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Environmental Impact for 3D Bone Tissue Engineering Scaffolds Life Cycle: An Assessment

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Abstract: With the development of additive manufacturing technology, 3D bone tissue engineering scaffolds have evolved. Bone tissue engineering is one of the techniques for repairing bone abnormalities caused by a variety of circumstances, such as injuries or the need to support damaged sections. Many bits of research have gone towards developing 3D bone tissue engineering scaffolds all across the world. The assessment of the environmental impact, on the other hand, has received less attention. As a result, the focus of this study is on developing a life cycle assessment (LCA) model for 3D bone tissue engineering scaffolds and evaluating potential environmental impacts. One of the methodologies to evaluating a complete environmental impact assessment is life cycle assessment (LCA). The cradle-to-grave method will be used in this study, and GaBi software was used to create the analysis for this study. Previous research on 3D bone tissue engineering fabrication employing poly(ethylene glycol) diacrylate (PEGDA) soaked in dimethyl sulfoxide (DMSO), and diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide (TPO) as a photoinitiator will be reviewed. Meanwhile, digital light processing (DLP) 3D printing is employed as the production technique. The GaBi program and the LCA model developed to highlight the potential environmental impact. This study shows how the input and output of LCA of 3D bone tissue engineering scaffolds might contribute to environmental issues such as air, freshwater, saltwater, and industrial soil emissions. The emission contributing to potential environmental impacts comes from life cycle input, electricity and transportation consumption, manufacturing process, and material resources. The results from this research can be used as an indicator for the researcher to take the impact of the development of 3D bone tissue engineering on the environment seriously.

Keywords: life cycle assessment; 3D printing; bone tissue engineering scaffolds; GaBi software.

1. Introduction

One of the strategies for assessing environmental effects is life cycle assessment (LCA). LCA was created to assess a product's environmental performance in order to establish its current state and allow for future improvements [1]. LCA is a tool for assessing the potential environmental elements and prospective aspects connected with a product or service, according to ISO 14040:2006. It is accomplished by generating a list of inputs and outputs, comparing prospective environmental impacts to those of inputs and outputs, and interpreting the results in light of the study's objectives [2].

Tissue engineering has developed in an attempt to develop biological alternatives that can be used to restore, replace, or regenerate damaged tissues. Tissue development is critical for controlling biological activities. Tissue engineering relies heavily on cells, scaffolds, and growth-stimulating signals. Typically, the scaffold is constructed of polymeric biomaterials that offer structural support for cell adhesion and subsequent tissue growth [3]. Since scaffold provides structural support for cells, the design properties are the key factor in bone tissue engineering and represent more than just a passive component. It will control cell and tissues growth by balancing mechanical function [4]. The regeneration of bone is complex, as it involves a number of molecular, cellular, metabolic, and mechanical stimuli, according to prior study. Appropriate macro and microstructures are crucial elements that can stimulate cell penetration, gas movement, and nutrient absorption [5]. Bone tissue engineering can also be used to repair bone abnormalities caused by a variety of factors. Seed cells, growth factors, and scaffold materials are the three primary components for bone tissue creation and regeneration *in vivo* and *in vitro* [6]. Artificial tissue or implants that create a 3D environment resemble the natural bone extracellular matrix (ECM) to encourage cell adhesion, proliferation, differentiation, and appropriate physical and mechanical qualities for new tissue regeneration are also known as biomaterials [7]. There are many different types of ECM in human tissues within each set of components and structure. As a result, the optimal scaffold for tissue engineering should be the native ECM of the target tissue, which can provide functions and features in terms of structures, tissue compatibility, bioactivity, and mechanical properties [3].

