Biomedical Manufacturing: A New Frontier of Manufacturing Research

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A new frontier of manufacturing research, biomedical manufacturing, is presented. Advanced manufacturing technologies, such as manufacturing processes, systems, and quality control, can be readily applied to improve the safety, quality, cost, efficiency, and speed of healthcare service and biomedical research. The analogy of the hospital as a factory is explored to broadly and inclusively define biomedical manufacturing. Characteristics and engineering needs of biomedical manufacturing are discussed. Examples of the grinding and cutting of plaque in interventional cardiology and laparoscopic surgery on minimizing the nerve tissue thermal damage in surgery are presented to demonstrate the broad spectrum of biomedical manufacturing. On education, the scope and pedagogy for teaching a new senior undergraduate/first-year-graduate level course in Biomedical Design and Manufacturing are discussed. [DOI: 10.1115/1.2896116]

1 Introduction

Globalization and the advancement of technology have brought rapid and profound changes to the worldwide manufacturing industry and research community. In the US, as shown in Fig. 1(*a*), manufacturing's share of the total employment has declined from 22.0% in 1977 to 10.4% in 2006 [1]. Industrial automation, advanced machine tools and processes, information technology, lean manufacturing practices, and global supply chain and service all contribute to the reduction of employment in manufacturing. Although the value of manufacturing has increased from $387 billion in 1976 to $1510 billion in 2005 [2], the share of manufacturing in the US gross domestic product (GDP) has declined from 21.2% in 1976 to 12.1% in 2006. The ratio of manufacturing's share of GDP to manufacturing's share of employment is shown in Fig. 1(*b*). The increase of the ratio from 0.95–1.0 before 1987 to about 1.3 in 2005 represents the overall steady but slow gain in productivity.

Healthcare spending in the US is represented by the national healthcare expenditures (NHE). The NHE is defined as the total amount spent to purchase healthcare goods and services as well as the investment in the medical sector to produce healthcare services [3]. In the past two decades, the NHE has grown rapidly from $\$153\times10^9$ in 1976 to $\$1990\times10^9$ in 2005 [3]. The ratio of the NHE to the total GDP, as shown in Fig. 1(*a*), has increased from 8.4% in 1976 to 16.0% in 2005. This number is expected to grow as the aging of the population continues [4,5].

The increase in healthcare costs is a burden to individuals, employers, and federal and local governments. The NHE can be subdivided into private and public funds. The percentages of the three varieties of private funds (out-of-pocket payment, health insurance payments, and other private payments) and three types of public funds (federal Medicare, other federal funds, and state and local funds) are shown in Fig. 2. The share of private out-of-pocket payments in the NHE has decreased from 47% in 1960 to less than 13% in 2005. The burden of healthcare costs is mostly transferred to three rising categories: private health insurance, federal Medicare, and other federal funds. Private health insurance, which is mostly covered by employers, has risen from 21% in 1960 to 35% in 2005. The Government is the largest contributor, covering almost 45% of the costs in the NHE, rising from only 24% in 1960. This analysis reconfirms the increase in healthcare costs for US companies and the government.

Manufacturing has changed in the past years and will continue to do so. In the 1950s, the three dominant manufacturing segments of the GDP were food, primary metals, and motor vehicles. In 2001, the top three segments have changed to chemical products, industrial machinery and equipment, and electronics and electrical equipment [1]. Based on data from the Bureau of Economic Analysis [2], the manufacturing GDP can be divided into durable and nondurable goods. Two segments of nondurable goods (chemical products and food/beverage/tobacco products) and four segments of durable goods (computers/electronics, motor vehicles, machinery, and fabricated metal products) are selected for analysis. Figure 3 shows shares of these six segments in the manufacturing GDP from 1976 to 2005. The continued rise in the share of chemical products, the steady share of food/beverage/tobacco products, the rise of computer/electronic products before 2000 followed by a sudden drop after 2000 due to the shift of production overseas, and the cyclical nature of motor vehicles can be identified. Manufacturing is clearly changing. As the society evolves, manufacturing needs will adapt to societal needs.

Transitioning its focus to healthcare related areas is an inevitable path for advanced manufacturing. Solving the challenge of the increasing costs of healthcare requires a multidisciplinary approach. Manufacturing is a critical part of the solution. Many manufacturing researchers have recognized this trend and the great societal needs. There are ample opportunities for manufacturing science and engineering to contribute to the rapid advancements of biomedical technology and improvements in the safety, quality, cost, efficiency, and speed of healthcare services. However, research efforts that are performed by the manufacturing sector in healthcare are sparse and not well recognized. There is a lack of a unified definition, coherent strategy, convincing examples, and critical mass to demonstrate the benefits of incorporating advanced manufacturing knowledge and technology into healthcare service and biomedical research.

