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Unveiling Efficiency: A Comparative Study of 3-Axis and 4-Axis Additive Manufacturing for pHEMA

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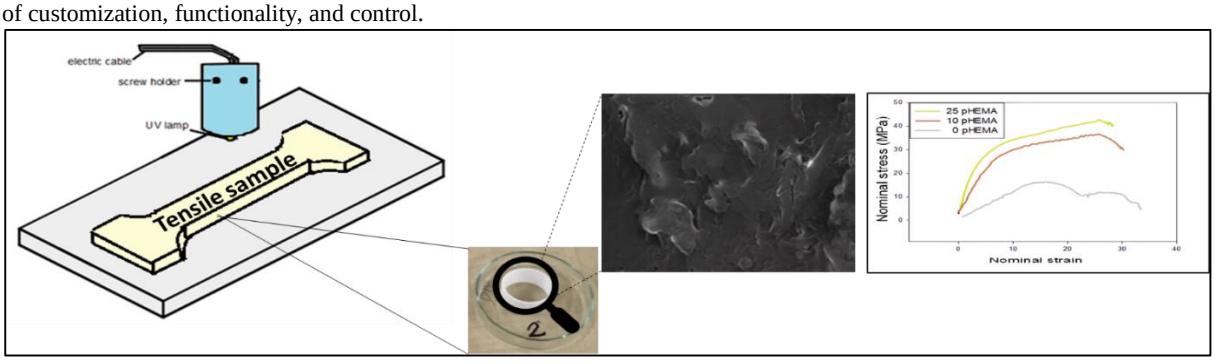
Abstract

This study presents a comparative analysis of samples produced on a device designed to produce an artificial aorta adapted to mimic living geometry using a 4-axis (4D) additive manufacturing device with a substrate that can rotate 360 degrees in the horizontal axis. The samples produced in the 4D device were cured with ultraviolet light (UV). The mechanical properties of the samples, which varied depending on the UV exposure time, were compared. The samples were fabricated using a biocompatible polymer, poly(2-hydroxyethyl methacrylate), pHEMA. For this purpose, firstly, we designed a device capable of 4Dadditive manufacturing by adding a rotating table to the bed of the device in addition to the three-dimensional cartesian system which can be used to produce biocompatible samples. The mechanical and structural properties of these samples were compared with those produced using the 3-axis (3D) additive manufacturing device. The results showed that the artificial aorta produced with the 4D device, incorporating UV curing technology under varying conditions (such as crosslinker concentration and polymerization time), exhibited an 11.53% increase in mechanical strength and a 36.98% reduction in biodegradation compared to those produced with the 3D device. This demonstrates that 4D additive manufacturing enables the production of promising biomaterials with slower degradation rates.

Keywords: Additive manufacturing, poly(2-hydroxyethyl methacrylate), artificial aorta, 3D, 4D.

Graphical abstract

4D additive manufacturing holds great promise for advancing the field of biomaterials by offering unprecedented levels of customization, functionality, and control.



1. Introduction

In addition to conventional manufacturing methods, new production techniques have been developed for object manufacturing. Researchers have recently focused on conventional methods (e.g., turning [1], milling [2], drilling [3]), unconventional methods (e.g., electro-erosion [4], electrochemical [5]), and new approaches, such as additive manufacturing (AM) [6]. The advancement of manufacturing technologies that meet demands beyond those achievable with traditional methods is inevitable. In the emerging field of additive manufacturing, objects are produced layer by layer. Due to its numerous advantages—including enhanced design flexibility, waste reduction, and minimized material usage—AM is increasingly preferred, especially in the medical field.

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These benefits contribute to shorter surgical procedure times, reduced implant rejection rates, and improved ergonomic and aesthetic outcomes [7]. In AM, objects can be produced from metallic [8] or polymeric materials [9]. For samples produced with polymer materials, AM technology is increasingly used to create biocompatible materials, such as liquid-form "inks" compatible with living systems [10].

