Forward We Go!

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Key Words: Democratization, Medicine, Minimally invasive surgery, Laparoscopy, Robotic surgery, Standardization, Surgery, Video-assisted surgery.

History of modern day minimally invasive surgery, where we are now, and where we are going to standardize and democratize surgery.

Technology has revolutionized many aspects of our lives from space to social media and telecommunication. Medicine and surgery have been one of the last beneficiaries of this advancement in technology. We predict this will change rapidly, revolutionizing medicine and surgery to standardize and democratize it. Here is how we see it happening…

The first successful vertical laparotomy was performed in the early 18th century by Dr. Ephraim McDowell and was initially negatively received by authorities in the medical community. Dr. James Johnson, the editor of the Medico-Chirurgical Review of London in 1817 wrote,

> "In spite of all that has been written respecting this cruel operation, we entirely disbelieve that it has been performed with success, nor do we think that it ever will."

Over a decade later, Dr. Johnson issued an apology:

> "A back settlement of America - Kentucky, has beaten the mother country, nay, Europe itself, with all the boasted surgeons thereof, in the fearful and formidable operation of gastronomy with extraction of diseased ovaria…. There were circumstances in the narrative of some of the first three cases, that raised misgivings in our minds, for which uncharitableness we ask pardon of God and Dr. McDowell of Danville."

One hundred years after Dr. McDowell's success, Dr. Hermann Johannes Pfannenstiel performed the first transverse laparotomy. He also, was criticized. It took another 100 years for the outcomes to be published, confirming Pfannenstiel's transverse laparotomy had lower complication rates than the traditional vertical approach.[1]

A similar progression has been seen with developments in endoscopy. The first endoscopy was done by Dr. Philipp Bozzini in the 18th century who used a light carrying instrument, a Lichtleiter, to look inside the bladder. Yet, it was not initially accepted. One hundred years later, Dr. George Kelling performed the first laparoscopy in the early 19th century.[2,3] Other virtuosos including Dr. Hans Christian Jacobeous, Dr. Raoul Palmer, Dr. Kurt Semm, and Dr. Victor Gomel used laparoscopy throughout the 20th century to perform intraperitoneal biopsies and lysis of adhesions among other minor procedures. Dr. Hubert Manhes did an ectopic pregnancy by laparoscopy in late 1970s. Dr. Victor Gomel was the first to perform successful laparoscopic salpingo-ovariolysis in the 1970's and 80's and Dr. Kurt Semm was the first to perform total laparoscopic appendectomy in 1981. Prior to Dr. Kurt Semm, Dr. Henk de Kok used a laparoscope to identify and mobilize the appendix and removed it through a 1-cm incision. In fact, he had done 320 laparoscopic appendectomies by 1980, but he downplayed his accomplishment because the medical establishment continued to be wary of laparoscopy. It was Dr. Semm who publicized the technique, and much of the surgical community in Germany persecuted Dr. Semm for

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Acknowledgements: We would like to thank Dr. Steven Lindheim for his editorial assistance in preparation of this manuscript.

Disclosure: none.

Funding sources: none.

Conflict of interests: none.

Informed consent: Dr. Camran Nezhat declares that written informed consent was obtained from the patient/s for publication of this study/report and any accompanying images.

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DOI: 10.4293/JSLS.2022.00073

