



3-Dimensional Printing and Bio-Based Materials in Global Health: an Interventional Approach to Addressing Healthcare Disparities in Low and Middle-Income Countries

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3-Dimensional Printing and Bio-Based Materials in Global Health:
An Interventional Approach to Addressing Healthcare Disparities in Low and Middle-
Income Countries

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for the Degree of Master of Liberal Arts in Extension Studies

Harvard University

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Abstract

Approximately 2 billion people in developing countries around the world lack access to essential surgical care and services, resulting in the avertable deaths of over 1.5 million individuals each year. These startling statistics reveal a hidden notion and key premise, this being “avertable deaths.” These are deaths that could easily be averted by garnering access to adequately equipped healthcare facilities that can provide provisional surgical care. Upon further examination, a fundamental barrier that inhibits access to surgical care is the lack of basic surgical instruments and supplies in healthcare facilities in developing countries. Without access to the most essential and basic surgical instruments and supplies, these facilities are extremely limited in their respective interventional scope and capacity to provide adequate surgical care. Upon reflection of this pertinent problem, a functional, yet dynamic solution must be improvised that is rooted in feasibility, this being 3-dimensional printing. The deployment of low-cost 3-dimensional printing technologies in developing countries could revolutionize the distribution and manufacture of surgical instruments in district-level healthcare facilities. While previous research has focused upon the applications of 3-dimensional printing materials for biological scaffolds or implants, limited research has examined the fabrication of simple, yet essential surgical instruments that are often in short supply in developing countries. Critical surgical instruments could be manufactured with sustainable, bio-based plastic materials at a fraction of the cost of conventional stainless steel medical supplies. Introduction of this new interventional approach could radically

alter the current surgical care paradigm that is faced today and potentially save the lives of millions of individuals that die each year from preventable conditions.

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Chapter I

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). Upon further examination, the inequity related to the access to surgical services becomes stratified based upon income distribution. 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: low-income countries (LICs) = \$1,045 or less, Middle-income countries (MICs) which are subdivided into lower-middle-income = \$1,046 to \$4,125 and upper-middle-income (UMICs) = \$4,126 to \$12,745, and finally high-income countries (HICs) = \$12,746 or more as shown in Figure 1 (Debas et al., 2015). This stratification in accessibility to surgical services is most prominent in low and middle-income countries (LMICs) in which nine out of ten people cannot access basic surgical care (Meara et al., 2015). This equates to approximately 2 billion individuals in low and middle-income countries that have almost zero access to essential surgical services (Debas et al., 2015). Of these 2 billion people, over 1.5 million people per 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 of these individuals.

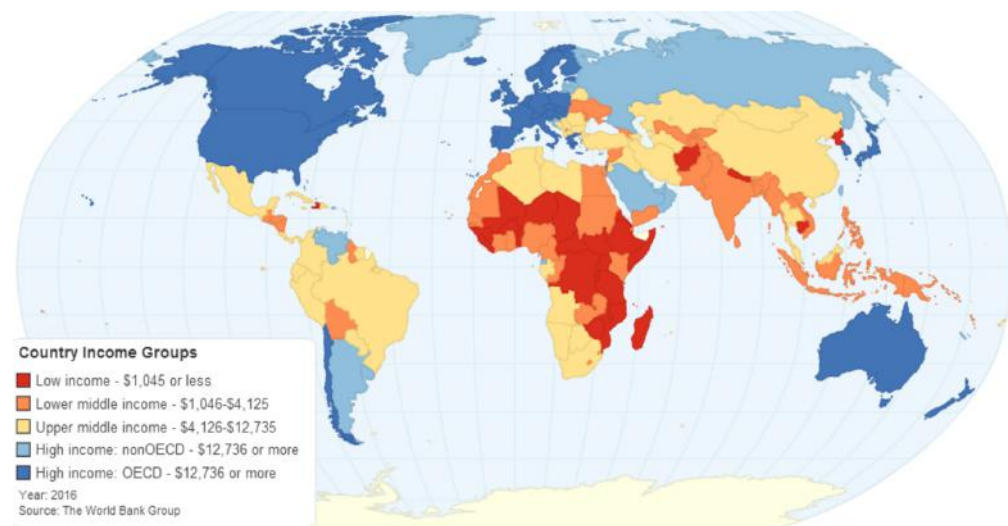


Figure 1. World Bank Country Income Group Classification (Country Income Groups, 2011)

Upon comparison of the access and delivery of surgical care in HICs vs. 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 Figure 2 below. 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.

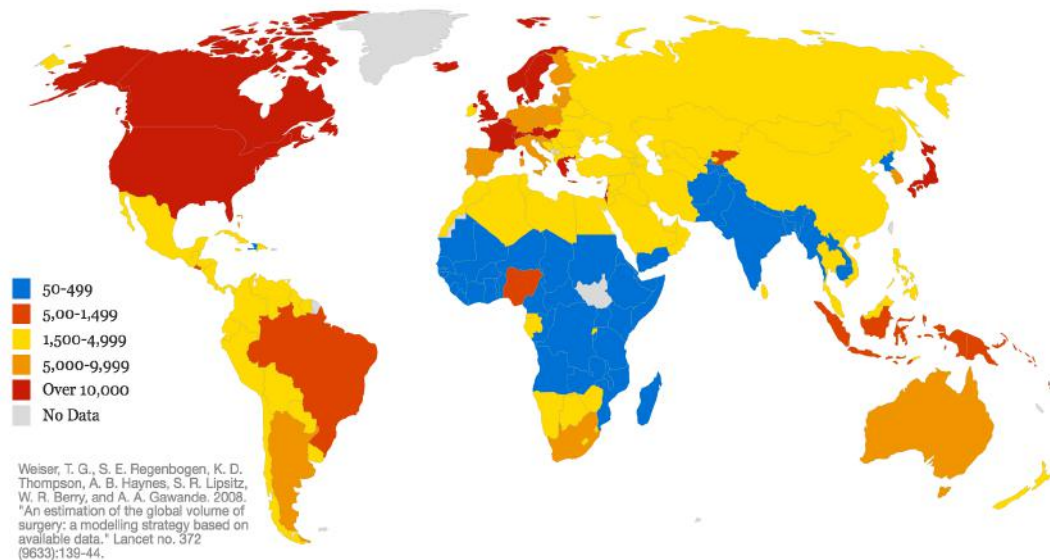


Figure 2. The global volume of surgical interventions per 100,000 individuals amongst HICs and LMICs (Weiser et al., 2008)

Given the low volume capacity for surgical interventions in LMICs, there are a number of critical surgical procedures that are specifically underperformed in LMICs. Death and permanent disability can be avoided through surgical interventions following abdominal emergencies, road traffic injuries, congenital abnormalities, pregnancy complications, fractures, burns, or acute infections that are highly prevalent in LMICs (World Health Organization, 2014). General, obstetric, and trauma surgeries are the most critical surgical interventions that are often underperformed in LMICs and must be increased in to further remedy the frequency of the conditions noted above (Debas et al., 2015). Pregnancy complications often require obstetric surgical intervention in the form of

cesarean section, 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 top 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.”

The Global Burden of Disease and Essential Surgical Conditions

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-cultural and demographic 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 few years. 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 as well as 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. 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 noted as “surgical conditions”, which consists of any pathology for which an invasive procedure may provide treatment, palliation or cure (Gunn, 2012). While surgical conditions consists of a broad spectrum of pathologies, particular interest is given to those that are deemed as “essential” surgical conditions. 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 World Health Organization (WHO) organizes essential surgical conditions three distinct categories as depicted in Figure 3 below. 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.

Category	Deaths (thousands)	DALYS (thousands)
Category 1. Communicable, maternal, perinatal, and nutritional		
Maternal conditions	280	19,000
Birth asphyxia and birth trauma	780	78,000
Category 2. Noncommunicable diseases		
Cataracts	< 1	7,000
Peptic ulcer disease	230	7,000
Appendicitis	38	2,000
Skin diseases ^a	90	16,000
Cleft lip and palate	5	< 1,000
Oral conditions ^b	< 1	13,000
Category 3. Injuries ^c		
Road traffic crash	1,160	72,000
Other unintentional injuries	1,550	96,000
Intentional injuries	540	34,000
Burden from these conditions	4,700	340,000
Total burden from all causes	45,000	2,400,000
Share of burden due to conditions addressable by essential surgery (percent)	10.4	14.2

Figure 3. The three categories of essential surgical conditions, including number of deaths and disability-adjusted life years per condition as depicted (Debas et al., 2015)

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 Figure 3 above, 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 (Alwan et al., 2010). The term was developed in order to compare the overall health and life expectancy of individuals amongst different countries (Alwan et al., 2010). 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. The reason that these conditions become chronic in nature is due to the lack of healthcare infrastructure and limited surgical care access and delivery (World Health Organization, 2002). This is of particular importance for pediatric patients in LMICs, as approximately 85% of pediatric patients in countries 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 for future generations. 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.

Surgically Avertable Deaths: Disparity of Surgical Service Provision in LMICs

Over 80% of deaths from non-communicable diseases, injuries, and trauma occur in LMICs (Alwan et al., 2010). The resulting fatalities resulting these conditions are termed “surgically avertable deaths”, with a vast majority of these conditions being

treatable with surgical interventions. 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 avertable deaths in LMICs (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). 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 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 vs. 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 anaesthesia 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 anaesthesia 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, multiple studies 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 Figure 4 below (Kushner et al., 2010).

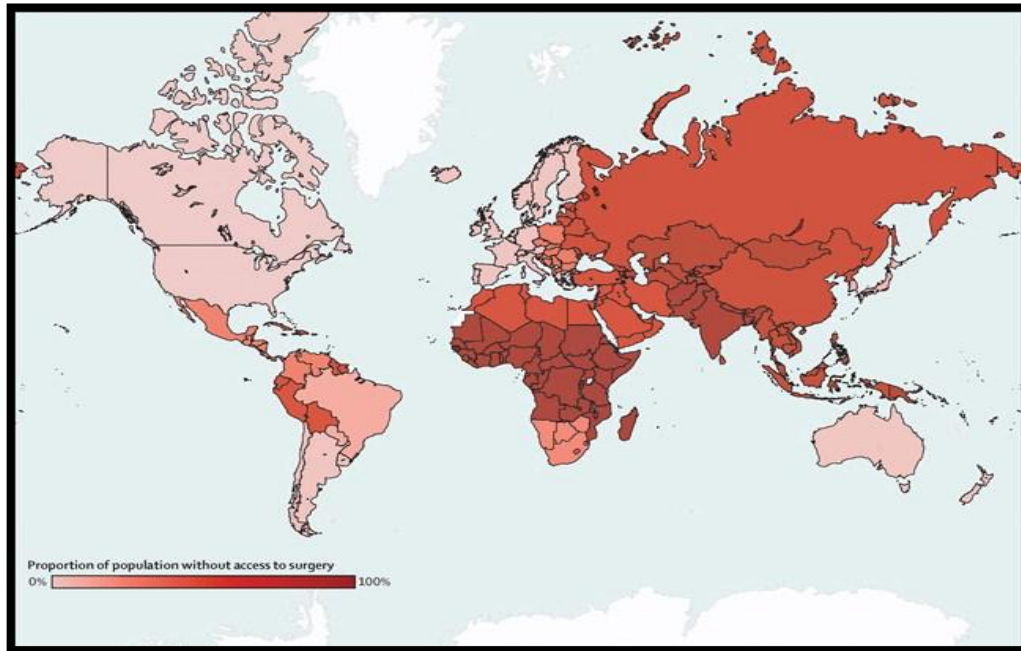


Figure 4. A depiction of the proportion of the global population without access to surgery based upon geographic locality. The darker shades represent increased lack of access to essential surgical care services (Alkire et al., 2015).

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 (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 Figure 5 below (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.

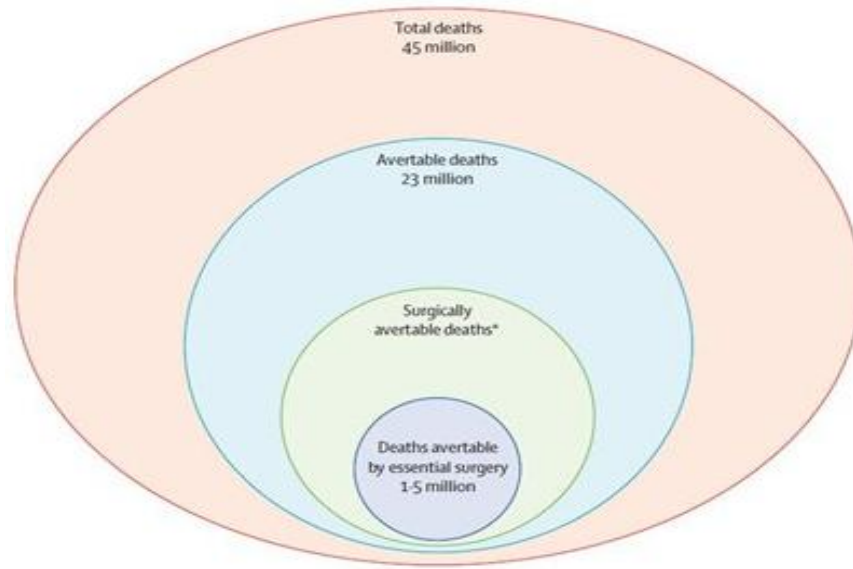


Figure 5. A provisional figure depicting the number of surgically avertable deaths in LMICs (Mock et al., 2015)

Surgery: A Highly Cost-Effective Health Intervention

The delivery of emergency surgical care has long been sidelined due to perceived 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 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 bednets to prevent malarial infection (Chao et al., 2014). In Figure 6 below, researchers 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 averted. 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).

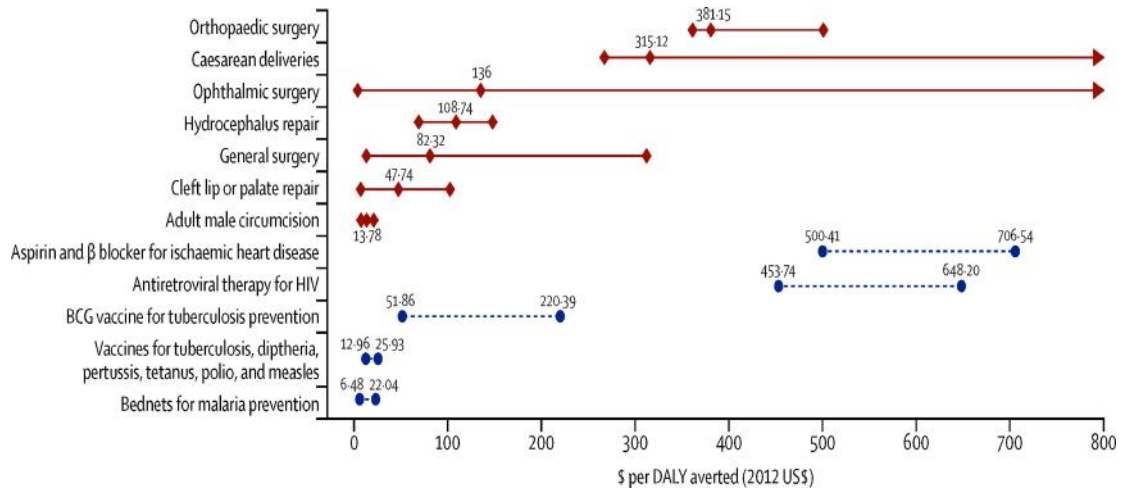


Figure 6. Cost-effectiveness of surgical interventions compared with other public health interventions (Chao et al., 2014)

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). With such high healthcare expenditures, individuals and families generally resort to reducing expenditures related to necessities such as food and clothing (World Health Organization, 2005). These reductions in expenditures can potentially become even more dire, as in many cases families are left unable pay for their children's education, effectively reducing investment in human capital and development in their respective communities as previously discussed. 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 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 Figure 7 below.

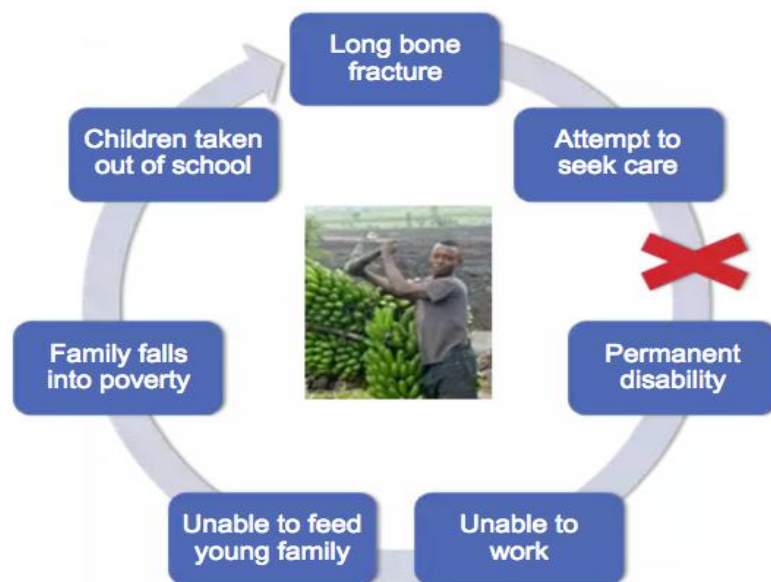


Figure 7. The cyclical nature of poverty in relation to the elective care of an acute trauma that eventually becomes a chronic condition if not properly treated (Dare, 2015).

