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UNIVERSITY OF CALIFORNIA

Los Angeles

The Fundamental Study of
Nanoparticle Effects in Metal Matrix Nanocomposite
for Biomedical Applications

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy
in Mechanical Engineering

by

Zeyi Guan

2020

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ABSTRACT OF THE DISSERTATION

The Fundamental Study of Nanoparticle Effects in Metal Matrix Nanocomposite for Biomedical Applications

by

Zeyi Guan

Doctor of Philosophy in Mechanical Engineering

University of California, Los Angeles, 2020

Professor Xiaochun Li, Chair

Metals have been widely used for biomedical applications, especially as bio-implants, due to their excellent mechanical properties that are suitable for load-bearing applications. Zn has recently attracted attention for being used as biodegradable materials for implants, especially for bioresorbable stent and biodegradable electrodes. The suitable corrosion rate and benign biocompatibility promote Zn as a potential candidate for bioresorbable cardiovascular stents. However, the lack of strength and thermal stability inhibited its practical application and commercialization. Alloying has been applied for strengthening but inevitably introducing side-effects, such as increased corrosion rate and decreased elongation. In this dissertation, a new class of materials, metal matrix nanocomposite, was investigated for biomedical applications, including biodegradable implants (e.g., bioresorbable cardiovascular stents) and medical devices (e.g., degradable nanowire biosensors). In the beginning, this work has developed and optimized the

fabrication methods of Zn matrix nanocomposite, enabling efficient nanoparticle incorporation and homogeneous dispersion. Additionally, through the characterization in microstructure and mechanical properties, this work has thoroughly investigated the nanoparticle interaction with the grain boundaries and intermetallic interfaces during the solidification process and aging process. Furthermore, this work has characterized the mechanical properties of Zn-based nanocomposites and has fabricated the prototype of bioresorbable stents for evaluation. For the application of biodegradable electrodes consisting of metal nanowires, nanoparticles have enabled molten metal viscosity/interfacial energy modification and fluid instability suppression to realize the high aspect ratio nanowire fabrication. This dissertation successfully establishes fundamental knowledge for metal matrix nanocomposite as suitable biomaterials for various medical applications, bridging the advanced manufacturing of novel biometals to innovative biomedical devices and providing innovative solutions for human health.

The dissertation of Zeyi Guan is approved.

Pei-Yu Chiou

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University of California, Los Angeles

2020

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Acknowledgement

Chapter III includes a version of

- Guan, Z., Linsley, C. S., Hwang, I., Yao, G., Wu, B. M., & Li, X. (2020). Novel zinc/tungsten carbide nanocomposite as bioabsorbable implant. *Materials Letters*, 263, 127282. <https://doi.org/10.1016/j.matlet.2019.127282>
- Guan, Z., Pan, S., Linsley, C., & Li, X. (2019). Manufacturing and Characterization of Zn-WC as Potential Biodegradable Material. *Procedia Manufacturing*, 34, 247-251. <https://doi.org/10.1016/j.promfg.2019.06.146>
- Guan, Z., Yao, G., Zeng, Y., & Li, X. (2020). Fabrication and Characterization of In Situ Zn-TiB₂ Nanocomposite. *Procedia Manufacturing*, 48, 332-337. <https://doi.org/10.1016/j.promfg.2020.05.055>

Chapter IV includes a version of

- Guan, Z., Linsley, C. S., Pan, S., DeBenedetto, C., Liu, J., Wu, B. M., & Li, X. (2020). Highly Ductile Zn-2Fe-WC Nanocomposite as Biodegradable Material. *Metallurgical and Materials Transactions A*, 51(9), 4406-4413. <https://doi.org/10.1007/s11661-020-05878-y>
- Guan, Z., Linsley, C. S., Pan, S., Wu, B. M., & Li, X. (2020). Zn-0.5Mg-WC as the antiaging biomaterial for the bioresorbable stent. *In preparation for publication.*

Chapter V includes a version of

- Guan, Z., Hwang, I., Pan, S., and Li, X. (July 5, 2018). "Scalable Manufacturing of AgCu40(wt %)-WC Nanocomposite Microwires." *ASME. J. Micro & Nano-Manuf.* September 2018; 6(3): 031008. <https://doi.org/10.1115/1.4040558>

- Guan, Z., Hwang, I., & Li, X. (2018). *Highly concentrated WC reinforced Ag matrix nanocomposite manufactured by molten salt assisted stir casting. Procedia Manufacturing*, 26, 146-151. <https://doi.org/10.1016/j.promfg.2018.07.018>
- Hwang, I., Guan, Z., Cao, C., Tang, W., Chui, C., & Li, X. (2020). *Thermal Drawing of Ultralong Metal Ultrafine/Nano-wires with Fluid Instability Suppressed by Nanoparticles. Nature Communication. Submitted.*

This work is funded by The National Science Foundation (NSF) under Grant No. CMMI #1449395 and the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number R01HL143465.

Throughout the writing of this dissertation, I have received a great deal of support and assistance.

I would first like to thank my supervisor, Professor Xiaochun Li, whose expertise was invaluable in guiding the research and methodology. His insightful feedback pushed me to sharpen my thinking and brought my work to a higher level.

I would like to acknowledge my labmates from Scifactoring Lab for their wonderful collaboration. I would particularly like to thank my labmate, Goncheng Yao, Shuaihang Pan, and Maximilian Sokoluk. I want to thank them for the scientific discussion that we had millions of times, which supported me to further my research.

I would also like to thank my first mentor when I was an undergraduate at UCLA, Dr. Peng Fei, for leading me into the world of academia and the world of science.

In addition, I would like to thank my parents for their wise counsel and sympathetic ear. They always support me financially and mentally without hesitation and encourage me when I am in a financial crisis, and when I am depressed. They are always there for me.

I would like to thank my girlfriend, Chen Zou. Thanks for her accompanying.

Finally, I could not have completed this dissertation without the support of my friends.

Vita/ Biographical Sketch

Zeyi Guan was awarded his Bachelor of Science in Mechanical Engineering with *cum laude* Latin honor, Department of Mechanical and Aerospace Engineering Henry Samueli School of Engineering at UCLA. He has published multiple works in core journals of his fields, including MMTA, ASME Micro&Nano Fabrication, Materials Letters. He has attended multiple international conferences, including NAMRC and TMS, with oral presentations given in public.

Chapter I: Introduction

Metals have been widely used for biomedical applications, especially as biomaterials, due to their excellent mechanical properties. An abundance of applications takes advantage of metals, because of their attribution to the strength, ductility, fatigue resistance, creep resistance, wear resistance, corrosion resistance, electrical conductivity, and thermal conductivity. Additionally, metal properties can be altered and modified through fabrication methods, aiming at different applications. Metals are mostly favorable for load-bearing applications, such as implants, because they can provide unique mechanical properties with both high strength and high elongation while ceramics and polymers cannot deliver.

Among the metals that have been studied for biomedical application, Zn has attracted attention in the recent decade for bioresorbable cardiovascular stents. The bioresorbable cardiovascular stent is defined as the expandable mesh tube to hold open the weak or narrowed arteries that will ultimately dissolve in the body. Because of the suitable corrosion rate of Zn in animal models, an increasing number of works have started to investigate the feasibility of Zn as bioresorbable cardiovascular stents to substitute Mg. This work focuses on the fundamental studies of nanoparticle effects on metals (e.g., Zn and its alloys) for biomedical applications (e.g., bioresorbable vascular stent and biodegradable sensors).

Since such load-bearing applications require much higher strength than that pure Zn could achieve, current research focuses more on the strengthening of Zn, including alloying strategy. However, the side effects of alloying are the loss of ductility, increased corrosion rate, and deterioration of biocompatibility. Although alloying strengthening by solid solution and precipitation is efficient, the introduction of additional elements usually results in other property deteriorations. Thus the practical use of such Zn alloys as stent material has been postponed.

In this work, nanocomposite was proposed as an innovative methodology to solve the dilemma of Zn strengthening without sacrificing other favorable properties. Nanoparticle induced strengthening would efficiently enhance mechanical strength without a loss of ductility while maintaining a favorable corrosion rate. This study focused on incorporating nanoparticles (e.g., WC, TiB₂) into Zn and Zn alloy matrix for enhancement of strength and thermal stability enhancement. The specific research objectives of this work include:

- Developing and optimizing a scalable fabrication method for Zn matrix nanocomposite with homogeneous nanoparticle dispersion
- Characterizing microstructures, mechanical properties, degradabilities, and biocompatibilities for Zn matrix nanocomposites
- Analyzing the material properties and establishing a fundamental understanding of nanoparticle interaction with the matrix for property modification
- Investigating the feasibility of the materials for biomedical applications
- Designing, optimizing, and fabricating the biomedical device, and preparing for *in vivo* trials in animal models

Nanoparticle induced strengthening is the most apparent effect on Zn, according to many relevant studies. Besides, chemically inert nanoparticles are supposed to maintain the corrosion resistance of Zn, where intermetallics in Zn alloys commonly have increased corrosion rates. More importantly, nanoparticle-induced thermal stabilization can inhibit the natural aging of Zn and thus introduce high-temperature stability in the human body environment.

The dissertation includes:

- Chapter II reviews the relevant literature.

- Chapter III aims at the fabrication and characterization of Zn matrix nanocomposite in order to investigate its feasibility as a new biomaterial systematically. This chapter has investigated the process optimization for an efficient and cost-effective production strategy. Furthermore, general material characterizations are carried out to evaluate the overall material properties, including mechanical properties, degradability, and thermal/electrical conductivity.
- Chapter IV aims at investigating the fundamental and technical aspects of bioresorbable stents made of Zn alloy matrix nanocomposite. Multiple characterization methods were conducted to fully understanding the effects of the nanoparticles in Zn-Mg systems. More specifically, the nanoparticle-induced microstructure modification (e.g., grain refinement and the modification of intermetallic morphology) and the resultant mechanical properties (e.g., ductility, fatigue resistance, and creep resistance) were studied. By further analysis, the specific interaction mechanisms between nanoparticles and the Zn/Zn alloy matrix (e.g., nanoparticle guided solidification, nanoparticle interaction with intermetallic precipitation, and nanoparticle interaction with grain boundary during shearing) were investigated. Beyond the material analysis, the bioresorbable stent prototype was fabricated after design, FEA simulation, and optimization, serving for early-stage animal trials. The functionality of the prototype was verified in on-bench deployment simulation.
- Chapter V aims at exploring an additional application, nanoscale metal bioelectrode, using various nanocomposites. This part investigated mechanical, electrical, and thermal properties of metal micro/nanowires (e.g., Zn, Ag, Ag-Cu) by thermal drawing, and uncovered a nanoparticle enabled fluid stabilization mechanism for the fabrication of metal nanowire by modifying the inherent material properties (e.g., surface tension and viscosity)

to break the fundamental limit. The material has been studied in realizing high aspect ratio nanowire fabrication by thermal fiber drawing. Furthermore, a new pinning mechanism to help suppress liquid instability by nanoparticles was proposed for ultra-long metal nanowire fabrication.

- Chapter VI summarizes the overall achievements and significance of this study.
- Chapter VII listed the future work and the long-term aims of this study.

Chapter II: Literature Review

2.1. Metals for microscale devices in medical applications

Metals have been widely used for biomedical applications, especially as implants, due to their excellent mechanical properties. Applications take advantage of metals because of the combination of high strength, good ductility, fatigue resistance, creep resistance, electrical conductivity, and thermal conductivity. Additionally, metal properties can be altered and modified through fabrication methods, aiming at different applications. Typical metallic biomaterials are used as permanent devices, including titanium alloys, stainless steels, cobalt-chromium alloys, gold, and silver. One of the critical properties required for biometals is biocompatibility, referring to the ability of a material to perform with an appropriate host response [1]. Long-term toxicity and complications are what doctors and patients worry the most. Thus, instead of metals, biodegradable polymers were investigated more frequently, since they can be absorbed and degraded into water and carbon dioxide [2]. The investigation on magnesium started about 20 years ago as a potential solution for biodegradable metal implants, especially for load-bearing medical applications. Mg is a suitable lightweight metal with Young's modulus similar to natural bone, and its ionic presence has a significant functional role in biological systems and in vivo degradation via corrosion in the electrolytic environment of the body [3]. However, Mg and its alloys obtained the undesirable corrosion rate, which could induce rapid loss of mechanical integrity and rapid hydrogen evolution during the degradation. Polymer coatings have been proven to preserve the mechanical integrity in early stages, but still has limitations on the mechanical properties [4].

In 2013, Zn was revealed to be a suitable biomaterial to substitute Mg due to its favorable moderate corrosion to many load-bearing applications, e.g., orthopedic and cardiovascular implants [5]. Furthermore, Zn has shown favorable ductility and non-toxicity as an essential

element in the human body. Still, an urgent issue of Zn is the inherent low strength, where a great deal of research is still contributing to strengthening the material by alloying. Even though the introduction of intermetallic phases could enhance the strength significantly, the side effects are the sacrifice of the ductility, corrosion rate, and biocompatibility. Furthermore, an age-hardening effect on Zn alloys was observed, which could deteriorate the mechanical properties (e.g., ductility) during the implantation and result in device failure [6]. Permanent materials for biomedical applications

Metals have been widely used in industry due to their excellent mechanical, chemical, and physical properties. The first use of metal devices, such as tools and weapons, can be traced back to more than 6000 years ago. However, due to their biocompatibility and toxicity, metals, especially heavy metals, are commonly thought “unfavorable” for biomedical applications [7]. Some heavy metals could combine with the body’s biomolecules, like proteins and enzymes, to form stable biotoxic compounds, while they can mutilate the molecular structures and hindering them from the functional bioreactions [8]. Because of the biocompatibility requirement, research on biomaterials used to focus on ceramics, which are much more stable, and polymers, which only have carbon, hydrogen, and oxygen elements. Some functional devices have been widely applied using ceramics and polymers to substitute metals. However, over 70% of the implant devices still significantly depend on metals because of their high toughness and durability [7]. These metals, mostly for permanent uses, include stainless steel, Ti alloys, Co-Cr alloys, noble metals (Au, Ag).

Ti and its alloys, including but not limited to pure Ti, Ti-6Al-4V (Ti64), and Nitinol (Ti-Ni alloy), are usually used for orthopedic implants because of the excellent biocompatibility, high mechanical strength, and good wear/corrosion resistance [9]. Ti has been thought of biocompatible and robust material for a long time, where the cytotoxicity of Ti has shown no negative influence

on cell growth [10]. Due to the high corrosion resistance and excellent biocompatibility, Ti alloys have been used for hip implants since the 1990s, but failure cases have been reported due to the wear resistance and chronic inflammation [11]. Other complications, such as non-biocompatible ion leaching, modulus mismatch, and stress shielding, were also discovered in the related studies [12].

Stainless steels have been the most practical materials for biomedical implants. SS 316L, austenitic stainless steel, is one of the most commonly used types [13]. However, people have found that a considerable amount of Ni, which was used to stabilize the austenite phase, could cause Ni allergy and results in complications involving immune system response, commonly seen in orthodontic appliances [14]. After a thorough development on Ni-free stainless steels, Mn and N have been used for stabilization instead of Ni, and have reached certain success [15].

Co-Cr alloys have also been proven to offer suitable mechanical properties (low Young's modulus- high strength) a long time ago. Research has always compared Co-Cr alloys with Ti alloys and stainless steel for orthopedic implants. Comparatively, Co-Cr alloys generally have higher wear resistance than Ti alloys but have allergy consideration with Ni, Cr, and Co [16]. Similar to stainless steel, Co-Cr has the problem of ion leaching the Co and Cr ion are considered non-biocompatible. Even though Co-Cr alloys are considered stable, they remain a potential threat to the human body where there is no proof showing the chronic biocompatibility till now.

Because of the potential risks of chronic inflammation, part of the recent research focus was on the improvement of the permanent metals devices regarding biocompatibility and toxicity. Thus, deferent surface modification methods and alloying optimization have been applied to the metals[17, 18]. Surface coating techniques could bring additional required functions to the devices, such as antibacterial, enhanced corrosion resistance, and enhanced cellular biocompatibility[19].

However, the surface modifications could only inhibit the side effects of the base metals in the beginning period of the implantation, and they could not completely solve the chronic problems brought by the inevitable ion leaching and cytotoxicity.

2.1.1. Biodegradable metals for biomedical applications

Permanent implant materials are frequently used in clinical cases that only require their presence temporarily. These situations are less-than-ideal as the long-term presence of implants is associated with many complications, including infections [20], implant migration [21], altered tissue growth [22, 23], stress shielding [24], toxicity [25-27], and subsequent surgeries. Because permanent metals listed abovementioned mostly have the inherent biocompatibility problem, there are always complications such as allergies and body responses, which indicate the unfavorable cellular response. Furthermore, permanent implants are also unsuitable for the pediatric patient population due to their inability to accommodate growth [28-30].

Conversely, bioabsorbable implant materials provide temporary support that allows for the restoration of a tissue's physiological integrity, followed by complete reabsorption of the implants. Most current bioabsorbable implants are polymer-based [31]; however, their lower mechanical strength and viscoelastic behavior have limited their clinical use for load-bearing applications, such as bone staples, fixation plates, ACL screws, cardiovascular and nonvascular stents, and spinal fusion cages and clips [32, 33]. Bioabsorbable metallic implants are an attractive alternative for suitable biomedical applications. Some metals have a higher mechanical strength and toughness necessary for load-bearing applications and have a proven history of biocompatibility *in vivo*.

Bioresorbable metals have been recently studied more frequently in recent decades. Compared with permanent metals, biodegradable metals have the inherent degradability [34]. Bioresorbable

metals, also known as biodegradable or bioabsorbable metals, provide temporary functions (e.g., mechanical support, electrical signal detection) and gradually degraded in the human body or absorbed by the human body [35]. Most of the metals will decompose to micro size pieces and are ultimately degraded to ions that will be delivered to the entire body by the circulatory system. For example, biodegradable metal implants are fixed and attached to the broken bones. Their primary function is providing temporary support to the broken bones and guiding tissue regeneration until the bones slowly heal. However, different than permanent metals, biodegradable metals are designed to decompose according to tissue regeneration rate. Thus, they could slowly transfer the supporting function to the bones and safely disappear when the bone tissues are entirely recovered. In the processes, patients no longer need to worry about the chronic inflammation caused by the implants, as well as they do not need a second surgery to remove the implants [36]. Besides the bone implants, another critical and representative application of biodegradable metals is cardiovascular stent [37].

Currently, metals that could be gradually absorbed in the human body attracted an increasing amount of attention in the bioimplant industry. Compared with the permanent metals, the advantages of the bioresorbable metals are discussed below:

2.1.1.1. Low risk for chronic inflammation, infection, and biocompatibility

Permanent materials usually mount an acute host inflammatory response. During the long-term contact with the host tissues, biomaterials like stainless steel and Cr alloy can generate corrosion byproducts, including iron, chromium, nickel, and molybdenum ions. These ions could be accumulated around tissues or be transported to distant tissues, and further inhibit the expression of lymphocyte surface antigens and inhibit the immune response [38]. Compared with these permanent metals, biodegradable metals degrade much faster and stay adjacent to tissues for less

than 24 months, giving less chance for the immune system to respond significantly to the implants. Furthermore, biodegradable materials like Zn and Mg have the byproducts of Zn and Mg ion, which are essential elements in human bodies [39]. Most of the byproducts will be absorbed by the body fluid and transported harmlessly [40].

2.1.1.2. No second surgery

Another important advantage of biodegradable material argues for the convenience of the patients during the treatment process. Patients that need implantation need implants for mechanical support within a certain amount of time before the fracture tissues heal, especially for young age patients. Human tissues have the self-healing mechanism such that broken bones could heal themselves when stem cells accumulated on the fracture surfaces and regenerate new bone cells. The implants are usually used for bone regeneration guidance (e.g., bone plates), especially in orthopedic surgeries. Thus, doctors tend to remove the implants once the broken tissues are fully recovered, which necessarily requires additional surgery. The implant removal surgeries bring inconvenience and pains to the patients. In contrast, a biodegradable implant no longer requires a second surgery to remove the implant, while the patient no longer needs to visit the doctors once the tissues are completely recovered.

2.1.1.3. Suitable for pediatric surgeries

Pediatric patients are different from adults due to several aspects [41], including:

- An accelerated ability to heal
- Better recovery of damaged tissues and functions, due to the assistance of growth and inherent ability to adapt
- Inherent rapid tissue growth

Thus, pediatric surgeries have to be treated differently in special cases, such as facial fractures and aorta coarctation. Bioresorbable implants have been utilized in bone fracture of pediatric patients frequently, but most of them implement polymers. Furthermore, a recent development on bioresorbable stents has involved the topics of pediatric patients due to the cases of congenital heart defects (CHD), which affected nearly 1% of newborns per year in the U.S. [42]. Although conditions such as coarctation of the aorta and stenosis in the pulmonary arteries could be treated in a minimally invasive fashion via stenting, stents commonly used for the treatment of adult arterial obstructions are unsuitable for pediatric patients since they have growing cardiovascular structures that would rapidly outgrow traditional metallic stents. Thus, bioresorbable stents (BRS) that can tolerate high-stress applications (e.g., aortic stenting) would greatly benefit this patient population.

2.1.2. Current applications of biodegradable metals

2.1.2.1. *Bioresorbable cardiovascular stent*

Bioresorbable stent (BRS) aims at providing temporary support to vessels before degradation, promoting vessel healing and restoration of vasomotion [43]. It provides an alternative minimally invasive surgical treatment to replace open chest surgeries that could hurt the patients. With the development of medical technologies, patients with artery diseases and heart disease will need the assistance of such biodegradable devices to save lives. The cardiovascular stent market is enormous and still expanding, with expected growth to reach \$13.1 billion by 2025, according to projections from Fortune Business Insights (Figure 1). The growth of the market is driven by the investigation and development of the drug-eluting system (DES) and bioresorbable stents. The bioresorbable stent market is valued at \$271.5 million and is expected to reach \$602.4 million by 2025, as reported by Brandessence Market Research. The bioresorbable cardiovascular stent has

been developed to substitute permanent metal stent and to avoid leaving foreign metal microstructures inside the vesicles. Poly-L-lactic acid (PLLA) has been first utilized as the material that could be ultimately converted to water and carbon dioxide via the Krebs cycle. Other materials, such as poly-D, L-lactic acid (PDLLA), and polylactic acid (PLA), also performed reasonably suitable degradation behavior. Absorb BVS (Abbott Vascular; Santa Clara, CA), as one of the leading company exploring this idea, has been investigating the commercializing product for years, but failed to provide a viable stent that could survive and cause no target lesion failure (TLF) and stent thrombosis (ST). Polymers have inherent disadvantages that are incomparable with metals, such as low strength and stiffness, low fracture resistance, slow degradation rate with rapid integrity loss, and non-ideal visualization [44]. The major problem for the commercialized polymer stents (e.g., ABSORB BRS) is the result of thrombosis, resulting in a remarkably high failure rate at the 3-year examination [45]. Following Abbott, a few companies have been working towards the commercialization of their polymer stents but struggling in the progress of successful clinical trials and FDA approval [46].

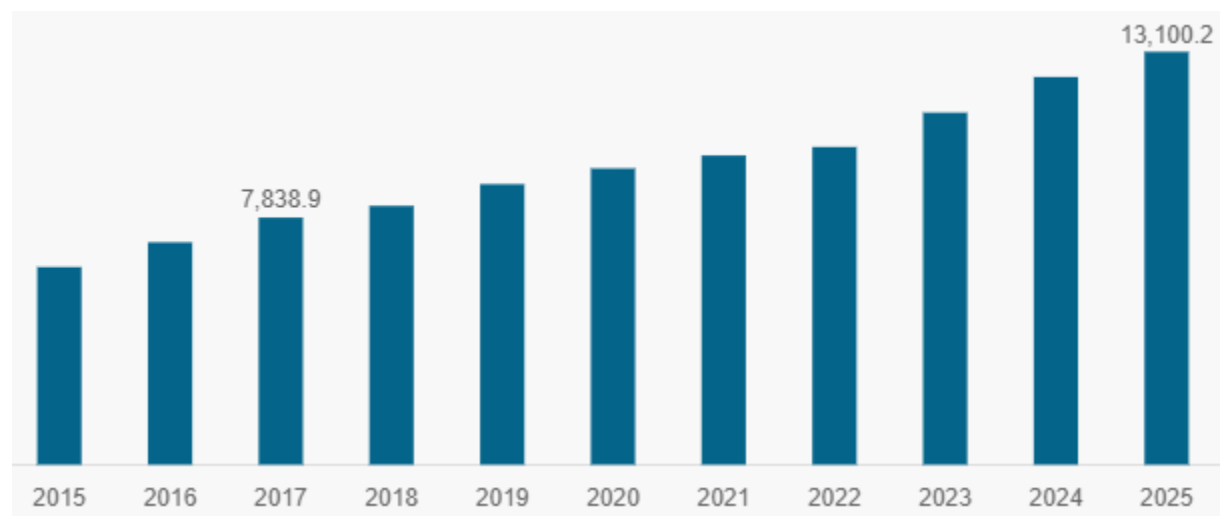


Figure 1: Global cardiovascular stents market size, 2015-2025 (US\$ Million), adapt from Fortune Business Insights.

Magnesium- and iron-based alloys have been extensively studied as candidates for bioabsorbable metallic implants with some success [47]. Among the metallic biomaterials, Mg and its alloys have been used for orthopedic implants due to their biocompatibility, low density, and low Young's modulus that is similar to bones [48].

The only bioresorbable metal stent is named “Magmaris” made of Mg from Biotronik. The product is a drug-eluting absorbable magnesium scaffold, which has been reported to have over 200MPa UTS with around 20% elongation. A reasonable degradation rate has been reported that about 95% of the Mg was resorbed at 12 months [49]. Compared with a current-generation permanent metallic drug eluted stent (DES) and an approved polymer BRS in porcine and rabbit animal models, Magmaris showed increased endothelialization and decreased thrombus formation at early ages (within a month) when comparing to BRS. It showed less inflammation level in the long term (1-2 years) when comparing to permanent metallic DES [50]. However, their drawbacks include the unfavorable corrosion rate and chronic inflammatory response [51, 52].

On the research side, different coatings were applied to enhance the corrosion resistance of Mg stent as the solution to retain mechanical integrity. Coatings can inhibit the rapid corrosion rate of Mg and Mg alloys through surface treatments or inert material deposition. Researchers have categorized the coatings into two types, conversion coating and deposited coating, shown in Figure 2.

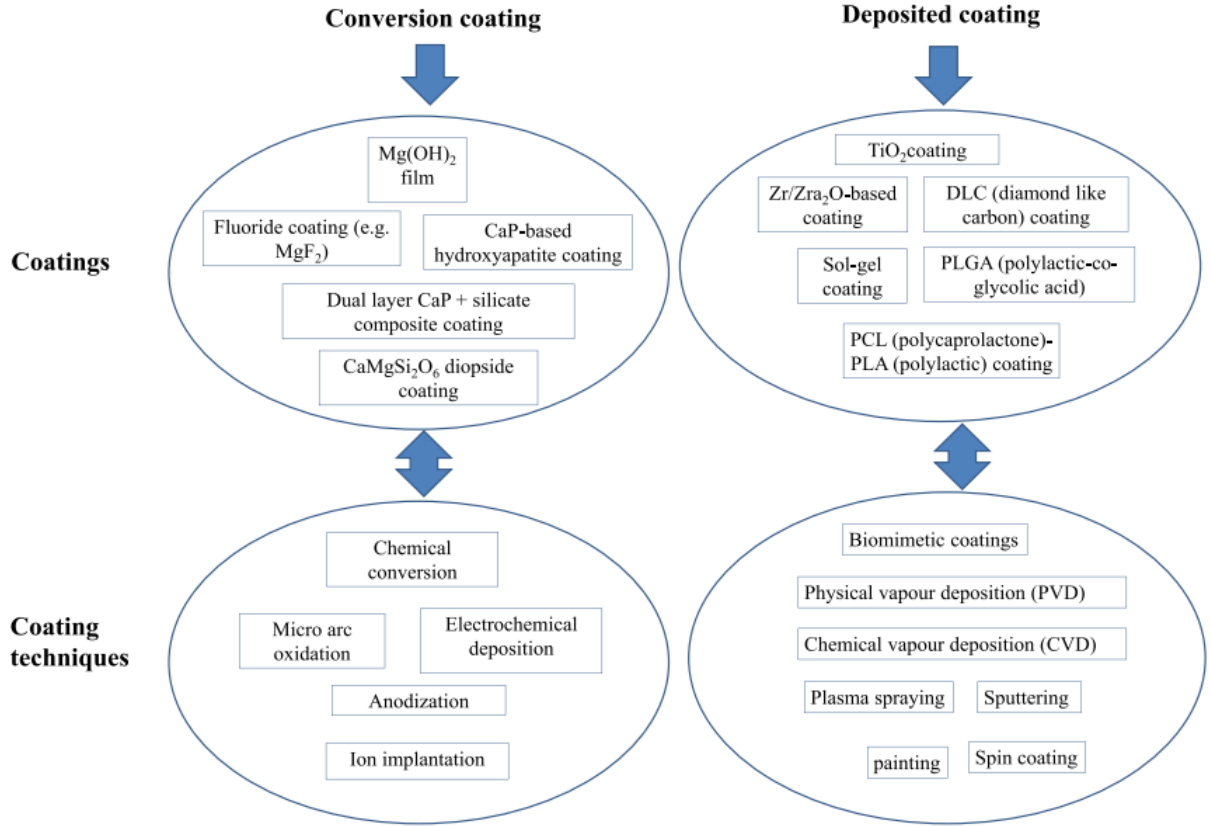


Figure 2: Classification of coatings and their corresponding processing techniques. Adapt from [53].

More specifically, coating materials could be categorized as the followings:

- Fluoride coatings, MgF₂ [54]
- Hydroxide film by solution treatment, Mg(OH)₂ [55]
- Organic coating, CaP by electrochemical deposition [56]
- Nanoparticle coating, HA [57], TiO₂ [58],
- Polymer films [59, 60]
- Oxides, micro-arc oxidation (MAO) [61], ZrO₂ [62]

While Mg has been thoroughly investigated with limitations, the research focus was partially moved to Fe-based stents. Fe has a much lower corrosion rate than Mg but results in better

biocompatibility and strength. Thus, investigations on Fe focused on developing the alloys that are expected to have high strength, high ductility, suitable corrosion rate, and high biocompatibility. Pure Fe was assessed on the aspect of degradability and cytotoxicity on endothelial cells, showing that a low concentration of Fe ion released from the degradation could result in a favorable effect on the metabolic activity of endothelial cells [63]. Through the development, Fe-Mn is a suitable alloy while approaching the gold-standard material, stainless steel 316L. Fe-Mn alloys (containing more than 29 wt.% Mn) are completely austenitic and anti-ferromagnetic and have shown sufficient *in vivo* cell viability, biocompatibility, and MRI compatibility, with a corrosion rate of around 520 $\mu\text{m}/\text{yr}$ [64]. Furthermore, their high toughness and tensile strength suggested the feasibility of being used as radial supports. However, such research is still ongoing, and clinical trials are urgently required before commercialization.

The corresponding requirement has been shown in the following Table 1.

Table 1: Desired properties for resorbable materials based on application, adapted from [65-67].

