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3D Printing and Bio-Based Materials in Global Health

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3D Printing and Bio-Based Materials in Global Health

An Interventional Approach to the Global Burden of Surgical Disease in Low-and Middle-Income Countries

Springer

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Preface

In taking a step back and looking at our world through a macroscopic lens, we soon realize that we are all functional constituents within the realm of global health and its sphere of influence. Global health affects everyone, in which threats to our health and well-being are prominent all around us, yet we as human beings have the innate capacity to challenge these threats and derive solutions through technological innovation and scientific breakthroughs. But what if these innovations and breakthroughs were only available and adapted to one segment of the population, while millions of others who desperately need these innovations have no access? Imagine if millions of people still die each year due to conditions that could be easily adverted and remedied by basic medical care…quite a shocking paradigm isn't it? We characterize this paradigm as the "global burden of surgical disease", a complex and multi-faceted global health threat that is not only characterized by the medical conditions and maladies it comprises, but also of the lesser-noted social and economic conditions upon which it afflicts. This is a unique "disease pathology," in which it is not defined by a microscopic entity such as a viral or bacterial agent, but rather by a host of surgically-treatable conditions clouted by social and economic components that influence the delivery of palliative surgical care.

While specifically these surgically treatable diseases are not classified as disease-pathologies, the manner and scope in which they impact human health is indeed quite similar. Specifically, the dissonance between healthcare access and delivery between different economic tiers of countries is staggering and allows for global health threats, such as the surgical burden of disease, to perpetually prey on low- and middle-income countries. A question that both my co-author and I have always pondered as researchers is, "how can we live in a modern era which is graced by continual advancements in science, engineering, and medicine, but still have millions of individuals that do not have access to these innovations, and in turn, suffer perpetually or succumb to conditions that could be easily remedied?" This question has no doubt crossed the minds of many researchers, and serves as a pillar of reflection and an impetus for future research initiatives.

In this book, we take a unique and integrative approach to examining the global burden of disease and in particular, the surgical burden of disease. We examine the

interventional capacity for modern technologies and innovations to be applied, adapted, and directly sourced in low- and middle-income countries. We specifically examine the interventional capacities of 3D printing technologies to fabricate surgical instruments and tools to be utilized to enhance surgical care and delivery in resource poor settings. In further following the true tenets of intellectual curiosity and innovation, we take a unique focus on the use of natural and sustainable bio-based materials in fabrication of these medical devices. In this book, we derive a multifaceted approach that examines everything from the social and economic elements related to the burden of surgical conditions on human health, to examining the tenets of applied frugal engineering of 3D printing technologies and the global medical device supply chain, to that of the materials science behind bio-based materials.

We first begin by setting the stage for the global burden of disease, in which we describe the economic tiers that countries are organized into and their respective capacities to deliver palliative care. We specifically define what types of surgical conditions are classified as "essential" and explore the premise of "surgically avertable deaths" and the social and economic impacts of surgical care. We further define the disparities in the access to surgical supplies amongst countries, and then explore a potential remedy for this supply shortage via the use of 3D printing technologies. Specifically, we discuss the use of RepRap 3D printing devices and break these technologies down to their fundamental components and processes, and examine the use integration of frugal engineering to adapt these technologies for resource poor settings. We then further explore the complementary use of 3D printing devices with bio-based materials, further expanding upon the chemical and physical materials profile of various printing filaments such as polylactic acid. We then transition to the feasible application and process analysis of utilizing these devices and their modified bio-based material components to fabricate a cohort of surgical instruments and tools to efficiently and effectively create a surgical toolkit for deployment in the surgical field. Lastly, we delve into the interventional capacities of 3D printing technologies coupled with bio-based materials in the global health field and their respective applications in low- and middle-income countries. The book examines the associated barriers to entry and adoption of these technologies as well as their impact on global medical device supply chains and the future realm of applications to improve global health.

While we indeed focus on only a subset of conditions and elements that contribute to the overall global burden of disease, we hope to foster intellectual inquiry and reflection by our readers and provide a platform that can effectively inform future policy decisions related to how we tackle the most pertinent health threats in our world today. It is through knowledge and inquiry, that we can effectively transform the theories of today into the interventions of tomorrow.

Cambridge, MA, USA

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Chapter 1
The Current Global Surgical Care Paradigm: An Introduction

Approximately 5 billion people around the world do not have access to safe, affordable surgical services when needed (Meara et al., 2015). In further exploring the nature of this startling figure, an interesting trend becomes further apparent. Inequities related to access to surgical services becomes stratified based upon relative income distribution of countries. Simply stated, accessibility to surgical services varies in each country based upon their respective income classification. The World Bank classifies countries according to four income groupings, in which income is measured using gross national income (GNI) per capita, in U.S. dollars (Debas et al., 2015). These four classifications are as follows: low-income countries (LICs) = $1045 or less, Middle-income countries (MICs) which are subdivided into lower-middle-income = $1046 to $4125 and upper-middle-income (UMICs) = $4126 to $12,745, and finally high-income countries (HICs) = $12,746 or more as shown in Fig. 1.1 (Debas et al., 2015). Upon examination of these income classifications, stratification in accessibility to surgical services becomes evident, with the countries having the lowest gradients in accessibility to surgical services being that of low and middle-income countries (LMICs).

In LMICs, nine out of every ten people cannot access basic surgical care, which equates to approximately 2 billion individuals in LMICs that have almost zero access to essential surgical services (Debas et al., 2015). Of these 2 billion people, over 1.5 million people each year die of surgically treatable and preventable conditions that were not adequately treated due to a lack of access to properly equipped district-level healthcare facilities (Debas et al., 2015). These surgically treatable conditions include injuries, malignancies, pregnancy complications, abdominal emergencies, and congenital anomalies, all of which could be prevented by improved access to basic surgical care (Mock et al., 2015). These conditions are typically viewed as low-risk in high-income countries (HICs), which have the highest gradient of surgical care and infrastructure to treat these conditions. In LMICs however, these surgically treatable conditions become exacerbated and chronic in nature, creating a perpetual dissonance in the health and overall well-being of these individuals. The chronic nature of these conditions can result in both

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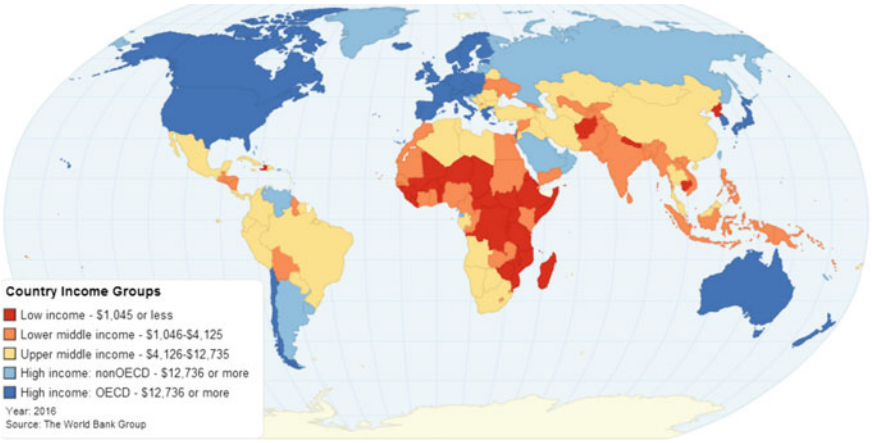

Fig. 1.1 World Bank country income group classifications (Country Income Groups 2011)

short and long-term effects not only related to an individual's health, but also their social, economic, and human capital, which can in turn affect the dynamics of local communities, and ultimately, the wellbeing of entire countries themselves.

Upon comparison of the access and delivery of surgical care in HICs versus LMICs, the disparities in provisional care are staggering and cause for great concern. Nearly 60% of all surgical operations take place in HICs, where only 15% of the global population lives, yet only 7% of surgical operations are performed in LMICs, where over 35% of the global population resides (Alkire et al., 2015). Specifically, of the 313 million surgical procedures undertaken worldwide each year, only 6% occur in LMICs, where over a third of the world's population resides (Meara et al., 2015). This dissonance in the volume of surgery allocated between HICs and LMICs is prominently depicted in Fig. 1.2. HIC countries such as the United States generally perform more than 10,000 surgeries per 100,000 individuals in the population, whereas LMIC countries such as Africa or India perform less than 500 surgeries per 100,000 individuals (Debas et al., 2015; Weiser et al., 2008). These statistics uncover a clear notion of dissonance displayed amongst the provisional surgical care capacities and accessibility gradients amongst various countries.

Given the low volume capacity for surgical interventions in LMICs, there are a number of critical surgical procedures that are particularly underperformed in LMICs. The most prevalent surgically treatable conditions that often plague LMICs include: abdominal emergencies, road traffic injuries, congenital abnormalities, pregnancy complications, fractures, burns, and acute infections (World Health Organization, 2014). Without adequate surgical intervention for these conditions, profound implications can incur, including that of permanent disability and death. General, obstetric, and trauma surgeries are the most critical surgical interventions that are often underperformed in LMICs and must be increased into further remedy the frequency of the conditions noted above (Debas et al., 2015). Pregnancy compilations often require obstetric surgical intervention in the form of cesarean section,

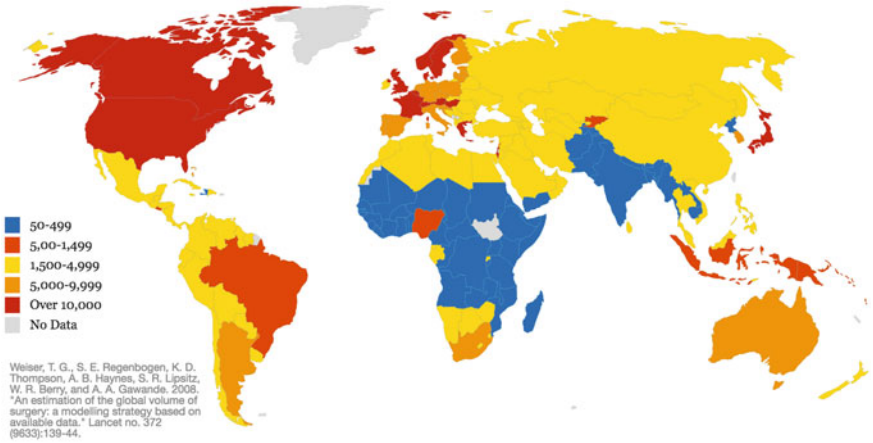

Fig. 1.2 Global volumes of surgical interventions per 100,000 individuals amongst HICs and LMICs (Weiser et al., 2008)

dilation and cutterage, cervical tear repair, obstetric hemorrhage control, and placental extraction (Debas et al., 2015). The provision of these obstetric surgical procedures are often underperformed in LMICs due to inaccessibility to medical supplies, hospital infrastructure, or medical personnel. General surgeries such as gall bladder removal, appendectomies, hernia repairs, infection incision and drainage, and tumor resections, are also underperformed and are much needed to reduce the burden of disability in LMICs (Debas et al., 2015; World Health Organization, 2014). Of these general surgical procedures, a commonly needed surgery is that of hernia repair, specifically that of umbilical, incisional, epigastric, inguinal, and hiatal hernias (Debas et al., 2015). In addition to the limited capacity for obstetric and general surgical capacities, trauma surgeries related to abdominal emergencies such as gastrointestinal perforation, intussusception, obstructed hernia, neonatal intestinal obstruction, appendicitis, and adhesive bowel obstruction are often underperformed and require perforation repair, hernia repair, and obstruction extraction procedures (Debas et al., 2015). Other trauma interventions related to road traffic incidents, a highly prevalent phenomenon in LMICs, are often limited in scope including closed and compound fracture treatment as well as burn treatment (Debas et al., 2015).

Although continual innovations in science, technology, and medicine are made on a daily basis, there is still a large segment of the global populous that does not have access to the most basic and essential elements of healthcare. The true tragedy lies in the fact that millions of individuals in the present state of humanity succumb to conditions and ailments that are easily treatable and remedied through access to basic surgical care. An interesting facet as noted by officials at the World Bank and the World Health Organization, is that although surgical care is deemed as an essential component in any functioning healthcare system, it has often been overlooked and even neglected within the realm of global health (Farmer & Kim, 2008). Upon acknowledgement of this revelation, research must further define the critical

role that surgery can play in global health, specifically that of addressing what is known as the "global burden of disease," specifically that of the "global burden of surgical disease" (Bickler, 2013).

1.1 The Global Burden of Surgical Disease: An Unubiquitous Global Health Threat

The global burden of disease (GBD) is defined as the entities responsible for disability and death amongst people across countries, time, age, and gender (Wang et al., 2016). The GBD is a comprehensive epidemiological study and tool that was formulated by the Institute for Health Metrics and Evaluation at the University of Washington in Seattle, in order to quantify health loss from hundreds of diseases, injuries, and risk factors (Wang et al., 2016). Each and every year, a new global burden of disease study is released that further examines the functional contributing elements and entities that are responsible for disease and health trends in various countries around the world. These contributing elements and entities include pathologies such as neonatal conditions, malaria, HIV/AIDS, diarrheal infections, malnutrition, and non-communicable diseases such as heart disease, stroke, and cancer (Wang et al., 2016). Upon assessment of the global burden of disease, the functional utility lies in the ability to derive targeted interventional strategies to improve and eliminate disparities experienced in various global health systems (Wang et al., 2016). As societies continue to advance and develop, the functional burden of disease affecting the human populous begins to change in a dynamic fashion, ultimately contributing to the ever-changing nature of the GBD. Innovations in the form of vaccines, drugs, and strategic public health interventions have significantly shaped and fundamentally altered the GBD in the last 100 years (Alwan et al., 2010). The latest GBD study was released in 2016, and provides comprehensive epidemiological analysis of the most current and up-to-date trends in human health and mortality.

The 2016 GBD study provides a functional analysis of an array of factors and elements that contribute to the global burden of disease, in which these factors are not only unique in the disease pathologies that they represent, but also in the socio-economic, cultural, and geographic arenas upon which they affect. For example, countries located in Sub-Saharan Africa experience a disproportional susceptibility to acute watery diarrheal diseases due to a lack of infrastructure that can provide clean water. Whereas developed countries such as the United States experience a disproportional susceptibility to heart disease and cancer, conditions that generally afflict affluent countries. As previously mentioned, the GBD is dynamic in nature, but recent epidemiological studies have identified a unique paradigm shift in the GBD that has been to manifest in the past decade. Non-communicable diseases (NCDs), injuries, and traumas have claimed increasingly more lives throughout the world, indicating a focal shift in human mortality from the most commonly touted communicable infectious diseases such as malaria and HIV/AIDS, to that of NCDs, injuries, and traumas. Upon acknowledgement of

this trend shift in the GBD, interventional strategies and capacities must be adapted to circumvent continued loss of life. One key element in addressing this shift in GBD includes adapting interventional strategies related to surgery, to remedy what is known as the "global burden of surgical disease."

In reflecting upon the global health threats that we as the human populace face in this day and age, we are inclined to perceive recollections of human suffering primarily at the hands of infectious agents such as HIV/AIDS, cholera, or malaria, all of which have been focal elements in the global disease burden. Infectious diseases are ubiquitously associated as prominent global health threats, in which eradication of such diseases can alleviate suffering on a global scale. While this is indeed certainly true, the true global burden of disease expands beyond just the realm of infectious agents to include other elements. What if there were global health threats present today that are not of infectious origin, but rather that of common, easily treatable conditions? Imagine if these treatable conditions become so chronic in nature that they plague and kill millions of people around the world to this day? These questions can be both described and accounted for in what has been recently described as the "global burden of surgical disease" (Bickler, 2013; Farmer & Kim, 2008). This is a specific segment of the GBD that focuses on examining the functional public health burden that surgically treatable conditions can have on the overall quality of life of individuals and the general global populace as a whole.

In tackling the global burden of surgical disease, it is obvious that expansion of the surgical interventional capacity of countries on a global scale is critical, as more and more health conditions related to NCDs, injuries, and traumas can be remedied with proper surgical intervention. Conditions that can be treated in a surgical manner are defined as "surgical conditions," which consists of any pathology for which an invasive procedure may provide treatment, palliation, or cure (Gunn, 2012). While surgical conditions consist of a broad spectrum of pathologies, particular interest is given to those that are deemed as "essential" surgical conditions. These surgical conditions are fundamental in contributing to the functional global burden of disease, and remedying these conditions could indeed substantially alleviate the global surgical disease burden.

1.2 Defining Essential Surgical Conditions in LMICs

In order to be classified as an essential surgical condition, distinct criteria must be met, in which the condition must be primarily or extensively treated by surgical procedures and other surgical care, the condition must occupy a large health burden, and finally, the condition must be successfully treated by a surgical procedure and other surgical care that is cost-effective and feasible to promote globally (Debas et al., 2015). These are surgical conditions for which basic interventions can provide coverage for approximately 80% of the most basic surgical needs of a community, especially in LMICs that often have scarce healthcare resources (King, Bewes, Cairns, & Thornton, 1990). The International Collaboration for Essential Surgery

(ICES) defines 15 essential surgical procedures of which can specifically provide coverage for over 80% of the basic surgical needs of communities in resource-poor settings where physicians are scarce (Cotton, 2016). These surgical interventions can be performed non-physician providers who receive specialized training in targeted surgical procedures at first point-of-care health facilities such as district-level hospitals, health centers, or primary healthcare facilities, equipped with basic surgical equipment (Cotton, 2016). This approach is formally known as "task shifting" and provides an affordable, viable, and sustainable solution that can indeed save time and most importantly, save lives (Cotton, 2016). These essential surgical conditions include: neglected obstructed labor resulting in obstetric fistula, severe post-partum hemorrhage requiring surgical care, infections resulting in abscesses that require drainage, severe wounds, severe head injury, airway obstruction, chest injury and infections, acute abdominal trauma, fractures and dislocations, severe limb ischemia, urinary outflow obstruction, hernias, cataracts, clubfoot, and cleft lip (Cotton, 2016). While task shifting does indeed serve as a viable option to remedy many basic surgical conditions, it is important to note allocation of advanced surgical care to treat certain surgical conditions such as congenital abnormalities such as neural tube defects and cleft lip and palate, eye conditions such as cataracts, and maternal conditions such as obstetric fistulas does indeed still rely on accessibility to specialized clinics shown in Fig. 1.3 (Higashi et al., 2015).

In addition to these 15 conditions, the World Health Organization (WHO) further organizes essential surgical conditions three distinct categories as depicted in Fig. 1.3. The first category is communicable, material, perinatal, and nutritional conditions, which primarily consists of maternal conditions and birth traumas. The second category is non-communicable diseases, which includes cataracts, appendicitis, skin diseases, cleft lip and palate, peptic ulcer disease, and oral conditions. The third category is injuries, which includes road traffic as well as intentional and unintentional injuries.

According to the World Bank, approximately 11% of the GBD can be treated with surgical interventions (Debas et al., 2015). Approximately 38% of injuries, 19% of malignancies, 9% of congenital anomalies, 6% of complications of pregnancy, and 4% of perinatal conditions can be treated and remedied by surgical intervention (Debas et al., 2015). In Table 1.1, the three categories of essential conditions are outlined with their corresponding number of fatalities each year. In addition to the number of deaths each year from each condition is the term "DALYs", which stands for disability-adjusted life years. DALYs are a quantitative measure of the overall disease burden expressed as the number of years lost due to ill health, disability, or early death, with time used as the common metric for mortality and health states (Alwan et al., 2010; Bickler 2013).

$$\text{DALY} = \text{YLL} + \text{YLD}$$

YLL = Years of life lost due to mortality
YLD = Equivalent Years of healthy life lost due to disability.

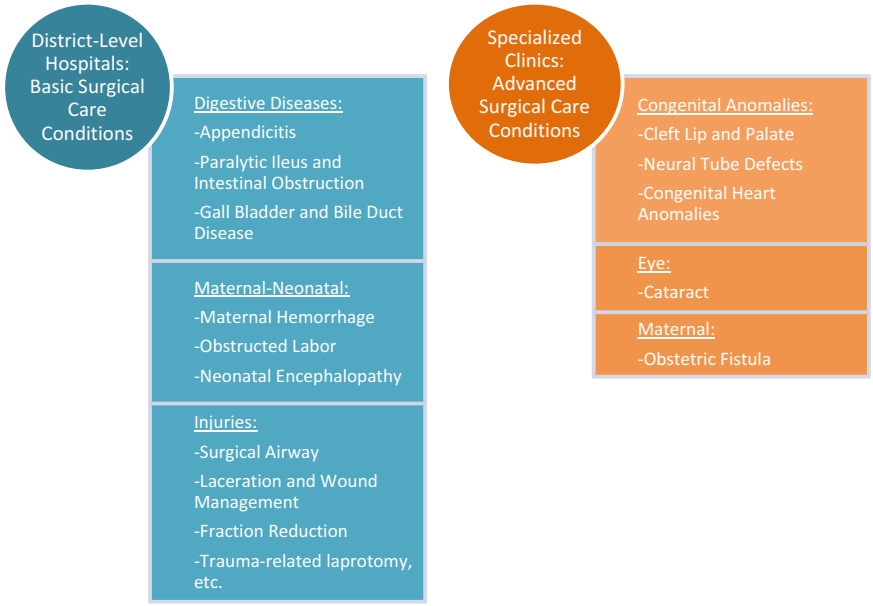

Fig. 1.3 Allocation of basic and advanced surgical care for various surgical conditions based upon healthcare facility access (adapted from Higashi et al., 2015)

Table 1.1 Three categories of essential surgical conditions, including number of deaths and disability-adjusted life years per condition as depicted (adapted from Debas et al., 2015)

Category	Deaths (thousands)	DALYS (thousands)
Category 1: communicable, maternal, perinatal, and nutritional		
Maternal conditions	290	19,000
Birth Asphyxia and Birth Trauma	790	78,000
Category 2: noncommunicable diseases		
Cataracts	<1	7000
Peptic ulcer disease	230	7000
Appendicitis	38	2000
Skin diseases	90	16,000
Cleft lip and palate	5	<1000
Oral conditions	<1	13,000
Category 3: injuries		
Road traffic accident	1160	72,000
Other unintentional injuries	1550	96,000
Intentional injuries	540	34,000
Burden from these conditions	4700	340,000
Total Burden from all causes	45,000	2,400,000
Share of Burden due to conditions addressable by essential surgery (%)	10.40%	14.20%

Based upon these statistics, it can be seen that surgery can indeed serve as a pertinent element in combating the GBD both in the short and long terms. This trend dynamic in increased mortality from NCDs, injuries, and traumas is of particular concern with regards to LMICs, which are often unsuited to support adequate treatment of these conditions. This is of particular concern, as individuals with these conditions are highly susceptible to these conditions becoming chronic and exacerbated. This ultimately leads to a perpetual state of illness or injury that can lead to catastrophic consequences in the form of lost income and human capital development. Previous studies have estimated that a minimum of 321.5 million surgical procedures would be needed in order to address the global burden of surgical disease for our entire human population of 6.9 billion in 2010 (Rose et al., 2015). In breaking down the more than 320 million surgical procedures needed, the rates of surgical need vary across epidemiological regions as shown in Fig. 1.4. Within each epidemiological region, the burden of surgical disease varies, thus the need for varying surgical procedures is distinct for each country as shown in

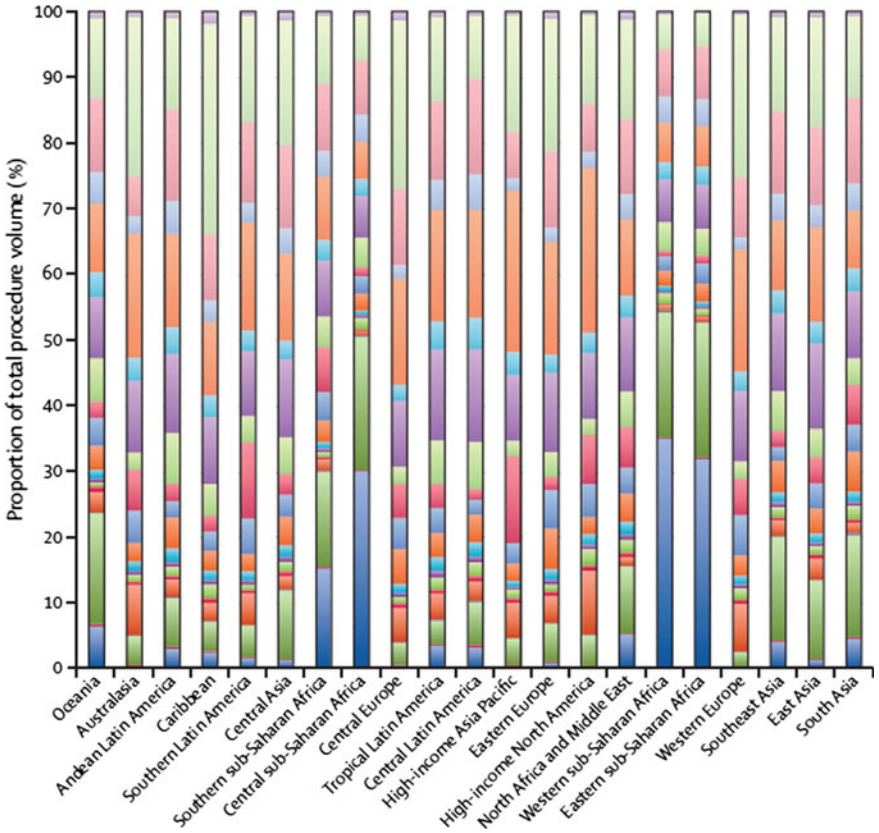

Fig. 1.4 Global surgical need estimates by country based upon World Health Organization Global Health Estimate disease subcategory (Rose et al., 2015)

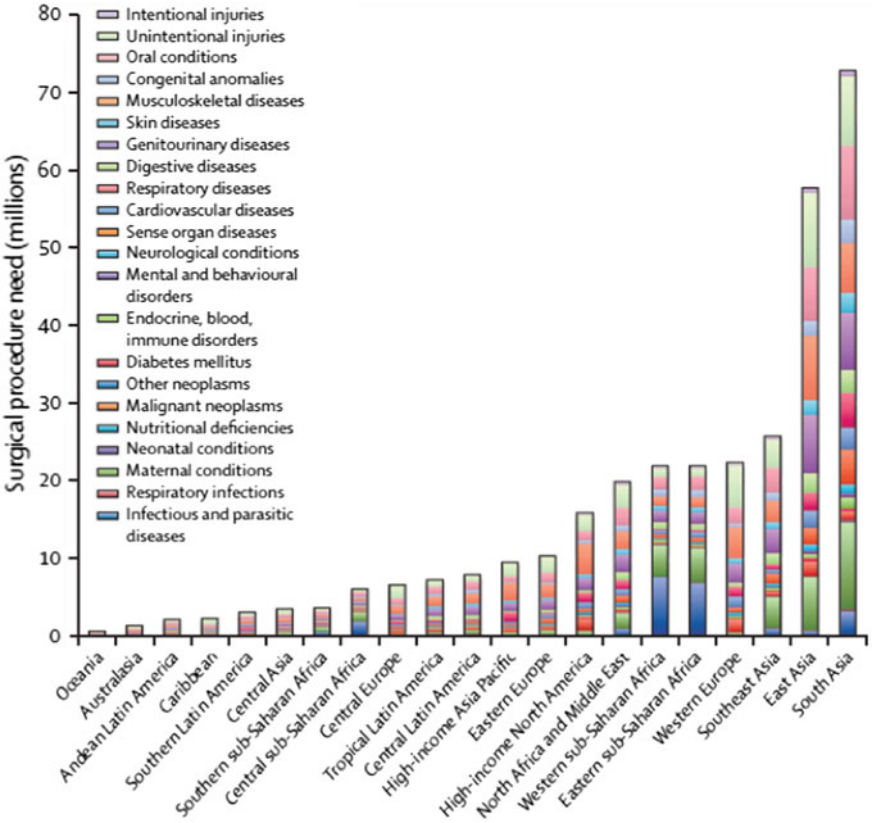

Fig. 1.5 Surgical procedure type and need based upon epidemiological region (Rose et al., 2015)

Fig. 1.5. Approximately 3383 operations per 100,000 would be needed in central Latin America, while 6495 operations per 100,000 would be needed in western sub-Saharan Africa (Rose et al., 2015). Upon examination of the various subcategories of disease, the number of surgical interventions needed varies, ranging from 131 to 412 procedures for nutritional deficiencies to more than 45 million procedures for unintentional injuries (Rose et al., 2015).

Without access to basic surgical elements, minor injuries become life threatening, common birth defects become life-long disabilities, and childbirth difficulties become obstetric disasters (Cotton 2016). This is of particular importance for pediatric patients in LMICs who hold the key to future growth, development, and advancement of LMICs. Approximately 85% of pediatric patients in continents such as Africa have a surgically treatable disorder by the age of 15 (Chao et al., 2014). In addressing these surgically treatable conditions at an earlier age, we can prevent the chronic and perpetual nature of these illnesses as these children continue to grow and develop, effectively reducing the functional burden of disease and setting the stage

for future generations of healthy individuals. Upon assessment of the GBD, it is vital that integrative solutions be garnered in a manner that can be scaled and adapted to meet the diverse healthcare needs of LMICs. The adaptability complex of these solutions must also be rooted in an interventional strategy that is financially feasible, but can still enhance surgical access and care.

1.3 Surgically Avertable Deaths: A Silent Anomaly

Over 80% of deaths from non-communicable diseases, injuries, and traumas occur in LMICs (Alwan et al., 2010). The resulting fatalities resulting these conditions are termed "surgically avertable deaths," which are deaths caused by conditions that could have been remedied and prevented via surgical intervention (Debas et al., 2015). These deaths are an often under-observed anomaly within the field of global health that is just as prominent as other health maladies. It is with proper surgical treatment that these conditions can be remedied and avert the eventual loss of life that could incur from these conditions in the short or long-terms. The functional burden of disability attributed to the lack of access to surgical care for traumatic injuries and nontraumatic chronic conditions, falls most heavily on people in LMICs (Farmer & Kim, 2008). According to the World Bank, provision of essential surgical procedures would avert approximately 7% of all deaths related to the GBD in LMICs including the primary super regions of Eastern Europe and Central Asia, North Africa and the Middle East, South Asia, East Asia Pacific, and Latin America and the Caribbean as shown in Fig. 1.6 (Higashi et al., 2015; Jamison et al., 2006). Correspondingly, this would also reduce the functional burden of disability incurred by these conditions, which is often chronic in nature and implicated in influencing the long-term health paradigms experienced in LMICs (Debas et al., 2015). There is indeed a "silent premise" related to the phenomenon of surgically avertable deaths, as the chronic and perpetual suffering of millions of people in LMICs from these conditions is often overshadowed by common fallacies that believe that modern medicine is indeed accessible to everyone. While many diseases commonly associated with global human suffering, such as cholera, malaria, typhus, and tuberculosis, result in fatality in a small timespan, surgical conditions are often quite the opposite. The reality is that a large majority of global burden of surgical disease consists of conditions that are chronic over extended periods of time. Afflicted individuals generally suffer for a prolonged proportion of their lifetimes due to a surgically avertable condition, which could be easily remedied in developed countries. The concern is that there is indeed ample time to intervene and remedy these conditions to alleviate human suffering, but often times these conditions become exacerbated and contribute to avertable death.

Upon further analysis of the concept of surgically avertable deaths, it is important to understand the underlying elements that are responsible for this increasing trend in

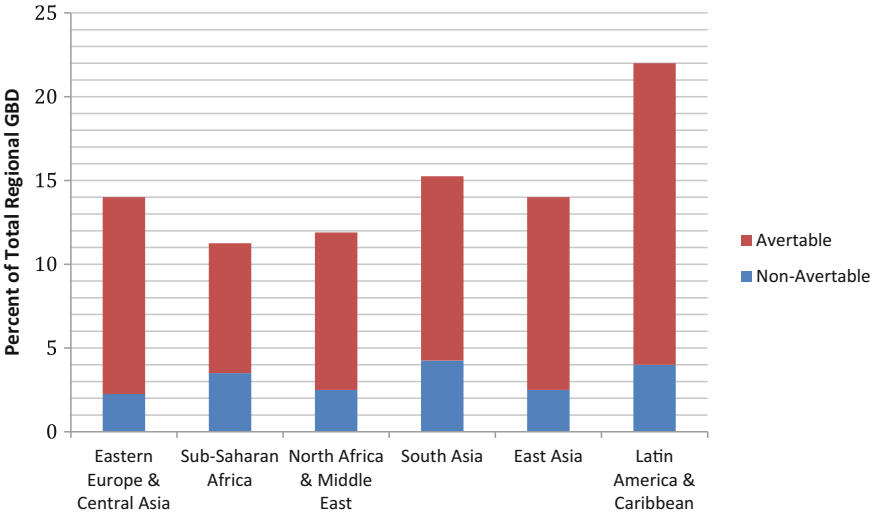

Fig. 1.6 Distribution of surgical burden by LMIC super regions including percentage of avertable and non-avertable conditions (adapted from Higashi et al., 2015)

preventable deaths experienced. One particular element that sheds light upon this phenomenon is that of the glaring disparities in the interventional surgical capacities of LMICs versus HICs. The World Health Organization Tool for Situational Analysis to Assess Emergency and Essential Surgical Care or EESC, is a tool utilized to assess life-saving and disability-preventing surgical services including emergency, trauma, obstetrics, and anesthesia in healthcare facilities (Elkheir et al., 2014). This tool has been employed in multiple studies to capture a healthcare facility's capacity to perform basic surgical and anesthesia interventions by investigating four categories of data: infrastructure, human resources, interventions provided, and equipment availability (Elkheir et al., 2014). This tool has been utilized in healthcare case analysis of multiple countries including Somalia, Tanzania, and Afghanistan (Elkheir et al., 2014). Upon employment of EESC, the results have revealed that there are enormous shortfalls in infrastructure, supplies, and access to surgical procedures at district-level health facilities in LMICs. This results in an overwhelmingly large proportion of the population having limited access to surgery, as depicted in Fig. 1.7 (Kushner et al., 2010).

