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Review

Material Challenges and Opportunities in 3D Printing for Hip Implant Applications

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Abstract

There is a current need for tissue and organ repairs, replacement, and regeneration for patients who suffer from diseased or damaged tissues or organs. This situation is continuously on the rise and the supply of this form of therapy does not meet the patients demand mostly due to lack of donors and biocompatibility issues which causes immune system rejection of the implants. To succeed through these limitations, researchers are currently investigating the use of scaffolds as another approach for implants. The conventional scaffold fabrication technique is limited due to the precision of pore design. The 3D printing technology on the other side can produce an extracellular matrix with a higher degree of complexity and matching details such as pore size and geometry suitably based on certain factors including tissue engineering, hip biomechanism, material suitability, ethical standards, future, and

challenges. This paper in particular focuses on materials challenges and opportunities addressing various issues at various levels to the materials-process-property relationship. It is comprehensive as it starts with hip biomechanism in gait and stress distribution to give the reader a clear perspective of the magnitude of challenges for hip implants and details to consider when designing the materials. This is followed by 3D printing for orthopaedic applications and 3D hip tissue regeneration. The hip replacement materials including polymers, composites, and metals are explored and correlated to conventional hip replacement materials. The work is concluded with some concluding remarks on opportunities, challenges, and future trends. The goal is to have scaffolds that have the capability of having a biomimicking design similar to the extracellular matrix with the advantage being the provision of structural supports for cell attachment, growth, and differentiation with the main goal of producing an operational organ or tissue. The knowledge derived from this review offers huge potential for providing a pathway for sustainable healing.

Keywords
3D printing; biocompatibility; biomaterials; cell adhesion; hip replacement; tissue regeneration

1. Introduction

The hip anatomy supports varying ranges of motion around the joint which includes climbing, running, and walking. The femoral head is attached to the femoral neck to the remainder of the femur. At the femur top, close to the femoral neck there is another bulge noticeable at the external of the hip which is referred to as the greater trochanter which attaches the muscles. Also, the presence of cartilage aids in preventing friction between the acetabulum and the femoral head, although there is a possibility of hip pain if the cartilage starts tearing down or gets damaged [1]. The illustration on Figure 1 displays the anatomy of the hip joint which comprises two bones which are the femur (thigh bone) and pelvis [2].

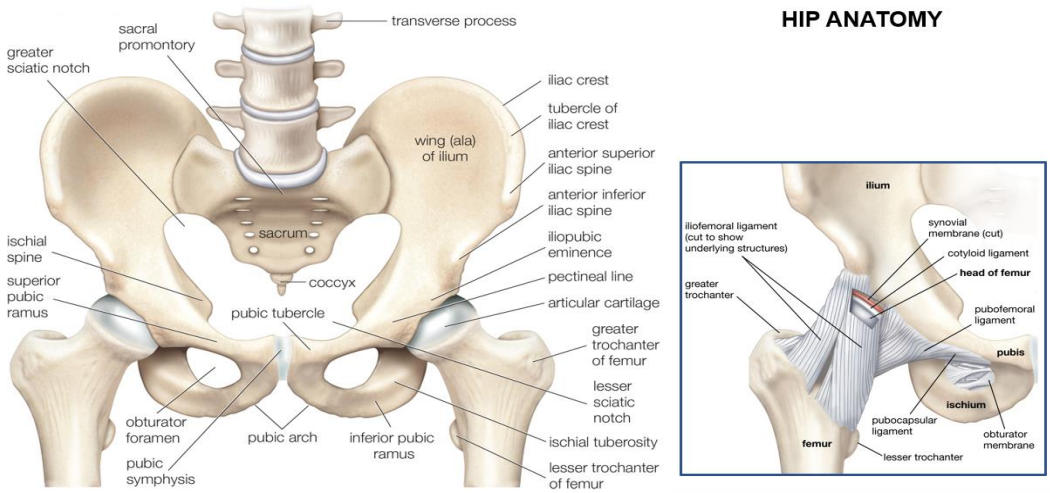

Figure 1 A labelled view of the hip joint [1, 2].

The ball and socket motion is regulated by various robust muscles which cling to the bones. These muscles called the glutes (gluteal) muscles, big and the robust muscles that cling to the hip bone, all make up the buttocks. The glutes attached to the greater trochanter have muscles that aid in holding the pelvis and the body well enough to reduce the likelihood of falling over and help in walking [3]. The top of the muscle layer (iliotibial band) is the long tendon that has a lot of muscle in the leg and hip connected to it (classification of these muscles can be seen in Table 1) [3-7]. It begins at the peak of the pelvis which is outside the hip joint and goes down to the leg. When the iliotibial band gets extremely stretched or over-utilized this can cause hip pain.

Table 1 Classification of muscle groups [3-7] and current non-surgical therapies and information about the procedures.

Muscle group	**Types**
Flexors	Psoas Major, Psoas Minor, Iliacus, Pectineus Rectus Femoris
Extensors	Gluteus Maximus, Semitendinosus, Semimembranosus, and Biceps Femoris (long head)
Adductors	Adductor Magnus, Adductor Longus, Adductor Brevis, Gracilis and Pectineus.
Abductors	Gluteus Medius and Tensor Fascia Latae.
Internal rotators	Tensor Fascia Latae and Gluteus Minimus.
External rotators	Gluteus Maximus, Gemellus Superior Gemellus Inferior, Obturator Externus Obturator Internus, Quadratus Femoris Piriformis.
Therapy	**Information**
Anti-inflammatories [4]	Also called non – steroidal anti-inflammatory drugs (NSAID) Mainly treats medium level pains which are inflammation-related Used as first-time treatment with a combination of strengthening training.
Physical therapy [5]	A non-invasive approach to treatment when surgery is not needed. The aim is to strengthen muscles, reduce associated inflammation, sustain joint motion and increase flexibility.
Physical fitness [6]	To maintain a healthy weight around the hip region.
Injections [7]	Prescribed for hip pain relief and diagnosis on the root source of pain.
Diagnostic	Numbing drugs are injected into the joint, a rapid relief will aid in confirming the joint as the pain source. If there is no relief observed, then further consideration will be required for a possible cause.
Pain relief	Intraarticular injections –ultrasound-guided cortisone is injected through to the joint which provides relief. Psoas injection – carried out under ultrasound, often deployed when symptomatic psoas tendon is the diagnosis and exists outsides the hip joint. Trochamatic bursa injections – prescribed when bursitis exists outside the hip and no form of therapy has provided relief.

Along with the family disease history, the known causes of arthritis include bursitis, hip fractures, hip labral tear, inguinal hernia, sprain and strains, tendinitis, meralgia paresthetica, sacrolites, Legg calve-perthes disease [8], leukaemia, osteoporosis, bone cancer [9] and synovitis [10]. The common forms of arthritis in the hip joints are Juvenile idiopathic arthritis (JIA), Osteoarthritis (OA), and Septic arthritis. Juvenile idiopathic arthritis (JIA) is more common in children. Most research revolves around the thoughts that a trigger virus causes this disease and coupled with genetic tendencies on children [2, 11]. Interested readers on the specific details on the JIA are referred to works by Ravelli et al, [12] and Thatayatikom and De Leucio [13].

The conventional approach has proven to be successful in relieving swelling and pain. For effective management of this condition, a physician determines the best method to be utilized. As can be seen in Table 1, when the therapies are applied but fail to reduce the hip pains to a suitable level this leads to poor quality of life with continuous unbearable pain. Lei et al, [14] presented the case of a 59-year-old man that had an intertrochanteric fracture in the left femur and previously had left hip fusion. The surgery was successfully carried out through the guidance of mixed reality and 3D printed scaffolds technology as a 3D anatomical structure that can overcome the pitfalls of conventional 2D data. Indeed, it provides a novel technique for real-time implantation. Furthermore, two cases involving 3 complex hip defects where hip arthroplasty was studied by Hughes et al, [15]. Through 3D printing, a life-size 3D model was fabricated for the actual three hips acetabular reconstructions which was successfully planned, trialled, and enhanced surgical precision and management with reduced complications. This proved to be impressive based on the accuracy and cost-effective technique for both cases and increased use is encouraged to be applied in future medical practice and academic pieces of training.

In our previous work, Okolie et al, [1], a review for understanding the fundamentals of 3D printing with bioprinting techniques was provided. Further, Bagaria et al, [16] and Aimar et al, [17] presented an overview of modern developments in 3D printing for orthopaedic applications, the drawbacks, and the prospects which make this field exciting. The objective of this review paper is to provide a sufficient understanding of modern biomaterials that can be utilized in 3D printing for hip implant design and orthopaedic applications. Hence enhances the level of hip implant functionality for the produced scaffold which aids in hip tissue regeneration. Herein, the area of emphasis is the selection of suitable biomaterials, their long-term performance, and holistic feasibility.

2. Influencing Factors for Surgeon's Decision on Hip Joint Surgery

The current methods for treating hip pains include the following which are hip surgery, exercise routines, and medications for hip pain treatment. The medicines aid to ease the pain, inflammation relief, reducing bone loss and modification of the duration of inflammatory disease as well as joint damage prevention. The exercises routines are however the best means to help the hips treatment. Exercise aid in maintaining varying ranges of motion and conditions/strengthens muscle supporting the hips. Tendon and muscle stretching of the joint surroundings can aid ease some hip-related pains and prevent future risks of injuries. More examples are bridging, heel slides, hip abductions, glute, quad, stomach, and squat exercises.

On the other hand, hip surgery involves hip replacement and an alternative surgical option for hip arthritis. When the treatments and medications applied do not soothe the hip pains to a suitable

level, this surgery for repositing or replacement of the hip joint may be the next solution. The hip surgeries that are currently commercially used include:

- Hip resurfacing – this is for young and active people; this is an alternative to total hip replacement. In contrast to total hip replacement, hip resurfacing does not need femoral head removal and can be trimmed and cemented to a smooth ball of ceramic or metal material. Instead, the destroyed femoral head is repositioned and attached to the ball covering that suits the socket [18].
- Total joint replacement – this is a renowned hip surgery, for this procedure, the destroyed hip is taken out and replaced with a prosthesis of either ceramic, metal, or plastic components. After the knee, the hip is the most replaced body part. Hip replacement is the gold standard solution when irreplaceable joint destruction disrupts its function and creates constant pain that cannot be healed by the conventional treatment [19, 20].
- Osteotomy – this is a major surgery in which the destroyed area of the hip is taken out and the joint is repositioned to fix any deformity and improve the function and alignment. An osteotomy will be suitable for a patient with arthritis in the hip joint, this may be used for young people at the early stages of OA [21].
- Hemiarthroplasty- this procedure replaces half of the hip joint (femur head) while keeping the other half intact. Usually carried out to replace the femur head when fracture disrupts blood supply, the removed femur head is replaced by a prosthesis [22].
- Arthroscopy – this is a minimally invasive surgery performed by adding a light and narrow device through little incisions in the skin on the joints. Arthroscopic surgery has since been in use to correct the knee joints and only recently started to be used in hip joint correction such as labral tears. The importance of most arthroscopic procedures remains uncertain [22].

About a quarter of the UK population needs a clinical check for MSK (musculoskeletal) conditions to be carried out at least once a year and above 25% or more of all the surgical routines handled by the NHS (National Health Services, United Kingdom) are mostly based on MSK conditions. There is currently a large variation in the rate of hip surgeries between the developed countries which influences a surgeon's decision. The reasons for these variations according to a study by Mailefert et al, [23] includes certain factors which are classified as:

- Univariate analysis – for evaluating potential pointers for the surgeon's decision and the key factor is the duration of the diseased joint post-diagnosis.
- Multivariate analysis – multiple variables were used for identifying potential factors that were based on the absence or presence of cardiovascular comorbidity (existence of more than one illness in the same body), joint space narrowing size, and quality of life.

Although the study by Mailefert et al, [23] was carried out in one country (France), there seem to be some similar characteristics with other countries [19]. The differences between the countries in the rate of hip joint surgeries, according to the study, are not based on intercountry differences in terms of the perception of the severity ranking at which these surgeries were appropriate. There is a possibility that factors such as the willingness of patients or patients' expectations, patient to the doctor ratio, surgery access, and health service policies might play a role. Another study by Huynh et al, [24] seems to agree that factors that affect the decision making are related to a higher level of symptoms and the level of severity from radiography.

3. Hip Biomechanism in Gait and Stress Distribution

Hip biomechanics deals with the understanding of both stress and strains acting on the hip. When the hip tissue/muscle is subjected to loaded forces from varying body movement forms such as running, walking, or standing, they undergo deformation either through compressing or stretching. For an efficient replacement of cells that forms tissues, they must be subjected to the appropriate stress, and the higher the frequency of the appropriate stress, the more efficient the metabolic process of the cells become, and the cell gets healthier. Gait analysis is a clinical technique utilized in analysing body movements. Gait analysis cannot be done in isolation, therefore must be performed in each direction and this makes the hip coordinates vital [25]. Gait analysis and evaluation are rapidly becoming a necessary tool for the provision of a qualitative description of a patient's gait variations. Not only can it be used for a proper diagnosis of walking disorders and source of hip pains, but it can also be used for treatment selection and analysis. While the kinematic and spatiotemporal (space-time) properties are mostly utilized in describing muscle and movement activity, kinetic parameters are rarely evaluated, although they provide an insight into the powers and moments that propel human walking. As a result, the kinematic parameters can connect abnormal motions to underlying bone misalignment and muscle malfunction [26]. Furthermore, the predictability of the hip joint centre locations which is essential during surgery is known to be different across the varying functional methods which pose a challenge [27]. Most novel experiments are designed to solve these challenges with the hip biomechanics, however, there is still a failure in defining the coordinate system. This makes the validation between research unreliable and an unnecessary challenge in predicting the experimental results to clinical facts [28].

In the past, it had been believed that the hip joints act as the fulcrum for the lever system. Studies have been carried out in the past to understand the partial centre of gravity, location to the major planes in the body, the effect of stress and joint pressure on the bones, abduction muscle function, and its relationship between the gluteal muscles angle of application to the joint pressure and the greater trochanter and values were derived from mathematical calculations although the basic information was inaccurate [29-31].

Assumptions which were made for calculation purpose are the following:

- The body mass focuses on one place or point also known as the centre of gravity.
- The line that links the centre of gravity to the earth is termed the line of body weight [32].

Figure 2 and Figure 3 below provides a graphical illustration of the assumptions stated above.

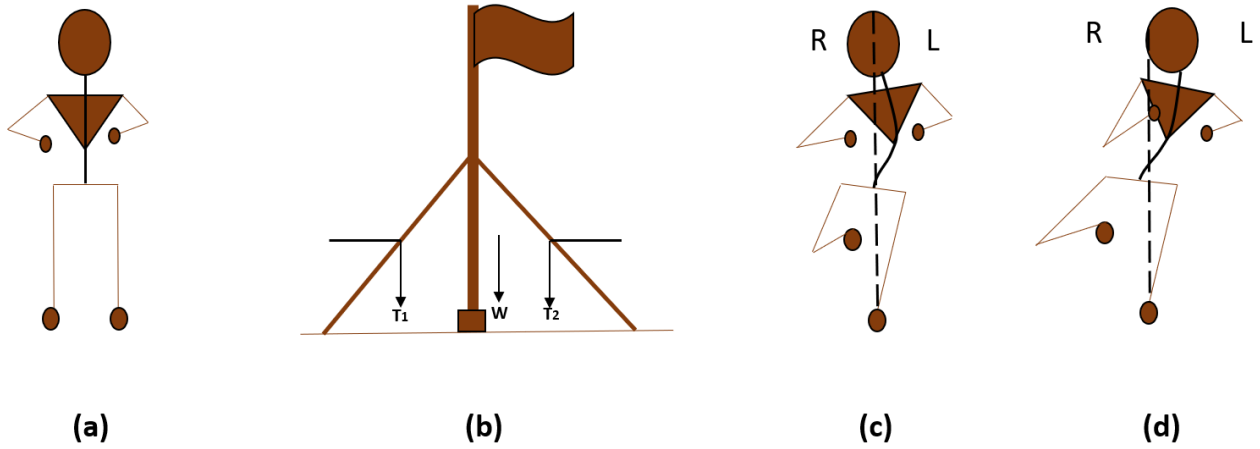

Figure 2 (a) Maintains balanced coordination of muscle groups (b) a free supporting stand weight is greater than the pole and flag weight (Pressure on the stand = weight of flag (w) + weight of poles (T_1 and T_2)) (c) when the whole body is standing on one foot, the bodyweight line splits the body into two equal parts (d) when one leg moves from the body centreline over the other (adduction), the body moves to regain equilibrium. Adopted from Ref. [32] and redrawn

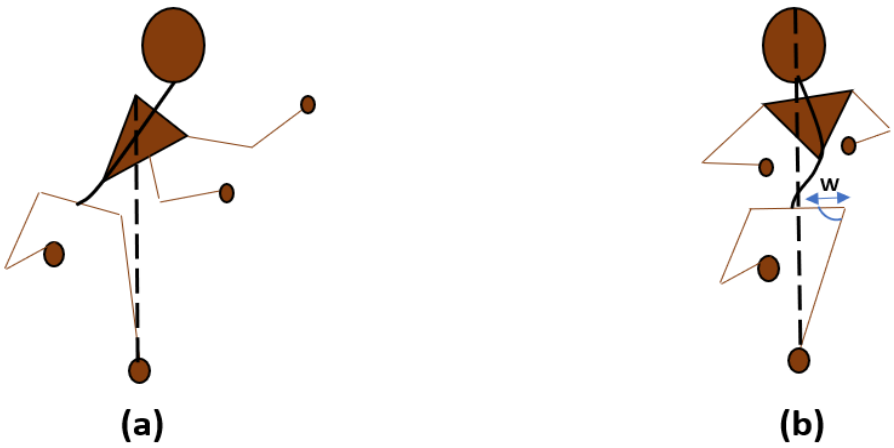

Figure 3 (a) There is a relationship between the hip joint and bodyweight line that can easily be changed (b) A representation of related forces acting around the hip joint. Adopted and redrawn from Ref. [32].

Although this remains the case, the bulk of the body weight mainly relies on the hip joint especially in single-leg support. An ideal scaffold should be able to fulfil this role. Clinical studies confirm that issues such as joint degeneration are not directly determined by bone structure or anatomy abnormalities [33, 34]. Herein, from cadaveric specimens, the detailed evaluation obtained confirms that deformed conditions and soft tissue lesions occur more than symptomatic degradation of hip function [34]. This finding leads to a need to understand the rationale behind the demands various activities place on the hip such as lifestyle, vocation, sprints, and capability of the joint functioning asymptomatically. Hip movements during gait mainly pertain to the femoral

movement as regards the pelvic region close to the hip joint centre. The range of motion for hips is larger than the normal three planes (Abduction of 0 to 45^0; Adduction of 45 to 0^0; Extension of 115 to 0^0) which this enables a 50^0 rotation, 70^0 adduction or abduction and 120^0 flexion or extension of 10^0 (displayed in Figure 4). Although these ranges are at maximum angles that is safe for the hips, these ranges are sporadically achieved during daily living activities. Therefore, the muscles subjected to these regular activities account for the provision of all rotational stability.