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 5,000 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 productivity, which is currently estimated at approximately \$12.3 trillion USD in the next 15 years as depicted in Figure 8 (Frilling, 2016; Meara et al., 2015).

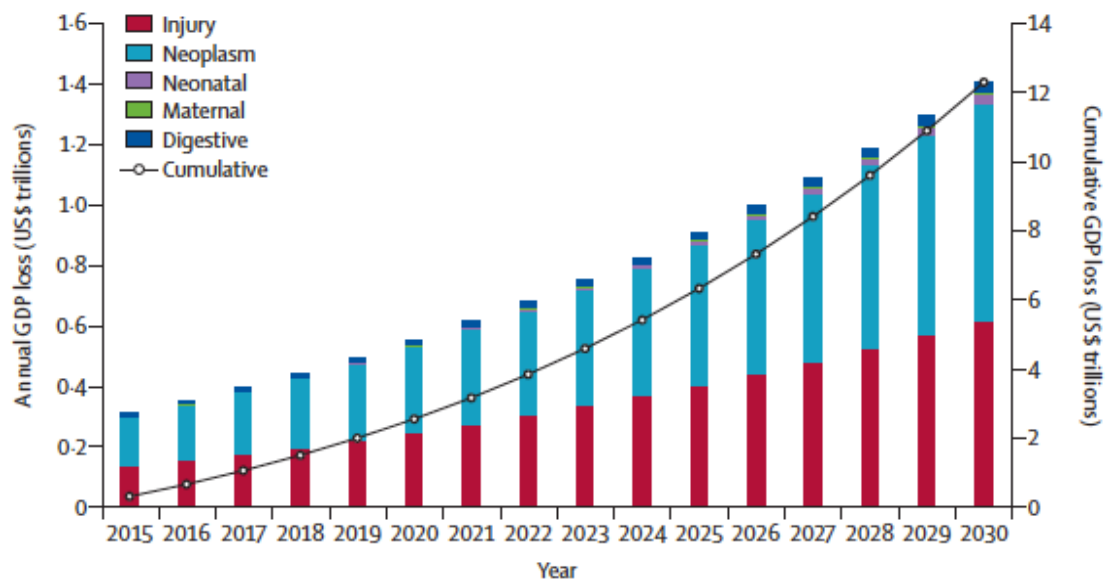


Figure 8. Annual and cumulative Gross Domestic Product (GDP) lost in LMICs from five categories of surgical conditions (Meara et al., 2015)

Disparities in Provisional Access to Surgical Instruments 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 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 GBD is eminent (Ozgediz & Riviello, 2008). This problem is especially important, as based upon current trend analysis and population dynamics, this of incidence ill-equipped medical facilities will likely become further exacerbated as healthcare demands of emerging countries increase and evolve (Alkire et al., 2015). The disparities experienced at district level health facilities in low 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 public health and economic gains, 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). 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.

Chapter II

3-Dimensional Printing and Bio-Based Materials: A Disruptive Innovation

In addressing such a profound problem such as the surgical burden of disease in LMICs, the need for what is known as “disruptive innovations” becomes necessary. These are innovations that 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. One particular disruptive innovation that could indeed serve as a focal element in combating the global surgical burden of disease and revolutionize the current global health paradigm is that of rapid device prototyping, more commonly referred to as 3-dimensional printing. With the glaring disparities in medical supply attainment and fiscal constraints in LMICs, the utilization of 3-dimensional printers has the potential to harness the productivity of an entire small-scale domestic manufacturing facility in a single, highly adaptable apparatus (Hostettler, 2015).

Over the past decade, research and development in 3-dimensional printing technology and software has increased exponentially. With this enhanced research, 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 upwards of \$20,000.00 in the past, these printing devices can now be purchased for as little as \$150.00 (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). Manufacturers of these units include such companies as MakerBot, DaVinci, Micro3D, and RepRap as well as a host of other new and innovative companies (Jones et al., 2011). 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 process (Gross et al., 2014). This process allows for the creation of physical objects and prototypes from a virtual model in a variety of materials such as plastic, steel, aluminum, and cobalt (Taneva, Kusnoto, & Evans, 2015). The process, as depicted in Figure 9, 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, Kusnoto, & Evans, 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, Kusnoto, & Evans, 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 Figure 10 (Taneva, Kusnoto, & Evans, 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 such as Cura 2.3.1. The G-code divides the 3D .STL file into a series of 2-dimensional horizontal cross sections generally between 25-100 μm ,

based upon fabrication technique (Gross et al., 2014). This digital 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).

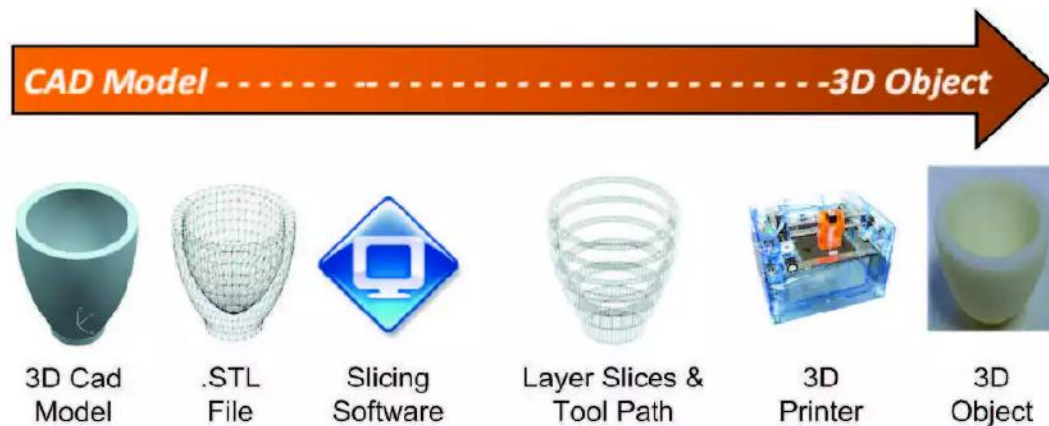


Figure 9. 3-dimensional printing process from 3D CAD Model to 3D object fabrication (Taneva, Kusnoto, & Evans, 2015)

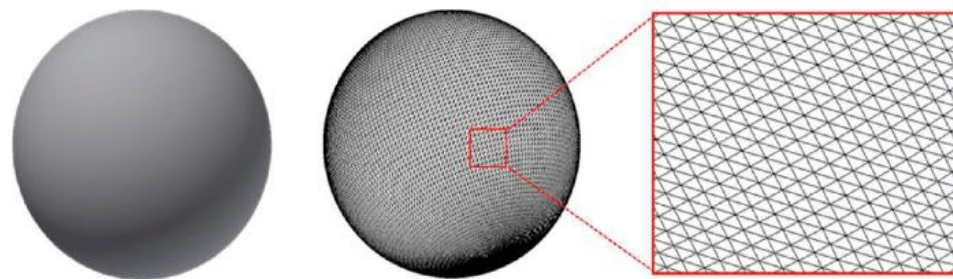


Figure 10. A graphical representation of the coordinate geometric configuration of information in an .STL file. The object as depicted on the left was created in a CAD program and saved as an .STL file. The graphical information displayed in the .STL file is shown on the right for the same object, with the surface of the object being represented in a coordinate triangulated pattern (Gross et al., 2014).

3-Dimensional Rapid Device Prototyping Processes

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. There are four types of rapid prototyping processes, each of which employ a distinct mechanical fabrication process and utilize specific printing filaments. These four processes as shown in Table 1 below are: stereolithography (SLA), selective laser sintering (SLS), fused deposition modeling (FDM), and inkjet printing (AlAli, Griffin, & Butler, 2015). Figure 10 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. Figure 11 below displays an overview of the mechanics of each rapid prototyping process and their respective functional attributes.

Type	Mechanism	Advantages	Disadvantages	Material	Other
SLA	UV light is used to create the object by curing and solidifying a liquid resin	<ul style="list-style-type: none"> • High-resolution prototypes • Good finishing at the surface 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Ability to produce complex/functional parts • Does not require support structure • High productivity 	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • No postcuring • Easy material changeover • Low-cost machines compared with others 	<ul style="list-style-type: none"> • 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)
INKJET	Spraying liquid or the photopolymer depending on the type of the jetting; binder or material	<ul style="list-style-type: none"> • A variety of material choice • High precision • Colored parts 	<ul style="list-style-type: none"> • Require postcuring 	Plastic, metal, and ceramics	Layer thickness: material: 0.013 mm (min) Binder: 0.09 mm (min)

Table 1. The four types of 3-dimensional printing processes: SLA, SLS, FDM, and Inkjet (AlAli, Griffin, & Butler, 2015)

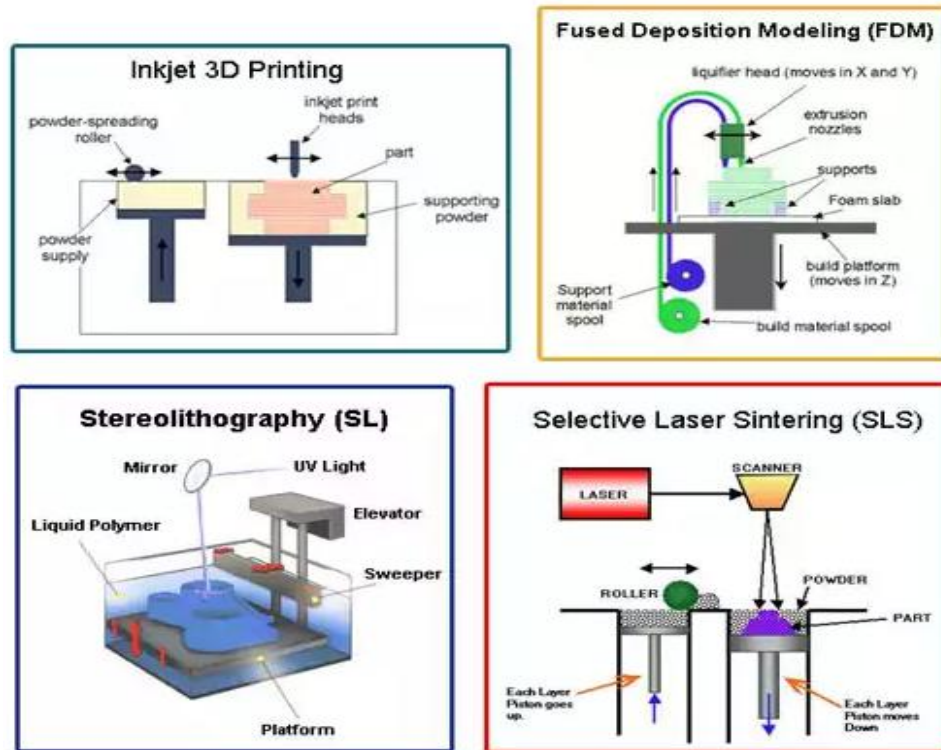


Figure 11. An overview schematic of inkjet, FDM, SLS, and SLA rapid prototyping processes (3D Printing)

The first process depicted is that of SLA or stereolithography printing, 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 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 sintering, 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 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 3D inkjet printing, which is a powder-based method where

layers of solid particles, approximately 200 μm in height with particle sizes between 50-100 μm , are bound together by a printed liquid material to generate a 3D model (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 (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). 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).

The final process is that of FDM or fused deposition modeling, 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 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).

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.

As previously stated, there are a variety of 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 pertinent (Tatham, Loy, & Peretti, 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,

Loy, & Peretti, 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.

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 Figure 12 (Jones et al., 2011). RepRap uses FDM fabrication to create objects from a variety of thermoplastic polymers including polylactic acid and acrylonitrile butadiene styrene (3D Matter, 2016; Jones et al., 2011). RepRap is an extremely unique printing apparatus, as it is designed to have the capability to automatically to print out a significant amount of its 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 ubiquitous parts and components that are cheap and available worldwide (Jones et al., 2011). The RepRap printer components, blueprints, and parts are also available via open-source to any party, without the need to provide royalty payments for device design or components (Jones et al., 2011). This makes this modular 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, Rodhain, & Barlette, 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, Rodhain, & Barlette, 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.

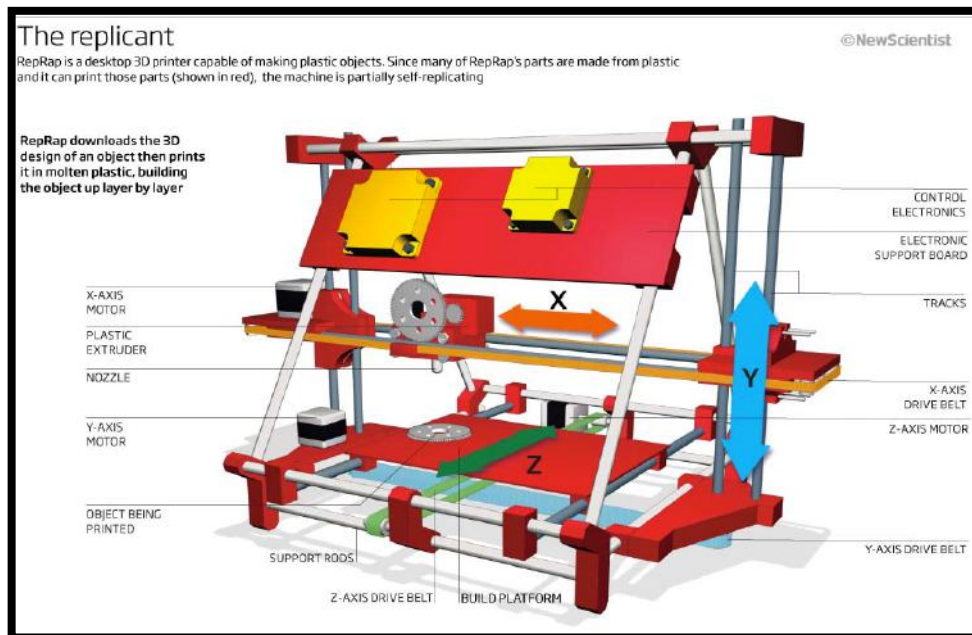


Figure 12. An overview schematic of the RepRap FDM 3D printer design and components (Simonite, 2010)

The RepRap printer consists of only the essential components to create a functioning 3D printer. These components are organized into seven distinct groups based upon the type of component and part for the printer. The first group of parts consists of the threaded rods and aluminum structural frame assembly, shown in Figure 13, which consists of the primary structural frame for the entire apparatus.

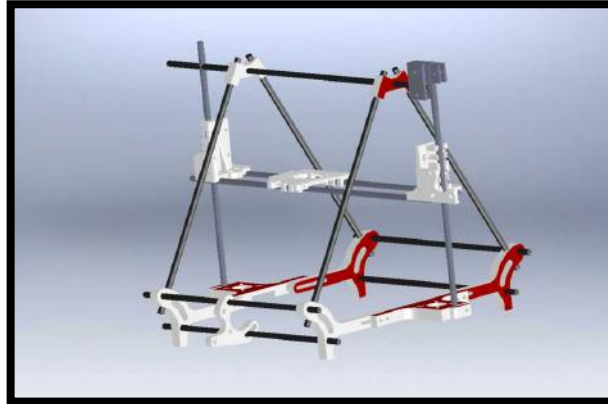


Figure 13. The threaded rod and aluminum frame assembly of the RepRap printing apparatus (Thompson, 2012)

The second group, shown in Figure 14, consists of the self-replicating printed parts that the device can fabricate by itself. This group of parts primarily consists of the axial connectors, casings, motor mounts, and platform assembly parts that attached over each of the connection assemblies in order to secure the entire device together.



Figure 14. A list of the self-replicated parts for the RepRap printing apparatus (RepRap Bill of Materials)

The third group of parts, shown in Figure 15, consists of the filament extruder parts, which are all necessary parts to fabricate the extrusion head and nozzle in order to feed the thermoplastic filament through. This includes such parts as the fan assembly, fan duct, extrusion body, and the primary extrusion gears for extrusion mobility.

