sagentia innovation

WHITEPAPER

Smart Surgery - a new era in surgical technology

Author: Rob Morgan

Smart surgery is a theme spanning many surgical disciplines and medical technology offerings. We see it as a trend that is distinct from the related themes of surgical navigation, robotic surgery and computer assisted surgery. Examples include smart surgical instruments, live data in surgery, novel visualisation systems and tissue sensing. The common thread is improved decision making by surgeons and other healthcare professionals, enabled by the novel provision of information.

The common thread is improved decision making by surgeons and other healthcare professionals, enabled by the novel provision of information

For surgical technology to become ‘smarter’, however, it must be driven by clinical need and provide health economic benefits; it cannot be driven alone by the availability of new enabling technology. By using the term ‘smart surgery’ and by highlighting this trend in the medical technology market, we hope to stimulate a cross fertilisation of ideas between different surgical applications.

To understand how this trend may develop we have reviewed the medical technology market to identify smart surgery products which have already been commercialised. Although not all of these products will be both clinically and commercially successful, they will have undergone rigorous scrutiny by their developers to ensure they target real clinical needs. Through looking at these products collectively, we have gained an insight into which clinical needs are being addressed and how similar needs might be addressed across different surgical disciplines; the result is a number of application themes. In doing so we have reviewed the technologies underpinning recent product developments and offer a view of how these technologies may develop. In the final section of this paper we offer a view on future trends in which the benefits of smart surgery are more fully realised.

The continuum of care

Smart surgery should be considered within the continuum of care of surgical patients, as illustrated in figure 1. In this continuum there is the opportunity to improve clinician decision making through provision of novel information at the point at which it is most needed. In some cases the information already exists through preoperative diagnosis and surgical planning but needs to be made easily available during surgery. In other cases data needs to be both collected and displayed during surgery. In each case the goal should be to efficiently provide data to decision makers, with minimal disruption to current treatment pathways and preferably resulting in improved surgical workflows. A related theme is the collection of outcomes data through novel surgical methods, for example through the use of smart implants.