Poly(2-hydroxyethyl methacrylate) (pHEMA), another preferred biocompatible material, was first synthesized by Wichterle and Lim using a radical polymerization technique [11]. It has been used in biomedical applications such as nasal cartilage [12], wound dressing [13], artificial cornea [14] and drug delivery systems [15]. With a short synthesis time and flexible polymer geometry, pHEMA can be easily synthesized via UV photopolymerization [16]. This study aims to produce biomaterial with enhanced mechanical and physical properties by leveraging the advantages of a fourth axis. To achieve this, pHEMA polymer was fabricated in an aortic geometry using a 4D printing technique. In addition to the traditional 3 cartesian coordinates, we introduced rotation around the Z-axis aligned with the print bed. In the UV photopolymerization process, 2-hydroxyethyl methacrylate, AIBN and EGDMA as a curing agent in varying amounts were magnetically stirred and polymerized at room temperature. Finally, the mechanical and physical properties of the artificial aorta compared with produced samples using 3D.

2. Methods

2.1. Materials

2-hydroxyethyl methacrylate (HEMA, Merck), 2,2'-azobis(2-methylpropionitrile) (AIBN, Sigma-Aldrich), ethylene glycol dimethacrylate (EGDMA, Merck), and phosphate Buffered Saline (PBS, Sigma-Aldrich) were utilized as received.

2.2. Manufacturing of pHEMA with UV-Photopolymerization and 4 Axis Printer

pHEMA was produced using the UV photopolymerization method in an aortic geometrywith slight adjustments to the polymerization parameters as described in the literature[17]. Briefly, 2-hydroxyethyl methacrylate (4 mL) and AIBN (50 mg) were magnetically stirred at room temperature for 30 minutes. Subsequently, varying amounts (10, 25,50,75,100, 200 μL corresponds to 0.2- 4.0 % v/v) of ethylene glycol dimethacrylate (EGDMA) were added as a curing agent, and the total volume was adjusted to 5 ml with phosphate-buffered saline (PBS). The prepared solutions were named sequentially based on EGDMA ratio as pHEMA, 10pHEMA, 25pHEMA, 50pHEMA, 75pHEMA, 100pHEMA, and 200pHEMA.

To fabricate a pHEMA-based aorta, a 4D additive manufacturing device with temperature, humidity, and air-control was used. This device utilizes spin coating technology along the Z-axis in addition to the three-dimensional cartesian system (Figure 1). The solution containing the monomer and curing agent was dispensed into a mold made of biocompatible polyvinyl alcohol (PVA) with dimensions of 30x26x30 mm using a dosing unit and exposed to UV light (365 nm). After photopolymerization, the pHEMA within the PVA mold was immersed in pure water, causing the PVA to dissolve and release the pHEMA structure.Finally, the obtained pHEMA was dried in a vacuum oven at 40°C.

2.3. Physicochemical and Mechanical Properties

The morphological structure of pHEMA samples was analyzed using a scanning electron microscope (SEM, TESCAN, Germany). Phase analysis of pHEMA was conducted witha Rigaku Ultima-IV X-Ray Diffraction system over a 2θ range of 2–90°, at a scanning rate of 0.02°/s.

To assess the stability of the artificial aorta samples based on pHEMA produced using both AM methods under in vitro conditions, the samples were dried at 40°C and weighed. They were then immersed in PBS (50 mM, pH 7.4, 20 ml) and incubated at 37°C with continuous agitation in a shaking water bath at 100 rpm for 30 days. At the end of each 10-day interval, the samples were removed from the solution, rinsed with distilled water to remove any salt residues, dried in a vacuum oven at 40°C, and weighed.

The mechanical properties of pHEMA films were evaluated via tensile testing,conducted according to the ISO 527-3 standard at room temperature. Five separate tensile tests were performed for each sample, prepared with dimensions of 20 x 5 x 4 mm. The tests were conducted at room temperature with a tensile load of 10 kN and a pulling speed of 3 mm/min.

