CANADIAN COUNCIL OF PROFESSIONAL ENGINEERS
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Tissue Engineering – A Professional Engineering Perspective

Prepared for:

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Abstract

The profession of engineering has undergone major changes in the last decades that have seen engineers move from more traditional single disciplines into multidisciplinary activities. One of the most rapidly advancing areas is bioengineering. The term bioengineering is a large umbrella encompassing all areas where engineers work with biological systems. Bioengineering has applications in many fields including biotechnology and biomedical engineering. A specific application of bioengineering is in the field of tissue engineering. This manuscript will define and explain tissue engineering, the role engineers have to play in this emerging industry, and what action the profession should take to ensure the field is adequately supplied with educated and qualified professionals. It is evident that tissue engineering will be carried out by teams of engineers, scientists, medical professionals and others, with a key role for engineers in specific applications that involve the practice of engineering.

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1.0 Introduction

Currently, tissue and organ failure accounts for half of the total annual expenditure of health care in the US (Persidis, 2000). The Canadian experience is unlikely to be significantly different. Although transplantation is commonly carried out as a solution to organ failure, many people who are on waiting lists will not receive transplants in time. Presently, there are no long-term solutions to this problem. Tissue engineering is emerging as a potential solution and/or alternative to current therapies, and this technology is receiving interest from many academic and industrial sources. The occupation of "tissue engineer" has been hailed as one of the hottest jobs of the 21st century (Rawe, 2000). Tissue engineering aims to assist the body in actually regenerating lost function, rather than masking symptoms as many therapies do today.

1.1 Bioengineering

Engineering can be broadly defined as applying scientific and mathematical principles to find solutions to practical problems. For example, APEGGA has defined engineering in this way (Appendix A). The United States National Institutes of Health (NIH) has published this working definition of bioengineering *(McIntyre et al., 2002)*:

> *What is Bioengineering? - Bioengineering integrates physical, chemical, mathematical, and computational sciences and engineering principles to study biology, medicine, behavior, and health. It advances fundamental concepts; creates knowledge from the molecular to the organ systems levels; and develops innovative biologics, materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health (NIH Working Definition of Bioengineering - July 24, 1997).*

In Figure 1, bioengineering is displayed as a new discipline of engineering. The figure is divided into disciplines, fields and applications. A traditional <u>discipline</u> is defined as an area of study that applies knowledge of physics, chemistry and mathematics to find solutions to specific problems. Traditional engineering disciplines include chemical, civil, electrical, geomatics, materials, and mechanical engineering. An exception to this is the field of environmental engineering, which also applies knowledge of biology. A new discipline of engineering – bioengineering – also applies knowledge of biology in addition to physics, chemistry and mathematics. Engineering disciplines are applied to fields. A <u>field</u> is defined as an area of specialization of one of the engineering disciplines. In this case, the two broad fields listed under bioengineering are biomedical engineering and biotechnology. Biomedical engineering is the specific application of engineering principles to solve medical problems. This

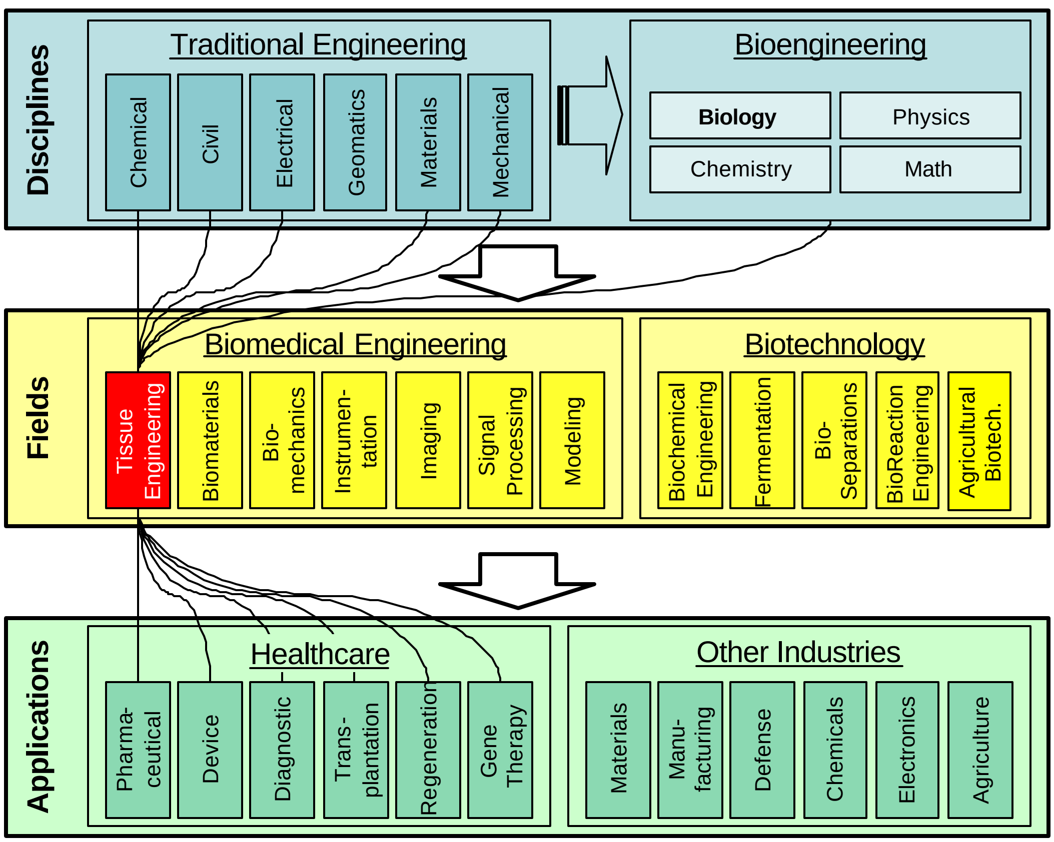

Figure 1 – The position of tissue engineering as a part of the field of biomedical engineering, building on many engineering disciplines (top row) and having applications in many industries (bottom row).