The goal of this paper is to define and broaden the scope of biomedical manufacturing. The definition of biomedical manufacturing, based on the US Food and Drug Administration (FDA) regulation, is introduced. Characteristics of biomedical manufacturing are presented. Examples from interventional cardiology and the use of a surgical thermal management system (STMS) for tissue machining are described to demonstrate the broad concept

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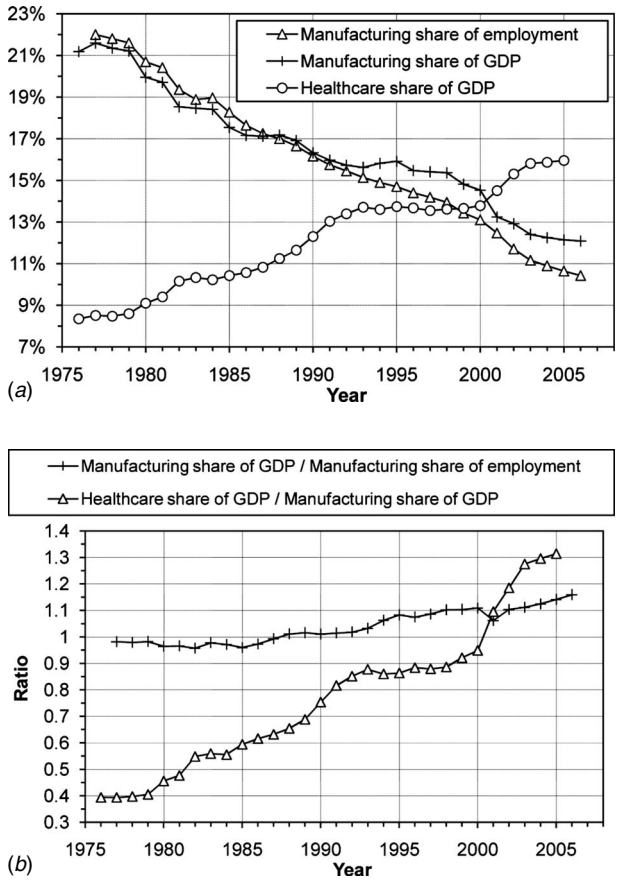

Fig. 1 (*a*) Manufacturing share of GDP and employment and healthcare share of GDP and (*b*) the ratio of manufacturing share of GDP versus the manufacturing share of employment and the healthcare share of GDP versus manufacturing share of GDP

of biomedical manufacturing. The educational aspects of biomedical manufacturing and collaboration with biomedical researchers are discussed.

2 FDA Definition of Manufacturing and Scope and Definition of Biomedical Manufacturing

2.1 FDA Definition of Good Manufacturing Practice. According to the US FDA's good manufacturing practice (GMP) [6], manufacturing is broadly defined to cover the detailed requirements and guidelines of quality assurance systems for the complete life cycle of medical devices. GMP consists of a combination of obtaining the requirements; determining the quality system; design; employee training; acquiring a facility; purchasing and installing equipment, drafting and updating the device record, procuring components and materials, producing, labeling, evaluating, packaging, servicing, and distributing devices; processing complaints; auditing; and FDA inspection [6]. The FDA has a broad definition of manufacturing—from the concept inception to the end of a device's life.

2.2 Biomedical Manufacturing: Scope and Definition. For biomedical manufacturing, a unified definition is lacking. It is too narrow to define biomedical manufacturing as the manufacturing of medical devices, which is only a small portion of healthcare industry. The definition of biomedical manufacturing needs to be broad enough to embrace current and future manufacturing research in healthcare.

Manufacturing has been part of healthcare technology development in the past. For example, the research in bone machining [7,8] was conducted in the 1970s. A series of papers have been published in the CIRP Annals on healthcare, including the review of assembly and automation technologies for healthcare products [9], machining of biocompatible magnesium alloys [10], bone machining in knee replacement [11,12], and surfaces in biomedical systems [13]. Other examples of manufacturing contributions to the realm of healthcare include micromachines for medical applications [14], robotic grinding and polishing of artificial joints [15], selective laser sintering to produce scaffolds for bone tissue engineering [16], application of radio frequency identification (RFID) for hospital equipment and people scheduling [17], coat-