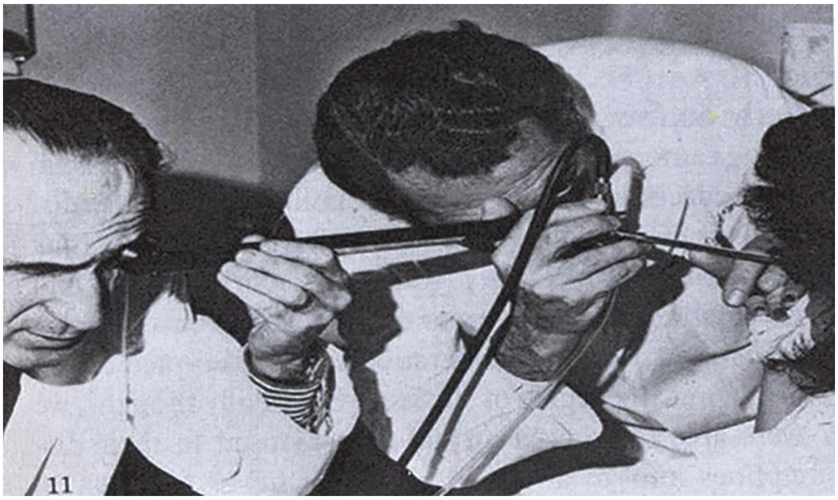


Figure 1. Dr. George Berci peering through a teaching attachment in 1977.

his work. Some surgeons asked for him to be suspended from medicine and many thought his actions to be unethical.

Broad acceptance did not follow and no advances were made in the field mainly because laparoscopy was a single eye procedure in which only the surgeon could see.[2–4] In some cases, there was an attachment for the assistants to see the procedure. In this picture published by Dr. Berci in 1977, one can see the limitations (**Figure 1**). Berci was a forerunner of endoscopy and cinematography, but even he was looking through the eyepiece of a telescope.

Since Dr. Camran Nezhat invented and pioneered videolaparoscopy (Video-Assisted Endoscopy Surgery) and demonstrated how it is more effective in treating pathology than laparotomy, modern-day operations have been revolutionized.[2,3,5–17] (**Figure 2**). Beginning with very big cameras that were developed for other purposes, Dr. Nezhat

Figure 2. Camran Nezhat, circa 1980, performing videolaparoscopy with one for the early video camera prototypes.

tried to fit them on the endoscope. Eventually, he was able to convince the industry to make custom-sized video cameras for endoscopes. Dr. Nezhat reported video laparoscopic treatment of stage IV endometriosis for the first time in 1985.[18] He observed that if stage IV endometriosis can be treated by laparoscope, almost all the surgical pathology could be managed by this route.[7,18]

Early adopters around the world, embraced this advancement by performing cholecytectomy in Europe (Prof. Dr. Med Erich Mühe of Böblingen Germany in 1985 and Dr. Philip Mouret of France in 1987) then in the United States (Dr. J. Barry McKernan and Dr. William B. Saye in Marietta, Georgia in 1988). The first laparoscopic radical prostatectomy was performed by Dr. Ralph V. Clayman. Dr. Harry Reich in the United States reported the first laparoscopic hysterectomy. Dr. Denis Querleu and Dr. Daniel Dargent, from France staged gynecological cancer. Dr. Nezhat and his team in collaboration with other surgical disciplines performed some of the most advanced procedures for the first time. For example, with urologists, Dr. Howard Rottenberg, Dr. Bruce Green, and Dr. Fuad Freiha, they performed the first laparoscopic, segmental bladder resection, first ureter-resection and re-anastomosis, ureteroneocystostomy with and without Psoas Hitch, and vesicovaginal fistula repair.[5,6,10–12,19] With colorectal surgeons, Dr. Earl Pennington, Dr. Wayne Ambrose, and Dr. Guy Orangio, the first bowel resection and repair including shaving, disk excision, and segmental colon resection.[5,6,10–12,19] With gynecologic oncologist, Dr. Benedict Benigno and Dr. Matthew Burrell, the first radical hysterectomy, para-aortic, and pelvic node dissection.[5,6,10–12,19] With Dr. Howard Brown, the first laparoscopic thoracic diaphragm resection.[5,6,10–12,19] With Dr. Nelson Teng, debulking of advance ovarian cancer.[20] With Dr. Sheryl Silfen, the first laparoscopy for management of adnexal mass during advanced pregnancy.[5,6,10,11,19] Some of the other procedures performed laparoscopically for the first time by Dr. Nezhat and his team were laparoscopic management of ovarian remnant syndrome, control and repair of major vessel injuries, isthmocele and niche repair, sacral colopopexy, and laparoscopic removal of endometriosis of the liver.[5,6,10,11,19,21]