Adapted from Reference 13.

includes instrumentation, imaging, signal processing, modeling, biomechanics, biomaterials and tissue engineering. Biotechnology includes biochemical engineering, fermentation, bioseparations, and bioreaction engineering. Biotechnology (from an engineering perspective) is primarily the application of engineering principles to the production of biochemical molecules, or the use of biochemical catalysts in processes (i.e. yeast in beer production). An application is defined by Merriam-Webster as "a use to which something is put". In this case the specific knowledge from an engineering field is applied to certain industries. Applications of biomedical engineering (including tissue engineering) include healthcare and many other industries.

1.2 Biomedical Engineering

The Whitaker Foundation defines biomedical engineering in the following way (Whitaker Foundation website):

> *"Biomedical engineering is a discipline that advances knowledge in engineering, biology and medicine, and improves human health through cross-disciplinary activities that integrate the engineering sciences with the biomedical sciences and clinical practice. It includes:*
>
> > *1. The acquisition of new knowledge and understanding of living systems through the innovative and substantive application of experimental and analytical techniques based on the engineering sciences.*
> >
> > *2. The development of new devices, algorithms, processes and systems that advance biology and medicine and improve medical practice and health care delivery."*

The Whitaker Foundation is a foundation that has primarily supported interdisciplinary medical research, with the principal focus being on biomedical engineering. It has contributed more than $615 million to universities and medical schools to support faculty research, graduate students, program development, and construction of facilities. As is evident from Figure 1, biomedical engineering encompasses tissue engineering and many other applications of engineering principles used to solve problems related to medicine and health.

1.3 Tissue Engineering

The position of tissue engineering relative to the engineering profession is displayed in Figure 1. The thin lines connect tissue engineering to the engineering disciplines that are involved (coming from above), and the specific applications of this technology (leading below). A more complete explanation of tissue engineering will follow in Section 2.0.

1.4 Summary

The following paragraph gives the knowledge and roles of engineers in the various disciplines, fields and applications shown in Figure 1. An engineer would typically obtain training in mathematics, physics and chemistry, and would apply this basic knowledge to solve practical problems in their field (i.e. chemical engineering). A bioengineer would also obtain training in biology and would apply this basic knowledge to solve problems with a biological component. The bioengineering discipline is then defined as the application of any engineering principles to any system involving biological molecules and/or cells to generate understanding of biological systems and practical technologies (MIT website, 2002). The biomedical engineering field would combine the approach of many engineering disciplines (including bioengineering) to solve problems in medicine and health. More specifically, a tissue engineer would be solving problems related to human health by growing or assisting in the regeneration of tissues and organs.

2.0 Tissue Engineering Fundamentals

We now know where tissue engineering fits into the engineering world, but what exactly is tissue engineering? According to the Pittsburgh Tissue Engineering Initiative (PTEI website, 2002):

> *"Broadly defined, tissue engineering is the development and manipulation of laboratory-grown molecules, cells, tissues, or*

> *organs to replace or support the function of defective or injured body parts."*

It is not evident from this definition what role engineers would play in such endeavors. What will become evident is that tissue engineering is a multidisciplinary, collaborative effort which could be lead by bioengineers, and must include engineers from many disciplines. Figure 2 shows the interdisciplinary nature of tissue engineering. The definitions of many of the biological terms can be found in Appendix A. Tissue engineering is at the intersection of engineering, materials science, medical sciences and biology. Individuals working in each of these areas play a key role in the design of a tissue engineered construct or device.