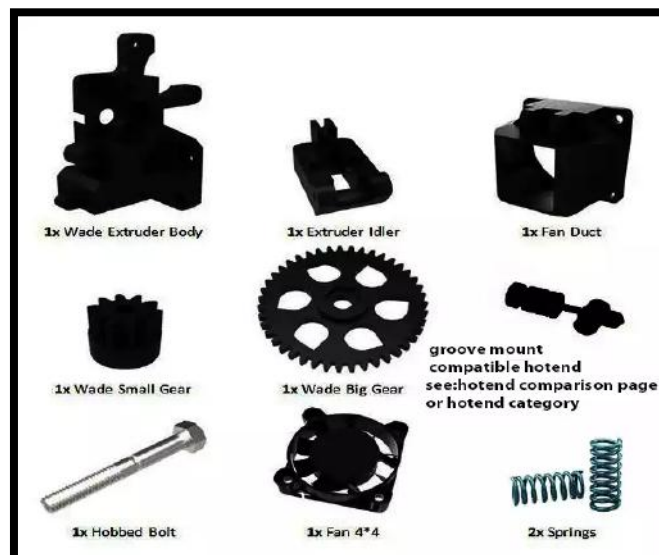


Figure 15. The extruder parts group (RepRap Bill of Materials)

The fourth group of parts consists of the RepRap mechanical parts, shown in Figure 16. This includes the various motors, pulleys, and bearings required for the operation of the RepRap apparatus.



Figure 16. The mechanical parts of the RepRap (RepRap Bill of Materials)

The fifth group of parts consists of the heated build platform components, shown in Figure 17, which consists of the heating transistor and physical build platform for the RepRap apparatus.



Figure 17. Heated build platform parts and components (RepRap Bill of Materials)

The sixth group of parts consists of the electronics, shown in Figure 18, which consists of the AC power supply and the microprocessor chips for programming the RepRap device.



Figure 18. The essential electronic components for the RepRap device (RepRap Bill of Materials)

The seventh and final group of parts consists of the bolts, nuts, and washers, shown in Figure 19, which are needed to assemble the entire printing apparatus.



Figure 19. RepRap assembly materials: bolts, nuts, and washers (RepRap Bill of Materials)

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 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 Figure 20 (Jones et al., 2011). 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 2kg coil reel otherwise known, as a filament spool, containing the 1.75mm thermoplastic filament is loaded in the machine (Jin et al., 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 temperature is also adapted based upon the filament material utilized, but is generally between 50-70°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 0.2mm above the build platform (Rengier et al., 2010). The thermoplastic filament from the 1.75mm filament spool is then fed through a driving motor in the extruder head and fed onto the 10x10 inch build platform as shown in Figure 21 (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.

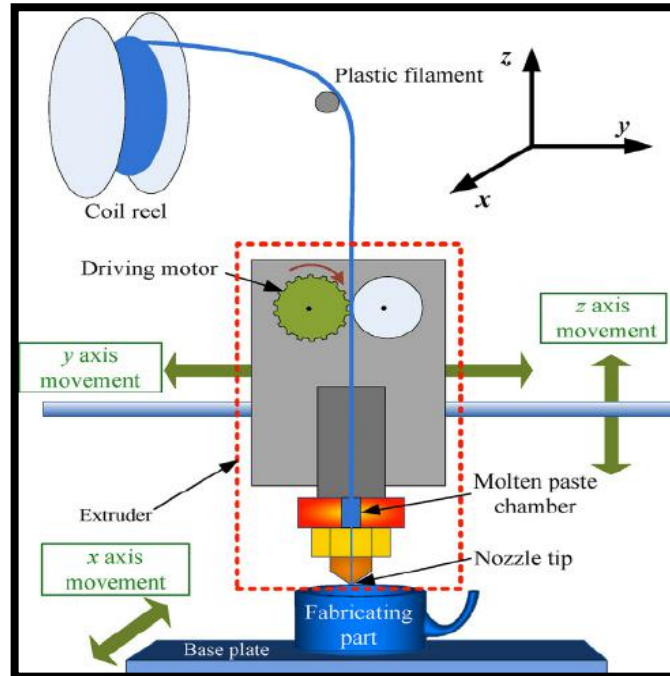


Figure 20. The internal and axial mechanics of RepRap FDM rapid prototyping (Jin et al., 2015)

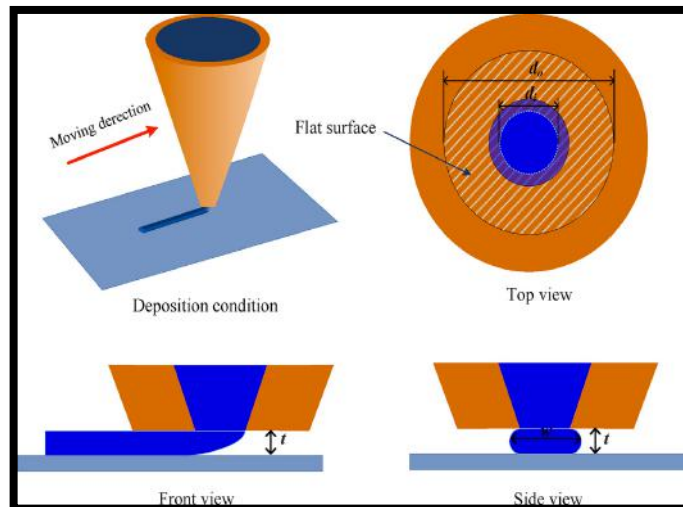


Figure 21. Extrusion nozzle directionality and layering schematic (Jin et al., 2015)

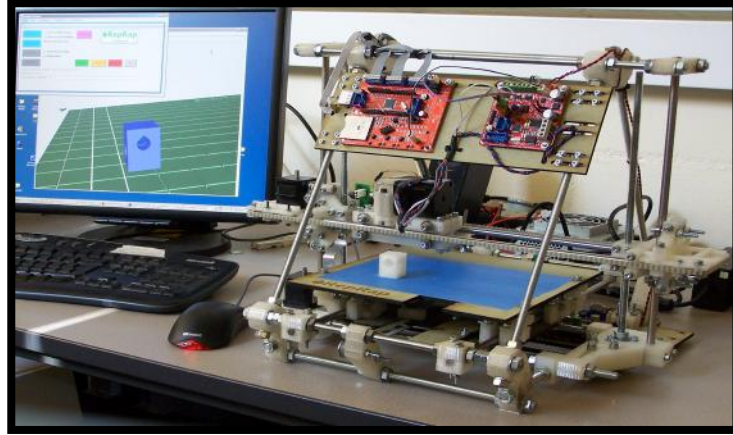


Figure 22. RepRap Version II, a smaller, lighter and simpler printing apparatus with a larger functional build volume and capacity (Jones et al., 2011)

Each year, the RepRap modular apparatus receives new updates to its fabrication methods and manufacturing processes. The most current model available is the Version II series that is more compact and integrates a larger build area than the previous generation as shown in Figure 22 above (Jones et al., 2011). Given this printer's innate flexibility and adaptability, these printers provide the ideal platform for fabricating surgical instruments in LMICs and are vital in stimulating domestic manufacturing initiatives to address medical device shortages in countries around the world. In utilizing these printers to fabricate 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 biocompatibility 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.

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

Research into the field of bio-based polymers specifically those derived from renewable resources have attracted great attention due to the increasing environmental and toxicity concerns associated with traditional petroleum-based polymers such as conventional ABS plastics (Davachi & Kaffashi, 2015; Neches et al., 2014; Zeng, Li, & Du, 2015). Specifically within the fields of medicine, biomedical engineering, and polymer chemistry, an innate push has been fostered to promote biocompatible materials that display the same modular material properties as petroleum-based plastics, but are safe and effective to utilize. 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 CO₂, biopolymers such as

polynucleotides, polyamides, polysaccharides, polyoxoesters, polythioesters, polyanhydrides, polyisoprenoides and polyphenols, as well as their respective derivatives (Sudesh & Iwata, 2008). In order to bioplastics to be utilized in additive manufacturing processes, these bio-based plastic polymers must have thermoplastic qualities.

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). Thermoplastics must be utilized in additive manufacturing, as printers must heat the plastic filament in order to be deposited onto the build platform in an additive fashion.

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, Li, & Du, 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). 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, H₂O and CO₂, are neither toxic nor carcinogenic to the human body, hence making it an excellent material for biomedical applications (Xiao, Wang, Yang, & Gauthier, 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, Wang, Yang, & Gauthier, 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 et al., 2014). PLA is utilized in bioabsorbable fixation devices 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 Figure 23 (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 (Figure 24) and the SR-PLA 96 stent can be used for stenting after ureteral repair (Hodsden, 2015; Pawar et al., 2014).

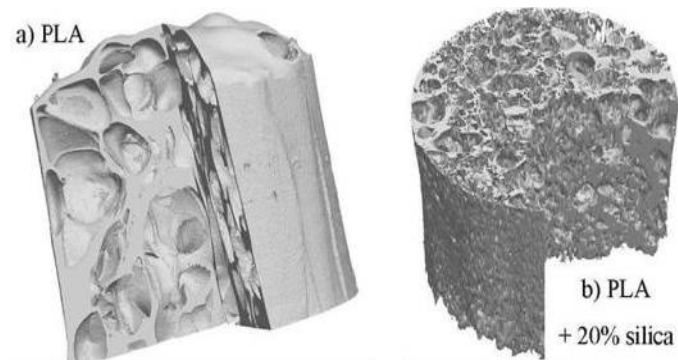


Figure 23. PLA bone tissue engineering scaffold (Tissue Repair, 2016)

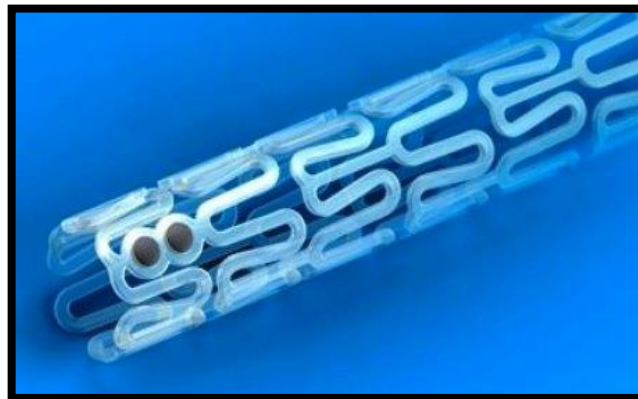


Figure 24. Abbott ABSORB II PLA Bioresorbable Stent (Hodsden, 2015)

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 processability in comparison to other biomaterials such as polyethylene glycol (PEG) or polyhydroxyalkanoates (PHAs) (Xiao, Wang, Yang, & Gauthier, 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 Polymeric Properties: Chemical and Physical Profile

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 et al., 2015). These polymer grades include pure poly-L-lactic acid (PLLA), pure poly-D lactic acid (PDLA), and poly-D, L-lactic acid (PDLLA) (Wang, Yang, & Gauthier, 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 Figure 25 (Xiao, Wang, Yang, & Gauthier, 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, Li, & Du, 2015).

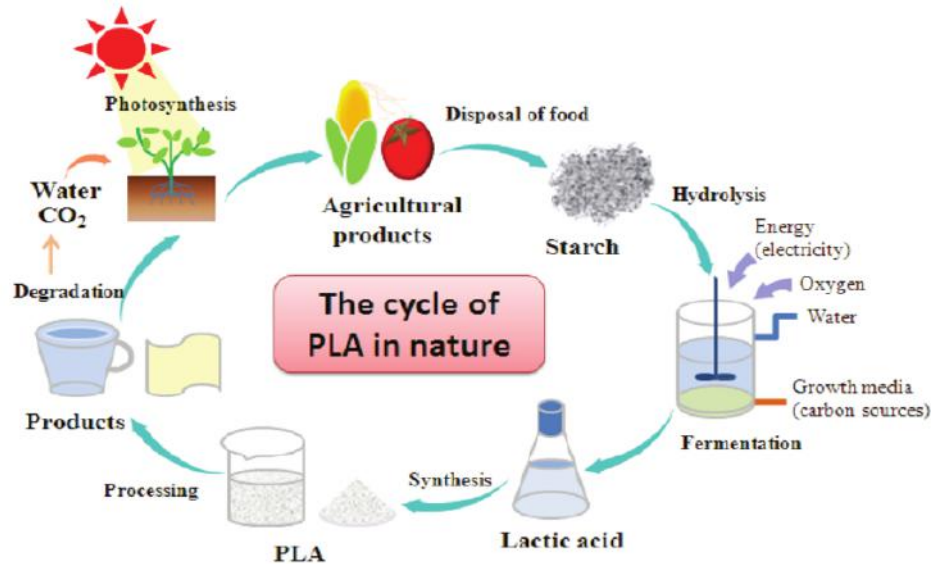


Figure 25. The natural cycle of PLA extraction (Xiao, Wang, Yang, & Gauthier, 2012)

PLA is a chiral polymer similar to lactic acid and contains asymmetric carbon atoms with helical conformation (Xiao, Wang, Yang, & Gauthier, 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, while the syndiotactic polymers contain sequential stereogenic centers of opposite configuration as shown in Figure 26 (Zeng, Li, & Du, 2015). The physical properties including melting temperature, crystallization behaviors, and mechanical properties of PLA depend strongly on its stereo-chemical compositions as shown in Figure 27 (Davachi & Kaffashi, 2015). Depending on the composition of the optically active L- and D-enantiomers, PLA can be crystallized into three distinct forms: α , β , and γ (Davachi & Kaffashi, 2015). The α -structure is more stable and has a melting temperature of 185°C compared to the β -structure, which has a melting temperature of 175°C (Zeng, Li, & Du, 2015). PLA homopolymer 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 additive manufacturing processes has a melting point of approximately 170-180°C due to imperfect crystallites, minor racemization, and various impurities (Zeng, Li, & Du, 2015).

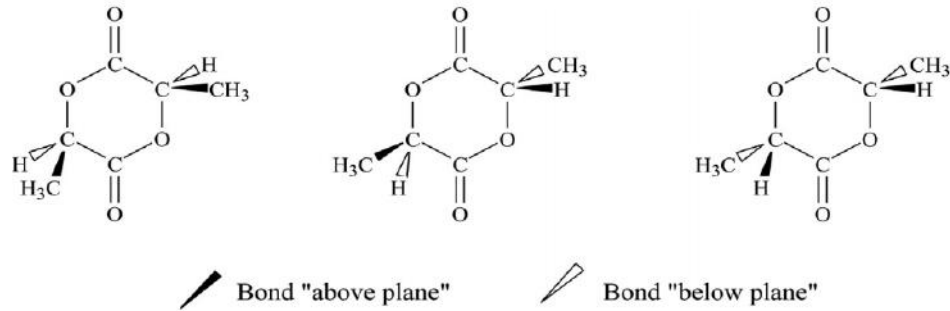


Figure 26. PLA stereo-isomeric conformations (McKeen, 2014)

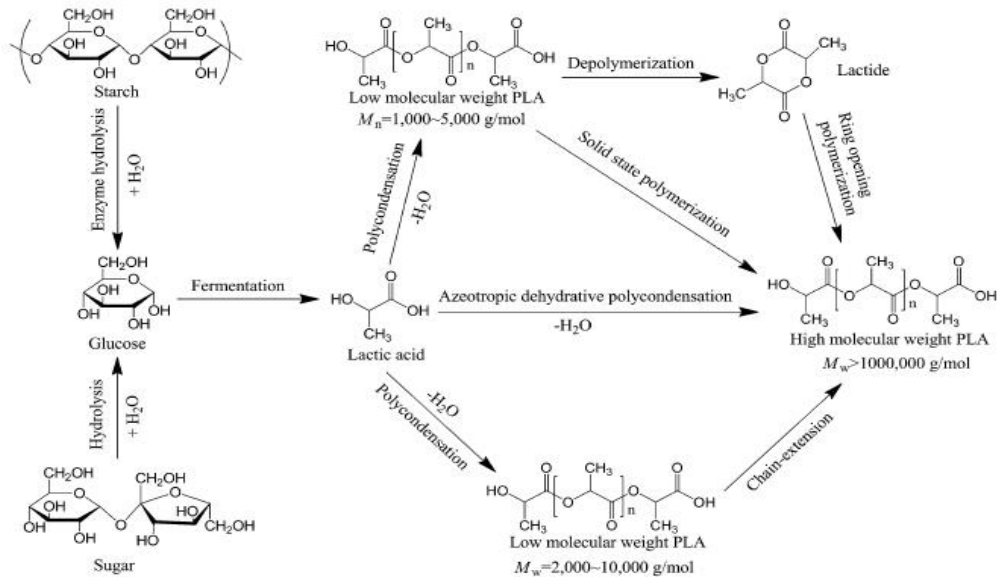


Figure 27. PLA isomeric conformations and molecular constituents (Zeng, Li, & Du, 2015)

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

(Hamad et al., 2015; Modjarrad & Ebnesajjad, 2013). Overall, PLA has above-average mechanical properties including enhanced Young's modulus, tensile strength, and flexural strength compared to traditional polymers, such as Acrylonitrile Butadiene Styrene (ABS), 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, polystyrene, and polyethylene as shown in Figure 28 (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).