While collaborating with surgeons from other disciplines, Dr. Nezhat encouraged them to use video assisted endoscopy. He started teaching his techniques beginning in 1982 in many postgraduate courses. Dr. Nezhat was one of the first gynecologists in the country to routinely perform cystoscopy and proctosigmoidoscopy in patients with endometriosis. Numerous hysteroscopy surgeons globally adopted the video augmentation to treat a variety of intrauterine pathologies. Video recording of surgeries became an integral part of teaching which made the techniques more reproducible.

Currently, the utility of video assisted endoscopy surgery has expanded such that it is routinely used for surgical management of even the most complex procedures, and operative video endoscopy is the preferred surgical method when a body cavity exists or can be created.[5,7,18] Video endoscopy surgery allows better visualization of the operative field, video augmentation, and turns macroscopic surgery into microsurgery. Among other advantages, the anatomy is magnified and by advancing the video endoscope to the most difficult to reach areas by laparotomy, visualization is improved. This facilitates better diagnostic and operative procedures and leads to better results. The limiting factors are the skill and experience of the surgeon and the availability of proper instrumentation.[5,7,11,18]

In spite of all of these advantages, in the 1980's and 1990's, there was significant resistance by medical journals and academics in accepting minimally invasive surgery (MIS). However, patients embraced and advocated for the use of video assisted endoscopic surgery. They described their experiences in widely known magazines such as *Time* and *Newsweek* in the mid-1980's[13–15] (**Figures 3–4**). Hence, the acceptance of MIS was initially driven by the patients. It was stated in a 1990's *Newsweek* article that, "In twenty years, laparotomy will be extinct."[13–16] At the time, many well respected medical authorities called video assisted endoscopy surgery and MIS a "gimmick" or "a bursting bubble", and even ridiculed the procedure.[22–25]

One reviewer stated that the paper was not publishable because:

> "Operating off the monitor and not looking through the scope while doing surgery is dangerous and only one out of 200 surgeons are capable of doing this and that the authors were advocating a dangerous technique."

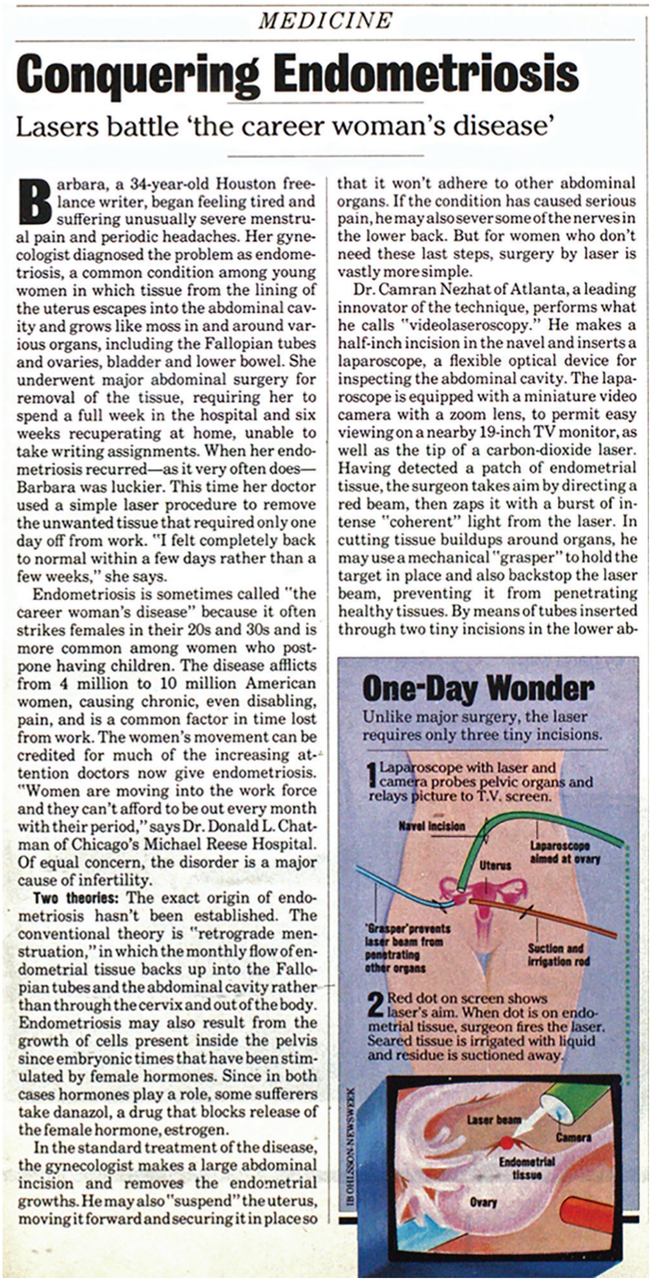
Some authorities in colorectal surgery called laparoscopic bowel resection barbaric [Camran Nezhat, M.D Personal communication.] Opposition towards MIS came from all angles. Even the Federal Bureau of Investigation, the Internal Revenue Service, the Justice Department, and multiple state medical boards were involved in investigating such cases at the same time; possibly because they had received accusations stating that such surgeons were "gangster surgeons or medical terrorists."[6,10,19]