In examining the disparities of surgical access amongst various countries, the global distribution of operating theaters and volume of surgery provides further insight. Nearly 2 billion people in LMICs live in areas with a density of less than 1 operating room per 100,000 individuals as opposed to in high-income countries, which occupy a density of 14 operating rooms per 100,000 individuals (Funk et al., 2010). Based upon these metrics, an estimated 140 million additional surgical procedures are needed in LMICs each year to save lives and prevent disability

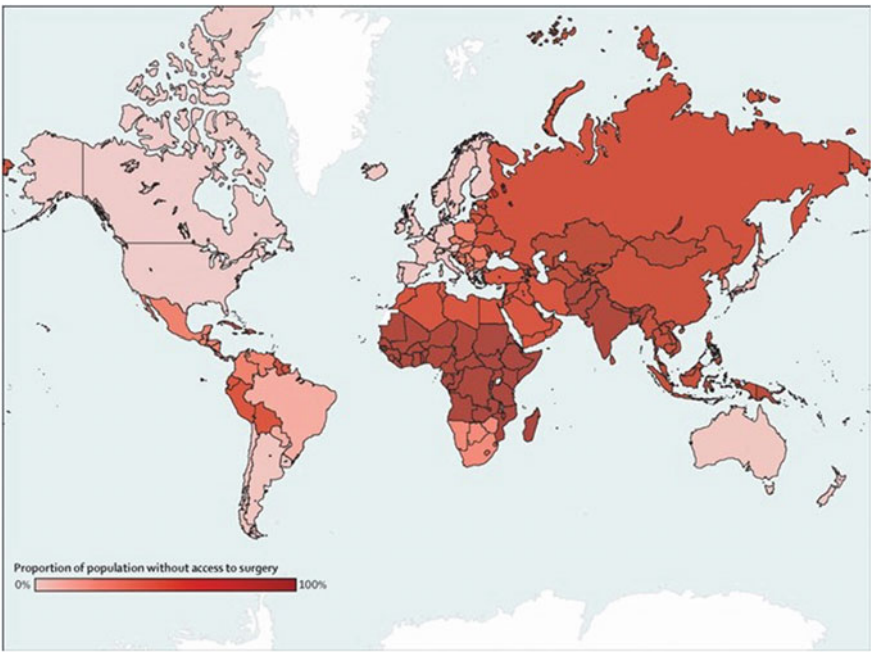

Fig. 1.7 Depiction of the proportion of the global population without access to surgery based upon geographic locality. The darker shades represent increased lack of access to essential surgical care services (Alkire et al., 2015)

(Meara et al., 2015). Previous studies have shown that low operative volumes in countries are indeed directly correlated high case-fatality rates from common, treatable surgical conditions, which indelibly contributes to the surgically avertable deaths of over 1.5 million people each year as shown in Fig. 1.8 (Debas et al., 2015; Meara et al., 2015). With this scarcity of surgical services in low and middle-income countries, the need for increased accessibility to surgical services to treat essential surgical conditions is imperative.

1.4 Surgical Interventions in Global Health: Social and Economic Implications

The delivery of emergency surgical care has long been sidelined due to perceived logistical complexity and cost (Smith et al., 2013). Human resources and science focused on global surgery as well as sustained financing mechanisms for surgical infrastructure lag behind other public health priorities, despite the growing need for access to quality surgical care (Smith et al., 2013). According to the United Nations, every $1 spent strengthening local surgical capacity generates $10 through improved

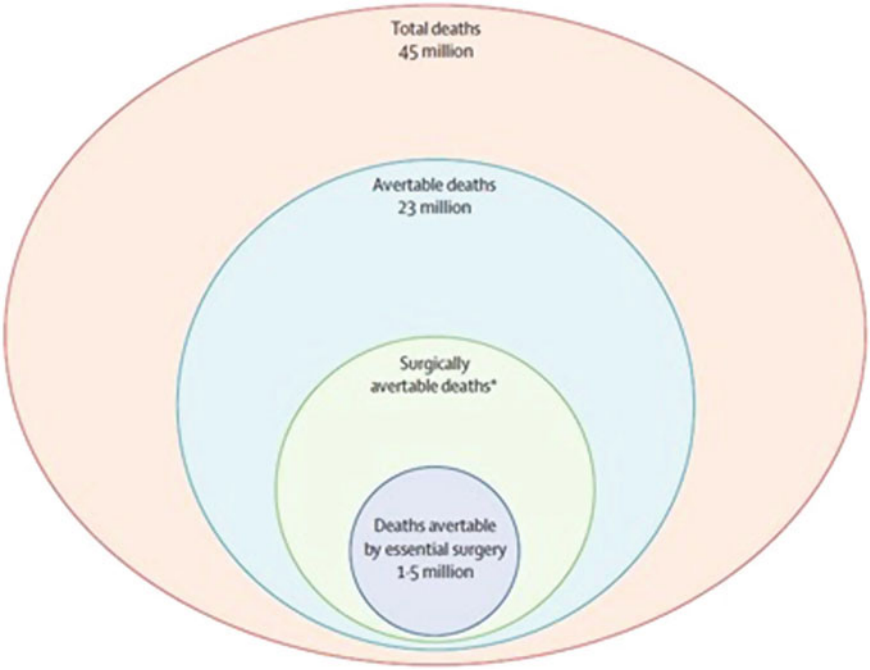

Fig. 1.8 Number of surgically avertable deaths in LMICs (Mock et al., 2015)

health and increased productivity (UN, 2013). In addition, studies have found that strengthening surgical capacity, particularly at the district-level hospital, is a highly cost-efficient solution to combating the global burden of disease (World Health Organization, 2014). WHO country assessments indicate that surgery is an integral part of primary health care and a cost-effective strategy of dealing with many health challenges specific to resource-poor settings (World Health Organization, 2010). Strengthening local surgical capacity is an approach that would provide a high degree of financial protection to populations and address the DALYs in a cost-effective manner (Jamison et al., 2006). Specifically, essential surgical procedures rank among the most cost-effective health interventions, with high-yield net positive social and economic gains (Mock et al., 2015). These social gains are in the form of increased human capital development, as a decrease in disease burden means that children less likely to miss or potentially drop out of educational institutions due to chronic illness.

Economic gains are directly related to the health of the workforce in domestic economies, in which individuals that are healthier can more readily contribute to the workforce, thus providing more income for their households and contributing to the economic well being of their respective country and community (Mock et al., 2015). This is especially true in LMICs, as a suitable number of these countries have economies that are primarily agriculturally based, with many families relying

on agricultural yields from tending to their crops. Agricultural jobs typically employ hard labor, thus it is pertinent for individuals to be healthy in order to continue to work and provide a suitable income for their families. In addition, with less money being allocated to the treatment of chronic illness, families can further invest in increased educational attainment for their children in the long run, eventually creating a socio-economic paradigm shift for communities (Mock et al., 2015). Specifically, future generations can transition from these largely hard labor-based jobs to that of more skilled positions with investment in education, resulting in higher incomes and enhanced development for these communities.

When discussing the applications of interventional surgical operations in global health, the perception of surgery as an expensive intervention does indeed serve as a barrier to widespread acceptance of its potential role in promoting global health, especially when compared with other public health measures such as vaccines or antiretroviral treatment (Chao et al., 2014). In combating this stigmatization of surgery recent studies have analyzed the cost-effective nature of essential surgery in comparison with other public health measures such as HIV/AIDS antiretroviral treatment, oral rehydration therapy, and insecticide-treated bed nets to prevent malarial infection (Chao et al., 2014). In Fig. 1.9, previous studies have determined that essential surgical procedures are indeed cost-effective in relation to other public health interventions and do yield positive net returns with regards to the cost per disability-adjusted life year adverted. Within the figure, DALYs are calculated by adding the number of years of life lost due to premature mortality to the number of years of healthy life lost related to disability, in which one DALY is defined as the loss of the equivalent of 1 year of life at full health (Chao et al., 2014). The median cost-effective ratio ($ per DALY averted) for specific interventions were: $13.78 for adult male circumcisions, $47.74 for cleft lip and palate repair, $82.32 for general surgery, $108.74 for hydrocephalus repair, $136.00 for ophthalmic surgery, including cataract and trachoma surgery, $315.12 for caesarean deliveries, and $381.15 for orthopedic surgery (Chao et al., 2014).

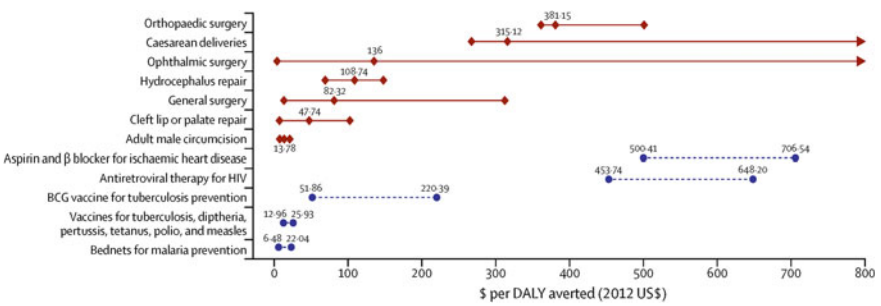

Fig. 1.9 Cost-effectiveness of surgical interventions compared to other public health interventions (Chao et al., 2014)

1.5 Catastrophic Healthcare Expenditures

In order to create increased accessibility to essential surgical services, it is vital that the burden of catastrophic health expenditures related to surgical procedures be addressed. Catastrophic health expenditure occurs when individuals or families pay fees or co-payments for health care services that surmise a large proportion of their relative income, resulting in financial catastrophe for the individual or entire household (World Health Organization, 2005). This specifically occurs whenever these expenditures are greater than or equal to 40% of a household's non-subsistence income, i.e. income available after basic needs have been met (World Health Organization, 2005). While there a general percentile threshold to deem a health expenditure as "catastrophic," any health expenditure, regardless of income percentile, that threatens a household's ability to maintain its subsistence needs can essentially be classified as catastrophic in nature (Su, Kouyaté, & Flessa, 2006). As opposed to households HICs, which are protected from catastrophic health spending by health insurance coverage or a tax funded healthcare system, households in LMICs have very high out-of-pocket payments, increased levels of poverty, and limited reliable access to healthcare insurance due to a general absence of risk-pooling mechanisms in health financing systems (Su et al., 2006). This makes households in LMICs exponentially more susceptible to catastrophic health expenditures, leading to a perpetuation of the cyclical nature of poverty (Su et al., 2006). Specifically, households in LMICs are susceptible to catastrophic health expenditures when they have a low income, are headed by an elderly or disabled person, or have a member with a chronic disease (Su et al., 2006). Households specifically afflicted with catastrophic health expenditures generally resort to reducing expenditures related to necessities such as food and clothing (World Health Organization, 2005). These reductions in expenditures can potentially become direr, as in many cases families are left unable pay for their children's education, effectively reducing investment in human capital development in their respective communities. This divestment from education typically leads to children dropping out of school and occupying hard labor jobs. While this does initially alleviate the financial burden for households in the short term, the long-term effects, which are often not taken into context, are of great concern. Without continued investment in children's education, these future leading members of society occupy less-specialized jobs and their respective income-earning potential becomes limited. This creates a perpetual state of stagnant growth without development and further contributes to a focal dissonance in the respective ability of developing countries to further grow and "develop" economically.

Approximately 44 million households, or more than 150 million individuals throughout the world face catastrophic healthcare expenditures, and about 25 million households or more than 100 million individuals are pushed into poverty by the need to pay for expensive surgical care services (World Health Organization, 2005). The relative impact of these out-of-pocket payments for health care does indeed extend beyond catastrophic spending alone. Many individuals in LMICs

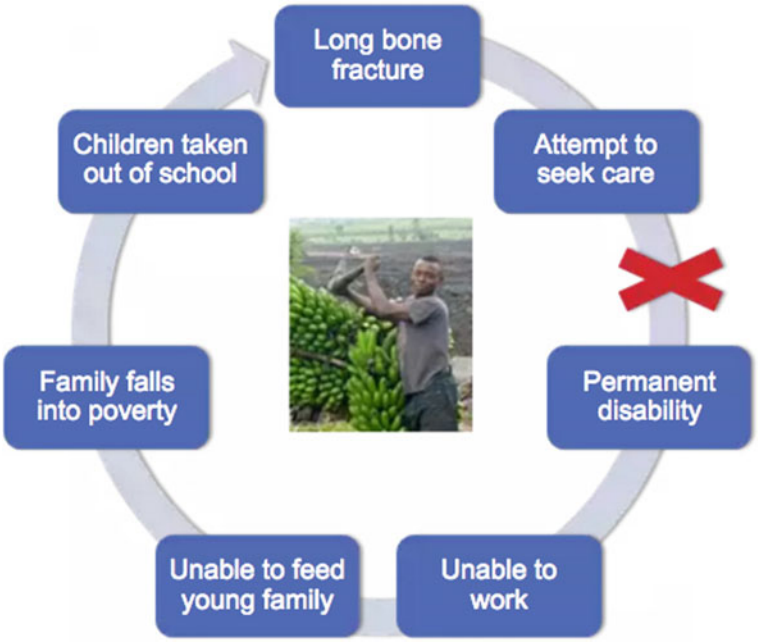

Fig. 1.10 Cyclical nature of poverty in relation to the elective care of an acute trauma that eventually becomes a chronic condition if not properly treated (Dare, 2015)

often decide not to utilize essential surgical services, as they cannot afford either the direct costs including consultations and medications, or the indirect costs including medical transport (World Health Organization, 2005). This contributes to the cyclical nature of poverty as low-income households progressively dive further into poverty due to the adverse effects of illness on their respective income and overall welfare as depicted in Fig. 1.10.

To prevent this trajectory of fiscal collapse, the affordability complex of essential surgical services must be addressed, as it is vital that the services rendered to patients is indeed fiscally feasible for the general populous in order to prevent financial catastrophe and impoverishment as a result of use of these services. Investment in surgical services in LMICs is indeed cost-effective, affordable, promotes economic growth, and most importantly, saves lives (Meara et al., 2015). It is critical that essential surgical care is scaled in a manner that can adaptively meet present and projected population demands. If LMICs were to scale-up surgical services at rates achieved by the present best-performing LMICs, two-thirds of countries would be able to reach a minimum operative volume of 5000 surgical procedures per 100,000 people (Meara et al., 2015). Without accelerated investment in essential surgical services to promote adaptive scaling to provisional service demands by their respective populations, LMICs will continue to have losses in economic

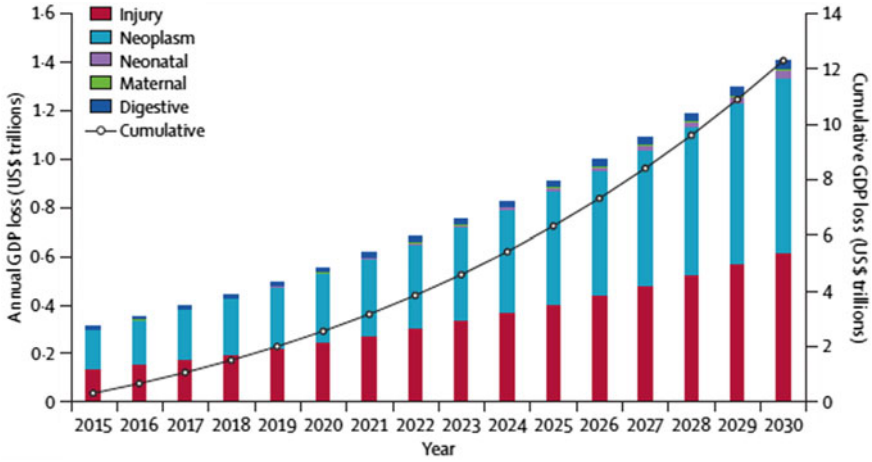

Fig. 1.11 Annual and cumulative Gross Domestic Product (GDP) lost in LMICs from five categories of surgical conditions (Meara et al., 2015)

productivity, which is currently estimated at approximately $12.3 trillion USD in the next 15 years as depicted in Fig. 1.11 (Frilling, 2016; Meara et al., 2015).

1.6 Disparities in Provisional Access to Surgical Supplies in LMICs

While the access to surgical care is influenced by a myriad of elements including human capital, access to medical personnel, and healthcare infrastructure, one pertinent element that has a focal impact on the degree of surgical care rendered is that of access to quality surgical instruments and supplies. Often times the most basic elements are overlooked in favor of complex, systemic interventions when deriving solutions to combat the GBD. In deriving solutions to combating the GBD from a surgical care perspective, one must take a step back and revert back to the basics. In order for palliative surgical care to be rendered in any locality, healthcare providers must have access to basic surgical instruments. This is an often-ubiquitous assumption that every hospital or healthcare facility has access to basic surgical tools, yet in many LMICs this is not the case and is element that is widely overlooked (Rankin et al., 2014). Surgical instruments are indeed a critical component in improving the access and delivery of adequate surgical care to combat the GBD in LMICs. If district-level healthcare facilities are not properly equipped with physical resources such as basic medical equipment and surgical supplies, a perpetuation of the global burden of surgical disease is eminent (Ozgediz & Riviello, 2008). Enhancing the interventional capacities of healthcare providers with access to basic surgical tools, allows for the adequate provision of critical care services, which can

ultimately improve patient care outcomes and quality of life. This problem is especially important, as based upon current trend analysis, this of incidence ill-equipped medical facilities will likely become further exacerbated as healthcare demands of emerging countries increase and evolve due to increased global population density (Alkire et al., 2015). The disparities experienced at district level health facilities in low-income and middle-income countries are staggering and display an obvious need for improvement in the surgical capacity of these facilities. Enhancing the surgical capacity of these facilities is vital in promoting communal health as well as economic growth.

Given the correlational nature of increased human health with that of increased economic gain, a comprehensive intervention can help shift the nature of these healthcare disparities experiences in the LMICs. One of the critical elements that EESC examines related to surgical capacity is that of access to critical surgical instruments and supplies (World Health Organization, 2014). EESC of multiple LMICs has identified massive supply gaps in district level health facilities, a pertinent element that drastically affects patient care and wellbeing (Elkheir et al., 2014). Access to proper surgical instruments and supplies allows for the physician to provide adequate care and can reduce the functional burden of disease that plagues many communities. The chronic nature of these non-communicable diseases, traumas, and injuries typically require surgical intervention, requiring access to basic surgical supplies in the form of surgical retractors, hemostats, needle drivers, tissue forceps, vascular clamps, etc., which are often in short supply in developing countries (Ibrahim et al., 2015; Rankin et al., 2014). This inaccessibility to basic surgical and medical supplies causes deficiencies in adequate patient care and treatment, impacting disability-adjusted life years (DALYs), as well as severely limiting the interventional capabilities of physicians (Ozgediz & Riviello, 2008).

When developing an interventional strategy to address this supply shortage, the most common fallacy tends to be the assumption that these supplies can be readily shipped and distributed on an international scale to remedy this problem. While this has been done in the past, there are indeed severe limitations to shipping supplies, particularly that of the associated costs and supply logistics (Hostettler, 2015). Often times when supplies are imported into LMICs there are associated import tariffs and taxes that are added in addition to the primary shipping price of the goods. Even after the supplies are "in-country" domestic transportation costs are further added and the timeline of supply shipment becomes extended further with added costs (Hostettler, 2015). This ultimately exponentially increases the cost of simple medical supplies, making them unfeasible to attain in a continued fashion based upon increasing demand. This is especially true for LMICs, which are often resource-stricken and plagued with supply chain deficiencies rendering traditional supply intervention strategies inept (Hostettler, 2015). In addition, the WHO Priority Medical Devices project suggests two potential causes for the problem of medical device allocation in LMICs (Diaconu, Chen, Manaseki-Holland, Cummins, & Lilford, 2014). The first is that medical device manufacturers often target high-income country economies due to a higher potential profit (Diaconu et al., 2014). This means that medical device supply and equipment designs are limited to

device specifications that are primarily suited for deployment in areas with advanced infrastructure and highly skilled and educated workforce. The second element is the physical distribution and procurement of medical devices in LMICs. The WHO Baseline Country Survey on medical devices shows that in contrast to HICs, LMICs undertake medical device procurement at national rather than regional or facility level (Diaconu et al., 2014). Upon acknowledgement of this paradigm, the need for an intervention that can be adaptively scaled to meet demand as well as promote domestic manufacturing of these medical supplies such as surgical instruments to completely bypass these supply chain inefficiencies, becomes ever more inherent. One particular solution that could indeed potentially solve these problems entirely is that of rapid device prototyping, otherwise known as 3-dimensional printing.

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Chapter 2
3-Dimensional Printing and Rapid Device Prototyping

Regardless of economic classification, humanity as a whole finds itself in a perpetual state of change and development that is nurtured by our intrinsic need as a species to consistently innovate in order to develop novel solutions to society's most pressing issues. In this perpetual state of change, elements such as our innate drive for intellectual inquiry and curiosity serve as impetuses for innovation. This intellectual inquiry and curiosity that is innately embedded in our human nature, provides a foundation for technological advancement in today's modern society. One particular technology that has recently grown exponentially is that of rapid prototyping (RP) otherwise known as 3-dimensional (3D) printing. 3D printing technology has seen a myriad of advancement since its initial inception in the early 1980s, and has been radically transformed with the advent of the Internet and innovations in the computer and software technology. With these rapid advancements in this technology coupled with continued research and development, these printing technologies have become more financially feasible and have vastly expanded in their respective interventional applications and capacities. Whereas 3D printers used to cost tens of thousands of dollars only a decade ago, these printing devices can now be purchased for hundreds of dollars (Hostettler, 2015). In addition, the scaling and applications of this technology has rapidly expanded, in which these units can be utilized to print mono-synthetic small-scale models to that of full-sized automobile parts (Hostettler, 2015).

2.1 The Dawn of Disruptive Innovation and Frugal Engineering

In addressing such a profound and dynamic problem such as the global burden of surgical disease in LMICs, the need for what is known as "disruptive innovation" and "frugal engineering" becomes essential. Disruptive innovation(s) refers to

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technologies that significantly alter or affect the way a particular market functions (Christensen & Raynor 2013). These technologies are not an iteration or reiteration of a previous technology, but rather something completely novel that transcends the market space upon which a previous technology had occupied. Disruptive innovations not only include disruptive technologies, but also the novel functional application of the technology (Christensen & Raynor, 2013). These innovations can be applied in the global health arena and are distinctly geared towards preserving and enhancing the quality of life for others. Disruptive innovations have the functional capacity to drive improvements in the health and well being of communities and entire countries by disrupting the cycle of poverty and improving health outcomes. Disruptive innovations can serve as an impetus for change and global development, fostering an era in which integrative, yet targeted solutions can be derived to address the most pertinent health threats facing societies today. In addition to disruptive innovations, the concept of frugal engineering serves as an equally important component that can drive future applications of advanced technologies in resource-poor settings.

Frugal engineering is essentially a minimalist approach to innovation and is defined as the process of reducing the complexity and cost of a good and its associated production (Maric, Rodhain, & Barlette, 2016). The core concept of frugal engineering involves taking a technology that has been manufactured for use and deployment in advanced infrastructure settings such as high-income countries and essentially breaking it down into its fundamental components to meet the needs of consumers in resource-constrained settings such as those of LMICs (Maric et al., 2016). In deploying the principles of frugal engineering, technologies that may have not been able to be feasibly deployed or implemented in resource-poor settings, can indeed be utilized and further adapted to meet the needs of its respective environment. In addition to physically breaking down technologies, frugal engineering seeks to redefine other aspects related to a technology's development and relative application. In constructing a holistic and integrative approach to frugal engineering, the essence of frugality plus innovation becomes unearthed, creating a defined element known as "frugal innovation" (Bhatti, 2012). Frugal innovation has the potential to not only redefine the physical design, manufacturing process, and distribution of a product, but the also the more theoretical aspects related to a product's business model, value chain, and market inclusivity (Bhatti, 2012; Christensen & Raynor, 2013). In modifying these various elements related to a technology, one can radically alter the application and adaptability complex of various technologies to be suited for markets in resource-constrained settings. This includes primarily reducing the materials cost for these devices so that they can be both affordable and accessible to more people. Coupling the fundamental concepts of disruptive innovation with that of the fundamental elements of frugal engineering can open the door to unparalleled possibilities. This is particularly pertinent for technologies related to global health, as making medical devices available to the

people that need them most is of the utmost importance to creating healthy world and for the sake of this book, pertinent in combating the global burden of surgical disease.

One particular technology that integrates the tenets of disruptive innovation and frugal engineering and could effectively combat the global burden of surgical disease and revolutionize the current global health paradigm is that of rapid device prototyping, otherwise known as 3-dimensional (3D) printing. Traditional fabrication and manufacturing processes are known as subtractive processes, in which objects are fabricated via the successive cutting of material from a solid block of material (Petrick & Simpson, 2013). This traditional process is highly inefficient and creates large amounts of excess material waste making it largely unsustainable. 3D printing creates a 3-dimensional solid object from a digital model via the use of an additive manufacturing process, in which material is successively added in a layering fashion (Petrick & Simpson, 2013). This allows for the fabrication of various parts and components in a highly efficient and sustainable manner that limits materials waste (Petrick & Simpson, 2013). The additive manufacturing process represents a focal disruption to the traditional manufacturing paradigm and ushers in an era of highly-customizable, efficient, and sustainable manufacturing processes. The dawn of disruptive innovations such as 3D printing coupled with the art of frugal engineering has unearthed previously unknown potential for developing countries. In settings such as LMICs where resources are often scare, the need for highly efficient, targeted, and direct manufacturing processes becomes of the utmost importance, not only to promote sustainability, but also to adequately meet the needs of resource-stricken consumers and communities.

With the glaring disparities in medical supply attainment, limited infrastructure, and fiscal constraints prominent in LMICs, the utilization of 3-dimensional printing technologies has the potential to harness the productivity of an entire small-scale domestic manufacturing facility in a single, highly adaptable apparatus that can be deployed in a plethora of settings and environments (Hostettler, 2015). These unique devices have limitless potential, specifically when it comes to the field of global health and medicine. The ability to fabricate low-cost, custom, and high-utility medical devices utilizing 3D printers in developing countries has sparked great interest in various fields of medicine and applied engineering including biomaterials research, prosthetics and orthopedics, medical and laboratory instrument design, as well as areas such as humanitarian and disaster relief (Ibrahim et al., 2015). In developing a solution to combating the global burden of surgical disease, deployment of 3D printing devices in LMICs could be feasibly implemented to fabricate a variety of medical tools such as surgical instruments. By delivering critical surgical instruments directly onsite and in an on demand fashion, one can drastically enhance the interventional capacities of healthcare facilities in LMICs and improve a fundamental component in enhancing surgical access and delivery. It is through this enhanced surgical access and delivery that human life can be saved both in the short and long terms.

2.2 3-Dimensional Printing: An Introduction to Rapid Device Prototyping and Extant Fabrication Processes

3-dimensional printing is formally defined as the synthetic fabrication and manufacture of 3-dimensional products from a computer-driven digital model via an additive fabrication process (Gross, Erkal, Lockwood, Chen, & Spence, 2014). This process allows for the creation of physical objects and prototypes from a virtual digital model in a variety of materials such as plastic, steel, aluminum, and cobalt (Taneva, Kusnoto, & Evans, 2015). 3D printing apparatuses come in a variety of sizes and variations based upon application specialty, in which some printers can print large-scale components such as automobile parts and even entire homes, and others can fit on a desk and fabricate small, high-definition parts and models (Hostetler, 2015). A common thread that connects all 3D printing apparatuses is the standardized printing and rendering process from digital modeling to physical object fabrication. The process, as depicted in Fig. 2.1, first begins with the creation of a 3D computer aided design (CAD) model, which is designed or obtained via scanning of a physical object and drafted in various computer software programs such as Solidworks or AutoCAD (Gross et al., 2014; Taneva et al., 2015). Once the CAD model is created in the software, the CAD model is then automatically converted into a stereolithographic file or .STL file (Taneva et al., 2015). This file stores the information for each surface of the 3D model in the form of triangulated sections, where the coordinates of the vertices are defined in a text file (Gross et al., 2014). The .STL file spatially defines the object surface in order to create a virtual design grid via coordinate geometric configuration of the object as shown in Fig. 2.2 (Taneva et al., 2015). The 3D printer interprets the digital geometric coordinate configuration derived from the .STL file by converting the file into a G-code file via slicing software (Taneva et al., 2015). The G-code divides the 3D .STL file into a series of 2-dimensional horizontal cross sections generally between 25 and 100 μm, based upon fabrication technique (Gross et al., 2014). This digital

Fig. 2.1 Depiction of the 3-dimensional printing process from 3D CAD Model to 3D object fabrication (Taneva et al., 2015)

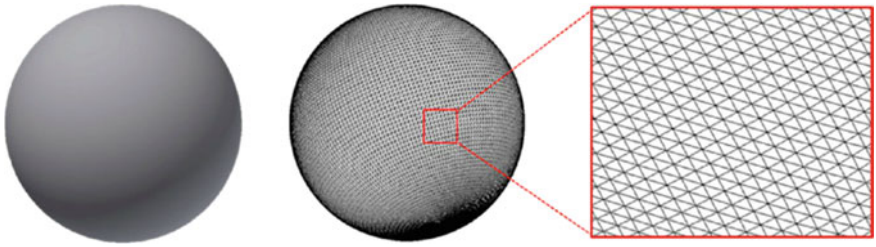

Fig. 2.2 Representation of the coordinate geometric configuration of information in an .STL file; the object as depicted on the *left* was created in a CAD program and saved as an .STL file. The graphical information displayed in the .STL file is shown on the *right* for the same object, with the surface of the object being represented in a coordinate triangulated pattern (Gross et al., 2014)

slicing of the object allows the 3D printer to print the object beginning at the base and the continue to fabricate consecutive layers in a additive fashion, essentially constructing the model from a series of 2D layers derived from the original CAD file (Gross et al., 2014).

While there are indeed a variety of different printing apparatuses and technologies that have come to fruition, it is important to note that not only does the scope of application matter when utilizing these technologies, but the manner in which they fabricate 3-dimensional objects. Rapid prototyping provides an ideal manufacturing method for 3-dimensional structures with complex, intricate, or distinct geometric configurations, which often times require custom fabrication processes typically not afforded with traditional manufacturing methods (Liska et al., 2007). While there are indeed an array of 3D fabrication processes, there are five primary types of rapid prototyping processes, also known as "extant" processes, that hold the most utility in fabricating medical devices (AlAli, Griffin, & Butler, 2015; Jones et al., 2011). Each of these fabrication processes employ a distinct mechanical fabrication process and utilize specific printing filaments. These five processes as shown in Table 2.1 are: stereolithography (SLA), selective laser slintering (SLS), fused deposition modeling (FDM), digital light processing (DLP), and inkjet printing (AlAli et al., 2015). Table 2.1 also describes the various attributes of each type of printing process including the mechanism, advantages, disadvantages, materials utilized, and the micron layer density of each process.

The first process depicted is that of SLA or stereolithography printing (Fig. 2.3), which was the first commercialized rapid prototyping fabrication method (Gross et al., 2014). Stereolithography works by focusing an ultraviolet laser onto a vat of photopolymer resin, in which the UV laser is used to draw pre-programmed designs on to the surface of the photopolymer vat (Gross et al., 2014). Since photopolymers are indeed photosensitive under ultraviolet light, the resin is solidified and forms a single layer of the desired 3D object (Gross et al., 2014). This process is repeated for each layer of the design until the 3D object fabrication is complete. The main advantage of this process is that it can fabricate high-resolution prototypes with adjustable micron layer density, in which manufactured prototypes are produced

Table 2.1 Five primary types of 3-dimensional printing processes: SLA, SLS, FDM, DLP, and Inkjet (AlAli et al., 2015)

Type	Mechanism	Advantages	Disadvantages	Material	Other
SLA	UV light is used to create the object by curing and solidifying a liquid resin	• High-resolution prototypes • Good finishing at the surface	• Support structure is needed • Require postcuring	Resin; a curable laser photopolymer or other plastic-like products	Layer thickness: 0.05–0.2 mm
SLS	Laser fuses the layers of a powder material	• Ability to produce complex/functional parts • Does not require support structure • High productivity	• Surface finish is rough	Plastic, nylon, polystyrene, metals; steel, titanium, and composites	Layer thickness: 0.06–0.18 mm
FDM	Extruding small beads of the melted plastic material, which hardens afterward	• No postcuring • Easy material changeover • Low-cost machines compared with others	• Slow processing, especially on large parts • Low detailing accuracy • Low surface finish integrity	Filament of thermoplastic polymer; ABS, PLA	Layer thickness: 0.15–0.25 mm (adjustable)
DLP	DLP projector projects the light in a repetitive process	• Good resolution • Fast processing time	• Support structure is needed	Liquid resin	Accuracy: 139 μm
INKJET	Spraying liquid or the photopolymer depending on the type of the jetting; binder or material	• A variety of material choice • High precision • Colored parts	• Require postcuring	Plastic, metal, and ceramics	Layer thickness: material: 0.013 mm (min) binder: 0.09 mm (min)

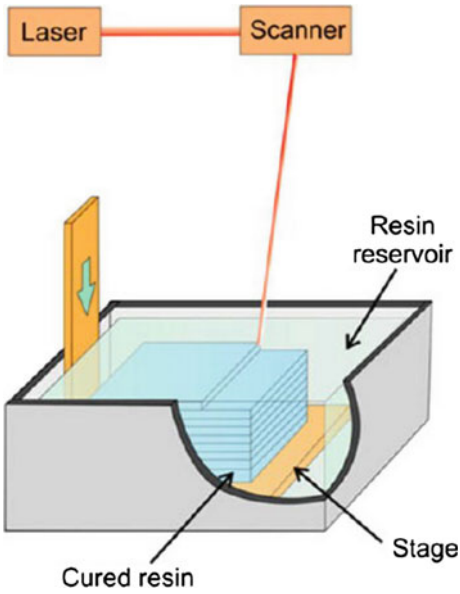

Fig. 2.3 Stereolithography (SLA) 3-dimensional printing process (Gross et al., 2014)

with a high-resolution and smooth finish (Gross et al., 2014). The main disadvantages of SLA printers are that they only utilize specific resin materials not conducive to bio-based materials, require extensive post processing in the form of rinsing the resin in isopropyl alcohol, and are generally more expensive to purchase and operate resulting in higher per-unit object costs (Gross et al., 2014).

