Surgery-led research: A priority theme for the EU Research Framework Programme

By Professor Nicola di Lorenzo, Director, Program "New technologies for Surgery ", Dept. of Surgical Sciences, Università di Roma Tor Vergata
Chairman, Technology Committee of EAES- European Association for Endoscopic Surgery

This report presents an overview of the general contribution and multidisciplinary implications of surgery calling for the inclusion of surgical research, development and innovation as a priority in European research programmes. It describes concrete topic proposals for each of the three main Health research areas in the Framework Programme and evidence of the economic and social impact of Surgery in the EU.

1. SURGERY CONTRIBUTION TO EU HEALTH

With the advent of industrialisation and new discoveries in science, disorders afflicting society have shifted from diseases of pestilence and infection to non-transmittable diseases that are today identified as common to all industrialised economies: ischemic heart disease, cerebrovascular disease, cancers and mental illness. Injuries also account for a large and growing amount of the disease burden, especially due to changes in transportation and technical innovation globally.

According to the World Health Organization, about 234 million major surgical operations are conducted each year. This includes over 63 million people who undergo surgery to treat traumatic injuries, 31 million for treating cancers, and another 10 million for pregnancy related complications. Sooner or later, many of us will have to go under the knife expecting to be treated with the latest technology and the most effective procedures.

Effectiveness and safety, therefore, must be upheld to a high degree of excellence. Studies conducted by the WHO conclude that complications following surgery result in disability or prolonged stay in 3-25% of hospitalized patients. That means that at least 7 million patients annually have post-operative complications, a figure which clearly indicates the need to investigate and develop better surgical procedures, instruments and training programmes.

In a time when drug pipelines are drying up and gene therapy has yet to deliver the anticipated breakthroughs, surgical procedures and innovative medical technology can offer a greater potential to solve many healthcare complications. It can also, in some cases, provide a viable alternative to lengthy drug-based treatments and costly mobility aid systems which can easily last a patient’s lifetime.
Given the current economic challenges and questions surrounding the sustainability of public finances, innovations in surgical procedures can improve healthcare delivery efficiency and cost-effectiveness from a 'providers' perspective. These are just a few examples to illustrate how surgical developments can help reducing public expenditure not only during the procedure but also after the patient is out of the hospital:

1. Off-pump CABG (Coronary Artery By-Pass Grafting): It can be performed without the patient having to go on a heart/lung machine which means a reduction in the resources required by the hospital in addition to benefits to the patient.

2. Percutaneous Aortic Heart Valve procedures: This technology is minimally invasive which means the patient's chest does not need to be opened. Consequently there is no need for heart/lung machines and the recovery time of the patients is much quicker which should equate to shorter hospital stays.

3. Laparoscopic surgery, and its most recent innovation – single site surgery – allows patients suffering of biliary stones (one of the most frequent surgical diseases) to be operated on a day surgery base, while the same cholecistectomy, performed some years ago, led to a week in-hospital stay.

Surgery should, therefore, be included as a key dimension to improving the quality of life of European citizens and improve the service that health systems provide in terms of costs, efficacy and efficiency. More specifically, surgery needs to be included as a priority in the Health work-programme of the next strategic framework for research funding.

2. MULTIDISCIPLINARY IMPLICATIONS

Surgery is by nature an interdisciplinary area of research constantly drawing on technologies, tools, and materials, which in many cases may have not been initially intended to be used in surgical procedures. At the same time, the work of surgeons has also served to make progress in other important areas. The cross-over with other disciplines within and outside the life sciences continues to be considerable and will become even more important in the future.

Therefore, surgery-led R&D is intrinsically best positioned to address the challenges in coordinating multi-agent and multi-disciplinary investigations. It will continue to be the bridge that connects the science behind many new applications and discoveries. The following are some examples of how the investigative nature of surgery has led to numerous advancements in medicine.

1. Neurosurgery: Intra and post-operative observation of neurosurgical procedures has facilitated the study and mapping of functions in different areas of the brain and the nervous system.