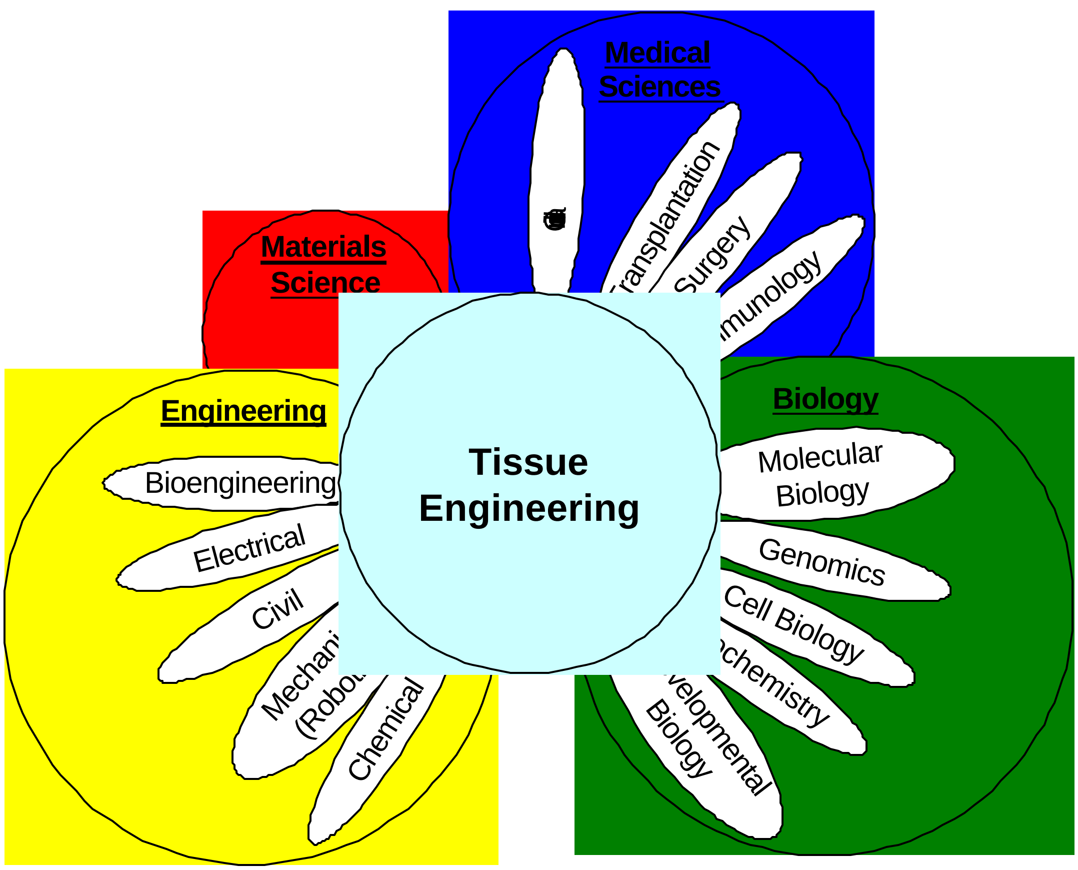

Figure 2: The interdisciplinary nature of tissue engineering.

A recent review article defines tissue engineering as "…devices or processes that (1) combine living cells and biomaterials, (2) utilize living cells as therapeutic or diagnostic reagents, (3) generate tissues or organs in vitro for subsequent transplantation, and/or (4) provide materials or technology to enable such approaches." (Lysaght and Reyes, 2001). A broader definition of tissue engineering is given by the NIH (Appendix A) (NIH BECON Website, 2002).

In a general sense, the three main constituents of any tissue engineering construct (or device) are:

1. Cells
2. Soluble Signals
3. Scaffold Materials

These three elements, together with the correct mechanical environment (a "4th" constituent), are necessary for the creation of a functional tissue engineered construct. The cells and the scaffold materials give the structural and functional properties of the tissue, while the soluble signals direct the actions of the cells. In the body, these soluble signals are found in blood and other body fluids and are produced by cells. Further, the scaffold is also produced and maintained by the cells. The correct combination of these four constituents is essential for a functional tissue, either *in vivo* (in the body) or constructed *in vitro* (in the lab).

2.1 Example Technology – Tissue Engineered Bone

The role of the different fields shown in Figure 2, and the different constituents listed in the previous section, can best be demonstrated by considering an example – the generation of tissue-engineered bone. In this case the objective would be to grow bone with the correct histological (looks like bone) and functional (works like bone) characteristics. The individual contributions from four fields – engineers, materials scientists, biological and medical scientists will be briefly considered.

Most mammalian tissue is composed of cells and what is termed an extracellular matrix. The extracellular matrix is comprised of large protein and sugar complexes which are produced and maintained by the cells in that tissue. Depending on the type of tissue, there may be more cells than matrix (e.g. liver tissue), or more extracellular matrix than cells (e.g. bone tissue). The ratio of cells to matrix helps define how the tissue functions and how the tissue is formed. Much of the initial tissue engineering applications are of structural tissues, like cartilage and bone, where the major constituent is extracellular matrix. Bone is composed of cells and an extracellular matrix (composed of mineral hydroxyapatite and protein collagen fibers). The cells are a small percentage of the total volume of the tissue, and the matrix makes up the rest of the volume.

Reaching the ultimate goal of fully functional bone tissue can be broken down into three steps. The first step is to completely understand what is happening inside the body, including normal tissue function, the initiation and progression of injury or disease, and normal tissue repair. The understanding must come from both an engineering and a biological science point of view. For example, chemical engineers, working with biologists, would model the interactions of growth factors and other stimulatory molecules on the proliferation (increase in number) and differentiation (acquiring of mature characteristics) of osteocytes, osteoblasts, and osteoclasts (all bone cells). Mechanical engineers would model the interaction of mechanical forces and loads on the cells and whole tissue. Scientists, with knowledge of cell biology, molecular biology and biochemistry will describe the growth and metabolism of the cells, including the uptake of nutrients and the production of waste products.

The second step is to design a device or process to replicate or assist the regeneration and repair process either in the body (*in vivo*) or in the lab (*in vitro*). This is where engineers, materials scientists and biological scientists will have a large role. It has been determined that mechanical loading of cells, while they are growing in culture, will increase the quality and amount of bone extracellular matrix that is produced. Engineers from all disciplines (shown in Figure 2) will need to design devices to culture the cells under such conditions. The knowledge of developmental biologists is also essential at this stage, because we are attempting to re-grow the tissue in a manner similar to the way it was grown in the first place (i.e. from embryo to fetus to adult). As bone is mostly extracellular matrix, materials scientists will help generate scaffold materials on which the cells will grow. This scaffold will temporarily perform the mechanical job of bone (i.e. weight-bearing), while the bone cells are producing their own matrix.

The last step is to implement the chosen device or process in a clinical setting. Medical scientists, including surgeons and immunologists, would have the largest role at this stage. Engineers would also be involved in scaling up any processes developed in the previous section. In order to treat a single patient, you need sufficient cells and scaffold to create the correct tissue, and in order to treat all of the afflicted patients, you need sufficient devices. In both cases, reproducible, scaleable processes are required – a major engineering role.

3.0 The “Engineering” in Tissue Engineering

As can be seen in Figure 2, engineers are one of the many different individuals that are necessary to build a successful tissue engineering construct. We have also seen in the previous section some of the roles that an engineer might play in the generation of tissue engineered bone. What we want to ask now, is in a general sense - *What role does the engineer play in tissue engineering?*

Engineers will be involved in the development and design of tissue engineering constructs. Many of the problems being encountered in tissue engineering can only be solved by engineers. First, an engineer’s approach to problem solving differs considerably from the hypothesis-experiment-conclusion approach of medical and science-trained personnel. Second, the scale of operations also sets engineers apart from scientists. Typically scientists will develop methods of culturing cells on a small scale (5-50 mL cultures). The growth of tissues and organs requires operating on a much larger scale (50-5000 mL). Only engineers are equipped to deal with all of the additional issues that arise at larger scales. These include mass transfer limitations, control systems, mechanical forces, etc. Engineers are also very adept at characterizing and analyzing the properties of materials (i.e. stress/strain) and designing new manufacturing and processing techniques. Engineering contributions may also include experimental design, and computer modeling.