The 3D bone tissue engineering scaffold is one of the most cutting-edge technologies for repairing bone abnormalities caused by various factors. Since the tissue engineering concept was first suggested, bone tissue engineering has been evolving rapidly. A case study outlines a few different material-binder system combinations for 3D printed bone scaffolds [8]. The development of 3D bone scaffolds involves the stage of material selection and manufacturing process that contribute to environmental exposure from energy consumption and emission to land, water, and air. Although careful measures in 3D printing have mostly focused on its energy performance, the product's environmental performance should improve at various points throughout the life cycle of the purposed tissue engineering scaffold [9]. Additive manufacturing provides opportunities to improve resource efficiency through technical approaches [10] and is approved by another researcher [11]. Also, previous studies focused on various materials used in 3D printing, from synthetic and natural polymers to ceramics and composites ink solutions [4,12]. Materials applied for fabrication of 3D bone tissue engineering consists of non-hydrogel based polymers, natural or synthetic hydrogels, and bio-ceramic powders as raw materials to formulate composite inks together with biodegradable and biocompatible polyesters such as poly (L-lactic acid) (PLLA), poly (vinyl alcohol) (PVA), poly-β-hydroxybutyrate (PHB), polyurethane elastomers, poly (D,L- lactic acid) (PDLLA), and polyurethane can be processed into wires, pellets, and powders as material extrusion for 3D process [5,13]. Previous research conducted to prepare scaffolds consists of a hydroxyl functionalized polyester pHM(GCL or poly(ε-caprolactone) (PCL) meet the specification for scaffolds in bone tissue engineering applications [14]. The most used synthetic polymers in fabrication of bone tissue engineering found was polycaprolactone (PCL) as PCL contains relevant properties such as viscoelastic properties, thermal stability long term biodegradability and easier to process due to low melting temperature (~58-60°C) [15]. 3D bone tissue engineering researches have various additive manufacturing technologies as the main manufacturing process to fabricate the scaffolds. It can be classified into stereolitography

(SLA), selective laser sintering (SLS), electron beam melting, extrusion based melting and ink based technologies [16, 17]. Majority of earlier studies focused on 3D printing as a method for fabricating bone tissue engineering. However, the study did not focus the process's environmental consequences, and there was little research on the product life cycle's environmental impacts on 3D bone tissue manufacturing scaffolds. As a result, this study proposes to use GaBi software to create an LCA model to analyse the environmental implications of 3D bone tissue engineering scaffolds.

This analysis, it will have an impact on a variety of areas, including society, the environment, and industry. Additive manufacturing has been used in the aerospace, manufacturing, and healthcare industries, where it has been used to help individuals with health issues. Implementing additive manufacturing in 3D bone tissue engineering paves the way for a future where value chains are shorter, smaller, more localized, and collaborative, as well as offering major sustainability benefits [10]. It has also been identified to have the potential for sustainability advantages such as less material wastage during the manufacturing process, capability to optimize geometries, and reduced energy consumption and transportation cost. The medical industry benefits from 3D printing, especially in producing biomaterials-based orthopedic implants and medical equipment, which is a sustainable process. The advancement of 3D bone tissue engineering applications significantly impacts the research and development time for new products, and it may be completed in less time [18, 19]. There are several LCA studies on different types of biomaterials and manufacturing methods. It is then observed that 3D technologies by using biomaterials show lower environmental impact for the fabrication of orthopedic implants and medical devices [20].

This research described the research background, which is relevant to 3D bone tissue engineering scaffolds, as well as how to use the LCA model to estimate the potential environmental impact. The 3D bone tissue engineering scaffolds stage required the involvement of raw material production, pre-manufacturing stages, printing process, transportation, and the conclusion of the product life cycle, which includes usage and disposal of the product, to assess the environmental impact. The implementation of this assessment will aid in identifying potential environmental impacts as well as weak environmental areas. Therefore, the tissue engineering scaffold technology can be improved to reduce the environmental burden.

2. Materials and Methods

2.1. Materials.

In this paper, the material involved to identify the environmental impacts through LCA analysis was from past research of fabrication on novel tissue engineering scaffold of polyethylene glycol) diacrylate (PEGDA), dissolved in Dimethyl sulfoxide (DMSO) and Diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide (TPO) as photoinitiator [21, 22].