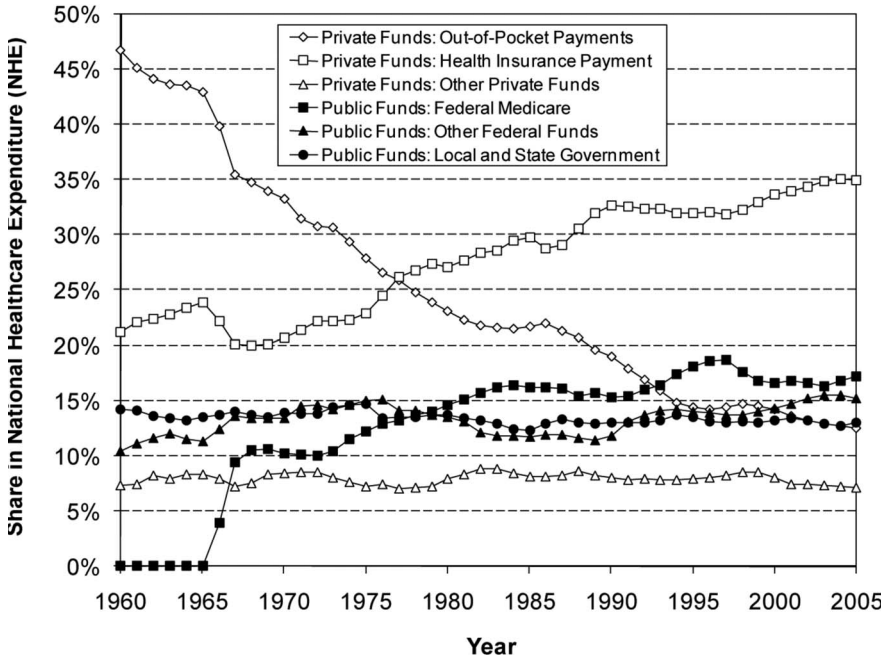

Fig. 2 Share of contributions in the NHE (data adopted from http://www.cms.hhs.gov/NationalHealthExpendData)

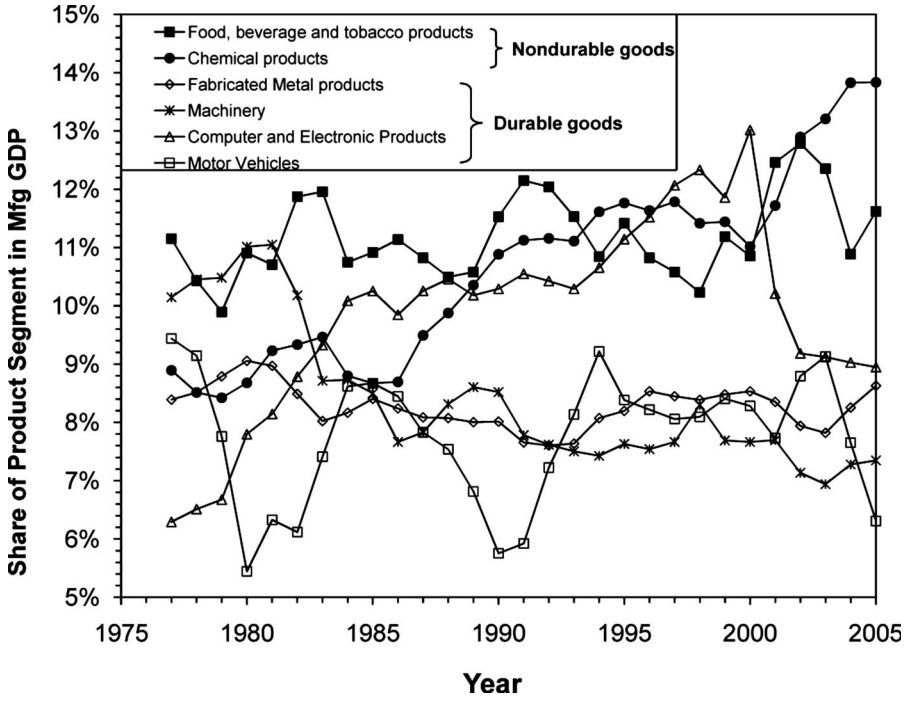

Fig. 3 Share of the manufacturing GDP from different segments (data obtained from http://www.bea.gov/industry/gpotables)

ings to improve the biocompatibility and mechanical properties of surgical tools [18], and equipment for inspecting medical device components, implants, and prosthetics [19]. There are many other examples of healthcare related manufacturing research, and they are very broad, covering all areas in healthcare services and devices.

In this study, a new approach to define biomedical manufacturing using the hospital-factory analogy is illustrated in Table 1. This is a broad perspective of biomedical manufacturing, with the purpose of extending manufacturing science and engineering to healthcare and biomedical research. In the hospital-factory analogy, the tissue/patient corresponds to a workpiece, the surgical instrument serves as a machine tool, the hospital bed is like a fixture, the doctor resembles an operator, etc. Based on this analogy, many manufacturing technologies and concepts can be readily applied to biomedical and healthcare situations. One reason to broadly define biomedical manufacturing in such a way is to create added value for manufacturing. If biomedical manufacturing is solely defined as the manufacturing of medical devices, its scope is too narrow and does not generate the high value associated with direct patient treatment and care.