Properties	Bioresorbable cardiovascular stent	Ref.
Biocompatibility	Non-toxic, non-inflammatory	[68]
	No harmful release or retention of particulates	
	Encourage endothelial cell attachment	
Mechanical Properties	Yield Strength > 200 MPa	[69]
	Ultimate Tensile Strength > 300 MPa	
	Elastic Recoil on Expansion <4%	
	Elongation to Failure (%Strain) > 15–18%	
	Low yield point	[70]
	Fatigue Strength > 256MPa at 10^7 cycles	[71, 72]

Mechanical integrity	Mechanical integrity 3–6 months	[73]
	Full absorption in 1–2 years	[69]
Corrosion behavior	Penetration rate < 20 $\mu\text{m}/\text{year}$	[72]
	Hydrogen evolution < 10 $\mu\text{L}/\text{cm}^2$ per day	[74]

2.1.2.2. Other applications

Despite the cardiovascular stent, other applications required the use of biodegradable implants. One of the applications that have been frequently mentioned is the orthopedic implants, also known as bone implants. Biodegradable implants were frequently used in human orthopedics, mostly to treat cancellous fractures or osteotomies [75]. The key factor of such implants is their modulus and strength because the suitable modulus could prevent stress shielding during the healing period. Mg has been studied thoroughly as a suitable material with Young's modulus around 40 GPa, which is similar to bone [76]. Also, Mg would degradation in the human body and gradually transfer the loading to the regenerated bones. Thus, Mg bone plants and screws for fixation have been used in orthopedics more frequently in recent years.

Another potential application is guided bone regeneration membranes. It is a well-established therapy to repair mandible and alveolar bone defects infected by periodontal diseases [77]. The membranes were designed to assist the tissue regeneration in dental implant and bone grafting materials, to prevent the generation of non-functional scar tissues. Polymer materials have been well studied, including polycaprolactone (PCL), self-reinforced polyglycolide (SR-PGA), and self-reinforced poly l-lactide (SR-PLLA) [78]. Polymer matrix composites were also studied to enhance the strength of the membrane materials. Still, there is plenty of room for metals being used in relevant applications.

2.1.3. Current development on zinc as bioresorbable stents (BRS)

Zn has recently generated significant interest as a suitable candidate for bioabsorbable metallic implants because of its excellent biocompatibility and tolerable corrosion rate [69, 79]. Compared to Mg, Zn and its alloys have better ductility and lower degradation rate, making them more suitable for the cardiovascular stent, especially for pediatric uses [69]. Zn has already shown great potential in biomedical applications, ranging from electrodes for batteries [80] and sensors [81] to micro/nanofillers for conductive paste [82] as the filament or alloying element. The electrical conductivity of Zn is much higher than most of the biocompatible semiconductors, making Zn a suitable option for bioresorbable electronics. As an essential element in basic biological functions, Zn is required for the proper function of numerous proteins that regulate the proliferation, differentiation, and apoptosis of cells, and is involved in nucleic acid metabolism, signal transduction, and gene expression [83]. Therefore, living tissues have transport mechanisms that regulate Zn levels, which combat toxic cellular levels [84, 85]. Additionally, recent *in vivo* studies have shown that Zn implants demonstrate steady corrosion rates with no severe inflammation, platelet aggregation, thrombosis, or intimal hyperplasia [69, 86-88]. Furthermore, Zn has a higher elongation to failure (60-80%) than magnesium (13%) and iron (18%) [86], positively influencing the fatigue resistance and fracture toughness of the Zn-based implants. However, despite these promising results, no commercially available Zn-based BRS are commercially available. Insufficient mechanical strength inhibits pure Zn from being used for load-bearing applications and limits its success as a structural material [79], even though recent studies have evaluated that Zn is a potential material for bioresorbable stents (BRS) for offering an ideal corrosion rate (10um/year), which would allow vascular healing to occur before the stent is completely

biodegraded. Enhancing the strength would make Zn an ideal candidate for clinical applications requiring implants to withstand high stresses.

Alloying can adequately enhance the strength by using a low concentration of a second metal element. The mechanisms mainly depend on intermetallic phase precipitation strengthening and solid solution strengthening [6]. However, the introduction of intermetallic phases most likely sacrifices other favorable properties, such as corrosion rate [89], ductility [90], and biocompatibility [91]. Moreover, some additional elements, such as aluminum, could cause potential human body inflammation responses [92]. Alloys like Zn-Mg and Zn-Li are options that achieved a combination of high strength, high ductility, degradability, and biocompatibility after severe plastic deformation, but their weakness in thermal stability resulted in rapid natural aging, where they lost their ductility within a few days [6, 93]. Thus, there are limitations to alloying strategies.

For cardiovascular stents, the advantages of the newly developed Zn biomaterial are specifically discussed below:

2.1.3.1. Suitable corrosion rate

Zn offers an ideal corrosion rate for a bioresorbable stent. It has been reported that the bioabsorption of a suitable biodegradable material requires maintaining mechanical integrity for 3-6 months and fully degradation in 12-24 months [94]. A specific requirement on the corrosion rate has been reported that a suitable material should have a penetration rate of less than 20 $\mu\text{m year}^{-1}$ [95]. Mg has been developed earlier for bioresorbable stent application, but Mg and its alloys innately experience a high corrosion rate over 1 mm year^{-1} , which makes them not suitable [96]. High corrosion rate results in a rapid degradation and rapid loss of mechanical integrity. Moreover, another side effect of high corrosion rate is the rapid hydrogen evolution due to the metal to ion chemical transformation. Compared with Mg, Zn obtains a relatively suitable corrosion rate of 20-

50 $\mu\text{m}/\text{year}$ [69, 97]. Its corrosion potential is -0.76V , which is intermediate between Fe (-0.44V) and Mg (-2.37V), which enable a suitable corrosion rate corresponding to the regular healing period of cardiovascular diseases [67]. The major advantage of the suitable corrosion rate is the lasting mechanical integrity of the stent during the recovery stage of the vesicle. To make sure that the vesicle diseases are fully cured, the stent must be fully functional to open vessels to avoid clots. A fast degradation could potentially result in stent failure and vesicle collapse, which consequently cause a clot and increasing blood pressure. Furthermore, since the corrosion usually starts at the grain boundaries, metal pieces fall off the device and could accumulate on tissues or be transported through the circulatory system. Sharp metal pieces would possibly further damage the vesicles and tissues.

2.1.3.2. Good ductility

Another advantage of Zn is its extremely high ductility, almost comparable to polymers. Pure Zn has been barely investigated on mechanical performance because it is so soft and alloying is commonly used to enhance the strength. Hot-worked Zn has an unprecedentedly high elongation to failure among all metals. Research has been reported that pure Zn (hot extruded) obtained 40% elongation to failure, even though the ultimate tensile strength (UTS) and yield strength (YS) were only 120MPa and 90MPa [90]. On the other hand, Mg has a limited elongation to failure that is less than 15%, whereas it has been observed that the fast degradation resulted in a rapid loss of ductility within a month (ductility reduced to less than 3% after 29 days) [98]. Comparatively, Zn obtains a high ductility that fulfils the requirement of ductility, because stents require at least 20% fracture elongation during the insertion and expansion operation in surgeries [67]. Furthermore, alloying is a commonly used strategy for both Zn and Mg to enhance the strength to support the narrowed vesicles, but it inevitably sacrifices the ductility in most cases. Thus, it is much worthy

of investigating in Zn alloys since there are more rooms to tune the alloying element concentrations to reach a combination of strength and ductility.

2.1.3.3. *Biocompatibility*

Zn has been investigated and developed as a biocompatible coating material in the dental industry more than 30 years ago, but showing relatively high cytotoxicity due to the rapid ion release [99]. However, research has shown that Zn is one of the most abundant nutritionally essential elements in the human body, with 85% existing in muscles and bones. Furthermore, Zn is essential to more than 300 enzymic reactions and participates in formations of DNA and protein expressions [100]. Thus, research has been investigating on the biocompatibility of Zn and its alloys to verify whether Zn would be a suitable metal for biodegradable implants that is harmless to cells and tissues.

A few *in vitro* studies have focused on the cellular response to indirect released Zn ions in simulated body fluid (SBF) and direct Zn substrate culturing. Human umbilical vein endothelial cells (HUVEC), human aortic smooth muscle cell (AoSMC), and human dermal fibroblasts (hDF) were usually used as the standard protocol to verify the compatibility since they are the vesicle cell that will directly contact the stent materials. Typically, standard tests start with indirect contact methods. Metal samples were immersed in the SBF solution and enabled ion leaching, where Zn ions concentration increased in the SBF. The solutions were used to culture cells, and cell proliferation was characterized by fluorescence microscopy. Some research reported good cell proliferation results, where cell number increased in such solutions [94, 97]. To further investigate the compatibility, direct contact methods were used by culturing the target cells directly on the sample plates. However, direct contact methods did not show a relatively good result, indicating a high concentration of Zn could significantly influence cell growth, shown in Figure 3 [94]. Other

Zn alloys have tested with direct contact methods, and unfortunately, the results were usually negative. Such results indeed proved that large Zn samples could not co-exist with cells for cell proliferation. However, different than the metal plates that were used in such standard *in vitro* tests, the actual medical devices, e.g. stents, were usually made of wires of 200 μm thickness, which will be fully covered with the surrounding cells within a few days after implanting. Thus, *in vivo* test will be more crucial to verify the biocompatibility for such degradable medical devices. Direct contact *in vitro* test could be a supplementary data to understand the mechanism of degradation and the interaction between cells and the implant materials.

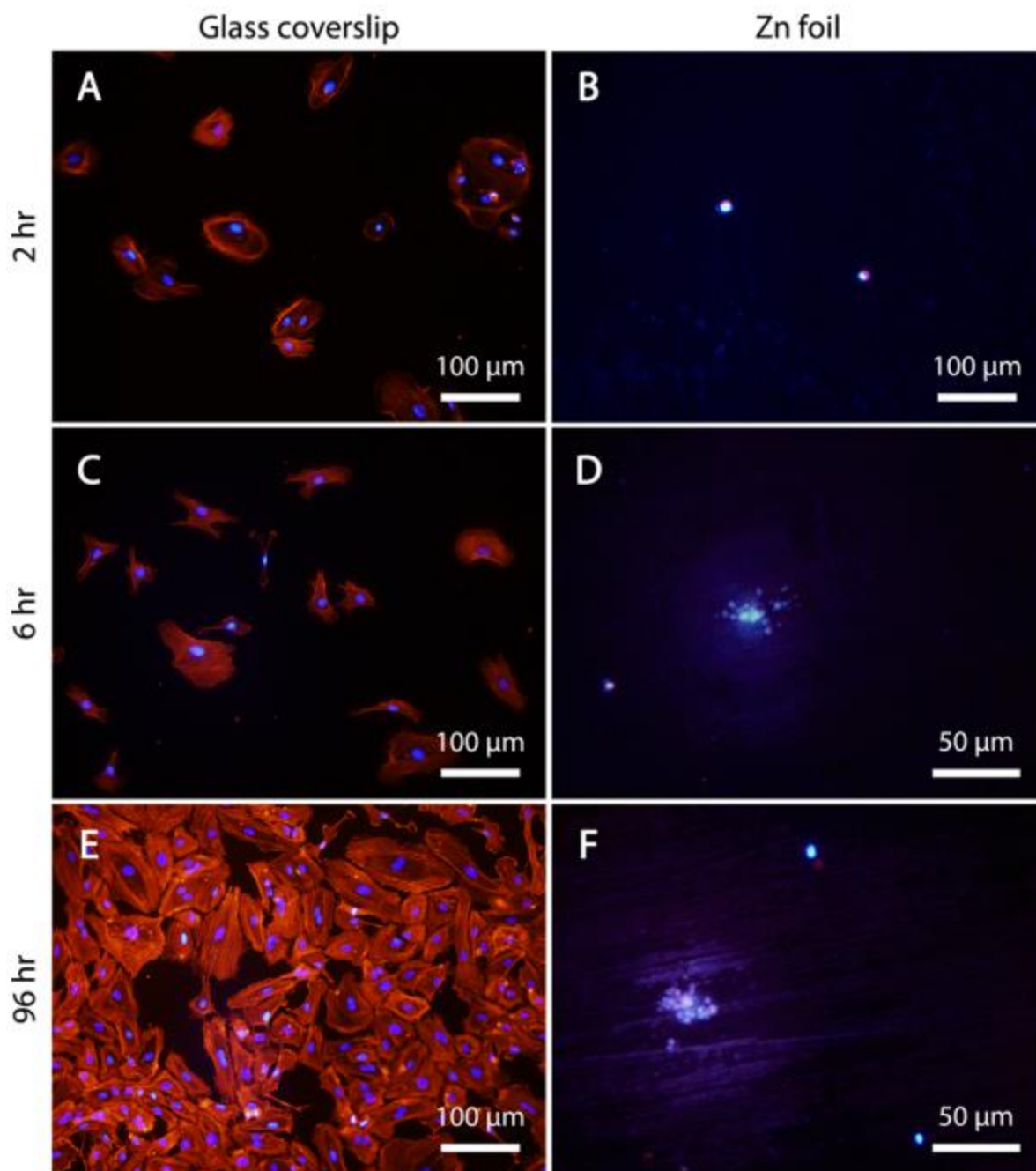


Figure 3: Fluorescent imaging of HUVAC cells on Glass and Zn foil

Another aspect of the biocompatibility is the *in vivo* toxicity experiment in animal trials. Due to the complex environment inside the human body, specific cytotoxicity and hemotoxicity tests could only show a limited response from the aspect of the cellular growth, and they cannot

generally reflect the overall response from the human tissues. Furthermore, stents are supposed to encounter a complex environment containing vesicle cell growth, blood flow, blood cell interaction, and vesicle contraction. Multiple effects could interact and induce new problems. Thus, such *in vivo* experiments focused on the actual animal response to the implants, which could indicate the overall biocompatibility before the viable human trials. The typical animal models are mouse, rabbit, and swine, where the later model has the vesicle that has the most similarity to humans. The recent development on the biocompatibility of zinc wires in *in-vivo* experiments has shown positive results in rat abdominal aorta lumen for 6.5 months and 1 year, suggesting that Zn did not provoke responses contributing to restenosis [101]. They have also indicated that Zn generated no severe inflammation, platelet aggregation, thrombosis formation, and obvious intimal hyperplasia through micro-CT, SEM, STEM [87].

2.1.3.4. Strengthening method by alloying

Zn is a very reactive metal for alloying, and almost all metal could form intermetallic phases with Zn for strengthening. Precipitation strengthening is commonly known as one of the most potent strengthening methods besides solid solution. A few commonly used alloying elements and the corresponding binary intermetallic phases are listed in Table 2:

Table 2: List of Zn alloys used for bioresorbable stents and their corresponding strengthening phase

	Alloys	Intermetallic phase	Reference
Nutrient elements	Zn-Mg	Mg ₂ Zn ₁₁	[102]
	Zn-Ca	CaZn ₁₃	[103]
	Zn-Sr	SrZn ₁₃	[103]
Essential elements	Zn-Fe	FeZn ₁₃	[89]

	Zn-Mn	MnZn ₉	[104]
	Zn-Cu	CuZn ₅	[105]
Other elements	Zn-Li	β -LiZn ₄	[93]
	Zn-Al	α -Al	[106]
	Zn-Ag	AgZn ₃	[107]

Strengthening effect on these alloys: There is much current research investigating on alloying strategies of Zn for strengthening. The ultimate purpose is using the least amount of alloying for the most efficient strengthening. Recent research has categorized the alloying element into nutrient elements, essential elements, and other elements [108]. Figure 4 has shown most of the alloys abovementioned, illustrating the phase diagrams of Zn alloys for a minimal alloying concentration. Such broad alloying options give Zn flexibility for strengthening, either by precipitation strengthening or solid solution strengthening, during the practical applications. Furthermore, by combining two or more elements, research has started to investigate ternary systems, where some could provide high strength and high ductility at the same time. Additionally, ternary systems could sometimes provide stable ternary phases as micro/nanoparticles, which offer high corrosion resistance, shown in Figure 5.

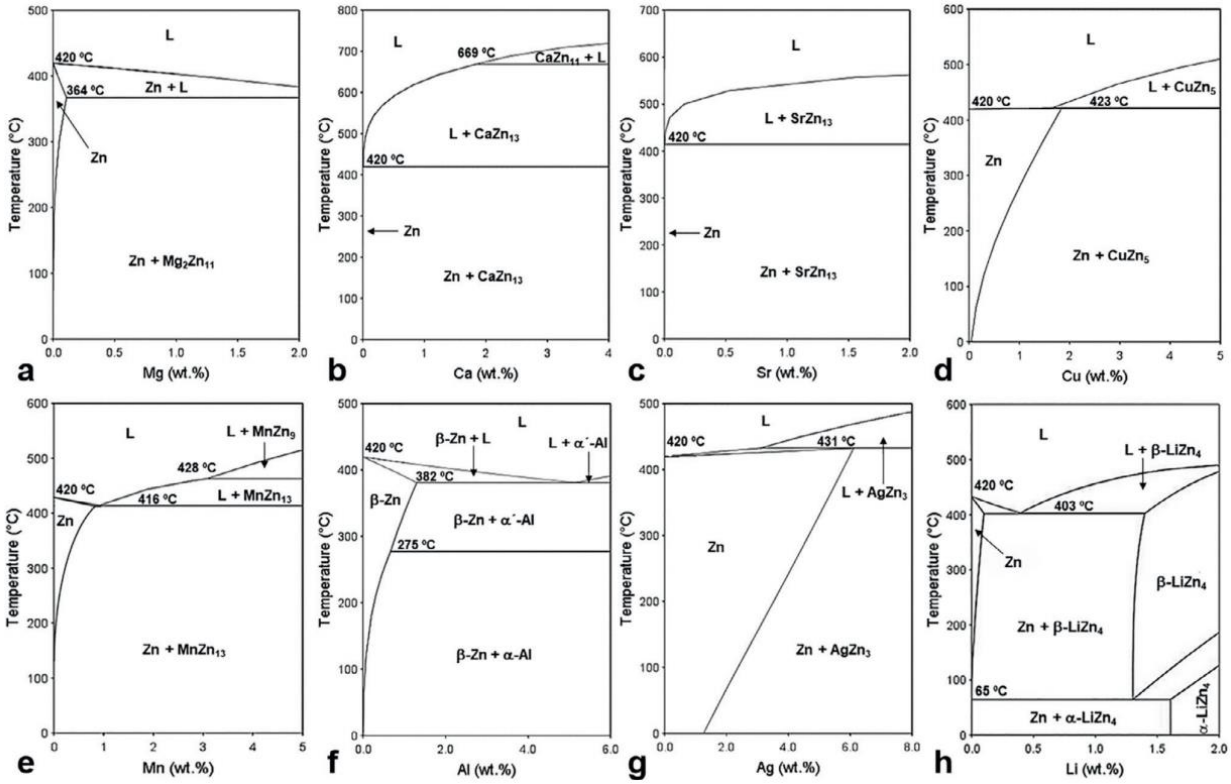


Figure 4: equilibrium phase diagram of Zn alloys, adapted from [109]

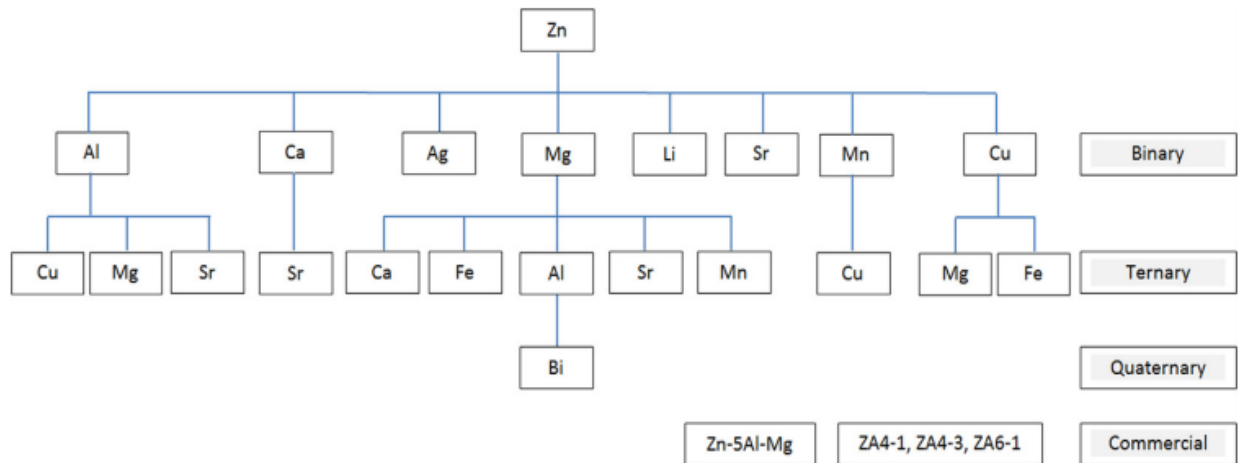


Figure 5: different Zn alloy combinations studied for biodegradable implant applications, adapted from [65]

Maintaining good ductility at a low concentration: Another limitation of alloying strategies is the limits of alloying concentrations. As commonly known, a tiny amount of heavy metal ions

could drastically alter the biochemical balance and ultimately cause deleterious health effects in humans [110]. The recommended daily intakes of Mg, Fe, Zn are 375-700mg, 10-20mg, and 6.5-15mg, correspondingly [65]. Similarly, according to *Recommended dietary allowances*, the recommended amount of the metal elements are listed in the following as the reference for Zn alloy design requirements [111, 112]:

Table 3: recommended daily dietary intake of metal elements for adults

Metal	Dietary intake (mg/day)
Zn	12.5
Mg	408
Ca	800
Fe	10
Cu	1.5-3
Mn	2-5
Li	10

Regarding the recommended daily intake of the metal element, a strict requirement is needed for alloy design to ensure biocompatibility, i.e., benign human body response to the metal ion release. Although such data is not rigid restrictions, researchers have to consider the side effects of overdosages due to corrosion of the alloys during the *in vitro* test.

2.1.3.5. Radiopacity

Pure Zn biomaterial has been tested by X-ray fluorescence radiation under standard X-ray conditions, demonstrating its radiopacity, shown in Figure 6 [113]. Zinc binary alloys have also

demonstrated excellent radiopacity. It helps to track the implant devices during interventional and minimally invasive surgeries [114].

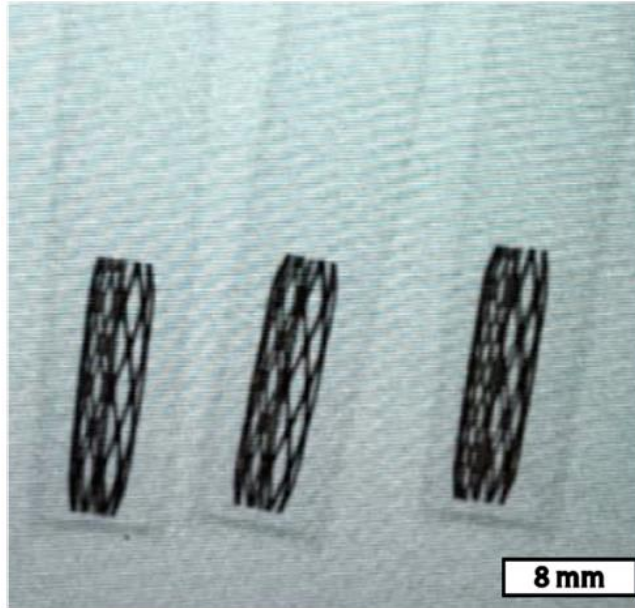


Figure 6: Radiopacity of three Zn stents, made via photochemical etching, after exposure to X-ray

2.2. Grand challenges

2.2.1. Innate weak strength

Zn innately has a weakness in strength. As-cast pure Zn has an insufficient mechanical strength, where the UTS is around 30MPa [115]. Hot rolled pure Zn only obtained a low intrinsic UTS of 120 MPa [93]. Even though its corrosion rate has been considered suitable for biodegradable implants such as bioresorbable stents, the low mechanical strength of pure Zn does not fulfill the requirement of a standard stent with a typical UTS > 300 MPa [116].

2.2.2. Dilemma on strength, ductility, and corrosion rate

Precipitation strengthening by alloying is effective in enhancing the mechanical strength. Multiple binary and ternary alloying systems have been investigated to strengthen degradable implants. Figure 6 summarizes the tensile test performance of typical Zn alloys. Typical high

strengthening effects, e.g., Zn-Mg and Zn-Li, have compromised the elongation, thus difficult in maintaining both high strength and good ductility.

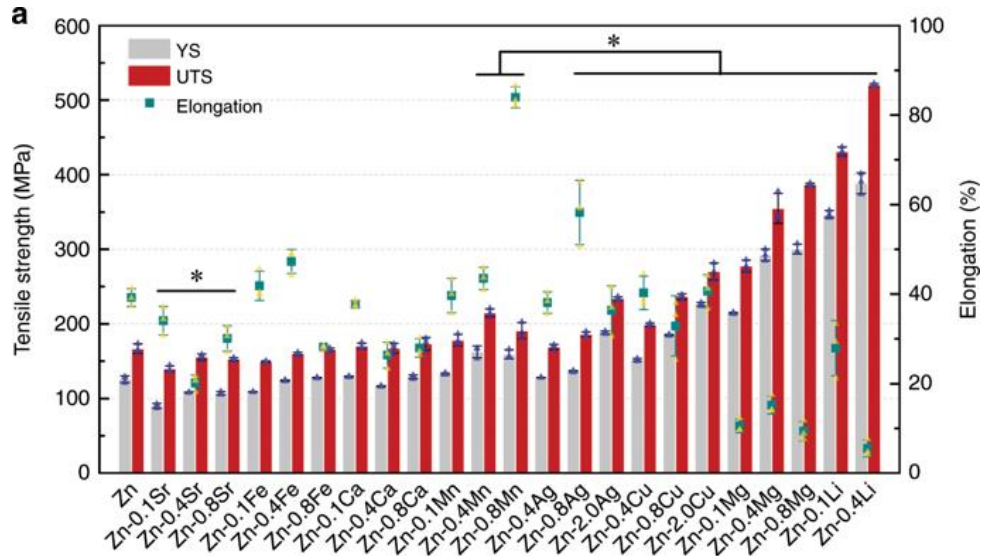


Figure 7: Mechanical tensile test of pure Zn and binary Zn alloys, adapted from [117].

Similarly, the corrosion rates of the Zn alloys abovementioned calculated on weight loss are presented in Figure 8. It suggests that the corrosion rate significantly increases if the alloying element concentration is higher, which also induce more intermetallic phases. Although such corrosion rates $\sim 30 \mu\text{m/yr}$ is still reasonable for some bioresorbable implant applications, the corresponding corrosion mechanism brought by the presence of intermetallic phases can be problematic. Intermetallic phases typically result in higher corrosion rates, where the interfacial corrosion would usually happen. Moreover, the intermetallic phases that generally exist at the grain boundaries, such as Zn-Mg and Zn-Li [6, 93], could result in metal grains peeled off the implants during degradation.

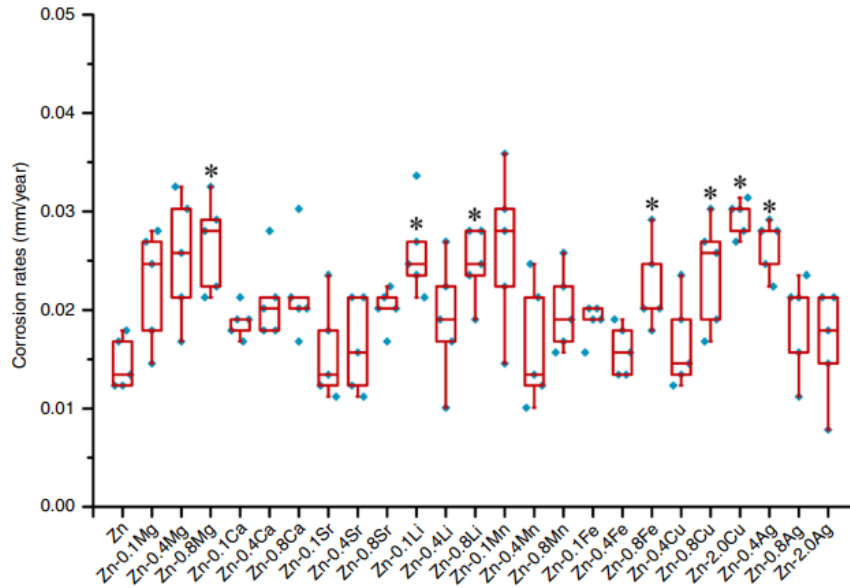


Figure 8: Corrosion rates calculated on weight loss ($n = 5$, independent samples). $*P < 0.05$ by one-way ANOVA with Tukey's post hoc test, compared with pure Zn. For box-whisker plots, box edges correspond to 25th, and 75th percentiles, lines inside the box correspond to 50th percentiles, and whiskers include minimum and maximum of all data points. Data adapted from [117]

Alloying methods require precise theoretical and experimental analysis on alloying concentration to reach the best combination of strength, ductility, and corrosion rate. However, there is a lack of studies and computer simulation methods to predict them. Thus, the practical method is an experimental trial and error to confirm their feasibility as novel biodegradable materials. Most alloying elements are not eligible for biodegradable applications due to their poor biocompatibility, such as Al and Ag.

There is a dilemma on the balance of strength, ductility, corrosion rate, and biocompatibility. Low concentration Mg and Li seem to be the most promising alloying elements for Zn currently. Their primary strengthening mechanism was the solid-solution strengthening when the Zn alloy samples were annealed, quenched, and hot-rolled/hot-extruded. They could provide a combination

of UTS of 300 MPa and elongation of 30% while offering positive results on corrosion behavior and cytotoxicity [6, 117].

2.2.3. Thermal stability/ mechanical integrity

Zn-Mg is a novel biodegradable metal with a better corrosion resistance than Mg. Also, it is significantly strengthened through precipitation. Meanwhile, in vitro cytotoxicity test results indicated great compatibility, illustrating that it is an excellent candidate material for load-bearing biodegradable implant applications [118]. However, due to the inherent thermal instability of Zn and its alloys, the natural aging effect could cause the loss of mechanical integrity and the loss of ductility at the physiological working environment temperature. It has been discussed that Zn-Mg alloy, with less than 0.1 wt% Mg, has an obvious age-hardening effect when the alloy samples were stored at room temperature for one year (Figure 9). It can be seen that after the fabrication of Zn-Mg wires, the ductility of the sample decreased significantly and rapidly after storage for a few days, and retain elongation of less than 15% after only 9 days. This rapid loss of ductility could result in the fracture of stents during the in-body expansion as well as a strict requirement for storage. This phenomenon is unfavorable for the bioresorbable stent application since the non-ideal thermal stability of Zn-Mg alloy could result in implants failure at the early stage of the implantation, consequently causing the devices dysfunction.