Figure 3. Camran Nezhat in *Newsweek* magazine, 1990.

All of this seemingly occurred because the development of video assisted endoscopy surgery (modern day minimally invasive surgery) was applied to the most difficult operations with equal or better outcomes. These promising results appeared to threaten the medical establishment. Probably many of these doubters were well intentioned and quite honestly believed they were protecting established surgical practice. They just could not conceive that one could improve on laparotomy and the profound impact video assisted endoscopy surgery would have on all surgical disciplines.[6] It was not until the 1990s and later, when The Society of American Gastrointestinal and Endoscopic Surgeons widely adopted video assisted endoscopy surgery and established guidelines leading to creation of the Fundamentals of Laparoscopic Surgery supporting the notion of video-laparoscopy as a legitimate alternative to open surgery in properly trained hands.[2,3,26]

When all was said and done, Drs. Camran, Farr, and Ceana Nezhat withstood accusations of barbarism, commercialism, medical terrorism, and even a surprising Stanford "suspension-ism" to be reversed by an apology and several months later by their reinstatement.[10,24] In the end, the Nezhats (and video assisted endoscopy surgery) were exonerated by respected medical authorities from all of these smear campaigns, which produced a victory for patients all over the world.[6,10] Forty years later in 2020, the American Medical Association (AMA) recognized Dr. Camran Nezhat, for his pioneering work with the Distinguished Service Award for his meritorious service in the science and art of medicine[27–30] (**Figure 5**). "Innovation is a key driver in transforming health care and Dr. Nezhat's pioneering work has fundamentally changed contemporary surgery and opened a path for surgeons around the world to help their patients", said AMA President Dr. Susan R. Bailey "He continues to push the leading-edge of advanced procedures and the development of the safest, most efficacious technologies to enhance patient care and improve outcomes."[27–30]

Thanks to pioneering and vision of other surgeons and interest of the industry in development of new instruments, performing operative endoscopy has become more common for numerous surgeons in different disciplines and more complex procedures. There is now overwhelming evidence that video-laparoscopy is superior to laparotomy. For example, obesity was previously thought to be a contraindication for the use of laparoscopy. It has now become the preferred method over laparotomy for surgical interventions in overweight patients.[31] Another misconception about video-laparoscopy was that of expense. To date, multiple Cochrane reviews have demonstrated that video-laparoscopy costs less than laparotomy because of less time spent in the hospital and reduction in postoperative



MEDICINE

Conquering Endometriosis

Lasers battle 'the career woman's disease'