2.2. Identification of LCA parameter.

Identification of LCA parameters is accompanied by procedures that must be conducted in accordance with ISO14000 guidelines. In this study, it is necessary to define the strategic features of the LCA study. This study adhered to the LCA methodology framework established by the international standard ISO 14040, which outlines four basic phases for LCA research. First, the analyses' goals and scope were established. Second, the inventory was created by deciding which materials manufacturing procedure would be the most suitable. Third, GaBi software was used to examine the probable environmental implications. Fourth, the findings were interpreted and evaluated, and the analysis was also updated. Finally, the results are presented by LCA software tools that help to reduce effort, time, and resources applying an LCA.

The life cycle of the 3D bone tissue engineering scaffold is the LCA model used in this study; it refers to the primary activities during the product's life cycle, including raw material production, pre-manufacturing phases, printing, transportation, etc usage, and disposal. This is called a cradle-to-grave approach, which is it is the full LCA from resource extraction, 'cradle' to the use phase and disposal phase, 'grave '[23]. In the LCA model development of 3D bone tissue engineering scaffolds, all of the product's key activities are referred to as the system boundaries. As a result, all aspects of the LCA approach outlined in the regulatory framework were considered. The analytical results are displayed using GaBi software graphs based on the inventory of all stages specified in the LCA development of 3D bone tissue engineering scaffolds.

2.3. Development of LCA model.

The LCA model was created by first developing the LCA framework for 3D bone tissue engineering. A framework for the environmental impact assessment must be defined before the LCA model can be installed into GaBi software. This framework was created with cradle-to-grave system limits in mind. To construct a comprehensive life cycle for 3D bone tissue creation, it began with preparing raw materials and proceeded through the manufacturing process until the end of life. The LCA Model considers the stages of raw material preparation for 3D extraction, the printing process for the 3D machine, and the disposal of 3D bone tissue as waste at the end of its lifecycle. Other additional data linked to LCA frameworks, such as transportation that uses diesel for product transportation, energy and electrical consumption for 3D machines, and material waste, are included in this research analysis.

All of the data for LCA Model needed are identified. Previous research claimed that PEG synthetic hydrogel polymer is usually used in tissue regeneration because of its non-toxic, non-immunogenic, and easily cleared from the body [22]. The application of PEG as photocurable resin also has gained much attention due to its high biocompatibility and hydrophilicity that are suitable in biomedical fields.

The 3D machine uses DLP 3D Printer and uses DLP (Digital Light Processing) is a printing process for bone tissue. DLP 3D printing is a common process for resin 3D printing. DLP 3D printing is a type of vat polymerization that uses liquid photopolymer resin that can solidify under light sources. DLP 3D printing as additive manufacturing is able to minimize the amount of material employed, lower energy use, resource demands, and related carbon dioxide (CO_2) emissions over the entire product life cycle [24]. However, although this technology has the potential to influence high levels of energy usage, suitable preventative precautions must be implemented. As previously said, additive manufacturing or 3D printing technology can be useful to the environment at times, but it can also be harmful because material utilization can lead to higher impacts per part due to higher energy use, more embodied material impacts, and more waste per part produce [25]. The LCA model that has been developed in GaBi software is shown in Figure 1.