Table 1 The hospital-factory analogous definition of biomedical manufacturing

Medical	Manufacturing
Hospital	Factory
Tissue/patient	Workpiece
Doctor	Operator
Surgical instrument	Machine tool
Diagnosis machines	Inspection machines
Bed	Fixture
Stretcher	Pallet
Tissue thermal damage	Workpiece thermal damage
Patient rooms	Inventory area
Waiting room	Loading dock
Sterilization	Cleanliness
Bracelets	In-process tags
Preclinical trials	Prototyping
Patient cycle time	Part-to-part cycle time
Patient scheduling	Production scheduling
Patient record	Job log

Based on the hospital-factory analogy, biomedical manufacturing is "the applications of manufacturing technology to advance the safety, quality, cost, efficiency, and speed of healthcare service and research." Examples are given in Sec. 4 to elaborate on this definition of biomedical manufacturing. Already, industrial manufacturing technology can be applied to improve healthcare. In the future, as biomedical manufacturing technology is further developed, it is expected that such manufacturing will become a prevalent and integral part of manufacturing research.

3 Characteristics and Engineering Needs for Biomedical Manufacturing

Biomedical manufacturing is technically challenging in many different ways. Manufacturing engineers usually do not have a basic training in anatomy and physiology and will need to learn basic biology and medicine to effectively communicate with collaborators in the healthcare community. With a learning spirit, a willingness to seek changes, and sound fundamentals in science and engineering, biomedical manufacturing has ample opportunities for innovation and growth.

3.1 Characteristics of Biomedical Manufacturing. Six unique characteristics that distinguish biomedical manufacturing are discussed below.

3.1.1 Highly Regulated Products and Services. Healthcare is highly regulated. Hospitals need to be accredited by a nationally recognized accrediting body, and physicians need to be board certified periodically in their relevant specialties. The Center for Devices and Radiological Health (CDRH) of the FDA is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the US. Medical devices in the US must meet FDA GMP and quality system regulation (QSR) guidelines. For most countries, a governmental regulatory organization

like the FDA's CDRH exists to ensure the safety and effectiveness of medical devices. New medical devices have to be approved by the FDA via a premarket notification (also known as a 510 (k)), which applies to a device substantially equivalent to an existing legally marketed device, or a premarket approval (PMA), which applies to new devices that support/sustain human life or are of substantial importance in preventing the impairment of human health.

Regulatory requirements become barriers for some, but can serve as opportunities for other healthcare service providers and medical device manufacturers. Government regulation can be used beneficially in the setup of a respected worldwide standard and elevates the level of international competitiveness. An example that reflects such a situation is the diesel engine emission regulations set by the US Environmental Protection Agency (EPA) in the past three decades. These emission regulations have elevated the technology and competitiveness of US diesel engine manufacturers such that they have become the world's leaders. It has already been shown that biomedical manufacturing, which is also under stringent and changing governmental regulations, will also benefit from the oversight of an effective government organization.

3.1.2 Highly Connected to the Insurance and Legal Sectors. In addition to the healthcare sector, the insurance and legal worlds are closely associated with biomedical manufacturing in matters of regulation, service, and product warranty. The decisions of an insurance company concerning the reimbursement of medical fees are critical to the success and cost of a device or service. Medicare is the largest healthcare insurer in the US and is also influential in its own reimbursement decisions on the success of a medical procedure or product. Due to regulatory and legal costs, the price markup of a medical device is very high, which, in turn, contributes to the high overall cost of healthcare.

3.1.3 Low Ratio of Material and Manufacturing Cost to Sale Price. Compared to the final market price of a medical device, the share of material and manufacturing costs is typically very low. This is due to the low production volume and high cost for legal fees, seeking insurance approval, regulatory compliance, and research/development. It is common that the yield for medical devices is more important than its cycle time in production.

3.1.4 No-Mistake Manufacturing. A landmark report by the Institute of Medicine, National Academy of Sciences in 1999 [20] pointed out the startling estimate that 44,000–98,000 people die each year in the US because of mistakes by medical professionals. The methodology and impressive results in the reduction of errors in aviation and manufacturing have been cited as benchmarks for healthcare to aim for [21]. The consequences of a mistake in a hospital or of a product failure inside a patient are dire. Product recalls are frequently followed by costly and lengthy legal proceedings, which are detrimental to providers and patients. There are ample opportunities to apply the technology and experience gained in manufacturing to prevent and reduce errors in healthcare.