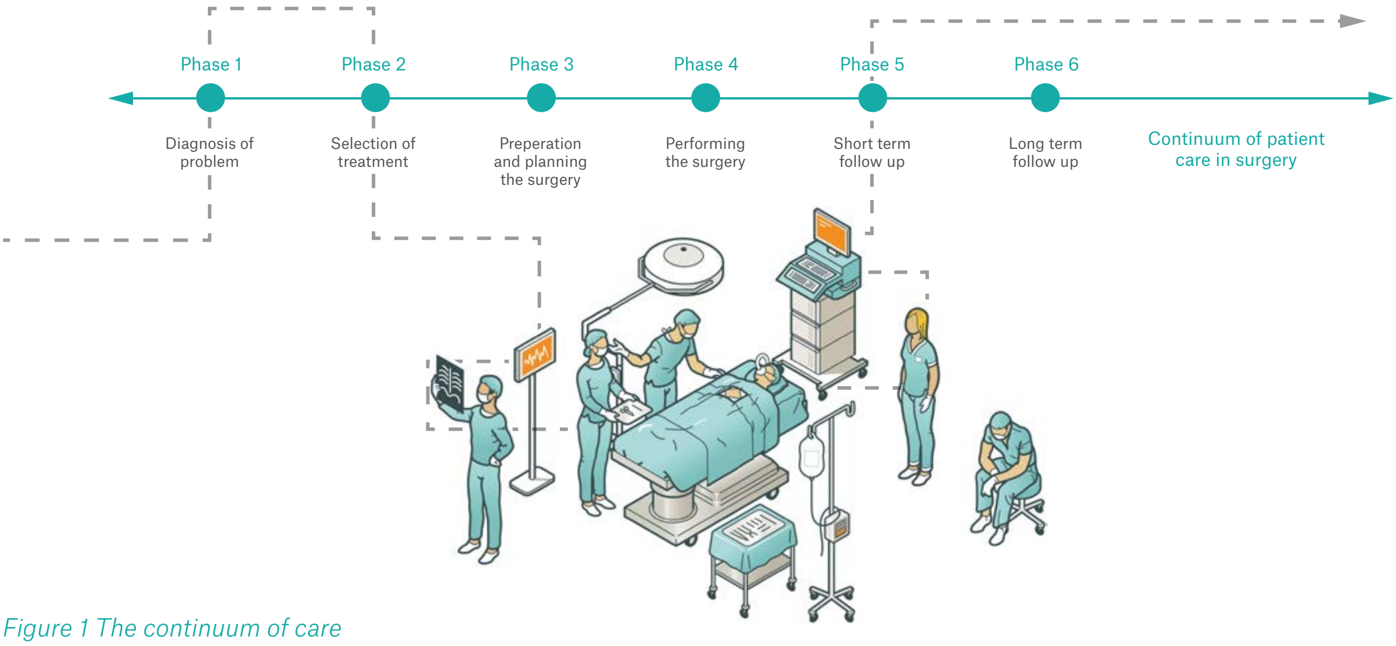

Figure 1 The continuum of care

Powerful imaging tools are routinely used preoperatively to characterise tissue properties, diagnose patient conditions and, in so doing, inform clinician decision making. Techniques such as magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) are used to non-invasively assess diseased tissue and characterise tissue properties. Whilst the use of such techniques has not been translated into the operating suite, except for specialised operating suites used predominantly in neurosurgery, the information obtained preoperatively is used intraoperatively, for example during computer assisted surgery and robotic surgery. Improved access to preoperative data in the operating room is being advanced by researchers and by GestSure Technologies using the Microsoft Kinect system. Likewise surgeons are experimenting with the use of Google Glass for accessing x-ray or MRI data both in the operating room and without having to switch their field of view away from the patient[1]. We can envisage a future state incorporating much greater use of image overlay of pre-operative data on live intraoperative feeds to improve tissue identification and characterisation in the OR.

Long term management of surgical patients may be improved by using data collected from devices implanted during surgery or by implanting implants which automatically sense and act (smart implants). Certain surgical implants, such as pacemakers, neurostimulators and implantable cardioverter defibrillators (ICDs), are inherently 'smart'. For example ICDs sense cardiac arrhythmia and deliver an electrical impulse in order to provide the patient with a long term management solution for their cardiac dysrhythmia. Likewise, modern pacemakers sense, stimulate and also wirelessly transmit data to allow clinicians to manage patients post operatively.

The transformation of traditionally 'dumb' implants to ones which sense is another avenue for technical advancement. The necessity and usefulness of such smart implants in improving post-operative management has to be clearly evaluated, however, because of the increased development complexity and increased risk to the patient introduced by embedding electronics within surgical implants.

Smart implants have been used as research tools in orthopaedic surgery to gain in vivo data for shoulder[2], femoral[3] and tibial prostheses[4] but have yet to gain traction as commercial devices; the development of smart joint replacements provides an informative case study. Superficially it would seem to be highly beneficial to monitor the performance of joint replacement implants postoperatively because such implants have a limited lifetime. A common reason for revision surgery is the wear of the bearing surfaces, generating wear debris to which the surrounding bone responds by resorbing away from the implant. The process is known as aseptic loosening. A smart implant could be used to monitor the progression of this process and inform the surgeon when the implant is starting to loosen. However, the patient's pain response to implant loosening is the key indicator that surgeons use in order to choose when to revise. Revising the joint replacement of a pain free patient is very difficult to justify, even though there is a rationale based on performing the revision before too much bone resorption has occurred. This case study demonstrates the need to ensure the parameters chosen for measurement are ones which will, in practice, drive a change in surgical decision making.

Unlike post-operative patient monitoring, the case for improved data provision during surgery is clearer because of the immediacy of the need to make treatment choices and perform accurate surgery. It is immediately apparent what to do with information describing the location of critical structures or of tumour tissue, so long as it is presented accurately and immediately during a surgical procedure. Potential upstream benefits relate to surgical precision, improved visualisation and surgical workflows. Downstream benefits could include improved patient safety, surgical efficacy and healthcare costs. Consequently in this paper we have focused on the opportunities for improvements in intraoperative data provision rather than post-operative monitoring.

Recent advances in intraoperative technology

Significant advances have been made in recent years in the development of products providing novel intraoperative information to surgeons and other healthcare professionals. These have been enabled by advances in underlying technology such as improved sensor technology, enhanced visualisation methods, increasing infrastructure to support wireless communications and the progressive miniaturisation of electronics. Surgical solutions include sensors that monitor a wide range of tissue properties including electrical, acoustic, mechanical, optical and thermal. Physiological parameters such as electrical impedance and oxygen concentration can be monitored in situ, and novel biomarkers are providing enhancements in measurement specificity. In this section we highlight a number of representative examples of applied technology in order to identify the direction in which the field is moving and to allow application hotspots to be identified.