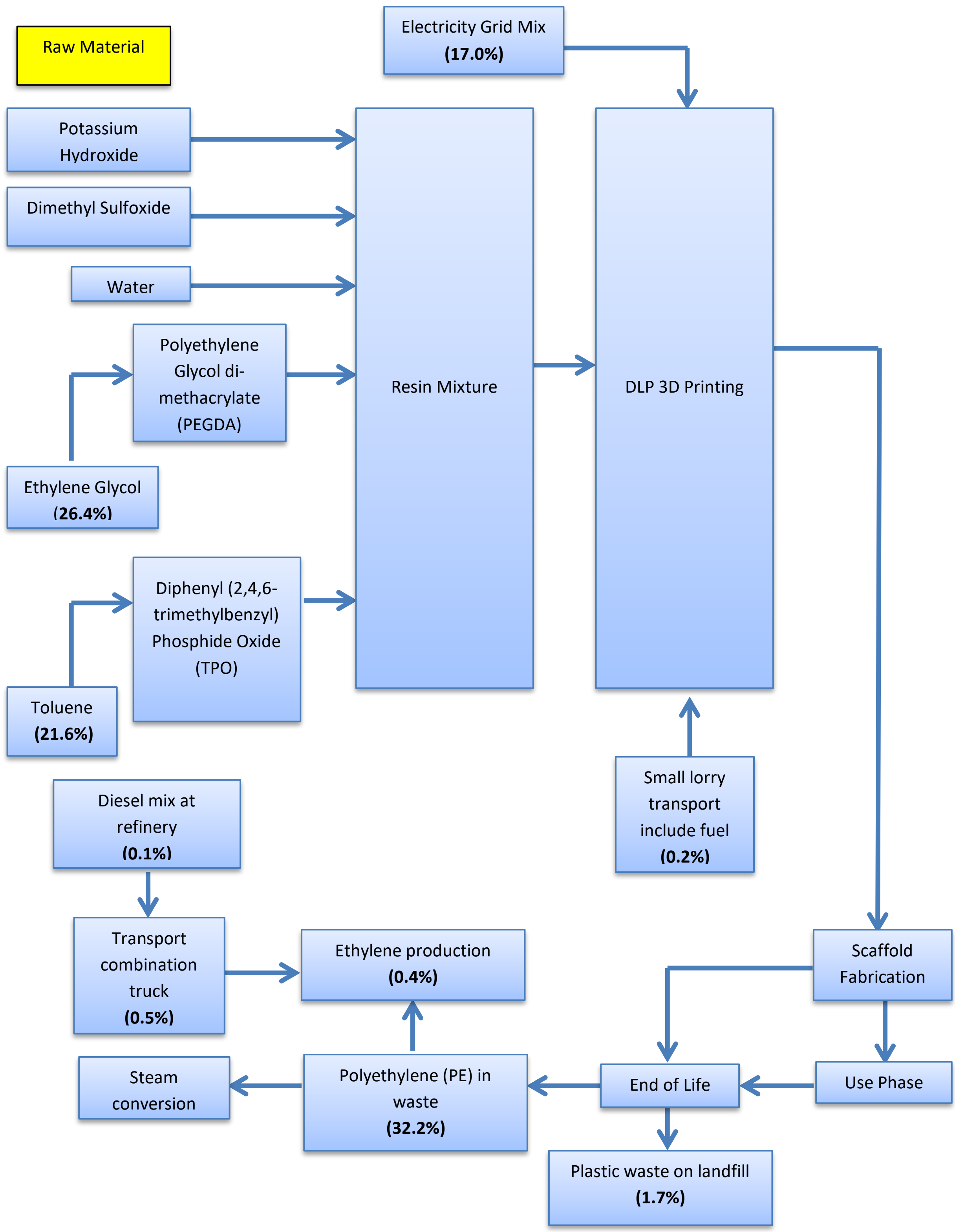


Figure 1. Complete 'cradle-to-grave' LCA model of bone tissue engineering scaffold in GaBi software.

LCA model shows all linked processes of 3D bone tissue engineering fabrication from raw materials as the resin mixture for material extraction in DLP 3D printing. Then, DLP 3D printing process consumes electricity and transportation consumption for the 3D operation. At the use phase, it continues to the end of life phase, showing wastage in landfills and polyethylene waste. At each process, give out the percentage value that contributes to environmental impacts. From the raw material, the values for ethylene glycol and toluene materials are 26.4% and 21.6%, respectively. At manufacturing process, electricity and transportation consumption shows 17.0% and 0.2%. Meanwhile, at the end of life stage, plastic waste on landfills contributes 1.7%, and polyethylene waste is 32.2%. The highest value of this LCA model comes from raw material polyethylene usage and electricity consumption in DLP 3D printing.

3. Results and Discussion

GaBi software is one of the LCA tools to analyze and generate results from the build-up LCA model. GaBi software helps identify the potential environmental impacts that contribute to human health and environmental emissions. For this research, the total life cycle of 3D bone tissue engineering scaffolds from raw material extraction, manufacturing phase till the end of life of product stage has been examined. This software applied CML (Centrum voor Milieukunde Leiden) method that has been developed by the Centre for Environmental Science at Leiden University [26]. The analysis has been analyzed by using CML 2001 - January 2016 baseline since it has globally been used in LCA software.