Barbara, a 34-year-old Houston freelance writer, began feeling tired and suffering unusually severe menstrual pain and periodic headaches. Her gynecologist diagnosed the problem as endometriosis, a common condition among young women in which tissue from the lining of the uterus escapes into the abdominal cavity and grows like moss in and around various organs, including the Fallopian tubes and ovaries, bladder and lower bowel. She underwent major abdominal surgery for removal of the tissue, requiring her to spend a full week in the hospital and six weeks recuperating at home, unable to take writing assignments. When her endometriosis recurred—as it very often does—Barbara was luckier. This time her doctor used a simple laser procedure to remove the unwanted tissue that required only one day off from work. "I felt completely back to normal within a few days rather than a few weeks," she says.

Endometriosis is sometimes called "the career woman's disease" because it often strikes females in their 20s and 30s and is more common among women who postpone having children. The disease afflicts from 4 million to 10 million American women, causing chronic, even disabling, pain, and is a common factor in time lost from work. The women's movement can be credited for much of the increasing attention doctors now give endometriosis. "Women are moving into the work force and they can't afford to be out every month with their period," says Dr. Donald L. Chatman of Chicago's Michael Reese Hospital. Of equal concern, the disorder is a major cause of infertility.

Two theories: The exact origin of endometriosis hasn't been established. The conventional theory is "retrograde menstruation," in which the monthly flow of endometrial tissue backs up into the Fallopian tubes and the abdominal cavity rather than through the cervix and out of the body. Endometriosis may also result from the growth of cells present inside the pelvis since embryonic times that have been stimulated by female hormones. Since in both cases hormones play a role, some sufferers take danazol, a drug that blocks release of the female hormone, estrogen.

In the standard treatment of the disease, the gynecologist makes a large abdominal incision and removes the endometrial growths. He may also "suspend" the uterus, moving it forward and securing it in place so that it won't adhere to other abdominal organs. If the condition has caused serious pain, he may also sever some of the nerves in the lower back. But for women who don't need these last steps, surgery by laser is vastly more simple.

Dr. Camran Nezhat of Atlanta, a leading innovator of the technique, performs what he calls "videolaseroscopy." He makes a half-inch incision in the navel and inserts a laparoscope, a flexible optical device for inspecting the abdominal cavity. The laparoscope is equipped with a miniature video camera with a zoom lens, to permit easy viewing on a nearby 19-inch TV monitor, as well as the tip of a carbon-dioxide laser. Having detected a patch of endometrial tissue, the surgeon takes aim by directing a red beam, then zaps it with a burst of intense "coherent" light from the laser. In cutting tissue buildups around organs, he may use a mechanical "grasper" to hold the target in place and also backstop the laser beam, preventing it from penetrating healthy tissues. By means of tubes inserted through two tiny incisions in the lower ab-

Figure 4. Camran Nezhat in *Newsweek* magazine, 1986.

pain. In addition, there are fewer complications and patients experience fewer lost workdays with minimally invasive surgeries.[32]

In 2004, a *New England Journal of Medicine* editorial described the overall benefits of video-laparoscopy, particularly for bowel resection. This is the same procedure that was called barbaric when it was first presented in 1988.[5,6,33–35] The editor of the *New England Journal of Medicine* wrote,

> "Surgeons must [move] beyond the traditional techniques of cutting and sewing . . . to a future in which . . . minimal access to the abdominal cavity [is] only the beginning."[36]

To his credit, the former editor of *Obstetrics and Gynecology* (the official journal of American College of Obstetrics and Gynecology), who was one of the original naysayers, acknowledged in 2010 that,

> "A substantial body of evidence has accumulated in recent years to support the laparoscopic approach to various gynecologic operations."[37]

Robotic surgery, also known as computer enhanced telesurgery, has also lead to the increased use of video-laparoscopy.[38,39] Urologists have taken advantage of the increased degrees of freedom available with the robot to work deep in the male pelvis and suture structures that were difficult or even impossible to suture before. Gynecologists have widely adopted video-laparoscopy, with and without robotic assistance, in benign conditions