Optics and fluorescence

Advances in intraoperative optical systems, particularly in the field of fluorescence imaging, have recently been applied in critical structure identification, tumour tissue detection and, in a broader sense, tissue characterisation.

Advances in the identification of critical structures have been achieved in part through the application of near infrared (NIR) imaging in both the detection of blood vessels and the visualisation of the ureter. The use of the NIR portion of the electromagnetic spectrum (700-900nm) has a number of advantages over the visible portion of the spectrum, including reduced background signal, due to the low level of NIR autofluorescence, and increased transmission through tissue. NIR radiation can penetrate to a depth of several millimetres, allowing subsurface structures to be imaged. Consequently, NIR imaging has been used for a number of years to assist in intravenous (IV) access, as used, for example, by the VeinViewer product marketed by Christie Medical and the system marketed by AccuVein.

Just as NIR imaging can be used to detect veins through the skin, similar technology

is being used during surgery to detect subsurface blood vessels. The SafeSnips product, under development by BriteSeed, is founded on the concept of embedding NIR emission and detection within a smart, energy based cutting tool. The goal is to detect blood vessels in close proximity to the tissue being dissected and alert the surgeon via the video monitor being used to visualise the surgical site. The InfraVision system, marketed by Stryker, uses an infrared (IR) emitting probe and an IR detection system to identify critical structures. One application involves the insertion of a fibre to transilluminate the ureter in laparoscopic procedures in order to reduce the risk of ureter damage. A further application, in laparoscopic oesophageal procedure, aims to eliminate the need for passing a bougie through the oesophagus.

Tumour detection during oncology surgery is being addressed by a number of different technological approaches. Molecular imaging technology, based on Cerenkov Luminescence Imaging (CLI), is being advanced by LightPoint Medical. This CLI approach uses radiopharmaceutical imaging agents from Positron Emission Tomography, which currently only find utility in preoperative imaging, to enhance intraoperative visualisation of tumour tissue. The use of optical detection methods to visualise the tumour promises lower cost and more portable systems than might be achieved by more conventional nuclear medicine approaches.

Intraoperative, fluorescence based, imaging and tissue characterisation systems are well established in neurosurgery. FDA approved systems are available from both Leica and Zeiss and both are designed to allow blood flow to be assessed in real time. Oncology surgery is now also being enhanced through the use of fluorescence imaging to improve the visualisation of tumour tissue. The Cysview (hexaminolevulinate hydrochloride) imaging agent, developed by Photocure, is being used alongside blue light cystoscopy equipment from Karl Storz to improve tumour resection in the treatment of bladder cancer; specifically nonmuscle invasive papillary bladder cancer (NMIBC).

A number of other fluorescent probes have been studied in conjunction with fluorescence image guided surgery (FIGS) and in the many studies the goal is cancer surgery. The most widely used NIR fluorophore is indocyanine green[5], which emits at 800nm. Indocyanine green (ICG) has a very long history of use in the clinical assessment of cardiac output and hepatic function, and in ophthalmic angiography, since being approved by FDA over fifty years ago in 1959. ICG is used as the contrast agent in Novadaq's SPY imaging platform designed for intraoperative imaging of blood vessel flow and tissue perfusion. A variety of other NIR fluorescence imaging systems are available for use in open surgery. Examples include HyperEye from Mizuho Ikakogyo and PDE from Hamamatsu. Reported applications include lympathic mapping in breast cancer surgery and blood vessel mapping in coronary artery bypass surgery – in both cases ICG was used as the contrast agent.

The development and regulatory approval of newer, more specific fluorophores will further improve the specificity of both tumour and critical structure identification during surgery. The assessment of nerve location during surgery is currently enabled by electromyography (EMG), in which electrodes are placed on the surgical instrument and on the patient's skin covering a selected muscle group. EMG systems include those designed for open surgery and, more recently, one designed specifically

The way in which fluorescence and other optical information is provided to surgeons in the operating room raises important human factors design questions that must be addressed in order to maximise adoption and minimise the risk of use related adverse events

for laparoscopic and robotic surgery from ProPep. By varying the current applied to the instrument electrode the relative distance of a nerve can be assessed and by varying the orientation angle of the instrument the approximate position of the nerve can be inferred. However, there is still a need to image nerve structures to allow for improved surgical navigation and encouraging progress is being made in the development of nerve specific fluorophores[6]. A number of approaches are being used including the use of biomarkers specific to the epineurium, the connective tissue forming the outer layer of peripheral nerves. One such biomarker has been conjugated to the fluorescent dye Cy5, which emits at 670nm[7], and so would allow it to be used in the future in conjunction with FIGS.