Upon acknowledgement of PLA's elongation and high-stress weakness, 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, Li, & Du, 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, Li, & Du, 2015). In addition to chemical copolymerization, recent studies have examined utilizing PLA composite 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 (Zeng, Li, & Du, 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, Li, & Du, 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, Li, & Du, 2015). In addition, natural fibrous blends can be created utilizing natural materials such as bamboo fiber and cellulose (Li, He, & Inoue, 2013; Shih & Huang, 2011). The result of these modified composite blends includes increased thermal stability and mechanical properties of the PLA filament including almost two-times higher tensile and flexural strength (Shih & Huang, 2011). Thus further creation of hybrid blends and reinforcement of PLA filament with natural components such as microcrystalline cellulose can create a high-strength PLA polymer that maintains its ideal bio-based properties (Mathew, Oksman, & Sain, 2005). 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.

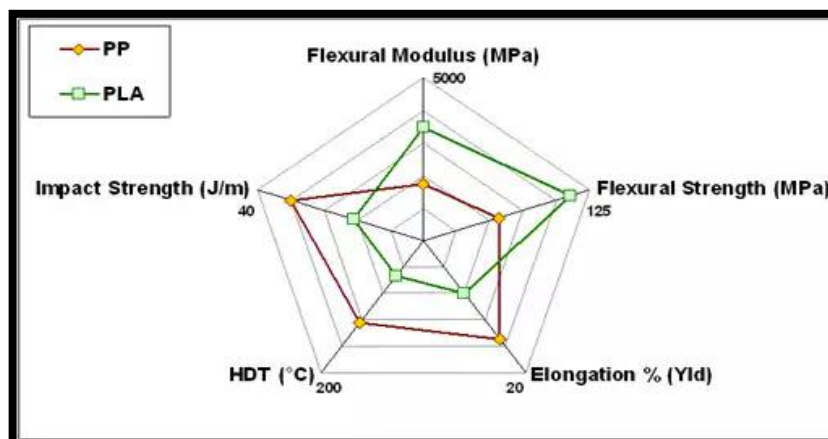


Figure 28. Polypropylene and polylactic acid mechanical comparison schematic
(Biodegradable Plastics and Composites, 2008)

Polylactic Acid vs. 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 integrative surgical toolkit transitions from theory to physical application. A novel component of the IST is 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. 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 bests ABS in 3 of 4 categories including compressive, flexural, and tensile strength, but is weak in overall impact strength as shown in Figure 29 below.

Impact (Un-notched IZOD)				Compressive Strength			
ASTM D256				ASTM D695			
PLA		ABS		PLA		ABS	
STD	1.8	5.7	STD	STD	2600	1100	STD
MAX	4.1	6.2	MAX	MAX	13600	7100	MAX
Impact Strength in ft-lb/in				Peak Stress in PSI			
Flexural Strength				Tensile Strength			
ASTM D790				ASTM D638 Type IV			
PLA		ABS		PLA		ABS	
STD	8970	5344	STD	STD	6783	4936	STD
MAX	13731	8646	MAX	MAX	9531	5532	MAX
Peak Stress in PSI				Peak Stress in PSI			

Figure 29. Comparative analysis of PLA vs. ABS impact, compressive, flexural, and tensile strength (PLA and ABS Strength Data)

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 leachate from instrument contact with the 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 100nm 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 et al., 2016; Stephens, Azimi, El Orch, & Ramos, 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 Figure 30.

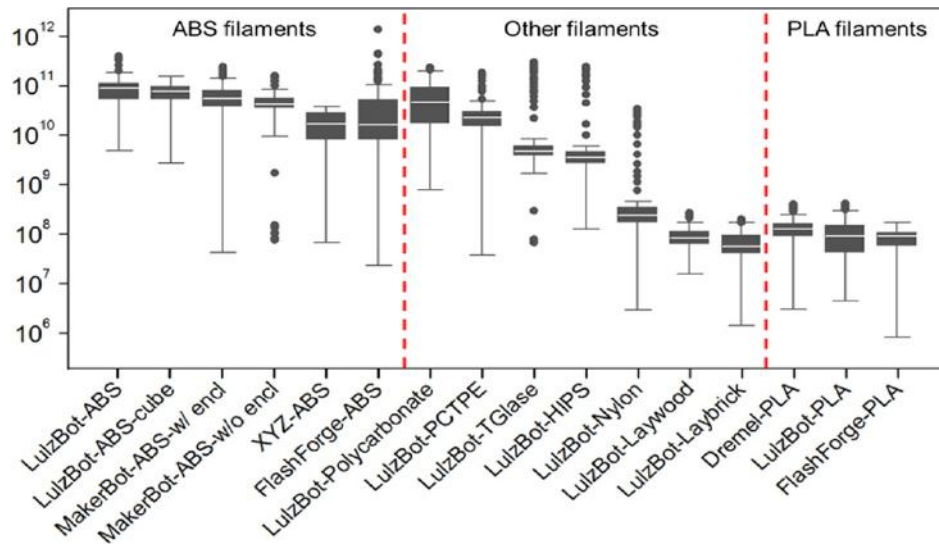


Figure 30. Summary of time-varied UFP emission rates for 16 different 3D printer and filament combinations. Each data point represents data from 1 min intervals, with the combination of data points representing the entire printing period (ranging between 2.5-4 hrs). Boxes show the 25th and 75th percentile 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).

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 31 below summarizes the volatile organic compound emission rates and provides estimates of the individual speculated VOC and Σ VOC emission rates from 16 different 3D printer and filament combinations (Azimi et al., 2016). The top three highest emitted compounds accounted for at least 70% of Σ VOC emissions in all cases, but for most of the printer and filament combinations, a single VOC dominated the Σ VOC 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 $\mu\text{g}/\text{min}$ (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 32 provides a overall comparison module for the total UFP and VOC emission output per mass of filament. According to this graphical depiction, PLA thermoplastic processing produces the least amount of UFPs and VOCs compared to ABS processing, thus providing further quantitative evidence in support of the high-net safety profile of PLA thermoplastic processing for surgical instrument fabrication.

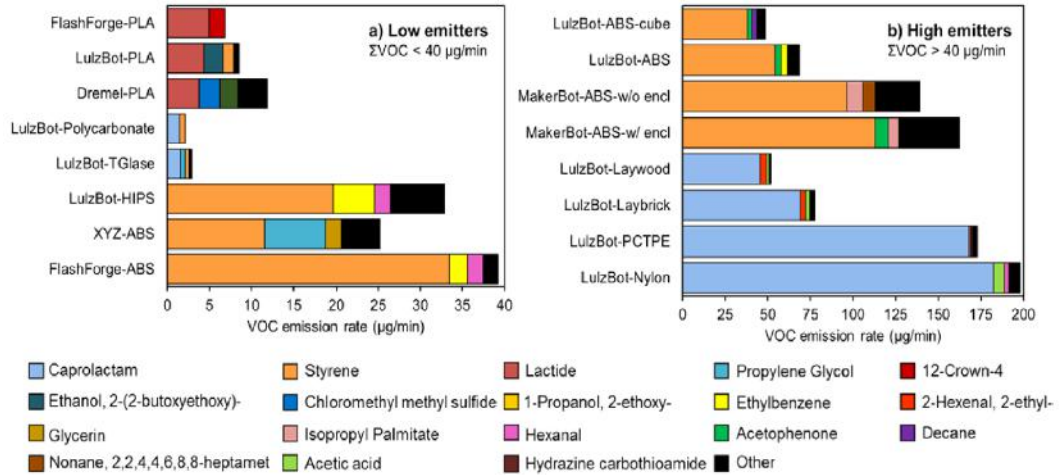


Figure 31. VOC emission rate and the sum of the top 10 detectable VOCs (Σ VOC) resulting from operation of 16 different 3D printer and filament combinations, which is divided into (a) low emitters, with Σ VOC < 40 μ g/min, and (b) high emitters, with Σ VOC > 40 μ g/min (Azimi et al., 2016)

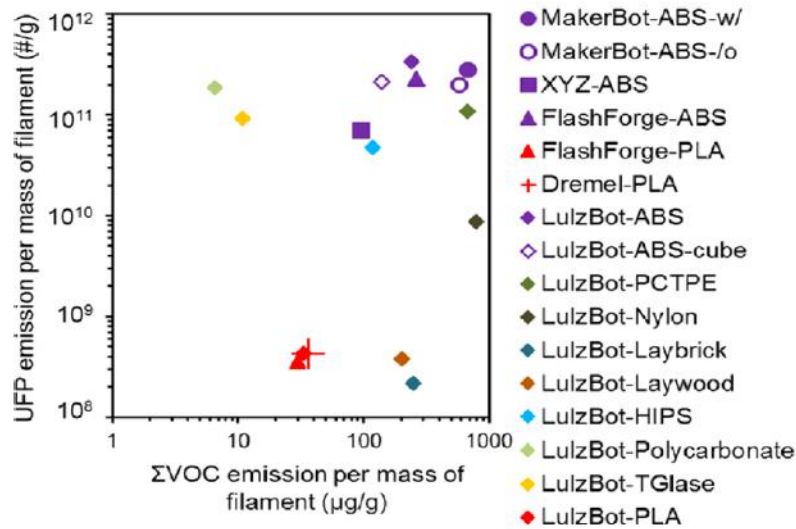


Figure 32. Comparison of total UFP and VOC emissions per mass of filament (Azimi et al., 2016)

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 prominently 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 detrimental environmental effects when not recycled properly. The use of PLA in LMICs is warranted as it presents a focal sustainable shift from non-sustainable petroleum based products such as ABS. 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.

Chapter III

The Integrative Surgical Toolkit

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 a self-contained, mobile integrated kit of essential surgical instruments could provide the basic tools necessary for vital surgical interventions on-site (World Health Organization, 2010). This toolkit, referred to as the “integrative surgical toolkit” or IST, provides a feasible solution to providing direct access to basic surgical instruments. In describing the components of this toolkit, 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.

The IST integrates 12 unique medical instruments/tools, 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 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 is that of handling of obstetrical complications including obstructed labor and hemorrhage (Jamison et al., 2006). The third is that of the surgical management of abdominal and extra-abdominal emergent and life-threatening conditions (Jamison et al., 2006). The fourth is that of 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 these integrative surgical toolkits, there are 12 distinct surgical instruments that have been selected based upon their ability to be 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. These surgical instruments include: Debaquey tissue forceps, scalpel handle, Kelly hemostat, Allis tissue clamp, needle driver, sponge clamp, Adson's toothed forceps, smooth tissue forceps, vascular clamp, Army-Navy general surgical retractor, a Senn retractor, and an umbilical cord clamp. These various instruments are shown in Figures 33, 34, 35, and 36.

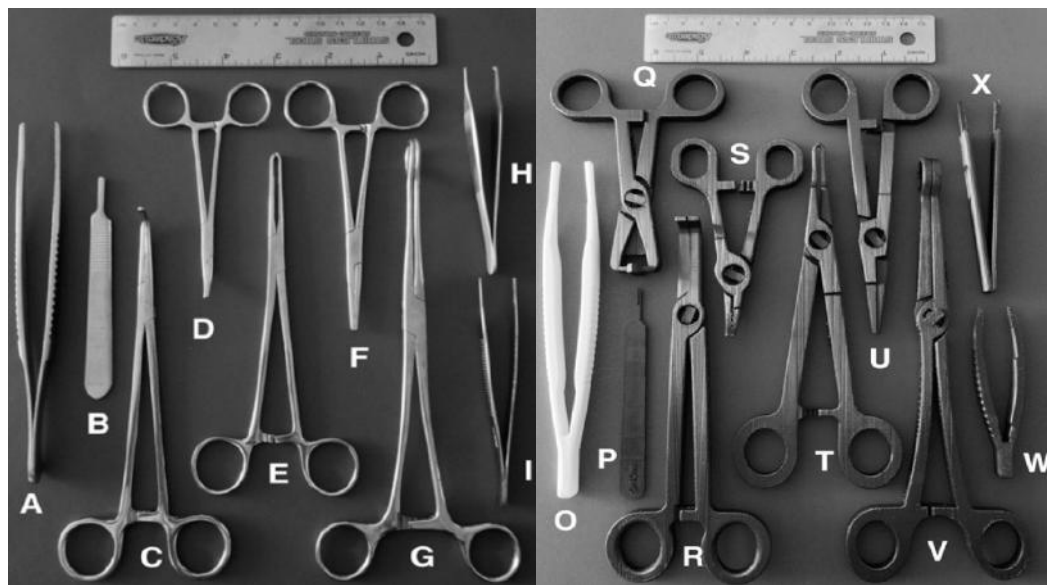


Figure 33. Surgical instrument profile: (Left Side) Stainless steel surgical instruments: A)

Debaquey 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) Debaquey 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)



Figure 34. 3D-printed polylactic acid Army-Navy surgical retractor (Rankin et al., 2014)



Figure 35. 3D-printed acrylonitrile butadiene styrene needle driver (Kondor et al., 2013)



Figure 36. 3D-printed acrylonitrile butadiene styrene umbilical cord clamp (Molitch, 2013)

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 as described in research studies including “On demand additive manufacturing of a basic surgical kit” and “3D printing of surgical instruments for long-duration space missions.” 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 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 37 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.

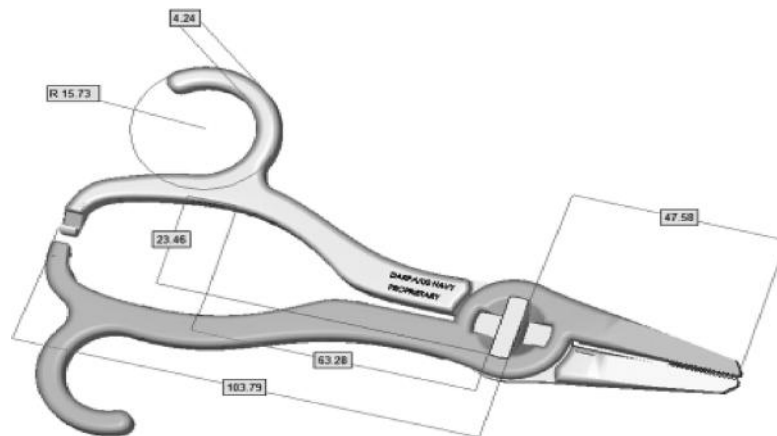


Figure 37. Modified CAD model with driving dimensions and two-piece hinge connection point (Kondor et al., 2013)

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 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% to 30% weaker than other directions, and that the max elongation was halved as shown in Figure 38 (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 Figure 39 as well as the infill pattern/geometry in Figure 40. The infill density refers to the overall amount of thermoplastic deposited within the internal scaffold of the 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 Figure 40 (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 10-20% 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 cross-section 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.