Table 1 show the role of engineers at the various scales involved in tissue engineering. The scales range from the molecular level (nm), through single cells (µm), tissues (mm-cm), bioreactors (cm-dm) and into the clinic (m). The roles of the engineer, along with some examples are shown. The examples show the application of bioengineering, electrical, chemical and mechanical engineering principles. The list is not meant to be complete, but merely an indication of the contributions engineers can make. Even at the small scale, engineers have much to offer. In order to gain approval for transplanting a tissue engineered product, one of the key features that have to be demonstrated is reproducibility and repeatability. The engineers' ability to model and predict performance at all scales will be essential in delivering tissue engineered devices in a clinical setting.

Table 1 – Role of Engineers in Tissue Engineering

Tissue Engineering Scale	Role of Engineer	Example
ALL	Modeling	Multivariable interactions and experimental design
	Imaging	Designing methods and instruments to view tissues, cells, molecules
Molecular (nm)	Materials	Design of polymeric scaffolds Patterning of scaffolds for cell attachment Design of polymer processing techniques
Single Cell (µm)	Impact of mechanical forces on cells	Response of cells (e.g. chondrocytes (cartilage cells)) to mechanical forces
	Modeling	Mass transfer of molecules to cells Molecular interactions with cells (kinetics of growth factor / receptor interactions) Kinetics of cell division, death, differentiation, adhesion, and migration,
Tissue (mm-cm)	Testing	*In vivo / in vitro* monitoring of construct performance
	Stress/Strain Analysis	Analyze stress/strain behavior of native and tissue-engineered tissues
	Impact of mechanical forces on tissues	Response of tissue (cells and extracellular matrix) to mechanical forces
	Modeling	Mass transfer of molecules to cells within tissues Combined heat and mass transfer during cryopreservation/thawing
Bioreactor (cm-dm)	Modeling	Fluid flow *in vivo* (blood vessels) and *in vitro* (within scaffolds, bioreactors) Mass transfer of nutrients / wastes within tissues and constructs
	Bioreactor Design / Optimization	Stationary / suspension culture / hollow-fiber bioreactors Bioartificial liver, pancreas
Clinic (m)	Materials Control Systems Quality Assurance Quality Control	Processing techniques Bioreactors

4.0 The Practice of Tissue Engineering

Tissue engineering, as a field of engineering, will need to be practiced by qualified, educated engineers. The next section will deal with the accredited bioengineering, biomedical engineering and tissue engineering programs at the undergraduate and graduate level in Canada and the US. This will be followed by a discussion of the state of the tissue engineering industry, and the role of professional tissue engineers in this industry.

4.1 Tissue Engineering Education

In Canada, engineering programs are accredited by the CCPE (Canadian Council of Professional Engineers). There are 36 universities offering accredited engineering programs in Canada. There are no accredited tissue engineering undergraduate programs in Canada. However, there are 10 bioengineering (including biomedical engineering and biochemical engineering) undergraduate programs (8 accredited), and 11 universities offering graduate programs in bioengineering. In addition, there are 11 universities at which there are individuals or groups conducting tissue engineering research. Appendix B contains a complete listing of the universities that are offering accredited engineering programs in Canada, along with their undergraduate and graduate programs in bioengineering. Also, the universities where tissue engineering research is occurring (within the faculty of engineering) are listed.

In the United States, engineering programs are accredited by ABET (Accreditation Board for Engineering and Technology). In 2001 there were 348 universities offering 1,627 accredited engineering programs in the US. There are no accredited tissue engineering programs in the United States. Of the accredited engineering universities in the US, 15 offer programs in Biomedical Engineering, 18 offer programs in Biological Engineering (or some form), and 7 offer Biosystems Engineering degrees (a total of 40 universities). The definition of Biosystems is very close to that of bioengineering, with more focus on agricultural and biotechnology applications.

The Whitaker Foundation has slightly different numbers, but in this case the programs may or may not be accredited by ABET. There are 91 Biomedical Engineering Programs or Departments in North America. Of these, 65 are offering undergraduate programs leading to a BSc, 74 are offering MSc, and 78 are offering PhD programs (Whitaker Foundation website). The number of Biomedical Engineering Programs / Departments (offering BSc degrees) that have been formed in the last 10 years (since 1992) is 39 out of the 65 (60%). The other 40% were formed in the previous 30 years. This indicates a great acceleration in the number of programs being offered that is not expected to diminish anytime soon.

There are other statistics available for the United States. While overall undergraduate engineering enrolment has remained steady at 350,000 students since 1979, the enrolment in undergraduate bioengineering programs has increased from just under 3,000 to over 6,500 from 1979 to 2000 (Whitaker Foundation Website). The fraction of bioengineering undergraduates has increased from 0.86% to 1.86% of the total undergraduate engineering students. The number of engineering graduate students has increased from 41,000 in 1979 to 81,000 in 2000, while the number of bioengineering graduate students has increased from 700 in 1979 to 2,500 in 2000. The fraction of bioengineering graduate students has increased from 1.70% to 3.09% of the total undergraduate engineering students. These trends are expected to continue in Canada, where biomedical engineering programs are in demand.