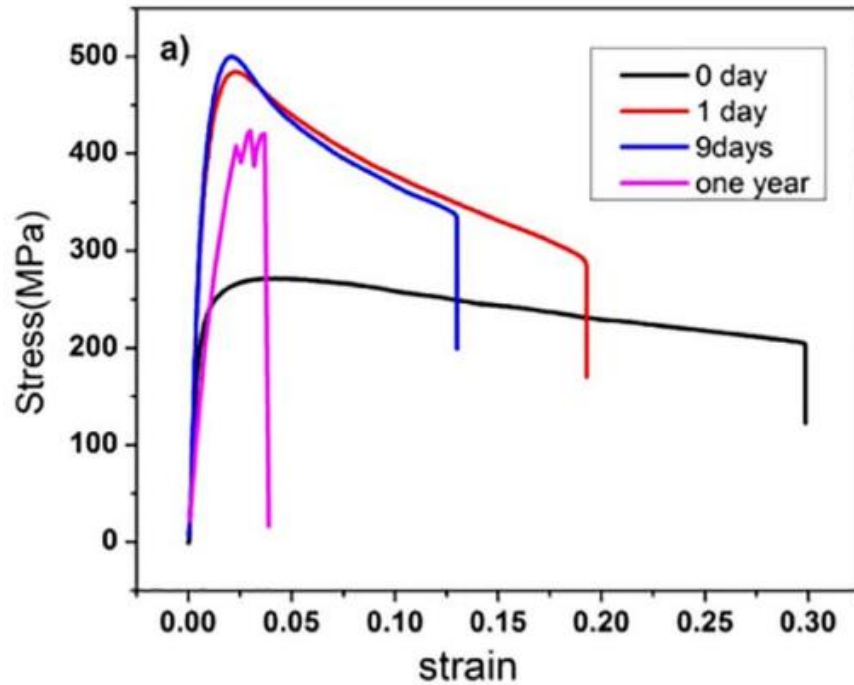


Figure 9: Representative tensile-stress curve of Zn-08Mg wires for different storage time at a strain rate of 0.0033/s. adapt from [6]

Researchers commonly followed the regular Zn and Zn alloy processing procedure to initial work hardening for Zn and Zn alloys, e.g., annealing – quenching – hot work. Especially for Zn-Mg alloys, high-temperature annealing (around 300-380 °C) and quenching will effectively dissolve the Mg elements and change the alloys to gain ductility. After hot working (e.g., hot rolling and hot extrusion), the ductility and strength of Zn and Zn alloy will increase significantly. However, such a procedure consequently make Zn alloy samples in a supersaturated solid solution, which is thermally unstable. Thus, at high temperature, which is defined as approximately half of the melting temperature, the alloy will gradually change the microstructure and form Mg_2Zn_{11} intermetallic phases (Figure 10). These brittle intermetallic phases exist at grain boundaries. The ductility of the samples would tremendously decrease with more precipitates. At the same time, due to the precipitation strengthening, the strength of the alloys could increase, as shown in Figure 9.

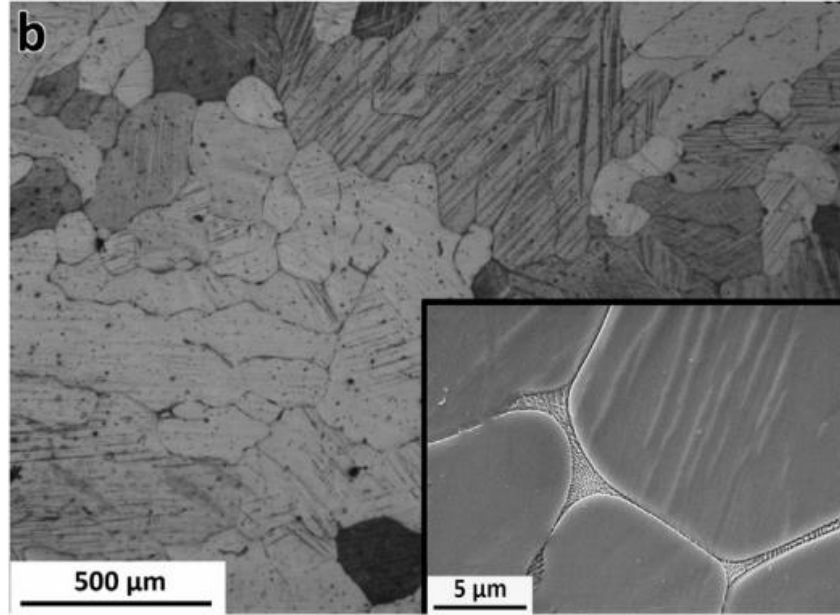


Figure 10: Microstructure of the investigated Zn–0.15Mg in the as-cast condition. Adapt from [90].

Similarly, Zn-Li has also shown its potential for good mechanical properties and biocompatibility as hot-rolled Zn-2Li samples offered a UTS of over 350 MPa and an elongation of 15% [93, 119]. Figure 11 shows the microstructure of Zn-Li alloy (as-rolled) with fine grains. However, researchers have concerns about age hardening in the Zn-Li system[120]. It seems that Zn-Li alloys still face the inevitable age-hardening phenomenon, which would hinder their use as biodegradable implant devices.

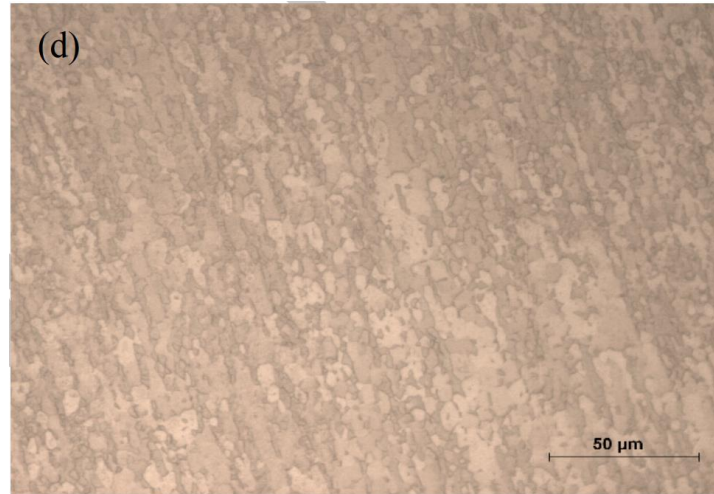


Figure 11: Optical micrographs of extruded-Zn-0.5Li alloy. Adapt from [119]

2.2.4. Grain structure

Grain size is of significance for biodegradable metals. Grain refinement has long been considered as an effective method to enhance the strength for Mg and Zn alloys, while alloying and plastic deformation was also used to strengthen metals [121]. Previous research has evaluated the grain size effect and suggests that the grain size is less than 10-12.5 μm for a stent strut thickness of 100 μm , because a finer grain size reduces the risk of a stent strut breaking [39]. Furthermore, because the corrosion normally tended to happen at the grain boundaries, smaller grains reduce the risk of large peeled-off metal pieces that could damage the vessel tissues.

2.2.5. Fatigue

Cyclic stresses, like those caused by pulsatile blood pressure, can lead to the initiation and growth of surface defects that often result in the premature mechanical failure of metallic stents. The material microstructure has a significant impact on the mechanisms of fatigue crack initiation and propagation due to the microstructural defects, such as grain boundaries and inclusions. Additionally, the aqueous environment can accelerate both the initiation and propagation of surface defects under such cyclic loading inducing corrosion fatigue [82]. Generally, metallic

implants owe their corrosion resistance to the passive layer (e.g., metal oxide layer) to prevent the underlying metal surface from contact with these aggressive ions. However, biodegradable metals, like magnesium and zinc, have a low resistance to corrosion because they generate soluble corrosion products [82,83]. As such, corrosion significantly contributes to the premature mechanical failure of biodegradable metal stents as well as to the rate of degradation.

For stent implant applications, despite the pressure applied to the temporary supporting implant, vessel contraction and blood flow also contribute to the mechanical stress and surface corrosion on the biodegradable implant. Thus, the biodegradable implants have to retain a high fatigue resistance to at least avoid device failure before the diseases are cured. Fe and Mg have been thoroughly discussed by different fatigue testing under either dry condition and wet conditions [122], as shown in Figure 12. Most Fe and Mg samples can endure 20% engineering strain for 10^7 cycles in the air but failed much faster in PBS solutions. The results, to some degrees, have indicated a lack of good fatigue resistance under wet conditions due to the additional corrosive effect from the SBF.

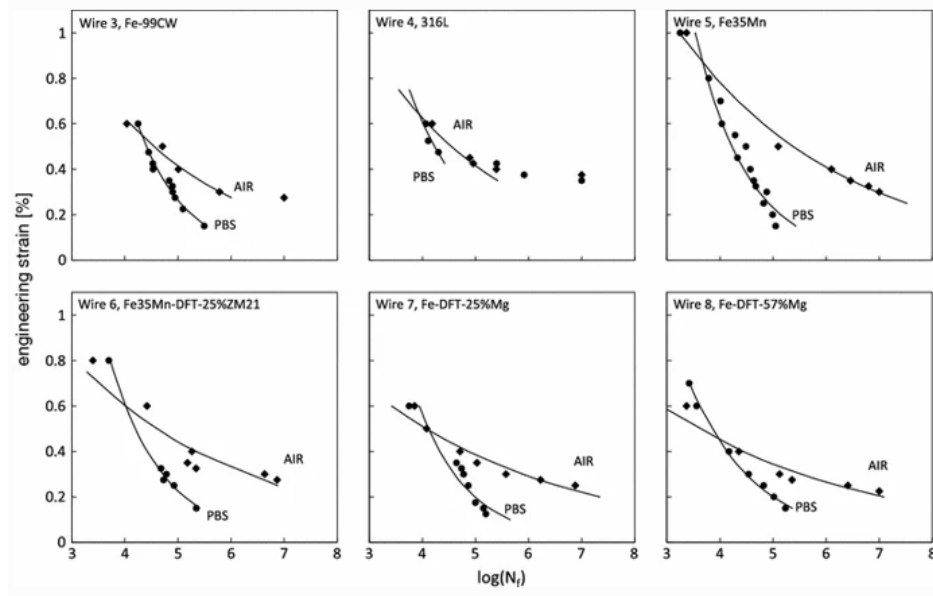


Figure 12: Fatigue strain-life (S - N) plots for each material tested in either air at $T = 298$ K (25 °C) or PBS at $T = 310$ K (37 °C), both tested at $f = 60$ Hz, $R = -1$, where $\log(N_f)$ represents the logarithm of the minimum number of cycles to failure for the tested alternating strain (strain amplitude) level. Adapt from [122].

Furthermore, corrosion fatigue has not been thoroughly tested on Zn and Zn alloys yet. Figure 13 illustrates the S - N curves of some Zn and Zn alloys, where pure Zn (polycrystals) can only endure 10^7 cycles at a stress of 10MPa [123]. Such low fatigue resistance prevented it from being a practical bioresorbable stent. Furthermore, Zn-Al and Zn-Al-Cu have been tested, showing a reasonably good fatigue strength comparable with permanent alloys, e.g., stainless steel, Ti, and Ti6Al4V[124]. However, toxicity studies revealed that Al is toxic to living organisms, especially for the central nervous system [125]. Thus, a more comprehensive study on the fatigue resistance of Zn alloys has to be accomplished in future research.

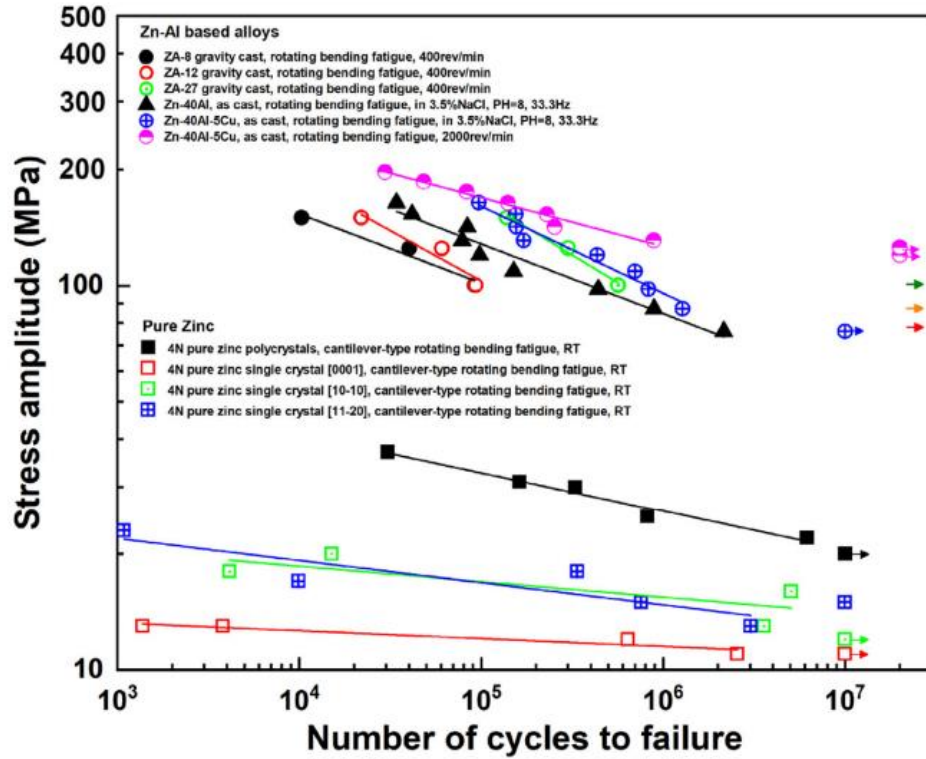


Figure 13: Summary of the S-N curves of pure zinc and its alloys adapt from [70]

2.2.6. Stent design

Although the stent design has been under development for more than a few decades, the optimization of designs for Zn needs to be performed based on its unique corrosion behavior and mechanical properties. Some of the current favorable stent designs, as shown in Figure 14, are mostly based on those of permanent metal stents (e.g., Ti alloys, nitinol, stainless steels) with both high strength and toughness, allowing the stent strut to be as thin as less than 50 μm . In those cases, wire braided stents are more commonly fabricated using micro-welding techniques [126]. However, biodegradable stents require thicker strut to compensate for the effects of lower strength, mechanical integrity, and corrosion rate, while the typical strut thickness is at the magnitude of hundreds of micrometers.

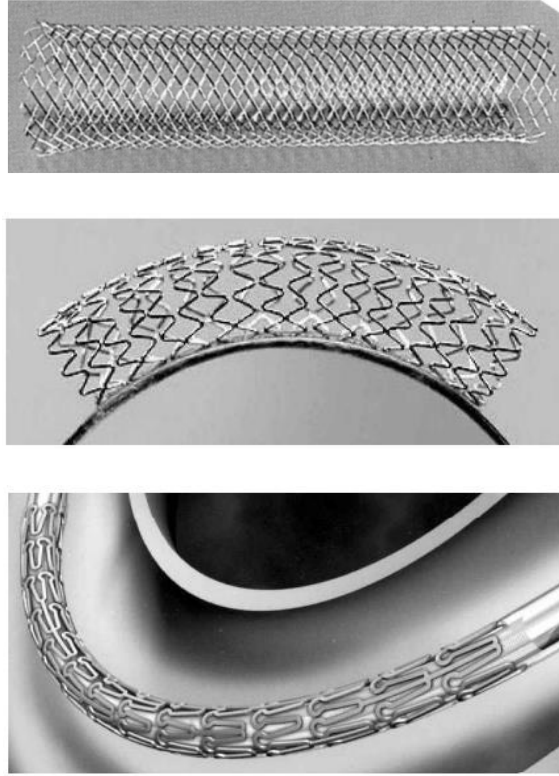


Figure 14: Different types of stent designs. From top to bottom: (1) WallStent, a braided stent fabricated from cobalt alloy wire; (2) AVE S7 stent: balloon-expandable open-cell sequential ring design with periodic peak-to-peak non-flex connections; (3) ACS Multilink: balloon-expandable open-cell sequential ring design, with peak-to-valley connections. Adapt from [126].

2.3. A potential solution to the current problem

A promising new method has been proposed to strengthen Zn based bioresorbable stents with nanoparticles. Metals reinforced with nanoparticles have emerged as an important class of materials that offer significantly enhanced mechanical, thermo-physical, and electrical properties [127, 128]. Nanocomposites have been reported as an effective method for mechanical strengthening in metallic materials owing to Orowan strengthening [127], grain refinement (Hall-Petch effect) [129], increasing the dislocation density [130] and load-bearing [127]. Furthermore, by using chemically and thermally stable ceramic nanoparticles [131], Zn matrix nanocomposites are supposed to achieve balanced biocompatibility, corrosion rate, and ductility. Currently, limited

success has been achieved by the research on the fabrication of Zn and Zn alloy matrix nanocomposite. The representative nanoreinforcements include tungsten carbide (WC) nanoparticles [132], silicon carbide (SiC) nanoparticles [133], alumina (Al₂O₃) [134], and hydroxyapatite (HA) [135].

Particulate-reinforced metal matrix nanocomposites have been under study for a long time, where multiple strengthening effects have been introduced, including Orowan strengthening, enhancement of dislocation density due to the residual plastic strain though the difference between the thermal expansion coefficients of the matrix and nanoparticles, and load-bearing effect [136]. A model has been used to predict the strengthening factors of metal matrix nanocomposites (MMNC), regarding the intra-granular type of MMNCs:

$$\sigma_{yc} = \sigma_{ym}(1 + f_l)(1 + f_d)(1 + f_{\text{Orowan}})$$

$$f_l = 0.5 V_p$$

$$f_d = \frac{1.25 G_m b}{\sigma_{ym}} \sqrt{\frac{12(T_{\text{process}} - T_{\text{test}})(\alpha_m - \alpha_p)V_p}{b d_p(1 - V_p)}}$$

$$f_{\text{Orowan}} = \frac{0.13 G_m b}{\sigma_{ym} d_p [(1/2 V_p)^{1/3} - 1]} \ln \frac{d_p}{2b}$$

where σ_{yc} is the yield strength of particulate-reinforced MMNCs, σ_{ym} the yield strength of the monolithic matrix under the same processing conditions as those of MMNCs, f_l the improvement factor due to the load-bearing effect, f_d the improvement factor associated with the enhanced dislocation density in matrix induced by the thermal mismatch between the matrix and the reinforcement particles, f_{Orowan} the improvement factor due to the Orowan strengthening effect, V_p the volume fraction of reinforcement nanoparticles, G_m the shear modulus of the matrix, b the magnitude of the Burgers vector of dislocations in the matrix, T_{process} the processing temperature,

T_{test} the test temperature, α_m the coefficient of thermal expansion of the matrix, α_p the coefficient of thermal expansion of the reinforcement phase and d_p is the particle size.

However, the grand challenge of metal matrix nanocomposite manufacturing is to realize homogeneous nanoparticle dispersion. Agglomeration and sintering of nanoparticles usually occurred during the incorporation, which could generate defects and cracks. Recently, a novel manufacturing method of high-performance metal matrix nanocomposite with uniform nanoparticle dispersion was developed according to the nanoparticle self-dispersion in the metal matrix [127]. Good wettability between nanoparticles and the molten metal would encourage the self-stabilization mechanism, where nanoparticles repel each other in molten metal.

In this study, Zn matrix nanocomposite is proposed as the methodology for strengthening the material with multiple advantages that could potentially benefit the biodegradable applications.

2.3.1. Orowan strengthening

Ceramic nanoparticles normally have high strength and high stiffness, enabling the particle strengthening, similar to the effect of intermetallic strengthening. The type of Orowan strengthening appears in the metal matrix nanocomposite are incoherent particles, where the dislocations are bowing around particles, following the equation:

$$\tau = \frac{Gb}{L - 2r}$$

where τ is the material strength, G is the shear modulus, b is the magnitude of the Burgers vector, L is the distance between pinning points, and r is the second phase particle radius. The governing equation expresses the strengthening effect is related to the particle size and particle volume concentration. The Orowan strengthening effect is significant in the strengthening of MMNCs, where a decreasing size and increasing volume could exponentially enhance the strength. The theoretical strengthening improvement factor can be calculated as:

$$f_{\text{Orowan}} = \frac{0.13G_m b}{\sigma_{ym} d_p [(1/2V_p)^{1/3} - 1]} \ln \frac{d_p}{2b},$$

where G_m is the matrix shear modulus, b is the matrix burgers vector, σ_{ym} is the monolithic matrix yield strength, d_p is the particle size, and V_p is the particle volume fraction.

For example, a 5 vol.% of Al_2O_3 nanoparticles of 10nm could theoretically enhance the strength of Mg to about 250 MPa, with an improvement factor of 1.5, shown in Figure 15 [136]. Orowan strengthening is generally the most crucial mechanism in strengthening metal matrix nanocomposites.

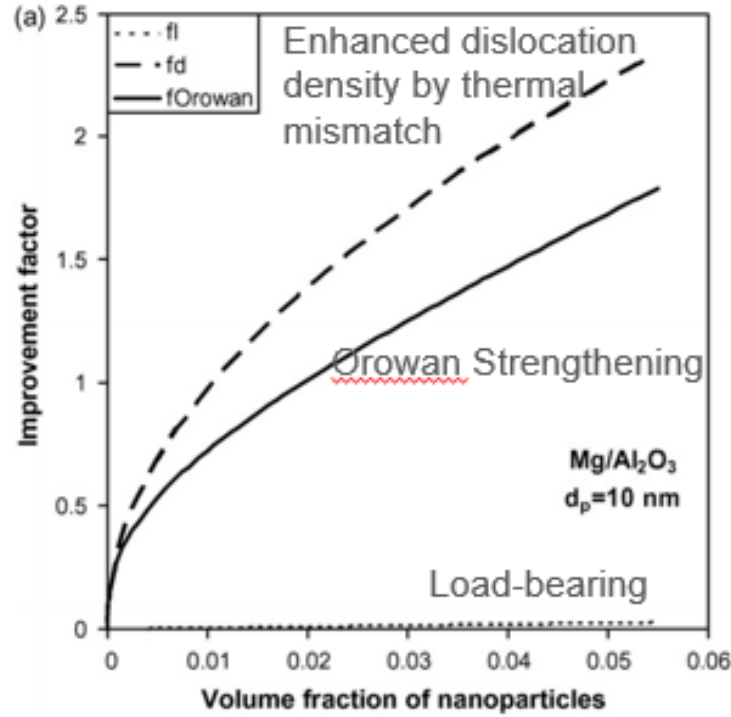


Figure 15: Theoretic improvement factor of strengthening mechanism in Mg-Al₂O₃ nanocomposite system

2.3.2. Grain refinement

Nanoparticle enabled grain refinement will strength materials by the Hall-Petch effect, referring to the equation:

$$\sigma_y - \sigma_0 = \frac{k_y}{\sqrt{d}}$$

where σ_y is the yield stress, σ_0 is a material constant for the starting stress for dislocation movement (or the resistance of the lattice to dislocation motion), k_y is the strengthening coefficient (a constant specific to each material), and d is the average grain diameter.

As-cast pure Zn barely has any functional applications due to the limited strength and elongation (30 MPa and <5%). Crystalline materials with HCP-lattice are generally less ductile than those with FCC/BCC, owing to the lack of slip systems. However, work hardening is typically used for strengthening of Zn by introducing grain refinement via plastic deformation, including hot extrusion and hot rolling. It has been discovered that hot-extruded Zn has enhanced the strength to 110MPa, and elongation to 70%.

2.3.3. Little alteration of corrosion rate

Theoretically, the corrosion rate of the biodegradable material is related to the inherent property and grain size, because often corrosion starts at the grain boundaries. The intermetallic phases are commonly where the corrosion initiates. The commonly used alloying elements, such as Mg, Fe, Li, Ca, usually form intermetallic phases where the corrosion rates are known to increase significantly. Instead of alloying, ceramic nanoparticles are commonly inert inside human bodies, where they cannot be easily degraded or absorbed. Furthermore, grain refinement due to nanoparticles will maintain the corrosion rate better than the intermetallic phase. Thus, nanoparticle hardening is generally a better strengthening method, while the corrosion rate would not be affected much.

2.3.4. Biocompatibility and toxicity

Biocompatibility refers to the capability of implants to existing in harmony with surrounding tissues [137]. Ceramic materials for biomedical applications, especially drug delivery, grow hastily,

including hydroxyapatite (HA), zirconia (ZrO_2), silica (SiO_2), titanium oxide (TiO_2), and alumina (Al_2O_3) [138]. Due to the chemical inertness, the biocompatibility of ceramic nanoparticles is relatively more sensitive to in vivo cell response.

As the major component of bones, hydroxyapatite (HA) is the most biocompatible ceramic material, with consistent sub-lethal toxic effects from in vitro and in vivo models [139]. Other oxide nanoparticles also indicate harmless effects to cells according to in vivo testing [140]. Compared with oxides, carbides and borides are barely studied, especially in the form of nanoparticles. A study in WC nanoparticle toxicity demonstrated that WC nanoparticles did not yield a toxic response up to 30 $\mu\text{g/mL}$ after 3 days of exposure in OLN-93 cell line, or the primary rate neuronal and astroglial cells [141]. Still, for stent application, hemotoxicity and cytotoxicity will need to be studied to validate that the device safety.

2.3.5. Thermal stability

According to the previous research, Zn-Mg alloy experienced an age-hardening effect, where a ductility loss as high as 55% occurred in as few as 9 days under ambient and physiological conditions. The fundamental reasoning for natural age hardening is the precipitate growth at room temperature. Due to the low melting temperature of Zn (419°C), room temperature is already close to the half melting point.

Nanoparticles inherently obtained the capability of enhancing material thermal stability by interaction with the microstructure. Nanoparticles have been reported as a thermal stabilization agent, where Al_2O_3 was used in aluminum alloy for strengthening and enhancing thermal stability [142]. Similar technology was used in metal during the recent decades in the field of 3D printing industry. In the recent development of aluminum laser additive manufacturing, nanoparticles have been used as agents to control the grain growth to form uniaxial grains, and ultimately enabling

high strength for light metals [143, 144]. Nanoparticles could affect the molten metal solidification process, including cooling, nucleation, and phase growth, whereas realizing fine grains via a slow cooling rate in the different metal matrix [145]. Such development on metal matrix nanocomposite has shown the effectiveness of nanoparticle interfering with the crystalline metal structure during the solidification and grain growth.

From the reported studies, nanoparticle interaction with metal matrix could potentially be the methodology to inhibit the age-hardening. The expected phenomenon could be:

- Inhibit the grain growth. Pure Zn has the intrinsic property of room temperature annealing due to the low melting point, so that grain growth during the functional application could increase the grain size to reduce the strength, due to the Hall-Patch effect. Nanoparticle could sufficiently control the grain growth by restraining the grain boundaries and pinning the grain growth fronts, shown in Figure 16 (left). It can retain good strength from hot working too.
- Inhibit the size of the precipitation of intermetallic phases such as Zn-Mg. It is proposed that nanoparticles could interact with the intermetallic phases during the high-temperature aging process, where nanoparticles could modify the morphology of the strengthening phases, shown in Figure 16 (right). The results in the fact that nanoparticles could control intermetallic morphologies that precipitate due to the age hardening and recover the ductility through the modification of the intermetallics.

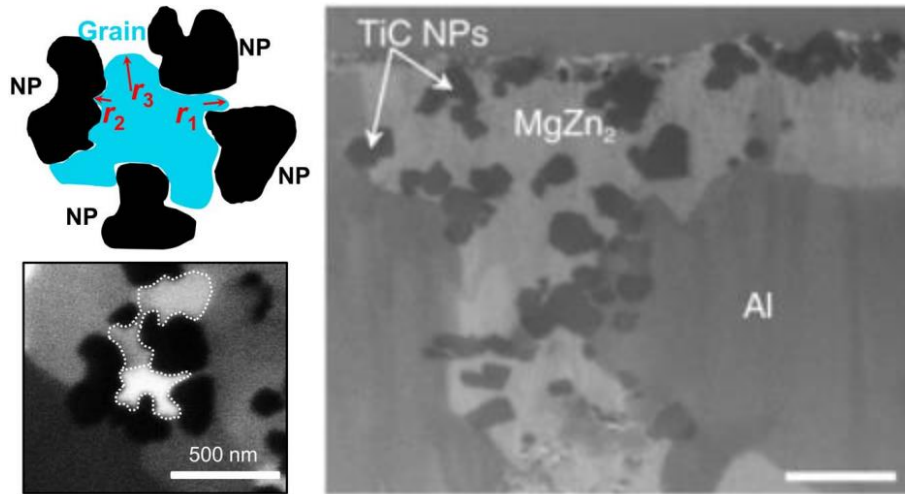


Figure 16: (left) Schematic illustration of the nanoparticle pinning effects and SEM image of a Cu grain refined by WC nanoparticles. (right) TEM sample showing the cross-section view of the modified secondary phase by nano-treated filler material. Adapt from [145, 146].

2.3.6. NP induced enhancement on fatigue resistance

Fatigue behavior is one of the most crucial aspects of stent application. Different than typical load-bearing devices that could encounter large stress and experience device failure, coronary stents usually experience periodic contraction due to the heartbeat. Long term study on stent implant has discovered that fatigue failure was more common than fracture [147]. This study proposed that, besides strengthening, nanoparticles could also enhance the fatigue resistance for to realize the desired properties.

The fatigue properties of nanocomposite have been well studied, especially in aluminum alloys, since research has been conducted on using nanoparticles to strengthen lightweight alloys. Al-Si alloy with SiC particle reinforcement was tested on its fatigue resistance, where the S-N curve was shown in Figure 17. The fatigue life increases as the weight fraction of SiC increases. The main reasons for the fatigue resistance enhancement are the load-bearing effect, where local stress is transferred to the stiffer particulate reinforcement, and the decreased elastic and plastic strain of

the composite. Another research on Al-TiC composite has shown that, with 15wt% TiC, the highest fatigue strength of Al-Si has increased from 133 MPa to 248 MPa, because the dispersed particles can resist the crack propagation, shown in Figure 18 [148]. The reason for the enhanced fatigue resistance refers to the crack reflection mechanism, where the particles within the matrix do not allow the crack to propagate easily and increase the time required to begin a crack.

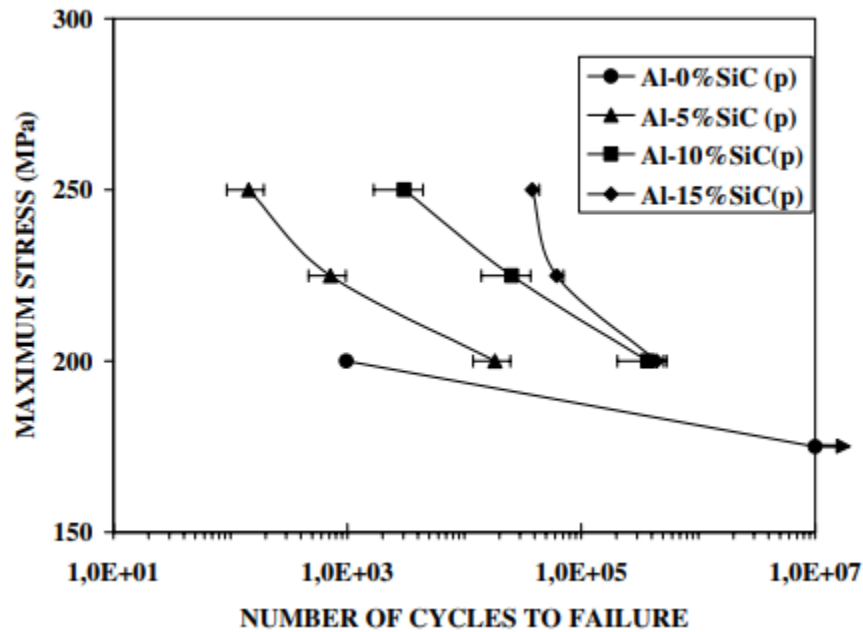


Figure 17: Effect of SiC particulates on the S–N behavior of the specimens. Adapt from [149].

