# Engineering, science and medicine: transforming healthcare

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# ENGINEERING, SCIENCE AND MEDICINE: transforming healthcare

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## Introduction

The treatment of disease is being revolutionised by the increasing use and capabilities of intelligent medical devices. Currently, there is a translational drive from basic research into clinical realisation, with multidisciplinary teams responsible for this synergistic effort. This work is forming the era of biomedical engineering, which is manifested in many aspects of medicine at both the bench and the bedside. Here, we focus on two different categories: imaging and medical robotics; and, tissue engineering. We introduce the underlying tenets on which these fields are built before discussing current research and the possibilities for tomorrow's practice.

## Imaging and medical robotics

Improvements in medical imaging, miniaturised components, implantable sensors, and new materials, coupled with a deeper understanding of human physiology, can offer those with disease and disability the prospect of an improved quality of life. The merging of imaging with robotic systems is allowing doctors to perform more efficient and accurate interventions, while intelligent assistive devices are replacing or repairing weak or impaired limbs, allowing those with disabilities to perform a wider range of tasks.

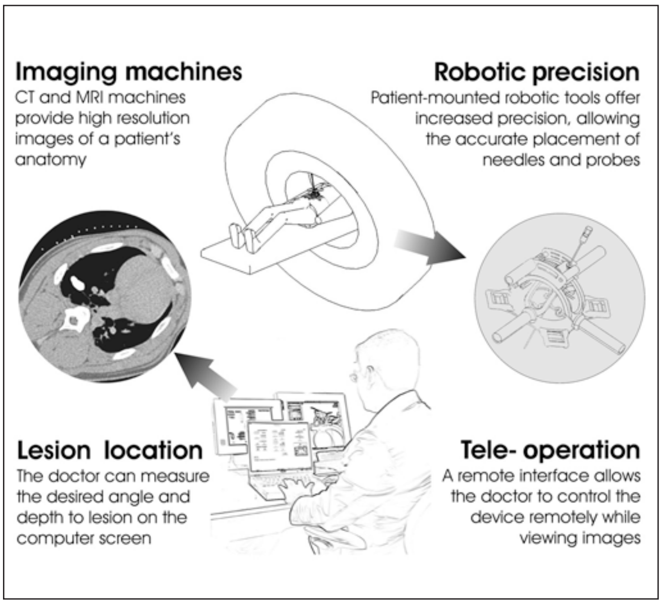
## Imaging

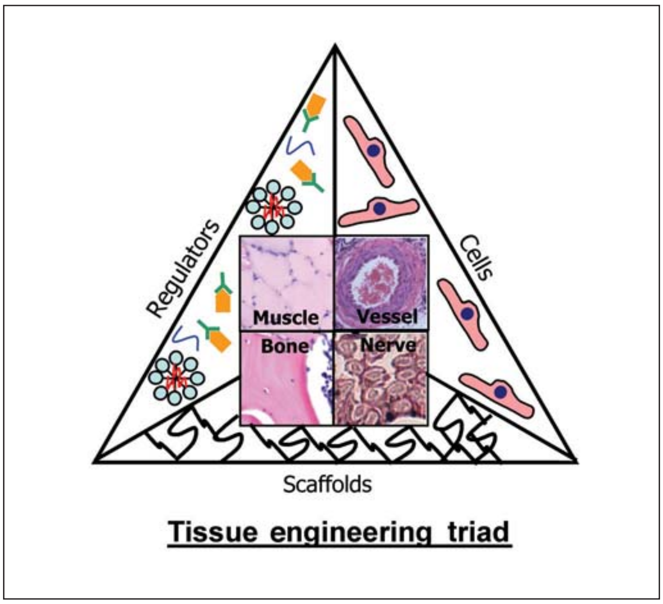
Due to advances in imaging, there has been a shift from invasive or open surgical procedures to minimally invasive approaches, resulting in reduced trauma and recovery time for patients. Miniature cameras and light sources placed inside the body – via small incisions and natural orifices – are enabling endoscopic and laparoscopic surgery, where doctors manipulate surgical tools while viewing their motion. Imaging techniques such as ultrasound and optical coherence tomography allow doctors to visualise the extent of pathology below the skin surface, offering the potential of a real time 'optical biopsy' of tissue and organs *in situ*.[1,2] Finally, whole body imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) are becoming the workhorses of hospitals as their imaging capabilities continue to evolve.[3]