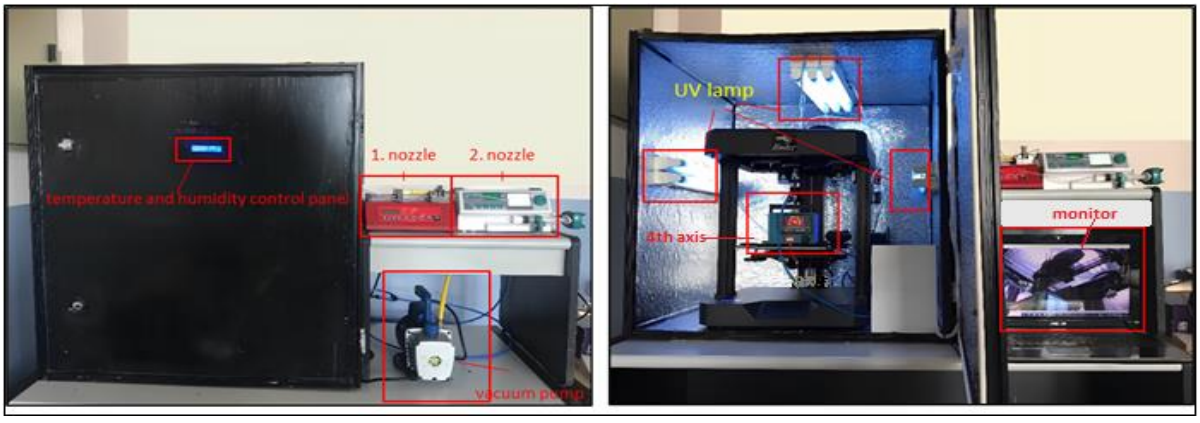

Figure 1. Integrated 4D additive manufacturing system with UV-photopolymerization

3. Results and Discussion

The pHEMA-based aortic biomaterial was developed through a straightforward, one-step process (Figure 2). Cross-linked pHEMAwas synthesized by exposing a HEMA monomer solution to UV light during photopolymerization in the presence of a photoinitiator (AIBN) and a cross-linker (EGDMA)

Artificial arteries with aortic geometry were successfully produced using both 3D and 4D printing methods. While no discernible differences were observed between the methods in terms of macroscopic features (such as cracks, fractures, or geometric irregularities), distinct variations were evident in the microscopic surface properties, degradation behavior, and mechanical characteristics of the products from each method. Figure 3 illustrates the pHEMA artificial artery produced using 4D additive manufacturing.