Recent Canadian statistics are also available for engineering enrolment (CCPE, 2002). Undergraduate engineering enrolment is listed as 48,600 students in 2000, while the enrolment in undergraduate bioengineering programs was just under 530 in year 2000 (CCPE, 2002). The bioengineering undergraduates represent approximately 1% of the total undergraduate engineering students. The total number of engineering graduate students was 10,200 in 2000, while the number of bioengineering graduate students was 148 in 2000. The bioengineering graduate students represent 1.45% of the total graduate engineering students. It is worthwhile to note that in the CCPE (2002) report, bioengineering is listed as biosystems engineering, which includes most bioengineering disciplines but does not include biochemical engineering. Also worth noting is the fact that the number of students enrolled in graduate bioengineering programs in Canada does not adequately reflect the number carrying out research in bioengineering (as well as being trained in this area). This is a result of the low number of accredited bioengineering programs at Canadian Universities.

4.2 Tissue Engineering Industry

As a result of the lack of any distinct tissue engineering undergraduate or graduate programs, the number of practicing tissue engineers is very difficult to estimate. Information is, however, known about the practice of biomedical engineering. These numbers may be used as a broad guide to what is occurring or will occur in the field of tissue engineering. According to the Whitaker Foundation, the number of biomedical engineers employed in the United States in 2001 was 7,221, and this number is expected to increase by 31.4% to 9,487 by 2010. The three largest industries (each with ~18% of the employed biomedical engineers) were 1) Hospitals, public and private; 2) Medical instruments and supplies; and 3) Self-employed workers, primary job (Whitaker Foundation website). The first and third of these industries would both hire tissue engineers. As mentioned in the previous section, the number of companies in Canada performing tissue engineering research is small, and the number of companies hiring biomedical engineers (or tissue engineers) is very hard to estimate. At the present time, no separate biomedical engineering industry statistics are available for Canada.

However, the Canadian biotechnology industry (which includes biomedical engineering) does provide statistics. In a recent published document, it was reported that the number of Canadian biotechnology companies has increased 183% from 1997-2001, which places Canada second in the world behind only the United States (Ernst & Young, 2002). In the same time period, the market capitalization in the biotechnology sector grew from $8 to $20 billion. The entire biotechnology industry in Canada includes sectors where biomedical engineers would be expected to work including: Therapeutics (57% of the total number of firms), Diagnostics (10%) and Medical Diagnostics (1%). This means that 270 companies are presently operating in Canada in areas that would hire biomedical engineers.

The most recently published survey of the CCPE (1998), which had an average response rate of 25%, also has some data on the number of practicing bioengineers in Canada. In 1997, 1486 of the 128,537 respondents (1.16%) considered themselves biosystems engineers (including biomedical engineers), while 124 (0.1%) actually considered themselves biomedical engineers. Of the biomedical engineers, just over half had undergraduate degrees in biomedical engineering. This low number is due to the fact that, as mentioned previously, most of the biomedical engineering undergraduate programs (60%) have been created in the last 10 years. This means that there has not been a lot of time for graduates to earn the required experience to be registered as a professional engineer.

In a recent review of the tissue engineering industry, it was determined that 73 firms were engaged in tissue engineering (Lysaght and Reyes, 2001). The United States is by far the leader in the commercialization of this technology with 55 companies (75.4%), followed by Europe with 17 companies (23.3%) and only one was located in Canada (1.3%). In Table 2, summary statistics for the industry are presented (world-wide).

Table 2 – Tissue Engineering Industry (Lysaght and Reyes, 2001)

Number of engineers, scientists and support staff (Jan. 1, 2000)	3300
Annual Spending Rate (Jan. 1, 2000 – Dec 31, 2000)	$610 million
Number of firms (Jan. 1, 2001)	73
Compound annual growth rate (1995-2001)	16%
Number of new startup firms (Average, 1990-2000)	4.4
Capital value of post-IPO companies (Jan. 1, 2001) (n=16)	$2.6 billion
Cumulative investment (1990-2001)	$3.5 billion

There has been a steady growth rate in the industry of 16% over the last 5 years, and the number of new companies formed per year has remained between 3 and 8 over the last 10 years. The tissue engineering industry, in contrast to other technology-driven industries such as the dot.com industry, has shown steady, aggressive growth over the last 5-10 years. This is in part due to the many different sectors in the tissue engineering industry. There are three main sectors – structural (skin, bone, blood vessels); metabolic (bioartificial organs, encapsulated cell therapy); and cellular (cell-processing, stem cell research, therapeutic cloning). Each sector has its own cycles of ups and downs which tend to balance each other. Presently structural companies employ 60% of the employees, cellular companies employ 27% and metabolic companies employ 11%. There are only two FDA-approved tissue engineering products on the market – Apligraf® (tissue engineered skin from Organogenesis, US) and Carticel® (tissue engineered cartilage from Genzyme Biosurgery, US), both of which are structural.

The tissue engineering industry is expected to show anywhere between a 22% and a 50% growth rate over the next decade (Persidis, 2000; Koopman, 2001). The tissue engineering industry is thriving in the U.S., but Canadian information is difficult to obtain. Judging by the ratio of the number of educational programs in bioengineering in Canada to the US (10/40=0.25), and the representative populations of the two countries ($30x10^6/300x10^6=0.10$), it is expected that the industry will flourish in Canada.

Another factor that may influence tissue engineering research and industry in Canada is stem cell policy. At the present time, stem cells (both embryonic, fetal, and adult) are a major part of the tissue engineering research. As mentioned previously, the three main parts of any tissue-engineered construct are 1) cells, 2) soluble signals, and 3) scaffolds. It is believed that the cells in this case will have to have a large developmental potential, and as a result, in many cases they will have to be stem cells. The regulations regarding the use of embryonic stem cells are much more generous in Canada, and that may drive many researchers and industry north from the United States.

4.3 The professional engineering aspects of tissue engineering

Professional engineers practicing as tissue engineers will have to follow the same standards of professionalism with regards to ethics, law, professional conduct, and the engineer's duty to society and the environment.

