devices for endovascular interventions: technical advances and translational challenges*. White pap., Natl. Inst. Health Res./Clin. Res. Netw., London, UK
90. Walker TG, Kalva SP, Yeddula K, Wicky S, Kundu S, et al. 2010. Clinical practice guidelines for endovascular abdominal aortic aneurysm repair: written by the Standards of Practice Committee for the Society of Interventional Radiology and endorsed by the Cardiovascular and Interventional Radiological Society of Europe and the Canadian Interventional Radiology Association. *J. Vasc. Interv. Radiol.* 21:1632–55
91. Di Biase L, Wang Y, Horton R, Gallingshouse GJ, Mohanty P, et al. 2009. Ablation of atrial fibrillation utilizing robotic catheter navigation in comparison to manual navigation and ablation: single-center experience. *J. Cardiovasc. Electrophysiol.* 20:1328–35
92. Riga CV, Bicknell CD, Rolls A, Cheshire NJ, Hamady MS. 2013. Robot-assisted fenestrated endovascular aneurysm repair (FEVAR) using the Magellan system. *J. Vasc. Interv. Radiol.* 24:191–96
93. Feng Y, Guo Z, Dong Z, Zhou X-Y, Kwok K-W, et al. 2017. An efficient cardiac mapping strategy for radiofrequency catheter ablation with active learning. *Int. J. Comput. Assist. Radiol. Surg.* 12:1199–207
94. Cordemans V, Kaminski L, Banse X, Francq BG, Cartiaux O. 2017. Accuracy of a new intraoperative cone beam CT imaging technique (Artis zeego II) compared to postoperative CT scan for assessment of pedicle screws placement and breaches detection. *Eur. Spine J.* 26:2906–16

95. Sears P, Dupont P. 2006. A steerable needle technology using curved concentric tubes. In *Proceedings of the 2006 IEEE/RSJ International Conference on Intelligent Robots and Systems*, pp. 2850–56. Piscataway, NJ: IEEE
96. Webster RJ. 2007. *Design and mechanics of continuum robots for surgery*. PhD thesis, Johns Hopkins Univ., Baltimore, MD
97. Furusho J, Ono T, Murai R, Fujimoto T, Chiba Y, Horio H. 2005. Development of a curved multi-tube (CMT) catheter for percutaneous umbilical blood sampling and control methods of CMT catheters for solid organs. In *Proceedings of the 2005 IEEE International Conference Mechatronics and Automation*, pp. 410–15. Piscataway, NJ: IEEE
98. Dupont PE, Lock J, Itkowitz B, Butler E. 2010. Design and control of concentric-tube robots. *IEEE Trans. Robot.* 26:209–25
99. Webster RJ III, Swensen JP, Romano JM, Cowan NJ. 2009. Closed-form differential kinematics for concentric-tube continuum robots with application to visual servoing. In *Experimental Robotics*, ed. O Khatib, V Kumar, GJ Pappas, pp. 485–94. Berlin/Heidelberg: Springer
100. Arabagi V, Gosline A, Wood RJ, Dupont PE. 2013. Simultaneous soft sensing of tissue contact angle and force for millimeter-scale medical robots. In *Proceedings of the 2013 IEEE International Conference on Robotics and Automation*, pp. 4396–402. Piscataway, NJ: IEEE
101. Burgner J, Rucker DC, Gilbert HB, Swaney PJ, Russell PT, et al. 2014. A telerobotic system for transnasal surgery. *IEEE ASME Trans. Mechatron.* 19:996–1006
102. Gosline AH, Vasilyev NV, Butler EJ, Folk C, Cohen A, et al. 2012. Percutaneous intracardiac beating-heart surgery using metal MEMS tissue approximation tools. *Int. J. Robot. Res.* 31:1081–93
103. Swaney PJ, Croom JM, Burgner J, Gilbert HB, Rucker DC, et al. 2012. Design of a quadramanual robot for single-nostril skull base surgery. In *Proceedings of the 5th Annual Dynamic Systems and Control Conference/11th Motion and Vibration Conference*, pp. 387–93. New York: ASME
104. Estape R. 2018. *Early acute in-vivo experience in gynecology oncology applications with the SPORT surgical system technology*. White pap., Titan Medical Inc., Toronto, Can.