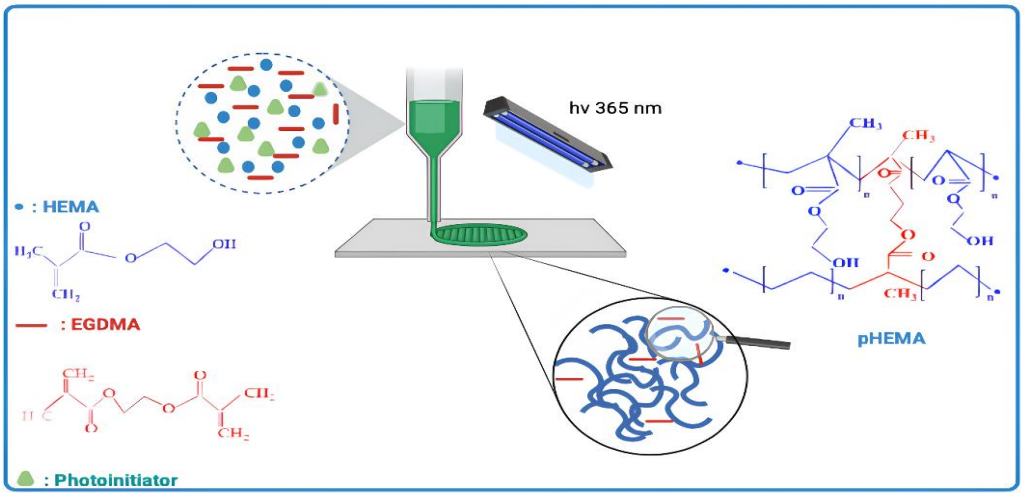

Figure 2. Schematic presentation of AM of pHEMA

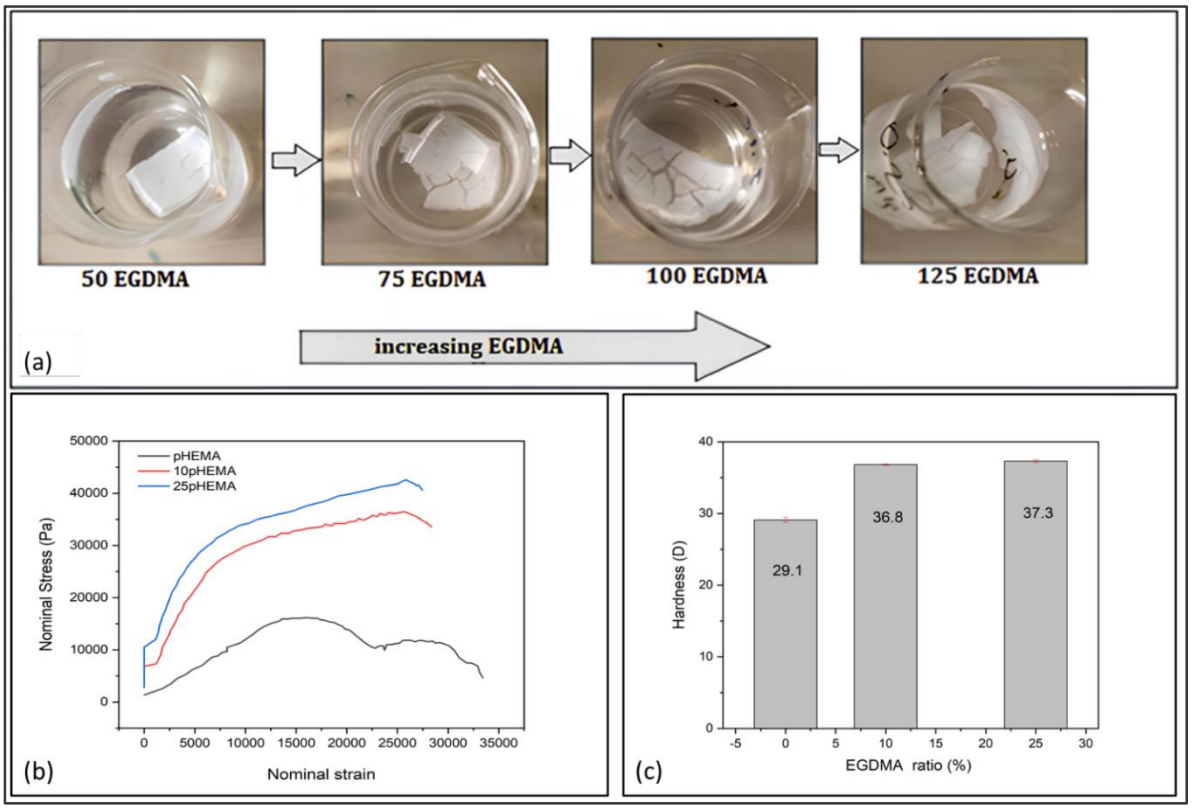

Figure 3. (a) Digital images of pHEMA: The effect of EGDMA concentration on AM (b) Stress - strain curves(c)Surface hardness