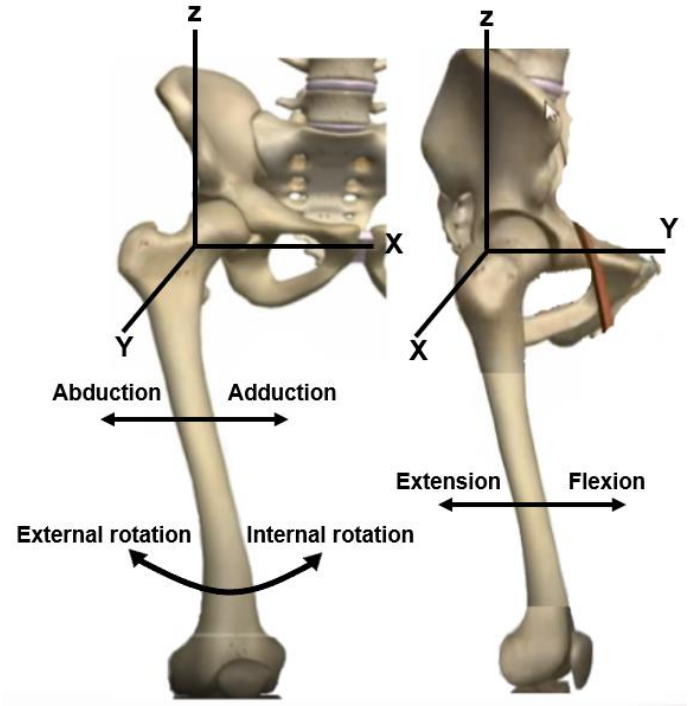

Figure 4 Rotation axis encircling the hip joint centre and the movement generated from the hip joint. Extension and flexion appear in the longitudinal plane surrounding the frontal/y axis. The movement of adduction and abduction appears in the frontal plane along the longitudinal /x-axis. The external and internal rotation appears in the transverse plane along the vertical/z axis. Adopted and redrawn from Ref. [35].

In determining the state of a healthy or diseased adult hip, an important factor to consider is the contact stress distribution in the hip joint [36-39]. A realistic approach to record contact stress is through direct measurement. The stress distribution in the hip is firstly measured directly through a measuring device by an in vitro process and subsequently by an in vivo process. This technique provides a thorough understanding of the features of a pristine hip. Through these methods, distinct areas can be measured instead of a general view [39, 40]. Clear models can be adequately utilized in evaluating contact stress distribution in regular surgical arrangements provided the cases are in related circumstances [41]. Also, it is worth noting that there will be differences between implant surfaces or transducers from the natural ones in terms of natural fluid film lubrication and natural cartilage microstructure.

Ipavec et al, [42] made certain assumptions prior to the modelling which include that the resultant hip forces rest on the forebody plane and that the articular cartilage indicates preferable elastic functionality where the dimensions repeat itself at regular periods, therefore cosine function is used for stress distribution. The study focused on a generalized model for a random direction for

the resultant hip force as ascertained in a state of motion. The centre of the right hip matches with the origin of the cartesian coordinate system which is aligned for the x and z-axis to lie in the anterior plane via the centre for the two hips. The y-axis stands in the rear – fore direction, the z-axis is perpendicular, and the x-axis direction towards the sideway–mid direction. The centre of the femoral head is the point that the resultant contact force for the hip origins [42].

There was an assumption that any tangential stress emanating from frictional forces is negligible when compared to correlated regular stress [43]. When the sufficiently lubricated femur, smooth and acetabular surfaces are roughly compatible, spherical, and are often used in intensely low friction coefficient (≈0.001) justifies this assumption [44].

Utilizing the spherical coordinate approach with origin in the centre of the articular sphere, the radius vector at a chosen point on the femoral head (articular surface) which is given by

$r = (rcos\emptyset sin\vartheta, rsin\emptyset sin\vartheta, rcos\vartheta)$, where r; the radius of the articular sphere, $\emptyset$; azimuthal angle and ϑ; polar angle. While the resultant hip force is provided by the vector

$\mathrm{R} = (Rsin\vartheta_R cos\emptyset_R, Rsin\vartheta_R, Rcos\vartheta_R)$, where R; the magnitude of the resultant force, ϑ_{R}; inclination angle in the direction of the resultant force to the vertical and $\emptyset_{\mathrm{R}}$; the rotation angle in the direction of resultant hip force to the horizontal axis.

The integration of contact stress over the weight-bearing area S gives the resultant hip force R.

$$\int sPds = R \tag{1}$$

With $ds = (sin\vartheta cos\emptyset, sin\vartheta sin\emptyset, cos\vartheta)r^2 sin\vartheta d\vartheta d\emptyset$

From the assumption that the radial stress on the hips articular surface is directly proportional to the radial strain of the cartilage surface, this radial stress (P) is also proportional to the cosine of the angle between the stress pole position (γ) and the articular surface [45].

$$P = P_0 cos\gamma \tag{2}$$

where P_0; stress value of the pole. The cosine of the angle **γ** can be expressed as

$$cos\,\gamma = sin\boldsymbol{\Theta} sin\vartheta cos\Phi cos\emptyset + sin\boldsymbol{\Theta} sin\vartheta sin\Phi sin\emptyset + cos\vartheta cos\boldsymbol{\Theta} \tag{3}$$

where **Θ**; a polar angle which the polar angular displacement from the vertical axis and **Φ**; azimuthal angle for the description of polar angular displacement in the direction of the horizontal plane on the x-axis in an anticlockwise rotation.

Where the weight-bearing area (S) can be described as the region of the articular sphere limited by the geometry of the acetabulum and the stress pole position. It is solely the positive stress values that are of interest. The centre boundary of S which relies on the pole stress position determines the line which stress Eqn (2) disappears and leads to

$$\cos\gamma = 0 \tag{4}$$

Arising from Eqn (4) the centre limitation of the weight-bearing area is determined, and this comprises all points within the radius far from the pole stress. This is taken as the articular sphere intersecting the plane going through the sphere centre. Therefore, the weight-bearing area is bound by the intersection of the articular sphere. The stress distribution at whichever body position provided can be evaluated by deciphering the three points of the vector in Eqn (1) and they are:

$$\vartheta_R + \boldsymbol{\Theta} \mp arctancos^2(\vartheta_{\boldsymbol{CE}} - \boldsymbol{\Theta})\pi \pm \pi 2 - \vartheta_{\boldsymbol{CE}} + \boldsymbol{\Theta} - 12\, sin\big(2.(\vartheta_{\boldsymbol{CE}} - \boldsymbol{\Theta})\big) = 0 \quad (5)$$

$$P_0 = 3R2r^2 cos\,(\vartheta_R + \boldsymbol{\Theta})\pi \pm \pi 2 - \vartheta_{\boldsymbol{CE}} + \boldsymbol{\Theta} - 12\, sin\big(2.(\vartheta_{\boldsymbol{CE}} - \boldsymbol{\Theta})\big) \quad (6)$$

$$\Phi = \emptyset_R\ or\ \Phi = \emptyset_R \pm \pi \quad (7)$$

where $\vartheta_{\mathbf{CE}}$; Wiberg angle by the vertical body axis [46].

From the Long and Rack [47] study, the analysis shows that in a situation where the pole of the stress distribution is positioned in the weight-bearing area, the position of maximum stress (P_{max}) concurs with the position of the pole and in this situation P_{max} equals P_0 (**Figure 5A, C, D**). However, when the stress pole is outside the weight-bearing area, the stress within the weight-bearing area is highest at the portion of the weight-bearing area nearest to the pole (**Figure 5B**).

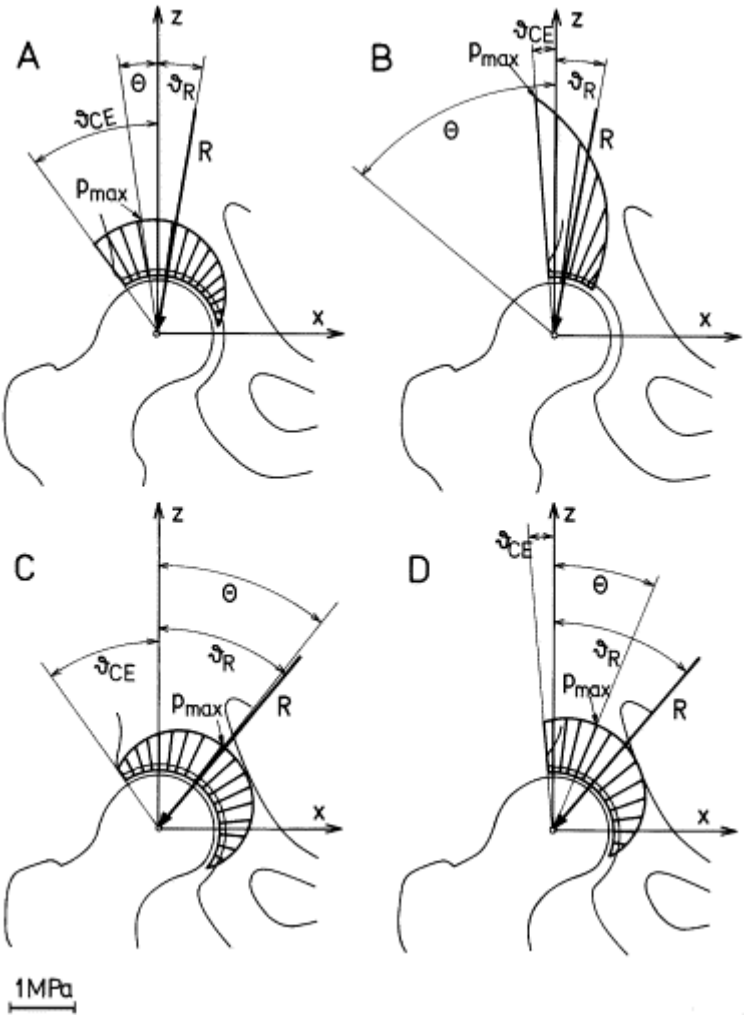

Figure 5 The evaluated stress distribution in the hip point at varying ϑ_R and $\vartheta_{CE.}$ (A) $\vartheta_{CE} = 35°$, $\vartheta_R = 10°$; (B) $\vartheta_{CE} = 5°$, $\vartheta_R = 10°$; (C) $\vartheta_{CE} = 35°$, $\vartheta_R = 40°$; (D) $\vartheta_{CE} = 5°$, $\vartheta_R = 40°$. With the values of the other parameter being: $\emptyset_R = 0$, r = 2.6cm and R = 2000N [41].

The value of **Θ** was resolved by the Newton iteration method and the hip resultant force R can be solved in varying phases of body posture with a total hip implant, R, ϑ_R and $\emptyset_R$ values are

determined by the coordinate system attached to the pelvis which leads to the evaluated stress distribution [48] and Figure 6 depicts the loading of the acetabulum. Although it is worth noting that it is solely the P_{max} value that is necessary, the stress shape distribution is also important [42]. The P_{max} value should be considerably low when the bodyweight is low as well and when the radius of the articular sphere is large.

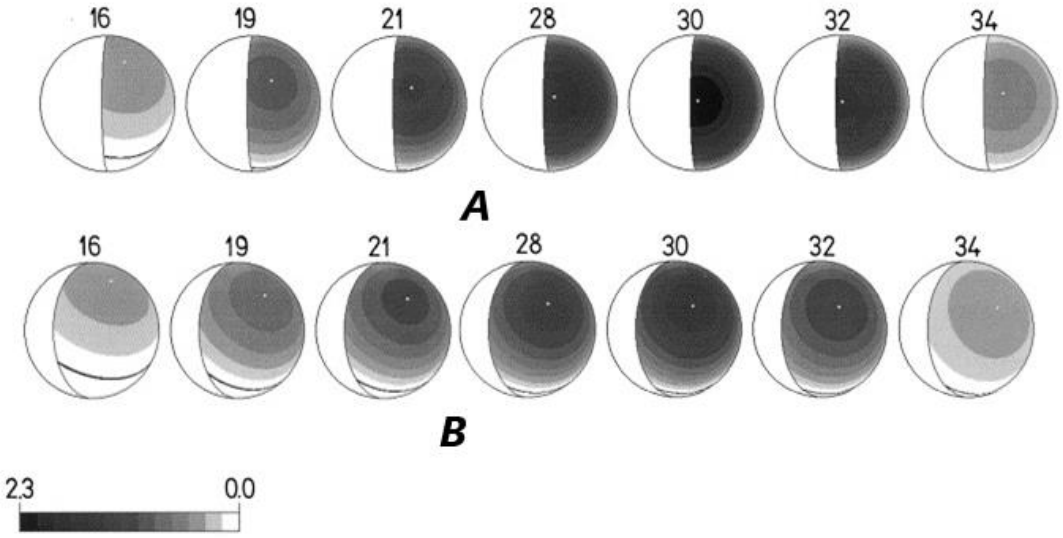

Figure 6 Distribution of contact stress on the horizontal plane in the pelvic coordinate system for two CE angles; (a) $\vartheta_{CE} = 5°$ (b) $\vartheta_{CE} = 35°$. The choice posture of gait (spotted by the numbers) is shown here. The stress measurement unit is $\frac{B\omega}{r^2}$ (BW = bodyweight force). The white dot marks the stress pole location. Adopted from Ref. [35] and redrawn. Adopted and redrawn from Ref. [35].

The importance of contact stress in the hip is to sustain the hip joint health maintenance and to ensure a pain-free movement. Any occurrence of odd contact stress is presumed to be the main cause of hip osteoarthritis. Although other factors of bone abnormalities like the impingement of the fermoacetubular and dysplasia tend to boost the disease growth. Understanding the distribution of stress as it contacts the cartilage surface of the hip joint during day-to-day functions is needed for a holistic knowledge of joint disease pathology and physiological operations. When performing the surgery and the overall handling of the implant/prosthetics, abrasions are bound to occur at the surface, this will lead to intensified stress at the abrasion points and create a spot with potential for crack growth propagation. From Figure 7, a depiction of the havoc level is shown and can be caused by a poorly designed implant [49, 50]. For proper utilization of an implant prior to application, the design safety with respect to mechanical behaviour should be ensured by a comprehensive analysis at varying loads. Most of the literature reviews analysed static finite element analysis (FEA) using loads with dimensions correlating to body weight [46, 51, 52].

Figure 7 Failure of an artificial hip prosthesis [53].

The key objective of hip implant design is to possess a displacement, wear, and displacement with an excellent fatigue life [53, 54]. For optimizing the ideal biomaterial and geometry process for the hip replacement implants, mechanical tests are advised to be utilized to ensure novel materials can guarantee the required resistance to the expected bodily load during static and gait postures. Colic et al, [54] studied the finite element modelling on the static loading of hip implants by stress analysing the hip implants doing various forms of motion including in extreme situations tripping. The loads are evaluated in accordance with experiments carried out by Bergman et al, [55] on patients weighing 860 N in an age group of 25 years. The analysis considered the motion on the flat surface simulation with the biomaterial for Ti6Al4v, CoCrMo, and 316L stainless steel-based ASTM guideline ASTM F-138 for Stainless steel ASTM F-75, F-799, F-1537 ASTM F-67 (ISO 5832/II) for cobalt, F-136 (ISO 5832/II), F-1295 for titanium [47]. From the von misses stress calculated, the maximum stress values were observed to be where the stress concentrations are expected. The study found FEA useful in predicting the mechanical properties and behaviour of implant models from the numerical analysis obtained the cross-section of the implant's hole matches to the hole location of the real implants.

Huiskes et al, [56] studied the interface stresses in a replaced hip joint through FEA for transmission of loads at the femoral head, this was based on the concept of surface replaced other than focusing on an individual patient case [57]. The model developed was split mathematically into smaller blocks with the nodal points being connected. The strains and stress values are the nodal points that are resolved by a computer program by sets of the equation. From the result an external force used as a distributed load on the outer cup leads to a peak compressive stress of 1.6×10^{-5} MPa/N within the cup, there was a transformation of the extreme load to bearing stress with a peak level of roughly 3.7×10^{-2} MPa/N and below it was bending stress in the region of 2.0×10^{-3} MPa/N. Although this cup behaves as an elastic shield, a section of the outer load was moved directly to the foundation of the cement (Figure 8) with a peak compression strength of roughly 9.4×10^{-4} MPa/N.

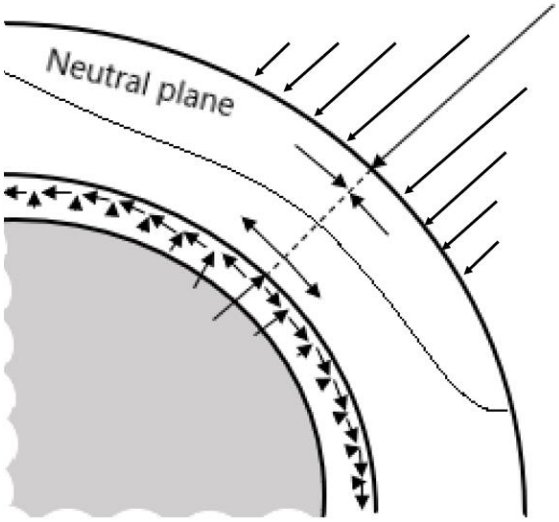

Figure 8 Pictorial demonstration of local load movement technique Adopted and redrawn from Ref. [56].

When a force is acting on the pelvis and femur while standing on two legs, a joint reaction force (JRF) act at the hip joint centre. Herein, the femur exerts force to the pelvis and the pelvis will subsequently exert an opposite and equal force on the femur as similar to Newton's third law. Although conventional studies have focused on 2 dimensional analyses, the musculoskeletal system is 3 dimensional. The illustration in Figure 9, displays that the JRF applied on the femur is in 3 dimensions. There are 3 mutually perpendicular forces exerted on the femur. F*d* acts from a distance, F*l* acts laterally and F*p* acts posteriorly.

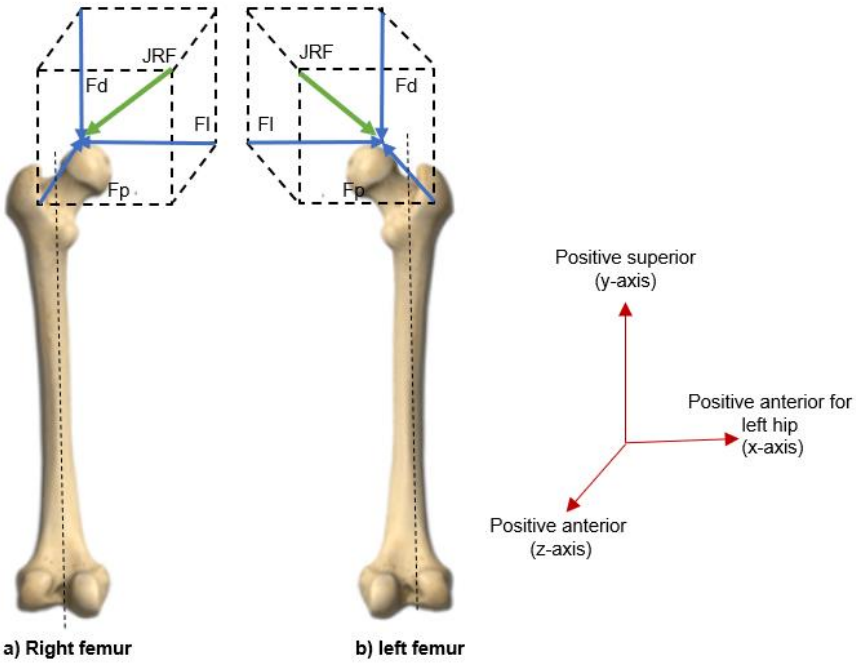

Figure 9 The joint reaction force applied on both (a) right and (b) left legs. Adopted from Ref. [58] and redrawn.