Methylene blue, which emits at 700nm, is widely used as a contrast agent in surgery and has more recently been used in NIR fluorescence clinical studies[8]. Autofluorescence is also being exploited, for example to enhance the visualisation of tumours. Novadaq's onco-LIFE autofluorescence detection technology is FDA approved for bronchoscopy and improvements in lung cancer detection have been demonstrated in a clinical trial comparing detection with white light alone. Visualisation systems offering both white light and fluorescence images allow the user to switch between views and, in some systems, overlay the images.

These recent advances have allowed tissues to be better visualised and identified. We expect there to be an increase in systems allowing improved tissue characterisation, starting with blood flow assessment and tissue perfusion. Such measurements are available in neurology and we expect other surgical specialty specific systems to emerge. Aimago, for example, is developing a portable microcirculation camera that uses laser Doppler imaging to measure tissue perfusion. The clinical applications being targeted initially are burns and flaps.

An additional optical method is being developed for tumour detection by researchers at the Mayo Clinic. The method uses blood oxygen measurements in the tissues surrounding a tumour and relies on the so called 'cancer field effect'. In a recent clinical study the method was applied to pancreatic cancer using a fibre optic probe passed through an endoscope to measure blood flow characteristics in the duodenum. Using the same spectroscopic method used in pulse oximetry, the researchers were able to demonstrate blood oxygenation levels were lower in the duodenum of patients with a pancreatic cancer[9].

The way in which fluorescence and other optical information is provided to surgeons in the operating room raises important human factors design questions that must be addressed in order to maximise adoption and minimise the risk of use related adverse events. Image overlay presents a promising method of communicating tissue sensing data during minimally invasive surgery. Novadaq's Pinpoint imaging system for endoscopic surgery, for example, allows fluorescence images to be combined with white light images in an overlay mode. Such optical imaging systems benefit from the ability to use the optical design to register the different images, avoiding the need for additional registration and associated image processing. An alternative method of displaying fluorescence images is being trialled by researchers at the Washington School of Medicine and involves the use of goggles which both sense the fluorescence and allow the user to view an overlayed image. Clinical trials are being conducted to assess the use of the goggles in visualising tumour tissue.

Nuclear medicine

Tumour biopsy surgery is facilitated by a number of techniques utilising local tissue sensing. The tracing of lymph nodes in cancer treatment is used in order to locate the sentinel node, which is considered to be the primary lymph node draining a cancer, so that a biopsy can be taken. The biopsy is analysed outside of the OR to assess the extent to which metastasising cancer cells have spread from the tumour. Preoperative imaging is typically performed using lymphoscintigraphy, which involves injecting a radionuclide near the tumour. It is combined with the intraoperative use of dyes, such as methylene blue, and radiation detection probes to trace the lymph structures back to the sentinel node. Such probes are now being deployed intraoperatively in the detection of tumour tissue using cancer specific radiopharmaceuticals such as fluorodeoxyglucose (FDG) and detection systems are available from companies including IntraMedical Imaging. Oncovision has developed an intraoperative imaging system, the Sentinella 102, which can be used in sentinel node detection.

Nuclear medicine is also being used intraoperatively to locate and image parathyroid adenomas – the benign tumours that can cause hyperparathyroidism. However, the position of the parathyroid gland within the thyroid can vary between patients and multiple parathyroid glands can occur. Physicians administer a radiopharmaceutical, such as Technetium-Sestamibi, that is absorbed by the parathyroid gland at greater concentration than surrounding tissue. In current clinical practice parathyroid imaging is performed preoperatively and postoperatively, but systems such as the Sentinella 102 now offer intraoperative imaging.

Ultrasound

Ultrasound is an example of a preoperative imaging technique that has been migrating into the operating room.