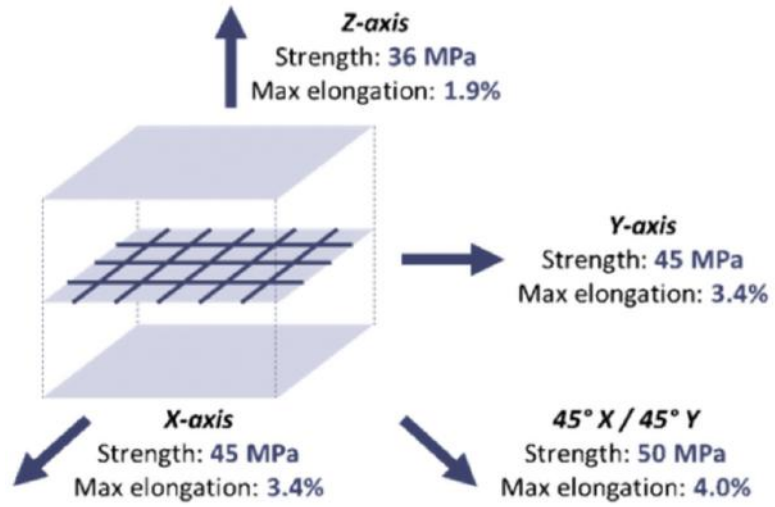


Figure 38. PLA axial mechanical properties (3D Matter, 2016)

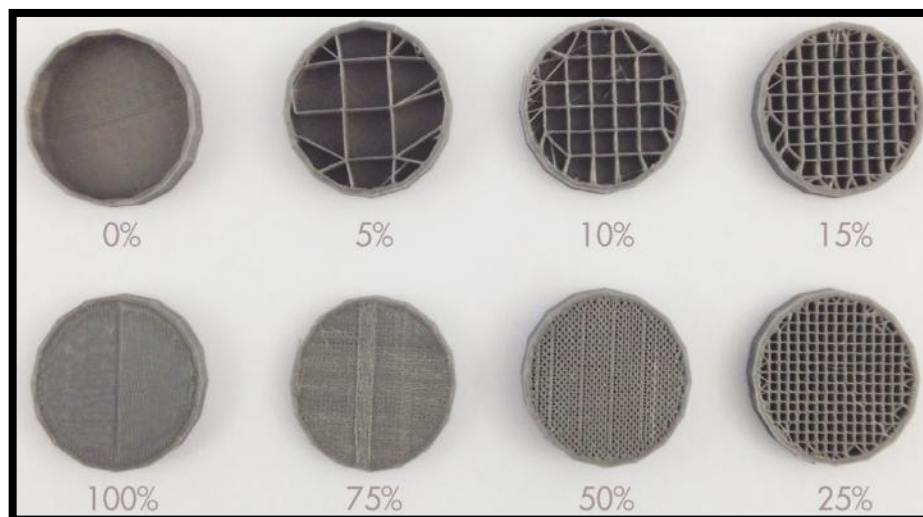


Figure 39. 3D Printer infill density configurations (Budmen, 2013)

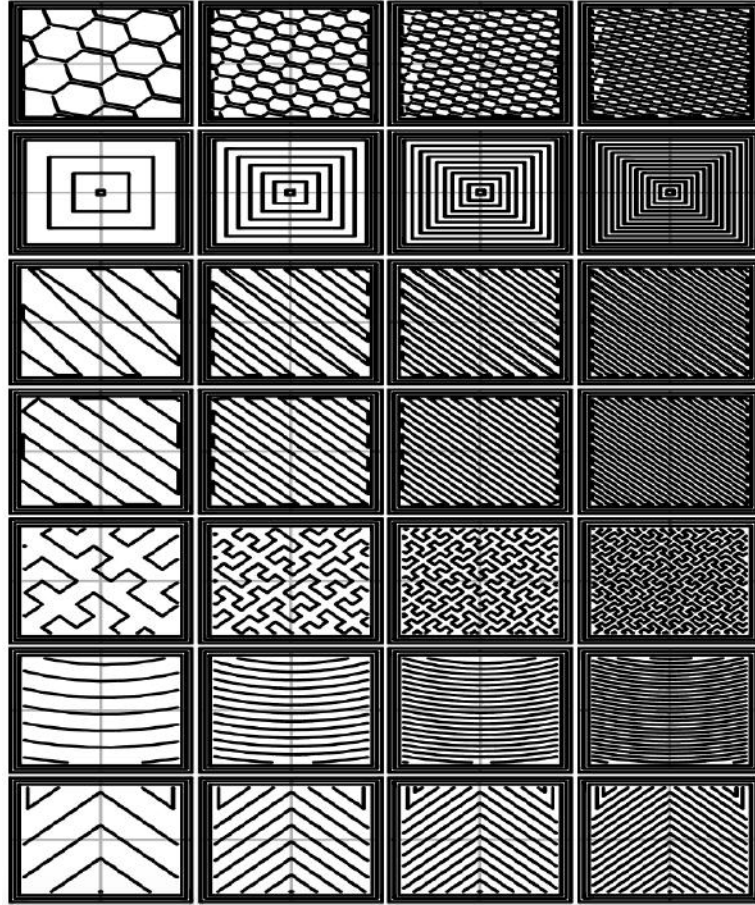


Figure 40. Infill patterns at varying densities. Left to Right: 20%, 40%, 60%, and 80%. Top to Bottom: Honeycomb, Concentric, Line, Rectilinear, Hilbert Curve, Archimedean Chords, and Octagram Spiral (Hodgson, 2016).

After modifying the instruments within the 3D CAD software, a limited run of IST prototypes were then 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. 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 5x5 inch 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 minutes. After fabrication of each surgical instrument, each tool remained on the build platform for approximately 5 minutes 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 an adjusted viewing angle as shown below in Figures 41-52.

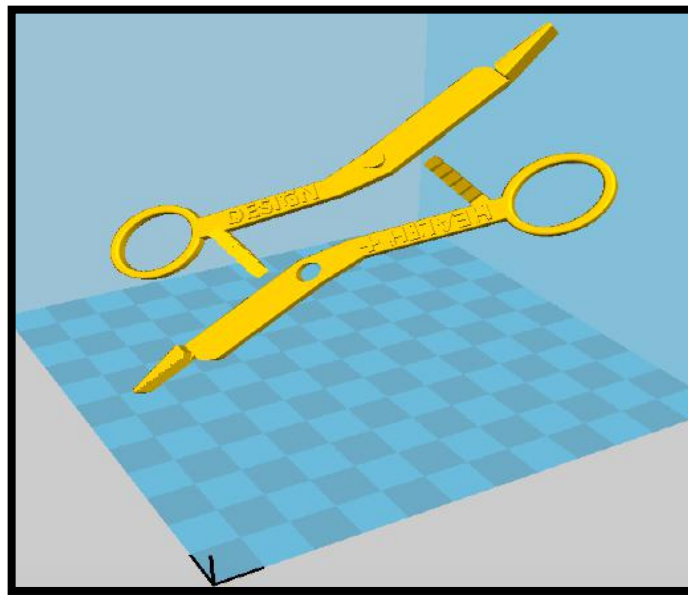


Figure 41. 3D CAD PLA Modified Kelly Hemostat (Pugliese, 2016)

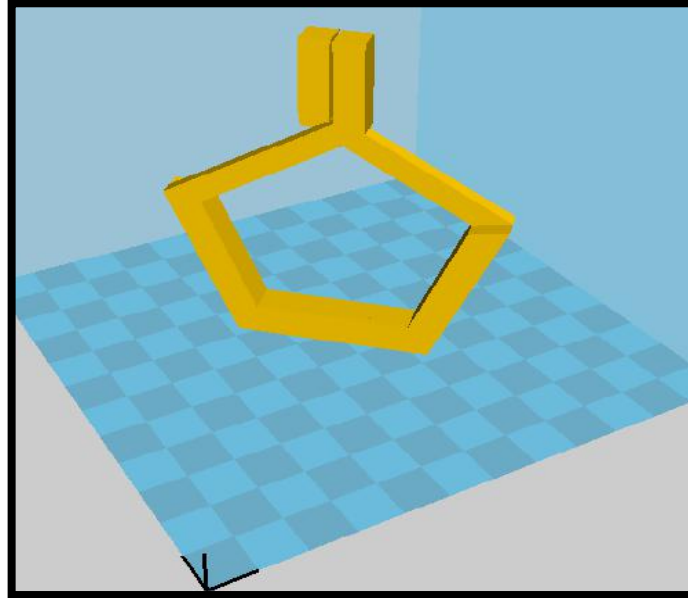


Figure 42. 3D CAD PLA Modified Vascular Clamp (Vascular Clamp, 2013)

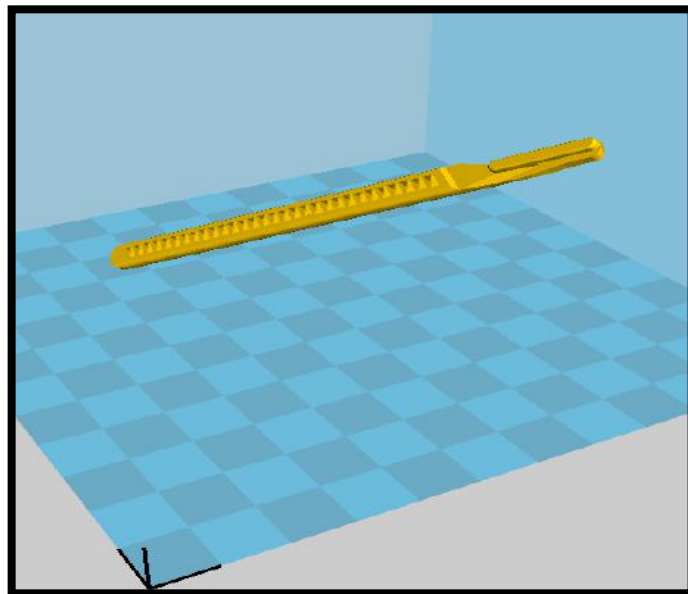


Figure 43. 3D CAD PLA Modified Scalpel Handle (Scalpel Truss Handle, 2016)

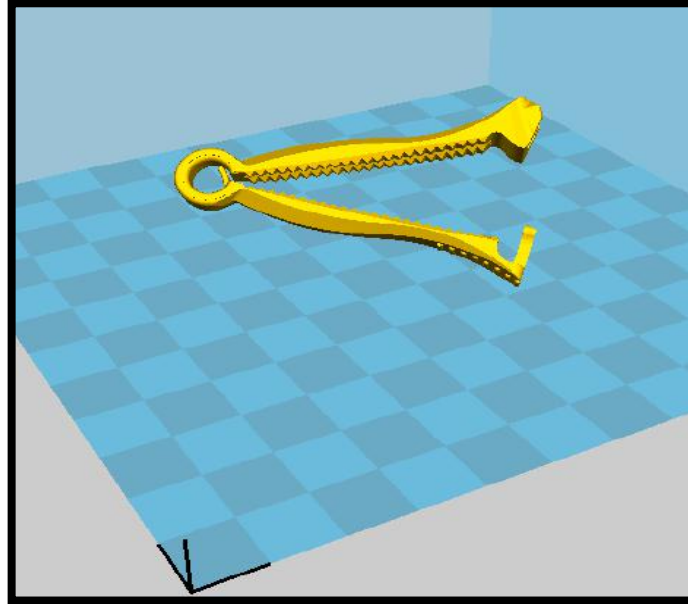


Figure 44. 3D CAD PLA Modified Umbilical Cord Clamp (Umbilical Cord Clamp, 2016)

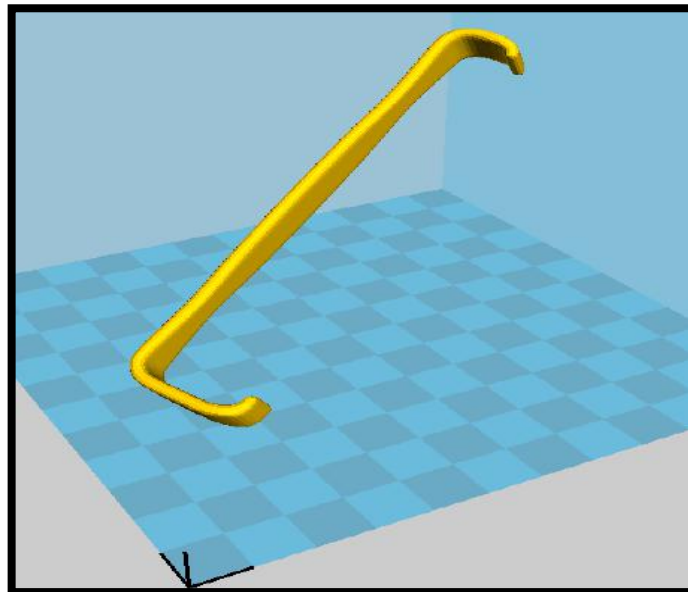


Figure 45. 3D CAD PLA Modified Army-Navy Surgical Retractor (Rankin et al., 2014)

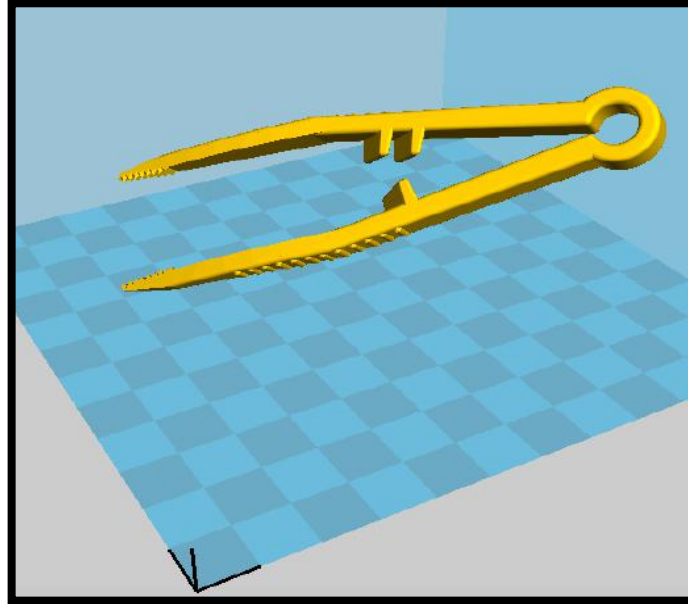


Figure 46. 3D CAD PLA Modified Adson's Toothed Forceps (Toothed Forceps, 2016)

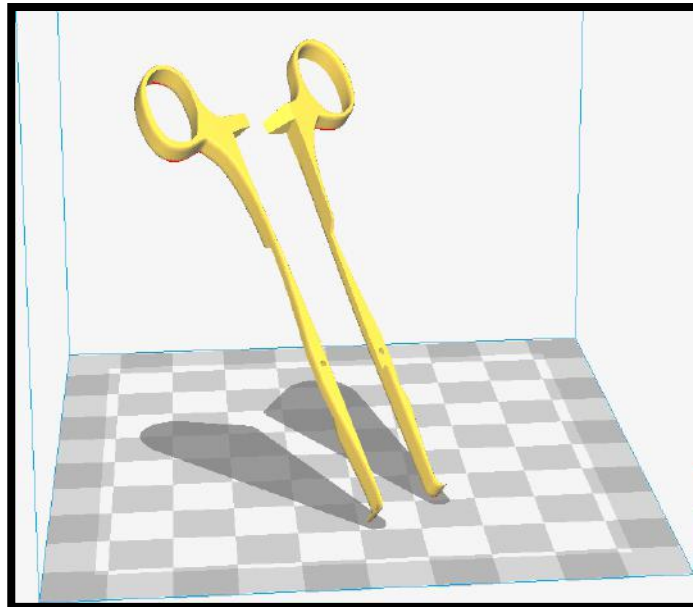


Figure 47. 3D CAD PLA Modified Allis Tissue Clamp/Forceps (Tissue Forceps, 2011)

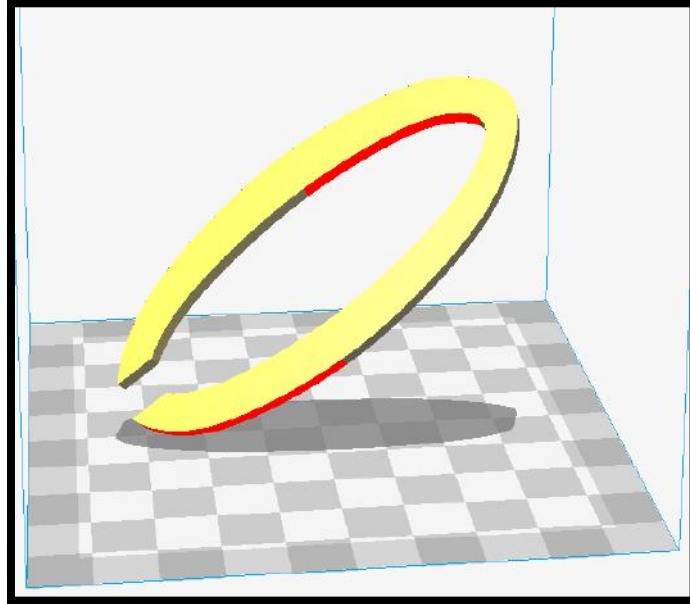


Figure 48. 3D CAD PLA Modified Smooth Tissue Forceps (Forceps, 2012)

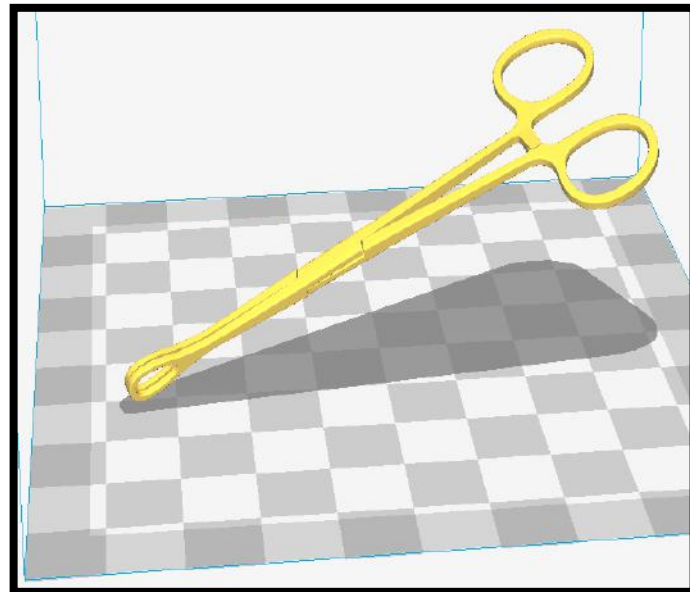


Figure 49. 3D CAD PLA Modified Sponge Clamp (Sponge Forceps, 2012)