The total JRF is the resultant of all the forces exerted at the hip joint is derived through.

$$JRF = \sqrt{Fd^2 + Fp^2 + Fl^2}$$

The magnitude and direction of the JRF ch based on the activity. It has been estimated that during normal walking the JRF magnitude at the hip is 300% of body weight while during jogging, JRF is measured at 500% of the body weight. To describe the force exerted on the limb in 3 dimensions, it is vital to establish a coordinate system and the anatomical orientation that connects them. When a coordinate system is established at a positive z-axis direction being anterior, the positive z-axis direction is superior and the x-axis direction is medial, this makes F*p* and F*d* will be negative for the right and left femurs. In the case of the left femur, the force is positive along the x-axis which acts laterally while for the right femur, the positive force in the x-axis acts across the centre. On the other hand, F*l* which acts laterally is going to be negative for the right femur while the left femur will be positive.

The peak shear stress in the upper cup section on the subplane ($\Theta = 0^0$) and at the top of the head is a coronal plane ($\Theta = 90^0$), resulting in 5.4 x 10^{-4} MPa/N and 5.8 MPa/N respectively. There is an indication for the pattern that a substantial part of the outer hip load is moved to the bone through the upper-cup-rim region.

While in the normal hip the large portion of the load is directly conveyed from the femur head to the medial cortex as stated in Brown et al, [45] at this point the foremost part of the head is partially avoided which thus leads to stress–shielding. From this study [56], a hypothesis was made that initiation of failure from elevated initial stress is not a major denominator but instead the failure propagation from a combination of both biological phenomena (gradual bone resorption) and mechanical effects (stress and micromotion increase) is the primary concern. Based on this study, it is perceived that the early failure of replacements could be caused by resistivity to reduce stability in comparison with other implant types. It was advised that a prosthetic design should be analysed based on its potential for failure propagation instead of solely initiation.

A scaffold must be completely attached to the bone for proper functioning and easing pain after surgery from loosely fitted implants. Currently two methods for ensuring this attachment which is through cementless and bone-cement applications. For the cementless approach, the whole hip is placed directly in the layer arranged in the skeleton while the bone-cement uses a fixation such as polymethyl acrylate (PMMA) on the implant to the skeleton (From Figure 10) [59].

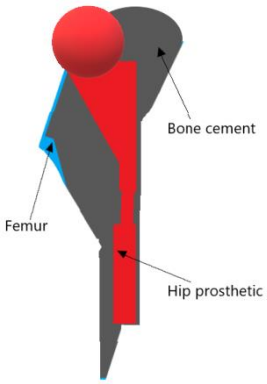

Figure 10 A cross-sectional view of the bone cement technique. Adopted from Ref. [59] and redrawn.

Kayabasi and Erzincanli, [59] studied finite element models and analysed body cementing techniques. This study was carried out in a dynamic loading condition. For their research, four varying shapes of stems were designed and the static and dynamic behaviour including the fatigue life of the created stem shapes were studied. The analysis of stem shapes was applied in titanium alloy (Ti-6Al-4V) and cobalt chromium materials. From the study, it was observed that all stem shapes overcame fatigue failure however the results from the simulator suggest that stem-2 will fail in bone cement and stem 2 was not able to resist fatigue failure on static and dynamic loading applications. The best stem shape was stem 3 which performed well under dynamic loading. A fundamental workflow for this study is depicted on (Figure 11) [60].

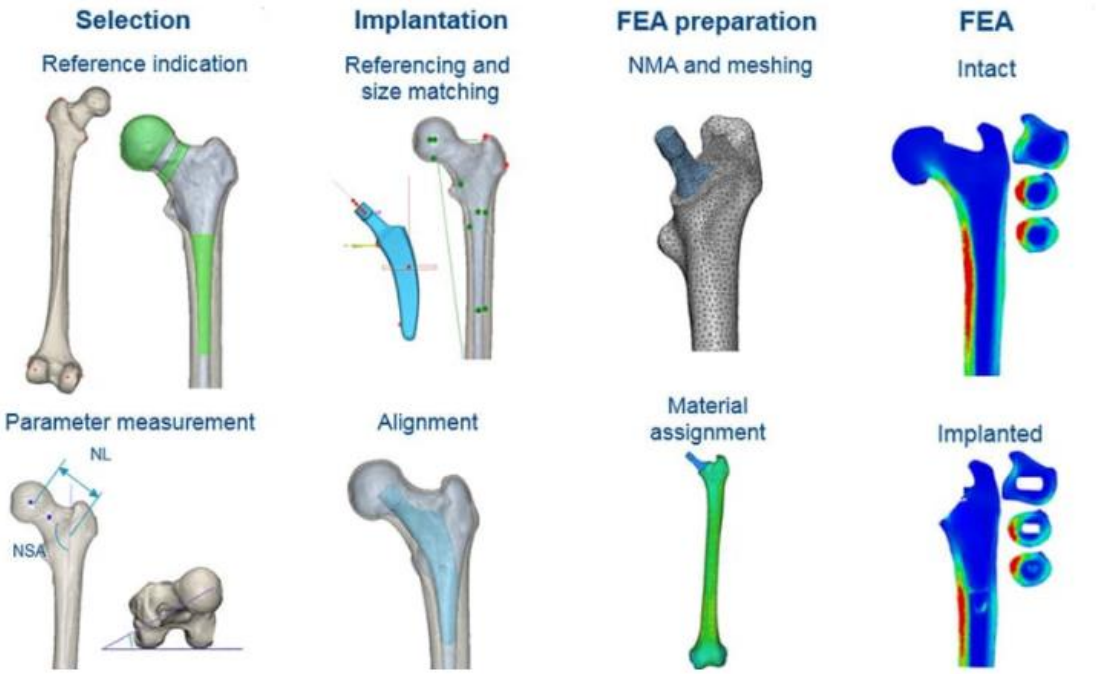

Figure 11 The basic workflow for using FEA models for implantation (NL and NSA are the neck length and neck shaft angle respectively) [60].

Lamontaigne et al, [61] researched the mechanism of the lower limb joint after hip surgery for standing and sitting tasks. A hypothesis was made which suggests that the powers and extensor moments become reduced after operating in comparison with healthier joints. There was a noticeable source of concern regarding a decreased force moment at the operated hip leading to the assumption that the unoperated hip is being overloaded leading to early signs of wear and tear of the unoperated knee and hips. Their study observed that the hip joint operated patients had reduced hip flexion at both an operated and non-operated lower limb for tasks. There was also an improved hip abduction. The operated patients also displayed a reduced hip extension moment, reduced extension support moments, and a small generation of power when sit-to-stand and absorption when stand-to-sit. These confirmed the original hypothesis, and it was concluded that the hip-operated patients showed a stand-to-sit and sit-to-stand kinematics and kinetics which was different from those with healthier joints and those that were non-operated. For hip replacements, the stress shielding, uniform stress distribution and stability effects are vital, or else the replacement cause pain in the thigh region. Another factor that may hamper the progress of hip replacement is

bone loss, therefore the geometry of the implant must be tailored to closely mimic the properties of the hip bone tissue which leads to reduced bone resorption with stress shielding. An approach to this solution is the design of porous 3D printed hip implants that cover the general activity stages of the implant development which includes concept generation, multiscale mechanism of the material, additive manufacturing, modification of the material structure, and performance assessment tests of the implant. The study by Zhang et al, [62] described a novel procedure for using accurate coordinates for precise implantation in hip resurfacing through reverse engineering and 3D reconstruction. Another study by Wang et al, [63] on the time for weight loading in the 3D printing patients was less than the traditional hip replacement implants. Furthermore, the post-surgery Harris hip score which is used to assess the result of hip surgery was higher in 3D printed implants. This signifies that 3D implants are the closest to the patient's anatomical structures and allow for improved coordination to human biomechanics.

4. 3D Printing for Orthopaedic Applications

There has been a significant improvement in bioimplants in the current decade where a wide variety of fabrication methods are being applied. The classification of these methods may be done in stages and the general classification is the prefabrication of production and post-fabrication focusing on surface finishing. The conventional fabrication processes such as compression moulding, casting, and sintering are sustainable and suitable for bioimplant fabrication with acceptable properties and improved functioning [64-67]. Currently, improved technologies for bioimplants utilize several processes that have the potential for accurate controllability which aids in obtaining a unique design.

In the human body, biological functionality is complicated and with huge differences in biomechanical properties from bone to bone. Such instance is the elastic modulus of the critical section of denser bones varying from 16-20GPa, this is a magnitude greater than the trabecular bone. Therefore, it can be understood that certain biomechanical errors are bound to happen between the recently implanted parts and closer bones with similar properties. Furthermore, from a medical perspective, these biomechanical properties may differ greatly from the body to the body. Hence, a need for fabrication techniques that can meet specific geometry for a precise injury/defect is justifiable. Additive manufacturing (AM) also often termed as rapid prototyping (RP) technology, is a common name for the fabrication technique depending on the type of surface development. From its emergence in the 1980s, this technique has been garnering research interest in the sector of manufacturing [64-67]. The conventional techniques for fabricating scaffolds are solvent–casting, particulate leaching, gas foams, fibre meshes/fibre body, phase separation and melt moulding. The limitations currently being faced are poor pore size precision, geometry, interconnectivity level, and mechanical strength. Further limitations include poor cell distribution due to anomalies when cell seeding is done manually. This becomes an issue since a high degree of precision while arranged in accordance with required and needed tissues such as osteoblast of tissues or the alignment of the endothelial cells [68]. In contrast to conventional implants, 3D printed implants can be tailored to several forms of diseases [67, 69]. With the possession of excellent design ability, 3D printed implants can solve certain challenges where it is complicated to insert and repair the different conventional implants together [70, 71].

The 3D printing technology is proving to be a useful tool for the fabrication of tissue scaffolds with a great level of accuracy and precision, producing well-detailed 3D scaffolds in biomimicry. The various techniques for 3D printing currently utilize a layer-by-layer process and they include the following: fused deposition modelling, selective laser sintering, and stereolithography. These techniques have been utilized in the fabrication of scaffolds that vary in sizes from millimetres to nanometres on the issue of reproducibility by the 3D printer. Bracaglia et al, [72] suggested that the introduction of chemical and physical gradients in scaffolds by integrating them enhances the functionality of the tissue engineering structure whilst also taking account of various 3D fabricating techniques to produce the scaffolds. A pictorial representation of the 3D printing process of scaffolds is displayed in Figure 12.

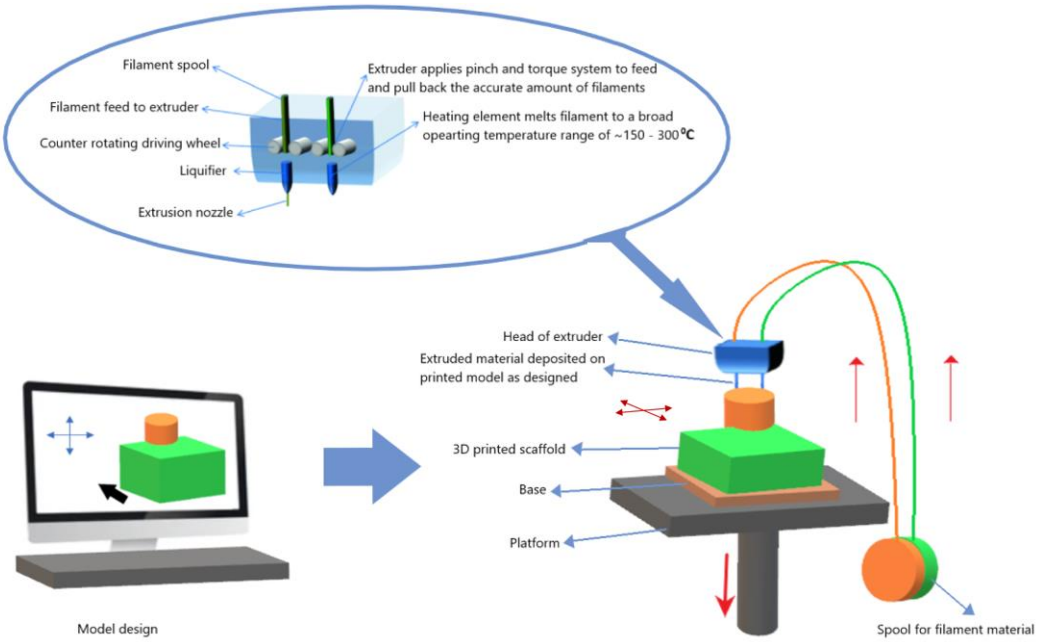

Figure 12 Basic working flow procedure of 3D bioprinting. Adopted and modified from Ref. [67].

What is also worth noting is that the terms additive manufacturing, 3D printing, and free form fabrication have been used interchangeably and are now becoming synonymous this past decade. The pros of 3D printing include the capability of bio mimicking extracellular matrix (ECM) and the ability to fabricate adaptable scaffolds regardless of the shape complexities for the cell distribution to be done homogenously. However, the major limitation is the accessibility of suitable biomaterials that possess the stability and necessary properties for the 3D printing of scaffolds. An additional limitation is a time required for scaffold fabrication and that time increases when the design becomes more complex and accurate [73, 74]. It is worth noting that 3D printers utilize varying powdered mixtures and materials, the size of the structures can easily affect the printability of the scaffold for most materials in 3D printing. For a material to be a viable choice for tissue regeneration, it should be printable with a great degree of reproducibility from 3D printing. These materials should be affordable, effective, and malleable to create the morphology required for the designed scaffold. Within the previous 4 decades, various 3D printing techniques have been suggested due to the processing approach. However, the ASTM/ISO 52900:2015 standard [75, 76] designated over 50 different 3D techniques which can be grouped as (i) Binder jetting (ii) Direct deposition (iii) Material

extrusion (FDM) (iv) material jetting/inkjet (v) powder bed fusion (SLS) (vi) sheet lamination (vii) stereolithography (SLA, DLP). For this review, the emphasis is on direct 3D techniques which usually utilize several forms in atmospheric conditions such as fluids capable of solidifying, nano fine powdered particles, layered sheets, and flexible filaments.

Currently, 3D printing (3DP) products do not have a formal legal standing that clarifies them both for implantable and non-implantable devices. Using Europe as the base reference, the whole 3D-printed products can be classified as customized tools under the regulation (EU) 2017/745 of the European Parliament and of the council of 5 April 2017 [17, 77]. It states that: *"any device specifically made in accordance with a written prescription of any person authorized by national law by virtue of that person's professional qualifications which gives, under that person's responsibility, specific design characteristics, and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs".* Varying from mass-produced devices *"which need to be adapted to meet the specific requirements of any professional user and devices which are mass-produced by means of industrial manufacturing processes in accordance with the written prescriptions of any authorized person shall not be considered to be custom-made devices"* [78]. In fact, manufacturers of customized tools will only be assured through a commitment of conformity assessment methods whereby the tools will comply with the performance and safety requirements [79].

Each technique uses a specific material form to fabricate a scaffold. However, specific materials foam to fabricate a scaffold. However, specific materials prepared in the form of choice for 3DP, it does not certify the material is 3D printable due to printing suitability in the right direction, therefore it is imperative to enhance the bonding strength in the interlayer of the fabricated material. As a result, the key aspect during object design for 3D scaffold production is dependent on the current material types at the beginning stage. Furthermore, the emphasis of incorporating 3D printable novel scaffolds and efficient technologies should be discovered in the future to transform the current biomaterial groups into a suitable feed material for 3D printing purposes. For example, a gelatine gel will cure when the temperature does not favour the growth of cells efficiently. This provides a path for novel method developments and mechanisms that requires simpler gelatine solidification e.g. a new hybrid method and enzymatic cross-linking of hydrogels and cells at very low temperatures [80, 81]. The most regularly used 3D printing techniques include inkjet direct printing, bioprinting, powder deposition printing (FDM), laser-assisted printed (SLS), and stereolithography (SLA) Therefore, the study aims to discover methods for novel biomaterial fabrication through 3D printing that can be used in hip implant design, applications and is a biocompatible tissue scaffold. Before the AM technique, 2D slice data is obtained from the designed surface of 3D structures. Required materials are fabricated through the combination of material layers [82]. As opposed to conventional fabrication techniques that take out materials from a whole, AM technique creates 3D materials by continuously adding layers instead. Currently, there is enough evidence of the economic production of these unique implants. The key types of this process are discussed in the sections below.

4.1 Digital Imaging, Precision Measurements, and Computer-aided Design (CAD)

The beginning of most 3D printing techniques is a computer-aided design (CAD) model that must be designed or obtained from a renowned organ structure. The initial structure is a 2D slice that is

stacked layer by layer to fabricate a 3D structure [69, 83]. For tissue engineering, tissue growth must match that of native bone to achieve it. These approaches can be utilized in fabricating scaffolds that mimic the native bone structure. The figures aid in providing information to scaffold drawings through similar parameters and morphology which is required for the scaffolds to match is irregularly arranged fractures/defects when tissue regeneration is needed. The shape of the scaffold also aids the growth direction of the cells and enables the end shape of the tissue. Importantly, the scaffold shape influences the manner of tissue regeneration as can be noticed in tissue regeneration of dentin with an oddly shaped scaffold utilizing dental pulp-obtained cells [84]. The complications are the structure and morphology of the tissues can be characterized via imaging techniques which include computed tomography (CT) and magnetic resonance imaging (MRI). These techniques will aid in obtaining a cross-sectional slice of the body parts and accumulate to a 3D image, hence the scaffold design to closely depict the native body parts [85].

MRI is often a better equipment than CT to fabricate an image with soft tissue and other body parts asides from bones due to the difference in closely packed organs which is easily viewed when the applied magnetic fields and radio waves charge. These magnetic fields and radio waves aid the possibility of the magnetic field and radio waves identifying the tissue of interest within the closely packed regions. However, the CT scans make improved quality images of the structures compared to MRI based on the poor concentration of water in the bones which leads to reduced hydrogen atomic emission energy to briefly produce a cross-sectional picture. Fabricating a scaffold straight from the picture is not always possible due to uncertainty in scanning damaged/ill organs. In this instance, a computer model is required to recreate the missing components of the tissues/organs. Through CT and MRI imaging techniques, their reproduction of both 3D and 2D images is a great tool device to recreate the complex tissue morphology. These devices will continue to aid in further research for predicting the precise fabrication of the required ECM to advance operational tissue creation.

For a simple prediction of bioimplant performances, characterization and full evaluation of the components is required in order to avoid implant rejections. The objective of this approach is to obtain a fast and reliable analysis and technique to be understood with the key emphasis on the precision of the geometric measurement. It is generally known that errors are bound to occur during fabrication. The contributing factors that induce the errors include environmental changes, tool wearing, machine build error, and vibrations [86]. In a bid to ensure the material meets the product specifications in geometry and surface topography is attained, metrology is critical in the chain of fabrication. With the advancement of manufacturing tending towards product mini scaling to produce innovative devices with suitable properties, measurement precision is of utmost importance.