3.1.5 Just-in-Case Production System. Product inventory and logistics in healthcare demand that the product be absolutely ready at the point of use, such as in a surgical operating room. This feature has made all healthcare providers and medical device manufacturers and distributors carry a large inventory to make sure that the right product is available at the point of use. This is named the "just-in-case" production system, in contrast to the just-in-time production systems in industrial manufacturing. This high inventory level is again reflected in the overall cost for healthcare.

3.1.6 High Level of Facility Management. Hospitals are subject to a regular board review. Any facility that manufactures medical devices is subject to random FDA inspection. Healthcare service and medical device manufacturing facilities require consistent and high levels of sterilization, cleanliness, and organization, along with clearly specified instructions to ensure sterilized operation to meet regulatory requirements.

3.2 Two Additional Characteristics of Medical Device Manufacturing. For medical devices, two additional characteristics are discussed below.

3.2.1 Advanced Materials and New Manufacturing Processes. The creation of advanced materials is the enabling technology for future medical devices. New metallic, polymer, ceramic, and foam materials (many are biocompatible) have been developed for biomedical applications. These new materials usually require new manufacturing processes to create the final shape, with desired bulk and surface properties. In addition, the knowledge of the behavior/properties of these new materials in manufacturing is typically lacking. Innovative manufacturing engineering is important and valuable for the development of new processes to convert these advanced materials into useful medical device components with consistent quality.

3.2.2 Miniature Feature Size, Tight Tolerances, and Unique Surface Features. Most medical devices incorporate precise miniature features to enhance performance. Manufacturing technologies need to achieve the required geometrical and dimensional tolerances and surface features. Surfaces of medical devices in contact with the human body usually require unique features, such as highly polished surface finishes or specialized textures, to promote healthy tissue-biomaterial interactions. The tribological phenomena occurring between tissues and device surfaces represent an open, untapped research field with little in-depth understanding.

3.3 Comparison of Biomedical and Automotive Manufacturing. Automotive manufacturing is commonly used as an example to illustrate the similarities and differences between traditional manufacturing and biomedical manufacturing. In terms of similarities, both are highly competitive and change rapidly as technology evolves. Both require timely technical innovations and management. The fundamental knowledge and skills required for biomedical and industrial manufacturing are the same. In contrast, the production volume in biomedical manufacturing is typically lower and more labor intensive. Manufacturing in healthcare has a higher growth rate, smaller size of product, lower production volume, tighter government regulation, more difficulty in testing long-term effects, higher costs, and more severe penalties for mistakes in design and/or manufacturing.

3.4 Engineering Needs in Biomedical Manufacturing. Manufacturing engineers in the highly regulated industry of biomedical manufacturing need to have a new set of knowledge and skills beyond the traditional expertise in machines, processes, and quality control. New knowledge in regulatory science, tissue-material interactions, legal compliance, advanced statistical quality control, and anatomy and physiology are required in the no-mistake and just-in-case production systems of biomedical manufacturing.

In the current world of globalization and an aging society, healthcare remains a localized service. In the past, patients did not often travel long distances to worldwide centers of excellence for treatment because of the needs for immediate care and family assistance, financial constraints, or insurance. Several new trends, such as overseas medical visits and home care, are emerging, but have uncertain future for expansion. What is certain is that the biomedical manufacturing, its market, and its research are global. Global perspectives and training are thus necessary for the next generation of biomedical manufacturing engineers.

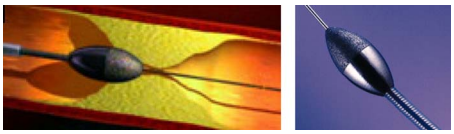

Fig. 4 Rotational atherectomy for grinding of plaque (courtesy of Boston Scientific)

4 Examples of Biomedical Manufacturing

To illustrate the broad concept of biomedical manufacturing, two examples, the grinding and cutting of plaque in interventional cardiology and surgical thermal management to prevent nerve damage, are presented.

4.1 Interventional Cardiology. Cardiovascular disease is the number one cause of death in the US, as well as in most of the developed and developing countries. In the US, a total of 6.8 million inpatient cardiovascular operations were performed in 2003, including 1.3 million cardiac catheterizations [22]. The most common type of heart disease is the buildup of plaque (deposits of fatty tissue), also known as atherosclerosis. As plaque accumulates in the coronary artery, it limits the supply of blood to the heart. This section reviews three methods (grinding, cutting, and stenting) to remove plaque blockages from blood vessels, which are routinely reopened, and discusses the connection to biomedical manufacturing.