## Surgical and image-guided robotics

Laparoscopic surgery is becoming commonplace as imaging quality improves and surgical tools become more sophisticated. Although this approach offers great benefit for patients, it does impose a number of visual and dexterity-related constraints on the surgeon, limiting the approach to less complicated procedures. As a result, various robotic systems have been developed to alleviate these constraints. The first recorded use of medical robotics occurred in a 1985 brain biopsy, and medical robots have since been applied widely in the fields of neurosurgery, orthopaedics, urology, cardiology, and interventional procedures.[4,5]

The da Vinci Surgical System is well regarded as the first commercially successful medical robot.[6] It offers a surgeon improved precision and dexterity by relaying video from miniature cameras to a remote console, where the surgeon uses a telerobotic system. The system restores the degrees of freedom lost in regular laparoscopy by placing a robotic wrist on the end of the arm inside the patient. In combination with tremor filtering and motion scaling, the surgeon is able to perform steadier, more delicate motions. In conventional open surgery, the surgeon interacts with internal tissues through a relatively large open incision. Replicating this tactile sensation is the goal of current work; research involves measuring the instrumental force on tissue and relaying this signal back to the control console.




A more recent advance in the field of medical robotics has been the development of robotic arms that integrate with CT, CT fluoroscopy, or MRI machines.[7-10] By utilising precise positional information, more accurate and efficient interventional procedures can be performed. For example, biopsies, tumour ablations, brachytherapy seed placement, drainages, and nerve blocks are all percutaneous procedures that can be improved by the increased accuracy of a robotic system. A significant engineering challenge here includes the spatial, radiolucent, and magnetic constraints imposed by these machines; new robotic technology will be required to tackle these issues.

Many of the robotic systems developed to date are general purpose, large and immobile, representing a significant capital expense for hospitals. However, a subset of procedures such as thoracic biopsies, catheterisation, and cardiac interventions require a limited and specific set of motions by a doctor. Subsequently, there is an opportunity to take a user-centric approach and design inexpensive (and even disposable) medical robots that augment only specific portions of a procedure while allowing the doctor to retain control.[11-13] Finally, imaging systems such as fluoroscopy will further drive the development of intelligent, image-guided tools that offer improved performance and a reduced radiation dose to patients and doctors.

## Prosthetics – replacing and repairing limbs

In the past, when a person lost a limb or its function, the damage was accepted as irreparable. Today the boundary between body and machine is blurring as we replace, repair or restore normal limb function with prosthetic and exoskeletal systems. An enhanced understanding of normal limb function, together with new actuators, power supplies, sensors and lightweight materials, are generating products that more closely resemble the body's own skeletal design and efficiency.

Lower and upper extremity amputees will be able to wear robotic devices that offer much greater functionality and dexterity than the passive limbs of today. We have already seen microprocessor-controlled artificial knees and ankles that offer natural leg motion and intelligently adapt to changing speeds and terrains. Such devices can help amputees walk more naturally and with improved locomotory efficiency.[14,15] Surface electromyography (EMG) sensors measure a muscle's response to nervous stimulation and have been used since the 1980s to provide a more intimate and realistic interaction with prostheses.[16,17] The next generation will see implantable peripheral and central neural faces that integrate directly into the nervous system, leading to improved control.[18]

Those who have suffered a stroke or spinal cord injury often sustain impaired or lost limb function, rendering them immobile. Current treatment is either labour intensive or consists of primitive mobility aids such as plastic braces and crutches. An emerging alternative includes robotic exoskeletal systems with motorised links attached to a patient's limbs. These rehabilitation robots replace or assist muscle function and facilitate the training of new neural pathways.[19,20] Robotic exoskeletons have the potential to drastically improve treatment by offering precise and consistent therapies; for example, progress in limb movement can be quantified by measuring patient–robot interaction, allowing therapy to be optimised. Previously, these machines were large and confined to research laboratories, but we are now seeing compact devices that can be worn by patients at home.

