The Royal Academy of Engineering

Regenerative medicine

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Biomedical engineering creates new medical technologies and systems that can greatly improve patient care and quality of life. The UK Focus for Biomedical Engineering is the Academy's forum for this increasingly important area of engineering in which the UK is taking a lead.

Introduction

The nation's ageing population and the increasing prevalence of chronic diseases that require management over prolonged periods, such as diabetes and chronic heart failure, contribute to an inevitable and large future healthcare demand. People throughout the world rightfully have increasing expectations for improved care to enable a healthy life into old age. While the challenge facing the UK is clear, a national strategic plan to address this will need to harness UK technological assets and require a transformation in the practice and delivery of healthcare – in which engineering will take a major role.

Regenerative medicine, which aims to restore the function of diseased/damaged tissues or organs through a variety of approaches, is one technology that could replace the long-term management of chronic diseases with cures for many major conditions. By addressing degenerative diseases associated with ageing, regenerative medicine can not only bring social benefits but also reduce the health demands of an ageing population. The field also offers the potential to establish a new industry based on new science in an area where the UK has centres of excellence that can serve a major future global market.

The technology

The science of regenerative medicine is advancing, driven by a rapid rate of discovery in cell and molecular biology, and related disciplines. Engineers with their tradition of bringing ideas to reality can uniquely contribute to the challenge of translating these scientific advances into useful clinical therapies and thereby align UK capability with the global economic opportunity regenerative medicine presents. However, to do this engineering must adapt its traditional practices and deepen its interfaces with biology and the clinic.

There is a growing body of clinical evidence demonstrating that cell therapy can improve cardiac function in cases of chronic heart failure which affects 800,000 people in the UK alone, using cells ranging from unmodified adult stem cells to specially engineered cells. However, there is still a need to understand what is the optimal cell type, what is the best way to deliver the cells and how the success of treatments can be assessed. Mechanisms of action need also to be discovered.

Cell therapies used to treat liver failure point to a distinction between the therapeutic potential of adult stem cells, which have the capacity to carry out repair work, and embryonic or other pluripotent stem cells that have the capacity to differentiate into any cell type in the body. While the ultimate promise of the latter is complete regeneration of tissues and organs, the former can be used for damage limitation. This could be very significant in treating liver failure, where function could be maintained through cell therapy until the organ repairs itself. People who have liver failure due to a drug overdose, for example, could be kept alive until their liver regenerates naturally. Otherwise, the consequences of liver failure are often fatal.

The academic research base of regenerative medicine is therefore becoming increasingly secure and there is mounting evidence of clinical efficacy from one-off treatments and small-scale clinical trials. However, for true clinical and commercial benefits to be delivered, regenerative medicine products must be manufactured at a scale to be available for routine clinical use and even off-the-shelf.

Key issues

Engineers have a key role to play in translating advances in cell biology and biomaterials into useful treatments. To do this, there is a need to engage more with biologists and clinicians to ensure engineering principles are applied. Beyond the basic research, the following are necessary:

- Ensure there is a market and define it explicitly
- Raise the finance – define the investment models
- Establish what price the market will pay and compare to cost of manufacture
- Understand the underlying science of the product in terms of critical attributes
- Acquire and equip production facilities
- Recruit and train staff
- Develop a stable process
- Make the product and develop quality control systems
- Liaise with the regulatory bodies
- Define and finance clinical trials.

The engineering role

The clinical proof of principle for regenerative medicine exists and is exemplified by the repairing of alkali burns to the cornea with limbal stem cell implants. There is a need for early collaboration between cell biology and engineering in the development

and commercialisation of these technologies.

While the advance of the biotechnology industry has fostered the development of robust methods for manufacturing protein drugs and other biologics, the move to regenerative medicine raises fresh challenges. Small molecules and more complex biopharmaceuticals can be reasonably well-defined for manufacturing. But stem cells, the likely basis for many regenerative medicine products, are much harder to characterise. Also, harvesting the cells is a part of the bioprocess that is very difficult to standardise.

Bioprocessors currently work delivering enough cells to treat five to 10 patients a year. Much higher volumes are needed for routine and economically viable therapies. The science is good, but early collaboration with engineers is essential to take the science into routine clinical practice. Research and the translation to viable therapies should be undertaken concurrently as the cells themselves can be the product and are the therapy.

Regenerative medicine as "therapies to enable or support a body's own repair" also encompasses scaffolds and their architectures, the molecular prompts that stimulate cells to grow and differentiate, and harnessing a patient's own cells for internal repairs. Engineering skills such as bioengineering design, biomechanics and simulation, manufacturing systems and bioprocessing, metrology and modelling, are relevant to the development of regenerative medicine products.

To satisfy the regulators and make regenerative medicine commercially viable, manufacturing has to be done to the same GMP (Good Manufacturing Practice Regulations) standards as medical devices and pharmaceuticals. Currently, regenerative medicine is a craft industry, relying on people who may be good at handling cells, but are not good at doing this in a repeatable manner. Processes for generating regenerative medicine products need to be automated to bring them under control and to help understand:

- What are the key process variables?
- What are the outputs of the manufacturing process?
- What machines are good for, and what people are good for?

Future work

To deliver regenerative medicine products it is necessary to apply multi-disciplinary science. The interaction between biology and engineering means the two disciplines must be intimately locked together. Clinicians should engage throughout the development process. Younger scientists have multiple sets of vocabulary and their multi-disciplinary contribution should be fostered. Incentives to foster and enable such multi-disciplinary partnerships to thrive are needed.

But creating a regenerative medicine industrial base able to treat many patients will require more than technology and setting up a business. It is necessary to incentivise investors and to understand their investment models.

To communicate the benefits of regenerative medicine engineers must assess how a proposed treatment might adapt to the pathway that describes the patient journey through the NHS. Engineering concepts could be applied to show how regenerative medicine can be integrated with other aspects of healthcare. In particular there are many opportunities for engineering to be applied to the value network aspects of delivering regenerative medicine. To build a bridge into the NHS for the adoption of regenerative medicine therapies, engineers will need to consider:

- Proof of clinical efficacy
- Providing evidence to demonstrate a step change over the current therapy
- Showing the benefit to the patient
- Showing the benefit to the NHS
- Assessing the impact on tariffs
- Setting out how the treatment can be integrated into current practice and any service redesign it will call for
- Considering if the implementation can be linked to NHS's key policies such as by demonstrating that it leads to improvements in patient safety
- Considering if the introduction of the treatment will require more, or fewer, skilled staff.

Conclusion

Venture capital investment currently is very limited because of the lack of commercial exits and without government support the industrial base will collapse. The situation calls for a national strategy to grow the industrial base and retain it in the UK.

A complex and challenging regulatory landscape is faced by UK companies and discourages inward investment. However, the specific focus that the Technology Strategy Board is putting on regenerative medicine should increase translational efforts. An engineering input is needed into the regulatory process, providing an engineering assessment of risk and benefit and the development of appropriate test methods to manage risk.

Cures based on regenerative medicine would be at a high cost per person, although there would be potential savings in community medicine. A challenge to be faced is the "silo budgeting" of health providers that presents a barrier to adoption. The solution is to take the Department of Health on a journey, persuading it that the clinical therapy works well by selecting clinical targets as the basis for showing how much money a cure, rather than a treatment, could save the NHS, and thus build the business case for getting it adopted and embedded as the standard of care.

For regenerative medicine to come into widespread clinical practice it is necessary to build a workforce, get people talking across disciplinary boundaries and invest in hospital facilities and infrastructure. Surgeons need to grow and learn alongside engineers, scientists, regulators, funders, the Department of Health and the NHS.

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