Ultrasound is available in the operating room for a wide range of surgical procedures and specialised transducer probes are available for use in minimally invasive and robotic surgery. Intraoperative systems are available from a number of providers including GE, Toshiba, Hitachi-Aloka and BK Medical. The use of BK Medical's intraoperative ultrasound system has recently been demonstrated in conjunction with Intuitive Surgical's da Vinci robotic surgery system. For example the system has been used in a robotic partial nephrectomy procedure, with the ultrasound being used to image subsurface tumour tissue. The use of ultrasound currently requires specialised surgical training or the presence of a radiographer in the operating room in order to interpret the images. Future developments in systems that remove the need for expert image interpretation would allow further uptake of ultrasound in the OR. Ultrasonic methods using transit time flow measurement (TTFM) are being used in coronary artery bypass surgery to measure blood flow in order to detect vascular graft failure. For example, Medistim markets an intraoperative ultrasound system, VeriQ, offering combined Doppler and TTFM for graft patency assessment in the OR.

In cardiology, intravascular ultrasound (IVUS) is being used to characterise plaques with the goals of improved stent positioning, improved surgeon decision making and improved postoperative care. Volcano Corporation's FDA approved VH IVUS system uses spectral analysis of backscattered ultrasound to classify plaque into different tissue types. It has been reported that suboptimal placement of a stent, such that the stent edge lies on the necrotic core of the plaque, increases the risk of stent thrombosis. The use of intravascular ultrasound in this application is being used to optimise implant positioning.

MRI and CT

The introduction of specialised operating suites now allows intraoperative MRI[10] (iMRI) and intraoperative CT (iCT). IMRIS has developed operating room configurations in which the MR magnet or CT scanner is moved into the OR on overhead rails when imaging is required. However, these are high cost, specialised operating rooms which are used only in specialised surgical procedures and the high infrastructure investment will preclude their use in the majority of surgical procedures for the short-medium term.

Force sensing

Force sensing instruments are being used to provide direct, real time feedback in surgical procedures. Biosense Webster recently gained PMA approval for their ThermoCool SmartTouch force sensing ablation catheter. The device uses radio frequency energy to prevent atrial fibrillation and differs from conventional instruments by giving feedback on the contact between the ablation electrode and the heart wall. Previously, indirect measures, such as electrogram parameters and impedance, have been studied but have been shown to be poor predictors of contact force[11]. The efficacy of the ThermoCool device has been backed up by clinical trial data which demonstrates improved outcomes versus treatment with traditional catheters.

Smart implants have been used clinically for a number of years in orthopaedics in order to inform device research and development. The development of implants with strain gauges, on board electronics and RF communication functionality has allowed in vivo loads to be monitored in patients. OrthoSensor has developed the Verasense product which is used as a trial during knee replacement surgery. The product has been developed to allow surgeons to optimise implant positioning and ligament balancing through intraoperative measurement of implant loads. Smart orthopaedic implants are also being developed to monitor post-operative tissue healing. For example Intellirod is developing an instrumented pedicle screw system for monitoring the spine surgery outcomes. In spine fusion surgery bone graft is implanted between vertebral bodies in order to generate bony fusion. The Intellirod concept involves monitoring load sharing between the pedicle screw and the fusion site, as a function of time, in order to track the progression of bony fusion.

Haptic feedback is a key goal of robotic surgery developers and we see great potential for the wider introduction of haptics into instrumentation systems used minimally invasive surgery.

Application themes

Advances in surgery are continually being made in order to improve outcomes, increase safety and reduce costs to the healthcare system. The significance of the latter goal has grown in importance in recent years due to the need to control healthcare spending in the developed world and the need to increase the provision of healthcare in the developing world. Having analysed the trends in recent advances in intraoperative smart surgery products, we offer a perspective on the application themes and related healthcare goals that can be addressed using smart surgery.

Minimally invasive surgery

Minimally invasive surgery has grown in popularity in recent decades but limitations in tactile feel and visualisation have prevented further adoption in certain applications. Laparoscopic hernia repair provides an example, since the proportion of inguinal hernia procedures performed laparoscopically is relatively low[12], despite there having been much greater optimism for adoption whilst it was being pioneered. The barriers to adoption include increased procedural cost, the longer surgical learning curve and the greater perceived risk of severe complications compared to open surgery[13]. Many open procedures are also being performed with smaller incisions, creating similar access and visualisation problems to those encountered in minimally invasive surgery. Similar issues also impact the wider usage of robotic surgery.