The next process is SLS or selective laser slintering (Fig. 2.4), which is a powder-based 3D model fabrication process. SLS utilizes a high power carbon dioxide laser to sinter polymer powders in order to generate a 3D model, instead of utilizing liquid binding materials to attach powder particles together (Gross et al., 2014). In the SLS

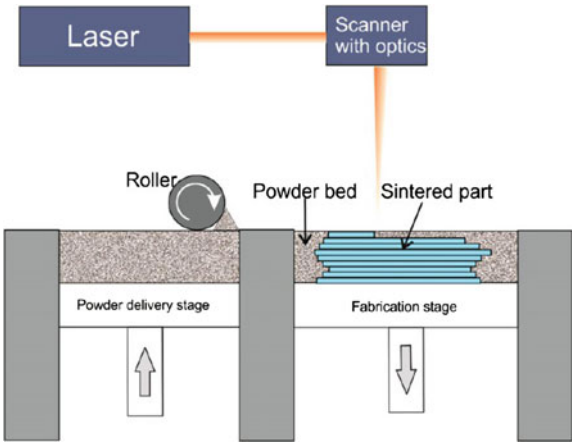

Fig. 2.4 Selective Laser Slintering (SLS) 3-dimensional printing process (Gross et al., 2014)

manufacturing process, an initial layer of powder is distributed onto a platform by a roller and is then heated to a temperature just below the powder's melting point. Following the cross-sectional profiles designated in the .STL file, a laser beam is selectively scanned over the powder to raise the powder's melting point to fuse powder particles together (Gross et al., 2014). After the first layer is completed, a second layer of powder is added, leveled, and sintered in the desired localities as indicated by the CAD model, and these steps are repeated to create a 3D model (Gross et al., 2014). The powders that are not sintered by the laser serve as structural support scaffolding for the model during the process and are removed after fabrication of the 3D object (Gross et al., 2014). One advantage of SLS is that a wide range of materials can be used, from polymers such as polycarbonate (PC), polyvinyl chloride (PVC), acrylonitrile butadiene styrene (ABS), nylon, and polyester to that of metal powders (Gross et al., 2014). In addition, a binding liquid material is not required, but SLS printed models are prone to shrinkage or deformation due to thermal heating from the laser and subsequent cooling and SLS printers are often expensive to purchase and operate (Gross et al., 2014).

The next process is that of FDM or fused deposition modeling (Fig. 2.5), one of the most commonly used manufacturing technologies for rapid prototyping. FDM fabricates a 3D model via the extrusion of thermoplastic materials such as polylactic acid (PLA) or acrylonitrile butadiene styrene (ABS), depositing semi-molten thermoplastic material onto a modular build platform layer-by-layer (McCullough & Yadavalli, 2013). The thermoplastic filament that composes the 3D models is

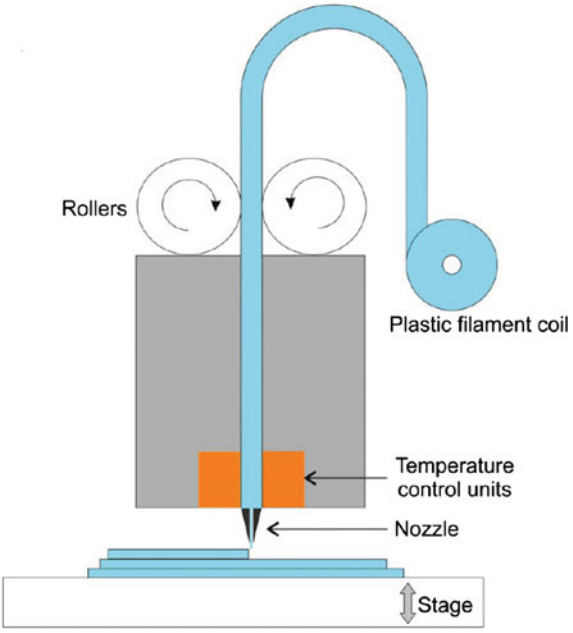

Fig. 2.5 Fused Deposition Modeling (FDM) 3-dimensional printing process (Gross et al., 2014)

moved by two internal mechanical rollers downwards towards to the heated nozzle tip of the extruder of the print head (McCullough & Yadavalli, 2013). The modular platform is generally heated to approximately 50–70 °C and the extrusion head is heated to approximately 190–215 °C based upon the thermoplastic material utilized (McCullough, & Yadavalli, 2013). As the print head traces the design of each defined cross-sectional layer horizontally, the semi-molten materials are extruded out of the nozzle and solidified upon the build platform in an additive fashion (Gross et al., 2014). These steps are repeated to fabricate a 3D structure layer-by-layer, with the outline of the part is usually printed first, with the internal structures on the 2D-plane printed layer-by-layer with various internal structural patterns (3D Matter, 2016; Gross et al., 2014). The advantages of utilizing FDM are that it is highly adaptable for the usage of various thermoplastic materials including bio-based thermoplastics and can be utilized a multitude of environments. In addition, the printing device itself has the lowest cost setup of all four processes and is extremely user friendly with regards to mechanical output and software setup (Rankin et al., 2014). The high extrusion temperature makes the printed objects sterile upon fabrication as well as extremely durable and malleable. The primary disadvantages of FDM are that the process is slower and has a lower micron resolution compared to other rapid prototyping processes (Gross et al., 2014).

The next rapid prototyping process is DLP or digital light processing (Fig. 2.6), in which a 3D model is fabricated via projection onto a liquid photopolymer basin (AlAli et al., 2015; Liska et al., 2007). DLP utilizes a light projector that displays a

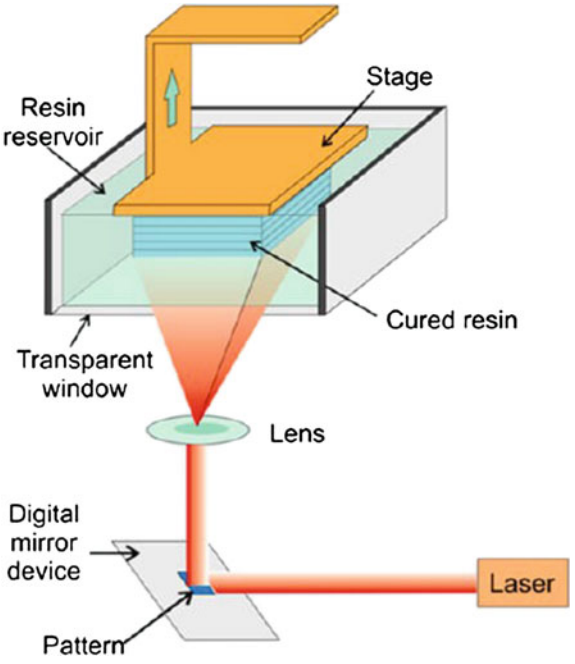

Fig. 2.6 Digital Light Processing (DLP) 3-dimensional printing process (Gross et al., 2014)

computer-generated image of the 3D model onto liquid photopolymer resin, in which the photopolymer hardens when exposed to the projection's light (AlAli et al., 2015). As the build plate of the printer proceeds downward in a y-axial trajectory, the liquid photopolymer is further exposed, thus further constructing the projected 3D model image, and is repeated until the model is fully fabricated and solidified (Gross et al., 2014; Liska et al., 2007). In examining the benefits of utilizing DLP printing, the primary advantage is that this process garners high-micron resolution models in a quick and efficient manner (AlAli et al., 2015). The primary disadvantages of this technology are that it is expensive overall, not only for the printing apparatus, but also specifically for the photopolymer resin, which typically costs hundreds of dollars. In addition, the support structure and 3D scaffolding that is fabricated to stabilize each model during the fabrication is integrated into the 3D model itself. This means that the support structure must be meticulously removed by hand in order to access the true model that has been fabricated. In doing this, there is indeed the potential to damage the model if the support scaffolding is not removed in an articulate manner.

The final process is 3D inkjet printing (Fig. 2.7), which is a powder-based method where layers of solid particles, approximately 200 μm in height with particle sizes between 50 and 100 μm, are bound together by a printed liquid material to generate a 3D model as shown in Fig. 2.7 (Napadensky, 2010). First, a layer of powder is distributed evenly on the top of a support stage by a roller, after which an inkjet printer head prints droplets of liquid binding material onto the powder layer at desired areas of solidification (Gross et al., 2014; Napadensky, 2010). After the first layer is completed, the platform drops and a second powder layer is distributed and selectively combined with printed binding material (Napadensky, 2010).

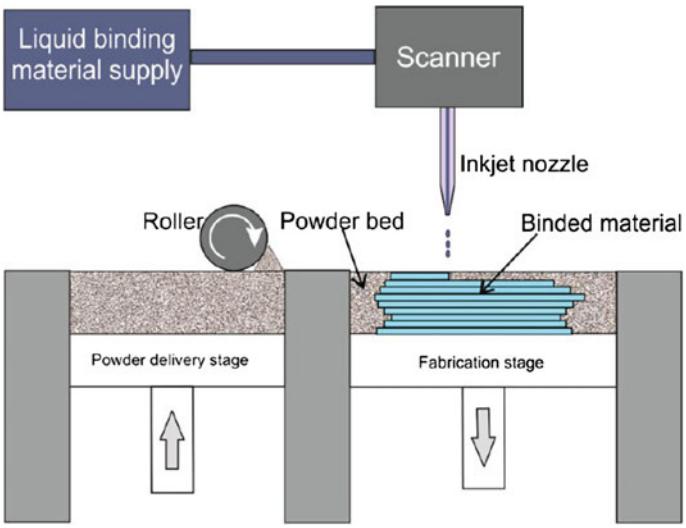

Fig. 2.7 Inkjet 3-dimensional printing process (Gross et al., 2014)

These steps are repeated continuously until a functional 3D model is fabricated, with the model being heat-treated afterwards, in order to enhance the binding of the powders in the object. The unbound powder serves as structural support scaffolding during the process and is removed after fabrication of the 3D prototype (Napadensky, 2010). The main advantage of the process is that it is relatively low-cost to purchase and operate and can utilize a variety of materials. The primary disadvantage of this process is that the unbound particles can result in significant porosity of finished materials and surface roughness, two critical elements that are importance when fabricating medical devices (Napadensky, 2010).

One of the most important elements upon deciphering the ideal additive manufacturing processes is the scope of application and the in-field deployment feasibility. These two elements are of critical importance, as these printing apparatuses would be deployed in healthcare facilities in LMICs, which often only have access to the basic support entities including infrastructure and fiscal capital (Ishengoma & Mtaho, 2014). This means that upon deployment of one these printing devices, the device would have to be cost and energy efficient, user-friendly, transportable, reliable, and deliver a consistent fabricated product that is functional and able to be directly deployed in the field. This is especially important for the fabrication of surgical instruments, as the printing device would have to print a consistent run of instruments that are free of any catastrophic mechanical or structural deficits (Ishengoma & Mtaho, 2014). Another important element is that the printing apparatus must have easily replaceable parts and support, in case of mechanical failure in the unit. If the unit has components that cannot be easily sourced or fabricated, it will be extremely difficult to source parts to be delivered to these often resource-poor settings (Tatham, Loy, & Peretti, 2015). Based upon these criteria, the process of fused deposition modeling proves to be the most ideal process for deployment in LMICs. The reason for FDM being the most ideal additive manufacturing process is that it is highly adaptable for utilization of bio-based thermoplastic materials, cost-efficient, and highly efficient. While this section has focused on the types of printing processes, thought must be given to the type of printing apparatus that will house this process and will actually be deployed in the field.

There are a variety of 3D printer makes and models such as MakerBot, DaVinci, and Micro3D, but given the unique circumstances that are faced upon deploying an advanced technology in often resource-stricken settings such as LMICs, the need for a basic, user-friendly, and highly adaptable modular printing platform become essential (Tatham et al., 2015). While it could indeed be feasible to ship other types of printing devices, as previously noted this is difficult given the supply chain inefficiencies and deficits as well as the fundamental problem of allocating replacement parts and support in case of printer mechanical failure (Tatham et al., 2015). This fallacy could indeed be catastrophic for deployment of an advanced technology such as 3D printers as most likely, if the device were to breakdown, most likely would not be fixed due to the complexity of the device parts and design, thus rendering the entire intervention a failure. Upon acknowledgement of these problems, one particular printing apparatus stands out above all else, this being the RepRap 3D FDM printer. Utilization of the RepRap modular rapid prototyping

printing apparatus can potentially serve as a cost-effective, highly efficient fabricator of surgical instruments in LMICs, a concept that will be examined further in this chapter.

2.3 Fused Deposition Modeling and the RepRap Rapid Prototyping Device

RepRap is a novel and innovative open-source self-replicating rapid prototyping 3D printer that utilizes a FDM rapid prototyping process to fabricate 3D objects as depicted in Fig. 2.8 (Romero et al., 2014). RepRap was developed and is still in development by an open community on RepRap.org, which was founded in 2004 by Adrian Bowyer at the University of Bath (Romero et al., 2014). The RepRap online community functions in highly unique manner, in which it develops and modifies RepRap 3D printing hardware via open-source publishing (Jones et al., 2011). This means that the RepRap design modifications, components, blueprints, and applications are available for anyone to access on the Internet, without the need to provide royalty payments for device design or components (Jones et al., 2011). The ultimate goal of this is to promote an open platform for inquiry as well as rapid device input, enhancement, and improvement (Romero et al., 2014). This open-source availability has fostered an unprecedented paradigm shift in 3D printing availability and accessibility. Individuals ranging from hobbyists to professional engineers and academics have all shared ideas to further improve the

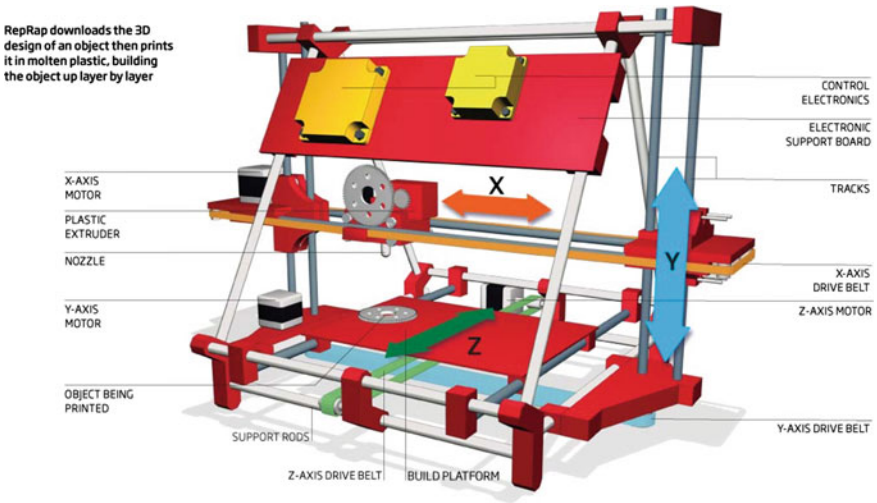

Fig. 2.8 Overview schematic of the RepRap FDM 3D printer design and self-replicated components shown in *red* (Simonite, 2010)

RepRap platform. This has led to rapid improvements in the design and application of RepRap devices in only a few years and has embraced the true essence of frugal innovation and engineering to create devices that could indeed be feasibly utilized in resource-poor settings.

Since RepRap devices are open-source, one could imagine that there could indeed be hundreds of variants, each of which have its own distinct components and design. While this is indeed possible, all RepRap 3D printers have three primary characteristics that are the foundational elements for these devices. The first is that they are machines that utilize FDM additive manufacturing to fabricate objects utilizing thermoplastic polymers such as acrylonitrile butadiene styrene (ABS) (3D Matter, 2016; Romero et al., 2014). The second is that there are four models that have been developed thus far, including: Darwin, Mendel, Huxley and Wallace (Romero et al., 2014). With these four models comes a variety of different variants including: Prusa Mendel, MendelMax, RepRapPro Huxley, and the RepRapPro Mendel (Romero et al., 2014). The final characteristic of RepRaps is that the accuracy of each model is widely determined by the diameter of the filament extrusion nozzle, which is generally between 0.4 and 0.5 mm (Jones et al., 2011; Romero et al., 2014).

RepRaps are an extremely unique printing apparatuses, as they are designed to have the capability to print out a significant amount of their own parts, a critical element when it comes to being deployed in resource-poor settings. The remaining parts that the device cannot print are generally parts and components that are cheap and available worldwide (Jones et al., 2011). This makes this modular printing apparatus extremely flexible when it comes to device repairs, improvements, and overall printing capacity. Another important element of the RepRap is that the device functions based upon the tenets of what is known as "frugal engineering," which is the process of reducing the complexity and cost of a technology and its production (Maric et al., 2016). This essentially refers to the removal of nonessential features from a technology in order to make it feasible to utilize and function in resource-poor settings (Maric et al., 2016). With the reduction of nonessential components, the RepRap apparatus is extremely cost-effective generally costing less than $150.00 and has the ability to be modified in order to meet the various manufacturing needs of the device user (Jones et al., 2011). The availability of open-sourced blueprints and designs allows for users of the product to address mechanical and fabrication issues instantly, thus allowing for proper unit operation.

The RepRap printer utilizes the FDM rapid prototyping process to construct 3D objects and utilizes a modular build platform that moves in conjunction with the extrusion head. The decision to utilize the FDM extant process for RepRap rapid prototyping devices was made based upon multiple factors. Any fabrication process that needed and operated utilizing a laser was rejected, as a rapid prototyping device could not fabricate its own laser, and because lasers are a costly component and likely difficult to source in a variety of environments and localities (Jones et al., 2011). In removing this functional laser component, this effectively removed selective laser sintering (SLS), stereolithography (SLA), and digital light projection (DLP) from being utilized in RepRap printing devices (Jones et al., 2011). In

addition, any process that required inkjet print heads was rejected, as it is rather unlikely that a RepRap device would feasibly be able to fabricate an inkjet print head by itself (Jones et al., 2011). With these four printing processes eliminated, only one process remained, this being fused deposition modeling (FDM). Fused deposition modeling provides the ability to fabricate objects with an array of various filament materials. This provides a significant advantage in the future, as the RepRap would be able to fabricate a larger proportion of its own components than could be created out of just one material (Romero et al., 2014).

The RepRap rapid prototyping device is a stepping-motor-driven Cartesian 3D printer, in which the basic components of RepRap machines can be classified according their respective function and attributes (Jones et al., 2011). The first group is that of the RepRap self-replicable plastic components, which are the components that can be manufactured by the RepRap printer. These components generally represent almost half of the total of the parts of the printer and are generally fabricated with ABS or PLA thermoplastic filament and primarily include the structural, extruder, and carriage print components shown in Fig. 2.9 (Romero et al., 2014).

The second group is that of the non-replicable components, which includes structural components such as the threaded and smooth rod frame assembly, washers, nuts, bearings, and belts. These components are generally made of metal, steel or aluminum, and the belts are rubber (RepRap Bill of Materials). The third group is that of the electronic components, which are vital for printer operation and include the microcomputer and electronic board, stepping motors, temperature and end stop sensors, resistances, and cables (Romero et al., 2014). The fourth group is that of the software, which includes the RepRap firmware and an external computer/laptop for 3D object splicing. The remainder of the parts that the RepRap

Fig. 2.9 RepRap self-replicated plastic components (Romero et al., 2014)

cannot fabricate by itself, other than the electronics and the motors, can be locally sourced from local hardware shops that occupy many urban centers in LMICs.

The RepRap operates an extruder nozzle that runs on the horizontal X and Y-axes and is driven by stepping motors that operate via toothed timing belts, which move at a feed rate of approximately 3000 mm/minute (Jones et al., 2011). The extrusion head moves on the x and y-axes adding a 0.15-micron thick layer for each layer of the object, while the build platform moves on the z-axis in a simultaneous fashion to allow for proper object fabrication on all planes as shown in Fig. 2.9 (Romero et al., 2014). Printing an object with a RepRap device follows the same schematic as any other FDM 3D printer. A 3D model file is uploaded and modified via the appropriate software and then sent to the printer, which requires a series of mechanical processes that the printer conducts in order to start fabrication. First, a 2 kg coil reel otherwise known, as a filament spool, containing the 1.75 mm thermoplastic filament is loaded in the machine (Jin, Li, He, & Fu, 2015). After this, the machine begins to simultaneously heat both the filament extrusion head as well as the build platform. This step is critical as each thermoplastic material has varying heating protocols and must be heated at a precise range otherwise the material will be compromised. The extrusion head is generally heated to approximately 190 °C for ABS thermoplastic and 215 °C for PLA thermoplastic (Chia & Wu, 2015). The build platform is temperature is also adapted based upon the filament material utilized, but is generally between 50 and 70 °C (Rengier et al., 2010). Once both these components are properly heated, the extrusion head is directed to the (0, 0) coordinate plane on the build platform and is lifted approximately 0.2 mm above the build platform (Rengier et al., 2010). The thermoplastic filament from the 1.75 mm filament spool is then fed through a driving motor in the extruder head and fed onto the 10 × 10 inch build platform as shown in Fig. 2.11 (Jin et al., 2015). A platform scaffold is generally fabricated as the model is created in order to provide support and attachment of the 3D object to the build platform (Fig. 2.10).

The RepRap printer consumes approximately 60 W when operating, and is designed to work off a single 12-volt power supply, which can be obtained by using the power supply from an old PC or even a car battery (Jones et al., 2011). Each year, the RepRap modular apparatus receives new updates to its fabrication methods and manufacturing processes. The most current open source model available is the Mendel series shown in Fig. 2.10, which incorporates a modular heated 10 × 10 inch build bed/platform, threaded aluminum rod frame assembly, and compact filament extruder (RepRapPro, 2017). Given this printer's innate flexibility and adaptability, these printers provide the ideal platform for fabricating medical devices such as surgical instruments in LMICs and could serve as vital elements in stimulating domestic manufacturing initiatives to address medical device shortages in countries around the world. While these devices are indeed highly adaptable for an array of field interventions it is important to note some limitations associated with the technology. RepRap printers in most cases, require an external computer to be physically connected to the printer, usually via a Universal Series Bus (USB) cable. As previously discussed, the external computer is responsible for calibrating the printer, running the 3D splicing software,

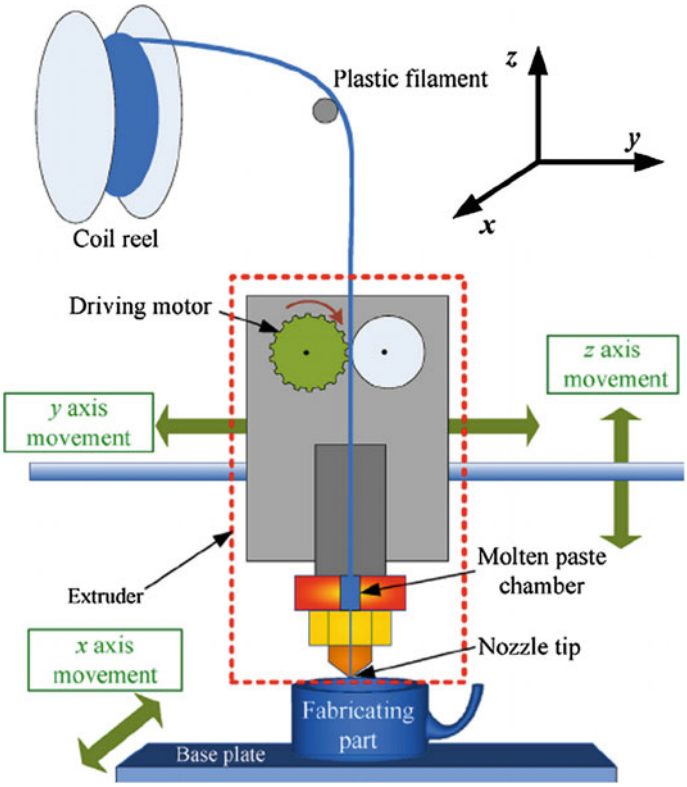

Fig. 2.10 Internal and axial mechanics of RepRap FDM rapid prototyping (Jin et al., 2015)

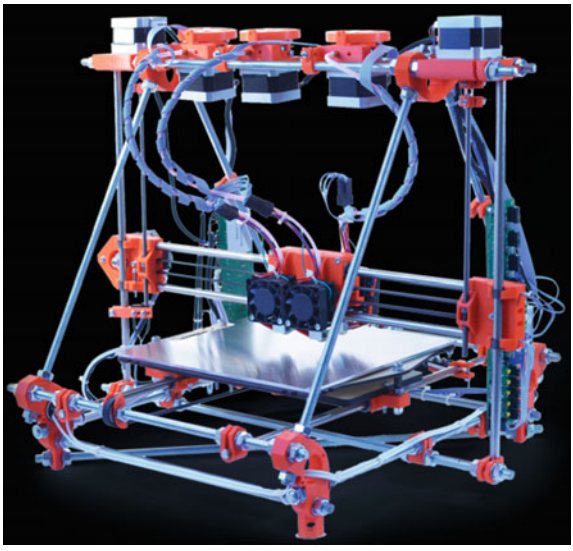

Fig. 2.11 A RepRap Mendel FDM 3D Printer with threaded aluminum rod frame assembly and modular build platform (RepRapPro, 2017)

processing the files into .STL format, and transmitting directions to the printer via G-code (Tatham et al., 2015). In addition, the computer must remain connected to the printer while the 3D model is printing. Recently, RepRap builders have devised way to eliminate this physical dependence on an external computer. Many RepRap machines can be retrofitted with controllers that include memory card readers such as micro-SD cards, in which .STL files can be saved as G-code instructions on these SD cards. This means that these printers can function independently without the need for an external computer and can be deployed in any environment that provides a suitable power source.

In utilizing these printers to fabricate medical devices such as surgical tools and instruments, the question of what type of material would be utilized is great importance. As previously stated FDM printers utilize a variety of thermoplastic materials to fabricate 3D objects, in which the most commonly used filament is ABS plastic. Previous studies have utilized FDM printers to fabricate instruments, but when utilized in medical devices, there are significant limitations. These limitations include nanoparticle aerosol emissions and mechanical application in addition to sustainability and toxicity complexes of the materials utilized. In cases such as these the use of bio-based materials instead of synthetic materials such as ABS provides a unique opportunity to harness natural materials that are biocompatible with human tissues, yet provide the same mechanical dexterity as conventional synthetic plastic polymers. The most feasible bio-based material that can be utilized in substitute of ABS plastic is that of polylactic acid or PLA.

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Chapter 3
3-Dimensional Device Fabrication: A Bio-Based Materials Approach

In the previous chapter, we defined the evolution and advancement of 3-dimensional printing technologies and the transformation of these devices from rather primitive machines to highly adaptable modular apparatuses. We further explored how the tenets of frugal engineering and innovation have led to the creation of a new breed of open-source 3D printing technology known as RepRaps and their potential application as an excellent platform to be deployed to fabricate medical devices in LMICs. Another component that has been briefly mentioned that is just as important as the type of printing apparatus is the type of filament utilized to create these 3D models. As previously mentioned, fused deposition modeling typically utilizes thermoplastic filaments, most commonly acrylonitrile butadiene styrene (ABS), to fabricate an object. As with all technologies, ability to improve and innovate is only limited by one's imagination and this is no exception for 3-dimensional printers. ABS plastics have been the go-to thermoplastic material for a plethora of applications ranging from case you may have on your phone to that of automobile and aerospace components (Van Wijk & Van Wijk, 2015). While indeed thermoplastics such as ABS are widely utilized in the production of goods today, the raw materials and resources that are needed to create ABS are largely unsustainable. As our human population continues to increase in population density, our consumption and demand for raw materials and resources will grow exponentially to satisfy our needs. These materials and resources such as fossil fuels required to make ABS plastics are limited and nonrenewable. In recognizing the potential exponential rise in materials consumption, the transition to more sustainable materials is eminent.

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3.1 Bio-Based Thermoplastic Polymers in 3-Dimensional Printing

In combining the two distinct elements of 3D printing and biomaterials, we combine a myriad of elements to create a paradigm shift in the way medical devices are developed and delivered. 3D printers allow for on-demand production, quick product development, and personalized design, in which coupling these elements with biomaterials allows for local production of sustainable and renewable products that could improve the social, economic, and human health of LMICs (Fig. 3.1). In keeping with the theme of this book, which bridges the gap between technological innovations and human health, we explore another type of thermoplastic filament. With continued advancements in 3D printing technology the potential to utilize a broader range of thermoplastic filaments has been recently recognized. Specifically, the use of "bio-based" materials as thermoplastic filaments such as polylactic acid (PLA) has garnered much attention due to its 3D printing potential, sustainability, renewability, and future medical device applications. In fabricating 3D objects with natural bio-based materials, we usher in a new era of utilizing natural polymers that display similar materials properties as their petroleum based counterparts, but promote enhanced sustainability and biocompatibility complexes.

Research into the field of bio-based materials and polymers derived from renewable resources has attracted great attention due to the increasing environmental and sustainability concerns associated with traditional petroleum-based polymers such as ABS plastics (Davachi & Kaffashi, 2015; Neches, Flynn, Zaman, Tung, & Pudlo, 2014; Zeng, Li, & Du, 2015). Specifically within the fields of

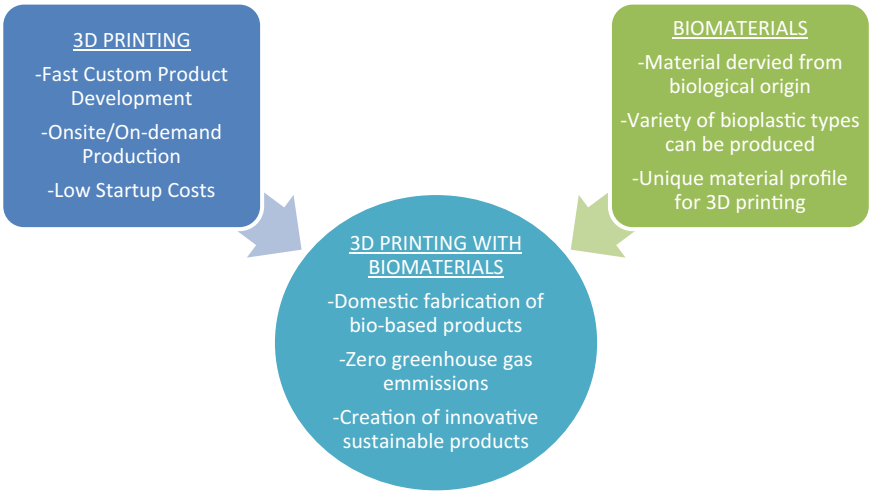

Fig. 3.1 Potential benefits of combining 3D printing technology with biomaterials (Adapted from Van Wijk & Van Wijk, 2015)

medicine, biomedical engineering, and polymer chemistry, an innate push has been fostered to promote the use of bio-based materials that display the same modular material properties as petroleum-based plastics, but are safe and effective to utilize particularly in the case of human tissue exposure, common in many medical settings. Bio-based polymers are polymers that are derived from specifically from organic biomass entities such as corn, sugarcane, or cellulose (Pilla, 2011). These bio-based polymers can be utilized to create bioplastics, which are a type of plastic that is derived from biological substances instead of conventional petroleum-based substances (Pilla, 2011). Bio-based polymers include not only naturally occurring polymeric materials but also to natural substances that have been polymerized into high molecular weight materials by chemical and/or biological methods (Sudesh & Iwata, 2008). This further expands the constituents of bio-based polymers to include various synthetic polymers derived from renewable resources and CO_2, biopolymers such as polynucleotides, polyamides, polysaccharides, polyoxoesters, polythioesters, polyanhydrides, polyisoprenoides and polyphenols, as well as their respective derivatives (Sudesh & Iwata, 2008).

To produce biomaterials, several types of crops such as maize, sugarcane, perennial grasses, and rapeseed can be used to extract sugars, starches, oils, or lignocelluloses (Van Wijk & Van Wijk, 2015). These crops can be converted into bio-based bulk chemicals through different biomass conversion techniques including gasification, pyrolysis, catalytic conversion, pulping, fermentation, and enzymatic conversion as shown in Fig. 3.2 (Thielen, 2012; Van Wijk & Van Wijk, 2015). Many bio-based plastics are starch and sugar-based due to their affordability and steady availability. By hydrolytic cracking, starch can also be converted into glucose, which again is used as a raw material in the fermentation process to produce other bio-based plastics such as polylactic acid (PLA) and polyhydroxy alkanoate (PHA). Sugars are also used for many bio-based plastics ranging from polyethylene (bio-PE), polypropylene (bio-PP) and polyvinyl chloride (PVC) (Van Wijk & Van Wijk, 2015). In order for bioplastics to be utilized in additive manufacturing processes, these bio-based plastic polymers must be thermoplastic in nature. Thermoplastics are plastic materials or polymers that become pliable or moldable once heated above a specific temperature threshold and become solid upon cooling (Modjarrad & Ebnesajjad, 2013; Pilla, 2011). The most important material selection criteria for FDM materials are heat transfer characteristics and rheology or the behavior of liquid material flow (Chia & Wu, 2015). Thermoplastic polymers are the most ideal printing material for additive manufacturing processes such as FDM due to their low melting temperature (Chia & Wu, 2015).

While there are indeed a plethora of biomaterials and bio-based plastics that can be derived from natural, sustainable resources, each material has distinct chemical and mechanical properties to be considered. The scope of application is as equally important as the materials properties of the bioplastics, particularly when discussing 3-dimensional printing processes. Materials processability is a core attribute when 3D fabricating devices with bioplastics, as these materials display varying chemical and mechanical profiles including varying extrusion temperatures, micron layer densities, thermal and hydro-degradability, as well as distinct dexterity, tensile,

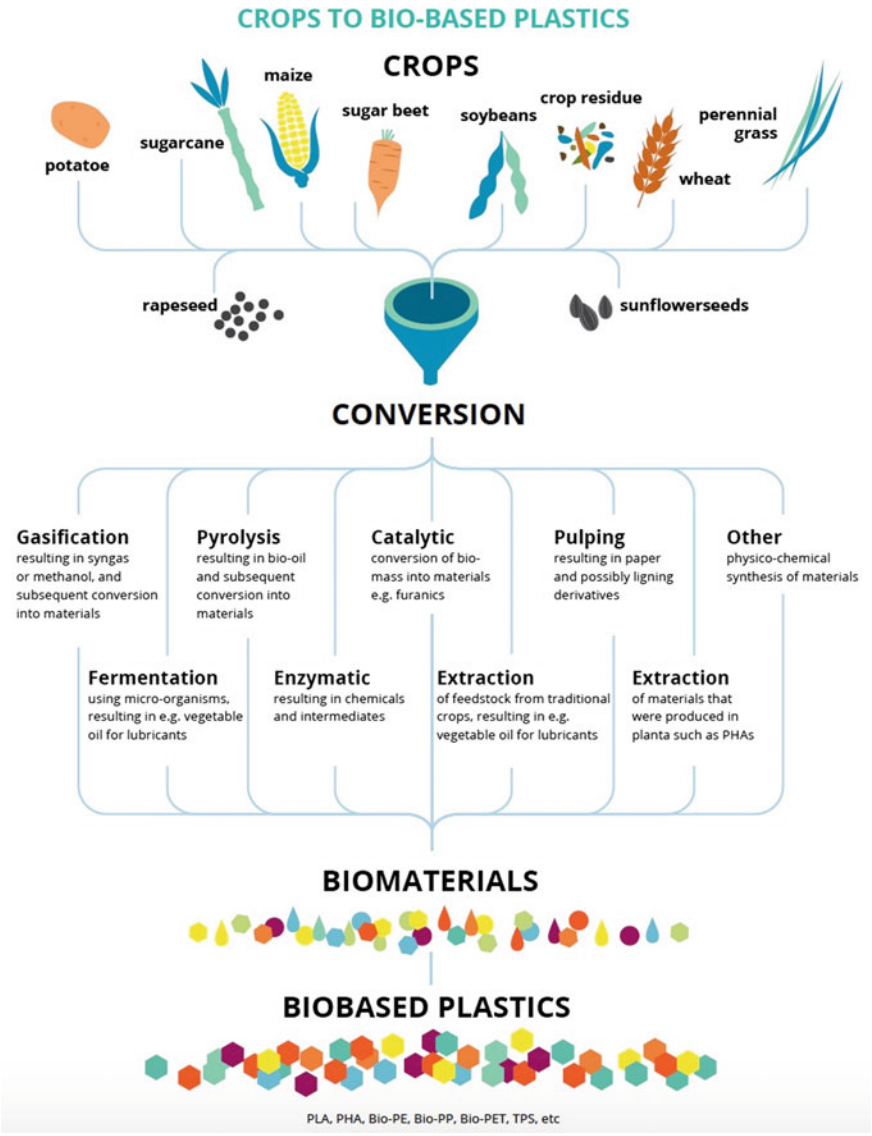

Fig. 3.2 Conversion of biomass into biomaterials and bio-based plastics (Van Wijk & Van Wijk, 2015)

compression, and load-bearing capacities (Bandyopadhyay, Bose, & Das, 2015; Chia & Wu, 2015; Thielen, 2012). There are four primary types of biomaterials that can be utilized to create bioplastics for manufacture, these include: cellulose derivatives, starch-based plastics, polylactic acid (PLA), and polyhydroxy alkanoates (PHAs). Each one of these of these biomaterials displays distinct materials

properties and processing capabilities, making each one unique in their respective application and use. Specifically, when utilizing an additive manufacturing application such as 3-dimensional printing, the bioplastic utilized must retain its ideal materials properties without being compromised during an extant process such as thermo-processing.