2. Intestinal surgery: Surgical resection of gastrointestinal segments has led to the discovery and understanding of certain hormonal patterns that determine patient’s recuperation rates after, for example, obesity, diabetes or pancreatic interventions.
3. **Transplantation surgery**: The development of organ transplantation has made it possible to study how the human immune system reacts in terms of rejection or acceptance.

4. **Heart and lung surgery**: Aggressive surgery in lung resection and cardiac repair of congenital and acquired diseases has led to the study of cardiopulmonary physiology and the functioning of the circulatory system.

5. **Prosthetics**: Biocompatibility of a great number of prosthetic materials has been definitively assessed by clinical use in cardiovascular, orthopaedic, otologic and general surgery.

6. **Deafness surgery**: Cochlear and brainstem implantation surgery has allowed a better understanding of VIII nerve and central auditory pathways pathophysiology;

7. **Laryngeal conservative surgery**: the increasing spread of conservative, subtotal and laser surgery has provided new insights into swallowing pathophysiology. This has resulted in a dramatic development in swallowing rehabilitation procedures, also in head-injured and ischemic patients.

### 3. Surgery in EU Research Programmes

An examination of the projects supported under the Seventh Framework Programme (FP7) shows that there is a need to place surgery at the forefront in the future. Currently, there are only 25 projects being funded that are related or have something to do with surgery. However, only four of these projects are within the work programme for FP7 Cooperation Theme Health. The majority of investigations are currently being done within the ICT Theme and most of them are exclusively focused on new imaging systems and virtual simulation. Surgery-led research seems to have lost its role as the driving force behind those breakthrough applications.

Frequently, surgery is just kept as a potential end use for certain technologies rather than the trigger for those investigations. For example, the ICT area includes activities such as nanoelectronics and robotic systems, but surgical applications are not stated as a research objective. Similarly, the nano-sciences and materials theme (NMP) offers space for topics with potential for surgery but actual calls for proposals targeting such applications remain marginal.

In currently funded projects, surgery has become the end rather than the point of departure. It is therefore necessary to stimulate R&D that is led by surgery from the beginning. Interdisciplinarity can be highly beneficial, especially in such a wide field, but policy makers and research managers must understand the requirements of surgeons and patients, who, at the end of the day, are the ones entering the operating theatre. The risk of not doing so raises the prospects of developing applications which the professional community may not embrace.

### 4. Advancing Research in Surgery: Proposed R&D Topics
The following are examples of some topic ideas to be considered for inclusion into the next Common Strategic Framework.


Innovative therapeutic approaches and intervention

Natural Orifice Surgery (NOTES/NOS) is one of the most promising areas of research within the emphasis of this thematic priority on non-invasive or minimally invasive approaches. Using this technique, operations can be performed passing an endoscope through mouth, anus, or urethra, for example, and then opening a small incision in the stomach, vagina or colon to perform the operation. Research has generally been conducted on animals, mainly pigs, but there have been some successful trials on humans to conduct gallbladder, kidneys and appendix removals through either the mouth or the vagina.

This revolutionary technique does offer many advantages: lower anaesthesia dosage, faster recovery time, shorter hospital stay and therefore a lower cost, less pain for the patient and also better aesthetic results due to the lack of visible scars. Applications could include battlefield surgery to wounded soldiers and operations in areas where establishing a sterilized setting would be difficult. There are two main topics for research regarding the Natural Orifice Surgery:

- Sterilisation and secure closure mechanisms that would lead to a low risk of infection and will guarantee a fast and painless recovery.
- Development of specific medical devices adapted to each particular natural orifice and the type of procedures that can be performed.

The two major European Societies active in the field, EAES (European Association for Surgical Endoscopy) and ESGE (European Society of Gastrointestinal Endoscopy) have settled the EURONOTES Foundation, which is currently coordinating most of the European researches in the field. Small grants, for a total amount of €500,000, have been provided thanks to companies support.