For patient-specific models through direct imaging for a more general approach to biomaterials, the study on establishing an animal model with a labral maxilla defect was carried out by Feng et al, [87] through virtual reality and SLS 3DP technique for dentoalveolar distraction osteogenesis (DO). The outcome showed feasibility and model suitability for reconstruction development purposes, this proved to be a novel technique. Also, Lee et al, [88] were able to create a nonsurgical endodontic therapy of the right mandibular first molar by 3 distal roots through the assistance of magnification. The material used in modelling was starch and through the 3D visualization and computer-aided rapid prototyping (CARP), 3 different distal roots were noticed namely distobuccal,

dentilingual, and middle distal. The CARP process proves to be an effective imaging technique to conduct a detailed study of irregular root anatomy in clinical dentistry.

Sannomiya et al, [89] utilized 3D bio models to simulate ameloblastoma which is a benign local lesion. This study covers the use of a 3D bio model before and after surgery. There was evidence that bio models allowed a predictable surgical process and prognosis if improved postoperative condition is applied the surgical time will be reduced. While Feng et al, [87] prescribed a method used in the design and fabrication of sensible facial prosthetics via 3D optical imaging and computer-aided design/manufacturing (CAD/CAM). The 3D data acquisition from the sensing system and CAD/CAM of the prosthetics aids in viewing the whole face without soft tissue defects and no discomfort to the patient due to radiation. The end prosthetic was adequate in size, shape, and aesthetic appearance which made it fit the affected facial area and met patients' requirements. Marafon et al, [90] assessed the dimensional accuracy of orbital prosthetics from reversed images produced by CAD/CAM through CT scans. The material used for the prosthetics was silicone with CT scans of 15 adults without congenital craniofacial defects. The research affirmed that orbital prosthetics from the CAD/CAM system can be applied in clinical procedures.

State-of-the-art software and hardware were suggested by Winder and Bibb, [91] to meet up with high-quality manufacturing of medical models through medical 3D printing (SLA and FDM). Medical 3D printed products should be conditioned to rigorous quality assurance in all manufacturing process stages. Surgeons should know the full extent of the inaccuracies in the models and cross-check the source images when the model integrity is not guaranteed. Pressel et al, [92] studied the biomechanical behaviour of pelvic osteotomy based on difficulty to evaluate from 3D pelvis anatomy. Thus, a suggestion for pelvis models is needed to aid in ideal biomechanical simulation. A polyamide-based hemipelvis is reversed engineered from a CT dataset of an 8-year-old child with a severe case of dysplasia of both hips through SLS. From the hip joint resultant force obtained, the hip extensor and abductor actuator forces counterbalanced the joint movements. This bony model was geometrically precise, while the joint irregularities were a result of cartilaginous structure neglect in the used model. It was concluded that these models increase joint contact area and reduce the forces on the hip joint. Rogers et al, [93] also studied the fabrication of advanced trans-tibial sockets through SLS. Where SLS was used based on its capability of fabricating these sockets using the suitable biomaterials for the prosthetic. Ciocca et al, [94] were able to restore and rehabilitate a nasal defect after surgery for a squamous cell centre. Prototypes for surgery assessment, classification, and planning such as an acetabular fracture can be successfully constructed through a 3D printing process supported by CAD data [95-97]. Some tools such as Bangor augmented reality education tool for anatomy (BARETA) combine virtual reality (VR) technology with models from various 3D printing technologies to simulate contact alongside vision [98]. Also, Webb, [97] has used 3D printing of didactic models to study foetal malformations through a combination of MRI and CT of foetuses and FDM technique. It is believed that physical models have a role to play in didactic, interactive, tactile and also contribute to the study of complex defects by various researchers. Concerning the fabrication of orthopaedic implants are designed to simulate the features of a joint such as the range of motion, weight-bearing capacity, and range of motion. The geometry and surface metrology of the implant is vital for meeting the specific performance of certain features which include coating adhesion, wear resistance, osteointegration, lubricant retention, etc. This specifically ensures the patients can benefit from the invasive surgery for as much as possible. With the overview being to enhance the lifespan of the bioimplant and attain

biocompatibility after replacement, the duo of contact and non-contact approaches is needed for the application on the finished products [64]. The examples of this approach include:

- Typical 2D imaging – this involves optical microscopy through a straightforward method for the characterization of surface structures. Additionally, this method is also adjustable in varying working conditions at different workpieces [64]. The practical optimized resolution for convectional optical microscope techniques can be achieved via a single-wavelength and great dynamic function limits. However, the depth and resolution of interest remain hindered. An example of 2D imaging is scanning electron microscopy (SEM).
- Coordinate measuring machines (CMM)– this is currently the mainly used device for the measuring of open parts when in contact state [86]. For the CMM process, the measurement is determined through a probe connected to the device where the 2D/3D displacements can be determined by the great resolution and poor contact forces. This probe is the main component of CMM. Typical probes are manual while recently that are usually attached to an optical/white, laser light for measurement of multi-sensors [99]. Currently, several probing systems are economically viable in carrying out varying measurement tasks.
- Scanning probe microscopy (SPM)- this is an appealing technique in studying atomic surface structures within a very narrow region [100]. Conventional types of SPM include scanning tunnelling microscopy (STM) and atomic force microscopy. The STM uses electrical near field interaction linked to a conductive surface and AFM is dependent on a sharp cantilever edge with little curvatures [86].
- Optical profiler- this is an alternative to the mechanical probe [101], this technique utilizes a light beam for a workpiece scan. Similar to the non-contact SPM technique, the key attraction of optical profiling is the avoidance of physical damages and chemical changes. The main forms of optical profilometers are interferometric profilometer and focus detection profilometer. An interferometric profilometer is dependent on the interference phenomenon. Within measuring, a pattern of interference between the reference and measuring beams is treated to be precisely obtained from the details on the height displacement. While the focus/laser detection profilometers keeps the projected beam focused on the work surface through the vertical movement of the lens. This movement demonstrates the height differences of the work material. The laser profilometer resolution is related to the beam size. For the optics, a laser profilometer can provide a better outlook of the surface roughness instantaneously.

4.2 Post Printing Surface Treatment Process

Most of the 3D printing techniques (e.g. SLS and FDM) produce objects with rough surfaces, when combined with the biocompatibility of the feed material, providing a pathway for the fabrication of multi-purpose high-surface-area substrate for biomedical application [102]. The capability of rapidly printing materials on demand of several custom profiles, shapes, and properties gives access to currently focus on difficult clinical requirements in bone replacement. Large area defects (voids) in the bone as a result of instances such as surgical cancerous cell removal will not rapidly regenerate in an adult body if no further treatment on covering the open spot is not carried out. The bulk properties can originally provide the material similarity for bio application, the chemistry and physical component of the material surface is also important to the biomedical device functionality.

Surface modification can be grouped into chemical and physical categories. Chemical modification can lead to carbide/nitriding/oxidizing/reduction of a surface, ion infusion, surface activation, and single/multi-layer coatings for various compositions. While physical modification involves alterations in morphology, geometry, and topography of the material surface with minimal effect on the chemistry of the material and this includes machining, grit blasting, and etching [103]. The renowned chemical techniques include atomic layer deposition, plasma, chemical vapour deposition, and electrochemical deposition. The purpose of surface modifying a biomaterial is to produce specific chemical and physical conditions that support favourable cell reactions in either soft or hard tissues. In occasions where tissue integration is required, the physical condition such as macro, micro, and nanoscale characteristics promote cells adhesion, proliferation, and distribution. It is noteworthy that in certain cases, a textured surface does no good to the functionality of the device e.g., cardiovascular tools and articulating surfacing. In the past, this has been resolved through a bone graft taken from my part of the body or a donor [104]. However, there are several limitations with this form of treatment such as site defects for the bone graft removed from the donor, also a possible immune rejection of the grafts, pathogen transfer from donor to host, poor supply of donor bone grafts available for specific demands and delayed union and non-union of bone grafts [105-107].

When the pre-fabrication is complicated, the final bioimplants are produced by applying finishing touches. Polishing is mostly utilized as the final step to obtaining a smooth and even surface which is mostly done manually leading to poor fracture toughness. Ceramic and metallic-based bioimplants are susceptible to brittle fractures from abrasive handling. Hence, polishing and precise grinding should be carried out to ensure the material property is sustained in the ductile region. From the reports by Costa [108] they are roughly 60 different steps involved in creating the simplest geometry of a ceramic implant in opposition with hip replacement parts, artificial knee replacements have more complicated surfaces that make it difficult to fabricate. In these scenarios understanding the basic geometric parts must be essential. A constant alteration of contact conditions during the grinding process should be considered to ensure a constant material output and great surface quality [109].

To enhance functional efficiency and decrease costs, general chains of the automated process are involved in fabricating bioimplants are designed. Costa et al, [108] have designed a sample that stands as a typical example. For this work, a series of calculations and modelling was applied to analyse the surface quality pre/post-grinding. The roughness peaks were reduced by following steps of polishing. It was revealed that a systematic process would aid to boost productivity, it was suggested that the polishing processes stood for 10-15% of the general cost of manufacture [110]. The goal is to reduce the possibility of shape deviations and the critical necessities in the polishing process include novel grinding techniques and highly accurate process development.

4.2.1 Precision Grinding

Typical grinding of hard brittle material is characterized by its power grinding ratio with a notable wearing of the wheel. Also, the debris from the grinding obstructs the wheel during grinding. Noticeably is the even distribution of the abrasive grains in the grinding wheel which slowly has an effect due to wear or debris sipping through. A boost in the forces of grinding would trigger the possibility of brittle damages, as a result, the level of precision is not assured. Such hindrances are

necessary for bioimplant fabrication as some specific areas of orthopaedic joints require certain surfaces. To resolve these issues, the use of electrolytic ion-process dressing (ELID) grinding was suggested [111]. This technology provides a new approach to handling metal-derived grinding wheels by using the electrolysis method. Strong abrasives are exposed at the anode while the metal-derived material and inner debris are the wheels are extracted through electrolyzation.

Previous studies show that ELID grinding is a great approach to fabricate smooth surfaces that possesses nanometric roughness within strong-brittle materials. Also, the abrasives undergo diffusion into the material surface during the process of grinding. This should aid in enhancing corrosion resistance as the outcome. Gibson and Shi, [112] proposed a prediction model for further analysis of kinematic roughness which covers material removal rates, the engagement area, and their geometric contact length. These achievements are understood to be a benefit for confirming good quality fabrication processes.

4.2.2 Polishing

The polishing process is viewed as an approach for fabricating high-grade surface finishes. In some instances, grinding solely cannot match the surface requirements for different bioimplants. Fabricating bioimplants through grinding processing and polishing of regions that debris removal is damaging [113]. It is expected that a smooth surface shows an enhanced corrosion resistance which aids in the longest life span of the implant. Also, the differences between the adjoining joints decrease the coefficient of friction and this makes it appealing in terms of the weight-bearing capability of implants. Typical polishing techniques include belt polishing, open abrasive polishing, and fixed abrasives, which have been fully studied in the past [114]. Currently, bioimplant polishing is usually integrated into a highly accurate CNC process to boost operation efficiency, hence an even material removal on the total surface. With the advancement in technology of polishing equipment, the roughness of polished materials can reach the nanoscale [115]. Cheung et al, [113] studied ultra-precision polishing and factors which affect it. This study aimed at suggesting strategies optimizing the free form surface finishes. From the study, an enhanced surface quality was attached with decreased time and costs. Asides from solely mechanical polishing, the chemical-mechanical polishing (CMP) process has proved to be a suitable approach to produce an optimized nano/microscale roughness in the bioimplants [116, 117].

Regular polishing techniques require a great deal of labour and are time-intensive, also noticeable residual stress on the surface layer, hence electrochemical polishing (EP) is highly recommended for the fabrication of the bioimplants [114]. For this process, the dissolution of the anode of the metal occurs in the electrolytes [118]. The non-homogeneity of the surface is sorted by the anodic levelling which is dependent on the variation of the rate of dissolution. This principle aids in handling very distinct geometries in a biomaterial.

5. 3D Hip Tissue Regeneration

The bone is the second most-transplanted tissue in the world, with over four million operations using bone grafts or bone replacement materials and these include hip replacements. The demand for this type of operation is constantly growing. Therefore, the development of bioactive three-dimensional (3D) scaffolds supporting bone regeneration has become an important area of interest in bone tissue engineering, including the 3D printing method of increasing importance. It should be

noted that individual groups of materials, including polymers, ceramics, and hydrogel they are not able to fully reproduce bone properties when used alone. However, when groups of materials are used together in 3D composite scaffolds, research shows that you can get beneficial properties and improve bioactivity. Bone is a heterogeneous composite material consisting of hydroxyapatite, type I collagen, lipids, non-collagen protein, and water. Therefore, during the production of scaffolds, it is advisable to use a composition of materials to obtain a composite scaffold, and thus potentially enabling greater scaffold bioactivity and structural biomimicry. The bioactivity of the scaffold is also increased by the inclusion of materials that can interact with or bind to living tissues. On the other hand, increased scaffold bioactivity can lead to better bone cell ingrowth (osteoconduction process), stable anchoring of scaffolds in bone tissue (osseointegration process), stimulation of immature host cells to transform into osteogenic cells (osteoinduction process), and increased vascularization. A perfect 3D scaffold should consist of a biocompatible, biodegradable material with similar mechanical properties to the tissue in which it is to be implanted. The scaffolds are not intended for permanent implants and ideally facilitate host cell deposition of the extracellular matrix (ECM) and replace the scaffold structure over time. Therefore, the 3D architecture of the scaffolding should be very porous with the connected structure to allow facilitate cell attachment, proliferation, and differentiation [119].

Tissue engineering as it is known currently is a multidisciplinary field that applies the concept of life sciences and engineering towards the continuous development of biological alternatives. This has rapidly evolved from the area of biomaterial development and entails the process of combining cells, scaffolds, and bioactive molecules into functional tissues. The objective of tissue engineering is to gather a functional structure that can repair, preserve and enhance tissue functionality or the whole organ [120]. On the other hand, regenerative medicine/tissue regeneration is a broad field that includes tissue engineering and also integrates advancement in self-healing which is a situation where the body uses its system, most of the times with the aid of foreign biomaterials to reproduce cells and restore tissues and organs.

The goal of tissue regeneration through surgery is to replace damaged/diseased tissues with healthy and performing tissues, tissue regeneration tends to focus on the cure rather than treating complex, often incurable diseases. This has been made possible through tissue engineering which requires extensive knowledge of the biological process necessary for differentiation and proliferation at the cellular level. This tissue engineering process often starts with a scaffold which is a 3D structure support material required for the suitable differentiation and proliferation of the cells immersed in the scaffold.

The area of tissue engineering and regeneration seeks to address these significant details for an improved implant application. This originally involved the transplanting of tissue from one area to another within the same body (autograft) or from one body to a different body (an allograft) which has been effectively used in replacing organs with reasonable results [121].

However, there still exist multiple problems with both procedures (autograft and allograft). The autograft technique is expensive and might cause an increased risk of infections, additional injury and is limited due to the unsuitable anatomical replacements from a different body region. While allografts are often not fully accepted by the immune system (immunosuppressant therapies) which is crucial and poses a threat from infection risks and may lead to the possible transfer of illnesses or diseases between the bodies. Most recently, there has been a surge in the study of tissue replacement designs that utilize physical, biological or/and mechanical components to restore

functionality [122-126]. Specifically, tissue engineering originally involved the concept of cell isolation from a body, proliferating than in vitro and growing them into a biomaterial that is subsequently implanted into the spot of the injury via in vivo. As such, the goal is to fabricate artificial tissues and organs to seek redress for the reduction of risks from the grafting methods (allograft an autograft). Several developed studies supply the needed information regarding how the cells interact with the extracellular matrix (ECM) to determine cell behaviour and function [127-130]. Where ECM in a 3-dimensional structure provides the mechanical support for cells around it. The potential for synthetic biomimicry mechanism development like ECM is an advantage of tissue engineering. A benefit of using 3D printers in hip replacement is that in certain biomaterials such as thermoplastics, cells can be inserted at the right temperature and precise location to produce a 3D implant that is based on the obtained clinical imaging. Through this process a strong hip implant is produced that is surgically inserted to heal the bone/tissue deformities, this implant biologically degrade with time to leave behind solely natural bone/tissues.

The biomaterials to be used for tissue engineering should have the following features [131]:

- Should be porous (to ensure nutrient movement, removal of waste, and cell growth), biocompatibility, reproducibility, cell/tissue compatibility, easy preparation, and biodegradable.
- Lead to the reduced inflammatory reaction, therefore, decreasing the possibility of immune system rejection.
- Advantageous if the biomaterial tissue scaffolds can act as substrates that support cellular fastening, growth, and differentiation.
- The cells grow and differentiate, this scaffold must have the ability to resist the forces put in by the cells else the scaffold will disintegrate and causes dismal diffusion of nutrients, waste, and oxygen.
- The scaffold structure should be mechanically stable to be capable of maintaining load-bearing and varying body movements in daily activity on the joint.

Hip replacement has witnessed a rapid advancement over the past decades and specific techniques for surgery have evolved. With the continuous advancement of hip replacement, the biological knowledge of orthopaedic tissues continues to advance. Likewise, the demand for biological solutions for pre and early defective hip remains a challenge for surgical hip treatment [132]. Furthermore, within the hip, there is a rich presence of vascular tissues, and this results in complexities during hip replacement surgery as adjacent vessels could be damaged during operation, an efficient preoperative planning procedure would significantly prevent this [133]. Other vital orthopaedic tissues include the articular cartilage, labral fibrocartilage, and ligamentum teres [132].

Tissue preservation or minimal invasive total hip replacement is currently becoming a priority with the focus being to reduce hospital stay, improve rehabilitation, and faster patient recovery [134]. The regenerative process replaces and renews the stem cells to facilitate the preservation, restoration, and reestablishment of optimum functionality for tissues and organs. At the early stages of some hip defects, simple injections of stem cells to the hip can position it to regenerate, heal the damaged tissue and bone cell lines [135]. The progress noticed in drug testing and regenerative therapy can significantly benefit from bioengineered human tissues developed via several cell types with precise 3D structures. However, there is a limitation with the production of

human tissues which are greater than the millimetre size and this is due to a lack of techniques for fabricating tissues with embedded life-supporting vascular networks [136].

5.1 3D Bioprinting of Hip Tissues

3D printing as a manufacturing technique is unique due to being customizable and precise, this makes it appealing to tissue engineering and regeneration. The inherent tissues in the human body are complex 3D cellular arrangements and structural proteins, however, they are also not similar as every human body is unique and peculiar. Techniques for directly printing 3D structures with cells that form organs and tissues are currently being developed. Through these bioprinting techniques, reproducibility with geometric accuracy of natural tissues is feasible. However, the challenge remains in deriving materials which recreate the biological and mechanical performance of the tissues. Directing cell growth to form the specific tissues on a laboratory scale is now considered as an alternative procedure. Most cells grown in vitro do not naturally reorganize themselves into 3D structures. To make this possible, the cell is encouraged to grow on a scaffold, and this offers the layout for the desired shape, for instance, a tubular scaffold utilized in producing blood vessels whereby the cells proliferate and laden the scaffold thereby taking the shape. With time, the scaffolds degenerate which leaves the cells organized into the shape of the desired tissue. Presently research on vascular tissue engineering has prioritized producing straight vessels. However, these vessels are not capable of accurately biomimicking the vessels of the human body and hinder their use in vascular surgery. 3D printing offers the perfect technological solution to this challenge as it is capable to fabricate organic and customizable shapes which are cost-efficient [137]. Another approach is the use of bio-inks which contains stem cells used for 3D printing of living tissue that can be introduced in the human body and facilitates the healing of a damaged joint. With this development, several hip defects such as arthritis and bursitis can be healed. These defects break down the rubbery-like natural cartilage tissues located in the joints which result in stiffness, swelling, and pains. However, the 3D printing technology enables new cartilage to be printed as required by utilizing the cells of a patient as the building blocks which is the principle for bioprinting [137].