From the LCA model build-up, inputs and outputs have been identified. The main inputs for this process are energy and material resources. The energy resources identified are non-renewable energy and renewable. Meanwhile, material resources give out renewable resources, non-renewable elements, and resources. All of the inputs show that raw materials, processes, transportation, and wastage come from two types of resources; energy and material resources. Figure 2 and Figure 3 show the value of material and energy resources that consists of non-renewable and renewable resources. The value justifies the accumulation percentage of resources from each type of process involved in the life cycle.

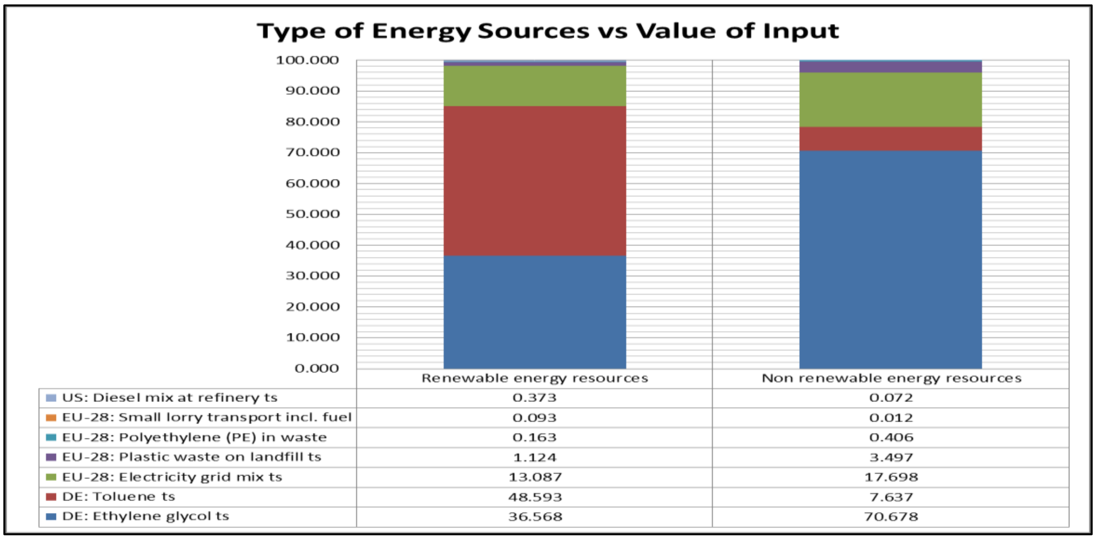
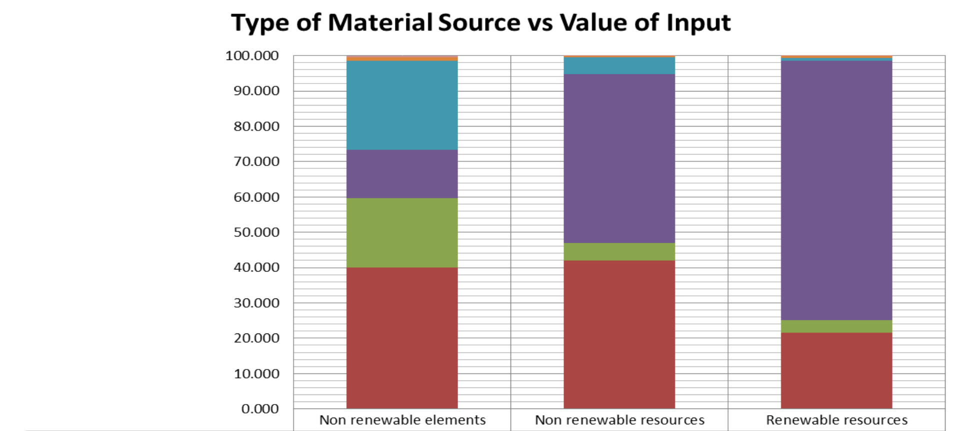


Figure 2. Value of energy sources from each process.