4.1.1 Rotational Atherectomy: The Grinding of Plaque. Rotational atherectomy, as shown in Fig. 4, is a catheter-based procedure to pulverize plaque within a coronary artery [23]. During rotational atherectomy, a high speed (about 200,000 rpm) diamond coated grinding wheel, called a rotablator, is guided to the plaque via a catheter, which is a thin, flexible, and hollow plastic tube inserted from the femoral artery and threaded through blood vessels to the heart. The grinding process breaks up the plaque into very small particles, typically with sizes smaller than red blood cells. These small particles can pass harmlessly through the circulatory system and will eventually be absorbed by the body. This process, introduced in 1993, is used in treating plaque blockages, which are (i) hardened plaque containing calcium deposits and difficult to remove by angioplasty (a mechanical expansion of the vessel by stenting or ballooning), (ii) too long for angioplasty, (iii) located at branch points or small arteries, and (iv) due to restenosis (the recurrence of a blockage) in a previously placed stent.

Rotational atherectomy is an internal tissue grinding process. The challenge in rotational atherectomy is the high, 30–50%, occurrence of restenosis. The healing process from the grinding wound in the artery often causes an overgrowth of cells and a recurrence of the blockage. For grinding engineers, the challenge is in designing the device, tool, and process that can minimize damage to the blood vessel and prevent regrowth of tissue.

4.1.2 Plaque Excision System: A Cutting System for Plaque Removal [24,25]. Plaque can also be removed using a rotating cutter in a plaque excision system, as shown in Fig. 5. This device, developed by FoxHollow, has been certified by the FDA to treat peripheral arterial disease (PAD), which causes plaque buildup in the arteries, most commonly occurring in the tibial-peroneal and femoral-popliteal vessels in the pelvis and legs. The device is again guided by a catheter to the site of the blockage. A miniature tungsten carbide cutting blade, rotating at about 8000 rpm, is activated and passed through the length of the plaque to cut or shave off the plaque from the arterial walls. The physician can reorient the cutting tool and retract/advance the tool several times until enough plaque is removed to restore normal blood flow. The removed tissue, which is analogous to the chips in cutting processes, is collected in the catheter for a postprocedure pathological analysis.

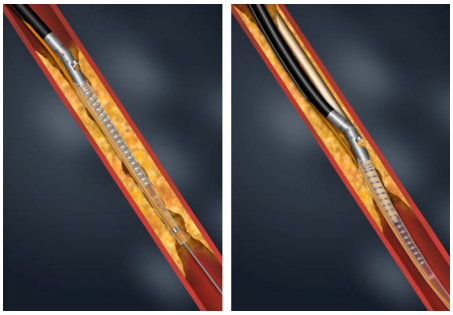

Fig. 5 Plaque excision system using cutting (courtesy of FoxHollow)

Plaque excision is a tissue cutting process. It is a good demonstration of the machining application in medicine, here treating the tissue as a workpiece. The micromanufacturing used to produce the miniature cutting tool is essential in enabling this medical technology.

4.1.3 Stent Manufacturing. A stent is an expandable wire mesh or hollow perforated tube that is inserted into a hollow structure of the body, such as a blocked coronary artery, to keep it open. Stent procedures are now conducted routinely, and a large quantity of stents is produced annually. In 2003, 664,000 angioplasties were performed in the US to remove obstructions in coronary arteries. A stent was inserted during 86% of these angioplasties [22].

Stents are commonly manufactured by precision laser cutting of a thin medical grade stainless steel tube [26], followed by microabrasive blasting [27], or other surface conditioning processes to remove the heat-affected layer and improve the surface and mechanical properties of the stent. The development of both drug-eluting and fine mesh stents has changed the treatment of coronary artery disease.

4.2 Tissue Machining and Surgical Thermal Management. Tissue machining is defined as the cutting and coagulation of tissue and blood in surgery. As far back as the Neolithic period, heat has been used to coagulate or to stop bleeding. Surgeons used to operate using a heated sharp blade to cut and coagulate tissue at the same time in surgery. This old technology has been replaced by modern energy-based electrosurgical and ultrasonic devices.

The first electrosurgical generator was developed by Cushing, a medical doctor, and Bovie, a physicist, in 1928. The basic principles used in electrosurgery are the electrical discharge machining (EDM) and resistance heating. Because human nerve and muscle stimulations cease at frequencies over 100 kHz [28], the electrical energy of alternating current of higher frequency (typically from 300 kHz to 1000 kHz) can be used safely to generate the sparks used to cut (or dissect, in medical terminology) and heat for coagulation.

Ultrasonic surgery uses a blade vibrating over 20 kHz to generate heat and denature tissue protein. Pressure exerted by the surface of the blade on tissue collapses blood vessels, allowing the coagulum to form a hemostatic seal. This process is similar to ultrasonic machining without abrasive particles.