Hence, 3D bioprinting is a new technology that has been used to embed live cells, extracellular matrices, and other biomaterials in user-defined patterns to build complex tissue structures "from bottom to top" [138]. The printing process usually begins with the selection of cells and biomaterials included in the bio-print design. Cells for printing can be obtained from tissue biopsies the migration of cells and nutrients. The scaffold surface should also be optimized for blood samples and other sources. However, their number can be increased by culturing to maximize cell density during bioprinting. An additional 3D cell culture step can also be performed to create cell aggregates for printing. Fennema et al, [139] showed that cell aggregates or spheroids have better intercellular communication and extracellular matrix development compared to cells grown in 2D culture, potentially accelerating the growth of printed constructs towards functional tissue after bioprinting [139]. At the same time, mesenchymal stem cell spheroids (MSCs) also show enhanced in vitro and in vivo osteoregenerative potential compared to MSCs grown in monolayer [140]. An important element is also the choice of material encapsulated in the delivery medium or bio-ink. The cassettes prepared in this way are loaded into a 3D bioprinter, which dispenses the bio-ink in a predetermined 3D geometry in accordance with the CAD model, which allows obtaining a product with a specific

architecture and construction [141]. After printing, the construct can be implanted directly into the patient or first matured in vitro. Biologically active culture media called bioreactors are also available to direct support cell growth towards specific types of tissues. Commonly used bio-printing techniques include inkjet, laser-assisted, micro-bio set printing, and extrusion. In the inkjet bio-print method, drops from the head nozzle are ejected due to thermal or acoustic forces. Thermal inkjet printers use heat to generate a pressure pulse in the printhead for a short time, causing a drop of bio-ink. Other systems rely on piezoelectric crystals that become mechanically stressed by applying a voltage, and as a result, change shape. Thanks to this, an acoustic wave is generated, which then generates pressure sufficient to eject droplets from the nozzle. The advantage of this method is its low cost and high printing speed. However, the limitation is frequent nozzle clogging, the risk of exposure of cells and materials to thermal and mechanical stress, heterogeneous droplet size, and its low viscosity [142]. In the bio-print laser assist system (LAB), material flow with living cells is possible with a laser beam. The big limitation of this method is the probability of cell damage and difficulties in creating 3D structures. Despite the restrictions on the use of this method, it has been used by Keriquel et al, [143] to print mesenchymal stromal cells associated with collagen and nano-hydroxyapatite directly in situ on a mouse skull defect to assist bone regeneration [143]. An interesting system is Bioprinting Microvalve, a system similar to LAB based on droplets that are dosed under constant pressure from cartridges by opening and closing a small valve. Microvalve systems can print cells, including MSCs, with high viability and functionality, with possible deposition of other biomaterials, such as collagen and morphogenic bone protein. Extrusion bio-printers, unlike the systems discussed above, extrude fibres of materials under pneumatic or mechanical pressure leading to deposit of very high cell densities. The microvalve system can be used to extrude tissue spheroids, tissue threads, cell pellets, cell-free matrix components, and cell-filled hydrogels [144]. Materials used for bone repair and regeneration include metals, ceramics, polymers, hydrogels, and related composites. Chou et al, [145] used 3D inkjet printing to create iron-magnesium (FeMg) composite scaffolds. As research has shown, the resulting FeMg constructs had an open, porous structure with similar mechanical properties when extended to the spongy bone. In vitro analysis showed good cell viability after exposure to scaffolds, with cell infiltration into the pores [145]. A representation of the basic difference between 3D printed and bio-printed scaffolds is provided in Figure 13.

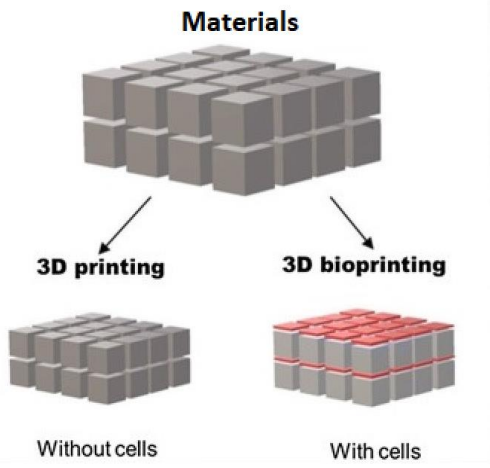

Figure 13 Schematic illustration showing the basic differences between 3D bioprinting and 3D printing. Adopted from Ref. [146].

Tarafder and Bose, [147] 3D printed a tricalcium phosphate (TCP) scaffold with polycaprolactone (PCL) and an alendronic acid (AL) coating of the scaffold made after manufacture [147]. It was found that local in vivo AL delivery from PCL-coated TCP scaffolds led to increased early bone formation compared to TCP exposed and PCL-coated scaffolds. The composition was then enriched with magnesium oxide [148]. Studies have shown that significantly higher bone and blood vessel formation was observed in Mg and Si-containing scaffolds compared to the unprotected TCP in vivo controls. It has also been shown that magnesium and silicon contained in 3DP TCP scaffolds can have the potential for future bone tissue repair and regeneration. An interesting group of biomaterials that have been used in bone tissue engineering (BTE) is bioactive glasses (BG), a glass-ceramic biomaterials that are amorphous, of which 45S5 Bioglass® is the most popular. After implantation, the dissolution of BG helps to form a biologically active hydroxyapatite (HA) layer on the glass surface, which in turn interacts with collagen fibres in the host bone to form a strong bond. In fact, the bond formed with the bone is so strong that BG can often not be removed after the fracture of the surrounding bone [149]. Westhauser et al, [150] studied the osteoinductive properties of scaffolds obtained by 3D method from 45S5BG ® coated with polymer inoculated with human mesenchymal stem cells (hMSC) in vivo [150]. The scaffolds were then coated by dipping either gelatine, cross-linked gelatine, or poly (3-hydroxybutyrate-CO 3-hydroxy valerate) and inoculated with hMSC. The scaffolds prepared in this way were implanted in immunodeficient mice. The tests showed bone formation on all received scaffoldings. Murphy et al, [151] used the 3D bio-print method to obtain scaffolds based on polycaprolactone scaffolding (PCL) / BG containing human adipose tissue stem cells (ASC). The conducted degradation study showed a weight loss of 23% after 14 days. Also, the cell viability after 24 hours was 70% and after 7 days was 58%. Scaffold pore sizes ranged from 100 to 300 μm, making them ideal for BTE. Bioactivity of the BG component was also observed, with the formation of HA crystals on the surface of the scaffolding. Therefore, this study showed the potential of solvent-based bio-print 3D to produce scaffold-containing cells and BG-polymer composites for BTE applications [151]. Zhang et al, [152] improved bioactivity of printed surfaces were obtained by coating mesoporous binder (pores with diameters from 2 to 50 nm) with bioactive active glass nanoparticles (MBG) on porous β-TCP scaffolds [152]. The conducted research shows that the obtained systems showed a high compressive strength of MBG-β-TCP scaffoldings in comparison with β-TCP scaffoldings without MBG nanolayer. The culture of human umbilical vein endothelial cells (HUVEC) showed increased cell attachment, viability, and expression of angiogenic genes compared to conventional β-TCP (BG-β-TCP) and pure β-TCP scaffolds. In addition, MBG-β-TCP scaffolds significantly increased new bone formation in vivo compared to BG-β-TCP and β-TCP scaffolds. Natural polymers fulfil very good properties for bone tissue engineering. Another benefit is that natural polymers often contain biofunctional molecules on their surface that can help cell attachment, integration, and differentiation on scaffolds. Literature data indicate that the use of polymers such as collagen, silk, alginate, chitosan, and hyaluronic acid are suitable but their use is limited due to poor mechanical properties and the presence of pathogenic impurities such as endotoxin [153].

Lyon et al, [154] received collagen-hydroxyapatite scaffolds in the compression moulding process to combine hydroxyapatite (HA), paraffin microspheres, and concentrated collagen fibres. The paraffin microspheres were then washed out, acting as porogens, and the collagen was chemically cross-linked [154]. The scaffolds obtained were characterized by pores with a size of 300-400 μm with walls with a thickness of 3-100 μm were found in micro-CT analysis with total porosity of 85-

90%. This is important because scaffold pores greater than 300 μm have been shown to promote osseointegration [155]. At the same time, mechanical properties were improved, with the best results being obtained for scaffolding with 60% HA content. HA-containing scaffolds showed significantly better bioactivity compared to scaffolds containing only collagen, according to other studies, with increased osteogenic differentiation [124]. In turn, research conducted by Meagher et al, [156] showed that the increase in HA content of the scaffold is directly correlated with the improvement of vascularity, cell density, matrix deposition, and mineralization [156]. For BTE, chitosan has been combined with many materials in scaffolding, including calcium phosphate, calcium sulphate, hydroxyapatite, and other natural polymers, including silk. Jing et al. [157] applied the lyophilization method to the 3D method of scaffolds based on hyaluronic acid (HLA) and chitosan. Chang et al. [158] investigated whether the use of HLA as an aqueous binder of hydroxyapatite / beta-tricalcium phosphate (HA-βTCP) particles could reduce the amount of bone graft needed and increase the ease of transplant management in clinical situations. Studies have shown that the addition of HLA to bone grafts not only promoted osteoconduction but also improved handling properties in clinical situations. McNamara et al [159] developed a new technique for producing HA silk porous scaffolds. In the first stage, silk was mixed with HA powder, and then silk macroporogens were added. The mixtures were then sintered, and the silk acted as a sacrificial polymer, forming a porosity. To obtain three-dimensional geometries, the obtained scaffoldings were machined [159]. Synthetic polymers that have been implemented in BTE include poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly (caprolactone) (PCL) and poly (ethylene glycol) (PEG), and copolymers such as poly (lactic-CO-glycolic acid) (PLGA) are also used. Kim et al, [160] used a combination of 3D printing, electrospinning, and a physical punching process to create composite PCL / alginate constructions with nanofiber content and improved mechanical strength [160]. Holmes et al [161] investigated PLA-based scaffolding using a 3D fused deposition printer that was chemically coupled to nHA to increase the differentiation of hMSC-inoculated osteoarthritis. Mechanical tests have also shown that scaffolding can withstand the normal mechanical load, demonstrating elastic properties [161]. Shaui et al, [162] obtained porous PLGA-nHA scaffolds with 3D printing using selective laser sintering. This method allowed the creation of well-controlled pore architecture and a high content of bioactive scaffolding surface on the scaffolding surface. Tests of mechanical properties showed an improvement in compressive properties, but nHA content above 20% caused deterioration of brittle mechanical properties [162].

Malda, [163] worked with these forms of 3D bioprinting in a project titled 3D-joint with the goal of making bio-printed tissues that can be implanted in living joints to replace the damaged section. With time, they mature into tissues that are similar to the initial healthy cartilage. As stated earlier where stem cells are deposited through 3D printers to the precise layout, it produces complex tissues via a layer-by-layerprocess. However, this does not imply that they can be immediately converted to new body parts/organs. Printing is not the end in itself for bio-fabrication as printing an organ does not instantly translate to functionality. The printed structure requires time, the right biophysical and chemical signals to mature into an effective tissue.

A major challenge is sustaining the right conditions required for cellular formation material. Conventional 3D polymers use polymers that are sufficiently flexible to pass through a printer nozzle but can also be solid enough to subsequently retain their shape. As bio-inks contain living cells, researchers are developing novel solutions. An option is the use of hydrogel which is a material that is composed of a network of sizeable molecules known as polymers that absorbs water. The

bioprinting technique with the material should be capable of keeping the cells alive. This will need aqueous conditions and fabricating under a low temperature, and this makes hydrogel-based materials the best prospect. While the soft nature of hydrogels makes them ideal for cell delivery and this also makes it their weakness, they fail to resist certain mechanical loads that the tissues encounter in the body.

To resolve the strength issue in hydrogels, Malda, [163] worked with additive materials that can make hydrogels sufficiently strong to behave as replacement cartilage. Reinforcing hydrogels makes them stronger, the study used a 3D printing combination of melted PCL with an electric field that produces very thin fibres. By using these microfibres, the created scaffold was combined with a cell laded hydrogel and these proved to be successful whereby the combination of the hydrogel with the fibres cooperates to increase the strength of composites while still permitting the cells to generate ECM and mature into ECM [163]. Based on Malda study [163], it is apparent that the future works is on increasing the scaling process to create bigger structures while providing varying materials for the combination of bone and cartilage tissue replacement with the ultimate goal being to use 3D printing for complete joint replacement. This will not only behave as replacements for damaged bone and cartilage, but the printing cells can also aid the body in restoring damaged tissues.

Daly and Kelly, [164] worked on developing joint printing which is still a relatively new field. There are previous examples where bio-printed tissues have been used to regenerate damaged tissues in clinical trials with animals. Daly and Kelly [164] are working on developing bio-inks that go beyond being printable to activating stem cells to create new cartilage by modifying the molecules to support and enclose the printed cells, facilitating them to generate the desired tissue. Emphasis is on newly printed stem cells contributing to the repair of damaged tissue after implantation. Daly and Kelly, [164] also developed substances that are called growth factors to stimulate new blood formation for damaged tissues. Currently, the vascular endothelial growth factor (VEGF) is added to bio-printed tissues to enhance the formation of new blood vessels in areas on the damaged joint or bone where bone growth is desired. Also, incorporation of the gradients of VEGF into the bio-printed tissues assists in directing the host blood vessel that forms to the exact area of the implants. Though most current research focuses on bone and cartilage growth, necessities on the joints can vary significantly which relies on the spot in the body. To fully test these printed tissues, mechanical testing is recommended for determining the elasticity, strength, and stiffness, supported by finite element analysis to develop improved knowledge on how the composition, structure, and stress behaviour of the implants can be tailored to function in certain conditions. It was concluded that bioprinting has a promising future and the potentially key applications are first, as a source for the discovery of novel tissues and organs for regenerative medicine and secondly, a device to fully know the human disease and provide a test for validating the efficacy and safety of drug delivery for these diseases.

6. Hip Replacement Materials

The advancement of material and design used for hip prosthesis has seen a rapid progression since the initial application. It remains a challenging issue in seeking new materials and pushing development in this century for implant manufacturing technology [165, 166]. These include metals, ceramics, polymers, composites, alloys, and most recently hybrids, with the goal being to improve

the quality of life for the patients and to evade the possibility of repetitive surgery. The timeline for this production is presented in Figure 14.

Figure 14 Brief timeline of hip replacement surgeries.

The bone is a component of the skeleton which is a dynamic and rigidly hard tissue in varying sizes, shapes, structures, and properties. It is necessary for organ protection. The matrix of the bone is similar to honeycombs and consists of 60% inorganic constituents (calcium-deficient apatite and trace elements e.g. zinc, copper, etc.) as reinforcement for composite like structure dispersed in the organic matrix of 40% (90% collagen bone type 1 and 10% non-collage protein e.g. decorin, hyaluronic, etc. [167-169]. In this context, the needed fracture resistance and toughness of the bone are supported by collagen type 1. This discrete composition results in having a strong tissue with lightweight. It seems that this key protein present in the bone ECM structure is accountable for cellular adhesion, distribution, and growth. Also, the other non-collagenous compounds control bone mineralization and adjust the hydroxyapatite arrangement [170]. Furthermore, the bone minerals can provide the required hardening and integrity retention as well as participate in collagen synthesis, stimulation of osteoblast proliferation, calcium-sensing receptor activation, inhabitation of osteoclast activity, differentiation, and angiogenesis [171, 172].

For bone metabolism activation, 3 cell types are needed, and they are osteoclasts obtained from split stem cells to monocytes, osteoblasts and osteocytes cells obtained from osteoprogenitor cells and macrophages participates in bone tissue resorption and biomineralization osteocytes are inactive osteoblasts which can be found in the lacunae. Osteoblasts are mononucleate cells that are located on the osteon surface that participates in osteoid production of bone formation and minerals and osteoclasts are multinucleated cells located on the bone surface that partake in bone disintegration by active enzyme secretion against minerals that produce new bones via osteoblasts [173-175] for the bone regeneration process.

The ECM can be grouped into 3 and they are demineralized bone ECM, deproteinized bovine bone, and decellularized bone ECM. Decellularization has the potential to lower immune rejection of the implant via antigenic cells removal. Several reviews show that the cortical role of a decellularized matrix in enhancing and stimulating regeneration, vascularization, and lastly alkaline phosphate activation [176-178]. Anyways, demineralized bone ECM comprising of organic bone parts without minerals and possible stimulation of osteoblast markers for cell growth, enhanced regeneration, and improved phosphatase activity [179]. In contradiction, deproteinized ECM is void of organic bone constituents and can boost osteoblast adhesion and growth [178]. While the study by Amerio et al, [180] suggested that the expression of bone morphogenic protein-2 can be decreased. Bone formation can be split into intramembranous and endochondral osteogenesis [181]. Intramembranous osteogenesis is noticed in clavide, parietal and frontal bone occurring via mesenchymal growth in the embryonic connective tissue membrane. While endochondral osteogenesis can be noticed in small, large, and irregular bone components and this begins with embryonic cartilage formation and subsequent conversion to mature bone [182, 183]. Cellular interactions (osteoblast and osteoclast) with the bone are required for bone metabolism and bone remodelling [184, 185]. Thus, bone matrix absorption and synthesizing will be noticed constantly based on the performance of osteoblasts and osteoclasts respectively. In view of this, functional balance provides regular bone formation and prevents [186].

The bone provides a range of functions such as internal organ protection, sound waves transmission, structural support of ventilation, storage of minerals e.g. amino acids, phosphates, calcium, bicarbonates, and phosphates, and also aids metabolic functions e.g. hormone secretion for the regulation of both energy metabolism and minerals. Therefore, the bone is subdivided into cortical and trabecular parts to achieve these functions.

It is estimated that roughly 80% of bone mass is in the cortical section and 30% of this volume is occupied by the vascular channel. The ratio of surface area to volume of the cortical bone is very low compared to the trabecular bone. The cortex gets porous with more ageing or diseases; therefore, it leads to more surface area but lesser strength. For longer bones, porosity increment close to the periosteal surface leads to strength loss rather than porosity increase close to the endocortical surface. A steady periosteal expansion throughout life repays for the strength loss, which is due to the bending strength being proportional to the radius of power 4 [187].