105. Iddan G, Meron G, Glukhovskiy A, Swain P. 2000. Wireless capsule endoscopy. *Nature* 405:417
106. Spada C, Spera G, Riccioni M, Biancone L, Petruzzello L, et al. 2005. A novel diagnostic tool for detecting functional patency of the small bowel: the Given patency capsule. *Endoscopy* 37:793–800
107. Gorini S, Quirini M, Mencias A, Pernorio G, Stefanini C, Dario P. 2006. A novel SMA-based actuator for a legged endoscopic capsule. In *Proceedings of the 1st IEEE/RAS-EMBS International Conference on Biomedical Robotics and Biomechatronics*, pp. 443–49. Piscataway, NJ: IEEE
108. Kwon J, Park S, Park J, Kim B. 2007. Evaluation of the critical stroke of an earthworm-like robot for capsule endoscopes. *Proc. Inst. Mech. Eng. H* 221:397–405
109. Ciuti G, Valdastrì P, Mencias A, Dario P. 2010. Robotic magnetic steering and locomotion of capsule endoscope for diagnostic and surgical endoluminal procedures. *Robotica* 28:199–207
110. Ciuti G, Donlin R, Valdastrì P, Arezzo A, Mencias A, et al. 2010. Robotic versus manual control in magnetic steering of an endoscopic capsule. *Endoscopy* 42:148–52
111. Rey J-F, Ogata H, Hosoe N, Ohtsuka K, Ogata N, et al. 2012. Blinded nonrandomized comparative study of gastric examination with a magnetically guided capsule endoscope and standard videoendoscope. *Gastrointest. Endosc.* 75:373–81
112. Popek KM, Hermans T, Abbott JJ. 2017. First demonstration of simultaneous localization and propulsion of a magnetic capsule in a lumen using a single rotating magnet. In *Proceedings of the 2017 IEEE International Conference on Robotics and Automation*, pp. 1154–60. Piscataway, NJ: IEEE
113. Kong K, Cha J, Jeon D, Cho DD. 2005. A rotational micro biopsy device for the capsule endoscope. In *Proceedings of the 2005 IEEE/RSJ International Conference on Intelligent Robots and Systems*, pp. 1839–43. Piscataway, NJ: IEEE
114. Simi M, Gerboni G, Mencias A, Valdastrì P. 2012. Magnetic mechanism for wireless capsule biopsy. *J. Med. Devices* 6:017611
115. Payne CJ, Yang G-Z. 2014. Hand-held medical robots. *Ann. Biomed. Eng.* 42:1594–605

116. Payne CJ, Rafii-Tari H, Yang GZ. 2012. A force feedback system for endovascular catheterisation. In *Proceedings of the 2012 IEEE/RSJ International Conference on Intelligent Robots and Systems*, pp. 1298–304. Piscataway, NJ: IEEE
117. Li J, de Ávila BE-F, Gao W, Zhang L, Wang J. 2017. Micro/nanorobots for biomedicine: delivery, surgery, sensing, and detoxification. *Sci. Robot.* 2:eaam6431
118. Zebda A, Alcaraz J-P, Vadgama P, Shleev S, Minteer SD, et al. 2018. Challenges for successful implantation of biofuel cells. *Bioelectrochemistry* 124:57–72
119. Ghelfi J, Moreau-Gaudry A, Hungr N, Fouard C, Véron B, et al. 2018. Evaluation of the needle positioning accuracy of a light puncture robot under MRI guidance: results of a clinical trial on healthy volunteers. *Cardiovasc. Intervent. Radiol.* 41:1428–35
120. Yang G-Z, Bellingham J, Dupont PE, Fischer P, Floridi L, et al. 2018. The grand challenges of science robotics. *Sci. Robot.* 3:eaar7650
121. Rafii-Tari H, Liu J, Lee S-L, Bicknell C, Yang G-Z. 2013. Learning-based modeling of endovascular navigation for collaborative robotic catheterization. *Med. Image Comput.* 16:369–77
122. Yang G-Z, Cambias J, Cleary K, Daimler E, Drake J, et al. 2017. Medical robotics—regulatory, ethical, and legal considerations for increasing levels of autonomy. *Sci. Robot.* 2:eaam8638
123. Bargar WL, Bauer A, Börner M. 1998. Primary and revision total hip replacement using the Robodoc system. *Clin. Orthop. Relat. Res.* 354:82–91
124. Marcus HJ, Payne CJ, Hughes-Hallett A, Gras G, Leibrandt K, et al. 2016. Making the leap: the translation of innovative surgical devices from the laboratory to the operating room. *Ann. Surg.* 263:1077–78