Figure 5. Camran Nezhat, MD, with American Medical Association's Distinguished Service Award.

and in management of endometrial, cervical, ovarian, and fallopian tube cancers;[40–48] to the extent that MIS currently is the standard of care for surgical management of endometrial cancer.[49] All of these advances have improved patient outcomes, and with similar results, the advantages of MIS has been confirmed in urology, gastroenterology, thoracic surgery, etc.[50–56]

Development and application of new technology such as florescent guided surgery (FGS) has made another step in minimizing the radicality of certain complex procedures. In pelvic and para-aortic lymphadenectomy or sentinel node biopsy, MIS enables less complicated surgery with less morbidity.[57–61] At the same time, encouraging results in use of neoajuvant chemotherapy for treatment of advanced ovarian cancer to decreases bulky tumors, prior to surgical debulking without compromising the patient's survival, has made the role of MIS more practical.[62–64]

It is now time to train, encourage, and educate future surgeons so they become proficient with MIS techniques, which will ensure that surgical procedures are standardized.[5] The development of enabling devices, such as the robotic arm, has made minimally invasive technology accessible and easier to learn.

Ideally, surgery should be customizable, replicable, and democratized. For instance, medical treatments are predominantly standardized on a global scale, as any patient receiving 325 mg of aspirin receives the same medication; but surgery is not like that. Two different surgeons performing the same procedure at the same hospital in neighboring operating rooms may do it differently. We must standardize surgery to ensure comparable metrics. Out of 8 billion people in the world, 5 billion do not have access to proper surgical care. It is estimated that 143 million more operative procedures are needed annually.[65] Nineteen million deaths can be avoided annually if proper surgery is done.[65] Studies show that the less experienced surgeon has higher a complication rate, 2.5-fold increased operative time, six-fold readmission rate, and higher mortality rates than those of high volume surgeons.[65]

How can surgery be standardized and as a result hopefully and gradually democratized? In the future, techniques of the best surgeons in each field will be combined to render standardized procedures for different pathologies, which will assure the highest quality of care is available to all. To do this, we must make better use of surgical technologies, which include digital surgery and subsequent new developments. Digital surgery is a combination of robotics, data analytics, machine learning, artificial intelligence, enhanced visualization, and enhanced instrumentation. It is a fusion of the human mind with artificial intelligence. We predict that ultimately intelligent robots will surpass human surgeons' capabilities by self-learning and scaling. Image-guided ultrasound therapy, prosthetic limbs, 3D printing, artificial vessels, genome editing, fluorescent guided surgery, and augmented reality, provide limitless possibilities, and will surely lead to incision-less surgical procedures (**Figure 6**).

The pace of advancement is accelerating. Improvements in farming during the agricultural age evolved over 8000 years, and manufacturing techniques during the industrial revolution improved over 100 years. In contrast,

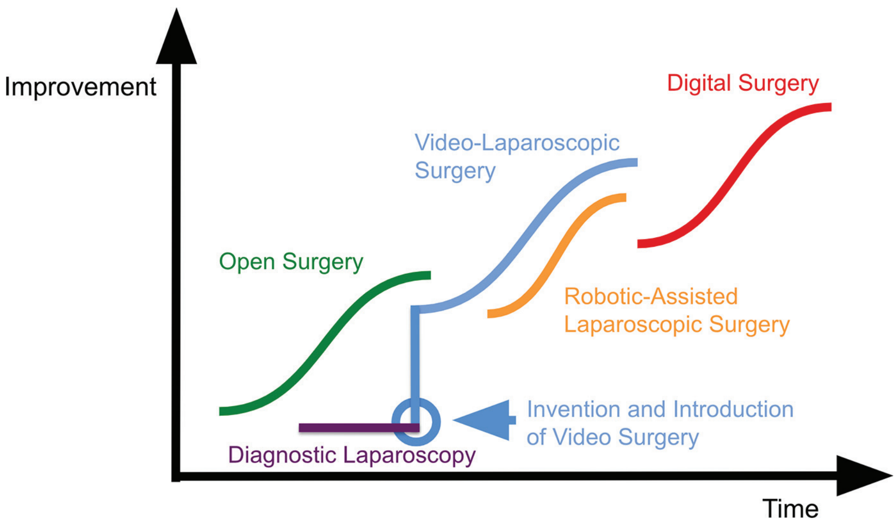


Figure 6. How video surgery with and without robotic assistance propelled minimally invasive surgery to replace open surgery.