Starch is a polysaccharide and solid carbohydrate produced by green plants for the storage of excess glucose. Natural starch displays a semi-crystalline structure, which undergoes thermal degradation before its melting point is reached (Shih & Huang, 2011; Storz & Vorlop, 2013). This means that it cannot be directly utilized and applied in thermoplastic processing and must be modified as thermoplastic starch (TPS) (Huneault & Li, 2007). TPS can be prepared from starch granules by mixing and heating them in the presence of one or more plasticizers, typically water and glycerol, in a process called destructurization (Storz & Vorlop, 2013). TPS has been proposed as an attractive bio-based material since starch is extremely cost-effective and abundantly available in large volumes (Storz & Vorlop, 2013). TPS also has a primary disadvantage in which it is extremely hydrophilic, rendering it unsuitable for applications in humid environments and requires it to be blended with hydrophobic plastics, which are generally incompatible with TPS (Huneault & Li, 2007; Storz & Vorlop, 2013). Though starch-based plastics are prominent in bioplastics market space, its use as a suitable bio-based plastic is limited because of the issues related to using high amounts of starch (greater than 30%) without compromising the material properties (Huneault & Li, 2007; Storz & Vorlop, 2013).

Another material that can be utilized to create bioplastics is cellulose. Cellulose and its associated derivatives display a high degree of crystallinity in its structure, and is more stable than starch and cannot be dissolved or plasticized with common solvents or plasticizers (Mohanty, Wibowo, Misra, & Drzal, 2003; Storz & Vorlop, 2013). Cellulose still needs to be modified for thermoplastic processing due to its propensity for thermal degradation. The most ideal thermoplastic cellulose material is cellulose acetate (CA), which is prepared by acetylation of the hydroxyl groups of pulp with acetic anhydride (Mohanty et al., 2003). The thermal and mechanical properties as well as the biodegradability complex of cellulose acetate depends on how much acetylation it undergoes (Mohanty et al., 2003; Storz & Vorlop, 2013). Although their monomeric building blocks are quite similar (Fig. 3.3), cellulose (and its derivatives) and starch exhibit different materials properties (Storz & Vorlop, 2013). Both starch and cellulose share a commonality in that they cannot be processed as a thermoplastic material for applications such as 3-dimensional printing, without prior chemical modification (Storz & Vorlop, 2013).

PHAs are a group of naturally occurring, semi-crystalline polyesters, which display excellent biocompatibility and biodegradability (Storz & Vorlop, 2013; Van Wijk & Van Wijk, 2015). PHAs can be produced via bacterial fermentation, via microorganisms, of renewable feedstocks or plants, in which there are a plethora of distinct PHA monomers and hydroxyalka-noic acids (Thielen, 2012). The properties of PHAs strongly depend on their molecular structure and composition, in

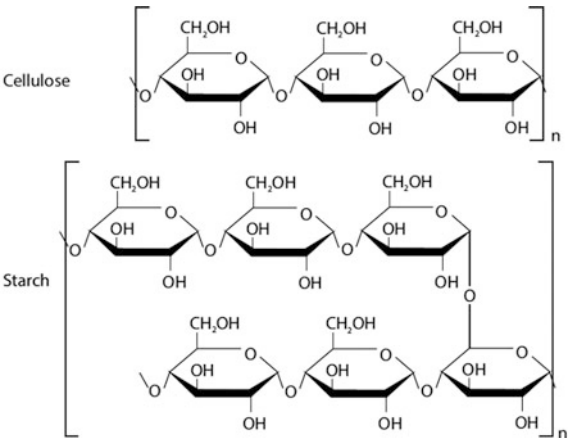

Fig. 3.3 Cellulose and starch chemical compositions (Storz & Vorlop, 2013)

which poly (3-hydroxybutyrate) or P3HB is very crystalline, and shows thermal and mechanical properties that is on par with PP and PE (Storz & Vorlop, 2013; Thielen, 2012). This however comes at a cost, as P3HB displays slow crystallization and the elongation at break, a measure of the flexibility, is lower compared to PP (Storz & Vorlop, 2013). The final natural biomaterial that can be utilized to fabricate bioplastics is that of polylactic acid or PLA. PLA bioplastics are semi-crystalline polyesters, which can be produced from lactic acid, a renewable fermentation product (Xiao, Wang, Yang, & Gauthier, 2012). PLA displays multiple advantages compared to all other previously discussed bioplastics, the first being that it can be processed on commonly available process equipment. Specifically, it displays a highly compatible nature with thermo-processing, particularly that of 3-dimensional printing, as PLA printing filament is highly prominent and utilized from FDM manufacture. An important property of PLA thermoplastics is the rate at which it recrystallizes upon cooling from the melt, in which rapid crystallization is required for many plastic applications with short cycle times such as 3D printing. Comparative Fig. 3.4 outlines the unique properties of each bioplastic material.

In examining the scope of application, we are particularly interested in the feasible deployment of RepRap 3D printing devices in LMICs in order to fabricate medical devices onsite to combat the global burden of disease. In focusing on the "big picture" the essence of feasibility is of the utmost importance. In defining the feasibility complex of interventions, the variables of resource-availability, accessibility, and in-field deployment dynamics are vital. While there are indeed a variety of potential bioplastic materials to utilize as previously shown, one must consider what materials can be feasibly deployed in a resource-poor setting and can be easily accessed. One of the most popular and versatile bio-based 3D printing filaments available today is that of polylactic acid (PLA).

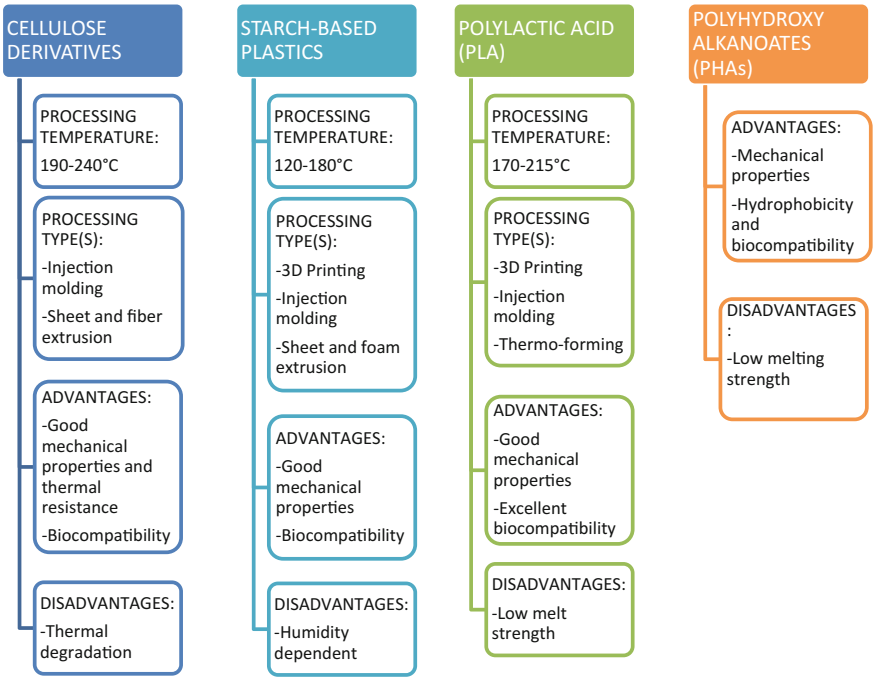

Fig. 3.4 Bio-based materials comparison table (Adapted from Van Wijk & Van Wijk, 2015)

3.2 Polylactic-Acid: Bio-Based Thermoplastic Polymer Properties and Medical Device Applications

Of the wide-array of bio-based polymers utilized to fabricate various bioplastic products, one particular sub-group has been of great interest with regards to its applications in 3-dimensional printing and fabrication of medical devices. 1–3 Polylactic acid, abbreviated as PLA, is one of the most extensively investigated bio-based thermoplastic polymers due to its high-modularity, mechanical strength, processability, renewability, thermodynamics, biocompatibility, sustainability, and low cost profile (Davachi & Kaffashi, 2015; Neches et al., 2014; Zeng et al., 2015). PLA has been widely utilized in a variety of medical applications ranging to the fabrication of tissue engineered scaffolds, orthopedic screws, sutures, stents, and drug-based delivery systems (Davachi & Kaffashi, 2015; Modjarrad & Ebnesajjad, 2013). Many in the field of biomaterials research have regarded PLA as the "most important" and ideal of all of the bio-based polymers currently available on the market (Van Wijk & Van Wijk, 2015). PLA is most noted for its biocompatibility complex, a critical property that is essential in the manufacture of medical devices including surgical instruments (Davachi & Kaffashi, 2015; Neches et al., 2014). The term biocompatibility refers to the properties of materials being biologically

compatible, in which they do not elicit maladaptive local or systemic responses from a living system or tissue (Ramot, Zada, Domb, & Nyska, 2016). PLA is derived from renewable and bio-based resources such as corn, rice and sugarcane, in which PLA and its associated degradation products, H_2O and CO_2, are neither toxic nor carcinogenic to the human body, hence making it an excellent material for biomedical applications (Xiao et al., 2012).

PLA has been approved by the U.S. Food and Drug Administration (FDA) and the European regulatory authorities for use in medical device applications, which often require direct contact with biological fluids (Xiao et al., 2012). Following regulatory approval, the applications of PLA and its polymeric composites have been utilized in wide-array of medical fields including: orthopedics, tissue engineering, ureteral stents, and biomaterials applications (Pawar, U Tekale, U Shisodia, T Totre, & J Domb, 2014). PLA is utilized in bioabsorbable fixation devices are for orthopedic and craniomaxillofacial surgery, in which these devices and ultra-high-strength implants are mainly composed of PLA and/or PGA polymers (Pawar et al., 2014). They are commonly used for the stabilization of fractures, bone grafting, reattachment of ligaments, tendons, and the PLA polymers reduce the risk of post implant infection (Pawar et al., 2014). PLA composites are also widely utilized in tissue engineering applications, in which these composites can function as effective scaffolds that stimulate cells/tissues for proliferation and osteogenic differentiation in bone tissue engineering as shown in Fig. 3.5 (Pawar et al., 2014). Cultured osteoblasts can be seeded onto bioresorbable PLA and PGA scaffold materials, in which the seeded scaffolds can withstand high-stress mechanics and promote bone growth and development (Pawar et al., 2014). PLA and its composites have been utilized in the fabrication of heart and ureteral bioresorbable stents for the treatment of ureteral injury and cardiovascular conditions. Specifically the PLA Abbott ABSORB II drug-eluting bioresorbable stent can be utilized to treat vascular occlusion (Fig. 3.6) and the SR-PLA 96 stent can be used for stenting after ureteral repair (Hodsden, 2015; Pawar et al., 2014).

PLA is an ideal bio-based material for 3-dimensional printing apparatuses as the material can be processed via FDM extrusion due to its greater thermal

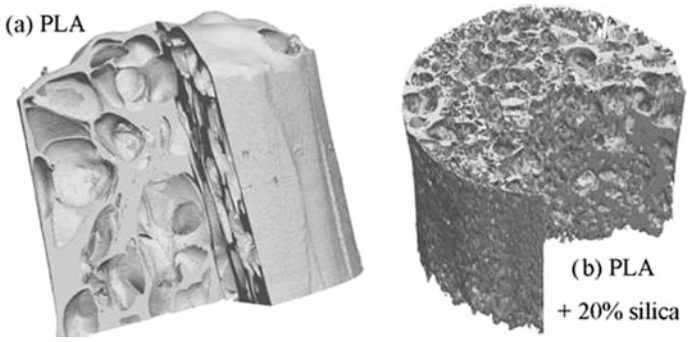

Fig. 3.5 PLA bone tissue engineering scaffold (Tissue Repair, 2016)

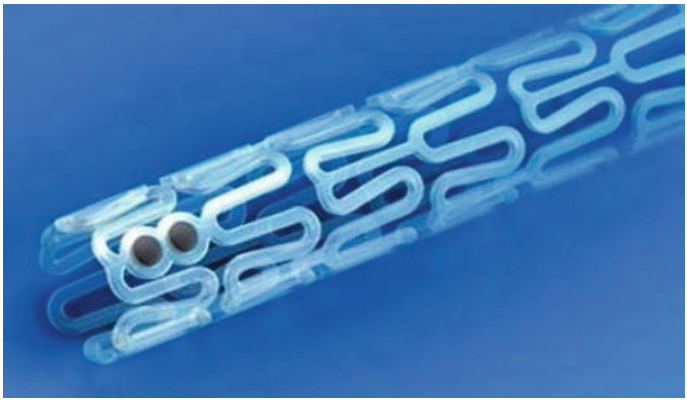

Fig. 3.6 Abbott ABSORB II PLA Bioresorbable Stent (Hodsden, 2015)

processability in comparison to other biomaterials such as polyethylene glycol (PEG) or polyhydroxyalkanoates (PHAs) (Xiao et al., 2012). In addition, PLA is superior to other bioplastics including polystyrene, polypropylene, and polyethylene terephthalate, with regards to the amount of energy and materials required to produce it (Kreiger & Pearce, 2013). The culmination of these materials properties makes the PLA thermoplastic polymer ideal for the additive manufacture processing and the fabrication of medical instruments (Kondor et al., 2013; Rankin et al., 2014). Polylactic acid is an aliphatic polyester derived from 2-hydroxypropionic acid, otherwise known as lactic acid, and is a multipurpose biodegradable polymer that is manufactured and produced in multiple polymer grades based upon application (Hamad, Kaseem, Yang, Deri, & Ko, 2015). These polymer grades include pure poly-L-lactic acid (PLLA), pure poly-D lactic acid (PDLA), and poly-D, L-lactic acid (PDLLA) (Xiao et al., 2012). The L-isomer constitutes the majority of PLA derived from renewable sources, as a large proportion of lactic acid from the biological sources exists in this form. Lactic acid is a natural organic acid that can be produced by fermentation of sugars obtained from the renewable resources such as corn starch, which contributes to the enhanced sustainability complex of PLA thermoplastics, which can be produced and used in an environmentally friendly cycle as shown in Fig. 3.7 (Xiao et al., 2012). These characteristics make PLA an ideal material to replace non-degradable petroleum-based plastics such as ABS in various commodity and medical-based plastic applications (Zeng et al., 2015).

PLA is a chiral polymer similar to lactic acid and contains asymmetric carbon atoms with helical conformation (Xiao et al., 2012). It has a stereogenic center in the main unit, which can display both isotactic and syndiotactic structures, in which the isotactic polymers contain sequential stereogenic centers with the same configuration such as the L and D-Lactides in Fig. 3.8, while the syndiotactic polymers contain sequential stereogenic centers of opposite configuration such as the Meso-Lactide in Fig. 3.8 (Mekonnen, Mussone, Khalil, & Bressler, 2013;

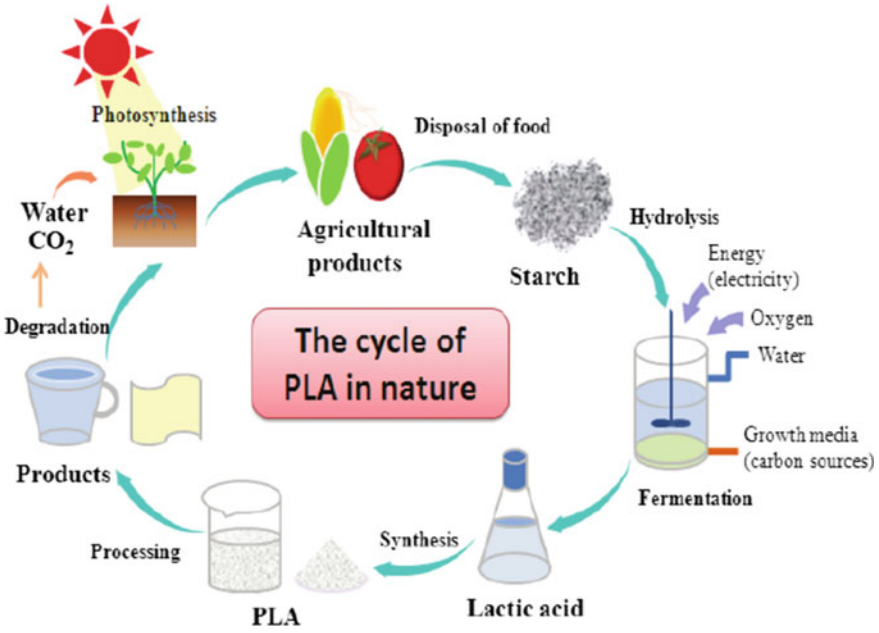

Fig. 3.7 The natural cycle of PLA extraction (Xiao et al., 2012)

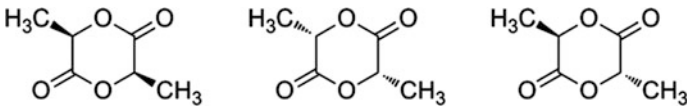

Fig. 3.8 PLA L-Lactide (*left*), D-Lactide (*middle*), and Meso-Lactide (*right*) stereoisomeric confirmations (Corneillie & Smet, 2015)

Zeng et al., 2015). The physical properties including melting temperature, crystallization behaviors, and mechanical properties of PLA depend strongly on its tacticity and stereo-chemical compositions (Table 3.1) (Davachi & Kaffashi, 2015). Isotactic PLA display a higher degree of crystallinity and enhanced thermo-degradability complex, with increases in both melting temperature (T_m), glass transition temperature (T_g), and the maximal decomposition temperature (T_{max}) (Corneillie & Smet, 2015). Isotactic PLA has the most ideal physical properties including increased Young's modulus, which measures elasticity via the amount of force a material can take before it breaks or becomes permanently bent, represented in unit form as gigapascals (GPa) (Corneillie & Smet, 2015; Davachi & Kaffashi, 2015). Atactic PLA, which has a random group orientation, displays amorphous qualities and lacks tacticity, thus making inferior in its mechanical qualities. PLA homopolymers polymerized from pure L-LA or D-LA has an equilibrium crystalline melting point of 207 °C, but most commercially available PLA that is utilized for

Table 3.1 PLA physical properties depend on tacticity and stereo-isomeric confirmation (Adapted from Marshall)

Polymer	T_m (°C)	T_g (°C)	Modulus (GPa)	Degradation time (months)
Isotactic PLA	170	60	2.7	>24 months
Syndiotactic PLA	153	45	N/A	N/A
Atactic PLA	Amorphous	55	1.9	12–16

additive manufacturing processes has a melting point of approximately 170–180 °C due to imperfect crystallites, minor racemization, and various impurities (Zeng et al., 2015). Commercially available polylactic acid (PLA) is typically available in the copolymer configurations of poly-L-lactic acid (PLLA) and poly-DL-lactic acid (PDLLA), in which PLLA is produced from L-lactides and *poly-DL-lactic acid* being produced form DL-lactides (Drummer, Cifuentes-Cuéllar, & Rietzel, 2012).

The stereoisomeric (L- and D-isomers) configurations of PLA are not only distinct in their chemical conformational nature, but also in their respective mechanical and thermal properties as well (Drummer et al., 2012). The thermal and mechanical properties of PLA properties depend on the ratio and the distribution of L- and D-LA in the polymer chains (Drummer et al., 2012; Mathew, Oksman, & Sain, 2005). For example, amorphous configurations of PLA containing 82% L-lactide and 18% D-lactide and semi-crystalline PLA containing 95% L-lactide and 5% D-lactide display very different thermal, optical, biological, and mechanical properties due to their intermolecular configurations (Mekonnen et al., 2013; Saeidlou, Huneault, Li, & Park, 2014). Amorphous polymers are isotropic and lack distinct definition in their molecular shape and pattern. These polymers have random structure, a broad melting point, and decreased mechanical properties including tensile, impact, and elongation at break strength (Fig. 3.9) (Zhai, Ko, Zhu, Wong, & Park, 2009). Crystalline polymers have a highly organized intermolecular structure that forms a crystal-like lattice, which results in a narrow melting point and increased mechanical properties including tensile and impact strength (Fig. 3.9) (Tabi, Sajó, Szabó, Luyt, & Kovács, 2010; Zhai et al., 2009). Increasing the L-isomer content and decreasing the D-isomer content, increases the crystallinity of the PLA constituent, which in turn increases the modulus and strength of elasticity as well as increases the heat deflection temperature (Tabi et al., 2010). Natural or native PLA is very brittle at room temperature, in which PLA consisting solely of L-LA blocks is semi-crystalline due to the high structural regularity (Storz & Vorlop, 2013). The crystalline regions of PLA provide additional mechanical strength, especially at elevated temperatures, which is ideal for thermo-processing involved in 3D printing.

In defining the materials properties of PLA for use in medical device applications such as surgical instrument fabrication, the physical and mechanical properties in addition to the chemical properties must be equally noted. Specifically the tensile, impact, shear, and compression strengths must be adequate enough for

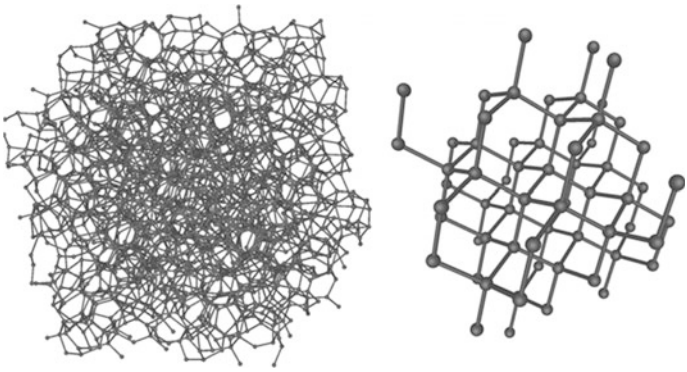

Fig. 3.9 Amorphous (*left*) and crystalline (*right*) polymer structures (Ströck, 2006)

deployment in the surgical field (Hamad et al., 2015; Modjarrad & Ebnesajjad, 2013). Overall, PLA has above-average mechanical properties including enhanced Young's modulus (materials stiffness), tensile strength, and flexural strength compared to traditional polymers, such as polypropylene (PP), polystyrene (PS), and polyethylene (PE) (Hamad et al., 2015). However, the elongation break and the impact strength of PLA are lower than other polymers such as polypropylene, polyamide, and polyethylene terephthalate (Hamad et al., 2015). Although the tensile strength and Young's modulus of PLA are comparable to other petroleum-based thermoplastics, PLA is indeed more susceptible to deformation at higher stress levels (Hamad et al., 2015). Although the tensile and flexural strength as well as the Young's modulus of PLA are quite good, the poor impact strength and overall materials toughness gradient has limited its use in applications requiring plastic deformation at higher stress levels (Hamad et al., 2015). This has led to increased interest in improving the overall "toughness" of PLA over last five years (Hamad et al., 2015; Oyama, 2009).

3.3 Chemical and Mechanical Profile Modification of Bio-Based Materials: Natural Biocomposite Enhancement

The PLA polymer has the unique ability to be adapted based upon user-specific applications. This element of adaptability is vital as this means that the PLA polymer can be modified and converted into a specific product by compounding, copolymerization, or polymer blending with other bio-based or petroleum-based thermoplastics (Zeng et al., 2015). This vastly expands the interventional applications of PLA, specifically in medical device manufacturing, as PLA can be further improved and developed to meet application-specific needs. This is important when

it comes to the fabrication of medical devices and supplies such as surgical instruments, as PLA can be further enhanced to improve the physical characteristics of these instruments in the surgical field. Characteristics such as tensile strength, flexibility, mechanical stress-points, and load-bearing capacity can be enhanced to further improve instrument utility and application. In addition, adding additives such as color pigments, UV stabilizers, impact resistance modifiers, flame-retardants, plasticizers, chain extenders, nucleating agents, can further optimize the properties for the planned application (Van Wijk & Van Wijk, 2015).

With regards to modifying and enhancing the materials properties of PLA, there are four primary modulatory components: plasticizers, chain extenders, nucleating agents, and biocomposites (Fig. 3.10). Plasticizers are small, non-volatile, organic molecules that are added to polymers such as PLA to effectively reduce brittleness and improve toughness as well as lower glass transition and melting temperatures (Mekonnen et al., 2013). Plasticization reduces the amount of polymer–polymer contact, thus decreasing the rigidity of a three-dimensional fabricated object (Mekonnen et al., 2013). The next type of PLA modifier is that of chain extension, which raises the molecular weight via interfacial adhesion of natural polymers such as PLA, resulting in higher melt-strength and toughness (Cherykhunthod, Seadan, & Suttiruengwong, 2015). Chain extending reactive agents such as peroxide (Perkadox) and multifunctional epoxide chain extender (Joncryl), have been utilized to enhance PLA blends and results in increased impact strength, elongation at

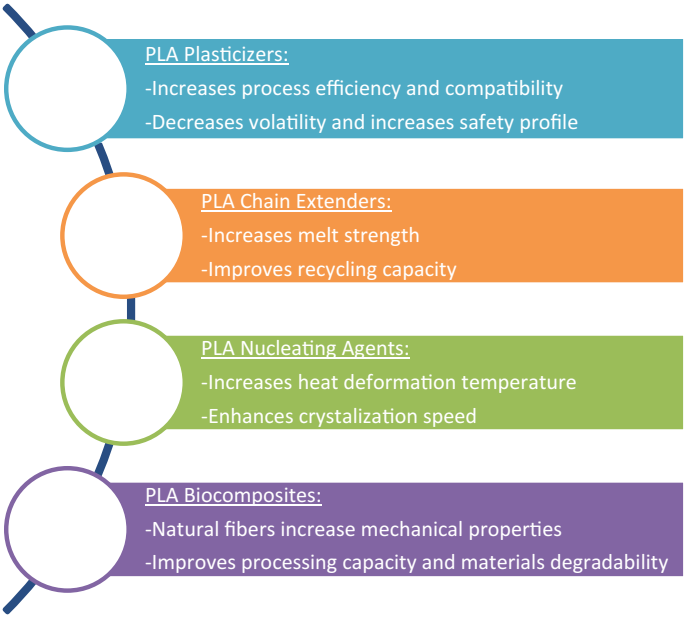

Fig. 3.10 Types of PLA materials property modifiers (Adapted from Hamad et al., 2015; Mathew, 2004; Van Wijk & Van Wijk, 2015)

break, and the overall mechanical nature of PLA (Cherykhunthod et al., 2015). The next type of modifier is that of nucleating agents, which are inorganic nanoparticles, such as talc, sodium stearate, calcium lactate, and carbon nanotubes, which modify the crystallinity complex of PLA polymers (Shi, Zhang, Phuong, & Lazzeri, 2015). The degree of crystallinity is an important element related to PLA processability, as it effects the structural, thermal, barrier and mechanical properties, and depends on the ratio of D to L enantiomers used (Shi et al., 2015). Nucleating agents serve as a catalyst PLA crystallization and improve its thermodynamic properties, making it further ideal for thermo-processing and enhance the overall toughness gradient of PLA.

PLA's mechanical materials profile can be further enhanced via integration with other biocomposite materials. With PLA displaying weakness in both its elongation and high-stress gradients, considerable research has been conducted to create stronger reinforced PLA thermoplastic polymers that can handle repeated high mechanical stress gradients in the field. The most widely used methods to modify the properties of polymers include chemical copolymerization and polymer blending (Zeng et al., 2015). PLA has been copolymerized with a variety of polymers including polyesters, polyolefins, and natural polymers through several polymerization techniques such as condensation polymerization (Zeng et al., 2015). In addition to chemical copolymerization, recent studies have examined utilizing PLA biocomposite blends, which merge various bio-based polymers with enhanced properties together, in order to create a strengthened fabricated product. Such blends include PLA with polyglycolic acid as well as poly(ethylene-glycidyl methacrylate) (EGMA), both of which act as a toughening agent for PLA (Okubo et al. 2009; Zeng et al., 2015). Specifically, these blends can improve the impact strength of PLA, as the crystalline matrix structure of high-molecular weight PLA becomes finer leading to the generation of more co-polymers in the interfacial regions (Okubo et al. 2009; Zeng et al., 2015).

Physical polymer blending is the most promising way of modifying properties of homopolymers such as PLA in a cost-effective and simple manner. PLA can indeed be blended with various plasticizers and polymers, in which the introduction of micromolecular or macromolecular plasticizers can exponentially improve the toughness index of PLA (Zeng et al., 2015). Specifically, the elongation break capacity can be enhanced due to the plasticization effect, which could reduce the glass transition temperature and thus increase the ductility of PLA (Zeng et al., 2015). In addition, natural fibrous blends can be mixed with PLA utilizing natural materials such as jute, kenaf, jute, bamboo, and silkworm fibers (Li et al., 2003; Shih & Huang, 2011; Tokoro et al., 2008). Figure 3.8 below shows the benefits of blending natural fiber blends with PLA, in which natural fiber blends are ideal for enhancing the mechanical properties of PLA. Specifically, fiber blends enhance PLA's overall toughness gradient including tensile strength, elongation-break, bending and impact strength, as well as elasticity and ductility. In addition to mechanical enhancement, certain fiber blends such as with bamboo fibers, enhances the thermal properties of PLA. This improves the thermo-processability of PLA and makes it even better suited for thermal extant processing.

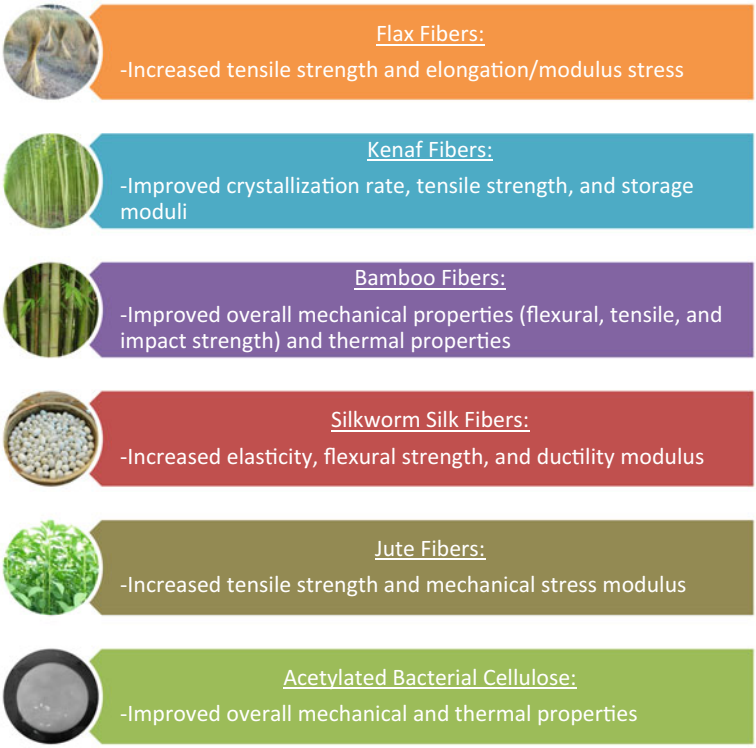

Fig. 3.11 Types of fiber biocomposite materials for PLA enhancement (adapted from Li et al., 2003; Shih & Huang, 2011; Tokoro et al., 2008; Xiao et al., 2012)

In looking at Fig. 3.11, we can see that the biocomposite fibrous blends greatly enhance the thermal stability and mechanical properties of PLA. The most feasible and popular biocomposite blends utilize bamboo fiber, which is easily sourced and complements many bioplastic polymers. Bamboo biocomposite blends display almost two-times higher tensile and flexural strength when compared to standard PLA (Shih & Huang, 2011). This reliably increases the structural and mechanical nature of PLA without compromising its ideal biocompatible properties for use in medical devices. Thus further creation of hybrid blends and reinforcement of PLA filament with natural components such as microcrystalline bacterial cellulose can create a high-strength PLA polymer that maintains its ideal bio-based properties (Mathew et al., 2004). An interesting facet related to bio-based polymers, is that not all of them are biodegradable, in which crystalline PLA is virtually non-biodegradable just like cellulose ester derivatives (Sudesh & Iwata, 2008). This decreased biodegradation profile further enhances the long-term efficacy of utilizing PLA in fabrication of surgical instruments that will be utilized repeatedly in the field. While there is indeed promise of utilizing polymer blends and biocomposite to further enhance PLA's material properties, these advances are limited by their

respective ability to be "scaled" for industrial manufacture. Many of these polymer blends and biocomposite materials do behave ideally in a lab setting, but the ability to readily apply these materials to the marketplace will take time. There are many confounding variables that must be examined before these materials can serve as a viable substitute for current thermoplastic materials, especially since many of these materials must be adapted for additive manufacturing processing. In addition, the price competencies of these materials must be examined, as they must serve as a viable option compared to current market alternatives, or if indeed they require a higher price point, they must justify it in a manner that makes it a better alternative than current materials offered in the marketplace. In an ideal situation, both the RepRap derivative devices such as the Mendel or Prusa i3 could be further modified in conjunction with these material advances to serve as an ideal fabrication and delivery platform for bio-based 3D objects and prototypes.