A tissue engineer wishing to begin practicing, whether in industry, management or private practice, will have to demonstrate competence (academically and experientially) in both engineering and biological/medical sciences. Determining the degree of knowledge required in each field is outside the scope of this report. As a result of the lack of undergraduate programs in tissue engineering, this may require competence testing in biology/medical science in addition to a basic or bioengineering undergraduate engineering degree. The reader is referred to a recent document published by the Professional Engineers of Ontario (PEO, 2001). This report recommended that a Core Body of Knowledge be established for Bioengineering, Biochemical/Food Engineering, Biomedical Engineering and Bioresource Engineering and that the provincial Academic Requirements Committee have access to this information. Within the Core Body of Knowledge, certain topics, such as cell biology, bioethics, and a bioengineering design project were required elements for a Biomedical Engineer.

As tissue engineering is a rapidly advancing field, it will be important for tissue engineers to maintain professional competence through continuing education, on-the-job training and a commitment to life-long learning.

Regulation of the tissue engineering profession will require individuals with tissue engineering knowledge to hold positions in, or be consulted by the appropriate federal (i.e. CCPE) and provincial (i.e. APEGGA, etc.) organizations.

The principles of engineering ethics hold for tissue engineers the same way they hold for all other engineers. There are obviously more ethical issues, which fall under the general heading of bioethics (medical ethics), as a result of the direct connection between tissue engineers and the healthcare industry. Issues such as quality of life versus quantity of life, euthanasia, cost of healthcare, and organ/tissue/cell donation and ownership all require much more treatment than this report can offer. The reader is referred to the NIH (NIH Bioethics website, 2002), American Journal of Bioethics (AJOB website, 2002), and the Canadian Bioethics Society (Canadian Bioethics Society website, 2002) for more information on and an excellent overview of bioethics. In addition, the consequences of not following the codes of professional practice become more complicated. The results of errors in a tissue engineer's calculations, for example, can have direct impacts on the health and well-being of individuals.

Tissue engineers, like engineers practicing in more traditional industries, will also have to deal with issues of product safety, quality and liability. However, a living product will have much more stringent specifications and quality control steps than an inert (non-biological) product such as a building, automobile, or non-medical chemical. Tissue-engineering devices are currently regulated by the FDA (Food and Drug Administration) in the United States as TEMPs (Tissue Engineered Medical Products). A detailed discussion on the role of the FDA with regards to a) Legislative authority, b) Product evaluation and regulatory process, c) Recent developments in product evaluation, d) Development of Standards (to ensure safety and effectiveness), and e) Communication with Industry can be found in Lanza *et al.*, 2000.

5.0 Actions by the Profession

The profession of engineering has a key role to play in the emerging field of tissue engineering. This section will deal with the steps that the profession should take in the areas of education, professional practice, public awareness, government influence and regulation.

5.1 Education

As there are no formal "tissue engineering" programs in place in North America, it is difficult at the present time to grant professional status to any engineers directly in this area. There are, however, accredited bioengineering programs throughout North America. Engineers wishing to practice tissue engineering could be granted professional status as bioengineers. Bioengineers should demonstrate adequate formal education and experience in engineering and biological/medical sciences, as would also be expected for tissue engineers.

An example should clarify the last point above. A chemical engineer, who wishes to practice as a chemical engineer in a specific industry (i.e. the petrochemical industry) must demonstrate adequate formal education and experience in chemical engineering (not petrochemical engineering). This is because petrochemical engineering is considered a subset of chemical engineering, and professional membership review boards do not look at specific applications, rather general headings. In the same manner, tissue engineers, as they are a subset of bioengineering, will have to demonstrate bioengineering (not tissue engineering) competence, including adequate formal education and experience.

One more point needs to be made regarding the formal education of tissue engineers. At the present time it may be detrimental to limit the number of people practicing tissue engineering by forcing individuals to have a formal bioengineering degree. The field is changing so rapidly, that valuable contributions may still be made by individuals with limited formal background in biomedical engineering. Adequate industry experience or post-secondary education should be sufficient, until adequate undergraduate programs in tissue engineering are available.

5.2 *Professional Practice (i.e. Membership, Regulation)*

Tissue engineering performed by engineers is still engineering, and thus would fall under the regulation of the provincial engineering associations. However, as seen in Figure 2, many aspects of tissue engineering are also supported by non-engineers including surgeons, clinicians, cell biologists, biochemists and other scientists. Obviously, these individuals do not fall under the regulation of the provincial engineering associations.

This is where a major difference between tissue engineering and more traditional engineering fields arises. Tissue engineering, by the nature of the field, will have to be carried out by teams of engineers and non-engineers.

Presently, any non-tissue-engineering project (i.e. plant design) requiring engineering has to be carried out under the guidance of a professional engineer. The engineer assumes responsibility for the project by affixing his or her seal to the drawings, specifications, plans, reports and other documents involving the practice of professional engineering (Andrews and Kemper, 1999). This means that the engineer prepared **or** approved the documents. If this relationship holds, any tissue engineering would be carried out under the guidance of a professional engineer. This tissue engineer would assume responsibility for the project under guidelines set by the provincial professional association. The role of engineers as the responsible parties in any tissue engineering project must be enforced when the project would involve (in any form) “the practice of professional engineering”.

In any case, as mentioned previously, regulation of engineers in the tissue engineering profession will require individuals with tissue engineering knowledge. The provincial professional engineering associations will still be charged with granting professional status to biomedical and tissue engineers. Adequately and accurately assessing the formal education and experience of biomedical and tissue engineers will be essential to maintaining the status of the profession.