## Tissue engineering/regenerative medicine

To our knowledge, the first technical report of tissue regeneration was made in 1980 by Yannas *et al*,[21] who constructed membranes consisting of bilayer artificial skin composed of a Silastic epidermis and a porous collagen-chondroitin 6-sulfate fibrillar dermis. This tissue was successfully used to close wounds in patients with burns covering 50-95% of their body surface area.[22] The term 'tissue engineering' was coined by Wolter *et al* in 1984 and, although technically distinct from 'regenerative medicine', the terms are now used interchangeably.[23]

It is useful here to consider the tissue engineering triad – the idea that three components lead to tissue development: scaffolds, cells, and growth factors.[24]

### Scaffolds

A scaffold is the delivery vehicle, physical structure, or scar-preventing agent of tissue engineering.[25] In many tissue engineering strategies, this temporary extracellular matrix consists of a natural or synthetic polymer scaffold. A scaffold can facilitate the migration of nearby cells into the defect site; alternately, autologous or allogenic cells can be cultured in the scaffold prior to implantation. Increasingly sophisticated scaffolds incorporate growth factors to stimulate differentiation, mitosis, migration or secretion.[26,27] Additionally, scaffolds can prevent scar formation and can guide development according to shape.[28,29] Scaffolds typically constitute the base product of tissue engineering devices and, in some cases, form the entirety of the device. Often, however, cells and growth factors are also required.[1]

### Cells

Repair strategies frequently include implantation of autologous or exogenous cells. For instance, cells may be required for very large wounds or when neighbouring cells lack migratory or mitotic ability. Isolated cell therapies, such as the repair of cartilage defects by autologous chondrocyte implants, have been successful.[30] The combined approach has been more widely reported; a variety of cell-seeded scaffolds including autologous, exogenous, differentiated, and undifferentiated cells of both embryonic and progenitor origin have been used in both *in vivo* and *in vitro* models.

In particular, stem cells have received significant attention. Stem cells are appealing in terms of cell-based therapies due to their properties of self-renewal and multilineage differentiation (they can generate many different types of cells); their ability to be harvested in large amounts via expansion in culture; their suitability for genetic engineering and gene delivery strategies; and, their good survival following grafting. Stem cells have already been used to generate bone, cartilage, blood, and neural and cardiac tissues, both *in vivo* and *in vitro*.[31]

Nonetheless, many challenges exist with stem cell technology; however, two recent developments offer the potential to overcome some of these constraints. The first is nuclear transplantation, whereby DNA from an ovum is replaced with DNA from a patient's somatic cell. Shock is then applied, and multiple cell divisions cumulate in blastocyst formation. Thus, pluripotent embryonic stem cells containing the patient's own DNA can be harvested (from the inner cell mass of the blastocyst), eliminating the host immune response following their transplantation. The second development is the 'reprogramming' of adult cells into embryonic stem cell-like states; in the past year, Yamanaka *et al* have identified four genes that, when activated, can accomplish this task.[32] If further developed, this technology can circumvent legal, ethical, and technical issues surrounding stem cell research and therapy.

In order to fully master cell technologies, we need to be able to instruct cells in the same way the body does. Cell communication is controlled by local chemical and mechanical environments; by controlling these environments, we can direct a cell to perform specific functions.

### Molecules

Control of cellular environments can be achieved through manipulation of the growth factors, enzymes, survival factors, and cytokines that influence cellular activity. Some of these molecules are naturally expressed as part of the remodelling process; in order to mimic this internal environment, engineered tissue products can be supplemented with growth factors. Alternatively, cells can be genetically modified to produce large amounts of trophic factors. In both scenarios, the additional molecular support enhances transplant survival. Some initial therapies have even employed isolated growth factor injections; for example, in the upregulation of bone formation and for repair of arthritic joints.[33,34] Cells also receive messages through integrins bound to the surrounding extracellular matrix. Recently, scaffolds have been designed to contain specific ligands that dictate cellular activity.[26] Finally, other therapies employ ultrasound or extracorporeal shock wave therapy to stimulate cell-mediated tissue remodelling, indicating that mechanical factors are also important in the local environment.

## Final thoughts

Here we have focused on the fields of imaging, medical robotics, and tissue engineering, but other key areas include targeted drug delivery, gene therapy, and pharmaceuticals. In the future, it is likely that technology will further integrate various fields into hybrid devices. Both robotic limbs and future robotic organs will be coated with polymeric drug delivery components, allowing temporal release of agents to prevent infection, and facilitate integration and implantation. The future will also see the integration of imaging modalities with operating rooms, enabling medical robots and surgeons from around the world to work in concert. Gene therapy will merge with tissue engineering strategies, leading to the advent of personalised medicine; by analysing the specific genetic make-up of each patient, tissue engineering strategies can be tailored to individual disease phenotypes. The next generation of therapies depends on research in each field and on the integration of various technologies. The science of today will be engineered into the medical devices of tomorrow.

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