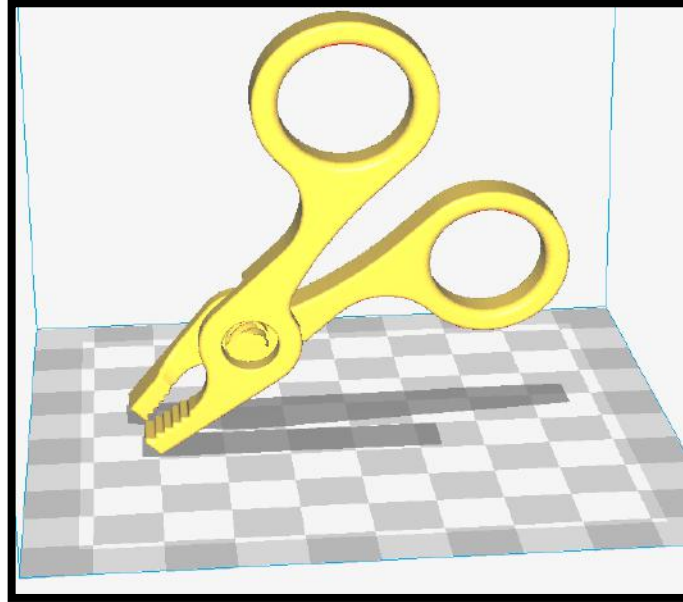


Figure 50. 3D CAD PLA Modified Needle Driver (High Quality Driver/Pliers, 2011)

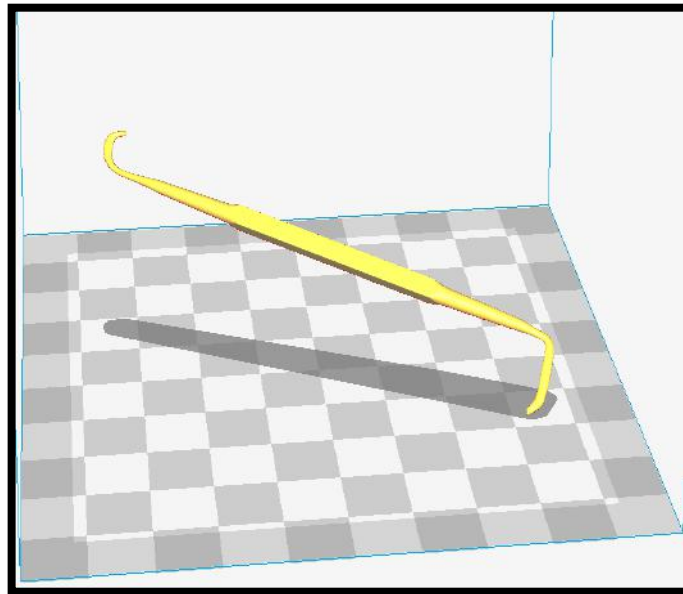


Figure 51. 3D CAD PLA Modified Senn Retractor (Senn Retractor, 2012)

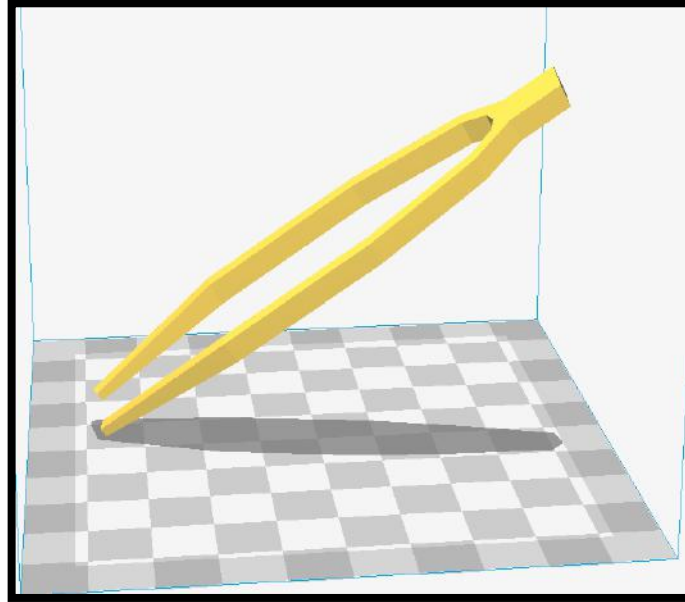


Figure 52. 3D CAD PLA Modified Debaquey Tissue Forceps (Tweezers V2, 2009)

The Integrative Surgical Toolkit: 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 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 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 the PLA integrative surgical toolkit. In particular, this toolkit is 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 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 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, Wang, Yang, & Gauthier, 2013).

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 strength and maintain the same degree of sterility when compared to other chemical sterilants (Athanasίου, Niederauer, & Agrawal, 1996). Glutaraldehyde sterilization entails device submersion in a 2.4% glutaraldehyde solution with a pH of 7.5 for 20 minutes 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 (Athanasίου, Niederauer, & Agrawal, 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 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, Wang, Yang, & Gauthier, 2014; Zeng, Li, & Du, 2015). In addition, PLA displays excellent shelf-life performance and storage capability on par with most petroleum-based plastics (Li, He, & Inoue, 2013). Polylactic acid retains its core materials properties when kept in relatively stable conditions that are free of direct ultraviolet light exposure and humidity (Li, He, & Inoue, 2013). 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.

Chapter IV

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

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

3D Printed Instrument Price Competencies and Barriers to Entry in LMICs

A core tenant behind the use of 3D printing is the ability to fabricate objects at a fraction of the cost of traditional manufacturing methods. This holds true for the fabrication of the integrative surgical toolkit, which can be created at a significant cost savings when compared to the conventional stainless steel instrument kit. 3D printing with PLA is very inexpensive and offers an impressive range of application for many common uses. 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). The RepRap printing apparatus costs approximately \$150.00 and 1kg 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 10-20g, 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. Even if these instruments were utilized as a one-time use, they are still less expensive than the cost of damage or 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 2 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 \$1,000.00 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 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.

Stainless Steel Surgical Instrument	Price (\$USD)	PLA Surgical Instrument	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
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
Umbilical Cord Clamp	\$3.50	Umbilical Cord Clamp	\$0.35
Vascular Clamp	\$427.76	Vascular Clamp	\$0.25
Total Toolkit Cost:	\$1,045.82	Total Toolkit Cost:	\$4.00

Table 2. PLA and stainless steel surgical instrument per-unit and total toolkit cost comparison

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.

Stable infrastructure must be provided or created in LMICs in order for the 3D fabrication process to work. Many LMICs often have poor resource and infrastructure gradients, but these elements are actually ideal for the RepRap 3D printer. The RepRap printer can receive AC 100-240V, 2 amps, and 50-60Hz making it internationally applicable and the power requirements are 24V DC at 6.25 amps, making it compatible with a small gas or hand crank generator, car battery, or solar photovoltaic cell setup (Figure 53), further enhancing the sustainability complex of device implementation (Jones et al., 2011; Wong, 2015).

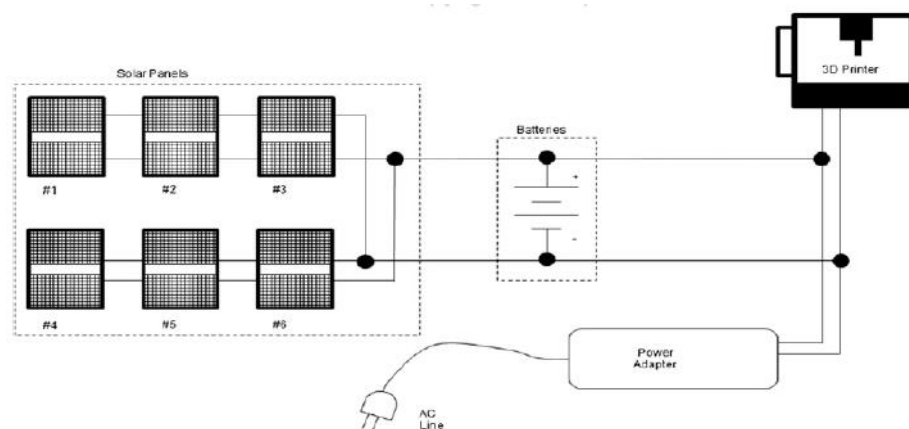


Figure 53. 3D Printer solar panel attachment schematic: six 9V solar panels deliver 27V into a voltage regulator that outputs a constant 24V to charge two lead-acid 12V batteries

(5Ah, 18Ah) in series, which provide the energy storage necessary to deliver the required current to operate a FDM 3D printer (Wong, 2015).

In addition to the minimal power needs of the FDM printing apparatus, access to printing materials including the parts to build the RepRap device, a laptop or computer to download the splicing software, Internet, and access to PLA 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 above, 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, the ideas proposed in this work are indeed extremely fiscally viable compared to other options. 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 more than \$2,000.00 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. The RepRap device has the ability to print over 80% of its 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 the integrative surgical toolkit 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 the Internet and would serve as ideal manufacturing and distribution hubs for these surgical toolkits to more rural hospitals and clinics.

A Paradigm Shift in the Global Medical Device Supply Chain: Manufacturing and Distribution at District-Level Healthcare Facilities

The enhancement of the surgical capacity of district-level healthcare facilities in LMICs is the primary interventional strategy behind the deployment of the integrative surgical toolkit and the RepRap modular printing apparatus. 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 the integrative surgical toolkit 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 Figure 55 (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 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 Figure 54 below (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.

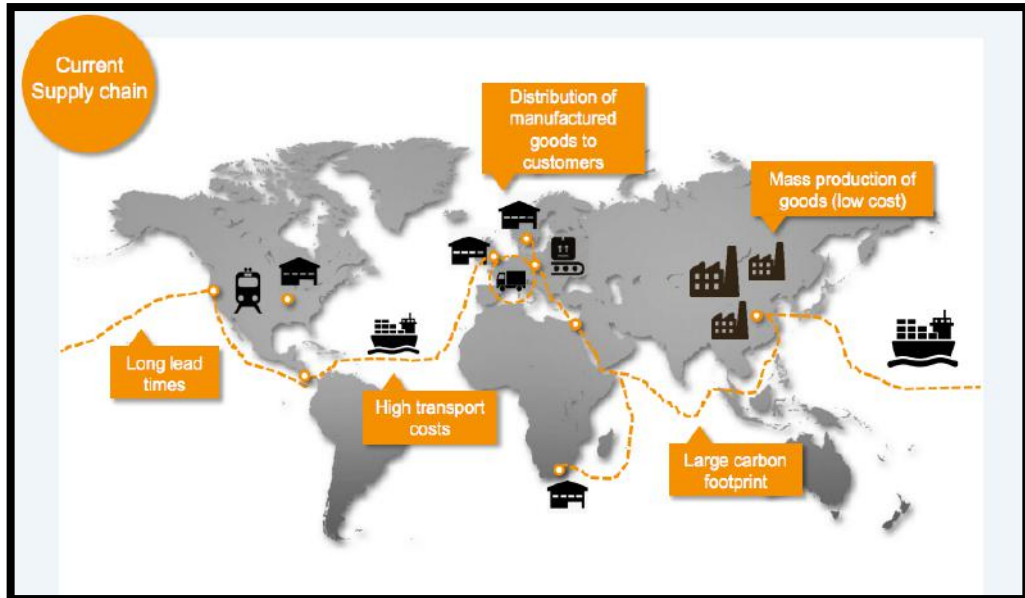


Figure 54. Current global medical device supply chain (Engel, 2014)

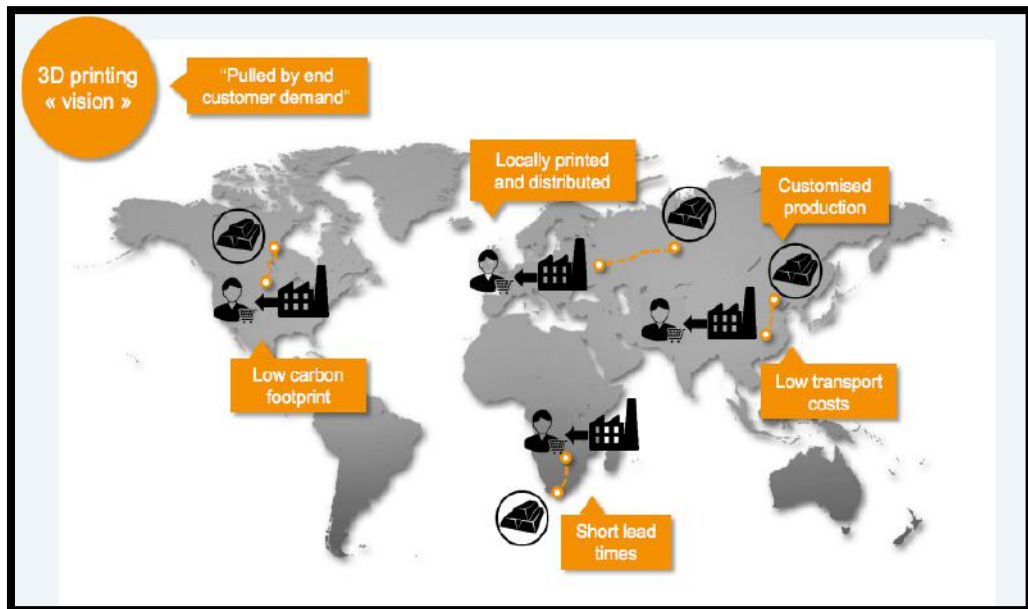


Figure 55. Global medical device supply chain schematic with implementation of 3D printing (Engel, 2014)

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. 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 Figure 56 (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 the integrative surgical toolkit. These facilities often have stable access to infrastructure entities such as electricity and 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 IST 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 \$8.00, thus eliminating fiscal barriers that would prevent distribution of these needed surgical tools to areas that need it most.

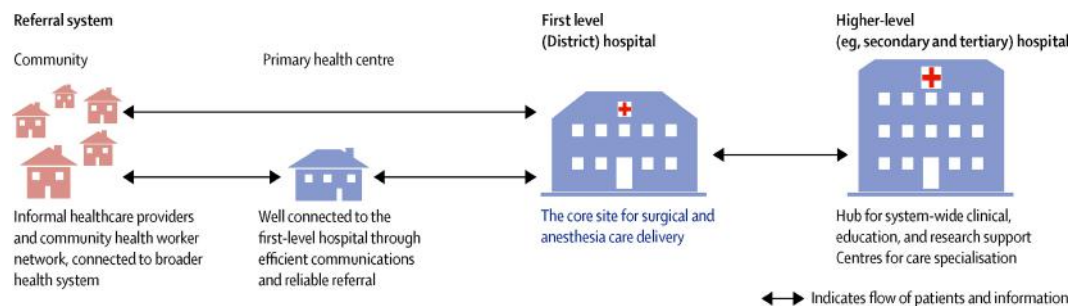


Figure 56. The district-level healthcare facility and its role in surgical care access and delivery (Meara et al., 2015)

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 medical 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 Figure 57 (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.

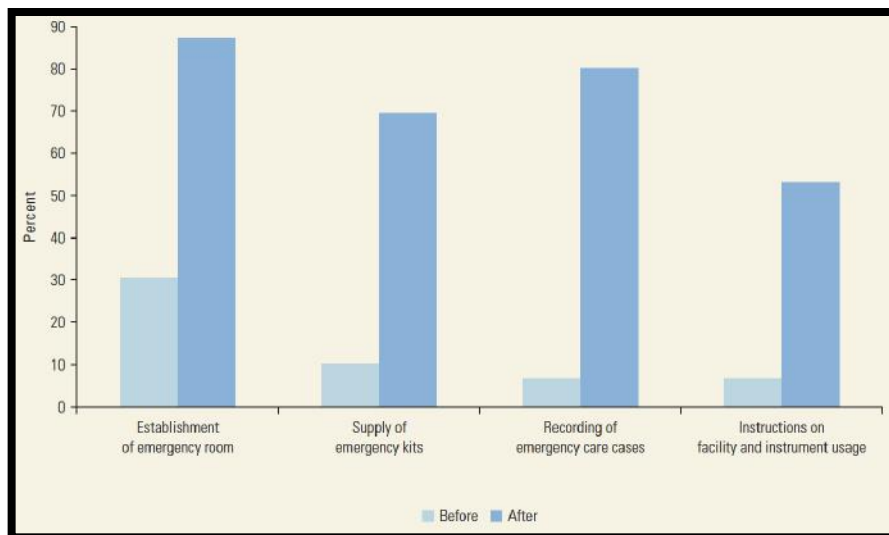


Figure 57. Access to fundamental surgical elements increases surgical output and delivery in LMICs (Henry et al., 2012)

A Discussion: Future Directions and Conclusions

In reflecting upon the multiple dynamics that have been explored over the course of this research, 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 researched are rooted in the functional capacity to reduce the global burden of disease and improve the lives of our fellow man. In answering the core question: “Can 3-dimensional printing of integrative surgical toolkits with Polylactic acid bio-based polymer filaments provide a safe, cost-effective, and interventionally feasible solution to improving surgical access and delivery in LMICs?” we can indeed say that this intervention is feasible and capable of being readily deployed in LMICs to combat the global surgical burden of disease. The utilization of alternative bio-based filaments such as PLA to fabricate the integrative surgical toolkit, 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 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.