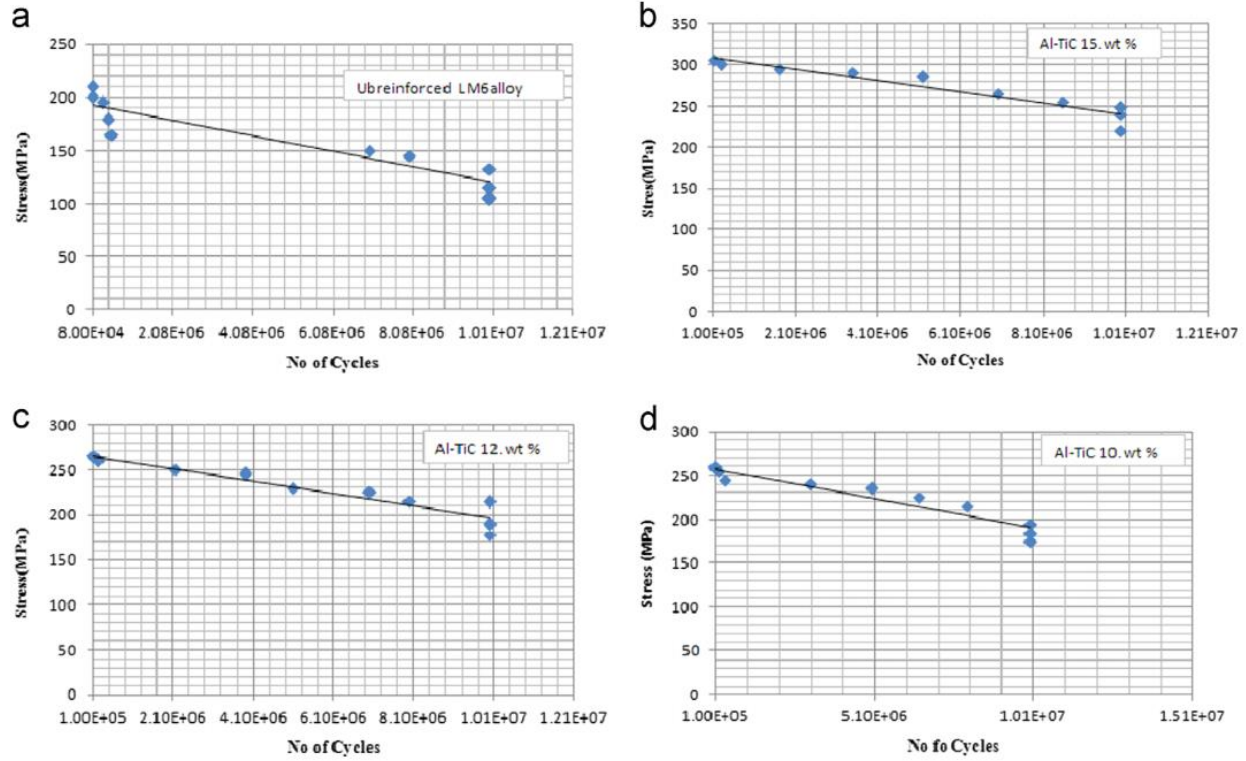


Figure 18: (a) Unreinforced LM6 alloy S–N plot, (b) Al–15 wt% TiC S–N plot, (c) Al–12 wt% TiC S–N plot and (d) Al–10 wt% TiC S–N plot. Adapt from [148].

2.3.7. NP induced enhancement on creep resistance

The creep resistance is not as important for stents, but could potentially be applicable when the materials serve as bone implants. Nanoparticles have been introduced to the Mg matrix to conquer its inherent deficiencies of poor creep resistance, along with low stiffness, high wear rate, high chemical reactivity, loss of mechanical strength at high temperatures [150]. SiC nanoparticles of 3 vol.% were incorporated into the Mg matrix by powder metallurgy, exhibiting a creep rate of about three orders of magnitude lower than pure Mg, shown in Figure 19 [151]. SiC nanoparticles could suppress grain sliding on the basal planes of 0001 by the pinning mechanism at the grain boundaries. Furthermore, they could block the dislocation movement to reduce the creep rate [152].

The strategy of the enhancing creep resistivity by nanoparticles is also applicable in Zn matrix nanocomposite, while Zn has a similar atomic structure and low thermal stability.

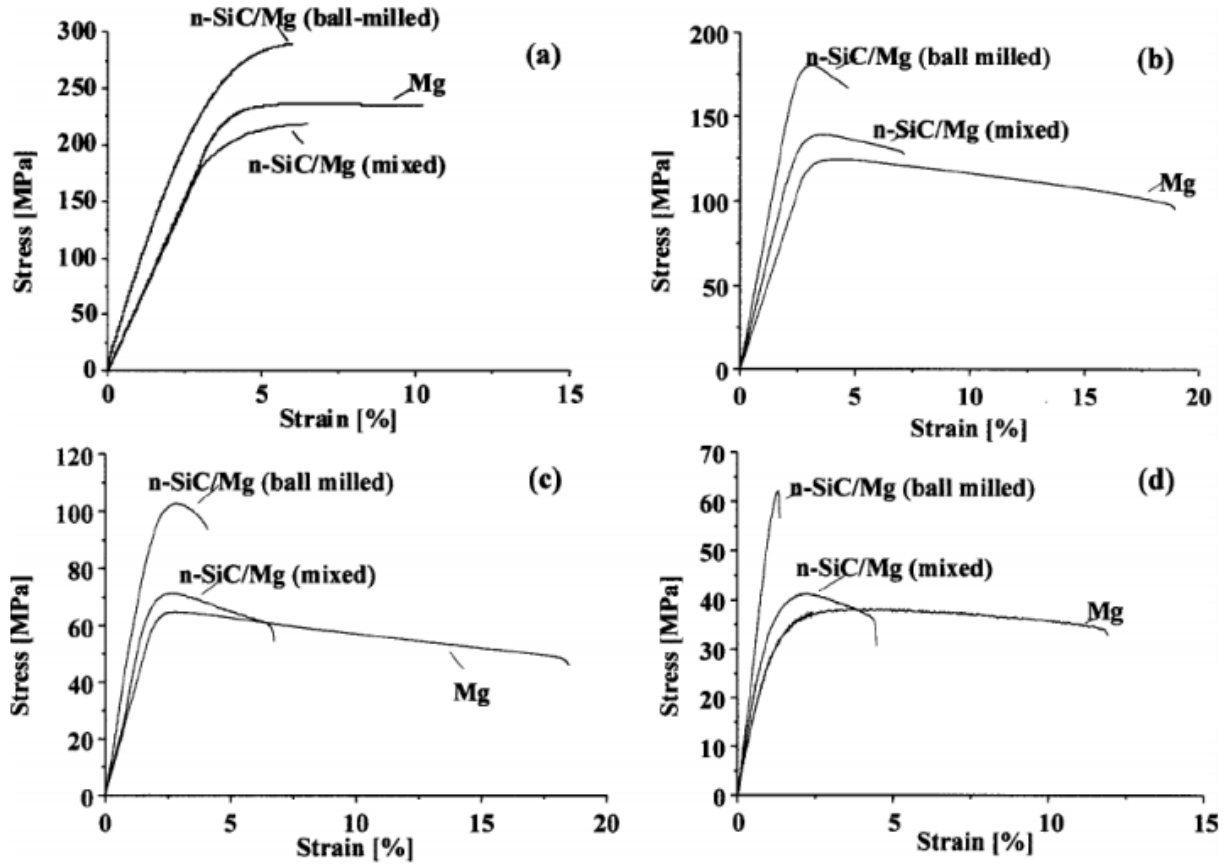


Figure 19: Stress-strain curves of pure magnesium and its nanocomposites at (a) room temperature, (b) 100, (c) 200 and (d) 300 °C. Adapt from [151].

2.4. Current development on micro/nanowires as biodegradable material

2.4.1. Micro/nanowires as electrodes for brain signal detection

2.4.1.1. Applications of micro/nanowires

Micro/Nanowire has already been a popular topic during the last decades that has been used in fields of microstructured photonic crystal fibers [153], optical micro/nanofibers [154], electronics in fibers [155], fiber-based metamaterials [156], fibers as a novel platform for sensing devices [157], studying chemical reactions [158], multi-material functional fibers [159, 160], and more recently fibers as a platform for fabrication of nanowires and nanoparticles [161-164]. Different from bulk materials, nanowires offered a speciality on linking the macroscale to the nanoscale,

providing a bridge to advance the knowledge of the nanoscale world. For instance, semiconductor nanowire has been well studied, demonstrating the possibility of exploring human tissue activities and cell activities. Moreover, metal nanowire, with its extraordinary electrical conductivity and high mechanical compliance, has performed a great number of capabilities in multi-functional devices[165, 166]. Due to the nano-size effect, nanowires, especially metallic ones, have broadened the applications on microdevices. For example, silver nanowires initiated the fabrication of stretchable, flexible, and transparent conducting film for human wearable transparent electrode devices[167, 168]. Conclusively, Si nanowires have been developed as biocompatible sensors that can be embedded in human bodies.

However, because of the difficulties in the fabrication and characterization process, the scalable manufacturing of metal nanowires is still a challenging task. Nevertheless, metal nanowires enable a high signal to noise ratio due to the generally good electrical and thermal conductivity. Also, degradable metals can be used for biodegradable devices, potentially advancing a new generation of devices in the biomedical industry.

2.4.1.2. Specific biomedical applications of nanowires

Conductive nanowires were known to be a favorite building block of many advanced cellular level nanoscale sensors in biomedical applications, for optical, electrical, and chemical interrogation of tissues and cells. Two silicon nanowire applications were published on a 3D macroporous nanoelectronic network as brain probes and vertical nanowire electrode arrays (VNEA) [169, 170]. The former application realized a macroporous nanoelectronic brain probe that could directly be implanted in the brain to record neuron tissue activities. The latter application further advanced extracellular electrodes that resided outside the cellular membrane, which were not capable of measuring sub-threshold events and prohibited precise cell-to-electrode registration.

Focusing on single cells rather than tissues, VNEA has the key probe made of 9 doped silicon nanowires (150nm diameter and 3um in length) used as intracellular nanoelectrode that could penetrate the membrane to interact with neuronal cells to receive biocurrent under stimulations. Similarly, a few other applications, such as submicrometer needles, were also proven to be suitable for intracellular applications[171].

However, it has been revealed that semiconductors were not the perfect material for biological probe applications. First, semiconductor nanowires did not have mechanical strength and hardness large enough to penetrate the tissue or the membrane, so that additional post-fabrication processing was required to protect the nanowires, such as the fact that 3D macroporous nanoelectronic network froze the polymer substrate to harden the probe. Second, low electrical conductivity results in a low signal-to-noise ratio and most silicon nanowire applications required a thin metal coating on the contacting surface to guarantee the signal reception. All these inevitable fabrication and the post-fabrication processes could be easily avoided if metal nanowires were used instead.

Metal nanowire could solve these two significant problems due to its inherent high mechanical strength and high electrical conductivity, but current technology did only apply micrometer size metal nanowires to such bioelectrode applications[172]. It has been reported that microwire array made of tin was used as probes for optical and electrical interrogation of neural circuits in vivo, where multiple tin wire arrays were fabricated through the thermal fiber drawing process. Such wires could be directly used on cellular signal detection without excessive post-processing.

2.4.1.3. Other applications of nanowires

Metal nanowires have already been applied to electronic devices, such as flexible wearable sensors and transparent electrodes. The combination of high transparency and high conductivity made metal nanowires the perfect building blocks for the transparent electrodes, which has already

been used in organic solar cells to increase the power conversion efficiency [173-175]. Also, functional applications, such as transparent sensors and transparent display, are promising for the next generation visual technologies and portable electronics[176]. Many of the researches on high conductivity nanowires (40-100nm diameter and ~10um length) targeted on forming nanofilms as the transparent electrode[167, 177, 178]. These thin films, though have been used on flexible microdevices such as transparent electrodes and ultra-thin high sensitivity sensor, inevitably ignored the advantage of the single nanowire, because loose connections between wires randomly affected the conductivity and increased the resistivity. To sum up, nanowire manipulation and arrangement are highly demanded further functional applications of electronic devices.

Metamaterials are artificially designed subwavelength composites possessing extraordinary optical properties, which can alter the electromagnetic wave propagation, resulting in negative refraction, subwavelength imaging, and cloaking[179]. Due to the large negative real part in its permittivity, silver was frequently used as the tuning element to fabricate metamaterials. A few numerical studies and simulations presented that silver nanowires embedded in silica tubes were aligned in an angular coordinate arrangement to function as the cloak to realize the invisibility in three-dimensional space [180]. Such a cloaking device could be potentially used for the military as far as silver nanowires could be scalable manufactured with a controllable arrangement. Most research has shown that metamaterial required precise alignment if metal nanowires participated, so that methods like electrospinning and chemical synthesis, which hardly obtained the capability of directional control, are not feasible for such applications.

2.4.1.4. Fabrication of nanowires

Multiple fabrication methods were used to reach the ultimate goal of mass production but being unable to overcome the technical difficulties. Furthermore, the integration of macroscale systems

with elaborate alignment, positioning, and post-synthesis technique for easy manipulation and handling is urgently required for more complex systems[162]. A few fabrication methods are presented in the literature reviews, followed by the discussion of their advantages and disadvantages, including thermal fiber drawing, chemical synthesis, laser drawn-cast, and electrospinning. Thermal fiber drawing utilized the size shrinkage of viscous coated claddings under high temperatures to reduce the core metal size, thus fabricating indefinite long metal/semiconductor nanowires from macroscale. Laser drawn cast was similar to thermal drawing while the heat source changed from furnace to laser, but also experienced the challenges that laser manufacturing was costly, and the process control was difficult. Scalable manufacturing using laser could be feasible in the future with simplified setup and better control over processing conditions. Electrospinning, on the other hand, could fabricate long metal nanowires, but since it required assistance from polymers, additional post-fabrication processing was required to enhance nanowire properties. This method also encountered the instability problem while it used the liquid precursor to form nanowires. Chemical synthesis was able to fabricate metal nanowires with diameters as small as a few nanometers but with a limited length up to tens of micrometers, and the critical problem was that this process was time-consuming and non-repeatable, and it could hardly be applied to mass production. The strict operation conditions, again, made it hard to adapt to the industrial environment. Representative methods and their corresponding nanowire fabrication results are shown in Table 4. From our point of view, thermal fiber drawing is considered as one of the best approaches to scalable manufacturing of ultra-long metal nanowires, considering the overall cost, fabrication feasibility, quality, and productivity.

Table 4: fabrication methods and their corresponding typical results

	Material	Cladding	nanowire diameter	Length	Author and year	Reference
Thermal fiber drawing	Sn95Ag5	PES	3.6 μm	Indefinite	Yaman, 2011	[162]
	Au	Fused silica	260 nm	20 μm	Tyagi, 2010	[181]
	Bi	Borosilicate	50 nm	1 m	Badinter, 2010	[182]
	PbSn	Borosilicate	~ 100 nm	1 m	Badinter, 2010	[182]
	Cu	Fused silica	6 μm	0.5 m	Hou, 2008	[183]
	PbTe	Borosilicate	400 nm	N/A	Hong, 2009	[184]
	CuP	Borosilicate	500 nm	N/A	Zhang, 2008	[185]
	Au	Silicate	330nm	2 cm	Gholipour, 2016	[186]
Laser drawn-cast	SiGe	Silica	15 μm	N/A	Coucheron, 2016	[187]
	Pd	Fused silica	250nm	140mm	Zhang, 2016	[188]
	Pt	Quartz	10nm	5 mm	Percival, 2014	[189]
	Au	Quartz	40nm	5 mm	Percival, 2014	[189]
Electro-spinning	Cu	50-200nm		100 μm	Wu, 2010	[190]
	Au	400nm		10mm	Wu, 2013	[191]
	Ni	120nm		>20 μm	Barakat, 2008	[192]
	Pt	50-70nm		N/A	Kim, 2010	[193]
Chemical synthesis	Ag	20nm		>500 μm	Lee, 2012	[168]
	Ag	70nm		8 μm	Tokuno, 2011	[194]
	Cu	300nm		9.42 μm	Xu, 2014	[195]
	Cu	78nm		Several mm	Zhang, 2012	[196]
	Au	15-100nm		20 μm	Lal, 2012	[197]

2.4.1.5. Thermal fiber drawing for metal nanowires

Metal microwire fabrication by thermal drawing in a glass cladding, known as the Taylor-wire process, has been in practice for decades. Schematics and the actual equipment are shown in Figure 20. As this conventional technique combines with the stack-and-draw approach, the fabrication of fine metal wires becomes possible. However, little success has been reported to fabricate long wires with a diameter of less than 1000 nm out of metals, especially those of higher melting temperatures, such as gold (Au), copper (Cu), zinc (Zn), and their alloys. Thermally drawn continuous Cu microwires of 4 μm in diameter have been demonstrated [183]. Au microwires of 4 μm diameter were fabricated over a length of several centimeters, and this continuous length shrank to 20 μm as their diameter was reduced to 260nm [181]. Fabrication of discontinuous Cu-phosphor wire with a diameter of 500 nm and length of tens of micrometers has been reported using Pyrex glass cladding [185]. Fiber drawing via laser-based heat source pulling of short pieces of Pt microwires has been used to fabricate quartz-sealed Pt nanowires. The resultant fibers were tapered down to 10 nm in diameter yet with a length of only 5 mm [189]. Alternatively, a polyol process, which is the synthesis of metal-containing compounds in ethylene glycol, was used to fabricate Ag nanowires with a length of up to 230 μm and a diameter of 60-90 nm [198, 199]. Low melting temperature metals such as tin (Sn), lead (Pb), bismuth (Bi), indium (In), and their alloys are mostly thermally drawn in polymer cladding. The smallest diameter reported for metal wires that can be reliably drawn into indefinitely long arrays is about 4 μm and is achieved from Sn_{0.95}Ag_{0.05} alloy with PES cladding [162]. Beads, discontinuities and structural deformation would be observed upon further size reduction. Nevertheless, thermally drawn functional fibers embedding Indium wires with diameter approaching 1 μm has been demonstrated [200]. While low-melting lead (Pb)-Sn alloys and Bi nanowires with a diameter down to 50 nm were reported

with a longer length, no experimental evidence was provided to support their continuity over the claimed drawn length [182].

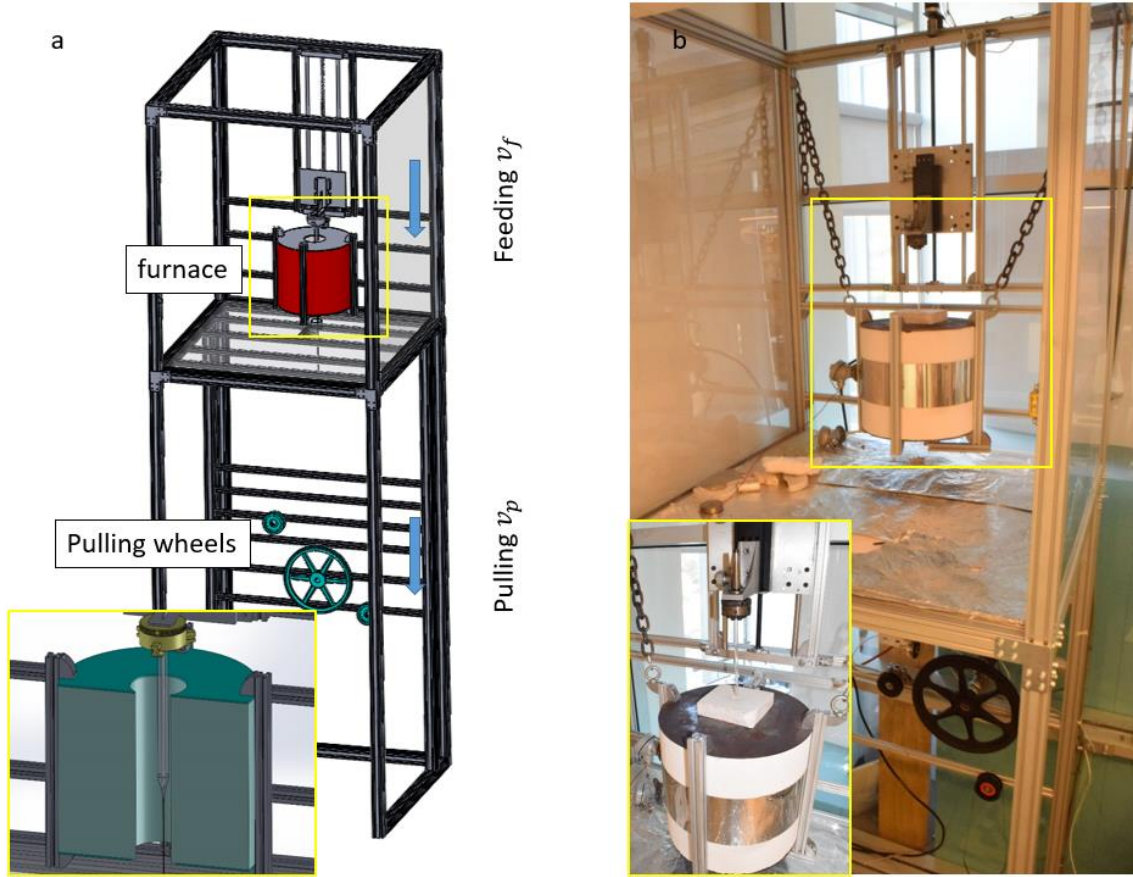


Figure 20: Drawing tower. (a) The schematic of the high-temperature thermal fiber drawing tower with the detailed section view inside the furnace, (b) the actual build-up high-temperature thermal fiber drawing tower with a detailed view of the furnace part. (CAD work contributed to Max Sokoluk)

Partially in this study, we apply thermal fiber drawing to fabricate ultra-long metal nanowires, demonstrating feasibility to scalable manufacturing, exploring novel metal nanowire properties and comprehend the fundamental physics behind, especially for mechanical and electrical behaviors, and developing functional applications.

Chapter III: Manufacturing and Characterization of Nanoparticle Reinforced

Zinc

According to the research, Zn is a very suitable biodegradable metal for cardiovascular stents, and potentially, Zn matrix nanocomposite could satisfy the stent requirement with a combination of optimized properties. Thus, this part of the research objective focuses on the investigation of Zn matrix nanocomposite fabrication and characterization to determine whether such materials could be suitable for biodegradable materials. The investigation of the materials included method optimization for dispersed nanoparticles, nanoparticle concentration optimization, and material processing optimization. The characterization included the evaluation of the mechanical property, microstructure, thermal stability, corrosion behavior. The ultimate target is to find a standard fabrication method for Zn matrix nanocomposite that could be applied for mass production with high production efficiency. Furthermore, the characterization of Zn matrix nanocomposites aimed at evaluating the properties and justifying if high strength, high ductility, suitable corrosion rate, and optimal biocompatibility could be realized. In this chapter, various ceramic nanoparticles were proposed for incorporation into Zn, and WC and TiB₂ have achieved certain success.

3.1. Fabrication of Zn-WC

3.1.1. Fabrication method

Molten slat assisted ex-situ stir casting was used to successfully incorporated WC nanoparticles into Zn. Ultrasound processing was used to realize a homogeneous dispersion of nanoparticles. Hot rolling has been used to homogenize the nanoparticle dispersion further and enhance strength and ductility for Zn-WC. Characterization of microstructure, mechanical behavior, corrosion behavior, and other related properties has been performed.

3.1.1.1. Molten salt assisted ex-situ stir casting of Zn-WC

Salt assisted stir casting was performed to mass-produce Zn-WC nanocomposite, as it has recently been demonstrated to be an efficient method for other composite systems [201, 202]. Schematics of the molten salt stir casting are shown in Figure 21. Induction furnace was used to melt potassium aluminum fluoride (KAlF_4) at 700°C in a 3kg-capacity graphite crucible (89mm in height and 130mm in inner diameter).

Bulk Zn (99.9%, RotoMetals) was weighed and added to the crucible. The molten salt was used to cover the metal and protect it from oxidation. WC nanoparticles (50-200nm) were mixed with fine KAlF_4 salt powders. This powder mixture was then slowly added to the crucible. A graphite stirrer was used to mix and incorporate the WC nanoparticles. The top layer of low-density molten salt was removed prior to casting Zn-WC to a 2-inch diameter disk with a 0.4-inch thickness.

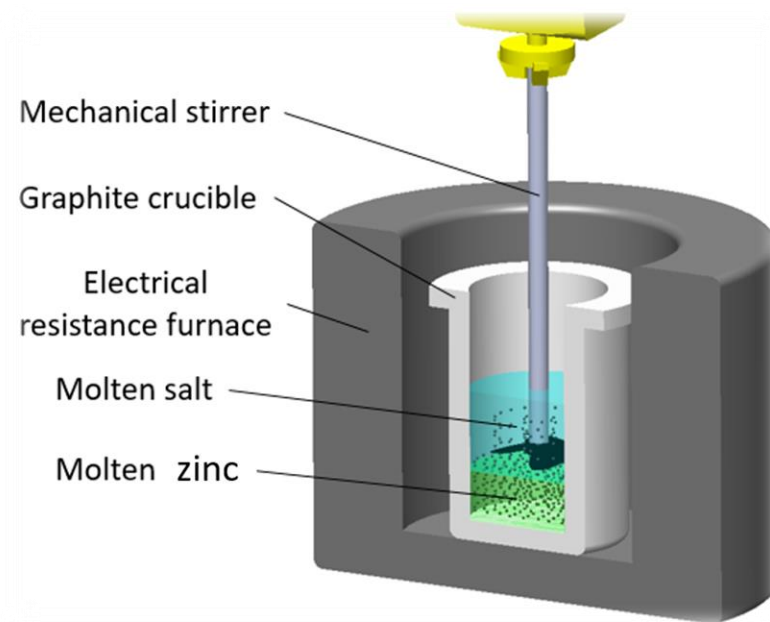


Figure 21: Molten salt assisted stir casting process

Zn-WC samples were cooled inside the crucible to room temperature. Samples were ground by manual polisher (Allied M-PREP 5™ GRINDER/POLISHER) through 60, 120, 240, 400, 600, 800, and 1200 grinding papers, and polished by 1 μm and 0.2 μm dispersed alumina solutions. SEM results are shown in Figure 22. A few observations can be found from the results:

- WC nanoparticles were successfully incorporated into the Zn matrix, indicated by the bright phases, demonstrating the efficiency of the molten salt stir casting method.
- WC dispersion remained as a problem due to the pseudo dispersion of nanoparticles, where micro size “clusters” of nanoparticles were observed.
- Some fluoride salt was trapped in the metal during the incorporation, indicated by the dark phase. Such a phenomenon was due to untuned operating parameters, where the high stirring speed and low amount of molten salt could result in turbulence flux of molten salt/nanoparticle mixtures.

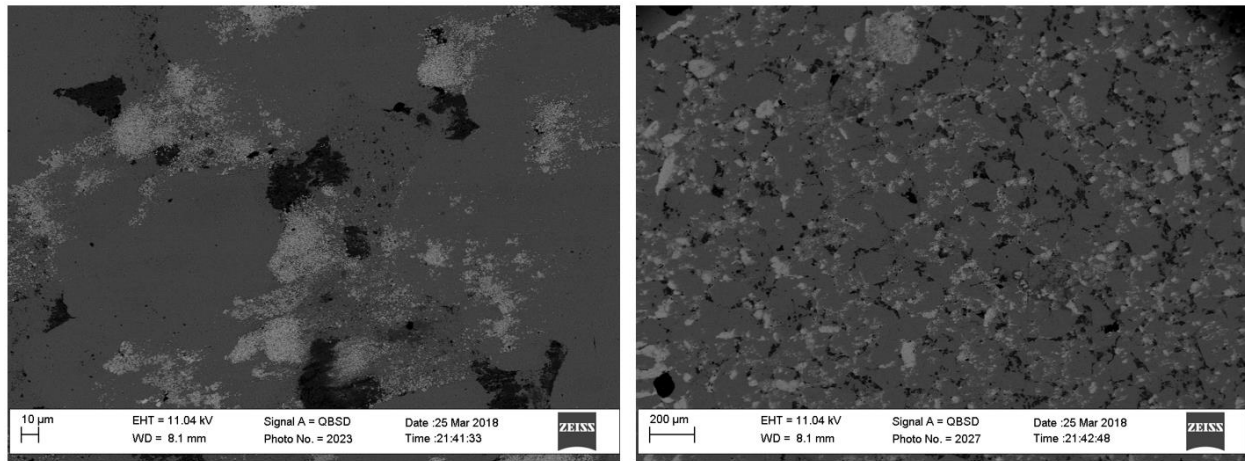


Figure 22: SEM results of Zn-5WC samples

- Samples cooled in crucibles had obvious nanoparticle segregation, where the top layer has much lower nanoparticle concentration than the bottom layers. As shown in Figure 23, the top part, represented by the left side, has lower WC nanoparticle density, and the bottom

half, represented by the right side, has a higher nanoparticle density. The reason could be the higher density of nanoparticles and clusters.

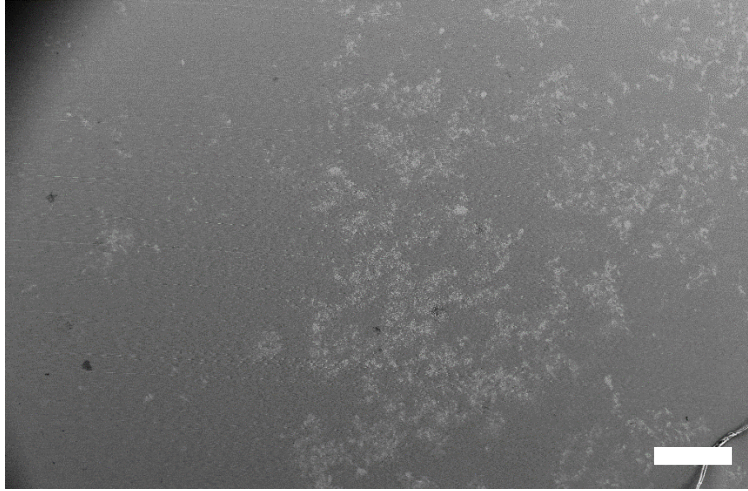


Figure 23: SEM images of Zn-WC cooled down in crucible, showing the sinking phenomenon, where the left part indicated the top, and right part indicated the bottom. The scale bar indicates 200 μm in the figure.

3.1.1.2. Parameter optimization and ultrasound processing for incorporation efficiency

To further improve the fabrication method, parameter optimization was applied to realized homogeneous nanoparticle dispersion in Zn. The optimized parameters are shown in Table 5. The optimized parameters were suitable for scalable fabrication of kilograms of Zn-WC nanocomposite with high volume concentrations of nanoparticle in a relatively short time.

Table 5: Molten salt assisted stir casting optimized operating parameters

Zn sample weight	500g – 1000g
WC concentration	0 – 15 vol. %
Stirring speed	400-500 rpm
KAlF ₄ to WC volume ratio	20 – 30
Temperature	750 – 850 °C
Time	45 – 60 minutes

Graphite propeller position	1/3 – 1/2 of the propeller should be immersed into the molten metal
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In order to further disperse the nanoparticles, ultrasound processing was used after the successful incorporation of nanoparticles. Ultrasound processor (Misonix S-400 Ultrasonic Liquid Processor, with a boron nitride (BN) coated Nb alloy C103 probe) was used to further homogeneously dispersed the nanoparticles and to eliminate molten salt that was trapped in the metal melt. The temperature was maintained at 800°C for 20 min, and the metal melt was cast to a BN coated steel mold. The schematics of the process are shown in Figure 24.