We recently conducted a survey of surgeons from a range of different surgical disciplines and we conducted a related survey with members of the medtech community. When we asked surgeons to rate the importance of new features in medical devices, enhanced visualisation scored highest. When we asked surgeons to then rate different advances in visualisation systems, real time diagnostics scored highly and above both High Definition (HD) imaging and 3D imaging

Critical structure detection

A common problem across different surgical procedures, including minimally invasive procedures, is the difficulty in identifying critical structures such as blood vessels, nerves and lymph structures. In each case, the surgeon’s knowledge of patient anatomy becomes critical and for new procedures is only fully developed after moving up the learning curve during successive surgeries. The location of critical structures varies between patients so increasing the risk of unintended damage. Nerves pose a particular problem because of the difficulty in knowing during surgery whether damage is being caused and because of the limitations in effecting a repair; damaged blood vessels can at least be repaired. There is a strong need for improved nerve detection in many surgical procedures, including spine fusion surgery and prostatectomy, in which the cavernous nerve can be damaged.

There are multiple examples of where instrument positioning and manipulation could be improved through the provision of real time tissue sensing data and we see this theme as a key area for future smart surgery innovation

Tumour tissue visualisation

Surgical tumour excision is a mainstay of cancer treatment and significant advances have been made in recent decades. Successful outcomes, measured in terms of reoccurrence and the need for second surgeries, are dependent on complete removal of tumour tissue, whilst a secondary goal is to spare as much normal tissue around the tumour margins. Difficulties in distinguishing between cancerous and normal tissue poses a challenge at the tumour margins, resulting either in unnecessary removal of the surrounding healthy tissue or incomplete removal of the tumour. In many open cancer surgeries the surgeon must rely on visual identification and palpation, and in minimally invasive cancer surgery the surgeon relies on white light reflectance images. There is a strong need therefore for enhanced visualisation methodologies that allow identification of tumour tissue in both open and minimally invasive surgery. This strength of need is supported by the variety of approaches identified during our technology review.

Instrument positioning and manipulation

Optimised instrument positioning and manipulation requires great surgical skill and judgement. In many cases it is limited by the access and visualisation available to the physician, particularly in minimally invasive surgery. A variety of technical approaches are being taken to address this theme in surgery, including computer assisted surgery (CAS) and surgical navigation to track implant position relative to preoperative imaging data and fiducial markers. Alternative smart surgery approaches are also being applied, and involve the provision of real time data on device performance and surrounding tissue properties. The difficulty in positioning and operating endovascular ablation devices provides an example. The application of RF energy to effect a change in surrounding tissue properties depends on the contact achieved between the probe and the tissue. In many uses of RF devices the contact with the target tissue can be well controlled and impedance measurements are used to incorporate feedback into the system. In endovascular applications the contact between the device and vessel wall can be less well controlled. Operation of the device can therefore be improved by providing real time force data on tissue contact. There are multiple other examples of where instrument positioning, operation and manipulation could be improved through the provision of real time tissue sensing data and we see this theme as a key area for future smart surgery innovation.

Tissue characterisation

Real time tissue characterisation is a theme which cuts across a number of surgical specialities. Intraoperative blood flow and perfusion assessment has found application in plastics, neurovascular, cardiovascular and vascular surgery. Vascular characterisation has been pursued because the characteristics of blood make it readily measurable: it contains cells which reflect light and sound in Doppler measurements and ICG is a well tolerated and long established marker that enables fluorescence measurements. As further enabling technologies are applied in surgery we expect further advances in tissue characterisation to become available.

Common themes

A need that spans all of these themes is timely, accurate and actionable presentation of information. The goal is to improve surgical decision making, resulting in tangible benefits to the healthcare system. Ease of use and human factors engineering are therefore key considerations in developing products that will deliver these benefits. Data display and image processing will also be key.

Future trends

Potential benefits to smart surgery:

- Better & more informed surgical decisions
- Increased surgical safety
- Improved outcomes
- Optimised surgical workflows
- Reduced re-operation
- Device performance & usage monitoring

We see smart surgery as a trend that will continue to develop and find greater application across different surgical disciplines. A key driver will be the desire of medical technology companies to find new ways of competing in the current healthcare environment and the trend will be enabled by the progressive development of enabling technology. Across the continuum of care we see the greatest opportunity in OR based solutions.