It has been noted that the polymerization environment plays a significant role in the production of artificial arteries using AM. With increasing EGDMA ratios in the polymerization environment, the products extracted from the mold were observed to exhibit cracks and fractures (Figure 3a). A higher EGDMA ratio increases the availability of reactive monomers, accelerating the polymerization reaction rate. However, the elevated EGDMA concentration also results in a higher degree of crosslinking within the polymer, leading to stiffer and consequently more brittle materials. Figure 3b illustrates the tensile strength of 10pHEMA and 25pHEMA, which are approximately 2 and 3 times higher than that of pHEMA, respectively. This increased strength can be attributed to the crosslinking of EGDMA between pHEMA chains, which promotes elastic behavior by binding the polymer chains together during tensile loading (Figure 2). Similar observations have been reported previously. Seo et al. indicated that increasing the divinyl benzene (DVB) ratio from 0.4% to 2% in pHEMA raised tensile strength from 0.3 MPa to 0.7 MPa [18]. In another study, it was noted that varying the EGDMA ratio between 0.1 mol% and 5.0 mol% resulted in the highest tensile strength at a 5% EGDMA ratio, measuring 1.5 MPa (150 N/cm²) [19].

Additionally, it is known that the length of cross-link chains significantly impacts the mechanical properties of polymers [20]. The polymerization rate, which increases with EGDMA concentration in the polymerization medium, may lead to shorter cross-link chain lengths, thereby reducing mechanical strength. Linear pHEMA exhibited the lowest hardness value, while 10pHEMA or 25pHEMA demonstrated highest hardness values, similar measurements (36.8 and 37.3) (Figure 3c). These results indicate that the hardness and biomechanical properties of the polymer are strongly influenced by the cross-link chain length. Considering all mechanical test results, the properties of cross-linked pHEMA polymers-particularly 10pHEMA- were evaluated as suitable for use as artificial aortic materials following the 3D and 4D additive manufacturing processes. Petersman and colleagues investigated the mechanical properties of 3D-printable polymers [21]. They observed that, except for PEEK, the tensile strength of the materials was close to reference values, with tensile speed identified as a significant factor in durability.

As a result of the mechanical evaluations, the effect of curing time on the production of 10pHEMA artificial veins using 3D and 4D processes was investigated. Figure 3d shows that a curing time of 2.5-minutes was insufficient for both methods. Additionally, an increase in curing time resulted in higher tensile strength. However, further extending the curing time led to a slight reduction in tensile strength due to excessive cross-link density. A similar observation was reported by Nasri et al. [22]. The tensile strength of the 10pHEMA sample produced with the custom-designed4D additive manufacturing device was 11.53% higher than that of the produced using 3D additive manufacturing device.