3.4 Polylactic Acid Versus Acrylonitrile Butadiene Styrene Thermoplastics

In deploying a FDM rapid prototyping-printing device such as a RepRap in the field, there are two primary filaments that are most likely to be utilized, this being ABS or PLA. As previously mentioned, the PLA and ABS thermoplastics are the two most commonly used printing filaments in FDM printing. While there are indeed a plethora of other distinct hybrid bio-based sustainable filaments that are being developed, the interventional capacity for these printers lies on the premise on in-field deployment feasibility and accessibility to these filaments. When it comes to printing surgical instruments, a functional comparison of these two filaments is warranted to provide support for the use of bio-based materials over petroleum-based materials in fabricating surgical tools. In fabricating surgical instruments, two elements are of the utmost importance, this being mechanical strength and biocompatibility/fabrication process toxicity. It is through the culmination of these two critical elements that the future of bio-based surgical toolkits transitions from theory to physical application. The ability to utilize sustainable bio-based polymers that are non-petroleum based and maintain the same fundamental mechanical and thermoplastic properties of petroleum-based plastics such as ABS would foster a new era of sustainable medical device fabrication. In first comparing the mechanical elements of ABS and PLA thermoplastics, the impact strength, compressive strength, flexural strength, and tensile strength are the four most important components. In comparing these four qualities, PLA was compared to ABS in four separate testing methods including: ASTM D256, D695, D790, and D638 Type IV (PLA and ABS Strength Data). ASTM is an international organization that develops consensus standards for materials, properties, and systems, in order to derive optimal standards (Langer & Grellmann, 2014). The ASTM D256 test is a standard testing method that analyzes the impact resistance of a material by

utilizing an un-notched IZOD pendulum to strike the material and measure the strength in foot pounders per inch (ft-lb/in) (Langer & Grellmann, 2014). In comparing the PLA and ABS specimens in all four tests, two infill densities were selected, one being standard density (approx. 50%) and the other being maximum density (100%) (PLA and ABS Strength Data). In the ASTM D256 test, ABS bested PLA at both standard and maximum infill densities (Fig. 3.9). The ASTM D695 test is a standard testing method that analyzes the compressive strength of a material by utilizing a tensile testing machine that compresses the material between two steel compression platens and measures the peak stress in pounds per square inch (PSI) (ASTM International, 2015). In the ASTM D695 test, PLA bested ABS at both standard and maximum infill densities (Fig. 3.12). The ASTM D790 test is a standard testing method that analyzes the flexural strength of a material by utilizing a universal testing machine and a three-point bend fixture to bend the plastic material test bars to acquire the peak stress in pounds per square inch (PSI) (DeWolfe, 2010). In the ASTM D790 test, PLA bested ABS at both standard and maximum infill densities (Fig. 3.9). The final mechanical test is the ASTM D638 Type IV test, which is a standard testing method that analyzes the tensile strength of a material by measuring the force required to pull the plastic specimen to its breaking point (ASTM International, 2014). In the ASTM D638 Type IV test, PLA bested ABS at both standard and maximum infill densities as well (Fig. 3.9).

The second element that is of importance when fabricating surgical instruments via FDM manufacturing, is that of biocompatibility and toxicity related to the fabrication process as well as the surgical instruments themselves. By this we refer to two primary elements, this being nanoparticle aerosol emission related to FDM additive manufacturing and nanoparticle lechate from instrument contact with the

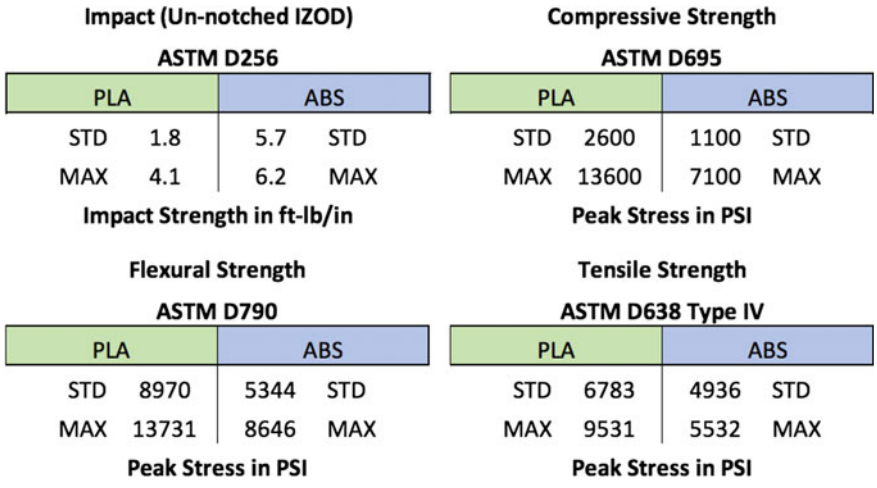

Fig. 3.12 Comparative analysis of PLA versus ABS impact, compressive, flexural, and tensile strength (PLA and ABS Strength Data)

bodily fluids and tissues. Nanoparticle aerosol emission has recently been of great concern for additive manufacturing processes, as when thermal processing anytype of thermoplastic material such as ABS or PLA, gases and ultrafine particles (UFPs) are aerosolized and emitted in the surrounding area by the printing apparatus. Ultrafine particles or nanoparticles are defined as particles less than 100 nm in diameter, which can inhaled by individuals within the immediate area of the 3D printing apparatus and can indeed be highly toxic depending on the material that is being processed (Stephens, Azimi, El Orch, & Ramos, 2013). Previous studies have shown that exposure to emissions from thermal decomposition of thermoplastics has been shown to have acute toxic effects in animals, and exposure to UFPs from other sources has been linked to a variety of adverse human health effects including respiratory arrest and cancer (Azimi, Zhao, Pouzet, Crain, & Stephens, 2016; Stephens et al., 2013). This is a critical factor when comparing ABS and PLA printing filaments, as ABS additive manufacturing processes are highly toxic in nature and must be performed with caution. Upon comparison of these two filament extrusion processes, PLA thermoplastic processing emits significantly less UFPs when compared to ABS filaments as shown in Fig. 3.13

Given the higher emission of UFPs via ABS thermoplastic processing, it is important to note what types of UFPs are emitted. These UFPs emitted via thermoplastic processing are in the form of volatile organic compounds (VOCs), which vary based upon the type of plastic being processed. Figure 3.14 below summarizes the volatile organic compound emission rates and provides estimates of the individual speculated VOC and ΣVOC emission rates from 16 different 3D printer and filament combinations (Azimi et al., 2016). The top three highest emitted

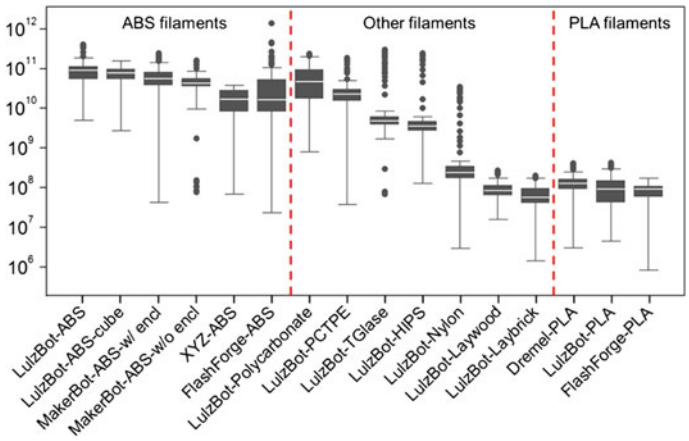

Fig. 3.13 Summary of time-varied UFP emission rates for 16 different 3D printer and filament combinations. Each data point represents data from 1 min intervals, with the combination of data points representing the entire printing period (ranging between 2.5–4 h). Boxes show the 25th and 75th percentile values with the 50th percentile in between. Whiskers represent upper and lower adjacent values, and circles represent outliers beyond those values (Azimi et al., 2016)

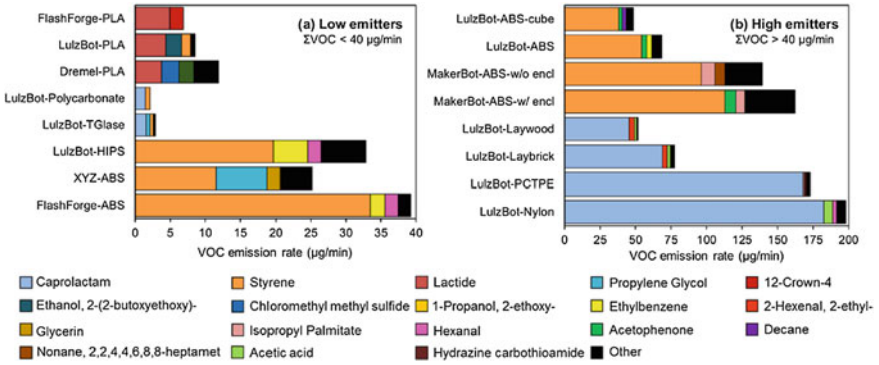

Fig. 3.14 VOC emission rate and the sum of the top 10 detectable VOCs (ΣVOC) resulting from operation of 16 different 3D printer and filament combinations, which is divided into **a** low emitters, with EΣVOC < 40 µg/min, and **b** high emitters, with EΣVOC > 40 µg/min (Azimi et al., 2016)

compounds accounted for at least 70% of ΣVOC emissions in all cases, but for most of the printer and filament combinations, a single VOC dominated the ΣVOC emissions (Azimi et al., 2016). The primary VOC emitted from all ABS filament and printer combinations was styrene, with estimates of styrene emission rates with these filaments ranging from 12 to 113 µg/min (Azimi et al., 2016). PLA thermoplastic processing primarily released lactide, a harmless organic compound with inert properties, thus making the processing of PLA extremely safe and non-toxic. Figure 3.15 provides a overall comparison module for the total UFP and VOC emission output per mass of filament. According to this graphical depiction, PLA

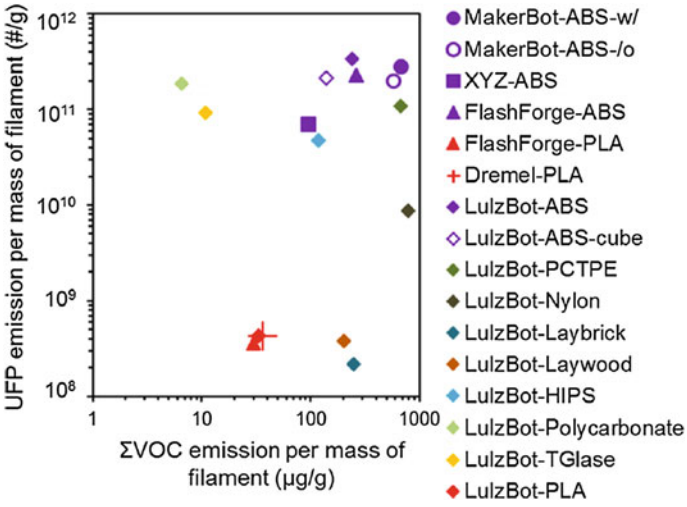

Fig. 3.15 Comparison of total UFP and VOC emissions per mass of filament (Azimi et al., 2016)

thermoplastic processing produces the least amount of UFPs and VOCs compared to ABS processing, thus providing further quanitative evidence in support of the high-net safety profile of PLA thermoplastic processing for surgical instrument fabrication.

In reviewing the use of PLA and ABS thermoplastics in medical devices, both materials are relatively biologically inert and stable in their final processed form. It is only when ABS thermoplastics are thermally processed via FDM extrusion that it becomes toxic in nature and presents a threat to human health. Both PLA and ABS are indeed hemocompatible, non-cytotoxic, and do not release any harmful or toxic leachates (Lithner, Nordensvan, & Dave, 2012). PLA thermoplastics are generally considered more hypoallergenic than ABS and are overall more recommended for continual exposure to bodily fluids and tissues (Rankin et al., 2014). In addition, PLA is equally noted for its sustainability complex and ability to be derived from simple bio-based elements such as corn or sugarcane, which are present in many LMICs. PLA prototypes and instruments can be composted and recycled easily without any harmful environmental effects, while ABS is not compostable and can have negative environmental effects when not recycled properly. The use of PLA in LMICs is warranted is it presents a focal sustainable shift from non-sustainable petroleum based products. This can ultimately contribute to further enhancing human and environmental health in LMICs and promote future sustainable interventions.

Upon review of the materials properties of PLA, the functional utility in utilizing this bio-based material in the fabrication of surgical supplies and instruments is promising. PLA presents as an excellent bio-based material, in which it displays exceptional biocompatibility, flexibility, and strength. Furthermore, with continued advances in polymer and bio-based materials blending such as with polyglycolic acid and banana fiber, the materials qualities of PLA can further be enhanced. These noted qualities make PLA ideal for the fabrication of surgical instruments to combat supply deficiencies in LMICs to combat the global surgical burden of disease. Specifically, we can utilize this bio-based material to fabricate a novel entity known as the "integrative surgical toolkit" or IST. The integrative surgical toolkit could indeed revolutionize global access and delivery of pertinent surgical care in LMICs and create a multi-faceted paradigm shift in medical supply delivery and accessibility. Specifically, the utilization of 3D printing apparatuses in conjunction with sustainable bio-based materials can create opportunities for healthcare advancement, delivery, human capital development, domestic manufacturing, medical device attainment, and social innovation.

Figure 3.11 Picture Credits (Listed in order of appearance in figure)

Flax Picture
Cuyler, S. (n.d.). Flax Fiber-Linen. Retrieved February 27, 2017, from https://www.emaze.com/@ALCQROOZ/Flax-Fiber-Linen

Bamboo Picture
McMathis, J. (2014, August 22). Could a bamboo fiber composite replace steel reinforcements in concrete? Retrieved February 27, 2017, from http://ceramics.org/ceramic-tech-today/biomaterials/could-a-bamboo-fiber-composite-replace-steel-reinforcements-in-concrete

Silk Fiber Picture
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Kenaf Fiber Picture
Properties of Kenaf (for Papermaking). (2016). Retrieved February 25, 2017, from http://www.paperonweb.com/Kenaf.htm

Bacterial Cellulose Picture
Cai, Z., & Kim, J. (2010). Preparation and characterization of novel bacterial cellulose/gelatin scaffold for tissue regeneration using bacterial cellulose hydrogel. Journal of Nanotechnology in Engineering and Medicine, 1(2), 021002.

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Chapter 4
3-Dimensional Printing of Medical Devices and Supplies

Applications 3-dimensional printing technology, specifically that of the RepRap FDM printing apparatus, can vastly enhance the surgical capacity of health facilities in developing countries. In defining the problem of disparities and lack of adequate surgical care, once again the fundamental problem of medical supply sourcing comes to fruition. Provisional surgical care relies heavily on the ability to allocate critical surgical tools and instruments to perform life-saving interventions. 3D printing technologies provide a cost-effective solution to provide needed medical supplies in a direct, on-demand fashion onsite, to further enhance the physicians interventional capacity to render surgical services (Ibrahim et al., 2015). Printing essential medical equipment can greatly reduce the functional burden of disease in developing countries. As previously, described 3-dimensional printing can deliver prototypes via FDM onsite, but what is the functional capacity of this device and how exactly can it aid in improving healthcare access and delivery in a variety of settings and environments in LMICs? The answer lies in the development of self-contained, mobile integrated kits of essential surgical instruments that could provide the basic tools necessary for vital surgical interventions on-site (World Health Organization, 2010). These surgical toolkits, referred to as the "integrative surgical toolkits" or ISTs, provides a feasible solution to providing direct access to basic surgical instruments. In describing the components of these toolkits, the term "integrative" takes to fruition, creating a novel entity that can provide the necessary instruments to surgically treat a variety of pertinent surgical conditions that often plague individuals in LMICs and contribute to the surgical burden of disease.

4.1 Fabrication of High-Utility Surgical Toolkits

The fabrication and deployment of high-utility integrative surgical toolkits is a concept and feasible idea that could indeed serve as a viable component in combating the global burden of surgical disease. A core tenet behind the fabrication of

S.K. Bhatia and K.W. Ramadurai, *3D Printing and Bio-Based Materials in Global Health*, SpringerBriefs in Materials, DOI 10.1007/978-3-319-58277-1_4

these surgical toolkits is that they must provide real, functional utility and encompass a variety of medical instruments/tools. For the sake of this book, we explore the feasible fabrication of 14 surgical devices/instruments, each of which is vital in defining surgical outcomes in the four common categories of surgically treatable conditions that afflict public health in developing countries. The first category is the provision of initial surgical care to injury victims to reduce preventable deaths and decrease the number of survivable injuries that result in personal dysfunction and impose a significant burden on families and communities (Bhatia, 2010; Jamison et al., 2006). The second category is the handling of obstetrical complications including obstructed labor and hemorrhage (Jamison et al., 2006). The third category is the surgical management of abdominal and extra-abdominal emergent and life-threatening conditions (Jamison et al., 2006). The fourth category is the elective care of simple surgical conditions such as hernias and hydroceles (Jamison et al., 2006). In providing comprehensive and adequate surgical care for each of these four identified surgical categories, the proper surgical instruments must be utilized. Since each of these surgical categories is distinct in nature, comprehensive integration of multiple high-utility instruments must be implemented in order to provide proper surgical care for each of these categories.

In creating such high-utility integrative surgical toolkits, we examine 14 distinct surgical instruments that have been selected based upon their ability to be 3D printed with bio-based materials such as PLA, and utilized in life-saving general and emergency surgical procedures most commonly present in LMICs. The World Health Organization as well as multiple surgical studies have defined these instruments pertinent tools in providing broad-spectrum surgical care, and critical in enhancing the interventional capacity of surgeons to combat the surgical burden of disease (World Health Organization, 2014). These instruments can be utilized in a plethora of critical surgical interventions ranging from simple wound stitching with a needle driver to complex surgeries such as vehicular accidents involving the use of tissue forceps, surgical retractors, and vascular clamps employed in a simultaneous fashion (Wong & Pfahnl, 2014; World Health Organization, 2014). One critical element related to the choice and use of these instruments for the integrative surgical toolkit is the ability of these instruments to be fabricated via 3D FDM printing. Previous studies have defined the feasibility of creating 3D CAD files of these instruments and utilizing commercially available 3D FDM prototyping to create actual functional devices that could indeed be utilized in surgery. Wong & Pfahnl, Rankin et al., and Kondor et al., have explored the fabrication of instruments utilizing ABS plastic filament and a MakerBot 3D printing apparatus. These medical instruments and supplies span a variety of applications and printing environments, in which Wong & Pfahnl explored additive manufacturing of surgical instruments in space to create a surgical kit for use on space missions. Rankin et al. explored fabricating a single Army-Navy surgical retractor out of PLA and Kondor et al., explored created a small trauma care kit for deployment in combat zones. These 14 surgical instruments that we explore for use in integrative surgical toolkits include: Debakey tissue forceps, Senn retractor, needle driver, Pennington clamp, sponge clamp, smooth tissue forceps, Allis tissue clamp, Adson's toothed

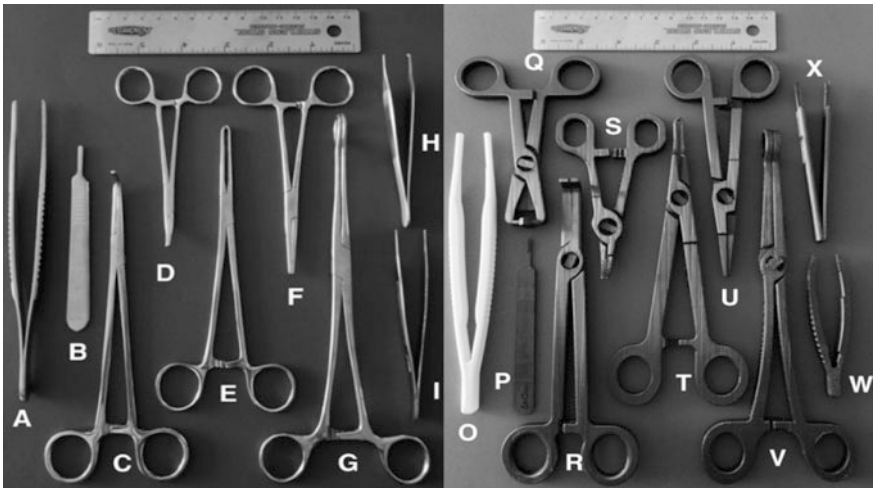

Fig. 4.1 Surgical instrument profile: *Left side* Stainless steel surgical instruments: *A* Debakey tissue forceps, *B* scalpel handle, *C* right angle clamp, *D* curved hemostat, *E* Allis tissue clamp, *F* straight hemostat, *G* sponge clamp, *H* Adson's toothed forceps, and *I* smooth forceps. *Right side* 3D-printed acrylonitrile butadiene styrene surgical instruments: *O* Debakey tissue forceps, *P* Scalpel handle, *Q* Towel clamp, *R* Right-angle clamp, *S* Curved hemostat, *T* Allis tissue clamp, *U* Kelly hemostat, *V* Sponge clamp, *W* Smooth forceps, and *X* Adson's toothed forceps (Wong & Pfahnl, 2014)

forceps, Army-Navy general surgical retractor, umbilical cord clamp, vascular clamp, Tenaculum, Kelly hemostat, and scalpel handle. These various instruments are shown in Figs. 4.1, 4.2, 4.3, and 4.4.

Debakey tissue forceps, (B) scalpel handle, (C) right angle clamp, (D) curved hemostat, (E) Allis tissue clamp, (F) straight hemostat, (G) sponge clamp, H) Adson's toothed forceps, and (I) smooth forceps. (Right Side) 3D-printed acrylonitrile butadiene styrene surgical instruments: (O) Debakey tissue forceps,

Fig. 4.2 3D-printed polylactic acid Army-Navy surgical retractor (Rankin et al., 2014)

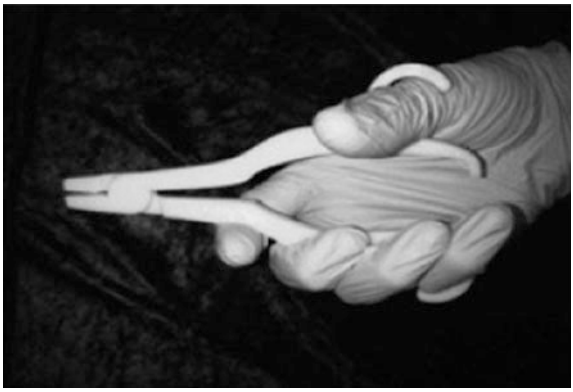

Fig. 4.3 3D-printed acrylonitrile butadiene styrene needle driver (Kondor et al., 2013)

Fig. 4.4 3D-printed acrylonitrile butadiene styrene umbilical cord clamp (Molitch, 2013)

(P) Scalpel handle, (Q) Towel clamp, (R) Right-angle clamp, (S) Curved hemostat, (T) Allis tissue clamp, (U) Kelly hemostat, (V) Sponge clamp, (W) Smooth forceps, and (X) Adson's toothed forceps (Wong & Pfahnl, 2014).

Previous studies have examined the fabrication of 3D printed ABS thermoplastic surgical instruments as shown above, and have indeed shown feasibility context of creating these devices. In order to create functional prototypes of the integrative surgical toolkit utilizing polylactic acid, the digital functional prototypes and models of each instrument were downloaded from multiple sources. This includes obtaining permission rights from open source 3D CAD file and .STL websites such as 123AutoCAD.com and thingiverse.com. These files were then modified and redesigned in Cura 2015 computer aided design (CAD) software, utilizing a Macintosh OS.X platform based workstation. Upon attainment of these CAD design files, many of the surgical instrument models were modified based upon the printer apparatus utilized, specifically that of the FDM printer and the PLA polymer

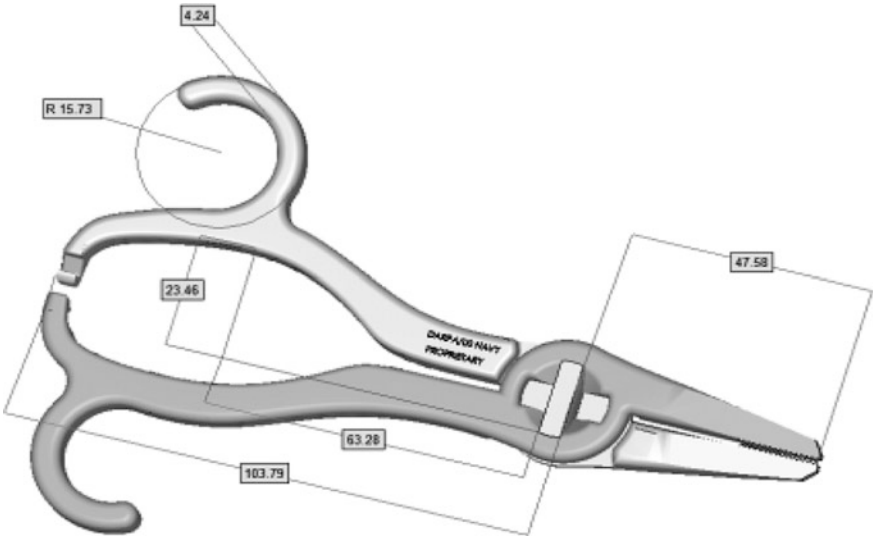

Fig. 4.5 Modified CAD model with driving dimensions and two-piece hinge connection point (Kondor et al., 2013)

properties. Many of the models were parameterized with key dimensions including arm lengths, and finger loop positions and custom designs were generated via alteration of the values of the key dimensions within the CAD application (Kondor et al., 2013). Instruments such as the vascular clamp and the Kelly hemostat were further modified to account for the limitations of printing suspended curvature components as well as device clamp locking mechanisms. Driving dimensions also known as the geometrics of the models were modified in the CAD model to generate unique instrument profiles and enhance the design compatibility with the PLA polymer filament. These modifications were made based upon previous studies that have identified ideal instrument configurations for FDM processing and PLA filament properties. Figure 4.5 shows the CAD model with driving dimensions that were modified for hemostat device to be fabricated via FDM with a thermoplastic polymer filament. After instruments were sized to and tailored to general hand mechanics, the CAD model was exported, and saved in the .STL file format.

Basic functional instrument designs for the IST were modified to replicate the mechanical performance of standard stainless steel instruments and adaptation of the designs was necessary to accommodate the properties of the polylactic acid thermoplastic polymer filament. An important element related to the fabrication of these instruments is that of the anisotropic quality of PLA 3D printing (3D Matter, 2016). The anisotropic quality means that the properties of the PLA material utilized depend

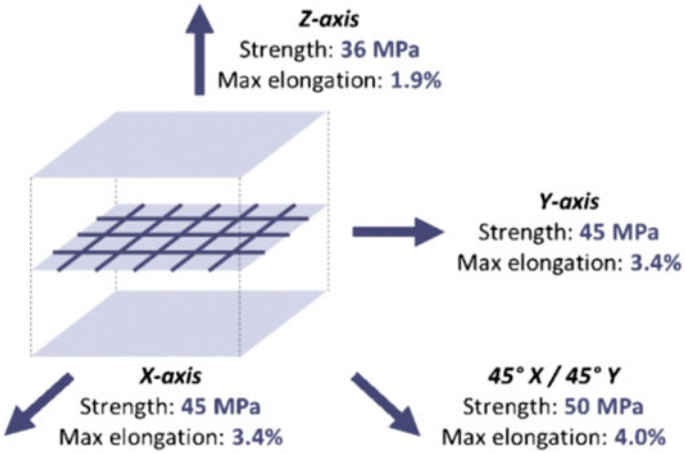

Fig. 4.6 PLA axial mechanical properties (3D Matter, 2016)

on the x, y, and z-axial direction. The process of 3D printing inherently tends to create weaknesses along the z-axis, because the interface between layers is not as strong, in which the z-axis direction is approximately 20–30% weaker than other directions, and that the max elongation was halved as shown in Fig. 4.6 (3D Matter, 2016). These axial configurations were taken into consideration and instrument x, y, and z-axial design modifications were performed using the Cura 2.3.1 software. This included modifying the infill density of each instrument's modular design as shown in Fig. 4.7 as well as the infill pattern/geometry in Fig. 4.8. The infill density refers to the overall amount of thermoplastic deposited within the internal scaffold of the

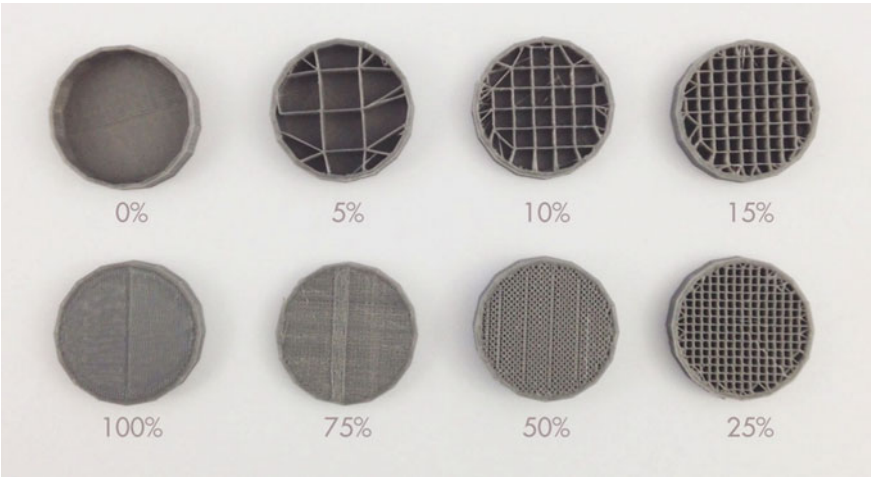

Fig. 4.7 3D Printer infill density configurations (Budmen, 2013)

3D printed instrument, in which a higher infill density means that there is more plastic deposited within the print, therefore creating a stronger object (3D Matter, 2016). The infill geometry or pattern refers to the pattern that the extrusion nozzle draws or follows to fill the 3D object (3D Matter, 2016). These patterns can come in a wide array of geometric configurations such as Honeycomb, Concentric, Line, Rectilinear, Hilbert Curve, Archimedean Chords, and Octagram Spirals as shown in Fig. 4.8 (Hodgson, 2016). These various infill patterns/geometric configurations varies with regards to flexibility, strength, and compression bearing capabilities, thus proper infill geometry must be determined for optimal PLA instrument functionality.

Based upon previous studies, an infill density between 10 and 20% will suffice for basic 3D prototypes, but for fabrication of surgical instruments the infill density must be higher (3D Matter, 2016; Rankin et al., 2014). According to previous research, increasing the infill density of an object increases its mechanical strength and durability, but comes a cost. Increasing the infill density results in decreased instrument flexibility, prolonged printing time, and increased materials cost (3D Matter, 2016). In order to preserve optimum instrument function coupled with enhanced flexibility, strength, and processing time, optimum fill density and fill geometry must be determined. Upon analysis of previous literature, the honeycomb fill pattern/geometry was determined to be the ideal internal structural scaffold matrix for PLA instrument functionality (3D Matter, 2016; Hodgson, 2016). With regards to the infill density, previous studies had identified that a baseline 60% infill density preserves optimal instrument mechanics and flexibility (3D Matter, 2016). This infill density however, must be modified at various stress points in certain instruments in order to prevent mechanical failure in the surgical field.

The infill density was particularly increased to 80% in specific localities including the crossection of the forceps arms on the x, y, and z-axes for the smooth tissue forceps design. These densities were increased at critical instrument mechanical stress points, specifically that of the pivot hinges present in multiple instruments such as the Kelly hemostat in order to provide enhanced mechanical strength and stiffness (Kondor et al., 2013). Instruments such as the Senn retractor were also thickened at key stress points such as the elbow bends located at each end of the retractor. All devices that required a functional rotational hinge were printed as two-piece modular components, which would be assembled afterwards. This includes the Kelly hemostat, Allis tissue clamp, sponge clamp, and needle driver, in which these instruments would be assembled via simply connecting the two pieces at the male and female hinge point.

After modifying the instruments within the 3D CAD software, a limited run of surgical instrument prototypes was physically printed utilizing a FDM printer outfitted with a PLA thermoplastic filament spool. The IST devices were fabricated directly from the .STL digital files using a Monoprice Mini desktop FDM printer, with the files being prepared for FDM fabrication using Ultimaker's Cura 2.3.1 2016 3D printing software running on a Macintosh OS.X based laptop computer.

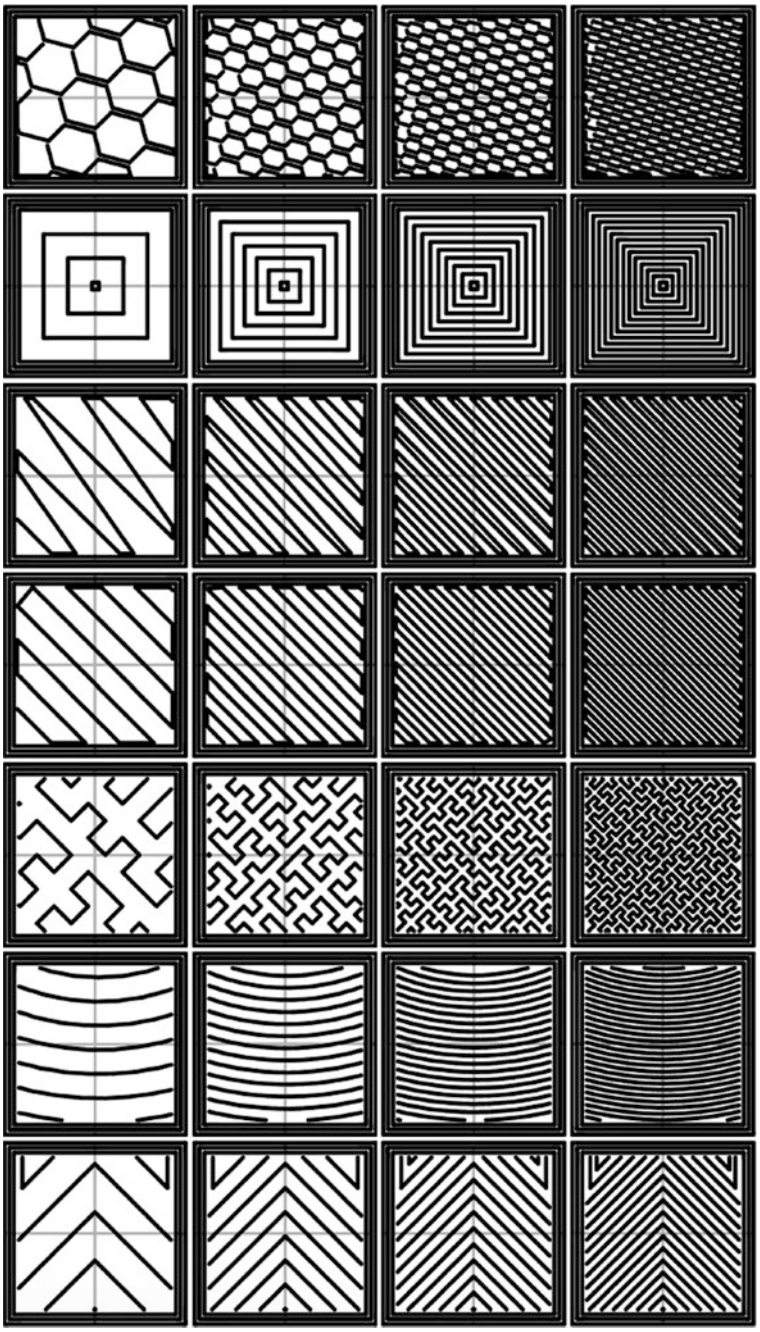

Fig. 4.8 Infill patterns at varying densities. *Left to right*: 20, 40, 60, and 80%. *Top to bottom*: Honeycomb, concentric, line, rectilinear, hilbert curve, archimedean chords, and octagram spiral (Hodgson, 2016)

After each model was adequately modified, the .STL file was saved and then delivered to the printer apparatus for processing and filament extrusion on a modular build platform. Based upon the modifications and the mechanics of each surgical instrument, the average fabrication time for a functional prototype ranged from approximately 45–240 min. After fabrication of each surgical instrument, each tool remained on the build platform for approximately 5 min to cool down and was then assembled. Each instrument was fabricated as a single modular piece or split into two complement pieces to be assembled after fabrication. The modified 3D CAD PLA surgical instrument .STL designs downloaded from 123AutoCAD.com, thingiverse.com, yeggi.com, 3dprintingforhumanity.com, 123.dapp.com, and grabcab.com were opened in Ultimaker's Cura 2.3.1 software and digitally snapshotted with Cartesian axial configurations and an adjusted viewing angle as shown below in Figs. 4.9, 4.10, 4.11, 4.12, 4.13, 4.14, 4.15, 4.16, 4.17, 4.18, 4.19, 4.20, 4.21, 4.22, 4.23, 4.24, 4.25, 4.26, 4.27, 4.28, 4.29, 4.30, 4.31, 4.32, 4.33, 4.34, 4.35.