We believe the following trends could be significant in the future of smart surgery:

- The indications for smart surgery systems will widen – for example fluorescence enabled imaging systems will become more prevalent in ORs, surgeons will find new uses for these systems and companies will seek regulatory approval for new indications
- The communication of real time data to OR decision makers will become more sophisticated, will take more account of human factors and will result in improved surgical workflows
- The first wave of products will typically require additional surgical footprint for data processing, control and display modules. A second wave of products will involve increased incorporation into existing devices and reduced surgical footprint
- Local sensing solutions for optimising implant and instrument positioning will emerge as lower cost alternatives to surgical navigation systems
- The operation of energy based devices will be optimised by local tissue sensing and real time feedback
- The adoption of MIS and robotic surgery will be increased by the availability of smart surgery solutions

References

1. Peregrin, T. Surgeons see future applications for Google Glass, Bulletin Of the American College of Surgeons (2014)
2. Graichen F., Arnold R., Rohlmann, A., Bergmann, G., Implantable 9-channel telemetry system for in vivo load measurements with orthopedic implants, IEEE Transactions on Biomedical Engineering, 54, 253-261 (2007)
3. Taylor, S. and Walker, P., Forces and moments telemetered from two distal femoral replacements during various activities, Journal of Biomechanics, 34, Issue 7, 839–848 (2001)
4. D'Lima, D.D. et al, Tibial forces measured in vivo after total knee arthroplasty , Journal of Arthoplasty, 21, 255-262 (2006)
5. Alander, J, T., Kaartinen, I., Laakso, A. Patila, T., Spillman, T., Tuchin., V. V., Venermo, M. and Valisuo, P. A review of indocyanine green fluorescent imaging in surgery, Int. J. Biomed. Imag. ID 940585
6. Gibbs, S. L., Near infrared fluorescence for image-guided surgery., Quant. Imaging Med. Surg., 2, 177-187 (2012)
7. Whitney, M. A., Crisp, J.L., Nguyen, L.T., et al. Fluorescent peptides highlight peripheral nerves during surgery in mice, Nature Biotechnology, 29, 352-356 (2011)
8. Vahrmeijer, A. L., Hutteman, M., van der Vorst, J.R., van de Velde, J. H. and Frangioni, J. V. Image-guided cancer surgery using near-infrared fluorescence, Nat. Rev. Clin. Oncol., 10, 507-518 (2013)
9. Patel, M., Gomes, A., Ruderman, S., Hardee, D., Crespo, S., Raimondo, M., Woodward, T., Backman, V., Roy, H. and Wallace, M, Polarization gating spectroscopy of normal-appearing duodenal mucosa to detect pancreatic cancer, Gastrointestinal Endoscopy, In press.
10. Bradley, W.G., Achieving gross total resection of brain tumors: Intraoperative MR imaging can make a big difference, ANJR Editorial, 23, 348-349 (2002)
11. Nakagawa, H., Kautzner, J., Natale, A. et al., Locations of high contact force during left atrial mapping in atrial fibrillation patients: electrogram amplitude and impedance are poor predictors of electrode-tissue contact force for ablation of atrial fibrillation, Circ. Arrhythm Electrophysiol, 6, 746-753 (2013)
12. Darzi, A. and Mackay, S., Recent advances in minimal access surgery, British Medical Journal, 324, 31-34 (2002)
13. Trevisonno, M., Current surgical approaches to the treatment on inguinal hernias and factors associated with the use of Laparoscopy., M.Sc. McGill University, Canada, (2013)

About Sagentia Innovation

Sagentia Innovation provides independent advisory and leading-edge product development services focused on science and technology initiatives. Working across the medical, industrial, chemicals and energy, food and beverage, and consumer sectors, Sagentia Innovation works with a broad range of companies from some of the world's leading and best-known brands, to start-up disruptors, new to the market. It is part of Science Group (AIM:SAG), which has more than ten offices globally, two UK-based dedicated R&D innovation centres and more than 400 employees. Other Science Group companies include Leatherhead Food Research, TSG Consulting and Frontier Smart Technologies.

sagentiainnovation.com

For further information visit us at:
sagentiainnovation.com or
email info@sagentiainnovation.com

Sagentia Ltd
Harston Mill
Harston
Cambridge
CB22 7GG
UK

Sagentia Ltd
First Floor
17 Waterloo Place
London
SW1Y 4AR
UK

Sagentia Inc
1150 18th Street
Suite 475
Washington
D.C. 20036
USA

sagentia innovation