Heat is necessary in surgical tissue machining for coagulation. Without coagulation, blood would spread around the area of the cut and block the view of the operating surgeon. However, heat has the significant side effect of damaging local tissue at high enough levels and, more importantly, the nerve or neurovascular bundle (NVB) near the surgical site [29,30]. Tissues are very sensitive to temperature. The threshold temperature for tissue damage typically starts at around 39 to 43 °C. This is particularly important in some surgical operations: prostatectomy and hysterectomy

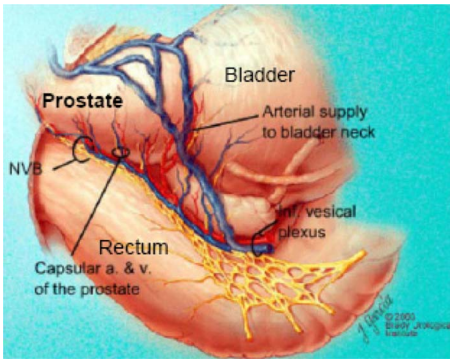

Fig. 6 Prostate and the NVB (courtesy of Brady Urological Institute, Johns Hopkins University)

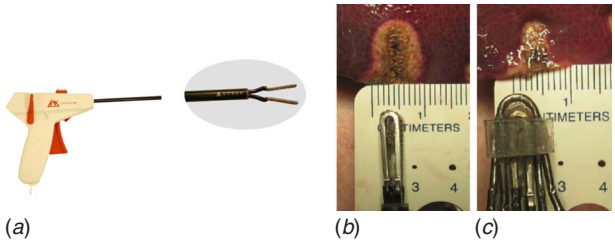

Fig. 7 Bipolar surgical thermal management: (*a*) a GyrusACMI laparoscopic bipolar surgical device, (*b*) tissue thermal damage on in vivo porcine spleen tissue using the bipolar surgical device, and (*c*) the cooling channel and corresponding reduction of tissue thermal damage in the porcine spleen test

procedures and neurosurgical operations, in general.

Every year in the US, over 167,000 men undergo prostate cancer surgery or have a prostatectomy (partial or complete removal of the prostate) [31]. This number increases due in part to advancements in screening that have made the early diagnosis of prostate cancer possible. The NVB, as shown in Fig. 6, is adjacent to the prostate. To completely remove a cancerous prostate surgically, heat from a surgical device for coagulation inevitably needs to be close to NVB. The heat from tissue coagulation can damage the NVB, resulting in up to 71% permanent loss of potency and urinary control capability, as reported by the study of Walsh et al. [32] at Johns Hopkins University.

Annually, over 600,000 women in the US have a hysterectomy, which entails the complete removal of the uterus [22]. The hysterectomy is the second most widely performed surgical procedure for women, second only to the cesarean section. This surgical procedure comes with the danger of increased urinary incontinence, up to as much as 40%, due to the thermal damage to NVB in surgery [33]. With the understanding of neural thermal damage, the robotic-assisted surgery with higher magnification and better dexterity to tie the blood vessels without extensively using energy-based surgical devices has been developed and adopted by surgeons to prevent NVB thermal damage.

Along with robotic surgical procedures, another recent development to protect against thermal damage to nerves is a STMS, based on advanced machining technology, which works to minimize thermal spread in energy-based surgical procedures. The problem is analogous to that of minimizing the thermal damage of the tool and workpiece in machining. New surgical procedures with better thermal management can reduce morbidity and preserve a postoperative quality of life for patients. This is becoming even more important because patients that are diagnosed with prostate and uterine cancer are now typically younger and healthier than those in the past [34]. Proper control of thermal damage during surgical procedures can also offer reduced tissue thermal damage and shortened recovery time after surgery.

Nerve tissue is especially vulnerable to thermal damage. Sapareto and Dewey [35] developed a relationship between tissue temperature and time of exposure until tissue death into a thermal dose model. All thermal doses are correlated with a corresponding dose at 43°C. In this model, tissue death is reached when the equivalent thermal dose at 43°C reaches an application time of 120 min. The definition of a tissue thermal dose $D(x,y,z;t)$, also known as cumulative equivalent minutes (CEMs) at 43°C, as a function of the treatment temperature $T(t)$ and time t, is

$$D(x,y,z;t) = \text{CEM at } 43°\text{C} = \int_0^t R^{[43-T(x,y,z;\tau)]} d\tau \qquad (1)$$

where R is an empirical constant. $R=0$ for $T<39°$C, $R=0.25$ for $39<T<43°$C, and $R=0.5$ for $T>43°$C.