Other entities, such as the New European Surgical Academy (NESA), have i.e. proposed designed a rigid two-joint Transdouglas Endoscopic Device (TED), which could enable single-entry abdominal surgery in women with high safety resulting from the low pressure needed. This instrument has already been engineered and anatomical studies were done at the Erasmus University of Rotterdam for a prototype with an estimated cost of €150,000.

In the United States, they have quickly embraced the enormous economic potential in this area derived from the high demand for new technologies that will arise in the coming years. The corresponding entity of EURONOTES, named NOSCAR Consortium, was established by SAGES (Society of American Gastrointestinal Surgeons) and ASGE (American Society of Gastrointestinal Endoscopy) in 2007 and received $2 million in grants from medical device manufactures to conduct research.

While the first reported human case of NOTES procedure was performed in Europe (April 21, 2007 – ANUBIS Operation, Strasbourg) there is now a high risk that Europe falls behind in developing the knowledge needed for leadership in this field.
4.2. Translating research for human health

Translational research in other major diseases: cancer, cardiovascular diseases, diabetes and obesity, rare disease, other chronic diseases.

Health risks such as cardiovascular diseases, obesity and diabetes are rising. Approximately half of the EU’s population was overweight or obese in 2003 and approximately 60 million people in Europe live with diabetes. This situation will be further aggravated due to decreasing level of nutritional habits in younger generations and sedentary lifestyle. Consequently, not only will the expenditure on healthcare systems sharply increase, but the workforce in the EU will also be impacted. Even though there have been innovations in other forms of therapy, surgery remains an indispensable remedy for most non transmittable diseases such as cancer and cardiovascular diseases. Recent research has also shown that surgery might be an effective cure against metabolic syndrome, diabetes and possibly Alzheimer’s.

For some cardiovascular conditions and obesity surgical procedures have already been proven to be effective. Currently, the level of safety has reached an acceptable threshold so, although there is research that could be done in those areas, the focus must switch now to other threatening diseases such as diabetes, Alzheimer’s and cancer. For this last hot issue, although basic research is improving its understanding of the mechanisms of cell’s degeneration to cancer, this will lead to effective prevention policies and therapies in the middle-long term. Surgery, for now and for the future, is the only treatment for many neoplasms, and will continue to play this role for advanced cases.

Moreover, surgery has been dominated by a market-based approach that does not guarantee the development of the necessary basic research to treat specific health conditions which may not be so profitable. That is certainly the case for many rare diseases which are usually left aside due to a lack of profitability. There is an urgent need to have more public funding devoted to research in this field. If surgery can be a solution, it should be carefully investigated and tested within the scope of EU’s research programmes.

5. Optimising the delivery of healthcare to European citizens

Translating the results of clinical research outcome into clinical practice including better use of medicines, and appropriate use of behavioural and organisational interventions and new health therapies and technologies

Patient safety and surgical safety should be the cornerstone theme for all parts of the programme. However, there is a lack of data on the effectiveness of new procedures and technologies, which makes it difficult to evaluate and present recommendations about the appropriateness of those therapies. Research about the necessary capacities to adopt innovative alternatives along with the implementation of surgical audit programmes would be highly desirable.

Comparisons of operations among different countries, for examples, are difficult not just because of the data, but also because of the introduction of new surgical methods not always performed according to standardised protocols. More, some operative methodologies are
based on routines that have never been subject to evidence-based studies. “Local traditions are among the major obstacles for progress in surgery”, which is also affected by strong hierarchical structures and the obvious fear of failure that hinders the development and implementation of new ways to operate.

For that reason, it is crucial to introduce and register surgical interventions in a systematic and standardized way. Technology can play a key role in recording the nature of operations to enable practitioners all around the world to learn, correct and improve their results. Collecting and measuring this type of information to develop procedural standards will help to reduce errors, design better curricula and portfolios for surgeons in training and reduce the learning time.