For the trabecular section, bone constitutes 20% of its volume and the remaining part is composed of fat and marrow. Mechanical loads are transferred to the cortical bone from the articular surface through the trabecular bone passing a larger surface area that is open to blood flow and bone marrow and thus has a higher yield than cortical bone [188]. Resorption also occurs on the bone surface for the trabecular bone while for the cortical bone the resorption flows through the same bone. The endocortical surface has a higher bone yield than either cortical or trabecular surfaces. The cortical bone is also more rigid, dense, and compact while the trabecular bone is more flexible, has lesser mechanical strength, sponge-like structure, and is less dense. Early researchers assumed the total isotropy on the femur strength which produces the early techniques for the evaluation of resistance and performance of the bone [189]. However, both the cortical and trabecular are necessary for bone strength although this relationship is complex.

The hip is always seen as a cortical bone site although both bones aid in femoral strength, the cortical bone contribution of bone density outweighs the tracebular in the femur [190]. In addition, the cortical bone provides support in the distal regime which bends the femoral neck while the trabecular aids the proximal load. From studies by Maharaj et al, [191] and Masood et al, [192] on the femur structural evaluation of a fully solid bone, the assumption was made that the femur has a sole composition which is made up of the cortical bone with the bone components neglected and bending stress was predominantly noticed with great distortion. The availability and mechanical design are the basis for general artificial biomaterials for human ailments. In terms of biocompatibility Yuan et al, [193] believe that an increase of porosity of a scaffold leads to better biocompatibility. However, there is a possible reduction in mechanical properties such as yield strength and young's modulus as porosity is viewed to be inversely proportional to the mechanical properties and can be attributed to the wall thickness thinning. While for biodegradation, the porosity has a crucial effect on corrosion resistance which is based on the degradation rate. With a reduction of the material porosity, there will be an increase in corrosion resistance which is based on the degradation rate. With a reduction of the material porosity, there will be an increase in corrosion resistance based on the specific surface area and vice versa.

The requirements to be met include biological, chemical, and mechanical criteria that must be satisfied prior to application in the body in conjunction with medical principles which makes the human body peculiar. The following properties should be exhibited by the proposed biomaterials [194, 195].

- The femoral stem surface should encourage bioactivity for osseointegration.
- Should exhibit great biocompatibility i.e. non-carcinogenic, corrosion-resistant, non-magnetic, non-toxic, and chemical stability.
- Suitable mechanical properties e.g. yield strength, hardness, and Young modulus.

- The stem should be capable of withstanding varying and great stresses in the human body gait motion through a great number of stress cycles such as fatigue stress cycles with induced stress corrosion.
- The implant surface should be devoid of imperfection which includes cavities, scratches, tool marks, holes, and other facts.
- The surface layer should have elastic modulus similar to gradients e.g. gradient-like distribution of pores on the surface.
- Suitable chemistry and adequate metallurgical alloy state e.g. good chemical and structure composition.
- Material availability and significant balance between durability, quality, and cost.

When choosing a material for a hip implant, first of all, its features should be taken into account, such as bio-functionality, bio-tolerance, including compatibility with the body, immunological and corrosive inertness in the environment of tissues and body fluids, no tendency to clot formation, uniformity of chemical composition, a specific set of properties mechanical (high compressive and tensile strength, bending and torsion strength, fatigue strength, adequate ductility, hardness, plasticity), ability to maintain mechanical, physical and chemical properties during operation, appropriate electromagnetic properties. Technological properties are also important, including first of all high quality and ensuring the desired surface quality, time of production process, and its cost. To ensure the proper functioning of the implant, the proper selection of the material, and the technology of its surface preparation, one should also take into account the reactions occurring at the implant-biosystem interface, where live cells and the surface layer of the material interact with each other. Therefore, the composition of the implant's surface layer is of the greatest importance for tissue acceptance of the implant and the osseointegration process. Osseointegration, i.e. a structural and functional connection between the living bone and the implant surface can be both biochemical and biomechanical (interlocking). Integration of the implant surface with the bone is a continuous process and involves the continuous absorption of bone tissue. It should be emphasized that biomechanical osseointegration (the process of overgrowing an irregular surface of the implant with bone tissue) is a long-term process, while the process of chemical binding of bone tissue with the surface of the implant is an immediate process. It is known from the literature that titanium does not have properties that allow biochemical binding to bone tissue, therefore implants made of this material require chemical modification. The modification of materials should be carried out in terms of obtaining material that allows the process of osseointegration, including primarily by maintaining the appropriate deformation impacts. Therefore, in addition to such material properties as bio-acceptability or bio-tolerance, relevant mechanical properties such as, among others, Young's modulus, whose size should be similar to Young's modulus of bones, are important. It should be noted that the appropriate mechanical properties will ensure the strength of the connection between the bone and the implant. Table 2 gives more important criteria for the quality of biomaterials, including a set of requirements for implants.

Table 2 Examples of requirements for materials used for surgical implants (according to [47]).

Mechanical properties	Technological properties	Bio tolerance
Tensile strength	Ensuring the assumed quality of the biomaterial	Reactions with tissues and body fluids
Yield strength	Ensuring the required surface and implant quality	Stability of mechanical, physical, and chemical properties
Fatigue strength	The suitability of the material and product for effective sterilization	Degradation is associated with local implant damage (harmful changes) and systematic corrosion effects (harmful damage)
Hardness	Minimum production costs	
Abrasion resistance		
Rigidity		
Plasticity (elongation, constriction)		
Ductility (fracture toughness)		

The process of implant design requires several works which include the geometrical features of the implant based on anatomical and physiological conditions and selection of the planned surgical or surgical technique. It is important to perform an analysis of the dimensional characteristics of the implants corresponding to the anthropometric characteristics of the adult, children, men, and women population of different ages and physiques. In addition, an analysis and assessment of the state of stress and displacement in the implant-tissue system should be made. Another element is the correct selection of implant material that should meet the criterion of mechanical and biophysical properties. When selecting a material, possible reactive and immunological reactions, as well as bio-tolerance of the material in the environment of tissues and body fluids, should be taken into account. The final stage is the development of construction, technological and acceptance documentation.

For medical devices, which include hip replacement materials, please note that they are subject to a Regulation (EU) 2017/745 of the European Parliament and of the council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Official Journal of the European Union L 117/1). Medical devices must meet the general requirements set out in Annex I of MRD 2017/745. Conditions for placing medical devices on the market and use:

- The product must meet the general safety and performance requirements.
- The medical device must be classified.
- A conformity assessment procedure should be carried out.
- The medical device must be CE marked.
- The manufacturer meets the requirements of MDR 2017/745.
- Established quality management system (EN ISO 13485: 2016).

This is a requirement that applies to the methods of design and manufacture of medical devices so that they do not endanger the health and safety of patients or users when they are used.

The requirements apply to the following areas:

- chemical, physical and biological properties,
- protection against infections and microbial contamination,
- construction and environmental factors,
- requirements for products with a measuring function,
- radiation protection,
- requirements for active products,
- information supplied with the product (label and instructions for use).

Before placing a product on the market, manufacturers shall carry out a conformity assessment of that product in accordance with the applicable conformity assessment procedures set out in Annexes IX-XI. Technical documentation is created for the conformity assessment procedure confirming the product's compliance with the essential requirements. The conformity assessment procedures depend on the product class. Several materials that have been used as hip implants are presented in the following order below.

6.1 Polymers

Polymers portray great subtypes of biomaterials with potential for 3D printing of scaffolds and can be classified as natural or synthetic. A material study by Kim, [196] has indicated that using 3D printed polymer-based implants can be efficiently used as a controlled drug delivery vehicle through built-in reservoirs and micro-channel networks and also introducing antibiotics directly to the polymer during fabrication [197]. Polymers such as natural gelatine methacrylate (GelMA) and poly (ethylene glycol) diacrylate (PEGDA) are both utilized in creating hydrogels which are natural polymers [198]. Hydrogels are appealing due to their flexible characteristics, possess great biocompatibility, and capability of retaining their hydration and 3D structure when insoluble and these hydrating characteristics make them able to bio-mimic the tissues [199, 200], however hydrogels like most natural polymers cannot be solely used as implants as they do not possess great mechanical properties. Polymers such as poly (o, l-lactic-co-glycolic acid) (PLGA) and poly(ε-caprolactone) (PCL) scaffolds have been produced using 3D printing. Their salvaging of the defects in a rabbit tibia shows that they are non-toxic and can promote the regrowth of bone tissue [201]. Although loading can occur which results to wear and tear as a result of biodegradation with the possibility of basic nutrient absorption from the blood to the implant for these polymer implants, biodegradability can also be an advantage to polymers based on its low toxicity and another benefit is that polymers possess clear ease of manufacture.

The major advantage of utilizing PCL and PLGA as a synthetic biomaterial is its acceptance for medical uses by the food and drug administration (FDA) [200]. This is due to low toxicity during the material degradation pathway. A limitation of PLGA is that it can lead to an inflammatory reaction when acidic oligomer accumulates [202]. Inflammation is a major factor in tissue regeneration [203] hence the necessity for regulating this reaction. Therefore, it is essential to properly understand the inflammatory effect of specific biomaterial utilized in the scaffold structure for the generation of the tissue. As of 2016, the FDA has lifted the limitation on 3D printed implants in the class of the 510K approval system, which allows 3D printed materials to be applied by regular surgical

procedures [204]. It is expected that with this approval there will be full acceptance of 3D printed scaffolds and a necessity for technological advancement, which will permit the simpler fabrication of a large variety of biocompatible materials with great precision.

Also, a key feature of these polymers is the biodegradation rate, which is most times it is rapid when PLGA is applied and declines when PCL is applied. In an assay carried out on polymer degradation of scaffolds, it demonstrates that with relative concentrations of PCL and PLGA, degradation of PLGA was 18% within 14 days and for 28 days was 56% while for PCL was 33% within 21 days and for 28 days was 39% [205]. Nonetheless, both PCL and PLGA may still possess valuable regeneration features based on the injury type [201, 206]. Durable healing is required for open bone fractures because the bone has gone through the skin and can cause infections which increases the healing period [207, 208]. PCL is probably a better option for open fractures based on its slower rate of degradation. This slow rate of degradation of PCL aids the scaffold to give support to cell growth for the necessary time for the build-up of dense tissues [201]. For instances of closed fractures where the bone does not penetrate the skin, PLGA will be a good alternative for bone regeneration.

PCL-based copolymers which include PLGA-PCL-PLGA [208] and PCL-PEG-PCL [209] are synthesized to regulate the PCL degradation during drug release control applications. Nonetheless, these copolymers can possibly be used for application for tissue engineering. A variety of synthetic polymers used in scaffoldings are poly(hydroxybutyrate), polyglycolic (PGA), and poly (propylene fumarate) (PPF). Natural polymers which include polysaccharides and proteins are also used for the fabrication of scaffolds and within polymers, the renowned option in tissue engineering is the collagen type 1 [210, 211]. Recently, collagen scaffolds filled with cationic PEiPDNA complexes to produce a scaffold with the ability for bone regeneration with scalp defects in rats [211]. With post-treatment and novel fabrication techniques, more polymers could produce great interconnectivity and high-resolution scaffolds which forms the basis of the concept of this study.

Some of the studied polymers include polymethyl methacrylate (PMMA). The use of PMMA in orthopaedic application spans several medical implants which include cranioplasty, rhinoplasty, and also bone cement for THR [212-214]. However, structural osseointegration with other structures is not aided by PMMA when they are in contact which limits its range of application. Therefore, Gonçalves et al, [215] proposed two varying formulations that introduce the growth propagation of calcium phosphate on a cemented disc surface to encourage osseointegration. Porous PMMA spacers were created for orthopaedic use when repair proves difficult. These spacers can also support the close tissues and possibly supports the healing process of soft tissues in damaged structures. The major issues of the bone cement are fatigue and interfacial deterioration between the bone and implant of the cement, which will further result in mechanical defects and instability. Further advancement on the material utilized for the implant has been structured on several materials which include stainless steel, reinforced titanium alloys, and UHMWPE or Kevlar with the emphasis on peak temperature reduction for cement polymerization. Testing on the tissue growth of PMMA path implants proves the fibrovascular tissue growth from close tissues with little symptoms of infections [216]. With the rapid development of 3D printing, the use of PMMA for patient-specific implants has been on the rise based on the ease of fabricating custom-made flexible structures [217]. The interfaces between PMMA cement and bone were studied by Freeman et al, [218] human knee joints were studied with time, and radiography was carried out. For joints in the radiolucency line at the bone-cement interface, there was no correlation between the radiography

line and the cement surface orientation. The future of PMMA applications hinges on providing solutions to patient custom problems.

Polydimethylsiloxane (PDMS), silicones, are the next candidates that are applied to a large variety of medical functions due to their non-reactive compounds. Research on PDMS shows it is more reliable for durable encapsulation of the body in relation to polyurethane coatings and epoxy resins due to their even surface and reduced surface energy. These characteristics also discourage polymer absorption of essential nutrients. Further, Teo et al, [214] reported lesser defects noticeable on the silicon surface which suggests better protection. Khorasani et al, [219] blended PDMS with UHMWPE as acetabular cup materials in a bid to find the solution for UHMWPE debris release. The test for biocompatibility was by an in-vitro cell culture test. The result for the in-vitro cell culture techniques is that the blend has a favourable surface to encourage cell response and growth, this depicts surface biocompatibility.

Another candidate material is polyurethanes (PU) which can be applied in a large variety of implants including biomedical applications because they can be easily modified to fit the purpose. However, PU can be chemically attacked in vivo and thus lead to material degradation. If the degradation is handled properly, it can be used to enhance tissue regrowth [220]. Also, PU is known to have a low water permeability which can be reduced additionally by inducing isopropyl myristate in low concentrations [221]. The research by Baj-Rossi et al, [222] discovered that epoxy-based PU membranes could retain enzyme activities for an estimated 35 days when implanted in a mouse within 30 days it was noticed that the sensor integration with close tissues was enhanced and reduced. Inflammation was noticed. A biodegradable PU binder and mineralized allograft bone fragments were used to fabricate a nonporous composite and it was discovered that the composite was osteoconductive and possessed great strength which makes it ideal for load-bearing utilizations. This reveals that PU composites have a huge potential for progressing tissue engineering and can also be modified to fit varying applications.

Thermoplastic PU also demonstrates great potential when combined with PDMS for implant applications due to its enhanced thermomechanical, surface, and biocompatible characteristics [223], although this technique is still at a novel stage and more research are still ongoing to evaluate the thermoplastic PU properties. PU nanocomposites have been successfully produced via iron(iii)oxide nanoparticles and biobased high branch PU which showed magnetic features with improved biocompatibility, shape recovery, bioactivity, and biodegradation contrast with the original [224]. Analysis of the physicochemical properties of softened and vulnerable PU grades (shore hardness 80A-85A) and a biostable corethane 75D shell was (very hard content) was implemented [225]. This was done on 37 mature merino weathers (3 years old) of an average weight of 55kg with common genetic background for THR with gait motion for 5Km and was subsequently characterized. It was concluded that in only one instance that the corether 75D fracture and was attributed to fracture and impingement. However, this shell fracture did not cause loosening or degradation in the corethane 80A softer layer which was intact the whole time. However, wear impingement on the acetabular cup remains a challenge. This material should be a model for smart biomaterials for several orthopaedic applications to surpass conventional limitations.

Polyamides (PA) are polymeric molecules that have amide bonds as repeating units. Polyamides can occur as both synthetic and natural. The emphasis for biomedical applications remains the synthetic polymer where nylon is the most common form of PA and often depends on fibres as a composite to enhance the mechanical strength and has been applied in suture and dentine implants

[226, 227]. However, PA is rarely utilized for packing films, albeit PA composites are considered safe for application as bone formation scaffolds and are mainly used as nanofillers to enhance the mechanical features of composites [227, 228]. The research conducted by [229] PA was tested with other materials to evaluate the microbial contamination with PA showing low contamination in comparison with other materials. This reveals that PA can prevent bacterial growth. Another benefit is that glass fibre nylon composite can be easily fabricated via a 3D printing device.

Other noticeable biopolymers include polytetrafluoroethylene (PTFE), polyimide (PI), and liquid crystal polymer (LCP). Essner et al, [230] investigated polytetrafluoroethylene (PTFE) and UHMWPE based on the wear ratio, based on Charnley's earlier experiment with PTFE low friction arthroplasty (LFA) which was a disaster judging from the high wear rate (2.0-3.5 mm/yr.) while that of UHMWPE was a success with lower wear rate (0.07-0.22 mm/yr). Likewise, polyimide (PI) can be subcategorized into several groups depending on the functional group, polymerization, and hydrocarbon residue type of the polymer chain. These properties have a major effect in determining the physical properties and possible utilizations. However, PI is still used in the medical industry as encapsulators and insulators for medical equipment. Tests were conducted by Rubehn and Stieglitz, [231] to determine the durability of three different commercially produced PI. There were no noticeable changes in tensile properties when they are inserted in phosphate-buffered saline solution within a period of 20 months at both 60 months and room temperature to imitate body conditions that validate their application during this period. Liquid crystal polymer (LCP) possesses a very high impact strength and young's modulus amongst materials. LCPs are also appealing for application in microwave frequency devices. Studies indicate an increasing interest in LCPs used as biomaterials in several devices and implants which include neural and retinal prosthetic implants [232]. Neuroprosthetic implants which have been revealed to improve walking ability for stroke patients [233] was studied by Lee et al, [234] for the purpose of encapsulation through fusion bonding and thermoforming of LCP thin films which were found to have a significantly low level of current leakage via LCP encapsulation within 300 days by in vitro facilitated soak tests for implant performance.

Polycaprolactone (PCL) is a biodegradable polymer that can easily undergo gradual degradation when exposed to biocompatible bodies [235]. A novel coaxial electrospun PCL/polyvinylalcohol (PVA) hydroxyapatite (HA) blended with core-sheath nanofiber coating was fabricated for enhanced implant osteointegration and reduced bone infections. The research showed that the NF coating could support drug delivery efficiently in a structural in vitro rat model and also promote sufficient osseointegration. Future studies should be based on the inclusion of antibiotics in the NFs to bacterial control and cellular reactions while histological imaging will be necessary for proof of osseointegration in the body [236].

Polyvinylidene fluoride (PVDF) is known for its great flexibility, thermal stability, cost-efficient, lightweight, low mechanical impedance, and acoustic, which makes it possible for use as an artificial hip joint based on good biocompatibility [237]. It is used extensively in the medical industry and has been previously studied by several researchers globally. Its inertness positions PVDF as a suitable material for orthopaedic applications while the piezoelectric feature makes it ideal for inward healing and can also be applied as sensor substrates [214, 237]. However, pure PVDF film is rare to acquire for biomedical applications and this is due to the difficulty in formulating smooth films and weaker adhesion to other materials. The possibility of improving these properties of PVDF with other materials to produce composites has been accepted. There has been proof that there is

energy generation through blood vessels contraction and expansion when PVDF shows several potential applications with emphasis on multifunctionality ranging from substrates or sensing materials on a sole device as fabricated by Marques et al [238].

Recent advancements in materials require PVDF to form composites with other materials prior to being considered as being lamina. Although Sharma et al, [239] produced a 1-µm thick film of PVDF-Tr-Fe with the purpose of piezoelectric pressure sensor utilization through conventional lithography technique as a model for a potentially worthwhile batch processing. Due to the complex nature of PVDF film fabrication, more studies in PVDF fabrication is necessary for an effective application in nanoscale devices and would be of great advantage to the orthopaedic industry.