5.3 *Public Awareness*

The public perception of biomedical engineering as a whole, and tissue engineering specifically, is still lagging behind the knowledge of professionals in the field. This trend can be expected to continue as the rapid pace of discovery in this area continues. The situation is even sometimes exacerbated by the frequent news updates by the public media about the latest medical breakthroughs, particularly in the field of stem cells. It is important for the professional associations to begin educating their own members, the industries that will work with tissue engineers (healthcare, medical devices, pharmaceutical companies), the media, and the general public about the "engineering" in tissue engineering. Inadequate education is one of the largest barriers to public acceptance of tissue engineering technology.

The public perception problem is analogous to that of the genetic engineering industry 10-20 years ago. Genetic engineering is defined as "The manipulating of genetic material in the laboratory. It includes isolating, copying and multiplying genes, recombining genes or DNA from different species, and transferring genes from one species to another, bypassing the reproductive process." (Ifgene website, 2002). Using this definition, genetic engineering does not have a high degree of actual engineering, but the public perception of the field as engineering is still strong.

It is important that tissue engineering, if the term is continued to be used, be actually perceived as real engineering – the application of mathematical and scientific principles to solving practical problems. This is also essential to assigning responsibility for tissue engineering projects to engineers.

5.4 *Government Influence*

In Canada, healthcare is governed by both provincial and federal governments, resulting in a publicly-financed, privately-delivered health care system (Health

Canada website, 2002). The federal government sets policies regarding matters of national importance and issues transfer funds to the provinces to assist in financing. The provincial government is involved with planning, financing, and evaluating the provision of hospital care, physician and allied health care services, as well as managing and delivering health services (Health Canada website, 2002). In Alberta, with the advent of public and private healthcare, the emergence of companies offering tissue-engineering services may precede the offering of such services by provincial health care.

As is evident by the recent stem cell debate and resulting regulations both in Canada and the United States, government policies have the power to shape the emerging tissue engineering industry. The public debate over the use of tissue engineering therapies in common health care will undoubtedly continue for many years. The funding for this research comes from public and private sources. It is believed that governments will continue to publicly fund tissue engineering research in the near future, although due to the enormous commercial potential, a large fraction of the research is privately funded. As a result of regulations and public perception, the acceptance of such technologies may be hampered, but initial research demonstrates that the technology has the capacity to save lives. The continued role of the government in the evolving tissue engineering industry is unclear. The role of the FDA in the United States has already been discussed.

When the tissue engineering industry reaches maturity, and tissue engineering therapies are regularly used to treat injuries, as well as tissue and organ failure, the government will have a role to ensure that public safety is guaranteed. This role may overlap with the jurisdiction of the provincial professional engineering associations. Details regarding the exact nature of the relationship between federal healthcare policy, provincial healthcare policy and provincial professional engineering self-regulation will still need to be determined.

6.0 Conclusions

The field of tissue engineering is a multidisciplinary, rapidly evolving field with many challenges and opportunities ahead. Tissue engineering is a subset of biomedical engineering, which is itself an application of traditional engineering and bioengineering principles. Tissue engineering is at the junction of biological sciences, medical sciences, materials science and engineering. Engineers will play a large role in shaping this new industry, and the Canadian engineering profession needs to be proactive in determining the role of the profession. Currently, biomedical engineering education and accreditation is paving the way for well-educated tissue engineers. The role of these engineers as the responsible individuals in a tissue engineering project needs to be adequately justified, to ensure that the tissue engineering industry is regulated as an engineering profession. In addition, the perception of tissue engineers by the public, other engineers, and industry needs to be shaped by the professional engineering associations.

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8.0 Appendices

8.1 Appendix A - Glossary

Biochemistry – the study of the structure and function of biochemical molecules, such as proteins, carbohydrates, lipids, and nucleic acids and how they participate in reactions occurring inside cells (biochemical molecules and biochemical reactions)

Bioengineering - the application of any engineering principles to any system involving biological molecules and/or cells to generate understanding of biological systems and practical technologies (MIT website, 2002).

Biological Sciences – the scientific study of biology (i.e. living organisms)

Biomaterial – any man-made material (natural or synthetic) that is designed to interact with a tissue/organ/organism in order to control, modify, support or improve its functions or properties. A biomaterial is different from a biological material such as bone that is produced by a biological system.

Biomedical Engineering - a discipline that advances knowledge in engineering, biology and medicine, and improves human health through cross-disciplinary activities that integrate the engineering sciences with the biomedical sciences and clinical practice. (Whitaker Foundation website, 2002)

Cell Biology – the study of the life of cells

Construct – a tissue engineered device, usually containing cells, a scaffold, and soluble signals to direct the actions of the cells

Developmental Biology – the study of the growth and development of organisms from the single cell stage through the development of the embryo, fetus, and adult

Engineering - APEGGA (Association of Professional Engineers, Geologists and Geophysicists of Alberta) defines the practice of engineering " … as:

> *(i) reporting on, advising on, evaluating, designing, preparing plans and specifications for or directing the construction, technical inspection, maintenance or operation of any structure, work or process*

> *(A) that is aimed at the discovery, development or utilization of matter, materials or energy or in any other way designed for the use and convenience of man, and*
>
> *(B) that requires in the reporting, advising, evaluating, designing, preparation or direction the professional application of the principles of mathematics, chemistry, physics or any related applied subject, or*

(ii) teaching engineering at a university.

<u>Genomics</u> – the study of the role of genes

<u>Histology</u> – the study of the appearance of cells, tissues, and organs

<u>Immunology</u> – the study of the immune system of humans, including non-specific defenses (skin, white blood cells, fever, complement) and specific defenses (T-cells, B-cells, antibodies)

<u>*In Vitro*</u> – inside the lab (i.e. outside the body – strictly *ex vivo*)

<u>*In Vivo*</u> – inside the body

<u>Medical Sciences</u> – the study of science as it relates to human health

<u>Molecular Biology</u> – the study of the interactions of biological molecules and the role they play in the operation of cells, tissues and organs

<u>Organ</u> – an organization of <u>tissues</u> into a structural and functional unit. For example, liver is composed of epithelial tissue (mostly hepatocytes (liver cells) and endothelial cells (blood vessels)) and connective tissue (support cells for the liver cells as well as circulating white blood cells). Organs are combined in organ systems (i.e. the digestive system) in organisms.