The bar chart for energy sources claims the most renewable energy resources come from raw material, ethylene glycol, with 36.568%. The least resources are from small lorry transport, including fuel, with 0.093%. The non-renewable energy resources also give the highest value from ethylene glycol, with 70.678%, and the lowest value from small lorry transport includes fuel. Both bar charts show that raw material, ethylene glycol, is the main energy resource, and transportation is the least energy resource for the 3D bone tissue engineering life cycle.

As for material sources, ethylene glycol shows the highest value for non-renewable, 40.032%. The main sources of non-renewable and renewable resources are the electricity grid mix with 47.684% and 73.379%, respectively. Small lorry transport, including fuel, still shows the lowest value for material source for each type of source, with 0.041%, 0.008%, and 0.009%.

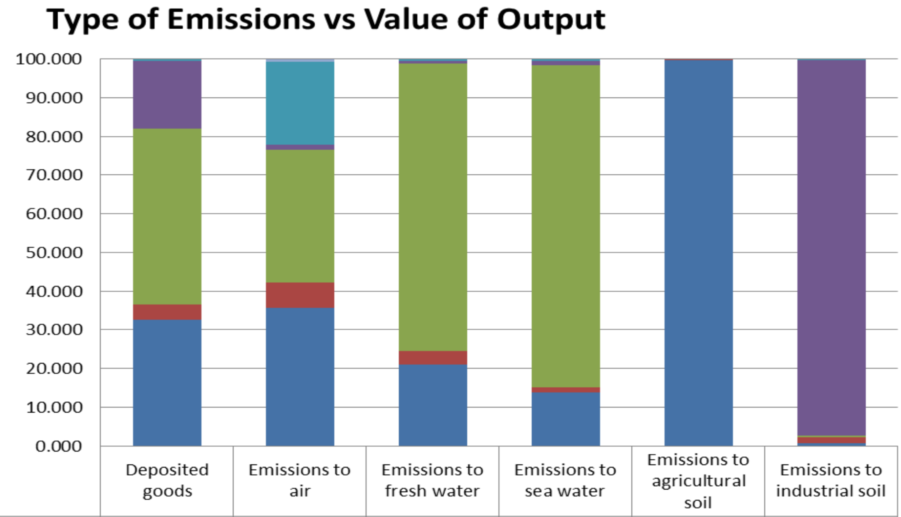


	Non renewable elements	Non renewable resources	Renewable resources
US: Diesel mix at refinery ts	0.431	0.031	0.022
EU-28: Small lorry transport incl. fuel	0.041	0.008	0.009
EU-28: Polyethylene (PE) in waste	1.041	0.422	0.662
EU-28: Plastic waste on landfill ts	25.042	4.814	0.795
EU-28: Electricity grid mix ts	13.822	47.684	73.379
DE: Toluene ts	19.591	4.979	3.595
DE: Ethylene glycol ts	40.032	42.062	21.536

Figure 3. Value of material sources from each process.

From both bar charts, it can be considered that raw material and electricity consumption is the main contribution input for this LCA analysis of 3D bone tissue engineering scaffolds. Raw material and electricity usage affect the energy consumption and potential environmental impacts for the whole life cycle. This research; electricity consumption is the main consumption for the 3D machine operation. The 3D machine requires huge electricity for long time usage. Consider that the machine operates for 12 hours long with a standard power usage of 70W, and the energy consumed is about 3MJ. Energy consumption from machine operation is affected by processing time producing higher product energy, and it is the main drive for environmental impacts in the additive manufacturing process [27]. Energy analysis in 3D printing technology transforms electrical to thermal or mechanical energy discharged as heat loss. Primary and secondary energy from the 3D machine is essential to change the material form and properties, while secondary energy is needed to support the printing process influenced by 3D printer capability [28]. The statistical approach in primary energy was chosen to sum together the same energy level, the numerous shares related to resource or material flows, and electric energy flows. The energy losses that occur at various levels during electricity conversion were traditionally accounted for during the conversion of primary to secondary energy [29].