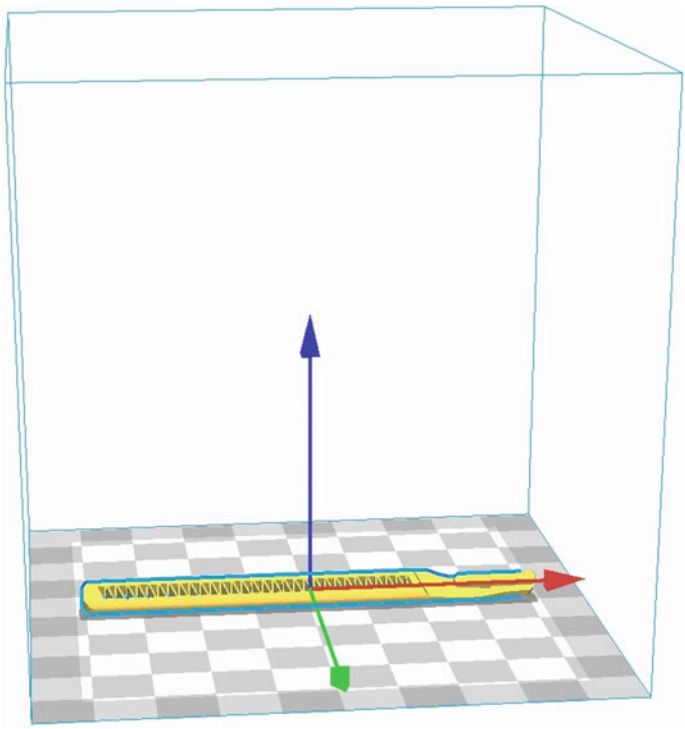

Fig. 4.9 3D CAD PLA modified scalpel handle, 3D coordinate plane (Scalpel Truss Handle, 2016)

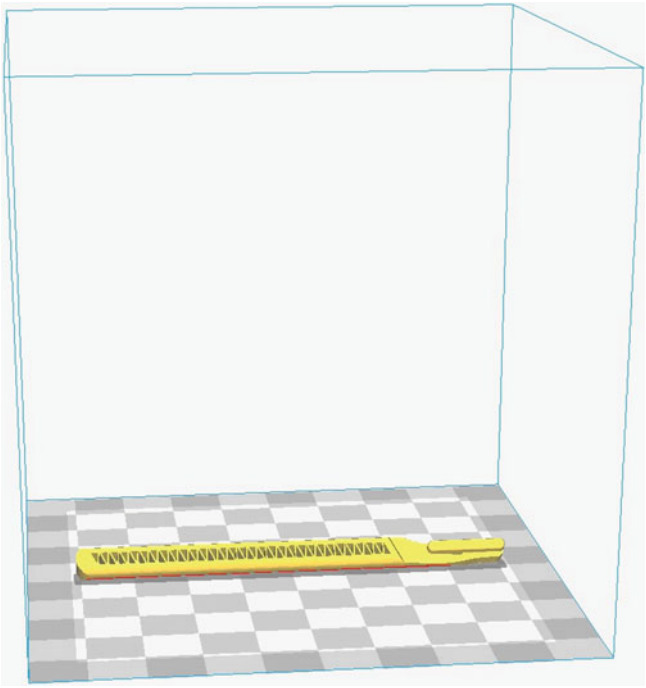

Fig. 4.10 3D CAD PLA modified scalpel handle, angular view (Scalpel Truss Handle, 2016)

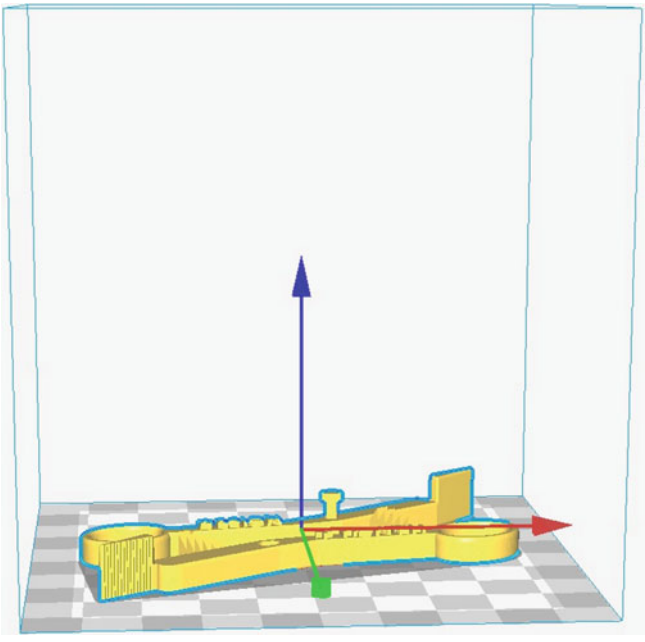

Fig. 4.11 3D CAD PLA modified Kelly hemostat, 3D coordinate plane (Pugliese, 2016)

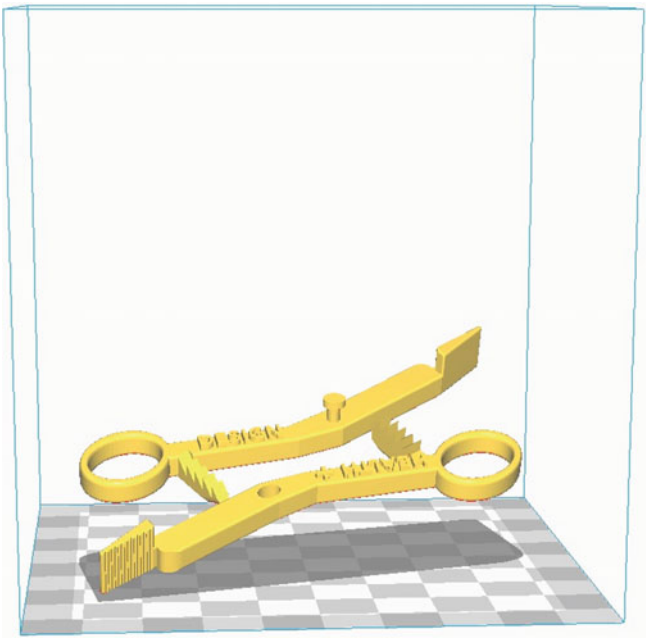

Fig. 4.12 3D CAD PLA modified Kelly hemostat, angular view (Pugliese, 2016)

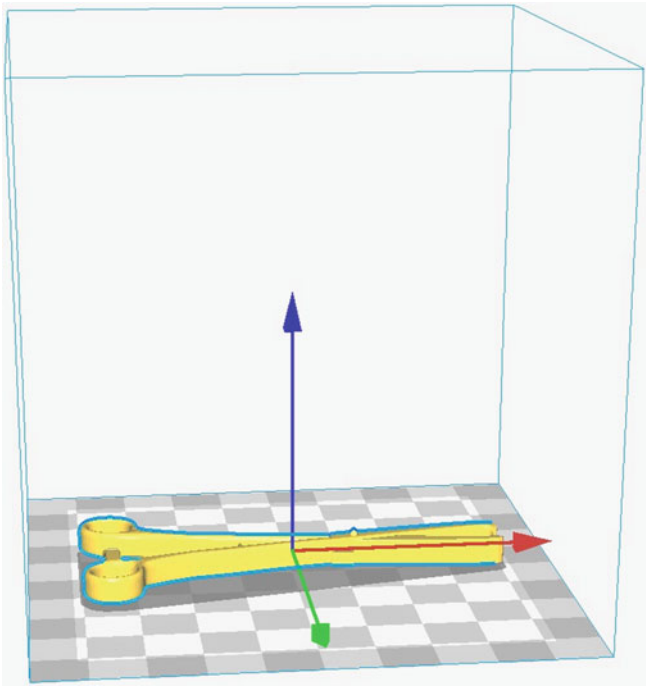

Fig. 4.13 3D CAD PLA tenaculum, 3D coordinate plane (Tenaculum 3D Model, 2012)

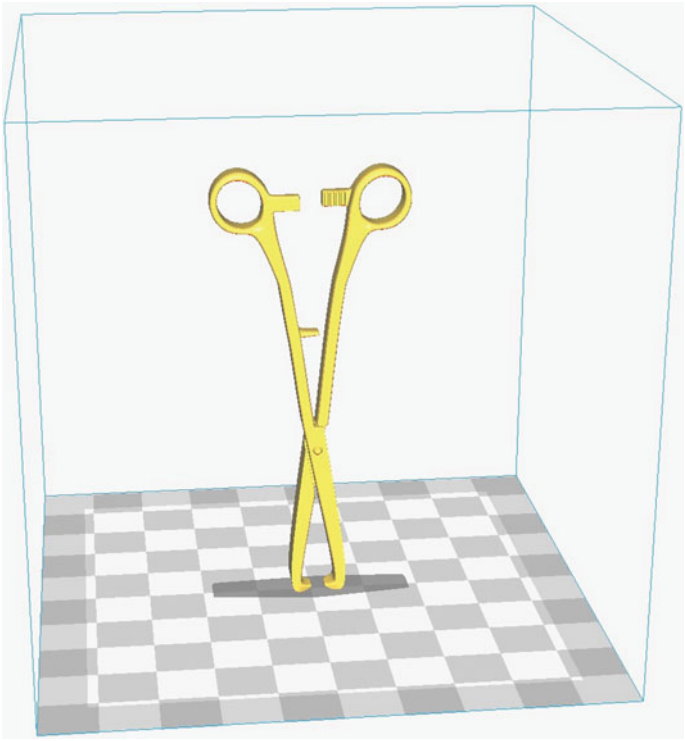

Fig. 4.14 3D CAD PLA tenaculum, angular view (Tenaculum 3D Model, 2012)

4.2 3-Dimensional Printing in the Surgical Field: Applications and Considerations

PLA has been proven to be an ideal bio-based material for surgical implantation and is a cost effective, safe, and environmentally suitable material for printing a functional integrative surgical toolkit. In fabricating this toolkit, instrument utility is of the utmost importance, specifically that of the ability of these instruments to tolerate the demands of the operating room. These instruments must be strong enough to perform their intended functions, be hypoallergenic, and tolerate repeat sterilization (Rankin et al., 2014). Finally, these instruments must be at least equivalent in cost, strength, and accessibility when compared to a standard stainless steel instruments in order to be considered as a viable option for deployment in LMICs. PLA is hypoallergenic, hemocompatible and displays an extremely high safety profile, in which it has been FDA approved for a variety of dermal applications (Modjarrad & Ebnesajjad, 2013; Rankin et al., 2014). Though not completely inert, PLA has an excellent safety profile and does not incite hypersensitivity reactions (Rankin et al., 2014). The FDA approval of PLA for implantation does indeed further reinforce

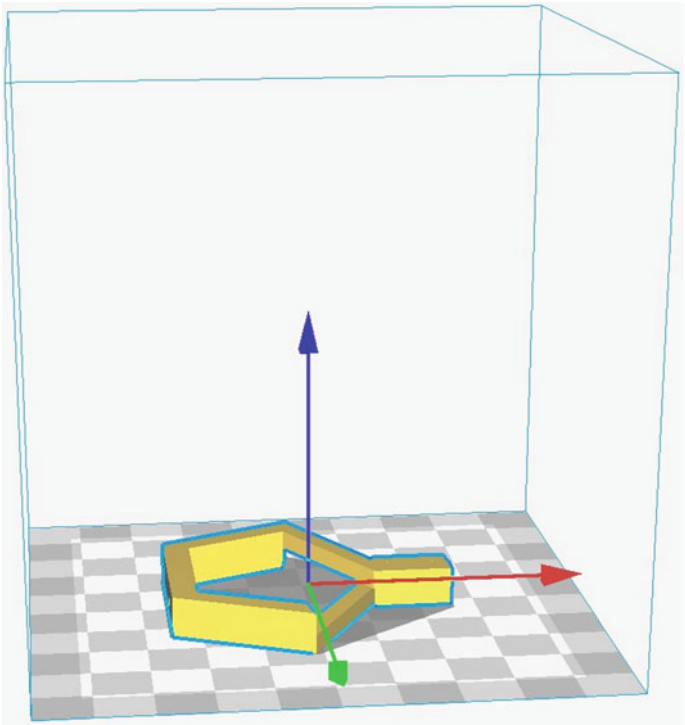

Fig. 4.15 3D CAD PLA modified vascular clamp, 3D coordinate plane (Vascular Clamp, 2013)

PLA as a safe bio-based material for transient human contact during an operation (Rankin et al., 2014).

Due to the limited scope and functional testing setting of the IST toolkit, the fabrication instrument prototypes, testing was not conducted in an actual surgical field. The instrument designs and modifications were made in accordance with prior studies that had previously defined the ideal fabrication methods and functional prototype designs of these instruments for deployment in a real-world surgical setting. Some of these instruments included in this toolkit such as the umbilical cord clamp and the Army-Navy surgical retractor have been printed and deployed in the surgical field. This further adds to the validity of these functional prototypes for use in the real-world surgical field scenarios. There is a clear difference between ideal and realistic surgical field applications and many confounding elements must be taken into consideration upon fabrication of surgical toolkits with bio-based materials such as PLA. In particular, entities such as these toolkits are indeed an applied medical device innovation, thus the core properties related to biomaterials and medical device fabrication must apply. Specifically, the thermal effects must be evaluated both during the production and use of the part or product, as molding temperatures seen during part production are typically much higher than end-use

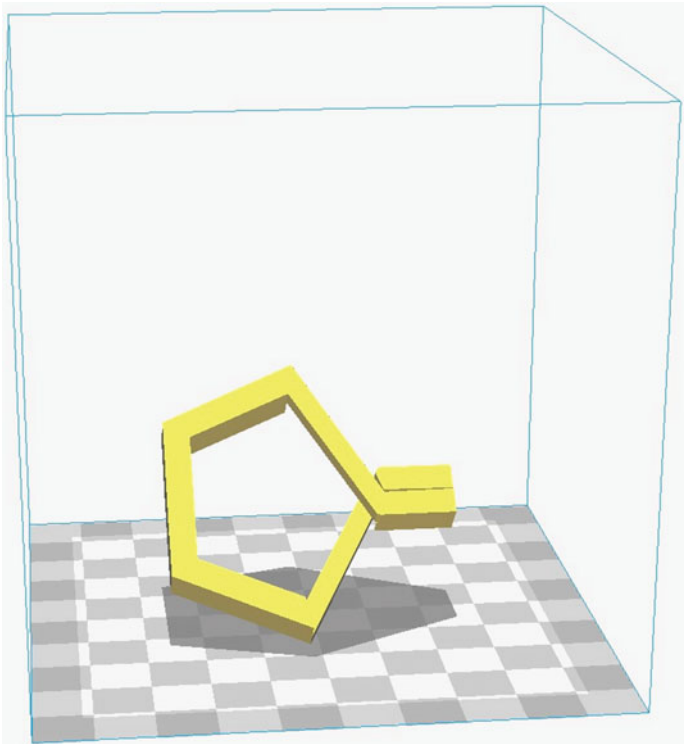

Fig. 4.16 3D CAD PLA modified vascular clamp, angular view (Vascular Clamp, 2013)

temperatures (McKeen, 2014). Thermoplastic material properties at melting temperatures, sterilization temperatures, and environmental conditions that include both temperature and humidity must be characterized. The polylactic acid thermoplastic polymer is indeed heat sensitive due to its nature as a thermoplastic and often becomes soft and malleable after exposure to temperatures above 140 °C (McKeen, 2014). This low heat sensitivity gradient is an important element with regards to the sterilization capacity of these PLA surgical instruments. One benefit of the high extrusion temperature of PLA in FDM processing is that the fabricated devices are completely sterile. Therefore, if an instrument were printed onto a sterile surface in a clean environment, such as an operating room, that device would be ready for surgical application as soon as printing was complete (Rankin et al., 2014).

The ability to sterilize a 3D printed instrument is critical to its application, in which PLA is extruded at temperatures well above the 121 °C recommended for steam sterilization and the 170 °C recommended for dry heat sterilization (Rankin et al., 2014). Many reusable medical devices such as surgical instruments will need to be sterilized by various methods such as steam, dry heat, ethylene oxide (EtO), electron beam, and gamma radiation (McKeen, 2014). These instruments must be able to withstand these conditions and still maintain their materials properties in

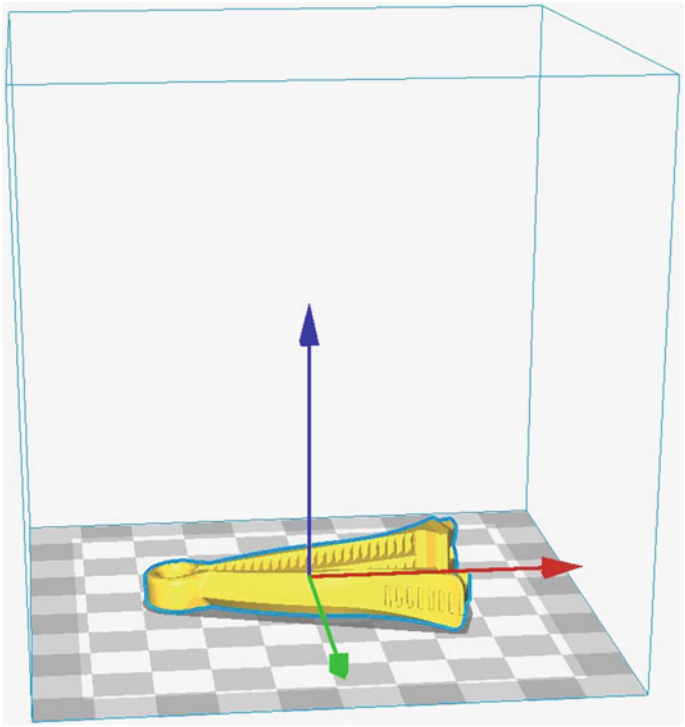

Fig. 4.17 3D CAD PLA modified umbilical cord clamp, 3D coordinate plane (Umbilical Cord Clamp, 2016)

order for these surgical instruments to be reused on a continual basis. Of particular importance is the hydrolytic stability for steam sterilization, thermal resistance to steam and autoclave conditions, chemical resistance to EtO, and resistance to high-energy radiation including electron beam, gamma, and ultraviolet radiation (McKeen, 2014). Autoclave and dry heat is a commonly utilized hospital sterilization technique that is usually performed at temperatures equal to or higher than 121 °C. PLA, PGA, and PLGA are susceptible to hydrolysis and their deformation at higher temperatures therefore limits the use of these sterilization methods (McKeen, 2014; Xiao et al., 2012).

EtO is chemically highly reactive and acts as a plasticizer for PLA, PGA, and PLGA, which can lead to changes in the polymer structure. EtO sterilization is performed at temperatures of 50–60 °C, which can lead to molecular weight loss, therefore EtO sterilization is not recommended for PLA instruments (McKeen, 2014). As previously noted, autoclaving compromises the structural integrity of PLA and although lower temperature methods of sterilization such as EtO sterilization do not impact PLA strength, harmful levels of ethylene oxide residue can be of great concern (Rankin et al., 2014). Given this knowledge, glutaraldehyde, an effective sterilant at room temperature, has been shown to retain the greatest PLA

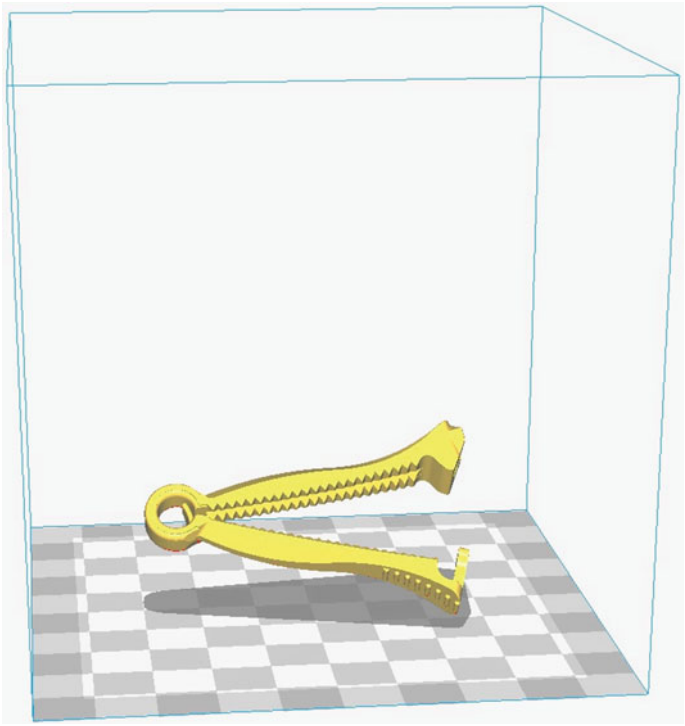

Fig. 4.18 3D CAD PLA modified umbilical cord clamp, angular view (Umbilical Cord Clamp, 2016)

strength and maintain the same degree of sterility when compared to other chemical sterilants (Athanasiou, Niederauer, & Agrawal, 1996). Glutaraldehyde sterilization entails device submersion in a 2.4% glutaraldehyde solution with a pH of 7.5 for 20 min at 25 °C in accordance with Centers for Disease Control (CDC) guidelines for critical medical device sterilization protocols (Rankin et al., 2014). A benefit of glutaraldehyde sterilization is its simplicity, cost efficiency, and reusability without impacting the strength or form of PLA (Athanasiou et al., 1996; Rankin et al., 2014).

The second element is that of chemical resistance, as any medical device including the integrative surgical toolkit would indeed require chemical resistance to various types of oils, greases, processing aids, disinfectant, bleaches, and other hospital chemicals (McKeen, 2014). Chemical resistance must be considered for the surgical instruments during fabrication, use and cleaning, as well as sterilization (McKeen, 2014; Modjarrad & Ebnesajjad, 2013). PLA is an excellent bio-based polymer that is highly chemical resistant and displays a high gradient of stability when exposed to these chemical elements. An important criterion for the use of plastics in medical device applications is quantifying the type and amount and identifying the material that is leached out or absorbed from the plastic when in

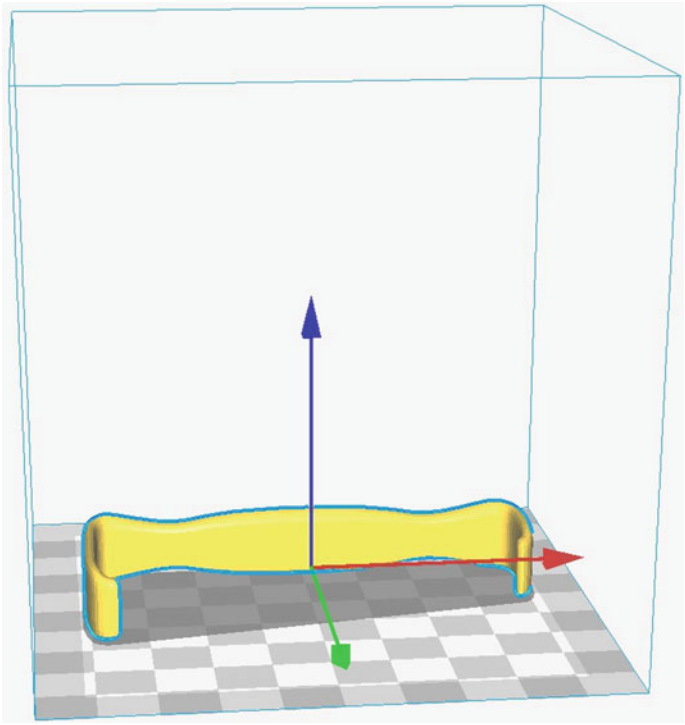

Fig. 4.19 3D CAD PLA modified Army-Navy surgical retractor, 3D coordinate plane (Rankin et al., 2014)

contact with chemicals, reagents, or bodily fluids during the end use (McKeen, 2014; Modjarrad & Ebnesajjad, 2013). This includes plasticizers, stabilizers, pigments, lubricants, catalysts, residual monomers and oligomers, residual solvents, and contaminants (McKeen, 2014; Modjarrad & Ebnesajjad, 2013). PLA displays a low-porosity and leachability gradient when utilized in additive manufactured prototypes, which allows the material to maintain a highly sterile nature and high biocompatibility index with host tissues without cytotoxic effects (Xiao et al., 2012; Zeng, Li, & Du, 2015). In addition, PLA displays excellent shelf-life performance and storage capability on par with most petroleum-based plastics (Li et al., 2003). Polylactic acid retains its core materials properties when kept in relatively stable conditions that are free of direct ultraviolet light exposure and humidity (Li et al., 2003). Long-term durability devices such as this surgical toolkit will still need to be further characterized via thorough field-based testing, as these devices must perform for prolonged periods of time under various environmental conditions, especially when deployed in resource-poor setting such as LMICs.

Previous chapters have defined the problem of the global surgical burden of disease and the polymer chemistry and engineering fundamentals related to the fabrication of the PLA bio-based integrative surgical toolkit. Now that the these

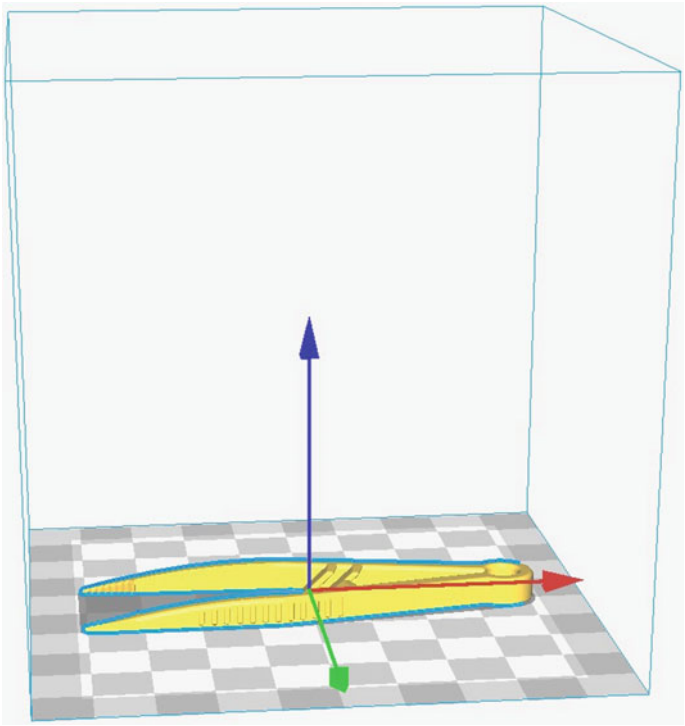

Fig. 4.20 3D CAD PLA modified Adson's toothed forceps, 3D coordinate plane (Toothed Forceps, 2016)

facets have been discussed in detail, the translational application of these entities takes fruition via definition of the interventional capacity of these bio-based surgical toolkits to combat the surgical burden of disease. The purpose of the integrative surgical toolkit is to provide a cost-effective, safe, and high-utility solution to combat medical supply deficiencies in LMICs and enhance the interventional capacity of physicians in district-level healthcare facilities in developing countries. This can significantly improve the outcomes of patients with surgically treatable conditions and serve as a tool in combating the surgical burden of disease. As previously stated, there are four surgical categories that define the functional surgical burden of disease in LMICs. Providing the surgical instruments to perform these categorical surgeries sets the stage for feasibly reducing the number of surgically avertable deaths globally. The first surgical category includes the enhancement of provisional surgical care to injury victims to reduce preventable deaths and decrease the number of survivable injuries that result in personal dysfunction and impose a significant burden on families and communities (Bhatia, 2010; Jamison et al., 2006). The second category is that of handling of obstetrical complications including obstructed labor and hemorrhage (Jamison et al., 2006). The third is that of enhancing the surgical management of abdominal and

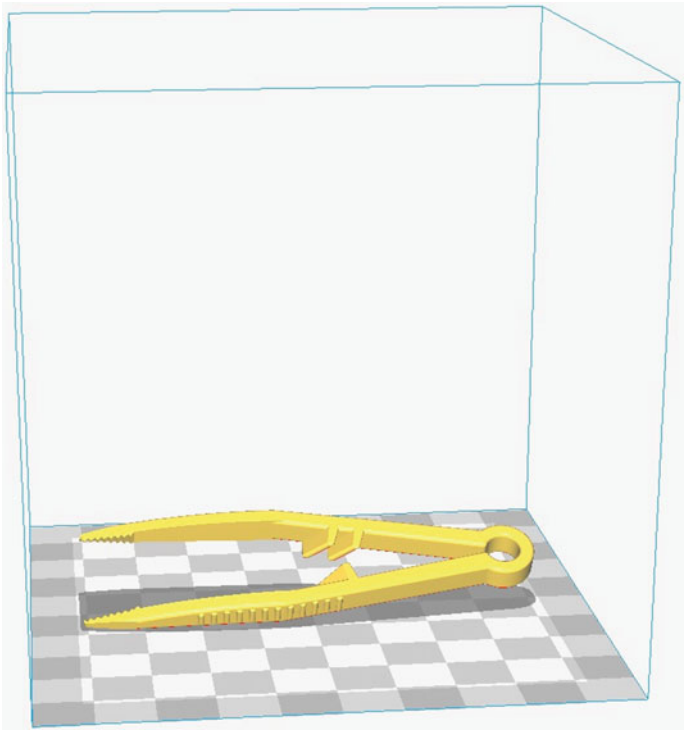

Fig. 4.21 3D CAD PLA modified Adson's toothed forceps, angular view (Toothed Forceps, 2016)

extra-abdominal emergent and life-threatening conditions (Jamison et al., 2006). The fourth is that of providing instruments for the elective care of simple surgical conditions such as hernias and hydroceles (Jamison et al., 2006).

The use of 3D printing apparatuses such as the RepRap allow for the fabrication of these toolkits on-site in a domestic manner, providing direct sourcing of critical surgical instruments. This means that healthcare facilities can harness the power of a manufacturing facility in an easy to use 3D modular printer than can print out a continuous set of surgical instruments for use immediately. This direct access can be critical in providing medical supplies to healthcare facilities that previously would not have these instruments. The premise of the integrative surgical toolkit is to provide access to a variety of broad-spectrum general surgery instruments directly on a fully customizable printing apparatus fabricated from local parts at a price margin that is far below the cost of conventional stainless steel surgical instruments.