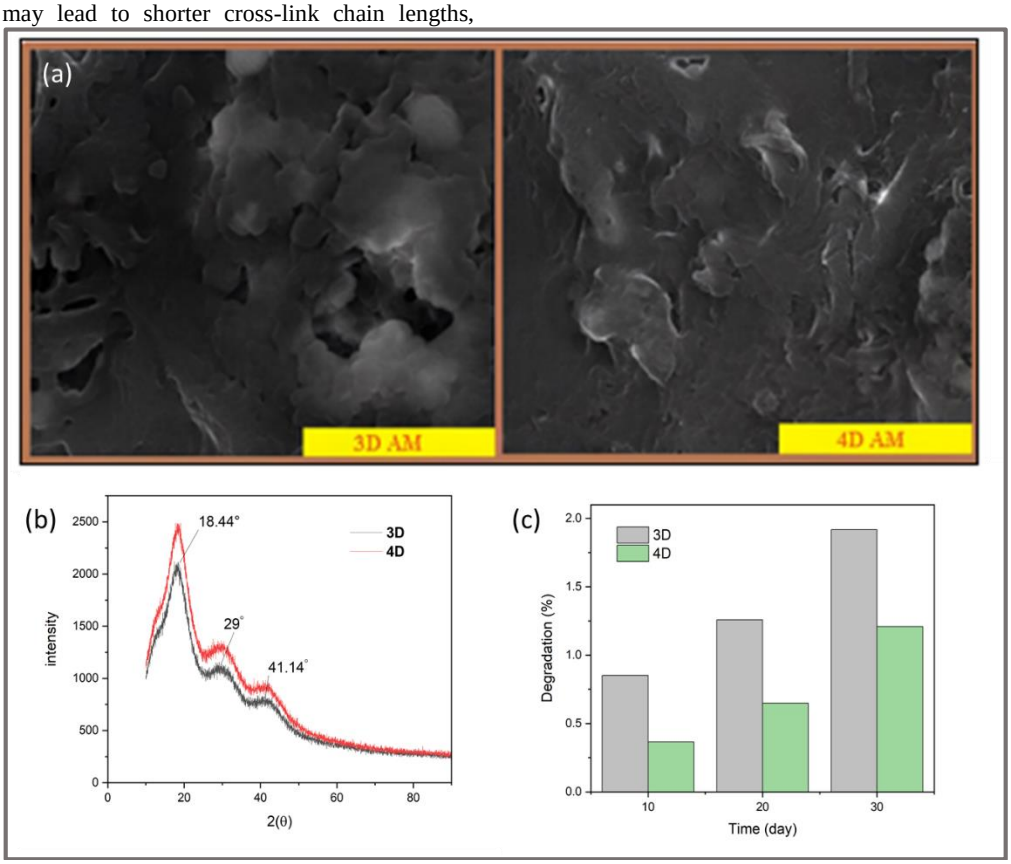

Figure 4. Comparison of physicochemical characterization of pHEMA produced by both 3D and 4D: (a) SEM micrographs (x35magnification), (b) XRD pattern and (c) Hydrolytic degradation

Figure 4a shows SEM micrograph of pHEMA aortic samples obtained by 3D and 4D AM (Figure 4a). Generally, voids in biomaterials can support cell growth. Surface roughness and voids facilitate cell adhesion and proliferation, aiding in circulation of nutrients and oxygen essential for tissue regeneration. However, the size, distribution, and quantity of voids are critical factors, as excessively large or abundant voids may adversely affect cell growth and tissue development [23]. According to SEM micrographs, 10pHEMA-produced via 4D AM may offer adequate surface characteristics as a biomaterial for promoting cell proliferation.

XRD pattern of pHEMA samples exhibited a broad peak at 2θ= 19.1° and 18.94° for the 4D and 3D production processes, respectively (Figure 4b). The intensity value at the highest peak was relatively higher in the sample produced using 4D manufacturing, which is attributed to an increase in the density of crystalline regions in the 4D manufactured samples[24]. The higher density of crystalline areas leads to increased peak intensities and sharper peaks. The measured peaks in both samples indicate that the4D manufacturing processresulted in improved mechanical properties,likely due to relatively denser crystalline regions. To date, the influence of the 4D on the polymer's crystallinity has not been explored in the literature.

Biodegradability of AM-manufactured samples was determined by hydrolytic degradation. As seen Figure 4c, the mass loss of 10pHEMA produced by 4DAM was approximately 1%, while the mass loss of samples produced by 3D was around 2%, indicating that4D additive manufacturing method may be an effective technique for producing pHEMA-based artificial aortas. In the literature, the degradation behavior of pHEMA has been tested in different environments. For example, Paterson et al. examined the degradation behavior of collagenase-degradable poly(2-hydroxyethyl methacrylate)-based foams in both hydrolytic and enzymatic environments. They reported that after a 16-day incubation period, pHEMA-based foams became fully hydrated, and the decrease in cross-linking led to the mass loss of polymer fragments [25]. However, although the degradation conditions used in our study (pH, temperature, etc.) simulate *in vivo* conditions, the complexity of human tissue-comprising various cell types and enzymes- requires further investigation.

4. Conclusion

This study successfully designed a 4D additive manufacturing device that enhances the production of biocompatible biomaterials by adding a rotating table to the traditional 3D Cartesian system. When compared to samples produced using conventional 3D additive manufacturing, those made with the 4D device exhibited 11.34% greater durability, attributed to a less porous structure. SEM analysis confirmed these differences in mechanical properties. Furthermore, degradation studies indicated that the 4D additive manufacturing method enables the production of slow-degrading biomaterials. These advancements suggest that the hydrogels produced through this method have significant potential to overcome the limitations of HEMA-based hydrogels, particularly in tissue engineering and drug delivery applications, where load-bearing capabilities are crucial.

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