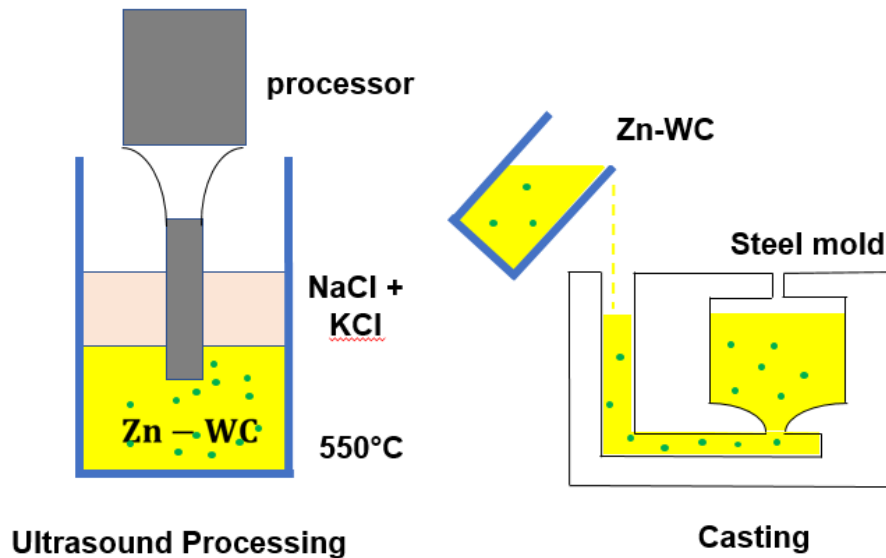


Figure 24: Schematics of ultrasound processing and casting

A long processing time using the ultrasonic probe will result in the desolvation of Nb into Zn to form intermetallic phases. During the experimental trials, such intermetallic phases were observed from SEM images once the ultrasound processing time exceeds 30 minutes, as shown in Figure 25. Additionally, because an ultrasound processor is not designated for high-temperature usages, flow air cooling of the processor was necessary during the ultrasound processing.

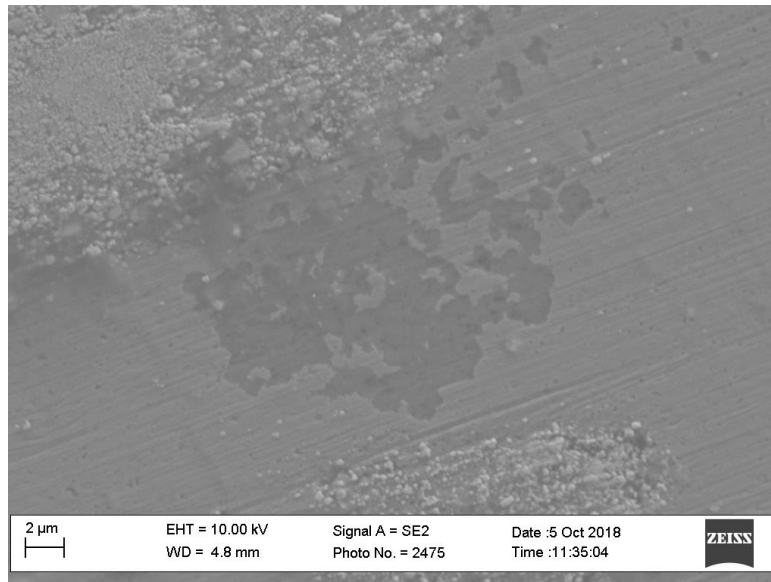


Figure 25: Long time (30 min) ultrasound processing resulted in Zn-Nb intermetallic phase formation in the Zn-WC nanocomposite

3.1.2. Fundamental dispersion theory behind the fabrication process

KAlF_4 reacted efficiently with ZnO on the top of the molten metal and dissolved the metal oxide during the incorporation. Such oxide acted as an interfacial barrier to hinder the nanoparticle incorporation into molten Zn. Due to the small size of nanoparticles, the gravity effect was relatively small. On contrast, interfacial energy dominated, while the high surface tension introduced by the oxide layer could block the nanoparticle's incorporation. The experimental phenomenon showed that, without a sufficient amount of fluoride salt, WC nanoparticles agglomerated on the top of the molten Zn and separated as an individual layer between the molten metal and molten salt. The agglomeration of nanoparticles increased the contact surface area with the oxide and further blocks the nanoparticle incorporation path.

The nanoparticle self-dispersion mechanism, discussed in multiple papers published by the Scifacturing group, is responsible for the phenomenon of homogeneous nanoparticle dispersion in the metal matrix [203]. The fundamental reason for the nanoparticle dispersion is the excellent

wettability between the selected nanoparticle and molten metal matrix, low van der Waals potential between nanoparticles inside the melt, and high thermal energy, shown in Figure 26. Once the wetting is good enough, it will result in a potential barrier that prevents nanoparticle agglomeration and sintering. High thermal energy will overcome the attractive van der Waals potentials between nanoparticles. Representative results have already been demonstrated in nanocomposite systems, including Mg-SiC, Al-TiC, and Cu-WC, shown in Figure 27 [145, 203, 204].

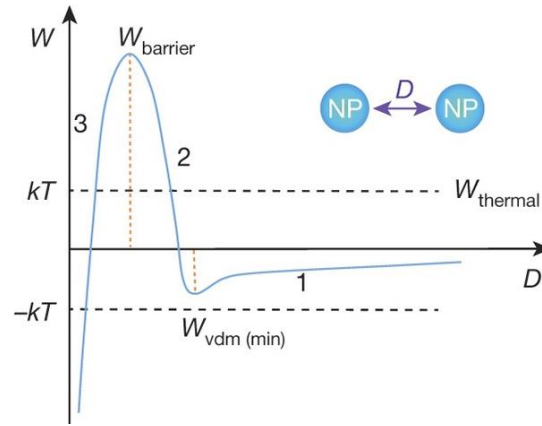


Figure 26: The principle of thermally activated dispersion and stabilization. The interaction potential W for two SiC nanoparticles (NPs; blue circles, separated by a distance D) that interact inside the magnesium melt is shown as the blue curve, which has three segments (labeled). Segment 1 is dominated by van der Waals interaction, segment 2 is dominated by the interfacial energy increase when the Mg–SiC interface is replaced by SiC surfaces, and segment 3 is the interfacial energy drop due to SiC nanoparticles contacting and sintering. $W_{vdw (min)}$ is the minimum van der Waals potential for maximum attraction, $W_{barrier}$ is the energy barrier due to the interfacial energy increase, $W_{thermal} = kT$ is the thermal energy.

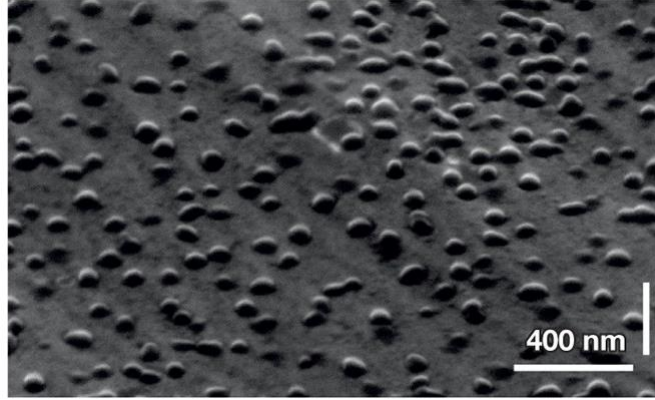


Figure 27: SEM images of the Mg₂Zn (14 vol% SiC) sample

3.1.3. Hot rolling

Hot rolling and hot extrusion are both typical methods for Zn and Zn alloys fabrication with high strength and high elongation to failure. Furthermore, such a plastic deformation process can introduce fine equiaxed grain structures, shown in Figure 28 [205]. In the fabrication of Zn-based stent, hot tube extrusion is used to form mini-tubes for a later laser cutting process.

However, due to the limitation of precision hot extrusion equipment, hot rolling was used in this work. Due to the inherent HCP structure of Zn (fewer slip planes than BCC/FCC), as-cast Zn samples are highly brittle with low strength. Hot rolling (150 – 200 °C) performed on Zn can enhance strength while reducing the anisotropic effect of directional rolling [206]. Hot rolling of Zn alloys has already been proven for efficient strengthening and improvement of ductility in studies of Zn-based stent [207].

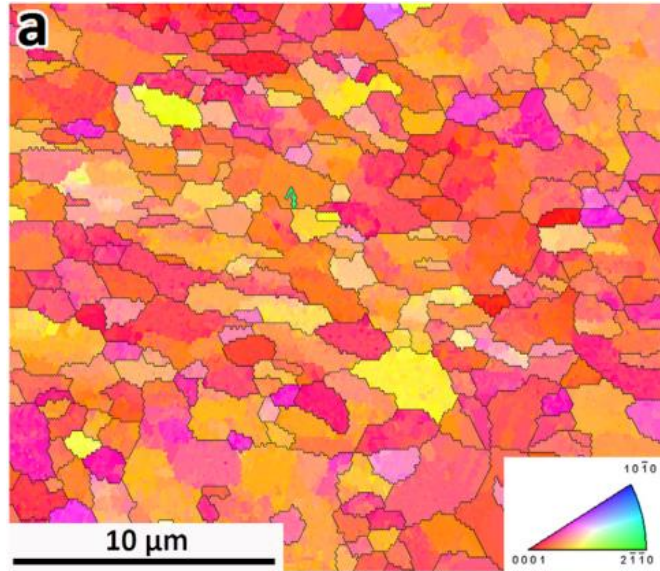


Figure 28: EBSD orientation map of Zn-0.5Mg

3.2. Characterization of Zn-WC

After the successful incorporation of the WC nanoparticles into Zn by the molten salt assisted stir casting, ultrasound processing for homogenizing dispersion, and hot rolling, characterizations were performed to study microstructure, mechanical performance, corrosion behavior, electric conductivity, and thermal conductivity.

3.2.1. Microstructure

SEM in backscattering mode was performed on the nanocomposite samples to investigate the nanoparticle dispersion, as shown in Figure 29. The bright phase represents the WC nanoparticles, while the darker phase represents the Zn matrix. Compared with Zn-2.6WC with scattered zones of dense nanoparticles, Zn-4.4WC achieved a better homogeneity of nanoparticles. In order to investigate the nanoparticle effect on the crystal structure, optical images were shown after etching (etchant: 20% CrO_3 and 5% Na_2SO_4 in distilled water). The grain size reduced from 17.4μm to 6.1μm with 4.4vol.% WC nanoparticle incorporation.

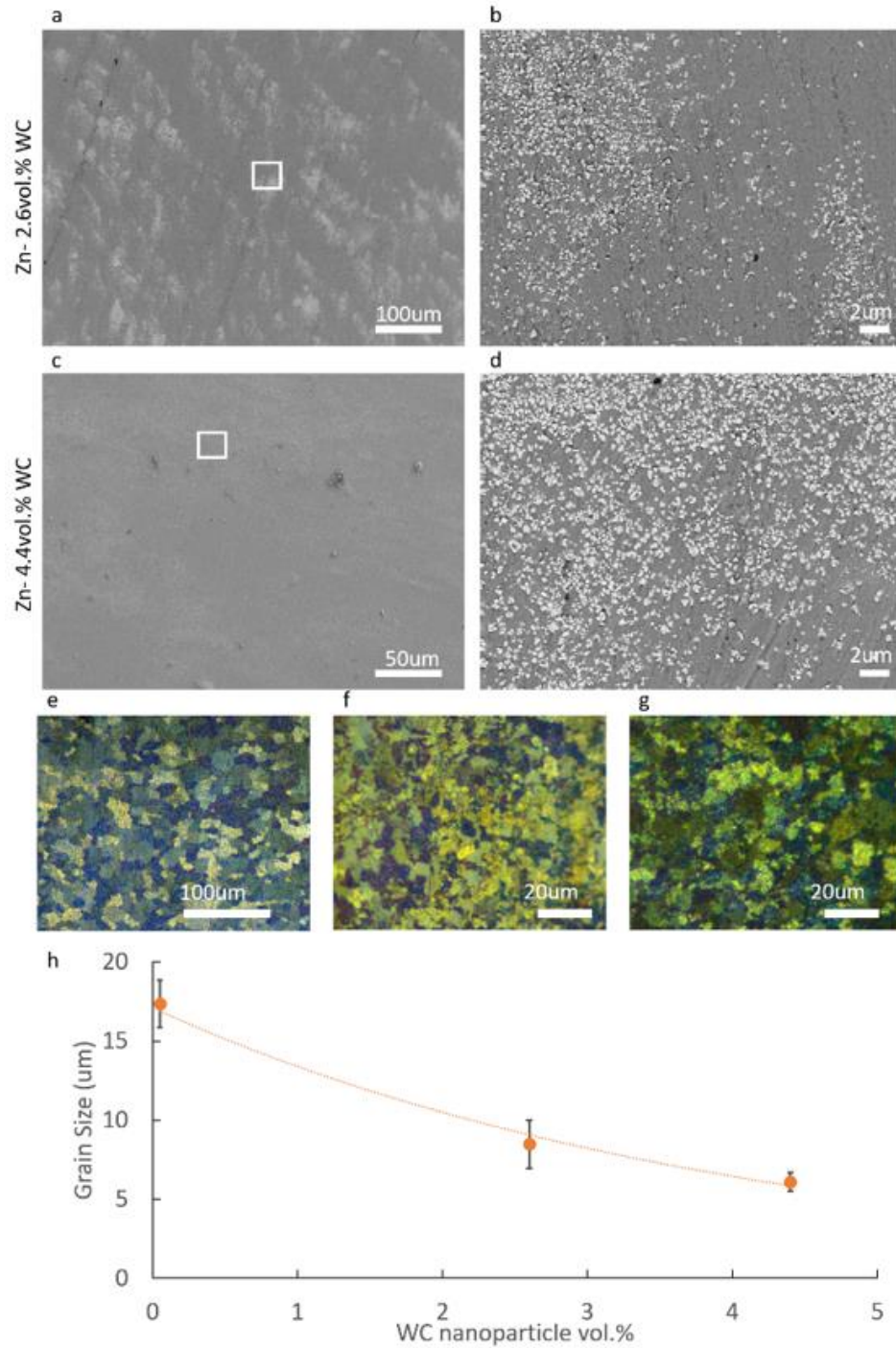


Figure 29: Zn-WC nanocomposite microstructure from SEM in backscattering mode. (a) and (c) represent Zn-2.6 vol.% WC sample and Zn-4.4 vol.% WC samples, while (b) and (d) are the magnified images. Optical images of hot-rolled samples for grain size measurement, including (e) Zn, (f) Zn-2.6WC, and (g) Zn-4.4WC. (h) shows the grain size refinement effect with respect to the nanoparticle concentration.

Good wettability between WC and molten Zn enables a self-stabilization mechanism through a force balance between the particle-particle van der Waals force and the particle-molten metal surface tension [127], effectively enabling nanoparticle self-dispersion within the molten Zn. However, when the nanoparticle size is not small enough, pseudo -dispersion occurs, where there is a favorable particle-particle distance (e.g., approximately a few nanometers in the Zn-WC system). Thus, pseudo-microcluster was observed in Zn-2.6WC. Zn-4.4WC, on the other hand, obtained a much better nanoparticle dispersion due to the higher concentration. The problem of non-uniform dispersion could be solved by using smaller sized nanoparticles.

Zinc's grain size is one of the determinant factors for mechanical strength. For instance, cast zinc with 100 μm grain size only has a UTS of 30MPa. The nanoparticle-induced grain refinement in this study is mostly due to grain growth impedance by nanoparticles during solidification. The finer crystalline structure (6.1 μm grain size) enables a better grain-boundary strengthening, also known as Hall-Petch strengthening, by impeding dislocation propagation. Another contributor to the increased mechanical strength is the Orowan strengthening effect directly from WC nanoparticles. The nanoparticles block dislocation movement, which means dislocations need higher energy to shear through/around the nanoparticles (i.e., Orowan mechanism)[208]. Other strengthening mechanisms include load-transfer and thermal expansion coefficient/elastic modulus mismatch.

Previous studies on nanoparticle reinforced metals reported that nanoparticle agglomeration, sintering, impurities, and voids would negatively impact the ductility of the matrix. Such defects can cause premature fracture through crack propagation during tensile testing. In this study, salt assisted stir casting effectively prevented these defects by avoiding zinc oxides, nanoparticle agglomeration, and sintering. A good nanoparticle dispersion was achieved by the self-

stabilization mechanism, and hot extrusion processing could further enhance the dispersion homogeneity by shearing [209].

TEM was used to reveal the microstructure of Zn-WC. TEM samples were prepared by Nova 600 SEM/FIB and were examined by TF20 High-Resolution EM, CryoEM, and CryoET (FEI). TEM image further reveals the homogeneous dispersion of WC nanoparticles, shown in Figure 30. The darker phase indicates the microstructure of the single crystal WC, as confirmed by selected area electron diffraction. WC has a hexagonal crystalline structure, where (111) plane and (201) plane are presented with an angle of 27° as indicated in the diffraction pattern. The interfaces between WC nanoparticle and Zn matrix nanoparticles were indicated by the yellow dash line, showing that no particle sintering or agglomeration during the fabrication process.

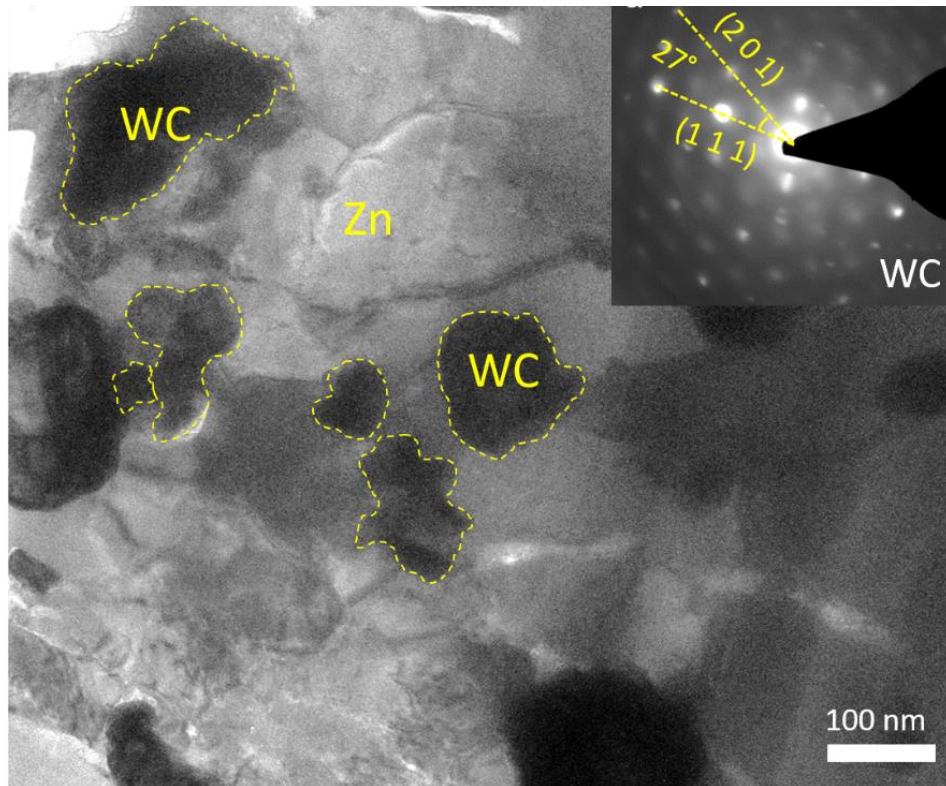


Figure 30: TEM image of Zn-WC nanocomposite. The small figure on the top right plots the diffraction pattern of WC on the darker phase after fast Fourier transformation.

To accurately determine nanoparticle concentrations and dispersion inhomogeneity, ICP-MS was used to measure metallic element concentrations. Zn-WC nanocomposites were ground to small pieces, and aqua regia was used to extract elemental W. The results were converted to WC concentrations in volume percentage, as shown in Table 6. In this study, Zn-WC nanocomposite samples had a lower than designed WC content due to the imperfect nanoparticle incorporation during manufacturing. The final Zn-WC nanocomposite formulations were Zn-2.6 vol.% WC and Zn-4.4 vol.% WC, which were characterized and compared to pure Zn samples, processed under the same conditions.

Table 6: ICP-MS result of Zn and Zn-WC nanocomposite samples (10mg per sample and 3 tests were performed on each sample)

	Concentration [mg/g]		
	Zn	W	WC (vol.%)
Zn	769.2±4.5	1.2±0.0	0.0
Zn-2.6 WC	761.4±1.7	42.0±1.5	2.6
Zn-4.4 WC	802.7±0.2	75.8±2.3	4.4

XRD was performed on the nanocomposite samples and the reference sample to semi-quantitatively characterize the phase composition of the materials, shown in Figure 31. The diffraction peaks of WC could be observed on the XRD pattern for both Zn-2.6WC and Zn-4.4WC samples, where the diffraction angles are from 30 to 90 degrees. Furthermore, no byproducts were observed, indicating that WC nanoparticle did not react with Zn during manufacturing and processing.

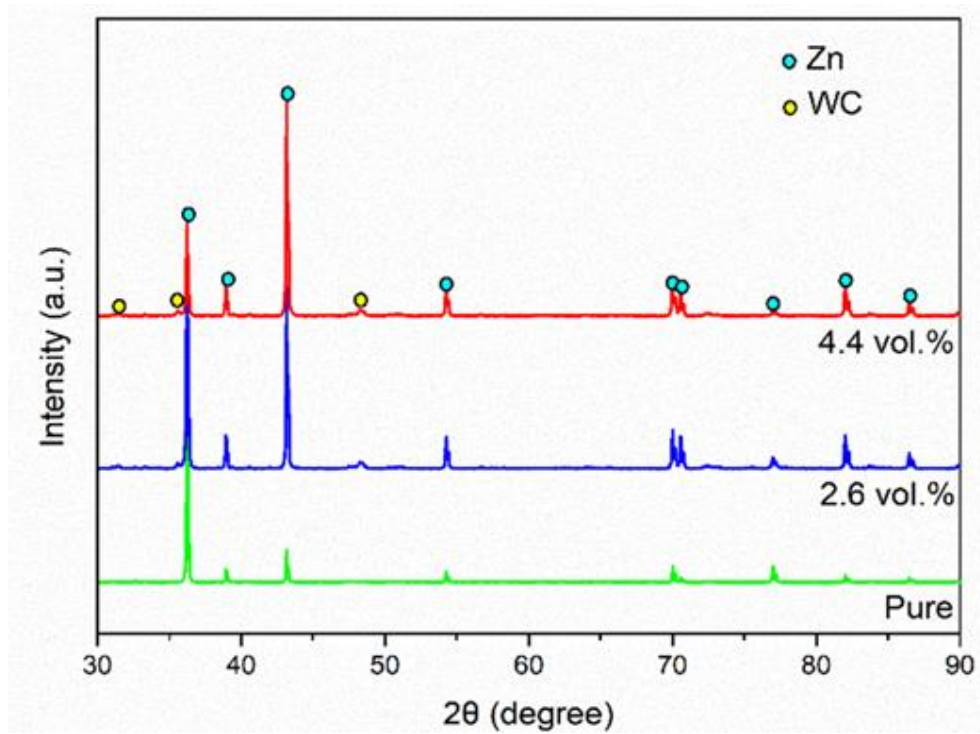


Figure 31: Diffraction pattern of Zn and Zn-WC nanocomposite samples.

3.2.2. Mechanical performance

The grain-size effect on the mechanical properties (Hall-Petch effect) was evaluated through Vickers microhardness testing and tensile testing. Microhardness was measured using 300 gf and 10 s dwelling time. Figure 32(a) shows that Vickers microhardness of the Zn-4.4%WC nanocomposite has increased by more than 43% from 34.9HV to 55.0HV. Tensile testing was performed using an Instron 5966 Dual Column Tabletop Testing system. The results show the ultimate tensile strength (UTS) of Zn-4.4WC increased by 87% from 89.1 MPa to 166.3 MPa, while the ductility only decreased from 70.1% to 65.1% (Figure 32(b) and Table 2). These results show that homogeneous nanoparticle dispersion could be used to avoid significant ductility reduction [210].

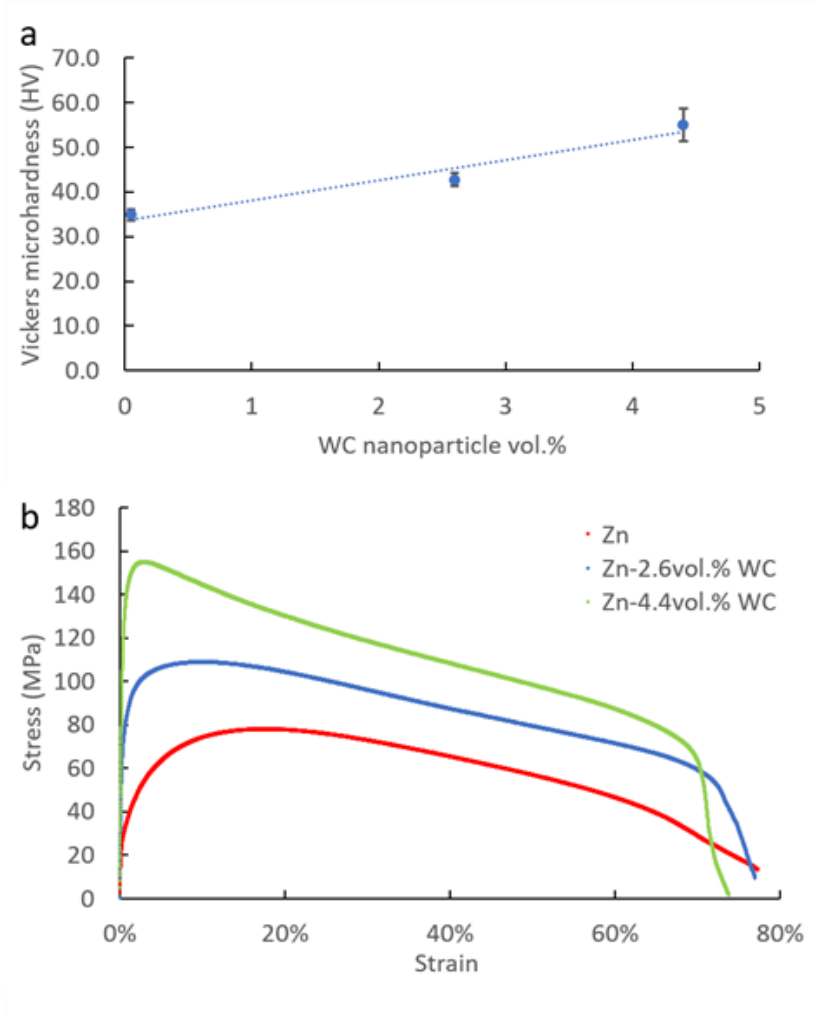


Figure 32: (a) Vickers microhardness Zn-WC nanocomposite samples; (b) Stress-strain curves of the Zn and Zn-WC nanocomposite samples from the tensile tests.

Table 7: Tensile test results of ASTM subsize dog-bone samples

	UTS (MPa)	Yield strength (MPa)	Elongation
Zn	89.1±15.4	35.6±10.4	70.1±10.2%
Zn-2.6WC	111.6±3.4	75.1±8.8	69.7±10.3%
Zn-4.4WC	166.3±15.7	126.9±2.7	65.1±12.3%

3.2.3. Corrosion performance

This part of the study includes the material characterization of degradability. As one of the most important properties for biodegradable material, the toxicity study of WC showed that WC nanoparticles have non-cytotoxicities in an *in vitro* characterization [211]. Theoretically, the biologically inert WC nanoparticles should maintain the favorable corrosion rate of pure Zn. The degradation rates were evaluated through the detection of ion release into the SBF at multiple time spots, and the change in surface morphology after immersion testing was evaluated. Compared with conventional strengthening methods (e.g., alloying), which commonly have an increased corrosion rate, Zn matrix nanocomposite fabricated in this work provided high strength and had a corrosion rate similar to pure Zn [90]. These results encouraged further investigation of Zn-WC nanocomposites for biomedical applications with the ultimate goal of creating safe and efficacious bioabsorbable metallic implants for many clinical applications.

Zn-WC nanocomposite was cast into a borosilicate tube by vacuum and went through thermal fiber drawing for microwires [212] to represent bioabsorbable devices for biodegradation characterization. The immersion test (ASTM G31-72) was carried out, where samples were kept in Simulated Body Fluid (SBF) for 14 days at 37°C. The SBF used in this study had ionic concentrations equal to that of human blood plasma, as well as an equal pH value (Table 8). Inductively coupled plasma optical emission spectrometer (ICP-OES) and ICP- mass spectrometer (ICP-MS) were carried out for Zn and W ion concentration measurement in the SBF. The changes in the surface morphologies after immersion were studied by environmental scanning electron microscopy (ESEM). The analysis was conducted with a ZEISS Supra 40 Variable Pressure SEM (VP-SEM) equipped with a Thermo Noran System 6 energy-dispersive X-ray spectroscopy (EDS) system. Vickers Microhardness test was performed before and after the emersion test.

Table 8: Ion concentration and pH values of simulated body fluid versus human blood plasma

Ions	SBF (mM)	Human Blood Plasma (mM)
Na ⁺	142	142
K ⁺	5	5
Mg ²⁺	1.5	1.5
Ca ²⁺	2.5	2.5
Cl ⁻	147.8	103
HCO ₃ ⁻	4.2	27
HPO ₄ ²⁻	1	1
SO ₄ ²⁻	0.5	0.5
pH	7.4	7.4

The statistical significance of differences between groups during immersion testing was determined using one-way ANOVA followed by Tukey post-hoc analysis. The SPSS statistical software package 24.0 for Windows (IBM, Armonk, NY, USA) was used for statistical analysis. Significance was established by a value of $p < 0.05$. Data were expressed as mean $\pm$ standard deviation (SD).

The results from the immersion test showed that the number of Zn ions released from the Zn-WC nanocomposites are statistically the same regardless of the volume fraction of WC nanoparticles and was similar to that of pure Zn micro-wires based on one-way ANOVA (Figure 33c). These results suggest that Zn retains the favorable degradation rate with the addition of WC nanoparticles. The degradation rate of the Zn-WC micro-wires was linear during the 14-day study length. The average corrosion rate of each sample per day was $0.25 \sim 0.4$, $0.33 \sim 0.43$, $0.31 \sim 0.33$ and $0.25 \sim 0.26 \mu\text{g}/\text{mm}^2/\text{day}$ at days 1, 3, 7 and 14, respectively, shown in

Table 9. These levels of Zn ion release are likely to be well tolerated *in vivo*. The National Academy of Medicine has set the recommended daily intake value of Zn at 2–3 mg/day for infants

up to 8–11 mg/day for adults [213], and normal serum and urine levels in adults have been reported as 1 µg/mL and 0.5 mg/g creatinine, respectively. Therefore, the toxic potential of the daily dose of Zn released from a Zn-based implant should be negligible[69, 214]. Additionally, no detectable levels of tungsten were released from Zn-WC nanocomposite microwires after 14 days of static immersion in SBF as measured by ICP-MS with a lower quantifiable limit of 0.5 ppb (0.5 ng/mL). Tungsten has historically been considered an inert metal; however, there are concerns that accumulation of tungsten within the bone may alter the bone biology as well as a result in higher exposure levels within the bone marrow, which contains part of the developing immune system [215]. However, relatively high doses of tungsten (15-500 ppm) are used in such toxicity studies [215-217]. Conclusively, these results indicate that WC remains chemically stable with minimal toxic potential *in vivo* [211], and its impact on the corrosion rate of Zn-based implants is negligible.

Figure 33d and Figure 33e show the surface morphologies of the Zn-WC nanocomposite micro-wires before and after soaking in SBF for 14 days, presenting that the surface immersed in the SBF for 14 days was similar to that before testing. A large amount of salt precipitation forms a layer to cover the sample's surface. According to EDS results, it is reasonable to assume that the layer of biodegradation products may contain ZnO, Zn(OH)₂, Zn₃(PO₄)₂, and Ca₃(PO₄)₂ based on the composition and insolubility of by-products in water and SBF.