The LCA analysis through GaBi software also generated the output value of emissions from each related process. Figure 4 shows the output value of emissions for each process. Emissions involved in the LCA analysis are deposited goods, emissions to air, freshwater, seawater, agricultural soil, and industrial soil. The bar chart shows each process emits to each type of emissions. The value shows the accumulation percentage emissions for each process. In deposited goods, the electricity grid gives the highest contribution with 45.565%, followed by ethylene glycol and plastic waste on the landfill with 32.532% and 17.466%, respectively. Emissions to the air show the highest emission comes from ethylene glycol and electricity grid mix with 35.632% and 34.181%. Fresh water and seawater emissions show electricity grid mix as the highest contribution with 74.373% and 83.291%. Meanwhile for emission to agricultural soil shows ethylene glycol as the main emission with almost complete emissions with 99.716%, and plastic waste on landfills contributes to 97.005% for emissions to industrial soil.



	Deposited goods	Emissions to air	Emissions to fresh water	Emissions to sea water	Emissions to agricultural soil	Emissions to industrial soil
US: Diesel mix at refinery ts	0.050	0.587	0.015	0.060	0.003	0.001
EU-28: Small lorry transport incl. fuel	0.005	0.191	0.007	0.008	0.012	0.002
EU-28: Polyethylene (PE) in waste	0.384	21.276	0.383	0.440	0.007	0.378
EU-28: Plastic waste on landfill ts	17.466	1.389	0.784	1.032	0.041	97.005
EU-28: Electricity grid mix ts	45.565	34.181	74.373	83.291	0.103	0.439
DE: Toluene ts	3.997	6.689	3.528	1.298	0.118	1.424
DE: Ethylene glycol ts	32.532	35.632	20.911	13.871	99.716	0.751

Figure 4. Output value emissions from each process involved in 3D bone tissue engineering scaffolds.

To summarize, electricity grid mix and ethylene glycol are the main factors for each emission and give rise to environmental impact in fabricating 3D bone tissue engineering scaffolds. This is because 3D printing technology requires high electricity consumption compared to other types of manufacturing processes, as the main driver for this fabrication comes from 3D machine operations. Therefore, electrical energy from 3D machine operation gives out the most important sustainability issues in potential environmental impact. The issues on energy utilization must be done at all phases in order to obtain high energy efficiency and low environmental impacts [30-32].

From all inputs and outputs identified in LCA analysis for 3D bone tissue engineering scaffolds, GaBi software then analyzes identified potential substances that contribute to environmental impacts. Figure 5 and Table 1 shows all the identified potential environmental impacts that consist of Global Warming Potential (GWP), Acidification Potential (AP), Eutrophication Potential (EP), Ozone Layer Depletion (ODP), Abiotic Depletion (ADP), ADP fossil, and Human Toxicity Potential (HTP). Each input and output shows the value for each potential environment. Table 1 shows the total value for each identified environmental impact. ADP fossil shows the highest environmental impacts value with 45.91MJ, and the lowest environmental impact has come from HTP with 0.0752kg DCB. In this analysis, ethylene glycol and toluene as the raw material for 3D bone tissue engineering scaffold contribute the most in ADP fossil with 16.8MJ and 24.7MJ, respectively. Another main input, electricity grid mix, and energy consumption illustrate the most in ADP fossil with 3.65MJ. Transportation and diesel are the LCA model inputs but show the lowest contribution for each environmental impact. For the output of the LCA analysis, plastic and polyethylene waste demonstrate a low contribution value for each potential environmental impact as the highest value for plastic waste is 0.956kg only and it contributes to EP; meanwhile, polyethylene waste contributes only 0.626kg CO_2 to GWP.