Polyethene (PE) can be classified by molecular weight such as high-density polyethene (HDPE) and low-density polyethene (LDPE), which can be utilized in wide ranges of applications depending on the characteristics. It is expected that with molecular weight increment, the yield strength increases while the elasticity is reduced. In previous research by Kurtz, [240] to create polyethene-based orthopaedic implants, it described the entire process beginning with the resin stage to the end product and mostly focused on the procedure and characterization of ultra-high molecular weight polyethene in the case of THR, the ceramic on UHMWPE implants showed a reduced fracture rate and squeaky sound when compared to the traditional ceramic-on-ceramic implant. Also, there was no osteolysis reduction and therefore for statistical validation, there is not a huge difference. However, the parts of PE can be synthesized to counter osteolysis. Furthermore, a study by Green et al, [241] discovered that porous HDPE possesses good elasticity, biocompatibility, and reduced toxicity and this makes it a suitable material for rhinoplasty surgery. It was suggested that surface modification is necessary depending on the level of the implant application. For instance, UHMWPE modification through laser radiation altered the sample's wettability and surface irregularities. This technique reduces the surface irregularities to 1.7 ± 0.5µm via a 532 µm wavelength laser. There was also a noticeable bone-bonding on the surface of the implant at 1 µm.

The research work by Cools et al, [242] on the utilization of pressurized plasma technique to modify PE implant surface for adhesion increase with PMMA bone cement. Also, in addition to a high concentration of the PET monomer, the PMMA structure was absorbed into PE film which leads to a smoother surface. Affafato et al [20] studied the wear pattern of conventional and cross-linked polyethene for THR with the long-term challenge of UHMWPE being poor wear resistance. A 12-station hip simulator was used to evaluate the wear performance of 5 varying polyethylenes combined with CoCr MO femoral head was analysed. The study was to understand a new XLPE derived from thermo-compression (XLPE-RT GUR1050) that produces less wear composed to XLPE GUR1020 and regular UHMWPE. The wear result was finalized by its crystallinity degree where XLPE showed a great wear reduction while XLPERTGUR1030 acetabular cups had a greater weight reduction while XLPE GUR1020. However, it is lower than regular UHMWPE.

Polypropylene (PP) is quite like PE in the sense that it can be modified as it relates to the density and classified into copolymer and homopolymer composites with the difference being material strength. Other materials have been understood to perform efficiently in the body than PP. finally, PP is a viable material, but its main disadvantage is based on the biocompatibility issues for biocompatible applications.

PP is mainly used as a surgical mesh for weak tissue reinforcement while still playing the role of a scaffold for the regrowth of fibre-collagenous tissues on the meshes and can also be used to treat prolapses [243]. Current research has been carried out on other body parts such as chest

reconstruction [244]. However, there has been a contradiction in the PP application. There have been speculations that such implants may induce inflammatory body reactions which slows the healing process [245]. Although Moailli et al, [246] suggest that the inflammatory reactions were a necessary unavoidable process during body healing and thus PP meshes can still be used. Also, PP is noted for being non-carcinogenic in the body and should be supported. However, the level of PP mesh biocompatibility cannot be ascertained totally. This situation can be salvaged by surface treatment to boost biocompatibility.

A recent technique that was employed by Abednejad et al, [247] for the PP membrane surface was with the infusion of PEG via graft polymerization. Bialecki et al, [248] evaluated the hip joint replacement produced from monofilament polypropylene mesh. For the technique, 6 lambs with varying weights of 12-15 Kg and 2 mature sheep weighing roughly 35 kg were used. From the results, the polypropylene mesh was similar for the femoral head, and a formation of stiff-elastic combination with the hip joint. An in-depth review of surface modification for bioimplants is presented in the section below. Table 3 provides an outline of the material properties of reviewed polymer-based hip implants used for orthopaedic applications, here the standards presented have varying fabrication techniques.

Table 3 Material property table for reviewed polymeric implants.

Polymer	Test standard	Tensile strength (MPa)	Yield strength (MPa)	Young modulus (GPa)	Elongation (%)	Ref
Poly (methyl methacrylate) (PMMA)	ISO 5833: 2002 and ASTM F451-99a	48-76	32-77	1.8-3.1	2-10	[214, 249, 250]
PA11		47		1.1-1.4	280	[214]
PA12		35-55		1.27-2.6	120-300	[214]
PA46		100	30	1-3	40	[214]
PA6 cast		55-85		0.7-3	10-350	[214]
PA6-3T		70-84		2	70-150	[214]
Polyimide		85-90	73	3.1	5-7	[214]
Nylon 6/6	ASTM F2033 - 12	76-85		1.7-2.0	12-300	[214, 249]
Poly (ethylene terephthalate)	ASTM F754 - 08(2015)	53	23-64	1.9-3.0	300	[249, 250]
Poly (lactic acid)	ASTM F1925 - 17	28-50	43-64	1.2-5.0	2-6	[249, 250]
Polypropylene Homopolymer		25-36	17-35	0.8-1.55	400-900	[214, 249, 250]
Polypropylene Copolymer		30-38		1.1-1.55	200-700	[214]

Polytetrafluoroethylene	ASTM F754 - 08(2015)	25-36		0.4-0.75	350-550	[214, 249]
Silicone rubber	ASTM F2038 - 18	2.8		Up to 10	160	[249]
HDPE	ASTM G 77, ASTMD 2714	20-32		0.6-1.4	180-1000	[214]
LDPE		8-12	15-20	0.2-0.4	600-650	[214]
Ultra-high-molecular weight polyethylene (UHMWPE)	ASTM F2759 - 19	>35		4-12	>300	[249]
Polyetheretherketone (PEEK)	ASTM F2026 - 17		60-66	3.2-4.8	1.9-2.7	[250]
Poly (vinylidene fluoride-co-hexafluoropropylene) (PVDF)		26-57	24-39	0.8-2.9	33-153	[214, 250]
Polyurethane thermoset		20-45			500	[214]
LCP		120-240		10-40	1.2-7	[214]
Parylene C		69	3200	2800	200	[214]

6.2 Composites

This material is made of two or more component materials and is important in tissue engineering based on its capability to enable 3D printing biomaterials to have better mechanical strength and complex designed scaffolds. A research group used a composite of calcium phosphate and type1 collagen by a 3D printer which is the Z printer 450 printer for printing scaffolds to understand the possibility of the process and to increase the mechanical and cellular characteristics in vitro [251]. In a different study by Serra et al, [252], PLA-based composites comprising of PLA and bioactive CaP glass were generated by a nozzle deposition system. These scaffolds were done with two varying layer designs which are; displaced double-layer (DISPL) and orthogonal layer configuration (ORTH) to verify the capability of nozzle-based additive manufacturing techniques to print scaffolds that are biodegradable with varying porosity and great mechanical properties [252]. This scaffold had great porosity and great mechanical properties that are based on the design, with ORTH scaffolds, produce roughly 3 times greater compression modulus (90KMPa) relative to DISPL scaffolds (-30kMPa).

The mechanical property of hydrogels can be significantly improved when they form composites. Composite hydrogels consist of ceramics that can sustain a hydrophilic polymer to bio-mimic the natural tissues and also boost the mechanical strength to resist compression forces brought by cell growth and distribution [199] composites use the potential for application in 3D printing of ECM such as scaffolds. Bose et al, [142] published a full review of 3D printed biomaterials in the engineering of bone tissues which includes the hip bone. It concluded that the search for suitable material/material blends for 3D printing is still a challenge. More research should focus on the

varying types of tissue replacements that require several specifications which include mechanical strengths, scaffold morphology, and pore sizes. Also, Wang et al, [63] assessed the use of 3D printed artificial hip joints for THR during a period of 2 years and finalized that the 3D printing technique indicated a better therapeutic effect that is in harmony with the anatomical characteristics and physiological structure of the patient, and it was suggested that the use of the 3D techniques will aid in improving the lives of many patients. Researchers are finding more efficient scaffolds with the ability to mimic scaffolds for cell attachment, growth, and distribution leading to a rise of functional tissue. Presently, most of the studies on 3D printed scaffolds have been based on bone tissues and hence more studies are needed in the tissue engineering area as it relates to other body tissues i.e. cardiac tissue. Novel designs of composites and synthetic biomaterials may take the lead for printing scaffolds with a 100% networking/interconnectivity, flexible pore size manipulation, >99% precision, and enhanced mechanical strength for varying tissue formation and load-bearing applications.

A novel composite material to match the cortical bone elastic modulus and possess an ultra-high flexural strength comprised of liquid crystalline polymers reinforced with carbon fibres was conducted by Kettunen et al, [253], this was fabricated through 2 stages of extrusion. The mechanical properties of LCP/CF seem promising for high load-bearing applications, for a bigger picture a bone-modulus fitting rigidity and high strength should ensure advantage is fracture fixations in comparison to a metallic implant for enhanced stability to encourage bone adhesion at fracture healing commencement. It was concluded that LCP/CF composites are suitable for orthopaedic applications due to their high flexural strength property and a high shear strength which is perpendicular to the fibre orientation. However, more studies on this composite should focus on wettability improvement of the reinforcement fibres prior to moulding and enhancement of torsional strength by applying an extra filament wound LCP/CF layer on top of the LCP/CF composite.

Carbon nanotubes (CNT) composites where CNTs are regarded as possessing unique mechanical, electrical, and surface properties that aid the functionality enhancements of its devices [254-256]. CNT composites are significantly the strongest materials among biomaterials for implants with high elastic modulus and tensile strength. However, the limitations of the composites are a relative weakness with shearing between facing skills, and due to their hollow structure, they are easily compressible. In a few structures, it was found that although there was no direct relationship between biocompatibility and key dimensions of carbon nanomaterials, from previous studies carried out it was ascertained that shorter CNTs have more biocompatibility than bigger CNTs [257]. CNT composites have been applied as coatings on metals for enhancing the packing density and porosity of the metal surface, thus reducing ionizations from the entire metal body [258, 259]. Research by Li et al [260] suggested that CNTs can be used as a competent coating for weight-bearing body implants and can encourage the generation of hydroxyapatite (HA) on these coatings.

A novel composite femoral stem was fabricated to meet the cortical bone properties and to reduce cortical bone loss due to stress shielding by Dimitrievska et al, [261]. The composite was fabricated via moulding and comprised of three distinct layers which are PA12/CF, PA12/HA, and was plasma spray-coated with HA. The biocompatibility test was in vitro through MG63 osteoblast-like cells while in vivo studies were based on the comparison of Ti64 rods studied on a rabbit femur. The in vivo studies demonstrate an adhesion and penetration of osteoprogenitor cells to the HA-coated composites. While for the case of in vitro, the three implants components enabled

osteoblast proliferation, and the HA-coated layer supported increasing bioactivity. This suggests that more research on the performance of PA12 components with HA coating will be worthwhile [261]. The demand for the fabrication of wear-resistant materials to be applied in artificial joints led to the study by Johnson et al, [262] to evaluate the wear behaviour of carbon nanotube and high-density polyethene composites. From the test data, there was confirmation that the addition of CNT to HDPE decreased the material wear rate with subsequent increase of weight percent will have a greater impact on the properties of the material. Also due to the structural similarity of HDPE to UHMWPE, it will also be beneficial to add CNTS to UHMWPE. However, novel techniques in proper uniform dispersion of CNT should be developed. Also, more tests on the bioreactivity of the wear debris and surface characterization should be carried out. The summary of the physical properties of reviewed composite-based hip implants used for orthopaedic applications can be seen in Table 4 below.

Table 4 Material property table for reviewed composite implants.

Composites	**Tensile strength (MPa)**	**Yield strength (MPa)**	**Young modulus (GPa)**	**Ref**
MWCNT-COOH (0.1)/PMMA (Simplex Ptm)	80-120		5-7	[263]
PA6/HANR-20	70.7	95.3	3.12	[68]
PA6/HANR-40	77.5	110.6	4.36	[68]
PA6/HANR-60	85.6	134.5	5.56	[68]
PCL + 1%ZnO		1.30-1.80	5.32-5.72	[264]
PCL + 2%Zno		1.05-1.29	4.16-4.40	[264]
PCL + 4%Zno		0.89-0.97	3.53-3.93	[264]
PCL + 6%Zno		0.87-1.09	3.57-3.98	[264]
UHMWPE + 10% HA		43.02	3.79	[265]

Therefore, for 3D printing of hip implants, the materials which have shown potential for meeting the requirements are the following; Acrylonitrile butadiene styrene (ABS), Carbon Fiber reinforcements, Conductive Filaments, Flexible Filaments, HDPE, Metal filaments, Polyether ether ketone (PEEK), Polyamide, Poly Lactic Acid (PLA), Poly Vinyl Alcohol (PVA) and T Glass/PETT. There is significant competition between these materials currently as each of these materials can be improved. The other materials which are used for fabricating conventional implants and can compete with 3D printed implants are presented below.

6.3 Conventional Materials

6.3.1 Metals

Stainless Steel. Stainless steel is a steel alloy comprised of several elements such as chromium with an estimated mass fraction of 11% and carbon (1.2%) which became popular in the 20th century [266] based on its manufacturing case and low cost. Although various grades of stainless steel are applied extensively in food processing, waste manifolds, vehicle parts, and surgical devices,

the austenitic 316L stainless steel is the sole grade that applies as a biomaterial due to its low cost and antiferromagnetic exhibition. It also possesses excellent toughness characteristics that are sustained low (cryogenic) temperatures. From cytotoxicity evaluation studied, they demonstrate relatively better compatibility [267-269]. Wiles, [270] first applied stainless steel as a biomaterial in total hip replacement in the 1930s with the subsequent decade heralding an interest in scientific studies on the bioimplant fabrication which leads to its large amount in the market with a share of 10–20%.

The mechanical properties of stainless steel are appealing to biomaterial fabrication due to the wide range of controllability it offers which grants these products to have enhanced strength and ductility for medical applications. Overall, the elastic module of the human bone (10-30GPa) is lesser than the stainless steel (roughly 200GPa). Although this relatively large fracture toughness and tensile strength indicate a suitable mechanical performance that can withstand enough plastic deformation prior to failure and significant loads, the mechanical model of functioning in a living body significantly varies with the external domain. Precisely, the bones undergo cyclic loading during the patients' movement. It is estimated that for a patient of above 20 years a cyclic number is roughly 1 x 10^7 cycles, the extent of loading may lead to fracture of materials that are lower than the yield strength [271]. Nonetheless, stainless steel implants experience fatigue because of relatively low failure strength. Hence stainless steel is mostly utilized in short-term implant materials. Another factor for the short time application is the uncertainty with regards to corrosion from studies that reported that there was a close correlation between the corrosion pits and fatigue crack initiation. Hence, surface treatments of polymers are normally utilized to boost the functioning prior to use [272].

Cobalt-based Alloys. The cobalt-based alloy was first adapted for use in bioimplants in 1936, over the next decade, studies were done based on medical applications with significant success being noticed [273]. Cobalt-based alloys are categorized based on the components into two groups. The Co-Ni-Cr-Mo is a form of cobalt alloy which comprises Mo (9–11%), Ni (33–37%), and Cr (19-21%). It started being used widely recently and usually undergoes wrought prior to utilization in heavy loaded bearing joints, for example, prosthesis skin [274, 275]. Co-Cr-Mo alloy is another form of Co alloy which components include Cr (27–30%) and Mo (5-7%). Currently, with a longevity span increment of 20 years, this material contributes immensely by acting as structural materials in fixed implants. For example, Co-Cr-Mo alloys having ultra-high molar weight polyethene which behaves as a liner is presently the main material suitable for prosthetic ankles and knees.

In general cobalt alloys have great biocompatibility due to their suitable corrosion resistance [274, 276]. Various studies on cobalt alloys revealed they are very corrosion resistant also in the chloride-abundant surrounding. A passive oxide layer is easily created on the surface which plays a key role in a barrier when corrosive materials are present and therefore reduces the possibility of corrosion occurring [277-279]. The X-ray photoelectron spectroscopy (XPS) analysis revealed that the oxide layer formation is greatly attributed to the large Cr amount. However, Ni and Mo had a similar but negligible contribution. It is worth noting that the main alloy components Cr, Ni, Mo, and Co are traced elements and highly toxic in the body when in excess quality. This can destroy the blood cells, liver, lungs, and kidney [280-282]. Therefore, a major concern on the use of cobalt-based alloy biomaterials is the release of ions/particles by shrink loosening and fatigue of the material.

When compared to stainless steel, cobalt-based alloys are durable and lower chance of fatigue failure [64, 65]. This can be attributed to the crystallographic structure of cobalt, ensuring all the alloys have great mechanical features. The ultimate tensile strength and Young's modulus of the cobalt are 430 – 1030 MPa and 220GPa respectively, this is roughly 10 times greater than the human bone. These unique mechanical properties present cobalt alloys as befitting a varying range of orthopaedic applications. However, the stress shielding results from a relatively high elastic modulus where the implant may bear most of the load around it and the required stress is not homogeneously transferred to other bones close to it. This will weaken the bone remodelling stimulus with time and can cause bone degeneration. Although the cost of manufacturing the alloys is high in relation to the medical market, cobalt alloys remain the better alternative for metallic implants in joint bearing utilization.

Titanium Alloys. Titanium and based alloys are highly attractive biomaterials due to various good features such as great biocompatibility, low density, model mechanical properties, and high strength [283-285]. The boost in demand for Ti alloys for utilization as a biomaterial has been noticed since the 1970s and possibly will continue. The most common form of titanium alloy used is Ti-6Al-4V which occupies 45% of the holistic implant manufacturing. Interestingly, the initial aim of Ti-6Al-4V development was for its application in the aerospace industry, its non-toxicity contributed to its application in the biomaterial field.

Titanium as an element does not exist within the natural body and its biological effect is uncertain but they are non-toxic and inert based on reports carried out [285]. Due to this inertness, Ti-alloys is an ideal biomaterial candidate but unfortunately, it caused an allergic reaction, and osteomalacia are noticed in patients. Ti-alloy-based implants were traced to the variation and aluminium alloy particle/ion release. A novel generation of Ti-alloys (β-titanium alloys) is currently in development with the objective being to replace Al and V with Ta, Mo, Zr, and Nb [47]. As stated earlier the biocompatibility of a material is hugely based on resisting corrosion and these easily make Ti and Ti-based alloy the best in that respective. Alloys like cobalt-based alloys through a passive oxide film, Ti-alloys offer higher corrosion resistance greater than that of stainless steel. The key difference is that due to the inherent properties of the sole titanium element, the alloys do not have enhancement via alloying to improve the corrosion resistance.

The impurity and structural level of Ti alloys determine the mechanical properties. From another perspective, the development of Ti-based alloy Ti-Nb-Zr-Tn (TNZT) discovered the lowest elastic modules of all the metallic alloys with the aid of modern alternative alloying elements. Importantly, although Ti-based alloy's elastic modules are lesser than Co-based alloys, stress shielding aftermath is still an issue because it can only be reduced but is hardly preventable. For comparison on ultimate tensile stress, the β titanium alloy values are quite like that of stainless steel but lesser than Co-based alloys [170, 283, 286]. To date, Ti alloys have a greater wear resistance than Co-alloy with this test from hip replacement simulators [47]. Although, the external stress which is applied to the implant can destroy the unstable oxide layer, and thus hardened oxide layer fragments are deposited on the body. These fragments subsequently split down the oxide layer and lead to the destruction of the implant surface. Hence, Ti-based alloys are highly recommended for application as parts of compatible constraints, instead of articulating with other materials. Long and Rack, [47] summarized metallic biomaterials of titanium and titanium-based alloys, cobalt-based alloys, and stainless steel as seen in Table 5.