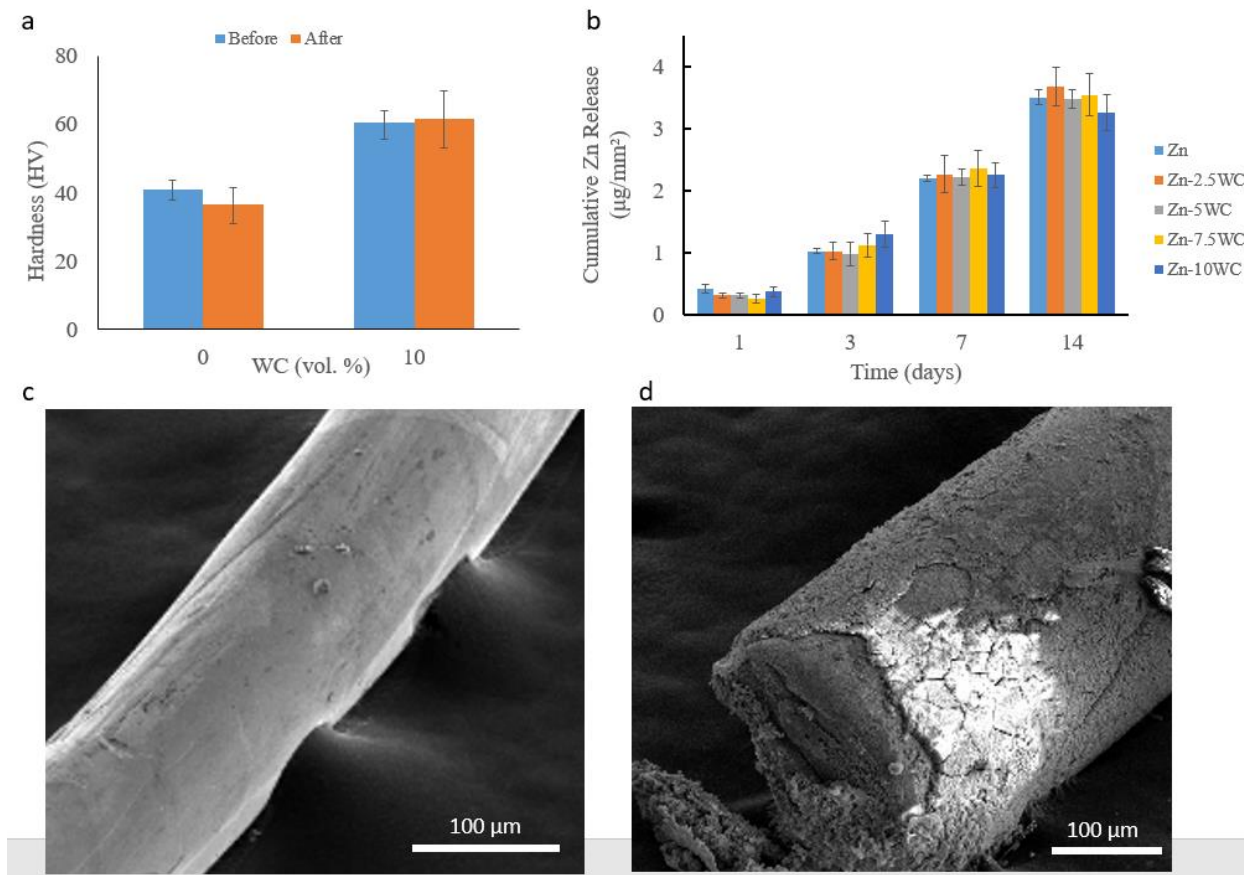


Figure 33: Biodegradability of pure zinc and Zn-WC nanocomposite. (a) Comparing the Vickers hardness of pure Zn and Zn-WC (10 vol. %) nanocomposites before and after 14 days of immersion in SBF. (b) Static immersion of Zn-WC micro-wires in SBF ($n=3$). No statistically significant difference ($p > 0.05$) was measured in Zn release between samples with increasing WC nanoparticle content based on one-way ANOVA. SEM images of Zn-WC nanocomposite micro-wire before (c) and after (d) immersion in SBF for 14 days.

Table 9: Average cumulative Zn ion release at day 14 of the immersion test

	Zn	Zn-2.5WC	Zn-5WC	Zn-7.5WC	Zn-10WC
Zn ion release ($\mu\text{g}/\text{mm}^2$)	0.329 ± 0.068	0.346 ± 0.047	0.299 ± 0.047	0.305 ± 0.070	0.338 ± 0.090
Significance level P	N/A	0.49	0.21	0.39	0.78

3.2.4. Electrical and thermal properties

Electrical and thermal properties have been characterized in this study. Because of the high electrical conductivity of metals, the relevant results shown in this part could potentially be useful for electronic devices in the future. The sheet resistance of nanocomposite samples was measured by *ResMap four-point probe* (Figure 34(a)), and thermal conductivity was calculated using heat capacity measurements from differential scanning calorimetry (DSC) and thermal diffusivity by laser flash analysis (Figure 34(b)). The electrical conductivity decreased from $10.2 \times 10^6 \text{ S/m}$ to $8.9 \times 10^6 \text{ S/m}$ for Zn-4.4WC, and the thermal conductivity decreased from 114.6 W/m-K to 91.0 W/m-K. According to one-way ANOVA analysis, electrical conductivity and thermal conductivity have p values of 5.5% and 7.0%, respectively, indicating that no significant reduction after nanoparticle incorporation. All related mechanical and physical results are presented in Table 10.

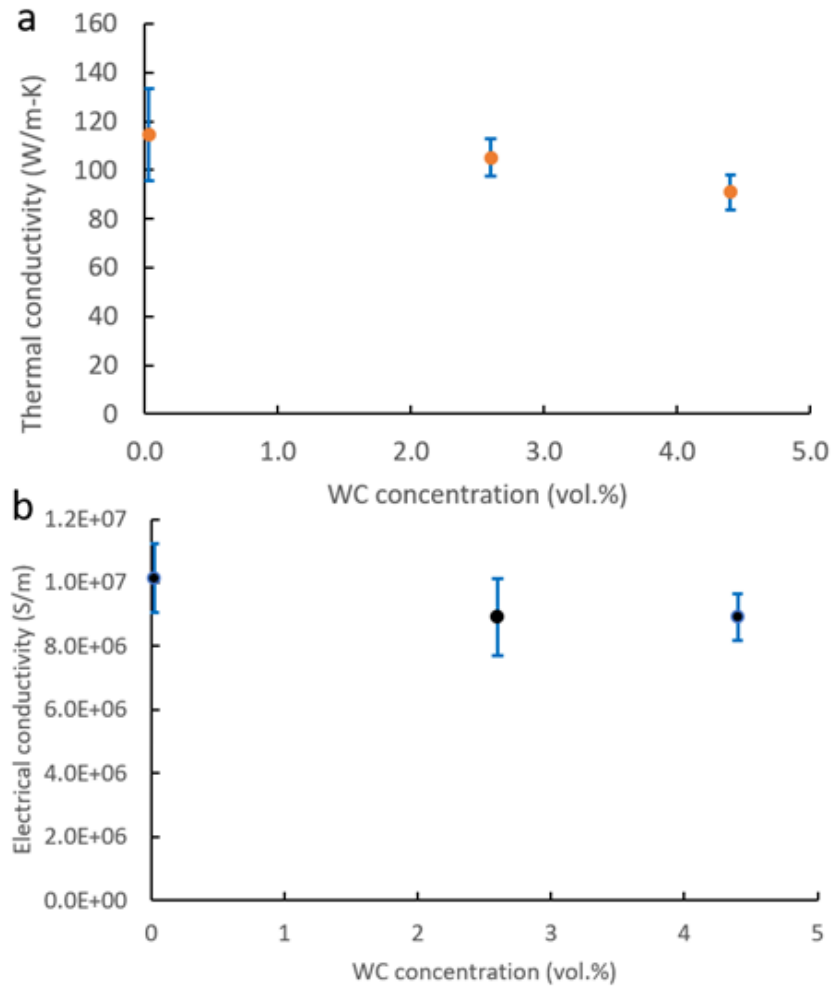


Figure 34: (a) Thermal conductivity of Zn-WC concerning the WC nanoparticle concentration; (b) electrical conductivity of Zn-WC concerning the WC nanoparticle concentration

Table 10: Physical properties of hot-rolled Zn/Zn nanocomposite plate

	Grain size (μm)	Vickers microhardness (HV)	Electrical conductivity ($\times 10^6 \text{ S/m}$)	Thermal conductivity (W/m-K)
Zn	17.4 $\pm$ 1.5	34.9 $\pm$ 1.2	10.2 $\pm$ 1.1	114.6 $\pm$ 19.0
Zn-2.6WC	8.5 $\pm$ 1.5	42.7 $\pm$ 1.5	8.9 $\pm$ 1.2	105.2 $\pm$ 7.8
Zn-4.4WC	6.1 $\pm$ 0.6	55.0 $\pm$ 3.6	8.9 $\pm$ 0.7	91.0 $\pm$ 7.2

Zn-WC nanocomposites could be used to create the next generation of bioresorbable electronics. The Zn-WC nanocomposites studied in this research have shown a good combination of material properties, including mechanical ductility (elongation > 65%), mechanical strength (UTS ~ 166.3MPa, YS ~126.9MPa), microhardness (~55HV), electrical conductivity ($8.9 \times 10^6 S/m$) and thermal conductivity (~91W/m-K). The high electrical conductivity provides a better signal-to-noise ratio in sensing, and high thermal conductivity provides faster heat release for electronics. The enhanced hardness of Zn-WC could also enable the application as biodegradable electrical contact materials, where the material toughness becomes the critical properties for such applications [218]. With an optimized combination of good toughness and electrical/thermal conductivity, Zn-WC nanocomposite would be suitable for applications such as electrodes and interconnects in bioresorbable electronics [81].

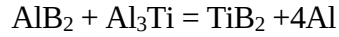
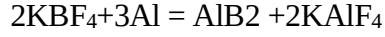
3.3. Fabrication and Characterization of In Situ Zn-TiB₂ Nanocomposite

In this part of the work, TiB₂ was incorporated into the pure Zn matrix and homogeneously dispersed through an *in-situ* synthesis method, known as flux assisted synthesis (FAS), with the addition of salt-assisted ultrasound processing and hot rolling [219, 220].

3.3.1. Method

FAS were used for TiB₂ particle synthesis and incorporation into the Zn matrix. High purity Zn (99.995%, ingot, Rotometal) and aluminum (Al) (99.999%, ingot, Alfa aesar) were used as the raw materials. Zn and Al (5 wt%) were melted at a temperature of 700°C. Mixed salt of potassium tetrafluoroborate (KBF₄), potassium hexafluorotitanate (K₂TiF₆), and the design of 3 vol.% TiB₂, was added into the ZnAl melt, with an atomic ratio of 2B/Ti (shown in Figure 35(a)). The reactions of salts in the metal melt to synthesize TiB₂ nanoparticles are shown below:





The molten salts were manually stirred for 10 minutes, and the salt slug was removed. New chloride salt (1:1:1 atomic ratio NaCl/KCl/ZnCl) was added and ultrasound was applied by an ultrasonic liquid processor (Misonix S-4000) installed with a Niobium probe for 10 minutes to remove the salt trapped in the metal melt at 500°C, to dispersed nanoparticles and to react with the Al residue in the metal melt (shown in Figure 35(b)). Zn-TiB₂ was then cast in a steel mold, as shown in Figure 35c. The nanocomposite samples went through hot cross-rolling (75% thickness reduction) at 250°C, as shown in Figure 35d.

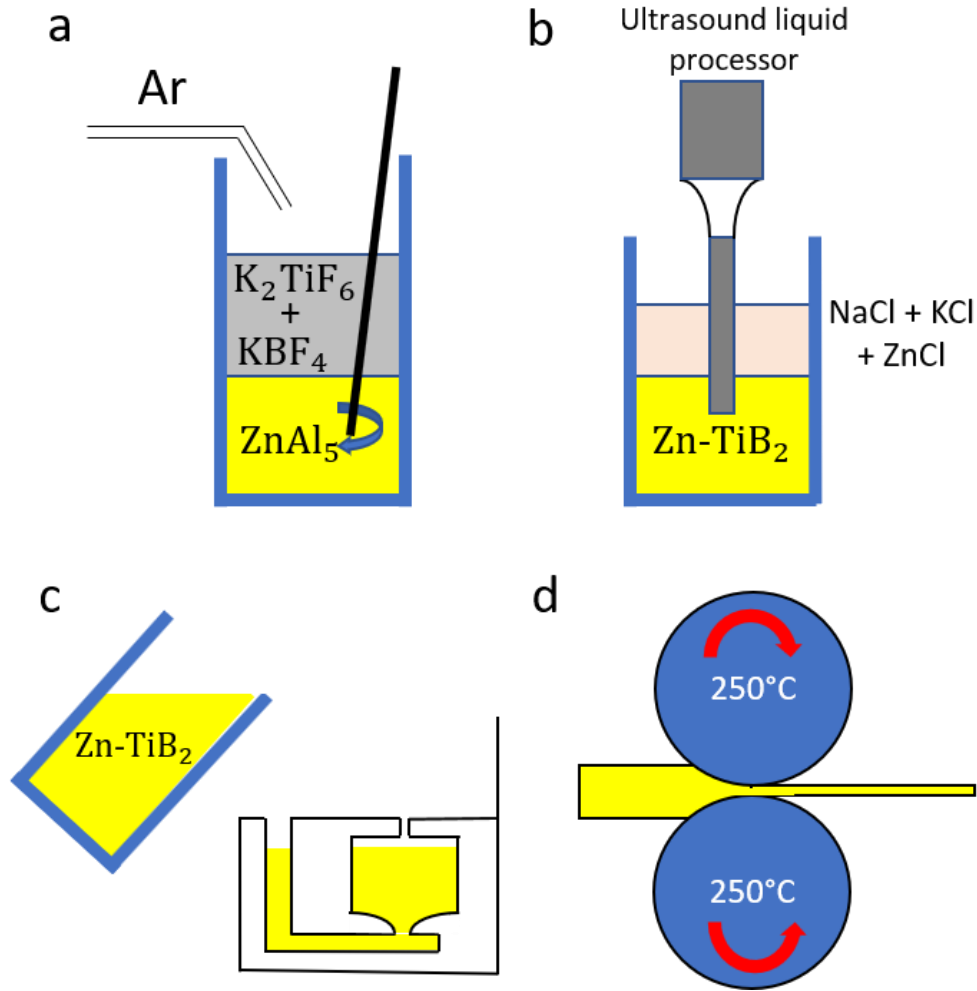


Figure 35: Schematics of Zn-TiB₂ fabrication procedure: (a) FAS for nanoparticle synthesis and incorporation, (b) molten salt assisted ultrasound processing for homogeneous nanoparticle dispersion, (c) casting in a steel mold, (d) hot rolling.

The high purity Zn and 3vol% Zn-TiB₂ nanocomposite samples, both hot rolled, were prepared by mechanical grinding, alumina nanoparticle polishing, and ion milling polishing for microstructure characterization using a scanning electron microscopy (ZEISS Supra 40VP SEM). The dispersion and size distribution of in situ TiB₂ nanoparticles was also investigated by SEM and energy-dispersive x-ray spectroscopy (EDS) analysis, with image processing through Image Pro. The microhardness test was performed covering the entire samples by LM 800AT microhardness tester using a load of 200gf with a 10 s dwell time. The tensile testing specimens

were fabricated by electrical discharge machining (EDM). The gage length and width of the tensile specimens were 10 mm and 4 mm, respectively (ASTM E8/E8M standard sub-size). Tensile tests were carried out using Instron ElectroPlus 1000 at a strain rate of 2 mm/min. 0.2% proof stress was used as yield strength.

3.3.2. Microstructures

Typical SEM images show that TiB_2 nanoparticles were synthesized and dispersed within the zinc matrix, owing to the assistance of the ultrasound processing and plastic deformation (e.g., hot rolling), shown in Figure 36(a). The aluminum residue was not observed through EDS map scanning. Darker phases represented the TiB_2 nanoparticles, and the brighter phases were the zinc matrix. Nanoparticle clusters of tens of micrometers were observed, which indicated pseudo-dispersion in local areas. However, nanoparticles were homogeneously dispersed within these pseudo clusters, without agglomeration and sintering, shown in magnified Figure 36(b). The corresponding Figure 36(e) and (f) were the EDS scanning intensity of Zn and Ti, in Figure 36(b). There were also areas of coarsely dispersed TiB_2 nanoparticles, shown in Figure 36(c).

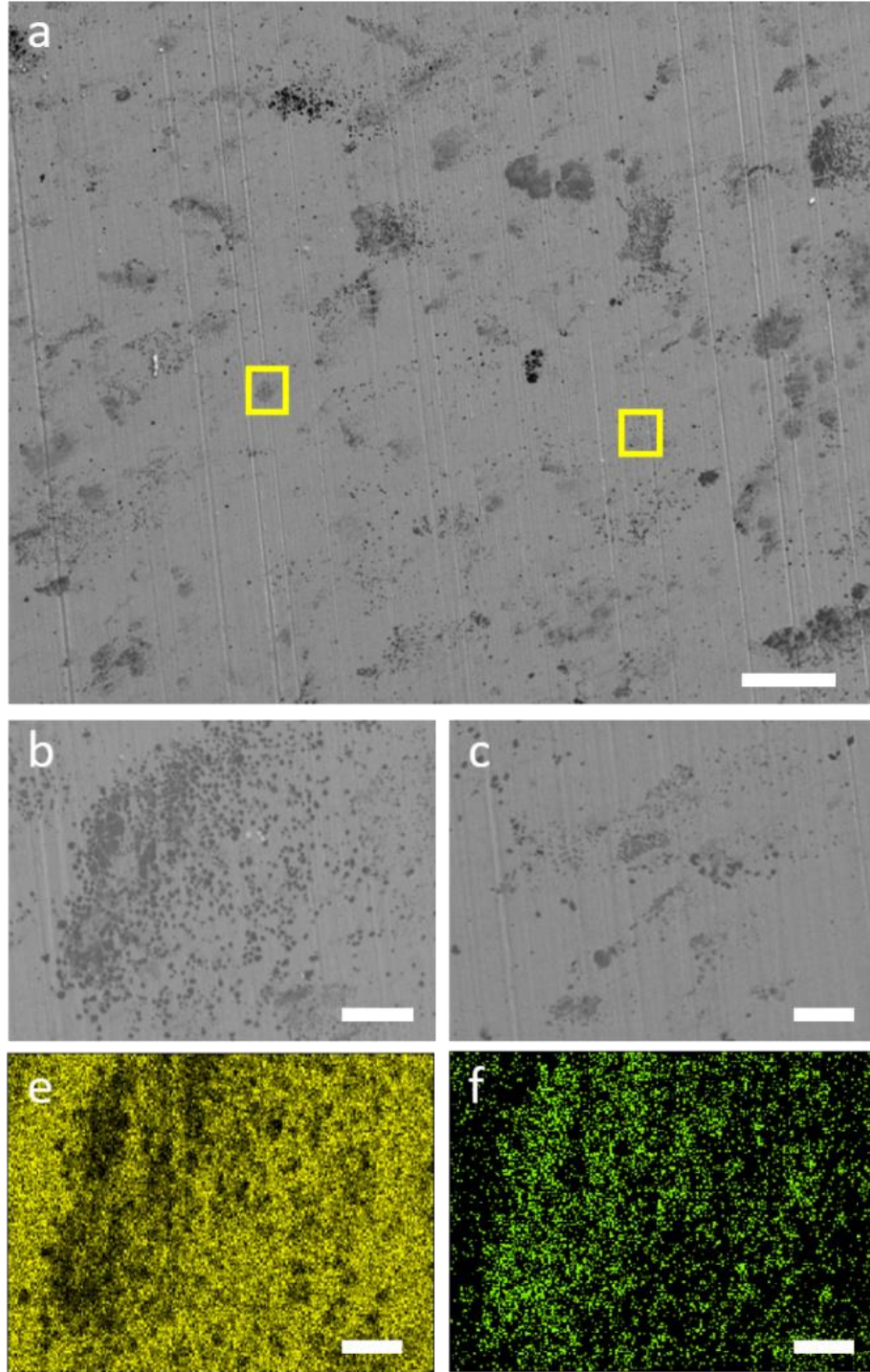


Figure 36: (a) Typical SEM images of Zn-3TiB₂ nanocomposite. (b) and (c) show the zoom-in SEM images at the local area, indicated in (a). Micrometer size pseudo-clusters containing many nanoparticles were observed. (e) and (f) correspond to the EDX scanning element intensity of Zn and Ti, respectively, shown in the local area (b). Scale bars indicate 20μm in (a) and 5μm in (b-f).

EDS point scanning was applied to distinguish further and confirm that TiB_2 nanoparticles were synthesized in the method abovementioned, shown in Figure 37. Point 1 indicated the darker phase area represented Ti elements, where Point 2 indicated the brighter phases represented the Zn matrix.

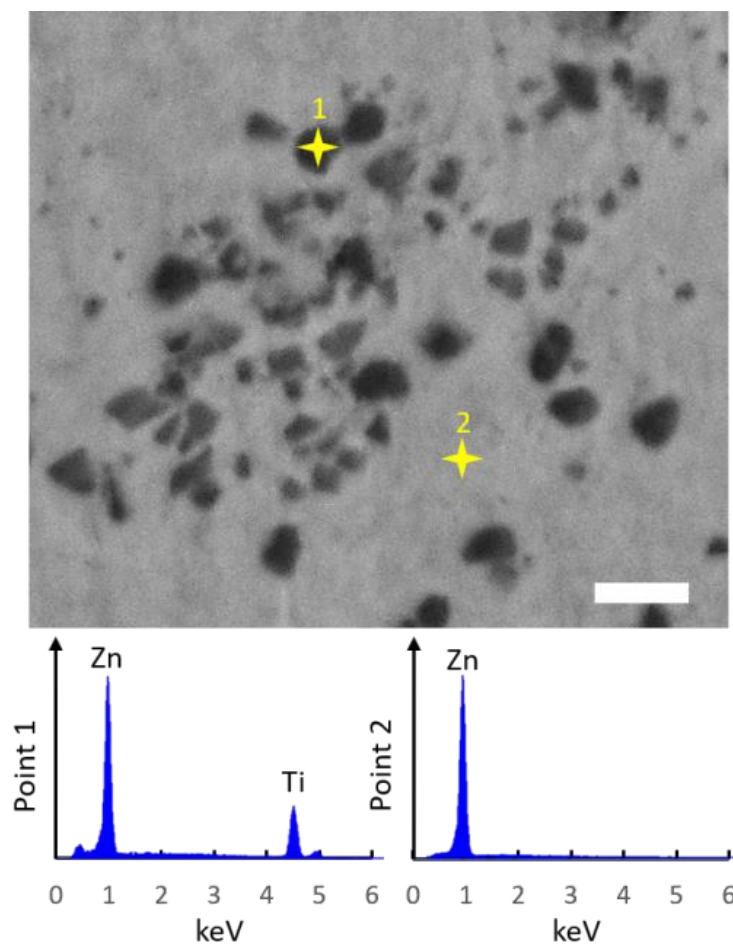


Figure 37: EDS point scanning on Zn-3TiB₂ samples to distinguish nanoparticles and matrix elements. The scale bar represents 1 μm .

A typical SEM image was captured for image processing of the nanoparticle size characterization (over 200 TiB_2 nanoparticles), shown in Figure 38(a). The corresponding histogram of TiB_2 nanoparticle size distribution was shown in Figure 38(b). The size of TiB_2 nanoparticles primarily falls in the range of 300-600 nm, with an average value of 454 ± 192 nm.

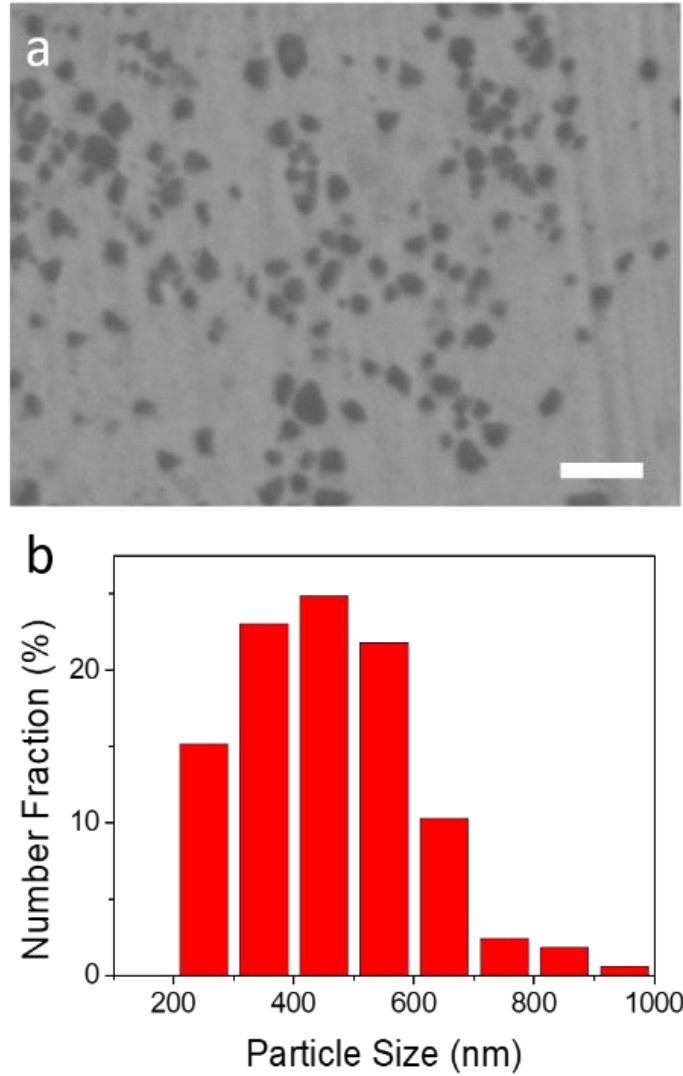


Figure 38: (a) SEM images of Zn-3TiB₂ under high magnification. (b) histogram of nanoparticle distribution after imaging processing. Scale bars indicate 1μm.

FAS has been used to produce TiB₂ nanoparticles in the Zn alloy matrix for strengthening, due to the good compatibility between the lattice distances of the hexagonal crystal structures of TiB₂ and η -Zn phases [220]. The dispersion was attributed to the good wettability between molten Zn and TiB₂ nanoparticles [221]. Following the similar manufacturing method, this work has performed with extra molten salt-assisted ultrasound processing to remove aluminum and disperse the nanoparticles. Further hot rolling was applied to further refine grains due to the dynamic recrystallization and the nanoparticle dispersion homogenization [222].

3.3.3. Mechanical properties

Vickers microhardness of HR Zn-3TiB₂ was compared with HR Zn, shown in Figure 39. This data indicated that 3 vol.% of TiB₂ nanoparticles have remarkably enhanced the hardness over 85%, from 34.4HV to 63.9HV. Compared with Al-TiB₂, in which 5 wt.% nanoparticles have only provided 10-20% hardness improvement [223], Zn-TiB₂ system has shown a significant efficiency on the improvement of hardness, indicating a fairly effective strengthening mechanism.

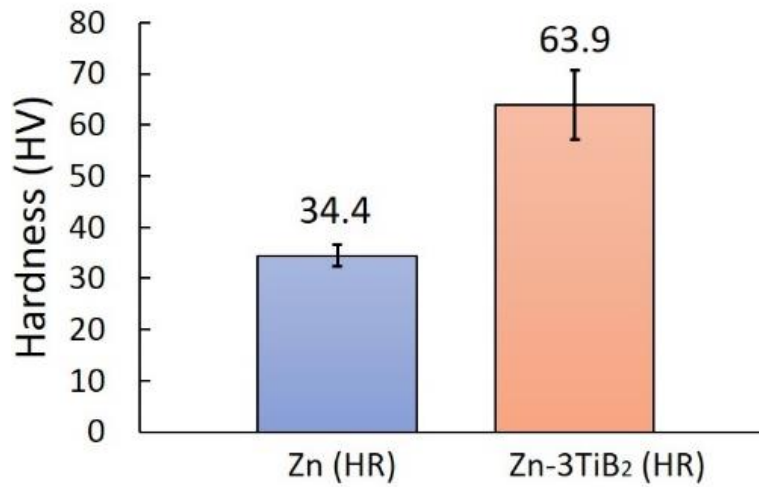


Figure 39: microhardness of Zn and Zn-3TiB₂ nanocomposite.

Mechanical behaviors of hot-rolled Zn-3vol.% TiB₂ and hot-rolled Zn have been further characterized by tensile testing, and the representative engineering stress-strain curves were shown in Figure 40(a). UT, YS, and elongation to failure have been modified from 98.9MPa to 143.8MPa, 36.6MPa to 70.2MPa, 71.9% to 22.8%, respectively. The results of the tensile properties are shown in Figure 40(b). Fracture surface SEM images of HR zinc and HR Zn-3TiB₂ were shown in Figure 40 (c) and (d), respectively. Arrows have indicated the dimples, which are the typical ductile fracture.

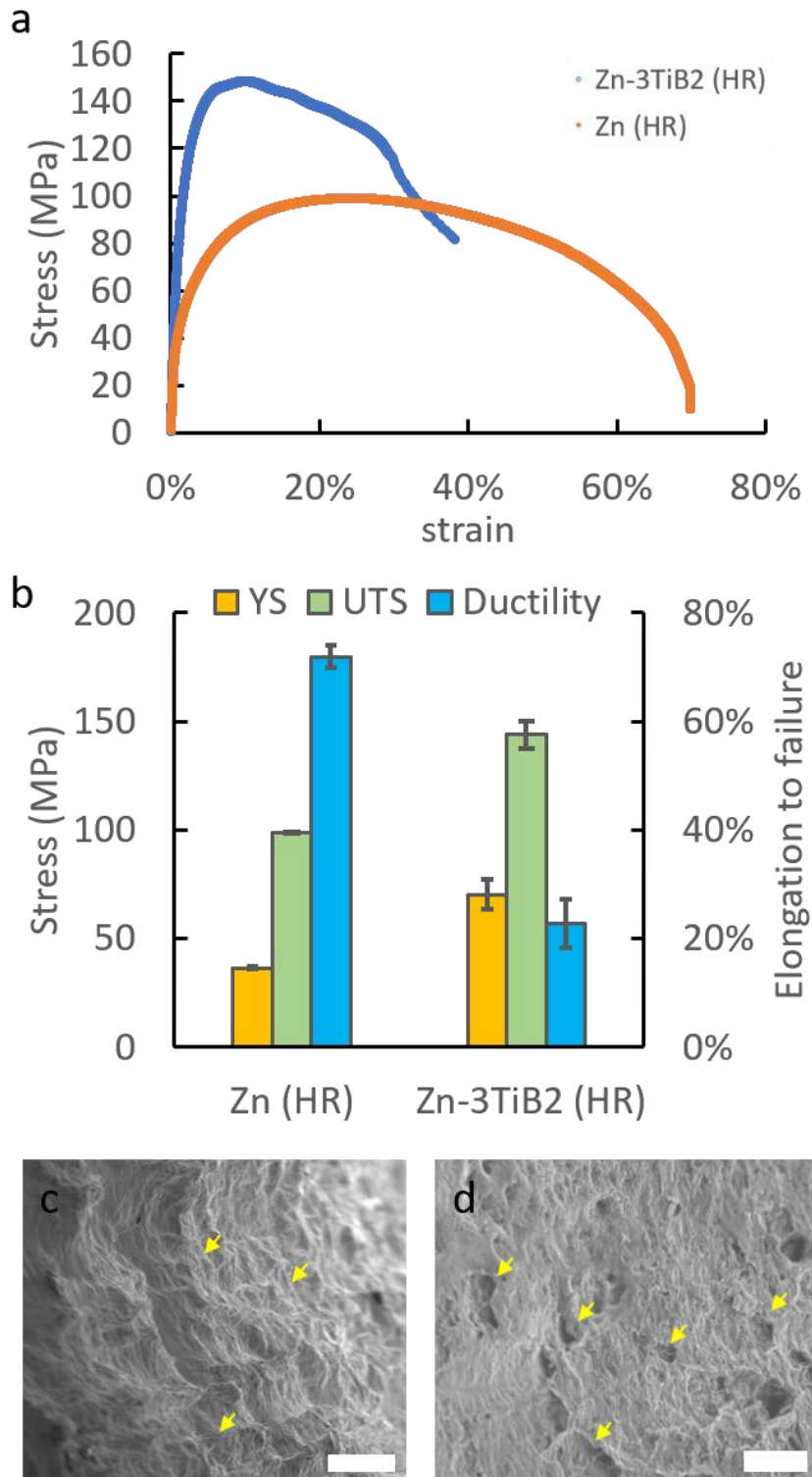


Figure 40: (a) Stress-strain curve of Zn and Zn-TiB₂. (b) Mechanical properties by the tensile test. Fracture surfaces of the tensile test specimen for Zn (c) and Zn-3TiB₂ (d). Ductile dimples are indicated by arrows. Scale bars indicate 20 μ m.