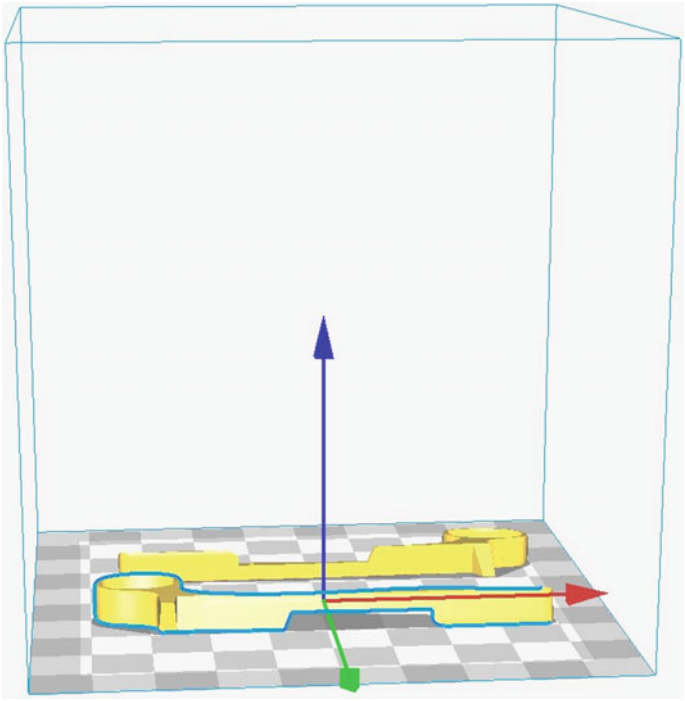

Fig. 4.22 3D CAD PLA modified allis tissue clamp/forceps, 3D coordinate plane (Tissue Forceps, 2011)

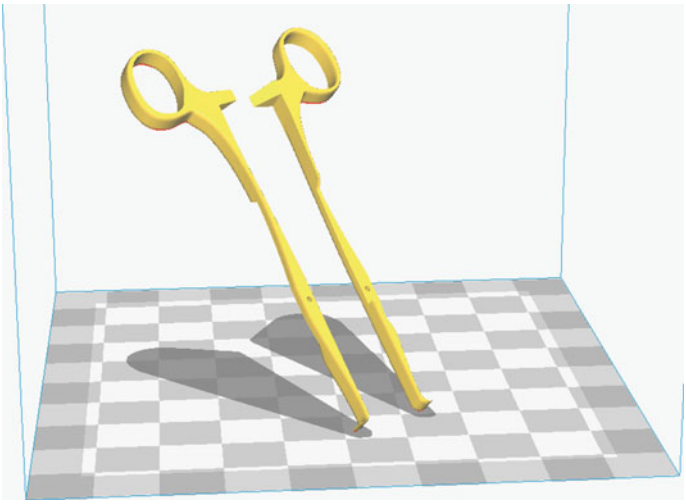

Fig. 4.23 3D CAD PLA modified allis tissue clamp/forceps, angular view (Tissue Forceps, 2011)

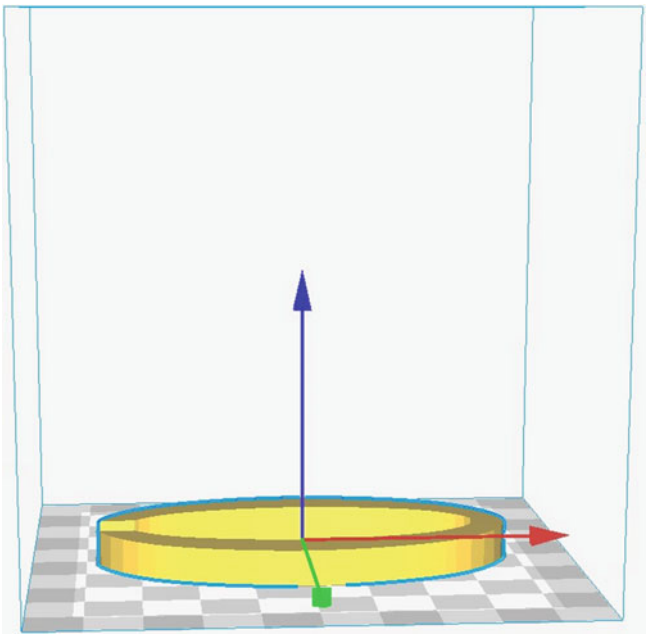

Fig. 4.24 3D CAD PLA modified smooth tissue forceps, 3D coordinate plane (Forceps, 2012)

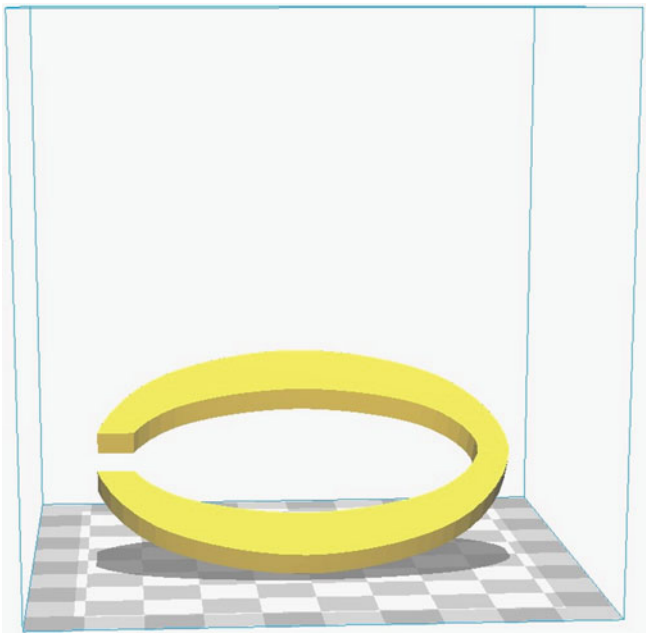

Fig. 4.25 3D CAD PLA modified smooth tissue forceps, angular view (Forceps, 2012)

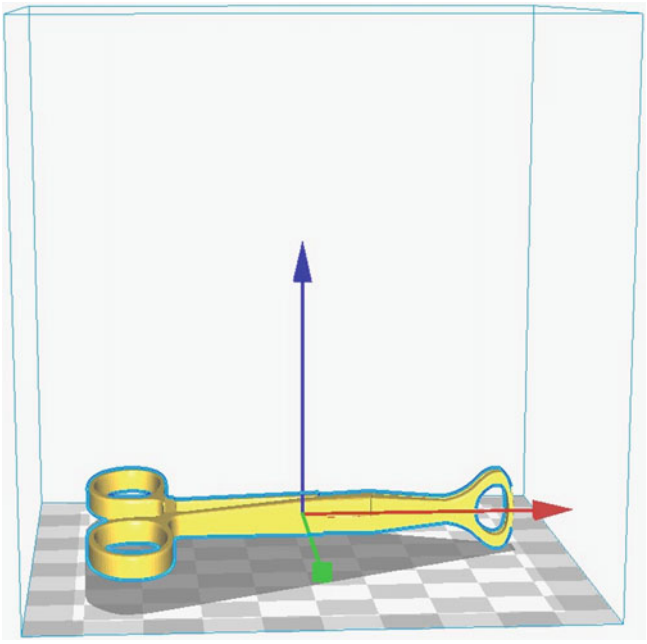

Fig. 4.26 3D CAD PLA modified sponge clamp, 3D coordinate plane (Sponge Forceps, 2012)

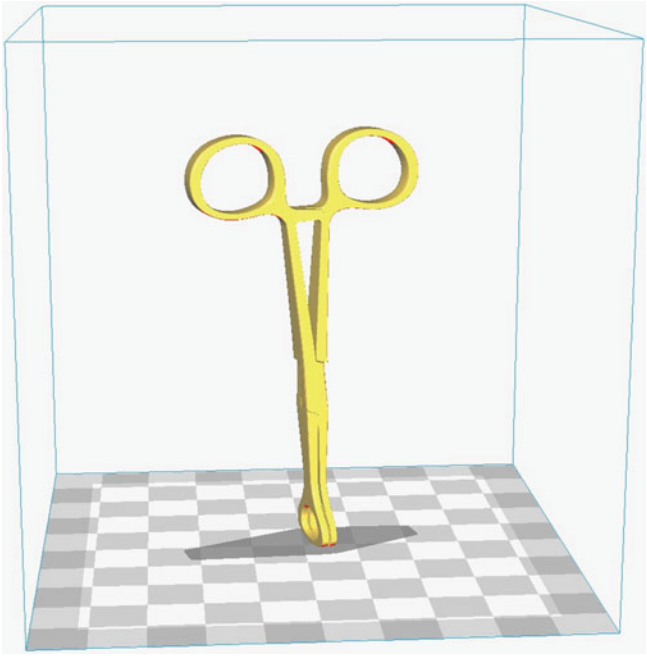

Fig. 4.27 3D CAD PLA modified sponge clamp, angular view (Sponge Forceps, 2012)

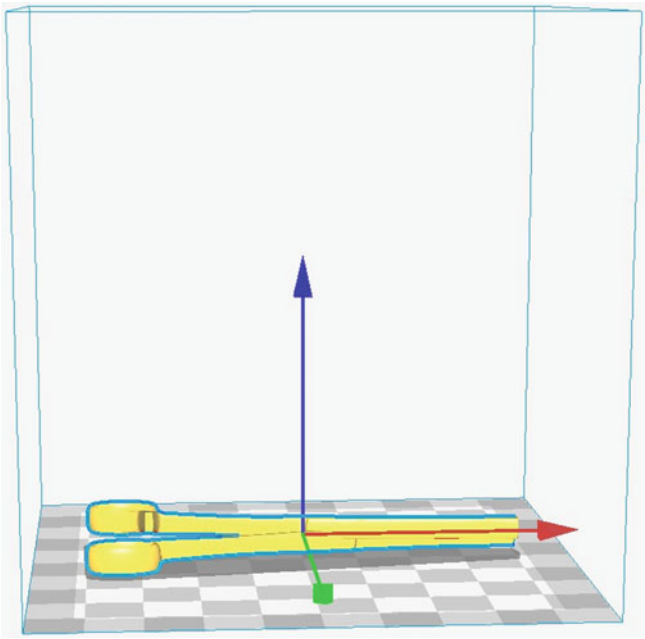

Fig. 4.28 3D CAD PLA modified pennington clamp, 3D coordinate plane (Pennington Clamp 3D Model, 2012)

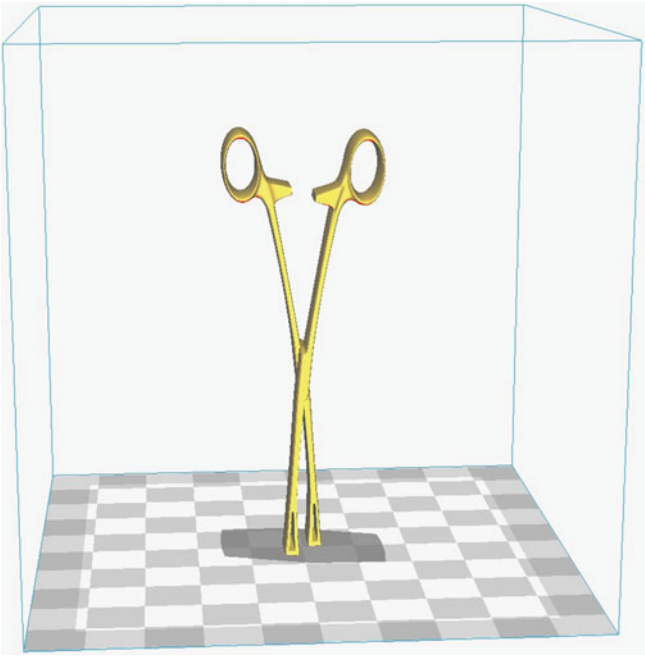

Fig. 4.29 3D CAD PLA modified pennington clamp, angular view (Pennington Clamp 3D Model, 2012)

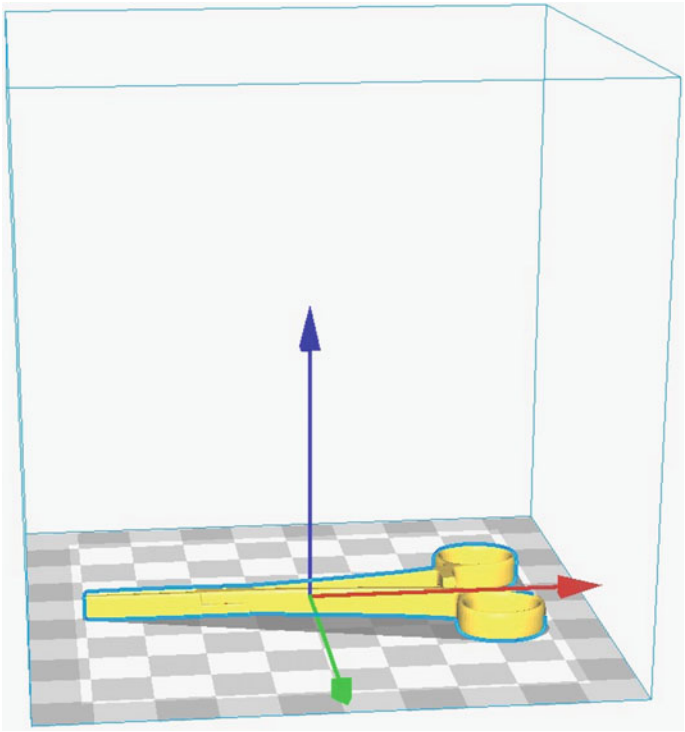

Fig. 4.30 3D CAD PLA modified needle driver, 3D coordinate plane (Needle Driver, 2012)

4.3 3D Printed Instrument and Medical Supply Price Competencies

Previous chapters have defined the problem of the global surgical burden of disease and the polymer chemistry and engineering fundamentals related to the fabrication of the PLA bio-based integrative surgical toolkit. Now that the these facets have been discussed in detail, the translational application of these entities takes fruition via definition of the interventional capacity of these bio-based surgical toolkits to combat the surgical burden of disease. The purpose of the integrative surgical toolkit is to provide a cost-effective, safe, and high-utility solution to combat medical supply deficiencies in LMICs and enhance the interventional capacity of physicians in district-level healthcare facilities in developing countries. This can significantly improve the outcomes of patients with surgically treatable conditions and serve as a tool in combating the surgical burden of disease. As previously stated, there are four surgical categories that define the functional surgical burden of disease in LMICs. Providing the surgical instruments to perform these categorical surgeries sets the stage for feasibly reducing the number of surgically avertable deaths globally. The first surgical category includes the enhancement of provisional

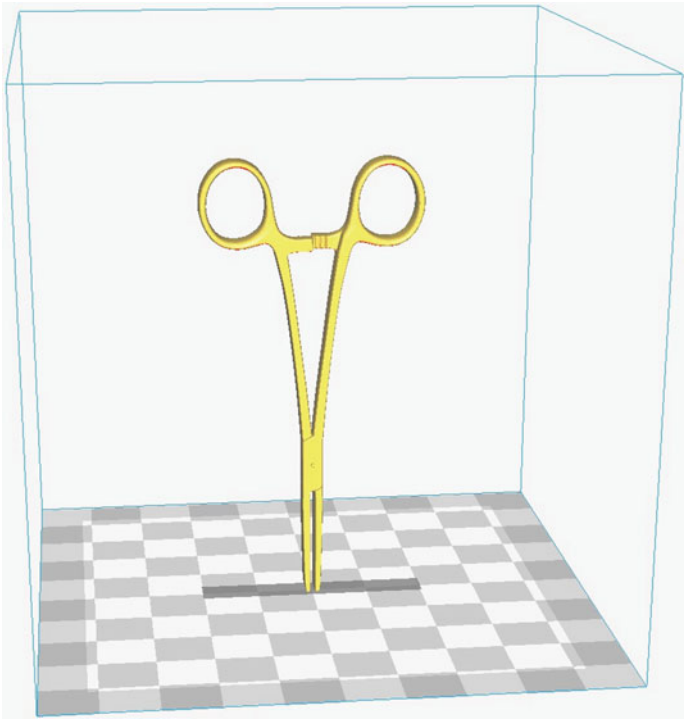

Fig. 4.31 3D CAD PLA modified needle driver, angular view (Needle Driver, 2012)

surgical care to injury victims to reduce preventable deaths and decrease the number of survivable injuries that result in personal dysfunction and impose a significant burden on families and communities (Bhatia, 2010; Jamison et al., 2006). The second category is that of handling of obstetrical complications including obstructed labor and hemorrhage (Jamison et al., 2006). The third is that of enhancing the surgical management of abdominal and extra-abdominal emergent and life-threatening conditions (Jamison et al., 2006). The fourth is that of providing instruments for the elective care of simple surgical conditions such as hernias and hydroceles (Jamison et al., 2006).

The use of 3D printing apparatuses such as the RepRap allow for the fabrication of these toolkits on-site in a domestic manner, providing direct sourcing of critical surgical instruments. This means that healthcare facilities can harness the power of a manufacturing facility in an easy to use 3D modular printer than can print out a continuous set of surgical instruments for use immediately. This direct access can be critical in providing medical supplies to healthcare facilities that previously would not have these instruments. The premise of the integrative surgical toolkit is to provide access to a variety of broad-spectrum general surgery instruments directly on a fully customizable printing apparatus fabricated from local parts at a

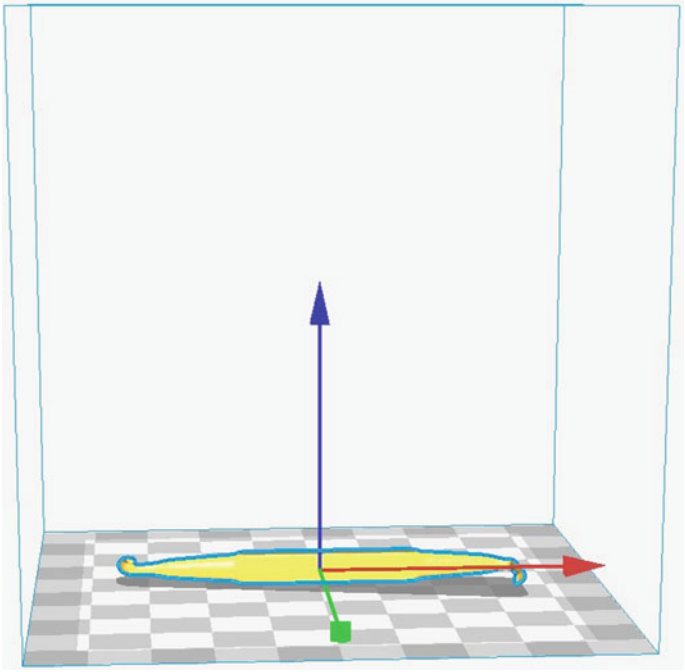

Fig. 4.32 3D CAD PLA modified senn retractor, 3D coordinate plane (Senn Retractor, 2012)

price margin that is far below the cost of conventional stainless steel surgical instruments.

A core tenant behind the use of 3D printing is the ability to fabricate objects on-demand and on-site at a fraction of the cost of traditional manufacturing methods. This holds true for the fabrication of entities such as surgical toolkits, which can be created at a significant cost savings when compared to the conventional stainless steel instrument kit. 3D printing with PLA provides an inexpensive, sustainable, adaptable, and feasible manufacturing material and method that can provide significant cost savings when deployed in resource-poor settings. For example, a set of two stainless steel Army-Navy surgical retractors is available through retailers for a retail price of $46.96 or $23.48 per unit (Rankin et al., 2014). A RepRap printing apparatus typically costs approximately $150.00 and 1 kg of PLA costs approximately $20.00, which can indeed be sourced in many localities (Jones et al., 2011; Rankin et al., 2014). Since the PLA fabricated retractor generally weighs between 10–20 g, depending on size and application, it is possible to fabricate more than 50 retractors per kilogram, which calculates to $0.25–$0.45 of PLA per instrument. By this metric, an individual would need to print only 8 retractors in order to cover the cost of the printer and make each unit cost the same as the stainless steel version (Rankin et al., 2014). Even if these instruments were utilized as a one-time use, they are still less expensive than the cost of damage or

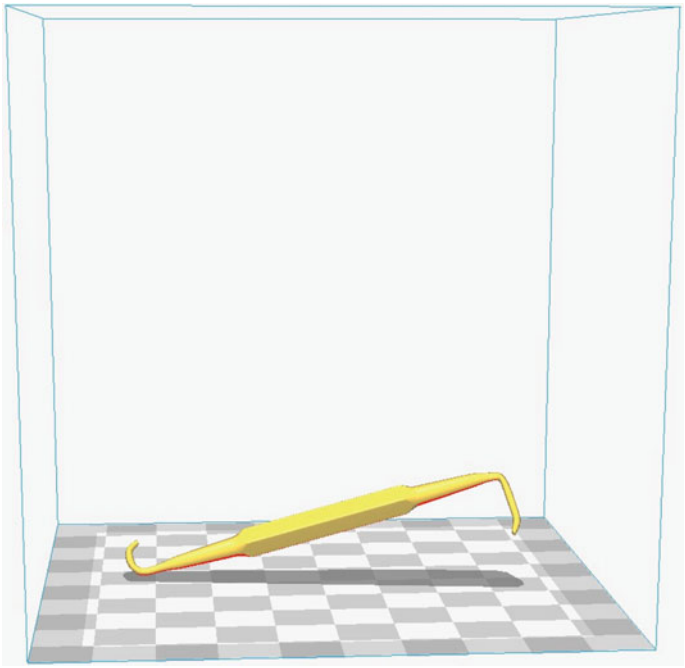

Fig. 4.33 3D CAD PLA modified senn retractor, angular view (Senn Retractor, 2012)

theft of stainless steel instruments (Rankin et al., 2014). The savings become even more apparent when considering other instruments such as a vascular clamp, in which the stainless steel version costs more than $400.00, while the 3D PLA printed device costs a mere $0.25 to fabricate.

Based on the per-unit costs of each instrument as shown in Table 4.1 below, if one were to price the entire PLA IST vs. a stainless steel or traditional counterpart, the IST including all 12 instruments would cost only $4.00 compared to over $1000.00 for a traditional stainless steel instrument kit. The metric costs for each PLA instrument was calculated based upon the instrument's weight calculated in the Cura 2.3.1 splicing software. A 1-kg spool of PLA has an approximate per-gram cost of $0.025 per-gram of PLA, thus multiplying the instrument's weight in grams times that of the per-gram cost of PLA yields its approximate total cost (Rankin et al., 2014). The approximate stainless steel instrument prices were obtained from 4MD Medical, a medical supply company that sells and distributes surgical instruments (4MD Medical, 2017). It is important to note that the stainless steel instruments do not factor in applicable taxes, tariffs, import, and shipping fees that are added when shipped internationally to most LMICs. This means that the per unit cost of these conventional instruments rises substantially, making them fiscally out of reach for district-level healthcare facilities that need them the most. In addition,

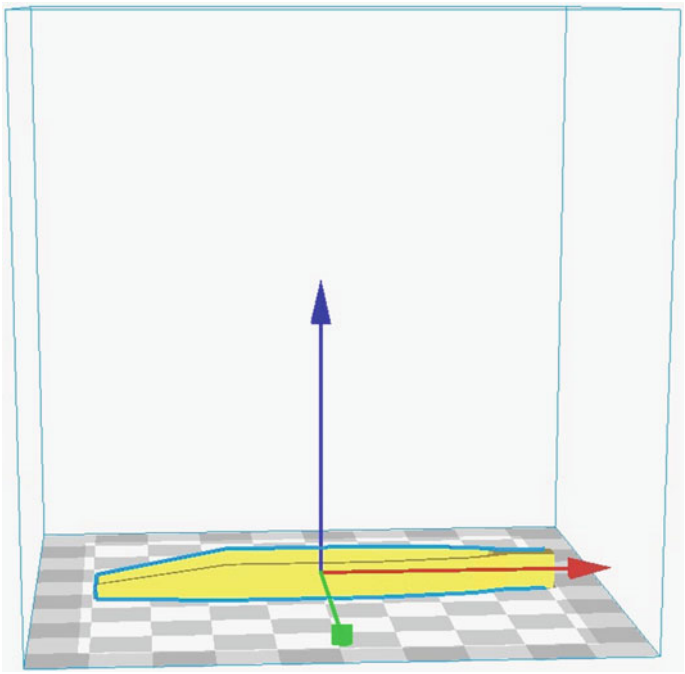

Fig. 4.34 3D CAD PLA modified debakey tissue forceps, 3D coordinate plane (Tweezers V2, 2009)

the approximate PLA instrument costs do not factor in printer power consumption, misprint and defective print allowance, as well as custom instrument configurations.

One can counter with the fact that perhaps stainless steel instruments can be donated to LMICs therefore absorbing the cost-burden associated with them, but this creates a "crutch" in which LMICs become dependent on other countries for medical equipment. 3D printers allow LMICs to harness domestic manufacturing processes in a compact and mobile unit that can allow them to create their own economies of scale based upon supply and demand metrics. Many times the cost of new technology presents a prohibitive force that contradicts its widespread use and adoption, but 3D printing with bio-based materials counteracts this by providing a modular set up that fabricates products on demand at an extremely low price point, therefore reducing the barrier to entry. Although these instruments are indeed extremely cost-effective and affordable, long-term durability tests must be conducted to examine the limits of 3D device functionality over an extended period of time compared to stainless steel instruments. Optimum device functionality, safety, and materials properties must be maintained in order to make 3D fabricated instruments a viable alternative.

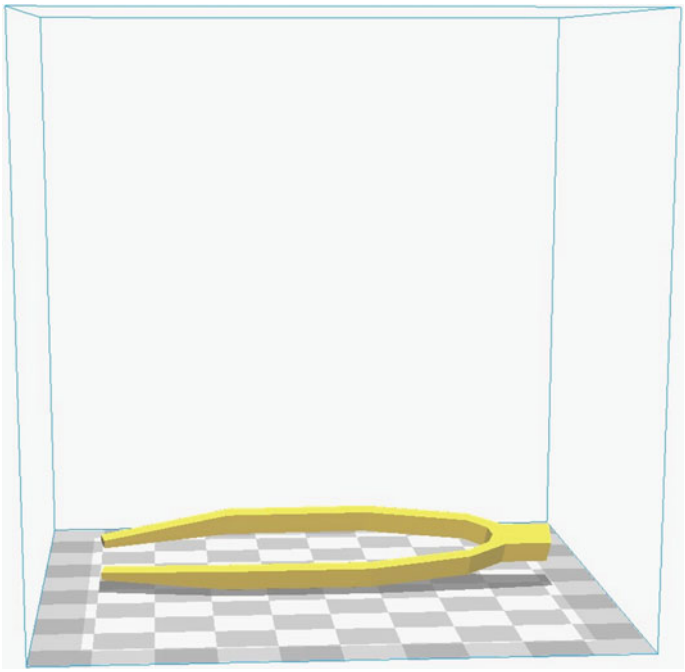

Fig. 4.35 3D CAD PLA modified debakey tissue forceps, angular view (Forceps V2, 2009)

Table 4.1 PLA and stainless steel surgical instrument per-unit and total toolkit cost comparison

Stainless steel surgical instrument	Approx. price ($USD)	PLA surgical instrument	Approx. price ($USD)
Adson's toothed forceps	$41.36	Adson's toothed forceps	$0.35
Allis tissue clamp	$43.23	Allis tissue clamp	$0.35
Army-Navy retractor	$23.48	Army-Navy retractor	$0.40
Debakey tissue forceps	$143.44	Debakey tissue forceps	$0.20
Kelly hemostat	$156.08	Kelly hemostat	$0.50
Needle driver	$33.28	Needle driver	$0.50
Pennington clamp	$52.95	Pennington clamp	$0.75
Scalpel handle	$27.50	Scalpel handle	$0.15
Senn retractor	$21.01	Senn retractor	$0.20
Smooth tissue forceps	$36.29	Smooth tissue forceps	$0.20
Sponge clamp	$88.89	Sponge clamp	$0.55
Tenaculum	$86.08	Tenaculum	$0.75
Umbilical cord clamp	$3.50	Umbilical cord clamp	$0.35
Vascular clamp	$427.76	Vascular clamp	$0.25
Total toolkit cost	$1184.85	Total toolkit cost	$5.50

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Chapter 5
3-Dimensional Printing: Interventional Capacities in the Global Health Arena

The global health arena surmises the entire span of our world and its human populous. This "arena" contains the entirety of our human population and with that population, the health threats that constantly shape our future. In acknowledging the global arena for which we find ourselves in, it is important that the innovations and technologies rendered to help our fellow man are also available to all within the confines of this metaphysical arena. Innovations in science, technology, and medicine must not be available to only a segment of individuals who understand and can harness it. Rather, it is within the adaptability complex of these innovations that the true essence of "innovation" comes to fruition. This is particularly true when it comes to rapid prototyping devices such as 3D printers. One could easily surmise that we could take a domestically manufactured printer in the United States and ship it to a locality in a developing country, but what are the consequences of this? For one, we are simply coming up with a quick solution that most likely will not work. The reason being is that in addition to the associated fiscally unsustainable costs of shipping and materials sourcing, there are indeed differences in the access to infrastructure and human capital amongst each country. But more importantly, we undermine the ingenuity of the local population as well as the entirety of the country for which we seek to help. In utilizing frugally engineered technologies, we create a catalyst for domestic manufacture and distribution that does not rely on international sourcing. More importantly, we create a hub for human capital development and open the doors for creativity fostered by individuals that understand the needs and applications of these technologies in their relative settings. This means that technologies can be further enhanced and improved upon in order to meet the needs of the people it is intended to serve. This is extremely important when utilizing technologies in LMICs, as the ability to adapt and redefine these devices can vastly improve the interventional capacity of 3D printing devices to effectively deliver high-quality medical devices and supplies to healthcare facilities. As individuals improve on the open-source device designs and applications, these modifications can be shared on a global interface such as the Internet, allowing for rapid information dissemination. This can allow for

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healthcare facilities in developing countries to connect with other facilities around the world to effectively improve medical device fabrication processes. This creates a true paradigm shift in which healthcare facilities in developing countries that previously were limited to relying upon international shipments of medical supplies and devices, can feasibly manufacture custom instruments in a domestic fashion to be utilized directly in the field. This creates an effective strategy to combating global health threats such as the surgical burden of disease.

5.1 Barriers to Entry and Adoption of Medical Device Innovations in LMICs

In acknowledging the potential behind 3D printing, it is important to understand the barriers to entry and adoption of the technology in LMICs. By this we refer to the elements and variables that limit the application and successful deployment of these technologies in developing countries. Typically barriers to entry concern logistical, fiscal, and political components such as costs, shipping logistics, import taxes and fees, access to human capital, international bureaucracy, and supporting infrastructure entities. Upon reflection of these plethora of confounding variables, we first address the most common fallacy related to international development and aid, this being equipment donation and adaptation of technology. It is indeed natural for one to ask that we should simply just donate medical supplies, which could easily address equipment deficiencies in LMICs. While this is true to a limited extent, initiatives that have taken this approach in the past have widely failed. Most healthcare technology is produced by companies from high-income countries (HICs) for their respective high-income markets, in which a vast majority of their sales take place in HICs (Goodman, 2004; Howitt et al., 2012). This means that healthcare technology is primarily designed for an environment that has access to an abundance of intellectual, physical, and infrastructure resources such as reliable energy sources, vast numbers of formally trained healthcare professionals, and advanced healthcare facilities (Howitt et al., 2012; Perry & Malkin, 2011). This creates a focal dissonance when equipment that is primarily designed to be deployed in HICs, is donated to LMICs, which typically have decreased fiscal resources, vastly underdeveloped infrastructure, and limited access to highly-trained healthcare workers (Howitt et al., 2012).

In the past, technologies from HICs have been deployed in LMIC settings without prior thought of how the technology will perform or the associated consequences of deploying a technology that was developed for a different environment or setting. What essentially happens based upon previous studies, is that these technologies become rapidly "useless," if not completely useless starting at their initial deployment (Howitt et al., 2012; Perry & Malkin, 2011). Upon further examination, we can see that rationale behind this, as previous studies have estimated that approximately 40% of healthcare equipment in developing countries is

non-functional and out of service, compared with less than 1% in HICs (Howitt et al., 2012; Perry & Malkin, 2011). Some low-income countries have received as much as 80% of their medical devices as donations, in which these donations come in the form of second-hand or brand-new surplus devices from hospitals in HICs (Jones, 2013; World Health Organization, 2010). While many may think this is indeed well intentioned and helpful, these donations actually place a burden on their respective recipients, and contribute to the accumulation of excess unusable technologies (Jones, 2013; World Health Organization, 2010). For example, oxygen concentrators donated to a Gambian hospital required a voltage that was incompatible with the electricity supply in that country, so the donated oxygen concentrators would not work (Howie et al., 2008; Perry & Malkin, 2011). Since the medical devices could not be retrofitted and adapted to the local power supply, these devices were essentially discarded since they had no functional utility or use (Howie et al., 2008; Perry & Malkin, 2011). Donations that have been carefully vetted and utilized to meet the specific needs of the recipient can indeed be very beneficial, but a better approach for LMICs is the use of frugal technologies, which can be specifically designed and adapted for use and deployment in LMICs to adequately address their respective needs.

A study by Zelenika and Pearce examined the barriers limiting adoption and scaling of open-source appropriate technology (OSAT) in developing countries. OSAT includes technologies such as 3D printing, in which non-profit organizations and academic researchers working in the field of appropriate technology (AT) and international development were interviewed to identify barriers to OSAT. The results of the study indicated that the primary barriers to the deployment of open source appropriate technology includes: (1) social barriers, (2) communication and information specific barriers, (3) barriers to open source technology, (4) barriers to technology (AT or in general), and (5) social and technical barriers connected (Fig. 5.1) (Zelenika & Pearce, 2011). Specifically in breaking down these barriers to adoption and interventional scaling, the researchers identified the need for better

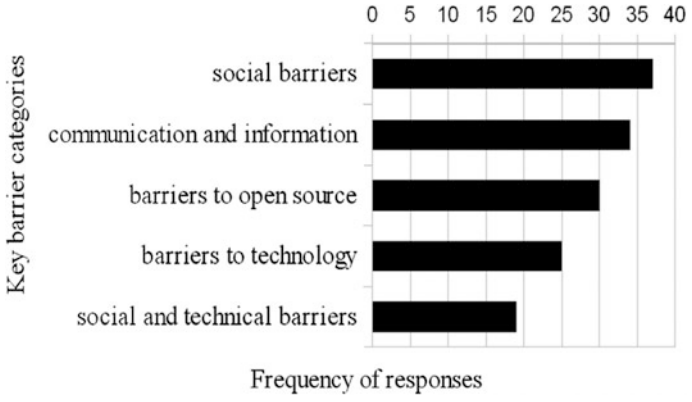

Fig. 5.1 Barriers to open-source appropriate technology (Zelenika & Pearce, 2011)

collaboration with locals, NGOs, and universities to share knowledge and feedback (Zelenika & Pearce, 2011). The social, economic, and science/engineering elements related to an intervention in developing countries must all be examined to promote feasible project implementation as well as sustainability. Project sustainability is indeed a prominent component when promoting an intervention related to international development, as many projects do indeed succeed initially, but fail to provide sustained benefits for its intended population. The ability to not only implement a project, but adequately educate and train the local population for which it is intended to serve is vital for empowering both the interventional capacity of the project, but also the people it serves.

We previously hailed frugal engineering as a tenet for sustainable innovations to grow and develop in LMICs, and while frugal technologies are ideal, there still needs to be functional access to basic and stable infrastructure in LMICs in order for frugally-engineered devices to function to their fullest capacity. Many LMICs often have poor resource and infrastructure gradients, which is where the adaptability complex and frugal engineering behind the RepRap rapid prototyping devices comes into play. RepRap series printers have a power requirement of 24 V DC at 6.25 amps, making it widely applicable for international settings and ideal due to its low power consumption (Jones et al., 2011; Wong, 2015). In addition, functionally compatible with other power elements such as a small gas or hand crank generator, car battery, or solar photovoltaic cell setup (Figs. 5.2 and 5.3), further enhancing the sustainability complex of device implementation (Jones et al., 2011; Wong, 2015).