125. Marcus HJ, Payne CJ, Hughes-Hallett A, Marcus AP, Yang G-Z, et al. 2016. Regulatory approval of new medical devices: cross sectional study. *BMJ* 353:i2587
126. Jeong IG, Khandwala YS, Kim JH, Han DH, Li S, et al. 2017. Association of robotic-assisted versus laparoscopic radical nephrectomy with perioperative outcomes and health care costs, 2003 to 2015. *JAMA* 318:1561–68
127. Jayne D, Pigazzi A, Marshall H, Croft J, Corrigan N, et al. 2017. Effect of robotic-assisted versus conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. *JAMA* 318:1569–80
128. Wright JD. 2017. Robotic-assisted surgery: balancing evidence and implementation. *JAMA* 318:1545–47
129. Keel G, Savage C, Rafiq M, Mazzocato P. 2017. Time-driven activity-based costing in health care: a systematic review of the literature. *Health Policy* 121:755–63
130. Liow MHL, Chin PL, Pang HN, Tay DK-J, Yeo S-J. 2017. THINK surgical TSolution-One® (Robodoc) total knee arthroplasty. *SICOT J.* 3:63
131. Shenoy R, Nathwani D. 2017. Evidence for robots. *SICOT J.* 3:38
132. Troccaz J, Berkelman P, Cinquin P, Vilchis-Gonzales A. 2002. Interactive robots for medical applications. In *Proceedings of the 6th Annual Conference of the International Society for Computer Aided Surgery (CARS 2002)*, pp. 175–80. Berlin/Heidelberg: Springer
133. Hungr N, Baumann M, Long J, Troccaz J. 2012. A 3-D ultrasound robotic prostate brachytherapy system with prostate motion tracking. *IEEE Trans. Robot.* 28:1382–97
134. Long J-A, Hungr N, Baumann M, Descotes J-L, Bolla M, et al. 2012. Development of a novel robot for transperineal needle based interventions: focal therapy, brachytherapy and prostate biopsies. *J. Urol.* 188:1369–74
135. Veron B, Hungr N, Troccaz J. 2016. Making a clinical device from a laboratory prototype: from Prosper to Prosper OR. In *Proceedings of the 6th Joint Workshop on New Technologies for Computer/Robot Assisted Surgery*. <http://hal.univ-grenoble-alpes.fr/hal-01455696/document>
136. Research and Markets Ltd. 2018. *Medical robots market to 2025—global analysis and forecasts by product; application, end-user and geography*. Report 4617877, Research and Markets Ltd., Dublin, Irel. <https://www.researchandmarkets.com/reports/4617877/medical-robots-market-to-2025-global-analysis>
137. Intuitive Surgical. 2016. *Annual Report 2016*. Report, Intuitive Surgical, Sunnyvale, CA. http://www.annualreports.com/HostedData/AnnualReportArchive/i/NASDAQ_ISRIG_2016.pdf

138. Köckerling F. 2014. Robotic vs. standard laparoscopic technique—what is better? *Front. Surg.* 1:15
139. Baek SJ, Kim SH. 2014. Robotics in general surgery: an evidence-based review. *Asian J. Endosc. Surg.* 7:117–23
140. Grimsby GM, Dwyer ME, Jacobs MA, Ost MC, Schneck FX, et al. 2015. Multi-institutional review of outcomes of robot-assisted laparoscopic extravesical ureteral reimplantation. *J. Urol.* 193:1791–95
141. Hughes D, Camp C, O'Hara J, Adshead J. 2016. Health resource use after robot-assisted surgery vs open and conventional laparoscopic techniques in oncology: analysis of English secondary care data for radical prostatectomy and partial nephrectomy. *BJU Int.* 117:940–47
142. Keel G, Savage C, Rafiq M, Mazzocato P. 2017. Time-driven activity-based costing in health care: a systematic review of the literature. *Health Policy* 121:755–63
143. Jeong IG, Khandwala YS, Kim JH, Han DH, Li S, et al. 2017. Association of robotic-assisted vs laparoscopic radical nephrectomy with perioperative outcomes and health care costs, 2003 to 2015. *JAMA* 318:1561–68
144. Childers CP, Maggard-Gibbons M. 2018. Estimation of the acquisition and operating costs for robotic surgery. *JAMA* 320:835–36
145. Kosugi Y, Watanabe E, Goto J, Watanabe T, Yoshimoto S, et al. 1988. An articulated neurosurgical navigation system using MRI and CT images. *IEEE Trans. Biomed. Eng.* 35:147–52