With 75% thickness reduction, Zn-3vol.% TiB₂ nanocomposites maintained a high elongation, further indicating the relatively good dispersion of nanoparticles with little particle agglomeration. Furthermore, the results showed a reasonable and comparable UTS where Zn-4.4vol.%WC nanocomposites offer 160 MPa in UTS. The combination of high strength and high ductility outperforms many zinc alloys and satisfies the standard requirement for biodegradable vascular stent applications [69].

Compared with Zn matrix nanocomposite fabricated by powder metallurgy, which could also achieve relatively good dispersion, this work has advantages for large-volume fabrication, and the standard size tensile bars were thus fabricated in the process. Tensile properties for standard specimen were never acquired for composite material produced in other research.

The strength enhancement is due to multiple, including Orowan strengthening, the grain boundary-induced Hall-Petch effect, and load-bearing.

$$\Delta\sigma_{Orowan} = \frac{\phi G b}{d_p} \left(\frac{6V_p}{\pi} \right)^{1/3} = \frac{2 \times 35 GPa \times 0.266 nm}{454 nm} \times \left(\frac{6 \times 0.03}{\pi} \right)^{1/3} = 15.7 MPa$$

where G_m , b , V_p , and d_p are the shear modulus of the matrix, the Burgers vector, the volume fraction, and the size of the nanoparticles, respectively. ϕ is constant.

$$\Delta\sigma_{HP} = k \cdot d^{-\frac{1}{2}} = 6.8 MPa \sqrt{mm} \times 0.05^{-\frac{1}{2}} = 30.4 MP$$

where d is the grain size and k is a constant. Although this work has not comprehensively tested the grain size of the nanocomposite samples, 50 μm grain size was estimated conservatively through other Zn nanocomposite works [132].

$$\Delta\sigma_{load} = 1.5 V_p \sigma_i$$

where σ_i is the interfacial bonding strength. TiB₂ normally has a high interfacial bonding strength with metals, especially aluminum, due to the good wettability [224]. However, such exact strength enhancement is unable to be calculated here.

Further optimization of nanoparticle concentration will be required for the specific applications as biomaterials. Although TiB₂ is commonly considered as a highly stable nanoparticle for high temperature, corrosive and reactive environments, its biocompatibility needs to be tested on whether human cells would have negative responses when in contact. Another important future work would be the *in vivo* characterization for Zn-TiB₂ nanocomposite on verifying whether nanoparticles would be successfully circulated and get out of the animal in time.

Chapter IV: Nanoparticle enabled microstructure control for zinc alloys

The previous chapter has investigated the dilemma where alloying alone cannot manage to balance the mechanical properties, corrosion behavior, and biocompatibility. It has also shown that 4.4 vol.% WC can increase the strength to more than 160 MPa in UTS. However, the strength was still lower than the bioresorbable stent criteria. Thus, this part of the study focuses on adding nanoparticle in Zn alloys along with a low concentration of alloying elements. The primary purpose of the nanoparticle is to influence the intermetallic morphologies in order to retain the excellent ductility of Zn. Secondly, nanoparticles act as microstructure stabilizing agents to avoid phase change at various temperatures. In this chapter, Zn-Mg-WC and Zn-Fe-WC systems were studied.

4.1. Zn-Mg-WC

4.1.1. Fabrication methods

A similar method regarding Zn-WC fabrication was applied for Zn-Mg-WC, shown in Figure 41. 3 vol.% of WC nanoparticles were incorporated into the metal melt. In the fabrication procedure of bioresorbable cardiovascular stent devices, bulk nanocomposite samples were cast in a steel mold, followed with plastic deformation for thin sheets fabrication. The metal sheet was cut to the designed shape using laser micromachining.

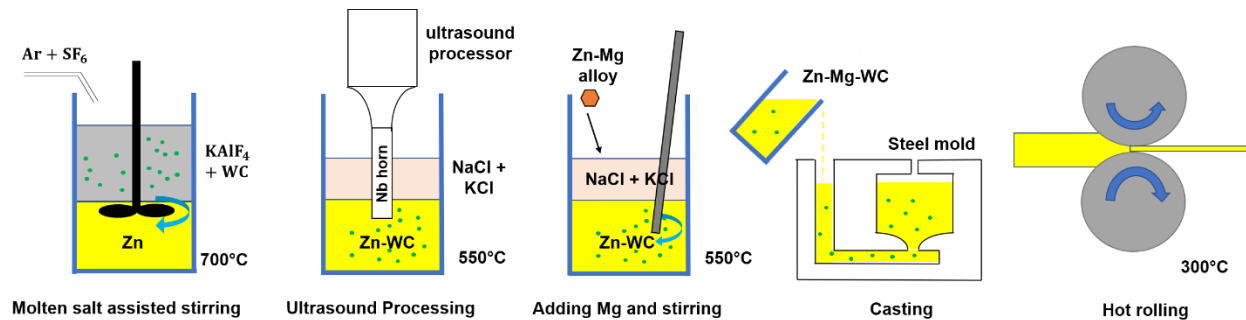


Figure 41: Fabrication procedure of Zn-Mg-WC

The fabrication procedure is as follows:

- Zn-WC incorporation - molten salt assisted stir casting: WC nanoparticles were mixed with KAlF_4 at a volume ration of 1:20, and then were added to metal melt with 60 minutes graphite blade stirring. The sample was cast into a steel mold, and the salt slurry was removed.
- Zn-WC homogenization - ultrasound process: Zn-WC was melted in the crucible with 15 minutes of ultrasound processing at a temperature of 600 °C. Niobium probe coated with BN as the ultrasonicator horn extender. 1:1 atomic ratio NaCl and KCl were used for surface oxidation protection.
- Zn-Mg-WC fabrication – adding Zn-Mg: premade Zn-Mg alloy (1:2 weight ratio) was added to the molten metal, and the nanocomposite sample was cast in a steel mold.
- Plastic deformation - orthogonal hot rolling: 3mm thick Zn alloy nanocomposite plate was hot-rolled at a temperature of 250 °C in orthogonal directions. The final thickness of the metal sheet was 250 μm . Nanoparticles are further dispersed homogeneously in the metal matrix.
- Stent fabrication - pattern design and laser cutting: stent pattern was designed in Solidworks and went through simulation for design optimization. A final design pattern was used in laser micromachining for production.
- Device finishing – ultrasound-assisted chemical etching and PLLA adhesive bonding: the laser cut samples went through chemical etching to polish the surface oxidation and reduce the toughness. PLLA adhesive was used to bond the produce to the final stent.

4.1.2. Microstructure characterization

The as-cast Zn-0.5Mg-WC was characterized under the SEM backscattering model the analysis of nanoparticle dispersion, shown in Figure 42. The brighter phases indicated the WC nanoparticles, and the grey phases indicated the Zn-Mg metal matrix. No severe agglomeration and sintering were observed from SEM images. The corresponding EDS scanning results were shown in Figure 43. The results further validated the WC nanoparticle dispersion. However, due to the low concentration of Mg, EDS cannot distinguish by showing an obvious peak.

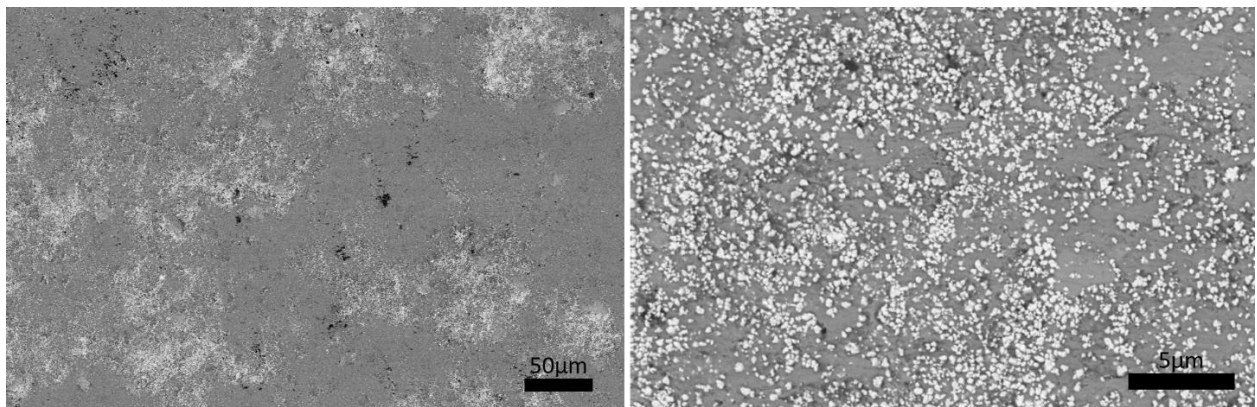


Figure 42: SEM images of Zn-0.5Mg-WC

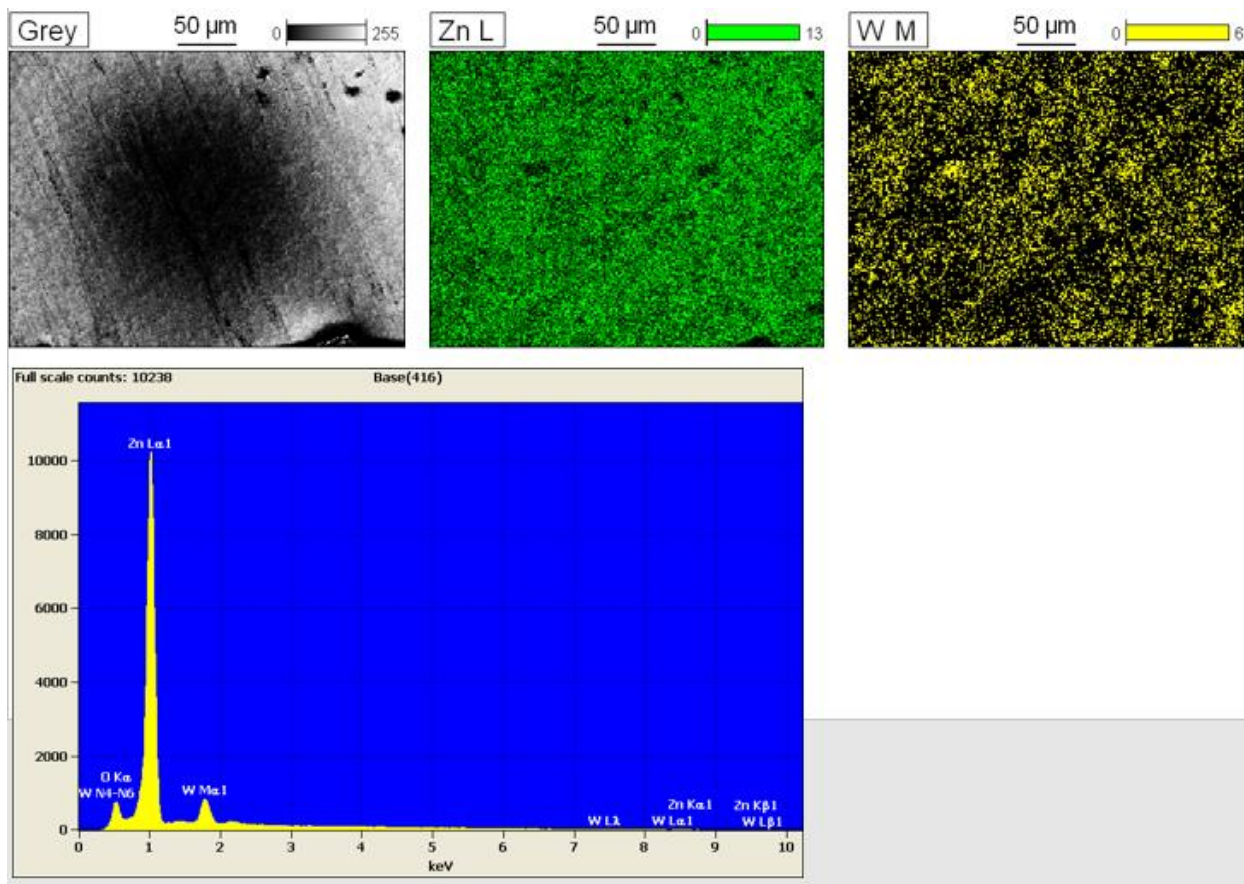


Figure 43: EDS scanning result of Zn-0.5Mg-WC

Due to the high diffraction intensity of WC nanoparticles, SEM with FIB was used to indicate the nanoparticle interaction with the intermetallic precipitation formation, shown in Figure 44. The sample surface was polished with ion milling, indicating sub-micron size grains with granular intermetallic phases.

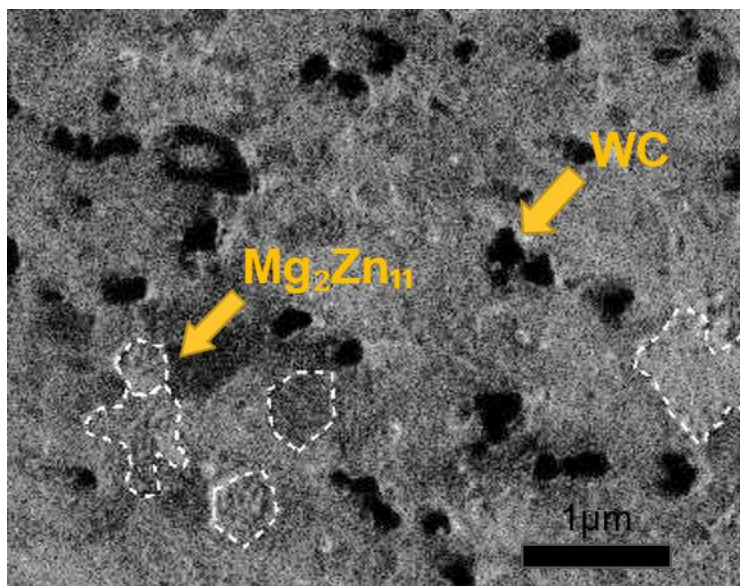


Figure 44: SEM image of Zn-0.5Mg-WC after ion milling in FIB

TEM samples were prepared for the characterization of the nanoparticle dispersion and the grain structure, shown in Figure 45. WC nanoparticles can be easily distinguished in the Zn matrix with a particle size of 100 - 300 nm. Most of the nanoparticles existed at grain boundaries, and nanosize grains were observed at nanoparticle adjacent zones.

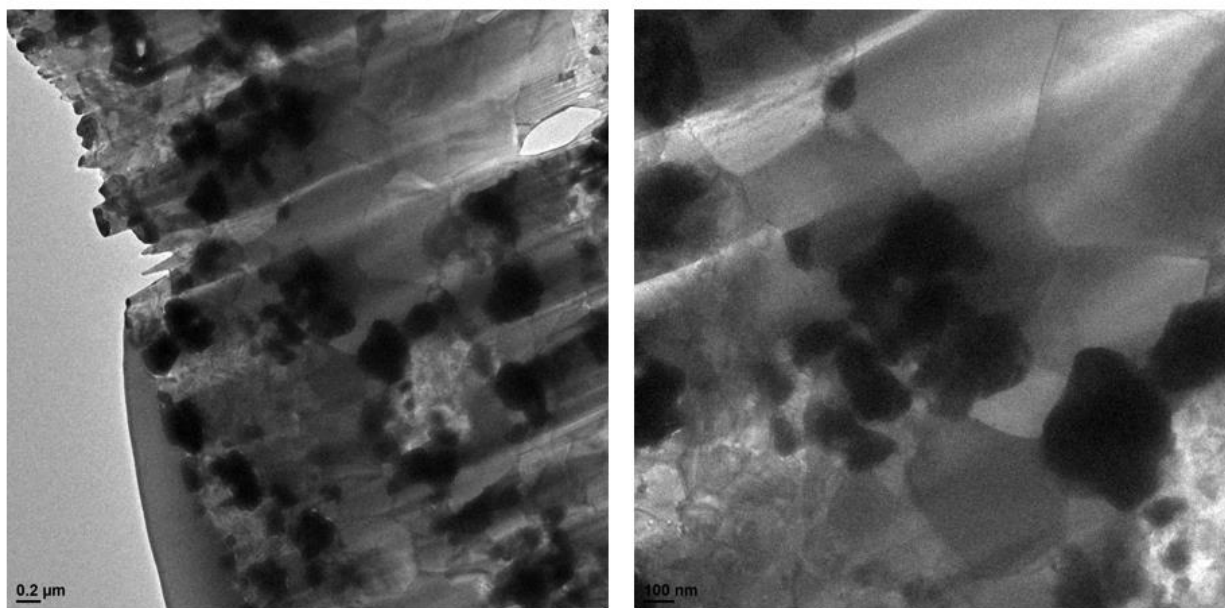


Figure 45: TEM images of Zn-0.5Mg-WC

Chemical composition analysis was done on Zn-0.5Mg-WC and Zn-0.5Mg, shown in Figure 46. Compared with Zn-0.5Mg, Zn-0.5Mg-WC has indicated additional peaks of WC. The diffraction peaks of WC from small angles to large angles represented (001), (100), and (101), respectively. Besides the reasonable intermetallic phase of Mg_2Zn_{11} , $MgZn_2$ phases were also observed in the XRD pattern. However, according to the Zn-Mg phases diagram and the related alloy research, $MgZn_2$ phases are uncommon in materials with less than 3 wt.%, shown in Figure 47 [225]. This unusual phenomenon can be understood as Mg segregation in the Zn-0.5Mg-WC sample. The existence of $MgZn_2$ phases indicated high Mg concentration at local zones, referring that WC nanoparticles interacted with the Mg element during the solidification process.

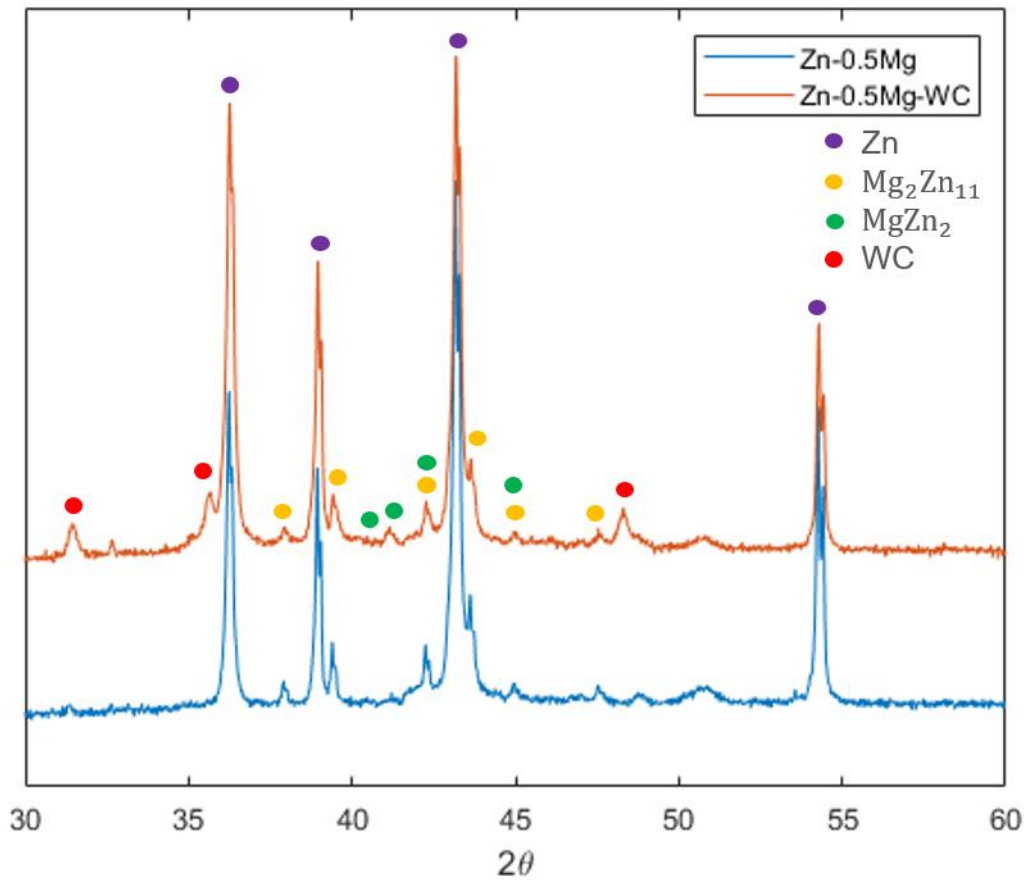


Figure 46: Chemical composition analysis by XRD for Zn-0.5Mg and Zn-0.5Mg-WC

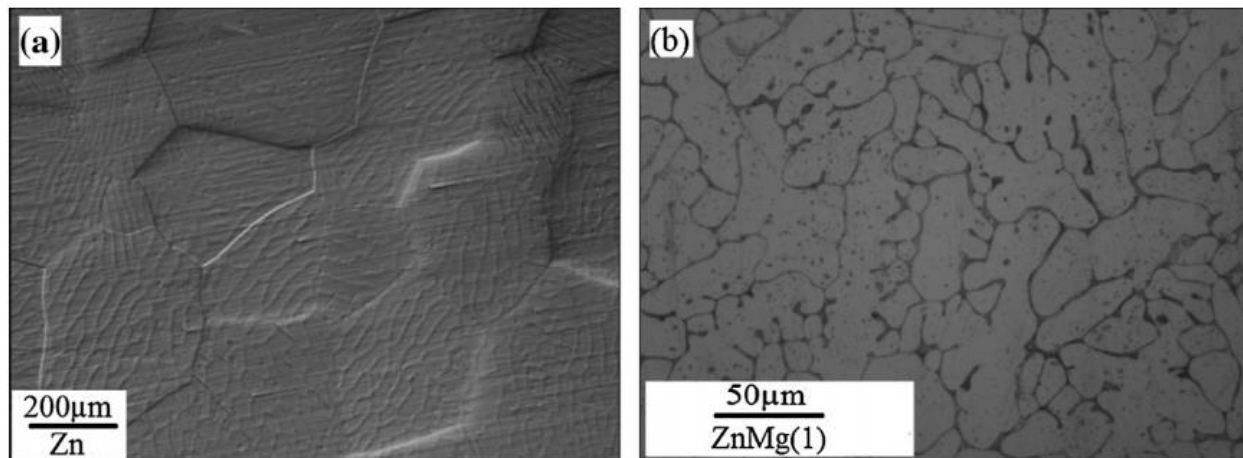


Figure 47: Micrographs of etched specimens with different Mg contents (0 wt.% and 1 wt.%).

DSC heat flow measurement was also conducted to understand the precipitate formation during the solidification, shown in Figure 48. A typical DSC cooling curve of crystalline alloys was observed. Solidification of HCP Zn rich phases occurred at 419 °C, and solidification of $\text{Mg}_2\text{Zn}_{11}$ was supposed to occur gradually in a temperature region, depending on the Mg concentration. However, Zn-0.5Mg-WC revealed a different heat flow curve, where an additional heat peak was observed about 50 °C lower than the major peak, corresponding to the solidification temperature of $\text{Mg}_2\text{Zn}_{11}$. It referred to rapid precipitate formation when nanoparticles existed, suggesting that the precipitate nucleation may be no longer initiated from grain boundaries, but other nucleation sites with higher free energies. It further proved the susceptible precipitation formation mechanism that nanoparticles could serve as the nucleation sites because of the high dislocation density and high energy in nanoparticle adjacent areas.

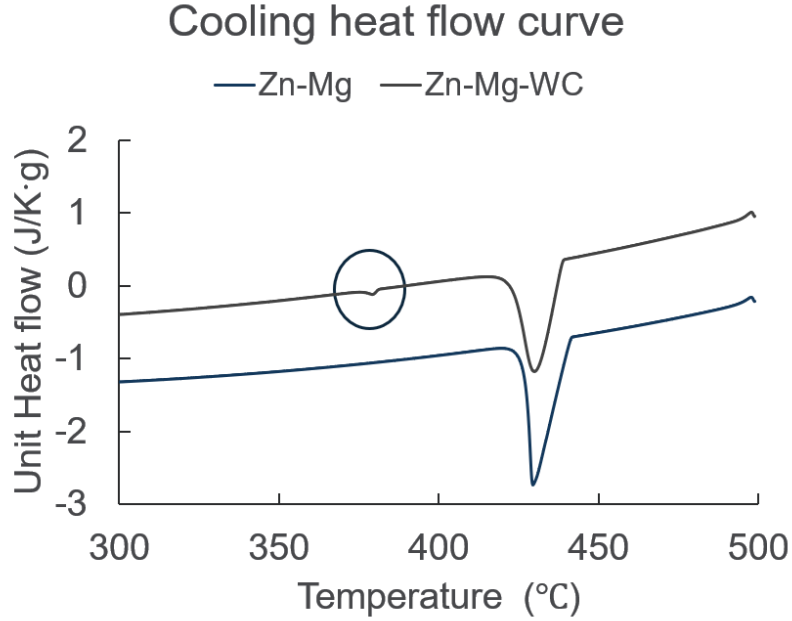


Figure 48: Heat flow curve during the cooling process of Zn-0.5Mg-WC and Zn-0.5Mg.

Pure Zn-0.5Mg typically has intermetallic precipitate forming at grain boundaries, and the intermetallic growth was relatively uniform, shown in Figure 49 [90]. Compared with pure metals, Zn-0.5Mg-WC showed a different microstructure with granular intermetallic morphology, shown in Figure 50. Brighter phases represented the $Zn_{11}Mg_2$ phases, which typically formed at the grain boundary in the process of precipitation. The darker background is that the Zn-rich phases contain Mg as solid solutions. The left image indicated the sample right after hot rolling. Intermetallic phases are granular with nanoparticles existed at the interfaces. The right image referred to the sample after 3-month immersion in a pure ethanol solution. Precipitation growth typically occurred at the nucleation site and propagated along the grain boundaries. However, WC nanoparticles were observed on the grain boundaries (WC nanoparticles on the bottom), and restrain the precipitate growth (in the direction from top to bottom).

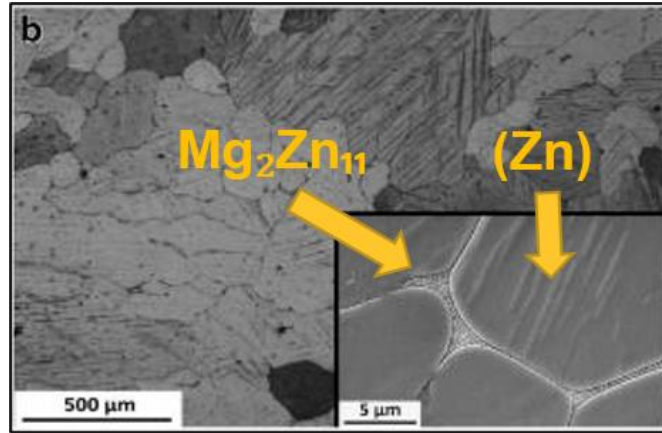


Figure 49: Microstructure of Zn-0.5Mg and the magnified image of the intermetallic precipitate.

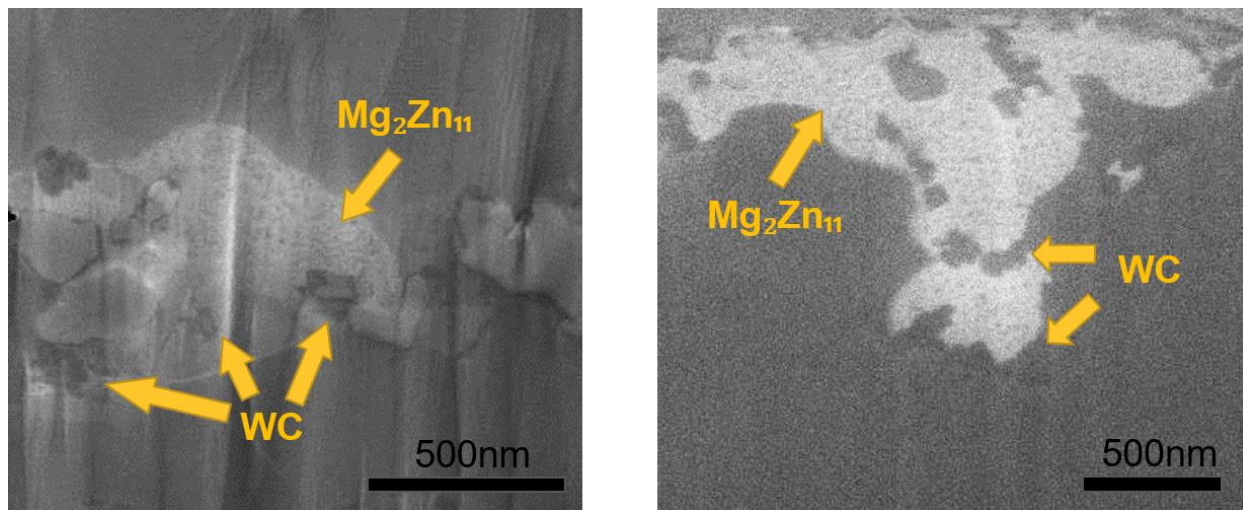


Figure 50: SEM of Zn-0.5Mg-WC under SEM with FIB cutting surface. The left image refers to the sample directly after hot rolling, and the right image refers to the sample preserved in ethanol for 3 months.

WC nanoparticles can be seen in the intermetallic phase and the interfaces. The intermetallic precipitates have granular morphology, instead of a net-worked shape in the grain boundaries. Due to the existence of nanoparticles, the precipitate morphology has been altered and modified. The corresponding intermetallic formation was proposed in the process shown in Figure 51. According to microstructure characterization and composition analysis by XRD and DSC, WC nanoparticles interact with the Zn matrix during the formation process, mainly in two aspects.