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.

The integrative surgical toolkit offers a highly versatile and adaptable surgical instrument 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. 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.

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.

During the course of this research study, a 10-question survey was distributed electronically to 54 individuals via Survey Monkey Inc., an electronic survey delivery interface, as shown in Appendices B and C. Selection criteria for survey correspondents was narrowed down based on education, profession, and experience, in which all surveyors had a minimum 4-year bachelor's degree and experience related to the subject matter. The surveyors were randomly selected based upon this criterion and have diverse professional backgrounds including experience in healthcare, academia, public health, and non-profit agencies. The individuals that agreed to partake in the survey were provided a 1-page synopsis document of the research in order to acquaint them with the material. The surveyors were then asked to answer each one of the 10 questions fully and submit them accordingly, in which each individual was compensated \$1.50 upon completion of the survey. In accordance with the survey and privacy contract guidelines, the identities and employment relations of the individuals surveyed were protected and the surveys were conducted anonymously, with response data analyzed and organized for each question as well as the demographic data that was provided.

There overall feedback with regards to use of 3-dimensional printing and bio-based materials in developing countries was indeed very positive. A large majority of individuals believe that the use of 3D printers and bio-based materials such as PLA hold promise for use in medical device fabrication in the next 5 years. In addition, almost 40% of surveyors stated that the use of sustainable bio-based materials in medical device fabrication was "very important." Surveyors also stated that the greatest obstacle in advancing the use of 3D printers and biomaterials in developing countries is that of

access to financial resources. Over 87% of surveyors agreed that distributing the integrative surgical tool kits from a district level hospital would be the ideal platform and could reduce the associate barriers to entry. Perhaps the most remarkable response was to Question 8 of the survey, which asked: “In assessing the lack of access to adequate surgical care and disparities in surgical capacities in developing countries, do you believe that the creation of “integrative surgical toolkits”, i.e. toolkits that contain multiple types of critical surgical tools, would be beneficial in enhancing the interventional capacities of hospitals and clinics as well as ultimately improve patient outcomes?” Over 90% of individuals surveyed agreed that deployment of ISTs could indeed improve patient outcomes.

It is important to note that while many proponents of this study have been hailed as feasible and innovative, there is indeed a plethora of confounding elements and variables that must be further examined and developed. A core principle of this study was translating 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 PLA 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. The application of 3D printing in LMICs continues to expand and develop each year, in which uses of the technology have been explored in everything from printing critical medical supplies for humanitarian disaster relief in Haiti to printing custom prosthetics and orthotics for amputees in Uganda (Hostetler, 2015). Furthermore, these printing devices have not only been utilized for 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 (Hostetler, 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 (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.

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 surgical burden of disease, characteristically defines who we are as human beings including our innate responsibility to help those that need it most.

Appendix A: Glossary

3-dimensional printing: a process for making a physical object from a three-dimensional digital model, typically by laying down many successive thin layers of a material

Acrylonitrile butadiene styrene: a conventional thermoplastic that is a specific type of plastic polymer made from the fusion of styrene and acrylonitrile with polybutadiene

Additive manufacturing: a process employed by 3D printing apparatuses, by which digital 3D design data is used to build up a component in layers by depositing material

Adson's toothed forceps: a thumb forceps with toothed or serrated tips used to pick up tissue or grasp gauze dressings

Allis tissue clamp: a straight grasping forceps with serrated jaws, used to forcibly grasp or retract tissues or structures

Biocompatible: compatibility with living tissue or a living system by not being toxic, injurious, or physiologically reactive and not causing immunological rejection

Bio-based material: a natural or synthetic material such as a polymer that is suitable for introduction into living tissue especially as part of a medical device

Curved hemostat: a small, straight or curved hemostatic forceps used to hold delicate tissue or compress a bleeding vessel

DALYs: an acronym for Disability Adjusted Life Years, the sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability

Debakey tissue forceps: a type of traumatic tissue forceps used in vascular procedures to avoid tissue damage during manipulation

District-level Healthcare Facility: a core healthcare facility that provides interventional surgical care and anesthesia

WHO EESC: acronym for the World Health Organization Programme for Emergency and Essential Surgical Care

Fused deposition modeling: a process of 3-dimensional printing where materials are distributed in layers in successive additive layers

Integrative surgical toolkit: (IST) a collection of various surgical instruments vital for common interventional surgical procedures

Kelly hemostat: a hemostat without teeth, introduced for gynecologic surgery

LMICs: an acronym for Low and Middle-Income Countries

Needle driver: a sharp instrument used for suturing, for puncturing, or for the guiding of ligatures

Polylactic acid: biodegradable thermoplastic aliphatic polyester derived from renewable resources, such as cornstarch, tapioca roots, starch, or sugarcane

Prototypical supply chain: the sequence of processes involved in the production and distribution of a commodity

Right-angle clamp: a clamp with a short 90° bend to its tip frequently used for dissection or passage of ligatures around vessels

Scalpel handle: a handle that holds a scalpel blade to facilitate use during surgery

Smooth forceps: an instrument that is used to move dressings or remove sutures

Sponge clamp: a clamp attachment for securing a surgical sponge

Straight hemostat: a surgical tool used in many surgical procedures to control bleeding

Army-Navy surgical retractor: a surgical instrument used to hold back organs or the edges of an incision

Tissue forceps: a surgical tool utilized to grasp organs and slippery or dense tissue during surgery

Towel clamp: an instrument used to hold towels or drapes in place on the surgical field

Umbilical cord clamp: a device that holds the umbilical cord in place when being cut

Appendix B: Survey Questions

1. Based on your personal opinion and perspectives, do you believe that medical devices fabricated with natural bio-based materials, such as polylactic acid thermoplastics, will be more widespread across the field of medicine in the future, and if so, when?

- A. Not at all
- B. Presently
- C. 5 years
- D. 10 years
- E. 20+ years

2. Based on your personal opinion and perspectives, do you believe that 3-dimensional printing technologies will be more widespread across the field of medicine in the future, and if so, when?

- A. Not at all
- B. Presently
- C. 5 years
- D. 10 years
- E. 20+ years

3. In using surgical instruments for performing surgical procedures, what qualities do you deem vital for proper instrument functionality in a surgical setting?

- A. Tensile strength and load-bearing ability
- B. Durability and flexibility
- C. Sterility and material inertness
- D. Sustainability and recyclability
- E. All of the above

4. What is the greatest obstacle in advancing the use of bio-based materials and deploying interventions such as 3-dimensional printing in developing countries?

- A. Financial resources and infrastructure
- B. Education and human capital
- C. Research and development
- D. Availability of natural resources
- E. Politics, ethics, and religion

5. Where do bio-based materials best fit in the relevant healthcare needs of developing countries?

- A. Pharmaceuticals
- B. Biomedical devices
- C. Diagnostic testing
- D. Surgical equipment

6. Often times health interventions in developing countries are viewed in the short-term, what long-term barriers do you believe will impact the overall efficacy of these 3D printers in their relevant settings?

- A. Device maintenance and mechanical failure
- B. Lack of continued technician training
- C. Limited supply accessibility to polylactic acid filaments
- D. Errors in printing processes and failure to improve instrument fabrication techniques
- E. All of the above

7. In examining the costs of the components for 3D printing devices to operate (power source, plastic filament, computer/internet, and training of technicians), do you believe that fabricating and distributing surgical instruments at a primary hospital, which has access to medical professionals and stable infrastructure would be a feasible way to reduce barriers to adopting 3D printing technology in developing countries?

- A. Yes
- B. No

8. In assessing the lack of access to adequate surgical care and disparities in surgical capacities in developing countries, do you believe that the creation of “integrative surgical toolkits”, i.e. toolkits that contain multiple types of critical surgical tools, would be beneficial in enhancing the interventional capacities of hospitals and clinics as well as ultimately improve patient outcomes?

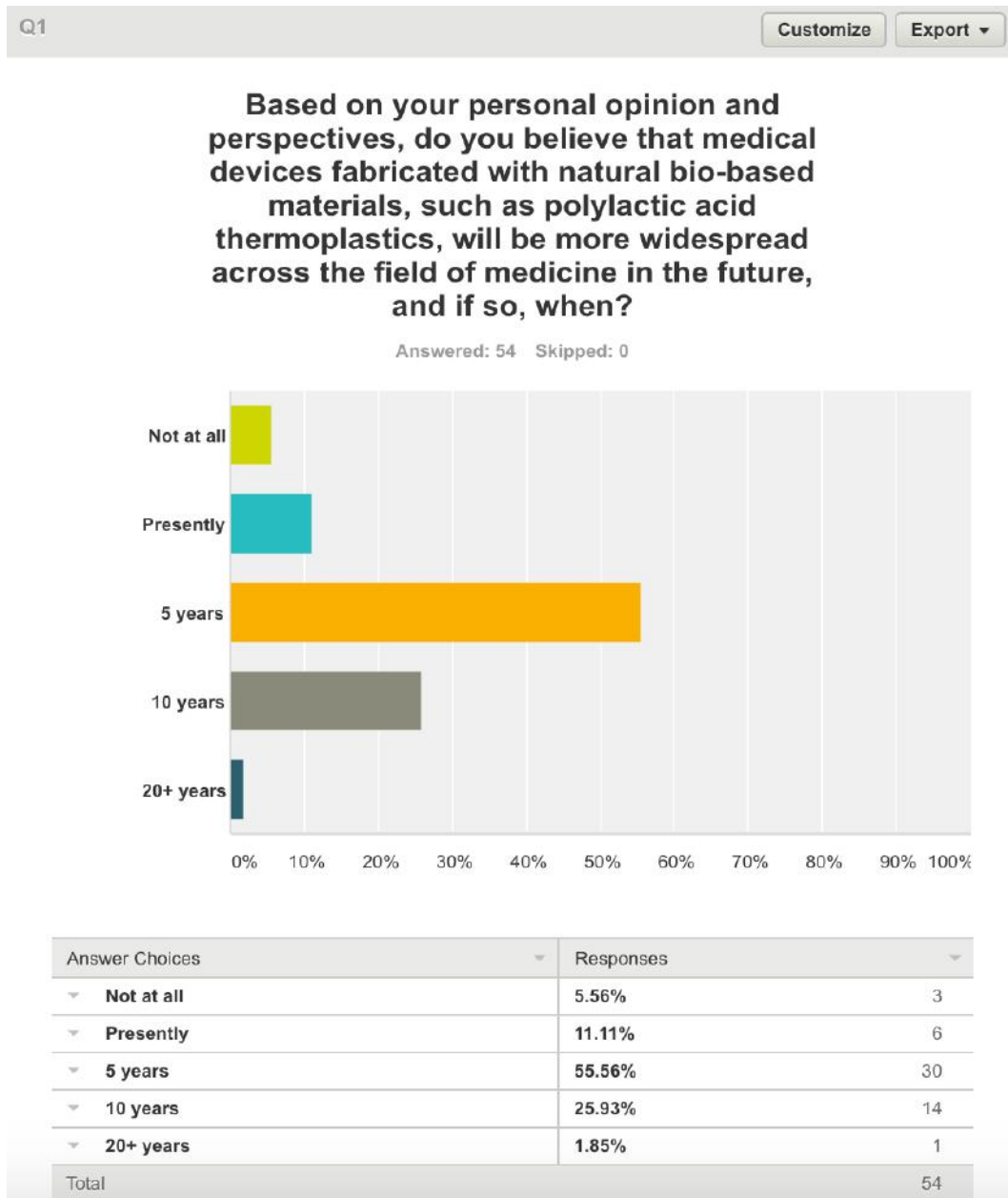
- A. Yes
- B. No

9. On a scale of 1-5, with 1 being “not important” and 5 being “very important”, how important would you rate the use of biocompatible, sustainable, and renewable bio-based materials in the creation of future innovative medical supplies and devices?

- | | | | | |
|---------------|---|---|---|----------------|
| 1 | 2 | 3 | 4 | 5 |
| Not Important | | | | Very Important |

Appendix C: Survey Results

Question 1 (Q1):



Question 2 (Q2):

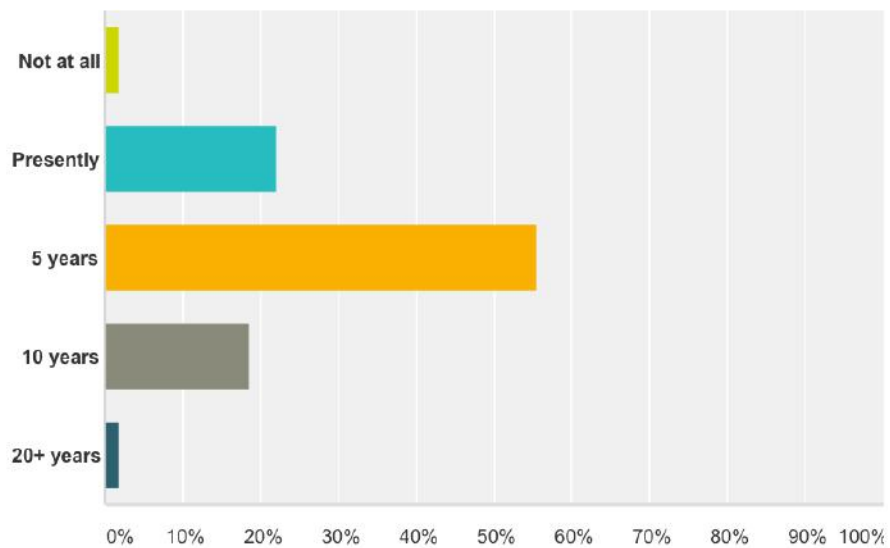
Q2

Customize

Export ▾

Based on your personal opinion and perspectives, do you believe that 3-dimensional printing technologies will be more widespread across the field of medicine in the future, and if so, when?

Answered: 54 Skipped: 0



Answer Choices	Responses
▾ Not at all	1.85% 1
▾ Presently	22.22% 12
▾ 5 years	55.56% 30
▾ 10 years	18.52% 10
▾ 20+ years	1.85% 1
Total	54

Question 3 (3Q):

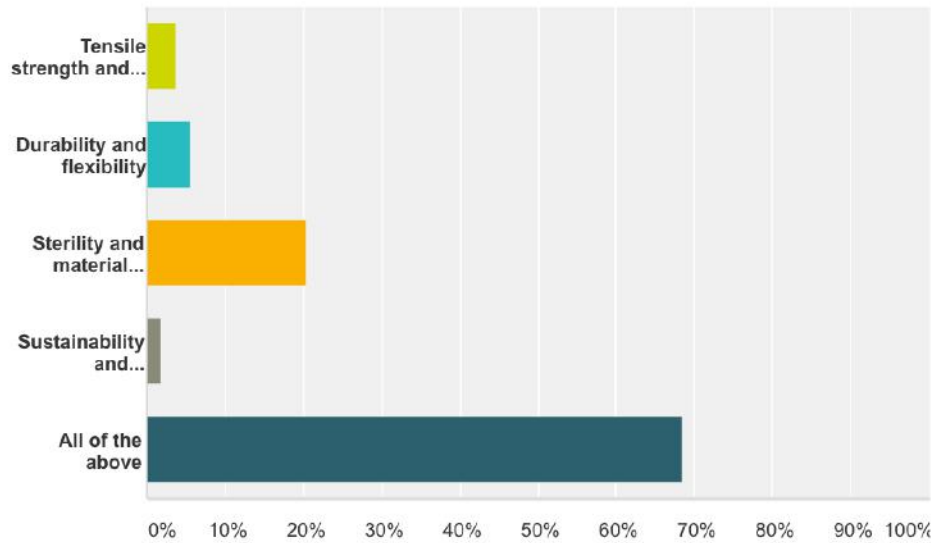
Q3

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In using surgical instruments for performing surgical procedures, what qualities do you deem vital for proper instrument functionality in a surgical setting?