The medical community has studied the hypothesis that surgical heat damages nervous tissues, which causes impotence and urinary control problems, in radical prostatectomy procedures. Research using open, instead of laparoscopic, surgery with unheated blades to remove a prostate was carried out by Catalona et al. [36], Walsh et al. [32], and Ahlering et al. [37]. Improved postoperative potency rates of 68–86% were reported. However, bleeding due to the lack of heat to aid coagulation was a challenge for the surgeons. Blood frequently blocked the visibility of the operative area, and the surgical time was extended. Further studies revealed that current laparoscopic, nerve-sparing prostate surgery has great variability in postoperative potency rates, depending on the surgical skills of the doctor [38]. Using a canine model, Ong et al. [29] confirmed the hypothesis that the current dissection procedure can result in NVB damage and poor postoperative potency outcomes due, again, to thermal damage of the NVB.

Machining research has studied workpiece thermal damage and heat partitioning between the tool and workpiece for decades. The technologies of workpiece thermal management can be readily applied to minimize collateral thermal damage to nerves and other tissues in surgery [39]. An example of the bipolar electrosurgical device made by GyrusACMI and the closeup view of its tip is shown in Fig. 7(*a*). Ice water flowing through the thin stainless steel cooling channel was shown to prevent heat from spreading out from the heated area during electrosurgery. Figure 7(*b*) demonstrates the effect of thermal spread in the *in-vivo* porcine spleen tissue after coagulation without the cooling channel. Using the same setup, but with the modified tip (surrounded by the cooling channel) shown in Fig. 7(*c*), the thermal spread outside the tip area is minimized. Quantitative tissue temperature measurements have further validated the observation.

5 Teaching of Biomedical Manufacturing

Education is an important part of biomedical manufacturing. A new senior undergraduate/first-year-graduate level course in Biomedical Design and Manufacturing has been developed. This new course is aimed at engineering students who are interested in learning biomedical manufacturing and who seek a career path within the medical device and healthcare industry. This course provides an opportunity for physicians and medical school faculty to mentor an engineering student team. Many medical researchers have innovative ideas, and they want to collaborate with engineers to realize these ideas. Engineering students, meanwhile, seek to learn more about the medical field and hope to work on medical device or healthcare service development. The goal of this course is to meet both needs.

This new course is designed to give students both the breadth and depth of knowledge in biomedical manufacturing. The breadth is accomplished by lectures in three sections. Fundamentals of biomedical design and manufacturing are taught in Sec. 1, lasting for 6 weeks. These lectures seek to provide an overview of

anatomy, physiology, tissue-biomaterial interactions, regulatory science, FDA GMP, manufacturing processes and systems for medical devices, and financial and operational functions in healthcare service. Section 2 features guest physicians and healthcare personnel that speak about their topics of expertise, including cardiovascular technology, surgical instruments, orthopedics and implants, endoscopy, neurosurgery, medical imaging, biomedical materials, hospital material and patient scheduling and flow, etc. Section 3 of the course is used to visit healthcare centers and medical device manufacturers.

The depth of knowledge is gained through working on two projects. The first is a midterm project to survey a medical technology, identifying its historical progress and future design/manufacturing needs. This is a relatively short individual project including a report and class presentation as deliverables. Sample projects include surveys of blood pressure monitoring, heart valves, magnetic resonance imaging (MRI), computed tomography (CT) scanning, artificial knee and hip joints, diabetes monitoring, endovascular grafting, etc. The second project is a semester long project, which is conducted by a team of two to three students and sponsored by either a physician or a medical device manufacturer. This project starts at the beginning of the term and lasts for the whole semester, with periodic milestone reviews. Physicians usually bring engineering students to their practice to watch operations, understand needs, and brainstorm ideas. The semester projects also include periodical reviews and an extensive report and presentation to sponsors.

Several valuable lessons have been learned after offering this exploratory course. First, it is difficult to separate design and manufacturing. Since biomedical manufacturing is not a mature research area, it is inevitable that design and manufacturing are intertwined. Second, it is important to establish a group of collaborators in the healthcare system and the medical device industry before offering this course. Third, sponsors need to commit their time to the project and also have a willingness to build a long-term education and research program with engineering. Fourth, the development needs to have a market in mind. Many good designs cannot proceed because of the lack of feasible route for commercialization.

6 Concluding Remarks

Biomedical manufacturing has been defined, starting with the hospital-factory analogy with an aim to broaden the scope of manufacturing research to include biomedical technology and healthcare services. Examples including the application of grinding and cutting for plaque removal as well as surgical thermal management to prevent nerve damage were used to demonstrate the underlying concept of biomedical manufacturing. The characteristics and engineering needs of biomedical manufacturing were also described.

It is the author's hope that this paper will encourage more researchers in manufacturing to seek collaborators in the medical device and healthcare service. Manufacturing engineers can apply their knowledge and skills to biomedical manufacturing research and eventually make a positive impact to the society.

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