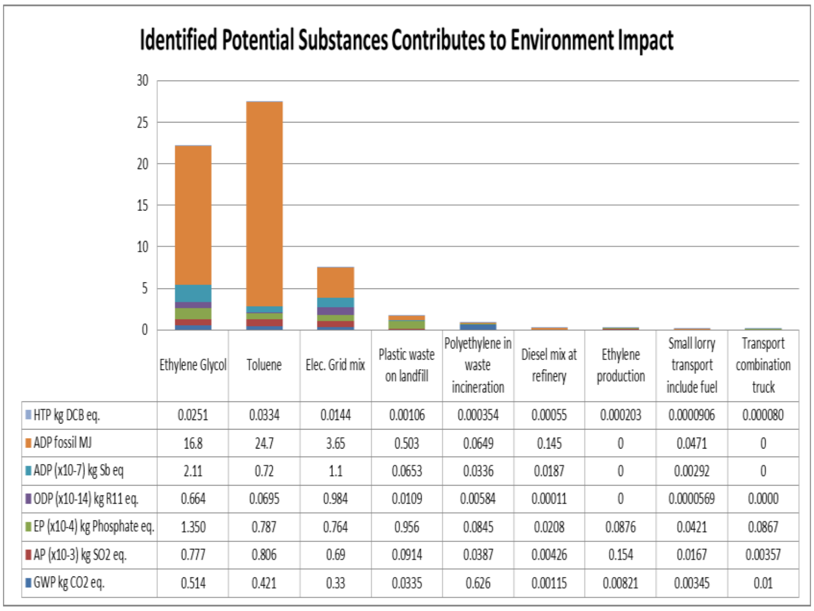


Figure 5. Identified potential substances that contributes to environmental impacts in 3D bone tissue engineering scaffolds.

Table 1. Identified potential environmental impacts and contribution values for each process.

	GWP	**AP ($x10^{-3}$)**	**EP ($x10^{-4}$)**	**ODP ($x10^{-14}$)**	**ADP ($x10^{-7}$)**	**ADP fossil**	**HTP**
	kg CO2 eq.	**kg SO2 eq.**	**kg Phosphate eq.**	**kg R11 eq.**	**kg Sb eq**	**MJ**	**kg DCB eq.**
Ethylene Glycol	0.514	0.777	1.350	0.664	2.11	16.8	0.0251
Toluene	0.421	0.806	0.787	0.0695	0.72	24.7	0.0334
Elec. Grid mix	0.33	0.69	0.764	0.984	1.1	3.65	0.0144
Plastic waste on landfill	0.0335	0.0914	0.956	0.0109	0.0653	0.503	0.00106
Polyethylene in waste incineration	0.626	0.0387	0.0845	0.00584	0.0336	0.0649	0.000354
Diesel mix at refinery	0.00115	0.00426	0.0208	0.00011	0.0187	0.145	0.00055
Ethylene production	0.00821	0.154	0.0876	-	-	-	0.000203
Small lorry transport include fuel	0.00345	0.0167	0.0421	0.0000569	0.00292	0.0471	0.0000906
Transport combination truck	0.01	0.00357	0.0867	-	-	-	0.000080
Total	1.94731	2.58163	4.1787	1.7344	4.0505	45.9100	0.0752

4. Conclusions

This research analyzed the total life cycle of 3D bone tissue engineering scaffolds by applying 'cradle-to-grave' analysis, from raw material extraction, manufacturing process till the end of product life with additional consideration from energy and transportation consumption. The analysis is then generated by the LCA tool, GaBi software, with the CML method to identify the potential environmental impact value. GaBi software for LCA analysis helps to determine the value much easy and fast compared to manual calculation. From GaBi software analysis, the value of input and output for each process has been determined, and the results show that raw material and energy consumption is the highest contributors to potential environmental impacts compared to other processes. To increase the printing efficiency, lowering the operation time will help in maintaining the low environmental impact. Another suggestion by using renewable energy for the 3D machine also may decrease the amount of environmental impact. As for raw material usage, many types of materials have been used for 3D bone tissue engineering scaffolds. Various types of materials will show the various contribution values for potential environmental impacts. Nowadays, many researchers focus on using recycled material as the main material for 3D bone tissue engineering scaffolds. Besides, current research on 3D bone tissue engineering scaffold fabrication focuses on eco-friendly material as the main material [33]. Since LCA analysis on 3D bone tissue engineering is still scarce, further studies need to be conducted. The development of bioprinting creates a high possibility for upcoming potential environmental impacts; thus, it is crucial to investigate and analyze the 3D bone tissue engineering scaffolds fabrication to create a healthy and sustainable process in the future.

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Conflicts of Interests

The authors declare no conflict of interest.

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