Answered: 54 Skipped: 0



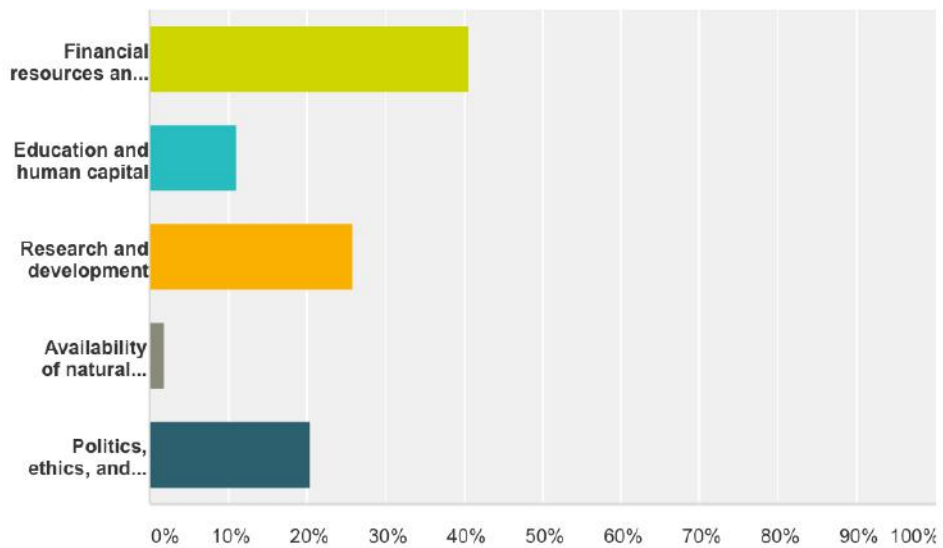
Answer Choices	Responses
▼ Tensile strength and load-bearing ability	3.70% 2
▼ Durability and flexibility	5.56% 3
▼ Sterility and material inertness	20.37% 11
▼ Sustainability and recyclability	1.85% 1
▼ All of the above	68.52% 37
Total	54

Question 4 (Q4):

Q4 Customize Export ▾

What is the greatest obstacle in advancing the use of bio-based materials and deploying interventions such as 3-dimensional printing in developing countries?

Answered: 54 Skipped: 0



Answer Choices	Responses
Financial resources and infrastructure	40.74% 22
Education and human capital	11.11% 6
Research and development	25.93% 14
Availability of natural resources	1.85% 1
Politics, ethics, and religion	20.37% 11
Total	54

Question 5 (Q5):

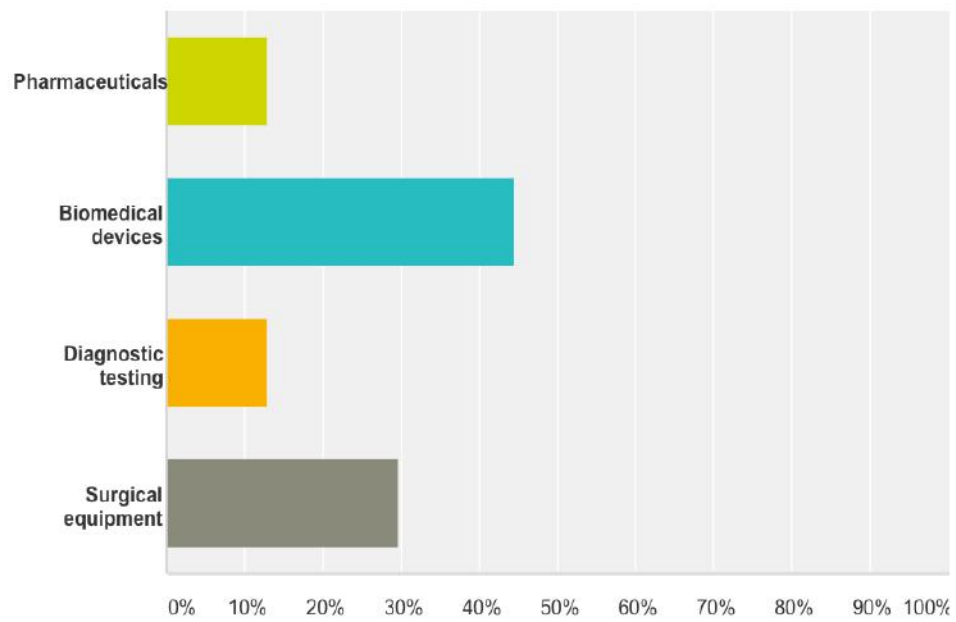
Q5

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Where do biomaterials best fit in the relevant healthcare needs of developing countries?

Answered: 54 Skipped: 0



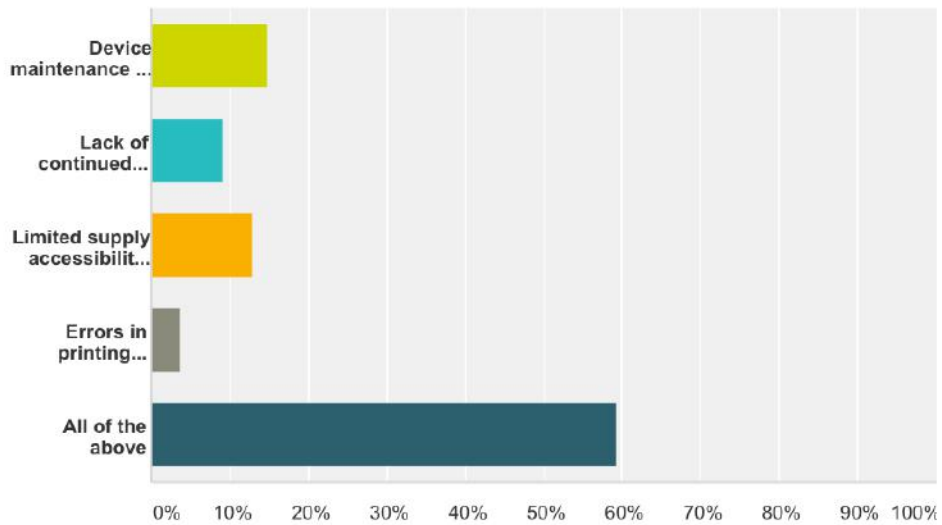
Answer Choices	Responses
▼ Pharmaceuticals	12.96% 7
▼ Biomedical devices	44.44% 24
▼ Diagnostic testing	12.96% 7
▼ Surgical equipment	29.63% 16
Total	54

Question 6 (Q6):

Q6 Customize Export ▾

Often times health interventions in developing countries are viewed in the short-term, what long-term barriers do you believe will impact the overall efficacy of these printers in their relevant settings?

Answered: 54 Skipped: 0



Answer Choices	Responses
Device maintenance and mechanical failure	14.81% 8
Lack of continued technician training	9.26% 5
Limited supply accessibility to polylactic acid filaments	12.96% 7
Errors in printing processes and failure to improve instrument fabrication techniques	3.70% 2
All of the above	59.26% 32
Total	54

Question 7 (Q7):

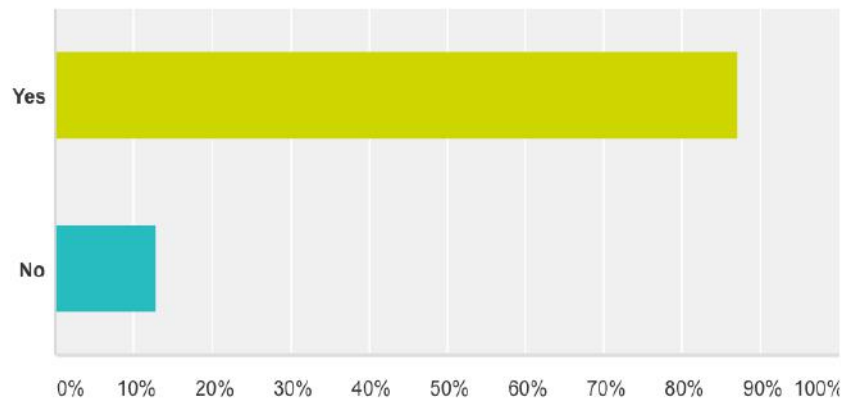
Q7

Customize

Export ▾

In examining the costs of the components for 3D printing devices to operate (power source, plastic filament, computer/internet, and training of technicians), do you believe that fabricating and distributing surgical instruments at a primary hospital, which has access to medical professionals and stable infrastructure would be a feasible way to reduce barriers to adopting 3D printing technology in developing countries?

Answered: 54 Skipped: 0



Answer Choices	Responses	
▾ Yes	87.04%	47
▾ No	12.96%	7
Total		54

Question 8 (Q8):

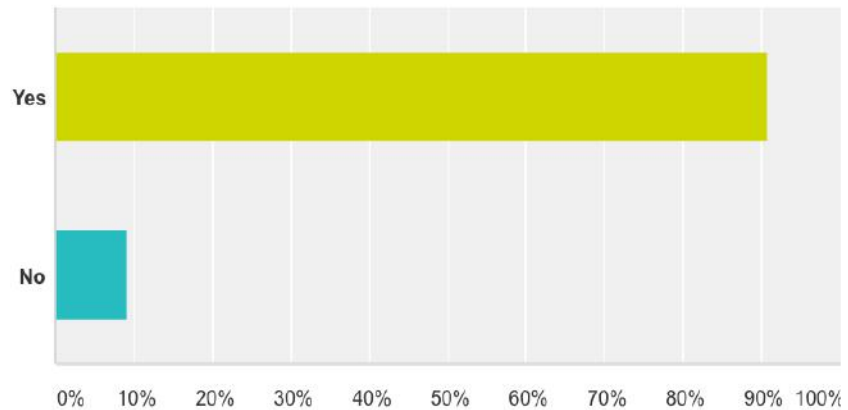
Q8

Customize

Export ▾

In assessing the lack of access to adequate surgical care and disparities in surgical capacities in developing countries, do you believe that the creation of “integrative surgical toolkits”, i.e. toolkits that contain multiple types of critical surgical tools, would be beneficial in enhancing the interventional capacities of hospitals and clinics as well as ultimately improve patient outcomes?

Answered: 54 Skipped: 0



Answer Choices	Responses
▾ Yes	90.74% 49
▾ No	9.26% 5
Total	54

Question 9 (Q9):

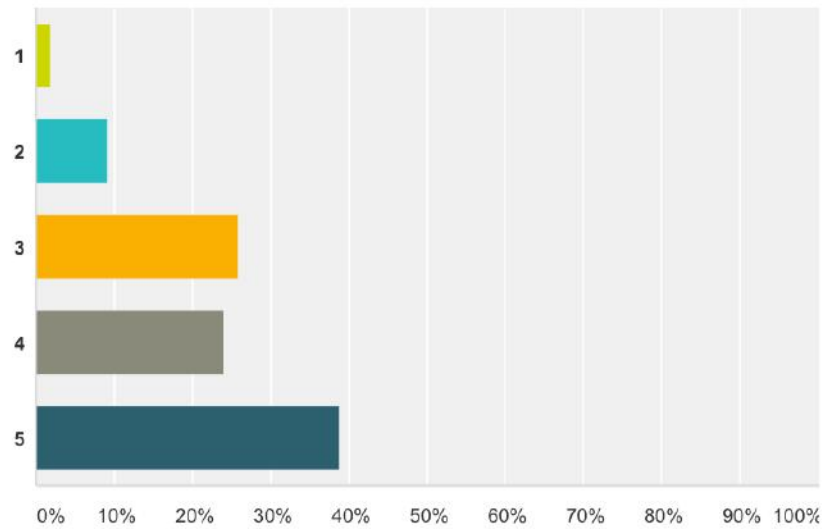
Q9

Customize

Export

On a scale of 1-5, with 1 being "not important" and 5 being "very important", how important would you rate the use of biocompatible, sustainable, and renewable bio-based materials in the creation of future innovative medical supplies and devices?

Answered: 54 Skipped: 0



Answer Choices	Responses
1	1.85% 1
2	9.26% 5
3	25.93% 14
4	24.07% 13
5	38.89% 21
Total	54

Question 10 (Q10):

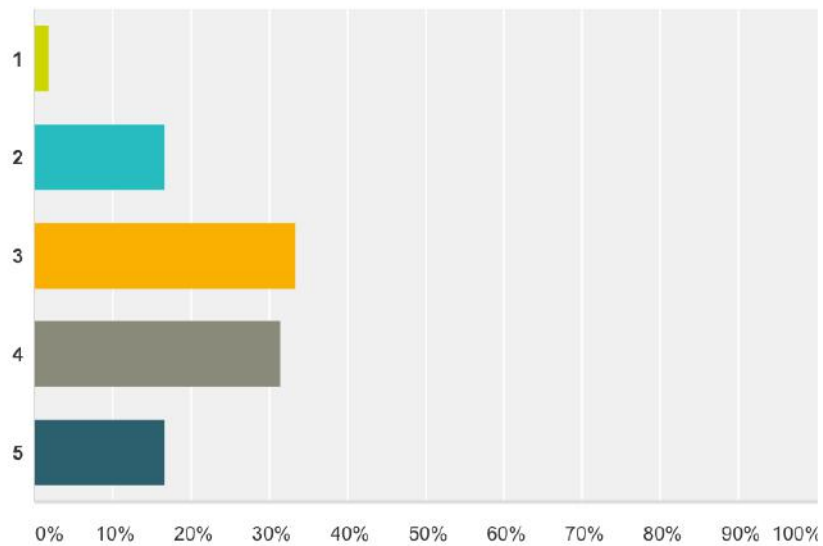
Q10

Customize

Export ▾

On a scale of 1-5, with 1 being "not feasible" and 5 being "very feasible", how feasible do you think the implementation of 3-dimensional printing devices in developing countries would be?

Answered: 54 Skipped: 0



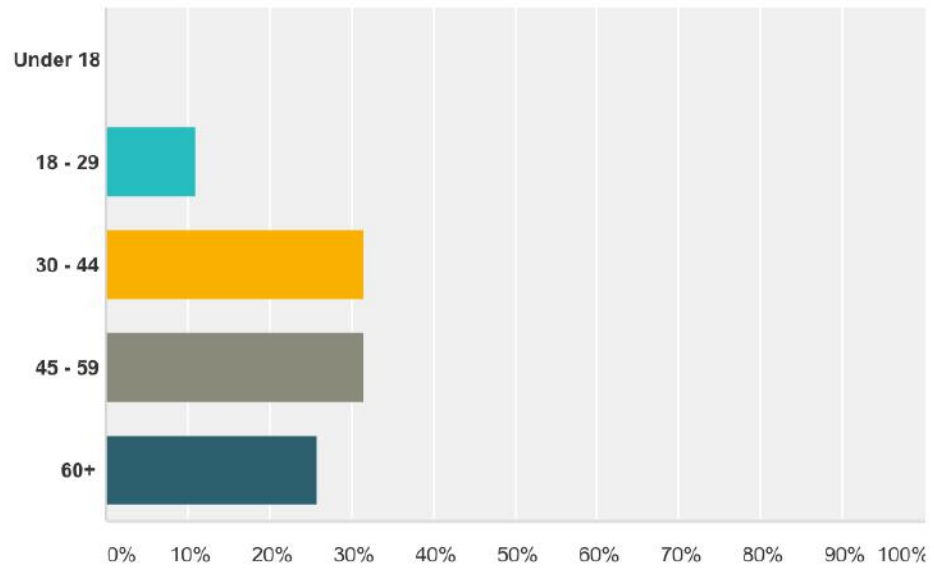
Answer Choices	Responses
1	1.85% 1
2	16.67% 9
3	33.33% 18
4	31.48% 17
5	16.67% 9
Total	54

Question 11 (Q11):

Q11 Customize Export ▾

What is your age?

Answered: 54 Skipped: 0



Answer Choices	Responses
Under 18	0.00% 0
18 - 29	11.11% 6
30 - 44	31.48% 17
45 - 59	31.48% 17
60+	25.93% 14
Total	54

Question 12 (Q12):

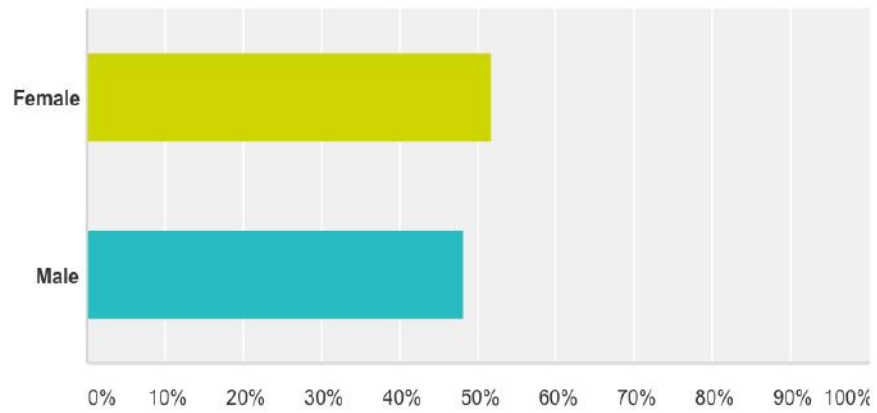
Q12

Customize

Export ▾

What is your gender?

Answered: 54 Skipped: 0



Answer Choices	Responses
Female	51.85% 28
Male	48.15% 26
Total	54

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