the universal use of the Internet since its inception occurred over only 20 years and sequencing of the genome required only nine years. A task that previously required 90 years to complete with a computer can now be done in one hour. Computing power and speed will soon surpass the human mind. We are on the cusp of transitioning to digital surgery and beyond.

Artificial intelligence (AI) follows a similar pattern and can be categorized into four main developmental steps: reactive machines, limited memory, theory of mind, and self-aware. The development of reactive machines proved that AI could be used for simple classifications and pattern recognition and useful in situations where all patterns are known, such as in chess. Google's MuZero chess AI was able to reach superhuman performance without knowing the rules and similar outcomes have been seen for Shogi, Go, and Atari. The current state of AI, limited memory, is a step past this in being able to handle more complex classifications and use historical data to make predictions, but remains vulnerable to outliers and adversarial examples. Self-driving cars, for example, use the set rules of the road in combination with observations from human drivers to make decisions, but are still susceptible to making incorrect decisions and causing accidents when others do not act according to the rules. The next milestone of AI, theory of mind (Metaverse), is where standardizing and democratizing surgery has the potential to come to fruition. This AI, improved by quantum computing, will be able to understand human motives and reasoning to deliver personal experience to everyone based on their motives and needs. In the future, we may experience the final form of AI, self-aware, which would exhibit human level intelligence, eventually bypassing our own intelligence and become superhuman in capabilities.

Over the last 10 years, noninvasive procedures have begun to replace surgery or radiation as preferred therapeutic modalities. For example, high-intensity focused ultrasound (HIFU) is now used to ablate many types of solid tumors and will eventually be used for many other applications. The precision associated with real-time imaging along with the use of sound waves makes HIFU a safe and cost-effective therapy. This is just one example of the many ways that new technologies will drastically improve the way we treat disease. Eventually, innovations in energy modalities could enable the Einstein equation ($E = mc^2$ or the relativistic energy-momentum relation) to advance our ability to precisely target cellular (and possibly subcellular) areas for treatment of cancer and to prevent other diseases. We already perform incisionless surgeries by combining new technology with new types of energy: HIFU, magnetic resonance imaging-guided ultrasound, and Cyberknife are now being used for solid tumors. 'Genome surgery' with CRISPR/Cas9 is already being used to repair or replace defective DNA.

"One key issue that surgeons and scientists are looking to resolve is visibility beyond the surface. Another is a way to distinguish critical structures from each other. Surgeons can only see so much inside the body under regular "white light," but some are optimistic that sensory improvements can help them detect in real time what cannot be seen with the naked eye. Florescence-guided surgery is one step toward visual enhancement in surgery. A popular fluorophore today is indocyanine green (ICG), which has been used in several medical specialties.[58–61,66] This technology may make the surgery safer, increase diagnostic accuracy, enable better treatment, decrease complication, and reduce overall cost.

An exciting future direction will be to combine the digitalized surgical methods with advances in energy generation and more accurately correct defective tissue and subcellular disease. Our vision is that all surgical procedures for tissue removal or debulking will be incisionless. Moreover, we believe that this brave new world, or at least a glimpse of it, will arrive in the lifetimes of those reading this report. This standardization, democratization, and expansion will start with automation and scaling of medicine first and then surgery. The standardization and democratization of communication and social media can be seen worldwide, even in less developed corners of the world. Technology will enable medicine and surgery to do the same.

We predict that by the year 2050, medicine and surgery will be more than 90% standardized and democratized. Forward we go!

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