While the power needs of these FDM printing apparatuses is minimal, there are indeed other elements that must be accessible for optimal printer functionality. This

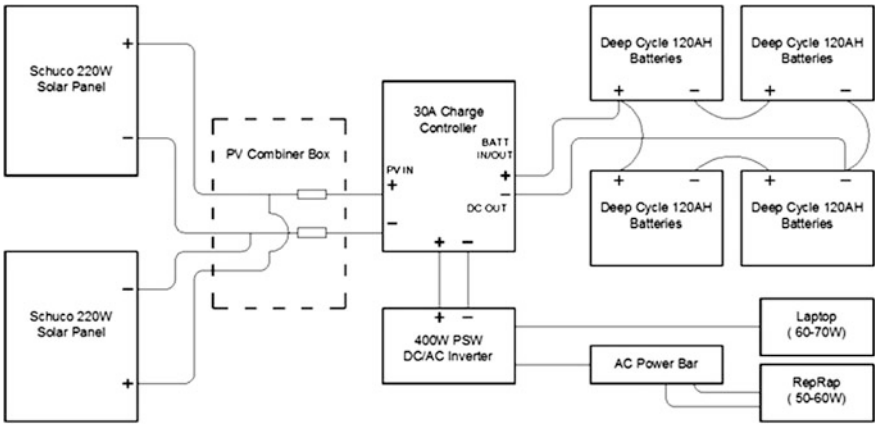

Fig. 5.2 Solar power printer schematic design. Photovoltaic cells are connected in parallel with a combiner box utilized to combine and drive the DC supply towards a 30-amp charge controller, to control the charging and discharging of the batteries. During charging periods four 120 AH batteries are fed DC current, while discharging continues to power the RepRap printer and a laptop through a DC/AC inverter (King & Babasola, 2014)

Fig. 5.3 Community-scale solar-powered open-source RepRap 3D printer system for off-grid communities (King & Babasola, 2014)

includes access to printing materials including the parts to build the RepRap device including a laptop or computer to download the splicing software, Internet, and access to PLA thermoplastic filament spools is critical. Most of the RepRap device components can indeed be sourced locally and blueprints for device assembly can be downloaded for free from the Internet. A basic PC or Macintosh computer or laptop can be used to run the splicing software such as Cura, which can be downloaded for free from the web and runs on a variety of platforms. Internet accessibility is indeed important in order to download the required software and blueprints and is very much useful for downloading the modular designs for other types of instruments or medical devices that are available via open source websites such as thingiverse.com, yeggi.com, or 123autoCAD.com (3D Matter, 2016).

Approximately 40% of the world's population has access to the Internet and this percentage has grown at an exponential rate over the previous decade (Rankin et al., 2014). This exponential increase is particularly prominent in LMICs in which, 54% of people in developing countries use the Internet (Pizzi, 2016). It is important to note that internet is not needed for device operation, in which the integrative surgical toolkit instrument designs can be pre-downloaded onto a micro SD chip or thumb drives and inserted into a computer to print the kit without having a direct internet interface. Another important facet and potential barrier is that of access to the PLA filament, in which in order to fabricate a steady set of toolkits, multiple filament spools will be needed over time. Based upon previous studies, many LMICs do indeed have access to PLA filament spools and in many cases it can be locally sourced without need for international shipping. While it is important to have access to the components mentioned previously, perhaps one of the most important elements is that of access to human capital. Human capital refers to the capacity to train a specific set of individuals in the operation protocols related to the

3D printer assembly and operation, 3D printing slicing software protocol, and prototype fabrication protocol. At least two individuals should be trained as technicians that know the fundamentals of 3D printing and operating the printing apparatus to fabricate a consistent product and deal with the various trials and tribulations of FDM printing. This includes modifying the device platform in case of misprints, in which the prototype device is not properly fabricated. Specifically, this can include the device not adhering to the build platform, errors in x, y, z axial configurations, filament jamming in the extrusion nozzle, belt drive jams, and a plethora of other distinct problems. It is important that the printing apparatus is ideally configured to produce a consistent product that is free of any flaws and can function in the surgical field. If individuals are not properly trained on how to utilize the printing device and supplemental components, the entire premise of the interventional becomes compromised. Specifically in developing countries, many times individuals are not properly trained or do not receive an incentive to train, in which many interventions fail as foreign devices that breakdown are not fixed and become neglected. This is a critical facet to recognize and understand, as it does indeed serve as a confounding element and effective barrier to entry to adopting new technologies in LMICs.

Typically, the effective cost of an intervention is a prominent barrier to entry, while this is indeed true in many respects rapid device prototyping is indeed a fiscally viable option when compared to other alternatives. Previous studies have fabricated medical devices utilizing costly printing setups and 3D printers that would simply not be practical in LMICs. Many researchers have utilized MakerBot printers, which are indeed the most ideal printers to utilize, but cost thousands of dollars per unit. In addition, if these devices were to breakdown, allocation of specific parts would be nearly impossible, and would have to be shipped internationally. This would effectively cripple the device for extended periods of time, rendering the intervention and fabrication of toolkits susceptible to failure. RepRap devices have the ability to print over 80% of their own parts, most of which are critical to device functionality (Jones et al., 2011). This limits the possibility of extended device failure and allows the device to be fixed immediately. As previously mentioned the fixed costs of the PLA filament and RepRap device are under $200.00. While there are indeed many other elements to take into consideration such as Internet accessibility, power, computer setup, and training technicians, the overall costs to achieve the production of 3D printed integrative surgical toolkits are extremely low. An important element to take into consideration is the exact locality where these printing devices would fabricate these toolkits. Rather than setup these devices in unstable environments such as rural clinics, these devices would be setup up in district-level healthcare facilities. These facilities often have access to stable infrastructure entities such as power and often times the Internet, and would serve as ideal manufacturing and distribution hubs for these surgical toolkits to more rural hospitals and clinics.

5.2 3D Printing: A Paradigm Shift in the Global Medical Device and Humanitarian Supply Chain

The enhancement of the surgical capacity of district-level healthcare facilities in LMICs is the primary interventional strategy behind the deployment of the RepRap modular printing devices and domestic fabrication of surgical toolkits. In defining the problem of surgical access and provisional care, once again the fundamental problem of materials sourcing in LMICs comes to fruition. In addressing these discrepancies in medical device attainment in LMICs, examining the global medical device supply chain is critical. 3D printing technologies could provide a cost-effective solution to provide needed medical supplies and create medical toolkits in an on-demand fashion directly in the surgical field (Ibrahim et al., 2015). These printers can be utilized in rural clinics and hospitals, localities that are often difficult to send vital medical supplies to due to distance, cost, and a variety of other factors. The ability to print these supplies within these clinics and hospitals can allow for enhanced patient care and treatment by local physicians that ordinarily lack access to basic surgical supplies and medical instruments. Printing essential medical equipment can greatly reduce the functional burden of disease in developing countries.

The RepRap printing apparatus can operate with minimal resources and has the ability to provide on-demand domestic manufacturing of the integrative surgical toolkit in LMICs. In utilizing additive manufacturing devices such as FDM 3D printers, this offers a high utility value that shifts the medical device supply chain from an international scale to that of a domestic scale. 3D printing promotes direct product to consumer approach, in which individuals receive the product i.e. surgical instruments in this case, in a direct fashion, significantly reducing amount of confounding variables often associated with international medical supply chains. The international medical device supply chain is often susceptible to long lead times, high transport costs, large carbon footprints, international tariffs/import taxes, as well as limited supply/market penetration (Engel, 2014; Hostettler, 2015). The direct access to medical devices such as integrative surgical toolkits fabricated by 3D printing in district-level healthcare facilities, can redefine the medical device supply chain in LMICs and globally on multiple fronts.

Fiscally, this intervention is highly cost-effective as surgical instruments are produced in an on-demand based upon need and also yields significant reductions in transportation, storage, and customs costs as shown in Fig. 5.5 (Hostettler, 2015). The initial input capital required to purchase the components for fabrication of surgical toolkits is immediately recouped from the first production run, thus returning a net-positive gain in the continued fabrication of these surgical device kits in the short and long terms. In addition, the direct source allocation and domestic manufacturing processes that allotted utilizing 3D printers results in increased market penetration of medical device products. The traditional supply chain allots for supplies to be sent to major ports or urban cities and then locally distributed, but generally these supplies are limited to the immediate surrounding

Fig. 5.4 Current global medical device supply chain (Engel, 2014)

areas. This means that medical supplies that may have never been able to be introduced into rural areas now have the distinct ability to be delivered in a domestic process, increasing access to these critical medical supplies. Additive manufacturing also reduces the uncertainty and delivery delays commonly associated with conventional international shipment of medical supplies as shown in Fig. 5.4 (Hostettler, 2015). This technology provides an ideal solution for improving the delivery and accessibility of emergency surgical care and can provide a cost-effective solution to providing essential surgical supplies, a critical component of enhancing the surgical capacity of district-level hospitals and clinics in LMICs.

One facet of global supply chain that is often overlooked is that of the humanitarian supply chain and logistics. This refers to the interventional capacity to deliver critical medical supplies to areas that need it most, with an applicable scenario being that of medical mission trips. Current estimates put the total U.S. based mission groups at more than 500, with an average of 10-trips/year/group, and a total annual expenditure of more than $250 million (Hostettler, 2015; Rankin et al., 2014). The bulk of expenses related to these medical trips are primarily attributable to transportation of medical materials and supplies. 3D printing has the potential to reduce these associated and often-widespread costs and can increase the dexterity of humanitarian logistics, in order to make future endeavors more efficient and effective (Shrinking the Supply Chain, 2015). The ability to employ rapid and customized manufacturing processes within a small, modular device that requires

Fig. 5.5 Global medical device supply chain schematic with implementation of 3D printing (Engel, 2014)

relatively little setup, can indeed alter the current and future states of humanitarian logistics. By manufacturing directly onsite and at the point of use, humanitarians can avoid ordering products that may take months to transport and clear customs (Shrinking the Supply Chain, 2015). In addition, the initial transport of printer components and materials such as raw filament spools is quite efficient, as it requires limited packaging and less space than finished goods (Shrinking the Supply Chain, 2015). Remote and rural clinics are often supply stricken and lack a variety of medical device instrumentation and supplies to accommodate the broad range of surgical and clinical treatment specialists, which perform procedures. This disconnect requires that campaigns travel with required instruments or substitute alternative tools, and additional logistical factors such as the potential for damage and theft of instruments is unaccounted for (Rankin et al., 2014). The ability to reduce traveling payload of medical supplies and fabricate high-utility medical instruments could benefit these efforts greatly and enhance the surgical capacities of healthcare facilities in LMICs.

One of the core entities associated with this disruption in the global medical device supply chain is that of the district-level healthcare facility. These are first level district hospitals that function as the core site for surgical care access and delivery as shown in Fig. 5.6 (Meara et al., 2015). These facilities provide the ideal setting for deployment of RepRap 3D printers and can serve as functional manufacturing and distribution hubs of medical supplies such as surgical toolkits. These facilities often have stable access to infrastructure entities such as electricity and

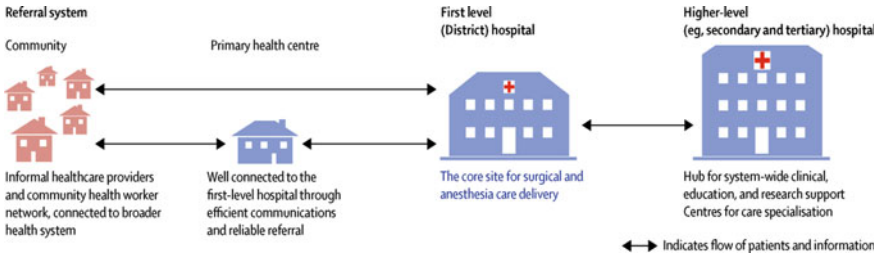

Fig. 5.6 District-level healthcare facilities and their role in surgical care access and delivery (Meara et al., 2015)

Internet as well as human capital in the form of medically trained individuals. These elements deem these healthcare facilities as the ideal locality for pilot studies examining the domestic manufacturing of surgical kits. In addition, these sites can serve as critical distribution hubs for these surgical toolkits. Ideally, these kits would be fabricated and stored in these facilities and then distributed to more rural localities such as remote clinics that cannot support 3D printing infrastructure. In creating a distribution hub, these facilities can indeed fabricate these kits for a specific price point and create a revenue generating schematic. These prices can be adjusted based upon the amount of kits produced and the relevant demand. A critical element is that these kits can be sold for a profit at a price of less than $10.00, thus eliminating fiscal barriers that would prevent distribution of these needed surgical tools to areas that need it most.

What we ultimately see is a focal paradigm shift in the overall medical device supply chain, in which LMICs can domestically manufacture increasing amounts of medial devices to be distributed locally. This can wean these countries off of relying on HICs for medical device donations and complex supply logistics that often plague medical resource allocation efforts in LMICs. In addition, previous studies have shown that increasing accessibility to emergency surgical kits can exponentially increase the percentage of surgical output and delivery in developing countries. For example, a coordinated country initiative to strengthen surgical service provision at district-level hospitals in Mongolia, had quantitatively measured effective output of surgical services based upon allocation of emergency kits and proper outfitting and establishment of an emergency room (Henry et al., 2012). This study had documented significantly increased capabilities to perform multiple critical surgical interventions including incision and drainage of abscesses, wound suturing, and wound debridement (Henry et al., 2012). This increase was due to the development of formal emergency rooms with adequate surgical supplies, which dramatically improved access to and delivery of these basic, yet critical surgical procedures as shown in Fig. 5.7 (Henry et al., 2012). This enhanced output of surgery can directly combat the surgical burden of disease and further result in enhanced patient outcomes and decrease the burden of disability that plague many individuals in developing countries.

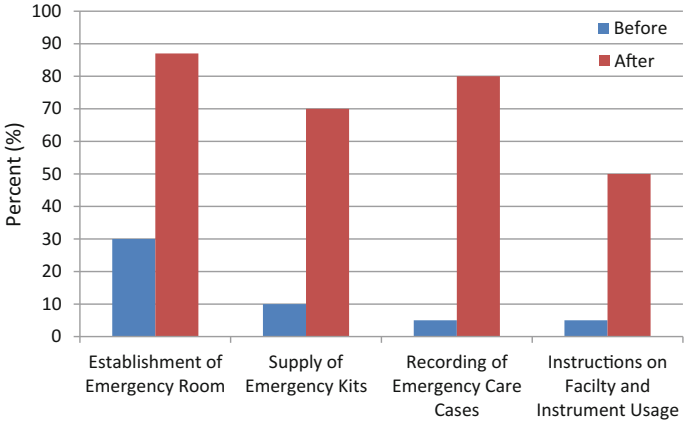

Fig. 5.7 Access to fundamental surgical elements increases surgical output and delivery in LMICs (adapted from Henry et al., 2012)

Upon further examination of Fig. 5.5 we see that there are indeed multiple facets that contribute to surgical output and delivery in LMICs. While access to emergency kits and supplies are a critical element, we can see that formal establishment of an emergency room, formal recording of emergency care cases, and formal instruction on facility and instrument usage are all critical factors that when combined, result in exponentially increased surgical output and delivery. As previously mentioned, the global burden of surgical disease requires an integrative solution and it is through the culmination of these interventions that we can effectively combat it in LMICs.

5.3 The Future of 3-Dimensional Printing: Bio-Based Materials, Medical Device Fabrication, and Open-Source Information Dissemination

With rapid advancements and innovations in applied science and engineering being made everyday, biomaterials science and additive manufacturing could be radically changed and improved in the near future. This is especially true for biomaterials research, as there are seemingly limitless possibilities of novel materials to be created via polymer blending, copolymerization, and biocomposites. We are currently in the midst of a focal paradigm shift from the use of unsustainable petroleum-based materials to using more eco-friendly materials that display enhanced properties. This shift has been noted in every field and industry ranging from the automobile and energy industries to that of medicine. Like all innovations regardless of application, the use of biomaterials is reliant upon their ability to appeal to a specific market segment, outperformer competitors, meet a consumer/market need, and be fiscally

Table 5.1 Future biomaterials for 3D printing (adapted from Van Wijk & Van Wijk, 2015)

Future biomaterial for 3D printing	Material profile	Material properties
Flex PLA or Soft PLA	PLA filament chemically-modified to make it more rubber-like	High overall flexibility and flexural strength
Nylon 11	Polyamide 11 (PA11) or Nylon 11 derived from vegetable oil	High flexibility, strength, and self-lubricating
Bio-Rubber	Thermoplastic elastomer (TPE) derived from rapeseed oil	High overall strength, thermo-resistance, and UV resistant
Arnitel Eco	Thermoplastic co-polyester made partially of rapeseed oil	Flexibility, high-tensile and compression strength
Biome 3D	Thermoplastic derived from plant starches	High flexibility and mechanical strength
Bamboo-Based	Filament derived from finely ground bamboo	High tensile, compression, and impact strength, low-cost
Straw-Based	Filament derived from rice and wheat stalks mixed with plastic binding polymer	High tensile, compression, and impact strength, low-cost
Laywood	Filament made of recycled wood with binding polymer	Wood-like qualities, low-cost, good mechanical properties

feasible. The ability for novel biomaterials to be developed and applied in the field heavily relies on these facets. Nonetheless, there are a variety of novel biomaterials that are being developed and adapted for current and future applications in additive manufacturing processing. Some biomaterials that are currently being developed are outlined below in Table 5.1 and vary based upon their respective material profile and properties as well as application. Some of the most promising materials for 3-dimensional printing include the development of bamboo-based and bio-rubber materials. These materials are readily available and their respective propensity to be processed into a viable thermoplastic material in conjunction with PLA is indeed feasible. While over the course of the preceding chapters have focused on the fabrication of various surgical instruments, the future of biomaterials spans broader applications and 3D fabricated objects.

With continued development and improvements in processing efficiency of these bio-based materials shown in Table 5.1, the ability to further utilize these materials in fabricate medical instruments and supplies becomes vastly improved. In particular, the use of materials such as bamboo- and straw-based fibers in PLA blends can further enhance the efficacy of their use in the additive manufacture of surgical instruments. These materials provide a natural, sustainable, and cost-effective component that can improve the mechanical and chemical properties of surgical tools and instruments, while simultaneously maintaining their ideal

biocompatibility complexes. Specifically, the ability to improve the impact, tensile, barrier, and elasticity properties of these instruments, while decreasing their relative susceptibility to thermal, humidity, and ultraviolet degradation processes can further enhance the application of these instruments. The true potential of these materials for use in medical device applications in LMICs further lies in the ability to domestically source these natural materials. Many developing countries are indeed agricultural-based economies that function on the harvesting and selling of domestic crops. Many of these domestic crops include sugarcane, corn, rice, maize, and other suitable bio-based materials that could be utilized in the domestic production and additive manufacture of medical devices. This can further decrease costs, improve medical device procurement, promote domestic manufacture, as well as serve as an impetus for innovation for future device development. Surgical instruments and tools can further be modified and adapted for process efficiency, materials compatibility, surgical-field performance and application in conjunction with these bio-based materials.

We have merely examined only a small portion of medical instruments, supplies, and tools that can be fabricated with the use of rapid prototyping processing. The fabrication of biological scaffolds for tissue engineering, an array of functional prosthetics, anatomical models, stents, sutures, orthopedic screws, etc., all can be modified with biomaterials and are the future for natural, biocompatible materials that respond in a positive fashion to our native tissues, anatomical processes, and biomechanics. With continued research in biomaterials, researchers and scientists have begun to see that nature is the most adept frugal engineer, who utilizes materials in the most efficient and effective manner that are unmatched by the bounds of mankind's artificial materials. In further tying-in the future of biomaterials in additive manufacturing, custom anatomical models and medical supplies such as casts, implants, and splints can be fabricated utilizing natural bio-based materials such as PLA.

In addition, we have only examined the fabrication of surgical instruments with bio-based materials and rapid prototyping devices. There have been multiple studies that have examined the fabrication of a multitude of other medical devices and supplies to be utilized in humanitarian aid and conflict relief. For example, researchers at the University of Toronto have fabricated prosthetic legs for children in Uganda and research from Worcester Polytechnic Institute have 3D printed trans-tibial prosthetic sockets for amputees in Uganda, and a pilot study in Haiti fabricated basic clinical medical supplies such as umbilical cord clamps, oxygen splitters, and IV bag hooks (Bender, Chartoff, & Hoppe, 2014; Dotz, 2015; Krassenstein, 2015). 3D-printing technology bridges the gap between theory and application, and specifically closes the gap between novel idea and actual rapid prototyping of that idea in the field. Since 3D printing files can be openly shared on global platforms such as the Internet, the ability to manipulate digital files is quite easy, and allows for ideas in one location to be easily duplicated or repurposed in another (Shrinking the Supply Chain, 2015). Although 3D printing requires the use of trained individuals, it is simple enough that affected communities can develop their own ideas to address humanitarian or livelihood needs (Shrinking the Supply

Chain, 2015). For example, Oxfam and MyMiniFactory.com, a open-source library of 3D object designs, launched a project to help rapidly design, manufacture and test items to address the water hygiene issues of Syrian refugees in Lebanon (Shrinking the Supply Chain, 2015). Designers, engineers, and enthusiasts from around the world were invited to submit designs for hand washing devices and the selected designs were then simply e-mailed to humanitarian workers for in-field fabrication, testing, and feedback (Shrinking the Supply Chain, 2015). This example shows how rapid prototyping devices in the field close the gap between idea and application. If this were to perhaps be conducted in another manner, logistical factors such as the war, conflict, cost, shipping, and bureaucracy could have indeed hindered the delivery of these hand-washing devices. The organization, Refugee Open Ware (ROW), is an international humanitarian organization that supports innovations to improve the lives of those afflicted by conflict. The organization has been utilizing 3D printers to fabricate prosthetics to assist Syrian refugees, Jordanians, Yemenis and other amputees from the Middle East that have been afflicted by war and conflict. ROW developed an open-source 3D printed prosthetic hand that was co-created with a 6-year-old Yemeni refugee was severely burned and treated by Doctor's Without Borders (Fig. 5.8). The total cost of the printed prosthetic was approximately $80 as compared to a cost of over $10,000 for a conventional prosthetic hand (Refuge Open War, 2017).

In addition to the current and future potential humanitarian elements related to rapid-prototyping devices, these devices hold promise in the fabrication and delivery of highly customizable medical components and anatomical models for patients. Specifically, we can fundamentally alter the medical device value chain, in which we can obtain patient data, develop a custom 3D blueprint, transfer the blueprint to the printing device, and fabricate a patient-specific device (Fig. 5.9).

Fig. 5.8 ROW 3D printed prosthetic hand (3D Printing and Prosthetics, 2017; Refuge Open War, 2017)

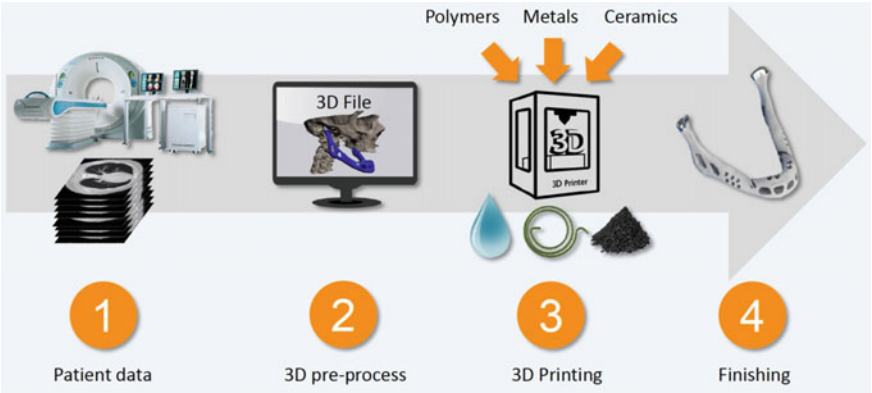

Fig. 5.9 3D printing and the medical device value chain (Engel, 2014)

This process is universal in that it could be applied to an array of medical and dental applications, such as in the fabrication of custom prosthetics, implants, casts, splints, braces, and 3D anatomical models of scans, all of which can be tailored to each patient. These devices can be fabricated for minimal cost and further enhance the treatment and palliative care rendered to patients.

The application of 3D printing in LMICs continues to expand and develop each year, in which these printers have not only been sought in printing medical devices and supplies, but also for medical education and training. These devices can print low-cost, high-resolution anatomical models of organs, bones, and vascular networks that can be utilized to train future medical practitioners in LMICs (Hostettler, 2015). These models can be custom configured, scaled, and printed on-site allowing for future generations to have access to high-quality medical models at a fraction of the cost of conventional ones. In addition to the fabrication of anatomical models for medical education, 3D printers can fabricate models from MRI or CT scans (Fig. 5.10) (Matisons, 2015). This provides the ability to create a 3-dimensional model of a patient's condition such as a tumor, vascular condition, or malignancy from a 2-dimensional interface such as a MRI or CT scan (Matisons, 2015). This can further enhance the interventional capacity of physicians to surgically treat conditions, resulting in enhanced patient outcomes. For example, a team of surgeons at the Hospital Sant Joan de Déu in Barcelona, Spain completed a fully invasive tumor resection in a pediatrics patient utilizing a custom 3D model of his tumor (Fig. 5.11).

The patient was diagnosed with neuroblastoma, which is an extremely aggressive cancer in children that develops in the nerve tissue and requires surgical resection of the tumor in conjunction with chemotherapy. In this particular case, the patient had presented with a tumor that was in between his spine and kidney, and surrounded by a plethora of blood vessels and arteries, making resection nearly impossible without endangering the patient's life. A scan of the patient's tumor was digitally processed and reformatted for 3D fabrication and printed utilizing a

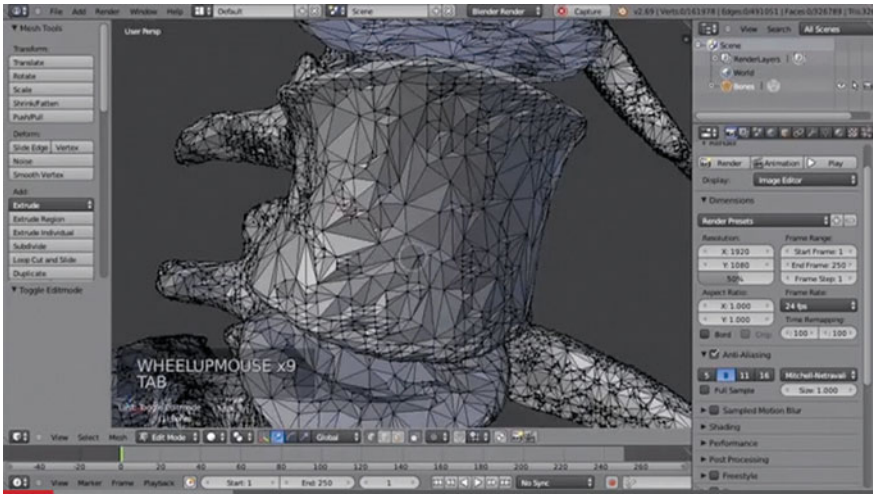

Fig. 5.10 Radiographic images can be converted to 3D print files to create customized anatomical models; radiographic image conversion of spinal segment into .STL format shown (Ventola, 2014)

Fig. 5.11 Surgeons extract tumor utilizing 3D-printed model (Surgeons extract tumor, 2014)

multi-material 3D printer and using this replica, surgeons were able to test the operation more than a week ahead of the surgery. In doing so, they were able to develop an effective tumor resection plan without damaging other tissues and allowed for an overall reduction in operation time.

As the world becomes increasingly globalized, the potential for the dissemination of information and innovations increases each and every year. With increasing

access to elements such as the Internet in LMICs coupled with the concept of frugal innovation, we can create an impetus for change and development. Increasing large segments of LMICs are becoming interconnected to the global network interface, allowing for the access and dissemination of knowledge that would not have been possible only a decade ago. This allows for novel interventions such as the one proposed in this study, to have the potential to be deployed in the areas that need it most. This is of particular importance for the advancement of 3-dimensional printing in LMICs, as open-source 3D printing websites and platforms contain free step-by-step fabrication manuals, troubleshooting facts and questions, prototype specifications, and filament property profiles that is critical for the sustained development and application of this intervention. With these sources being open-source and available online, district-level healthcare facilities can further improve upon the modular design and instrument profiles of these surgical toolkits to meet their own needs.

Future fabrication of entities such as 3D-printed surgical toolkits with bio-based materials offers a highly versatile and adaptable surgical instrument delivery platform. This means that these instruments and toolkits can be further redesigned and custom tailored to the needs of various healthcare facilities. The open-input design allows for physicians and technicians to provide instant feedback in order to further improve the instrument designs. These modified designs can then be instantly fabricated in the surgical field to deliver real-time device feedback and functionality. Perhaps the most important element is that these enhanced and modified designs can also be uploaded to open source websites and shared with individuals around the world. Websites such as the National Institute of Health's 3D print exchange provides a free, open-source online resource for sharing medical and scientific 3D print files and tutorials (Fig. 5.12) (Ventola, 2014).

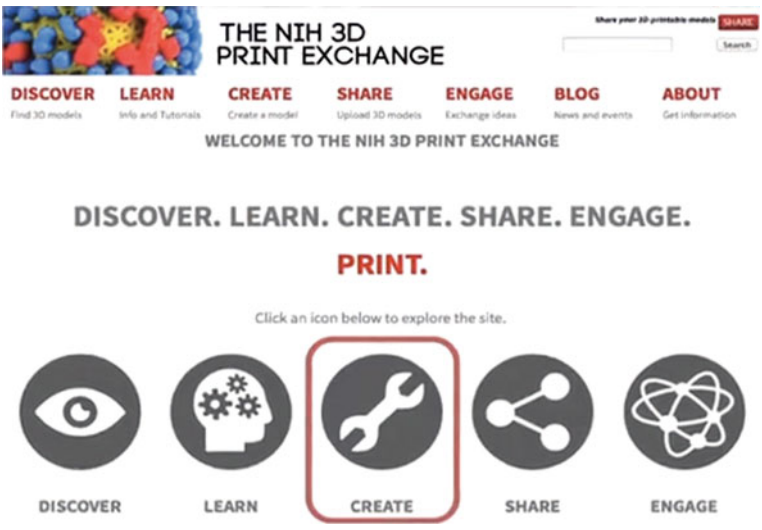

Fig. 5.12 The NIH 3D print exchange website (Ventola, 2014)

This means that anyone could have the opportunity to download these files and print them, in which they can also provide device feedback and potential modifications. This could potentially revolutionize how medical devices and supplies are designed and utilized in resource-poor settings such as LMICs. In addition, this information can be shared with other healthcare professionals and academic institutions around the world, which can provide input and feedback to further create enhanced versions of the instruments or perhaps completely redesign the instrument profiles. This essentially fosters an environment of connectivity and information exchange that can take the toolkit designs in this study to the next level. This can foster momentum for the fabrication of new and even better surgical toolkit designs that incorporate more efficient and effective materials, cost-effective designs, and enhance interventional applications.

5.4 Concluding Remarks

In reflecting upon the multiple topics, themes, and elements that have been explored over the course of this book, one can see how the interventional capacity of the bio-based PLA integrative surgical toolkit and RepRap modular printing apparatus in LMICs to combat the global surgical burden of disease is indeed multifaceted. The ideas and innovations that have been explored in this research are rooted in the functional capacity to reduce the global burden of disease and improve the lives of our fellow man. The utilization of alternative bio-based filaments such as PLA to fabricate entities such as integrative surgical toolkits, can indeed serve as a safe and effective biomaterial that is sustainable, sterile, non-toxic, and affordable (Kreiger & Pearce, 2013). The utilization of 3-dimensional printing technologies such as the RepRap rapid prototyping platform coupled with bio-based filaments such as polylactic acid, can provide an ideal delivery vehicle which provides a high-utility platform that is a cost-effective solution for providing access to and delivery of critical surgical toolkits in LMICs.

While this study has been limited in multiple capacities, including the device deployment and manufacture of instruments in LMIC healthcare localities as well as physical testing of these instruments in the surgical field, the ideas and innovations rendered are not steeped in theory, but in feasible application. The RepRap modular printing platform, bio-based materials, and surgical instrument designs are available to be utilized not in the future, but in the present. Furthermore the instruments proposed to be utilized in the surgical toolkit can and have been printed with the PLA filament. In order to further develop the use of bio-based materials for surgical instruments, in-field surgical trials must be developed and executed to further characterize the ability of these instruments to meet the rigorous demands of surgery. This is especially true for the reformatted and modified modular instrument designs that were created in this project in order to be fully compatible with the PLA filament and FDM processes. Modifications to the infill density, geometric infill pattern, as well as the x, y, and z-axial configurations can indeed impact the

functional mechanics of these instruments. This further reiterates the need for thorough field study of short and long-term outcomes of deploying these toolkits in resource-stricken settings such as LMICs. In addition to examining the materials properties of these instruments, a holistic approach must be garnered to examine the use and deployment of RepRap printers in district-level healthcare facilities in LMICs. While this has indeed been examined in several studies, the entire process from constructing the RepRap device to that of fabricating these toolkits as well as the elements in between such as training and education, must be further examined.

The open source dissemination of knowledge is indeed vital in promoting the further advancement and development of novel innovations in LMICs. But while this is important, another element that this open sourced access creates is a platform for health and economic development. As previously discussed, in combating the surgical burden of disease, we can create net-positive economic gains, in which individuals that are healthier contribute more to society and promote economic development. This means that healthy individuals can provide more for their families, further the education of their children, and contribute more overall to their respective communities, as they are not plagued by chronic nature of surgically avertable conditions. Health and wealth are indeed interconnected, but incorporating knowledge and human capital, we create something new. In utilizing additive manufacturing processes such as 3D printers, LMICs have the ability to fabricate their own medical instruments and designs and harness the power of domestic manufacturing processes. Open source information for 3D printing and medical device designs, means that these countries can transition from relying on medical supply donations from HICs to having the ability to address their own respective health needs. Of course this is only one facet, specifically related to creating certain medical devices, but we create new paradigm of independence.

It is important to note that while many of the ideas and innovations are indeed interventionally feasible, there is indeed a plethora of confounding elements and variables that must be further examined and developed. A core principle of this book was the translation of theory into action and providing a functional schematic of a feasible solution to a global health threat. While this has been extensively examined, like all innovations, there will be have to be further research and most importantly, collaborative efforts to see ideas such as these take fruition. Rapid device prototyping and additive manufacturing processes are in a continual state of change and development. Further advances in micron layer density, bio-based materials properties, and medical device designs are made each and every day. This study also only focuses on the fabrication of a limited range of surgical tools and instruments that can be feasibly fabricated utilizing current 3D printing devices. There are thousands more medical devices that have the potential to 3D printed, but the technology still is in its infancy and will need to be further improved to create truly outstanding medical devices that are on par with conventional stainless steel instruments. As technology becomes cheaper and more readily available, small innovations such as bio-based surgical toolkits can be further developed and improved upon. The true challenge lies in making these innovations available to the individuals that need them most and improving the lives of others. In

acknowledging this challenge, it is important to embrace the highly adaptable nature of 3-dimensional printing devices and diverse medical applications of printing technologies in LMICs.

As our world continues to further develop, and the challenges we face become more complex and dynamic, the need for targeted, adaptable, and integrative solutions becomes eminent. The quintessential notion of "real-world problems, requires real-world solutions" becomes ever so important as we continue to make advances in science, technology, and engineering. The dissemination of knowledge and the promotion of human capital development through the investment in the education of future generations, especially in LMICs, hold the key to health and economic success. Collaborative efforts between researchers, policy-makers, and governmental organizations is critical in tackling some of the most challenging and pressing issues that are present in today's global health paradigm. The ability to adapt and respond to new global health threats and challenges such as the global burden of surgical disease, characteristically defines who we are as human beings including our innate responsibility to help those that need it most.

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