**5.1. Clinical Trials**

The same principle should be applied to clinical trials, which play a very important role ensuring that new surgical procedures and devices can be safely used on humans. Currently in Europe, most clinical trials in surgery are carried out privately and financed by the very same companies that have developed the product or technique. This results into a lack of credibility and the migration of some of those trials to independent auditing bodies, mostly based in the US. If the EU aims at remaining competitive in the field of surgical innovations, new mechanisms to conduct surgical clinical trials must be put into place.

**5.2. Training and Education**

Every new technology or procedure in surgery will often have a steep learning curve for the practitioner to be qualified to perform adequately. It is therefore imperative to effectively deal with the learning process prior to clinical testing. Otherwise, the impact of the learning curve on the performance evaluation can be significantly negative.

Technology requires constant training and up-skilling so the development of new surgical training systems and methodology is a key facet of effectiveness. Virtual reality simulators (similar to those used for aerospace industry) have been developed in order to assure surgeons have the required skill before commencing the clinical research project and to avoid practicing on patients, which is an ethical concern. Though, their introduction in the European curriculum for surgeons in training must be considered a major goal for regulatory entities in Europe.

At the same time, periodic assessment of skill for surgeons in clinical practice (to be evaluated through the same simulation systems) is the necessary step to guarantee the highest standard of care in all European countries.

**6. COORDINATED SUPPORT ACTIONS FOR SURGERY**

One of the main obstacles for surgery to achieve adequate recognition has been the low level of participation from surgical associations in the definition of research priorities in Europe. Surgery is a very fragmented field divided in many disciplines and it is getting even more dismembered because technological advances that make certain interventions easier, has opened the doors to other medical practitioners and technicians that, in the past, were not able nor certified to perform surgery.
There is an urgent need for surgery to act with just one voice so research needs can be clearly defined and EU global support mechanisms for surgery can be implemented. It is very important to establish connections among all those professionals that work at the operating theatre. Especially among those institutions that have achieved a high level of professionalism and performance. They will, in the first instance, set an example for other organisations, but more importantly, they could define standards and safety procedures to be incorporated across Europe.

Coordination and support actions and the establishment of a network of excellence for surgery will help to bring together and coordinate this array of practitioners to promote and facilitate the share of knowledge and ideas not only about research projects but also about public health policies. This will eventually contribute to promoting the physical mobility of surgeons and also the free flow of knowledge-the fifth freedom.

7. INNOVATION IN MEDICAL TECHNOLOGIES FOR SURGERY

Surgery is one of the most important applications for medical technology and therefore a key element of competitiveness for the European Economy. European medical technology industry already invests some €5.8 billion in R&D and employs near to 529,000 highly skilled workers. This figure has grown by 15% since 2003. Sales in 2005 were of approximately €63.6 billion with an annual growth rate of the industry between 5% and 6%. The potential is great and the EU must give incentives to this steady path of growth that the medical technology companies have been following for the past few years.

Regarding the size of the sector, there were about 11,000 medical technology companies in Europe in 2005. More than 80% of them are Small and Medium Enterprises (SMEs). FP7 already recognises their importance and actively seeks to engage them in project participation. SMEs working in the field of surgical applications and devices could benefit enormously from those changes if surgery is given the appropriate recognition in future research programmes.

Open Surgery, for example, is worth more than €5.5 billion for instrument sales, while Laparoscopic Surgery today represents a global market valued at about €2.5 billion. Other areas such as Diagnostic Endoluminal Surgery are expected to explode in the next several years due to the increasing number of cancer cases in industrialized countries that must be adequately screening to be treated on time. Other areas with great market potential are Electro medical implants and Orthopaedics.

A market based approached should always be balanced with the public financial support for pure surgical R&D. Manufactures and health related private companies only carry out specific research programs to come up with new techniques and technologies that can be profitable. However, that does not guarantee the development of the necessary basic research to advance in fields that have not such a high sales potential. This is precisely one more reason why there is an urgent need to incorporate surgical R&D into the EU’s health policy agenda and related research programmes.