<u>Tissue</u> – an organization of <u>cells</u> into a structural and functional unit. There are four types of tissue in the mammalian body – epithelial tissue (i.e. skin, intestine), neural tissue (i.e. neurons), muscle tissue (skeletal muscle, stomach muscle, cardiac muscle), and connective tissue (i.e. blood, fat, tendons, ligaments, bone, cartilage). Tissue is organized into organs.

<u>Tissue Engineering</u> – An NIH funded report by the WTEC (World Technology Evaluation Center) has recently defined tissue engineering as:

> *"…the application of principles and methods of engineering and life sciences toward fundamental understanding of structure-function relationships in normal and pathological*

mammalian tissues, and the development of biological substitutes to restore, maintain, or improve tissue function. Sometimes also called reparative and regenerative medicine, tissue engineering is an emerging interdisciplinary area of research and technology development that has the potential to revolutionize methods of health care treatment and dramatically improve the quality of life for millions of people throughout the world. Some products are already in use clinically, and their number will assuredly increase rapidly in the future." (McIntire, et al., 2002)

8.2 Appendix B – Bioengineering Programs at Canadian Universities with Accredited Engineering Curriculums

University	Undergraduate Program*	Graduate Program	Tissue Engineering Research*	Website
Carleton University	N/A	N/A	No	http://www.eng.carleton.ca/
Concordia University	N/A	N/A	No	http://www.concordia.ca/
Dalhousie University / Technical University of Nova Scotia (DalTech)	Biological Engineering	Biological Engineering, Biomedical Engineering	Yes – 1,3	http://www.dal.ca/~engiwww/index.htm
École de Technologie Supérieure	N/A	N/A	No	http://www.etsmtl.ca/
Ecole Polytechnique	Biomedical Engineering#	Biomedical Engineering	Yes – 1,3	http://www.polymtl.ca/departement/dep/biomedic.php
Lakehead University	N/A	N/A	No	http://www.lakeheadu.ca/~engwww/
Laurentian University	N/A	N/A	No	http://www.laurentian.ca/index_e.asp
McGill University	Agricultural Engineering	Biomedical Engineering	Yes – 1,3	http://www.mcgill.ca/engineering/
McMaster University	N/A	N/A	Yes – 1,3	http://www.eng.mcmaster.ca/
Memorial University of Newfoundland	N/A	N/A	No	http://www.engr.mun.ca/
Queen's University	N/A	N/A	Yes – 1,2	http://info.queens u.ca/
Royal Military College of Canada	N/A	N/A	No	http://www.rmc.ca/
Ryerson Polytechnic University	N/A	N/A	No	http://www.acs.ryerson.ca/
Simon Fraser University	Minor (Stream) in Biomedical Engineering	N/A	No	http://www.ensc.sfu.ca/
Université de Moncton	N/A	N/A	No	http://www.umoncton.ca/udem/index.html
Université de Sherbrooke	N/A	N/A	No	http://www.usherb.ca/sca/
Université du Québec à Chicoutimi	N/A	N/A	No	http://www.uqac.uquebec.ca/
Université du Québec à Trois-Rivières	N/A	N/A	No	http://www.uqtr.ca/Departement/ecoleIng.shtml
Université Laval	N/A	N/A	No	http://www.fsg.ulaval.ca/index.htm
University of Alberta	N/A	Biomedical Engineering (with U of C)	Yes – 1,3	http://www.engineering.ualberta.ca/
University of British Columbia	Bio-Resource Engineering (Biological Engineering)	Bio-Resource Engineering (Biological Engineering)	Yes – 1,2,4	http://www.apsc.ubc.ca/engineering/
University of Calgary	N/A	Biomedical Engineering (with U of A)	Yes – 2,4	http://www.eng.ucalgary.ca/
University of Guelph	Biological Engineering	Biological Engineering	No	http://www.eos.uoguelph.ca/index.html
University of Manitoba	Bio-systems Engineering	Bio-systems Engineering	No	http://www.umanitoba.ca/faculties/engineering/
University of New Brunswick	N/A	N/A	No	http://www.unb.ca/
University of Ottawa	Biotechnology (Chemical Engineering+Biochemistry)#	N/A	Yes - 2	http://www.uottawa.ca/welcome.html
University of Regina	N/A	N/A	No	http://www.uregina.ca/engg/
University of Saskatchewan	Agricultural and Bioresource Engineering	Agricultural and Bioresource Engineering	No	http://www.usask.ca/communications/faq6.html

University	Undergraduate Program*	Graduate Program	Tissue Engineering Research*	Website
University of Toronto	N/A	Biomedical Engineering	Yes – 1,2,3,4	http://www.ecf.toronto.edu/apsc/ http://www.utoronto.ca/IBBME/
University of Victoria	N/A	N/A	No	http://www.engr.uvic.ca/
University of Waterloo	N/A	N/A	No	http://www.eng.uwaterloo.ca/
University of Western Ontario	Chemical and Biochemical Engineering	Biomedical Engineering, Chemical and Biochemical Engineering	Yes - 1	http://www.engga.uwo.ca/
University of Windsor	N/A	N/A	No	http://athena.uwindsor.ca/units/eng/EnginSplash.nsf/Engineering+main+page?OpenForm
Total Bioengineering Universities	10 (8 accredited)	11	11	-

Notes: (*) Research Areas: 1 – Biomaterials, 2 – Modeling, 3 – Tissue Engineering, 4 – Stem Cells
(#) Undergraduate Program not accredited by CCPE (June 30, 2002)