Table 5 Provision on the use and characteristics of metallic biomaterials and provides a perspective over the choice of Ti and Ti-alloys being the best in terms of biocompatibility [47].

Metallic scaffolds	Advantages	Disadvantage	Key use
Cobalt-base alloys	• Great fatigue strength • High corrosion resistance • Good wear resistance	• High modulus • Poor biocompatibility	• Prosthetic stems • Load-bearing parts in total joint replacements (wrought alloys) • Dental moulds
Stainless steels	• Lower cost • Readily available • Easy processing	• High modulus • Poor performance with time	• Mostly used in total hip replacements (large nitrogen) • Temporary mechanisms (fracture beds, high nails, and screws)
Ti and Ti-base alloys	• Reduced corrosion • Great biocompatibility • Minimum modulus • Good fatigue strength	• Poor shear strength • Low wear resistance	• Durable and permanent tools (pacemakers and nails) • For total hip replacements with separate femoral heads

The key advantage for metallic implants is their high strength, low fatigue degradation, easiness to shape, and can be easily sterilized while the disadvantage is that the metals corrode rapidly based on chemical reactions with internal acids and enzymes. This can lead to toxicity by metal ions in the human body. Some metal ions such as silver, copper, and Zinc can be antimicrobial which can be incorporated as antibiotics into polymers for 3D printing of customizable wound dressings as studied by Muwaffak et al, [287]. Where 3D printed PCL scaffolds were used to construct ear and nose 3D models and reduced the rate of infections on an individual patient. Gil et al [288] worked on AISI 316 L stainless steel which has been significantly used in the artificial knee or hip joints by attempting to optimize the corrosion resistance properties of AISI 316 L stainless steel due to ease of being examined via magnetic resonance. However, there was no significant improvement noticed, and this was attributed to the presence of chromium nitride.

Rieker et al, [289] stated based on the in vitro comparison that metal on metal (M.O.M) articulations had a smaller wear rate than UHMWPE articulation when used as alternatives, although biocompatibility was not considered as a determining factor. A long-term study (1965-1973) by August et al, [290] of 808 M.O.M cemented THR cases at Norwich and Norfolk hospital the

UK. There was over 49% with excellent results with 78% of these having slight or no pain, although the potential for regeneration was not examined. Dobbs, [291] confirmed that metal on metal prosthetics performed better than metal on polymer (M.O.P) prosthetics however both materials failed with time (1969-1972) due to loosening which was suggested as a wearing out process. This is supported by Black et al, [292] with the clinical study of Ti6Al4V on UHMWPE through PMMA cement, this led to a very high wear rate with revision carried out after 3 years. Tu et al, [293] studied porous standard Ti6Al4V dental implants fabricated from a laser sintered 3D printer to provide bone support to alveolar bone loss with the goal of designing a novel bioactive scaffold that can be used to replace bone defects. The results obtained from the histological, micro-CT scan, and X-ray reports show a significant bone formation which implies that Ti6Al4V is very promising for bone regeneration and repair of large bone defects i.e. hip and knee defects.

HA-coated titanium femoral prosthetic showed no deterioration with time and can potentially provide relief and durable implant from the study by Geesink and Hoefnagels, [294]. While a follow-up case study by Jacobsen et al, [295] with different patients with plasma spray-coated titanium implants demonstrated an excellent performance even in younger patients. A study on Chitosan coatings on medical-grade (AISI 316LVM) stainless steel by Finšgar et al, [296] shows that the coating protects the stainless steel from corrosion and also encouraged osteointegration on the implant.

The research by Kim, [297] confirms that a ceramic head (Zirconia) has a wear rate higher than metal [Cobalt] and attributed this to a smooth articulating surface of Zirconium. Another factor in M.O.M hip replacement is the cup orientation is based on the study by Angadji et al, [298], where larger cup inclination angles have a significant on M.O.M bearings and increase the total wear rate generated. Patel et al, [275] recommended that prospective behaviours such as compression/tensile strength, elongation, and fatigue resistance are crucial for alloy application in the future. In terms of failed metals and alloy implants, major causes of this are the severe level of gas porosity, high shrinkage, the introduction of foreign bodies, and irregular surface. Brown and Sandborn, [299] suggested that new forms of metallic alloys and improved manufacturing techniques will improve the several rates of hip devices.

In comparison to other materials, 3D printing of metal alloys is still a challenge due to the low level of advancement and difficulty in fabricating complex geometries. This can be attributed to more research emphasis on ceramics and polymers which is due to the technical growth of rapidly softening thermoplastics and ceramics with an increase of temperature and easy forms a product that rarely occurs in metals [109]. However, the bulk metallic glass is an ideal material for contradiction based on the study by Gibson et al, [109] where an FDM 3D printer was used to print samples and attributed this to the supercooled liquid region of the alloy and continuous softening on temperature increase. Currently, there is a maturity of 3D printing techniques to fabricate metals and alloys. However, there is still a lack of detailed research on metal-based 3D printed scaffolds and further research in this field should be encouraged. Table 6 outlines the material properties of reviewed metal-based hip implants that are used for orthopaedic applications.

Table 6 Material property table for reviewed metal implants.

Metallic	Test standard	Tensile strength (MPa)	Yield strength (MPa)	Young modulus (GPa)	Elongation (%)	References
Stainless steel	ISO 5832-9	861	496 (offset=0.2%)		46 (in 25 mm)	[271, 300]
Co-Cr-Mo	ASTM F75	655	450	248	8	[301]
Co-Cr-Mo	ASTM F799	1172	827	210-253	12	[275, 301]
Co-Cr-WN-i	ASTM F90	896	379	242		[301]
Co-Ni-Cr-Mo	ASTM F562	793-1000	241-448	228	50	[301]
Titanium (Ti)	ASTM F2516 - 18, ISO 5832-11:2014	760	485	110		[275]
Ti-6Al-4V	ASTM F2516 - 18, ISO 5832-11:2014	965–1103	896–1034	116		[275]

6.3.2 Ceramics

The use of ceramics as biomaterials began in the 1970s [302]. The special properties which include great biocompatibility make ceramics a choice material for bone treatments and joint replacements [303-305]. The benefits of ceramics are high compressive strength required for bone implants and there are also biodegradable while the manufacturing difficulty, minimized bone ingrowth, and implants ease of loosening (with time which it makes when displaced) limit the use of ceramics. From the level of reaction in the human body, bioceramics are normally grouped into three main types:

- Bioinert ceramics: they are mostly inert in the body. This can be attributed to the thin non-adhesive fibrous surface which forms at the bone and ceramics interface. This sort of material is viable for the replacement of prostheses due to its great durability.
- Bioactive ceramics: this refers to materials that have a direct capability of direct bone bonding with a typical example of the material being bioglass [305-307]. Where this material rapidly induces a bonding biologically to the close living tissues after implantation, therefore this form of bioceramics is mostly applied in metal prosthesis surface treatment (coating).
- Bioresorbable ceramic: this form of bioceramics gradually decomposes the host body with time and eventually replaces it by regenerating the bones [305]. Thus, they create advanced control of the bone replacement and biomaterial resorption process. Typical examples are calcite and tricalcium phosphate.

The most popular representative of bioinert ceramics is zirconia and alumina [305, 308]. They are both appealing for their biocompatibility where the chemical compositions are either having

little effect in the body or common ions present in the environment. Alumina is well known because of the fusion of great compression resistance, suitable wear properties, great corrosion resistance, and satisfactory fracture toughness. Boutin, [309] studied the first use of total hip prosthesis by alumna socket and head application in 1971, this leads to a spread in the use of alumina ceramic in medical applications. As of recent, alumina bioceramics is popularly viewed in femoral heads with an addition of a polymeric acetabular cup and metallic femoral skin for hip joint replacements and the wear plates for knee replacements [304, 310]. However, it is important to enhance the reliability of alumina ceramic as it was observed that there was crack growth with time in use. Other issues such as difficulty in fabrication, low fracture strength, and high brittleness can impair its future application. Zirconia is proposed as a better option to alumina-based on similar positives as alumina and they also have better fracture toughness [308, 310]. The utilization of zirconia in bio-medical application was initially introduced by Halmer and Duskell, [311].

Christel et al, [312] described the viability of zirconia in this fabrication of ball heads for hip replacements, which finally became a major application. In comparison with the utilization of alumina in hip implants, zirconia bioceramic permits a massive decrease in femur head diameter and this enables a greater degree of joint mobility freedom [313]. Currently, tetragonal zirconia polycrystal (TZP) was chosen by a ball head produced with very minute situations of clinical failure was recorded. Based on the suitable fatigue resistance where more than 300,000 TZP femoral heads being applied since 2002 [314]. This material is seeing a great time in development; however, zirconia is still seen as a novel material in the biomedical sector, with the failure/success rate still yet to be decided [314, 315]. Emphasis should be on the growth of gradual subcritical cracks and degeneration of toughness gradually. Therefore, long-term study is necessary to optimize the level of performance in biomedical applications.

Hydroxyapatite (HA) which is the popular type of calcium phosphate is appealing to bioceramic due to its great biocompatibility, chemical stability, similarity in bone structure, and lower density. Asides from the material features, the best characteristic of HA application in bioimplant is the great level of bone bioactivity (it aids in the ingrowth of hard tissue and bone integration after implanting). From the initial idea of bone repairs in the 1960s [196, 316] which was that a prosthetic body part can be firmly attached to the last bone either via outgrowth or ingrowth via a cementless approach, therefore HA is mainly applied on the metallic biomaterial. In the previous half-century, several studies affirm that enhancing the effect of ingrowth bone tissue boosted by the addition of HA coatings via the analysis of the bonding interface between bone tissues close and HA [307, 317]. From a biomedical point of view, these characteristics obtain a uniquely great therapeutic benefit of quick treatment for ill patients.

A great interest in bioceramic research is going to an advanced stage by the enhancement of biomaterial properties through the inclusion of nanotechnology. Previous research trials on the enhancement of the degree of crystallinity for HA reduced the particle size to nanometers. In comparison to conventional HA, these synthetic HA with nanoscales have a better surface area and free crystal-crystal bond which permits uniform resorption by the scaffold. Although the future of HA coatings based on clinical results seems promising, the limitations remain the poor mechanical properties which have the total HA lacking the required bending strength less than 100 MPa and tensile strength, also mechanical failure can probably occur due to long term usage. In addition, its application in load-bearing scaffolds is hampered by its influential brittleness. Hence, making the major reason behind HA being used as a polymer as composites or coating on metal. Although HA-

coated on metals from reports show a nice surface bioactivity the low metal/ceramic interfacial bonding cannot be overlooked because they may cause massive structure failure [82]. Also, the poor HA mechanical property should be the main reason why there is coating stability. Significant research has been undergone to boost the poor bonding strength of metal / HA interface with the coating technique having effects on the layer reliability, adhesive strength, and stability development on coating methods is thought to be the answer to this issue [318-320]. The material properties of reviewed ceramic-based hip implants used for orthopaedic applications are listed in Table 7 below.

Table 7 Material property table for reviewed ceramic implants.

Ceramics	**Test standard**	**Tensile strength (MPa)**	**Young modulus (GPa)**	**Hardness**	**Ref**
Alumina	ISO 6474-1	350	380	2200	[321, 322]
Mg—PSZ	ASTM F2393 - 12(2016)		200	1200	[321]
TZP	ISO 13356		210	1200	[321]
Zirconia	ISO 11491:2017	200-500	150-200		[322]
Pyrolytic carbon	ISO 14242-3-2013	280-560	18-28		[322]
Bioglassceramics	ISO 13779-2	56-83	22		[322]
Calcium phosphates	ISO 13779-2	69-193	40-117		[322]

7. Concluding Remarks, Opportunities, Challenges, and Future Trends

Most of the 3D printing processes are time-consuming and there is difficulty in fabricating large amounts. These restrict their adoption for medical purposes. Novel printing methods depending on the case and the scale of material processing should be improved. For instance, the projected SLA has introduced the use of digital light processing for efficiency in advancing the printing process. A photopolymer layer is fabricated in a single projection and drastically reduces the processing time. This same technique should be applied to other printing techniques. Another domain to be focused on for progress should be an efficient feedback system, that is, it stands now if an error occurs when printing, the whole process will be stopped which leads to a waste of material and time. The introduction of a feedback system will handle process changes better. More growth in 3D printing is to enhance printer resolution with reduced downtime or alter the geometry of unique products.

With 3D printing being a novel technique for tissue engineering, the acquisition of a 3D printer with a great resolution can come as an exorbitant investment (roughly $750,000 for a sole printer). Also, with the provision of suitable materials, cell culture promotes several cumulative factors that will increase the financial load. Finally, administrative guidelines and standards should be in place to ensure the implants reach a certain benchmark prior to the application [323]. However, the bountiful of premedical tests on 3D printing scaffolds depicts the possibility of applying this scaffold

in tissue regeneration and is plausible. It is essential that engineers, pharmacists, physicians, and scientists keep collaborating to improve the 3D printed scaffolds with respect to tissue regeneration, there is a high expectation of surpassing these barriers for clinical applications.

The general application of the 3D printer is greatly dependent on printable materials. Currently, it is mostly thermoplastic polymers that possess fitting melt viscosity, lower glass transition temperature, powder-based biomaterials, and a handful of powdered polymers that can be utilized in 3D printing. However, these studied materials hardly meet up with the advanced requirements for various industrial applications therefore material modification should be increased. Matrix material synthesis of unique properties where novel follows for reinforcement can be discontinued is necessary and also the accurate mix composition that is required for an enhanced composite printing process. Currently, there has been a concern about material impact in the environment, therefore sustainable materials seem promising to explore.

It is known that reinforcements enhance polymer composite performance. However, in comparison with conventional moulding techniques, 3D printed composites have lower mechanical properties and a good number of polymers cannot meet industry standards. Therefore, further treatment such as consolidation and infiltration has been previously employed to boost this printed product performance. However, this further increases the time and cost involved. The main cause of low mechanical properties is the presence of high porosity surfaces. The incorporation of reinforcements will likely enhance porosity as a result of weak interfacial bonding with the polymer matrix. Thus, the improvements from reinforcements will be balanced by the added porosity. Further research on the elimination of void formation when printing and promoting great interfacial bonding with the polymeric matrix and reinforcements are encouraged. Additionally, there are issues with reproducibility and consistency of these printed products which is not constant, therefore measures to promote even properties of the printed products should be studied.

However, 3D printing of polymers and metals for spinal implants is gaining momentum for recent novel designs that have 3D printing potential and this may, in turn, have an influence on hip implants. Multilevel materials fabricated through 3D printing which the produced device incorporates sensors can readily revolutionize the medical sector [324]. Also, more study on 3D printing techniques for varying surface modification is now being developed and is expected to have a large impact in exceeding the conventional porous metal coatings [325-327]. Another future concentration for growth potential points to enhance drug delivery based on the site-specific delivery alternatives with distinct geometry of the devices. Additionally, the addition of the time concept to 3D printing creates the fourth dimension and creates optimism in 4D printing for the future.

3D technology hastens the R&D time in novel materials/products. The design and development of a product can be enhanced through this technology to meet the requirements which include aesthetics, aerodynamics, and ergonomics. It aids in the faster modification of R&D for commercial products. With regards to the medical sector, it is monumental due to the difference in direct patient data. Therefore, it is mostly applied in devices, equipment, implants, and several other tools as required by the product.

3D printing will assist students, tutors, and researchers in understanding detailed facts with reduced hazards and a faster prototype production prior to industrial production, it also boosts innovation for the students in learning to develop novel ideas. In the aspect of medical training, it is a suitable device to run trial surgery prior to actual surgery. It will be easier to understand difficult

medical cases via the production of the patient customized prototype. Virtual environments such as BARETA have been incorporated in teaching anatomy although this can only cover anatomy shapes for the training [98].

It is critical to have improved design and development capability of a new product in various interdisciplinary areas. It can readily help in discovering defects in product assembly. For industrial utilization, 3D gives efficient concepts in the design, development, and manufacturing of the products. This technology enables the initial stage of product development via faster sample production. It also aids in the proper management of innovative ideas and manufacturing which is still lagging. 3D printing can achieve complex designs and lightweight components in a cost-effective approach.

3D printing as previously stated is utilized in the different industrial fields due to its contribution of enhanced flexibilities to obtain improved precision. The manufacturing of purpose-built complex products can be achieved through this technique, with this technique being applied in a range of sectors such as food, medical, and engineering. From 3D printing, the products are expected to have the following features based on the materials such as coloured components, cost efficiency, waste material recycling, better surface resolution/finish, and eco-friendly [328-330].

Although there is the availability of biomaterials showing huge potentials for bioapplications, knowledge obtained from the reviews on introducing graded properties needs further engagement. Thus, it is imperative to continually develop even scaffolds and total discernment of cellular interaction with the meantime. As stated by Zhang et al, [115] additional emphasis is on “flawed ECM-mimicking”, where some of the successfully fabricated scaffolds cannot mimic the necessary ECM notwithstanding they still aid in directing the needed tissue response. An instance is fibre tracking for nerve cells provides nerve cell external growth to cover a wound hole, even though this is not dependent on the current ECM structure [331]. 3D printing provides consistency, control, and precision necessary for the evaluation of chemical/physical gradients for in-depth tissue growth. However, a prime challenge is measuring cell reaction in uneven scaffolds. A future process that evaluates remote cellular reactions is crucial for the understanding of the gradient scaffold potential.

Recently with advancements in additive manufacturing techniques, 4D printing is garnering interest [332]. Li et al, [333] reviewed a novel shape memory polymer (SMP) that had the ability to maintain its temporary shape when stimulated by external forces and always returns to the original shape after stimulation making them smart materials. SMP was stated to be useful for biomedical applications such as aneurysm occludes, dental and suture implants. Conventional SMP preparation techniques are quite complex to achieve depending on the structure which requires high precision and discrete structures such as coronary and bone stents. The introduction of 4D printers resolves these issues. 4D printing which was first presented by Tibbits in 2013 [333-335] combines SMP and 3D printing techniques to function. Hence the 4D printed SMP structure can react to stimulus e.g. electric current, magnetic, humidity, temperature, and pH. of all the materials, polymers seem to be appealing due to an adjustable temperature, high deformation, high shape recovery rate, easy shifting ductility, low cost, and density. Shape memory PU, PLA, and PCL have potentials for biomedical applications but require further research for a full evaluation of the adoption range. 4D printing is a step above 3D printing based on its greater time dependency and enhanced predictability of materials. However, the limitation of 4D printing with regards to the biomedical application includes very few SMP materials suitable for it, where an efficient material selection

technique is always necessary for patient-based implantation. Software such as ANSYS GRANTA Materials Selector coupled with machine learning and artificial intelligence tools could go some way to provide a wide range of suitable materials to match this condition. Evidently, more study on SMP with low glass temperature, improved biocompatibility and biodegradability to fit 4D printing technology should be an area of development focus.

Author Contributions

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Competing Interests

The authors have declared that no competing interests exist.

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