- Interaction with intermetallic nucleation. The microstructure of Zn-0.5Mg-WC has indicated that WC nanoparticles served as nucleation sites for intermetallic formation, instead of grain boundaries (demonstrated in “intermetallic nucleation”). Cooling heat flow results have also indicated that nanoparticles induced the Mg segregation during the solidification, which is likely to occur at nanoparticle interfaces, where high dislocation density induced high free energy. Furthermore, the morphology of the intermetallic is granular rather than net-worked. Granular intermetallics are generally more favorable for tensile properties than acicular intermetallics since the crack formation is easier to happen at the tip of the particles [226].
- Interaction with precipitate growth. Since this work has also applied the typical manufacturing method, “annealing- quenching- hot working” for Zn-0.5Mg-WC, age hardening properties would still occur under room temperature. However, the existence of WC nanoparticle on the grain boundaries effectively restrained the precipitate growth. In the process of precipitation growth, Mg elements would segregate to nanoparticle adjacent areas instead of the grain boundaries. Instead of growing along the grain boundaries, $\text{Mg}_2\text{Zn}_{11}$ precipitates grew isotropically with nanoparticle restrain at the growth front (demonstrated in “precipitate growth”). The phenomenon could also enhance the thermal stability, while the precipitate growth will not initiate the loss of ductility due to the formation of net-worked intermetallic phases.

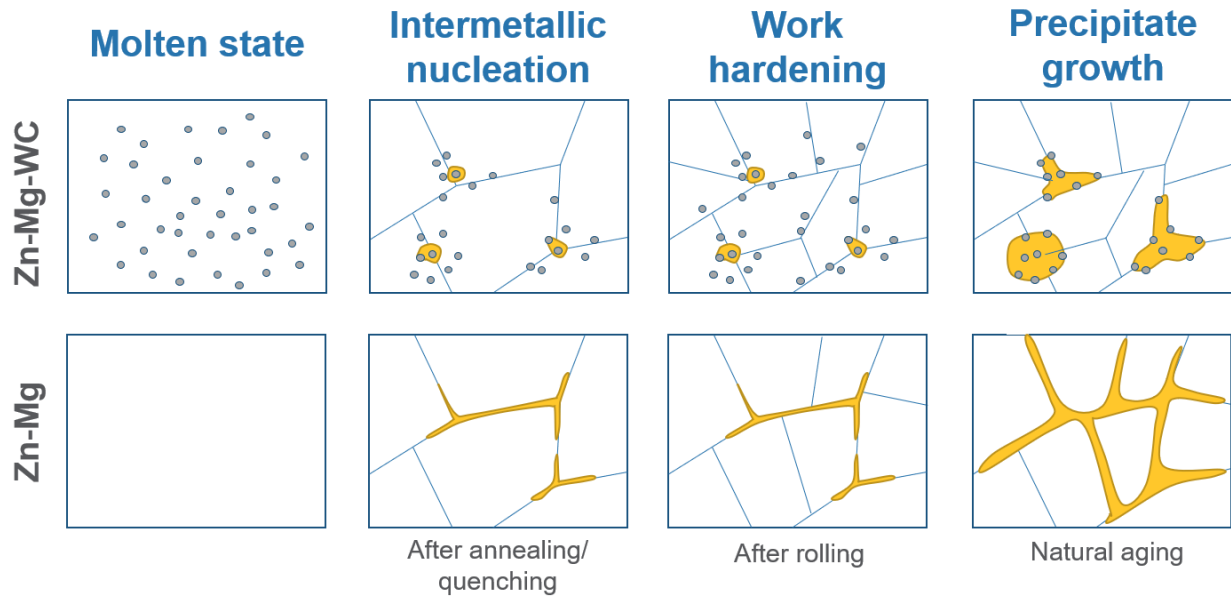


Figure 51: Proposed precipitate formation process of Zn-Mg-WC and Zn-Mg

4.1.3. Mechanical properties

The microhardness has been tested on both Zn-0.5Mg and Zn-0.5Mg-WC, shown in Figure 52. WC nanoparticle incorporation has limitedly improved the material hardness to 85 HV. Compared with nanoparticle strengthening effects in pure metals, e.g., Zn-WC and Cu-WC, the Zn alloys system did not show a significant improvement [132, 145].

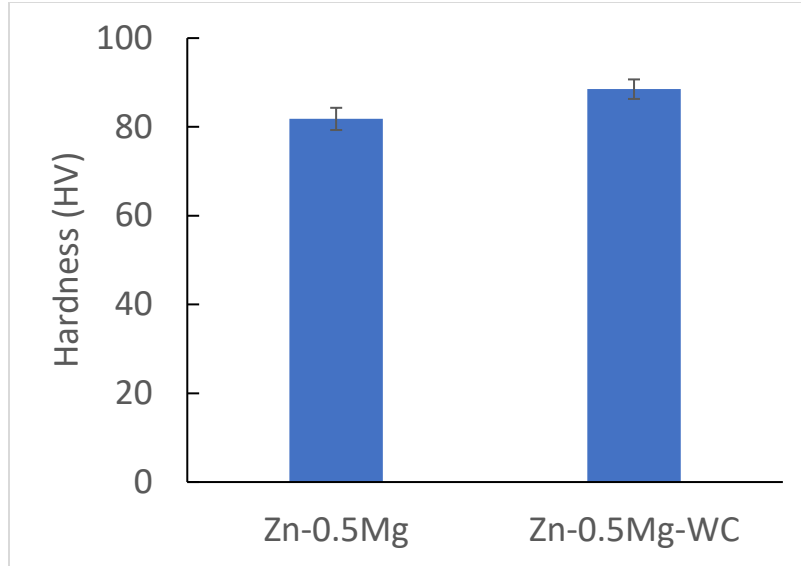


Figure 52: Vickers hardness of as-rolled Zn-0.5Mg and Zn-0.5Mg-WC

The tensile test specimens were fabricated by wire-EDM, according to stand ASTM E8 subsize type, shown in Figure 53.



Figure 53: Tensile and fatigue test specimen

The corresponding tensile properties, including UTS and elongation, were shown in Figure 54. Compared with pure Zn-Mg samples, which were obtained from literature, Zn-Mg-WC has shown different mechanical properties. Three distinguished sections can be observed:

- When Mg is less than 0.2 wt.%, nanocomposite has a slightly increased UTS with no ductility compensation. Due to the low concentration of Mg, most Mg elements existed as a solid solution in Zn, so that the effect of precipitation strengthening is not significant.

Furthermore, according to our previous study on pure Zn matrix nanocomposite, the elongation will not decrease once the WC nanoparticle dispersion is homogeneous.

- When Mg is between 0.2 to 0.6 wt.%, the UTS of nanocomposite is retained at a similar level with the pure alloys. In this region, the elongation enhancement is attributed to the intermetallic morphology altered by nanoparticles. Because the morphology of $Mg_{21}Zn_{11}$ intermetallics has been modified from networked to granular, the nanocomposites generally obtained better ductility. Furthermore, the nanoparticle Orowan strengthening effect was not obvious in this region, since the intermetallic dominate the strengthening effects.
- When Mg is larger than 0.6 wt.%, the elongation enhancement was not significant. Because the intermetallic volume fraction is higher than 20%, nanoparticles may be unable to overall control the intermetallic formation and precipitation. Thus, there may have intermetallic growth on grain boundaries.

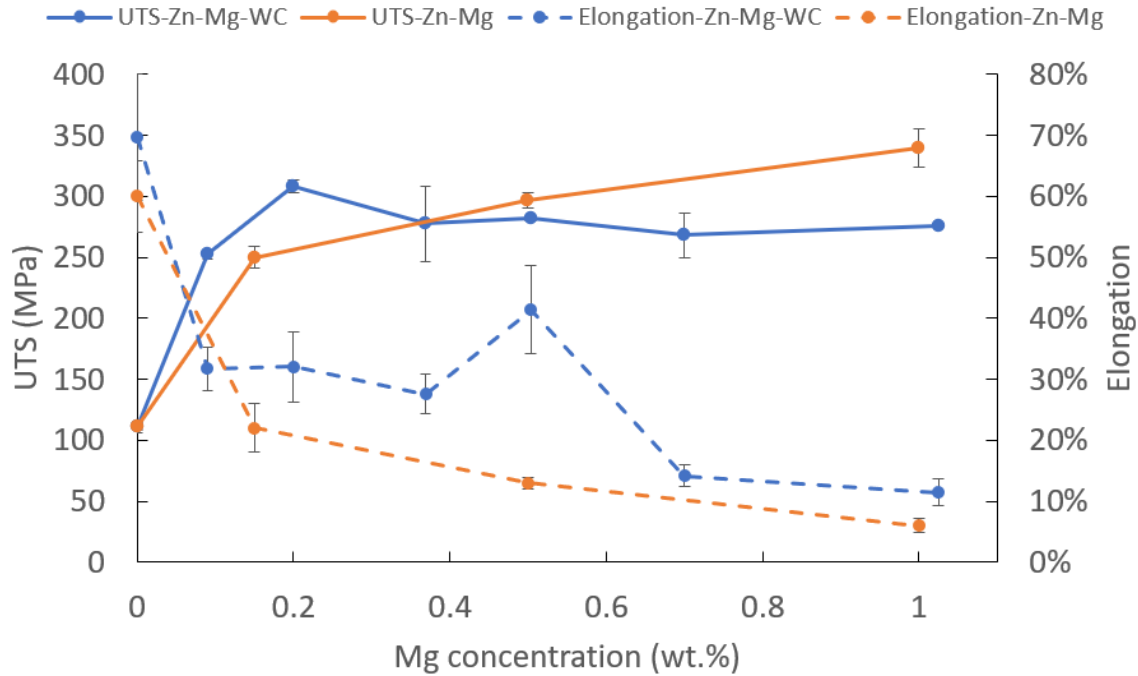


Figure 54: Tensile properties of Zn-Mg-WC nanocomposite, concerning the Mg concentrations

The fatigue property of the material is critical because the bioresorbable stents experienced a periodic contraction due to the heartbeat and blood pumping. The fatigue test was performed by Instron ElectroPuls E1000, and the testing specimen was subsize tensile bar with 500 μm in thickness. The fatigue result of Zn, Zn-0.5Mg, and Zn-0.5Mg-WC are presented in Figure 55. Stress was applied in a sinusoidal wave with a frequency of 60 Hz. The mean stress was determined based on the material tensile property, corresponding to 80%, 100%, 150%, and 200% of the yield stress. The results indicated that, with WC nanoparticle, the fatigue resistance of Zn-0.5Mg-WC improved significantly, where the specimen endure a 150% mean yield stress for more than 3,000,000 cycles.

It has already been reported that metal matrix composite obtained a particular fatigue behavior, where the reinforcement particles/fibers can initiate the crack at the particle-matrix interface and shield the crack tip from the applied stress and reduce the rate of crack growth [227]. The fatigue

resistance enhancement was also observed in the Al-SiC metal matrix composite system, which argued that SiC particulates improved fatigue resistance by acting as barriers to cracks and deflecting the growth plane of cracks, resulting in a decreased crack propagation rate [228]. A similar phenomenon was observed for the Zn-0.5Mg-WC specimen. The fracture surfaces of the fatigue samples were characterized by SEM, shown in Figure 56. Compared with Zn-0.5Mg, the nanocomposite sample has more dimples on the fracture surfaces. WC nanoparticles were also observed on the surface where the crack propagation occurred. It has suggested that the nanoparticles shield the crack propagation and decreased the propagation rate.

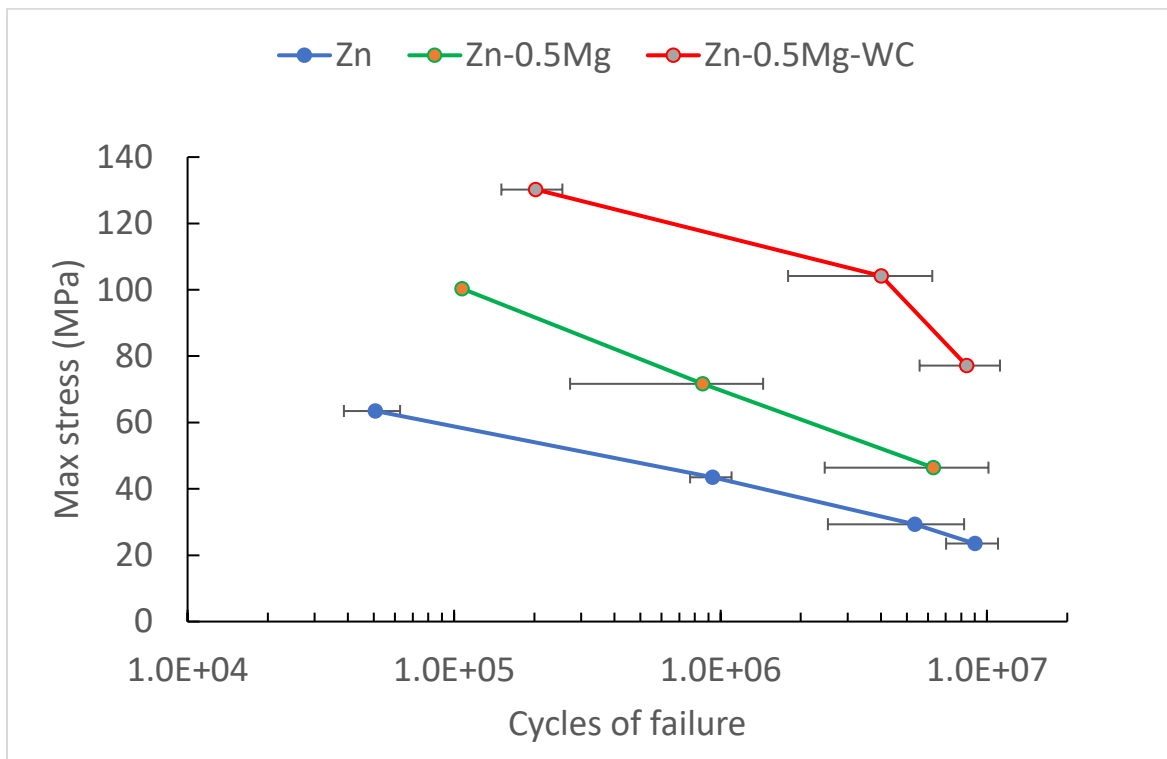


Figure 55: S-N figure of fatigue testing result for Zn, Zn-0.5Mg, and Zn-0.5Mg-WC

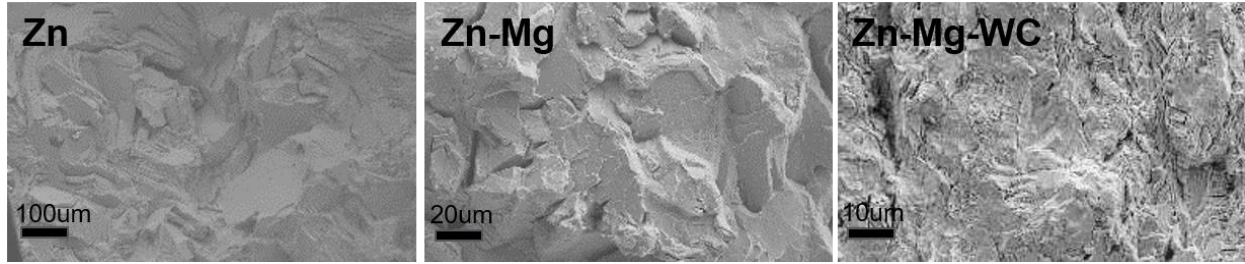


Figure 56: Fatigue fracture surfaces examined by SEM

4.1.4. Thermal stability and anti-aging effect

Immersion tests under 37 °C were carried out on the Zn-0.5Mg-WC tensile bar specimen for 3 months. Compared with the reported hot-extruded Zn-0.08Mg, which inherently obtained a natural age-hardening effect, Zn-0.5Mg-WC obtained the thermal stability and maintained stable mechanical properties during the 3-month study, shown in Figure 57. Its ultimate tensile strength was in the region of 250-280 MPa, and the elongation was 24-30%.

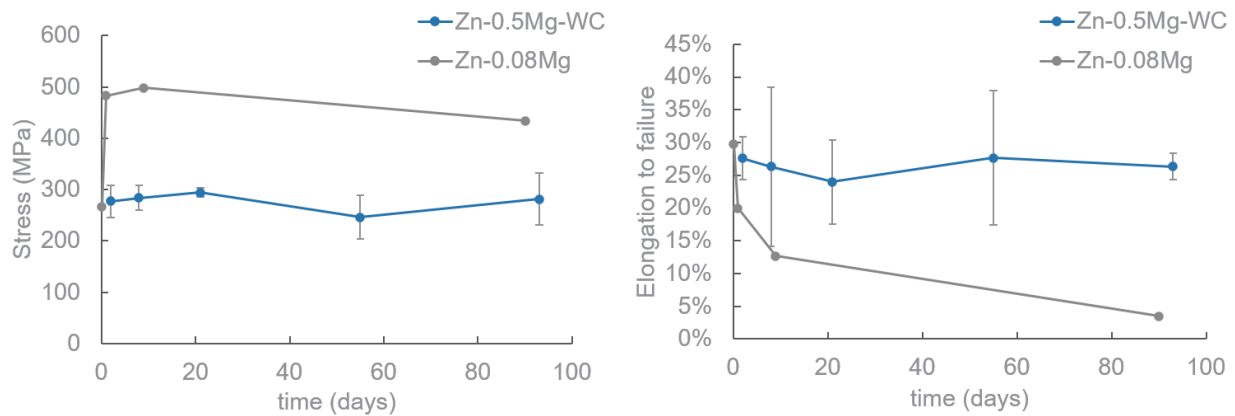


Figure 57: Stress and elongation changes regarding immersion time. Zn-0.5Mg-WC samples were immersed in silicon oil of 37 °C. Zn-0.08Mg data was acquired from [6].

This study only introduced the temperature effect to the specimen without corrosion effects. The Scifactoring group has already demonstrated the high-temperature stability for Cu and Al alloys [143, 145]. The corresponding anti-aging effect could be attributed to the microstructure

modification, and the isotropic precipitate growth as WC nanoparticles interact with the microstructure.

4.1.5. Corrosion resistance

The corrosion rate has not yet been finished in this work, but the proposed study has been demonstrated here.

Electrochemical testing was performed to investigate the corrosion resistance. Briefly, a three-electrode cell in a potentiostat/galvanostat/EIS (VersaSTAT 4, Princeton Applied Research) will be used to quantify corrosion resistance by studying the breakdown potential of stent prototypes, and levels of zinc and tungsten ions will be quantified by ICP-OES or ICP-MS. To correlate the results from the above experiments with the microstructure, SEM and EDS analysis will be performed, and surface morphology and microstructures post-testing will be compared with pre-testing images. This data will identify the relationship between grain size and nanoparticle content with the measured corrosion rates and fatigue life. Furthermore, corrosion is a dynamic process, and the corrosion rate is influenced by multiple factors, including environmental conditions and surface morphology, which both change as the corrosion process progresses. Therefore, long-term in vitro immersion tests in SBF will be conducted to understand corrosion behavior during degradation. Briefly, prototypes will be stored for up to two years, and supernatant will be collected monthly to measure released ions by ICP-OES or ICP-MS. At the 3, 6, 12, and 24- month time points, some of the samples (if still intact) will be weighed to measure mass loss. Changes in corrosion potential, rate, and resistance vs. time will be measured. By studying corrosion kinetics over the course of degradation, better theoretical predictions about the lifetime of the resulting stents can be made. The target degradation rate is 0.01 - 0.02 mm/year [67, 69].

4.1.6. Corrosion fatigue behavior

Corrosion fatigue testing on the Zn alloy nanocomposite was conducted (ElectroPuls E1000, Instron). The characterization is still in progress. The samples were immersed in SBF while undergoing tensile testing at 60 Hz frequency under various strains. The number of cycles to failure (fatigue life) was recorded, and the maximum stresses were calculated. BRS is expected to survive at least 10 million cycles before complete dissolution [67]. The rate of zinc and tungsten dissolution during tensile testing will be quantified with either ICP-OES or ICP-MS, and reported as the amount of metal released divided by the sample's surface area. However, for a more accurate study on the simulated environment, low frequency has to be applied since the periodic vessel contraction is at a much slower frequency.

4.1.7. Stent pattern design and fabrication

After successfully understanding the material properties and fabricating the materials, this work continued to develop the device fabrication. Due to the lack of an appropriate hot extrusion machine, thin metal sheets was used as raw material for laser cutting. The specific pattern was designed optimized with simulation using Solidworks. Laser cutting was performed on 200 μm thin Zn-Mg-WC metal sheets, and the device was fabricated by rolling the samples and applying adhesive for connection.

In the first iteration, a single cell stent with 6 crowns was finalized for laser cutting, shown in Figure 58. The corresponding material stress-strain curve was obtained from tensile testing in the early experiments. The crown structure was design to avoid high stress concentrated location to avoid fracture. The strut is designed to have a cross-section of 250 μm x 300 μm . Due to the lack of experience in laser micromachining, the sample was sent to professional companies for cutting.

The resolution of the design is set to be around 25 μm for relatively high-quality laser cutting. The corresponding 2D design and the actual parts were shown in Figure 59.

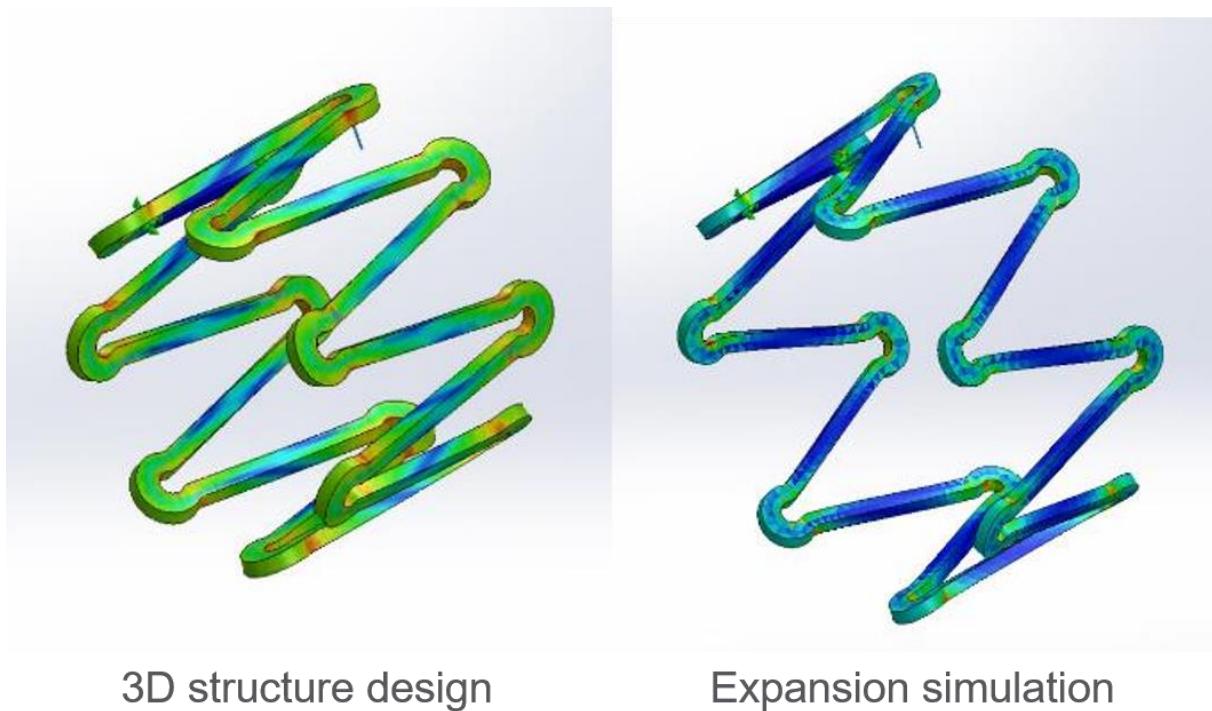


Figure 58: The first iteration of single-cell stent design

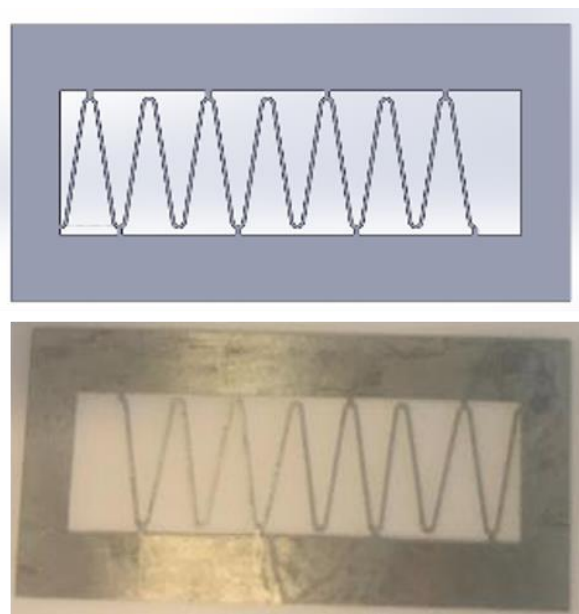


Figure 59: Laser cut V1 of single-cell design

After the fabrication, an angioplasty test (stent deployment) was performed on 8 mm balloon and 12 mm balloon, shown in Figure 60 and Figure 61. The very first iteration also aimed at testing the laser cutting capability and resolutions. The stent deployment was successful, especially with the 12 mm balloon, enabling a less than 5% recoil after the deployment. The expanded stent has a relatively uniform expansion, but still, require plenty of improvement.



Figure 60: Expanded V1 stent

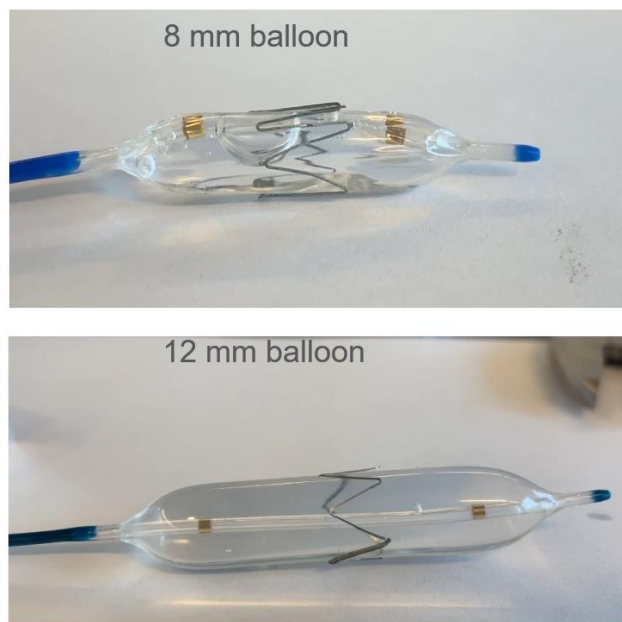


Figure 61: V1 stent angioplasty test on 8 mm balloon and 12 mm balloon.

The second iteration of the stent design was much closer to the real application, by demonstrating a close-cell, multi-cell design, shown in Figure 62. Although the simulation showed that the maximum local stress did not exceed ultimate tensile stress, some stents broke when using a 12 mm balloon, indicating structure failure, shown in Figure 63 and Figure 64.

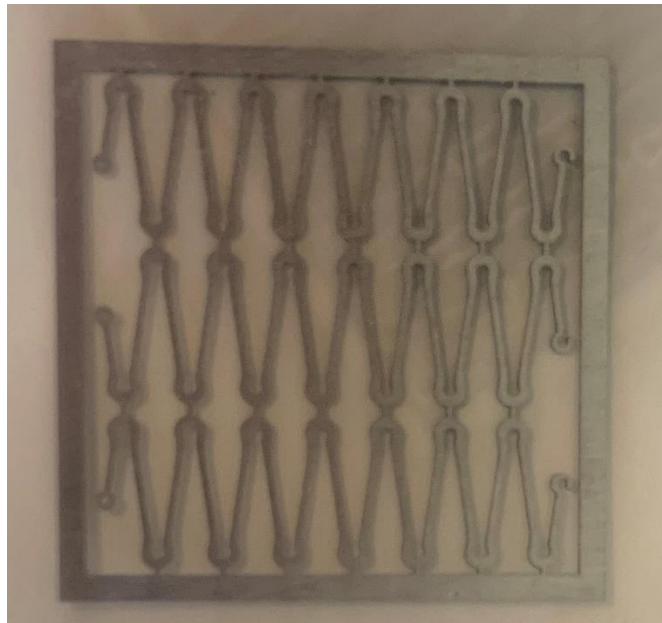


Figure 62: Stent V2 design and laser cut sample

This iteration was successful to some extent, with steady expansion observed. Furthermore, the close-cell design is successful. However, the problems were as followed:

- The stent samples were easy to break, partially due to the structure design and partially due to the surface roughness. More structure simulations are required to optimize the detail design, especially at the tip of the crowns.
- The adhesive used for this application is not strong enough. A better solution for connection is required in the next version.
- Stent recoil problems will need to be addressed in the next version.

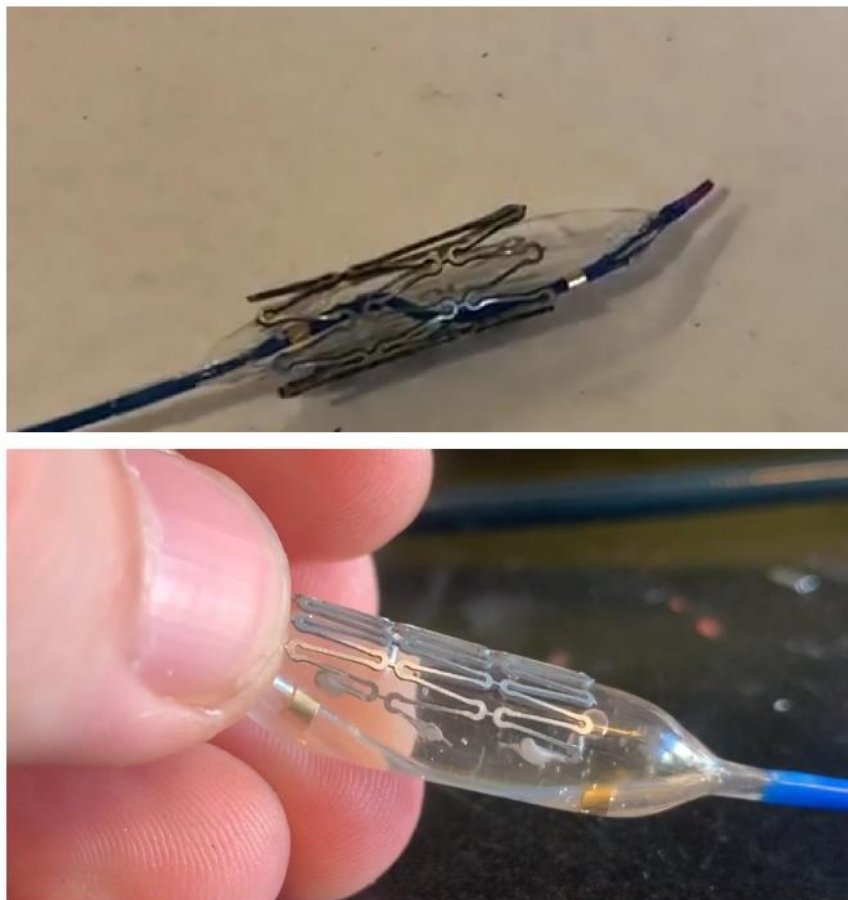


Figure 63: Angioplasty test for V2 stent



Figure 64: Successfully deployed stent using 8 mm balloon

The specific design has been analyzed by Solidworks simulation, and the weak points have been found on specific locations, shown in Figure 65. Blue arrows indicated the highest stress concentrated areas during the expansion. Furthermore, the device fracture location was analyzed, and optimization was carried out to solve the problems, shown in Figure 66. The green arrow represented the size reduction in the straight part, where the stress is the smallest. The yellow arrow referred to the strengthening of the expanded curvature, where the largest deformation occurred. The red arrow indicated the buffering of the tip of the crown, which could induce minimal recoil after expansion. The 3D CAD model on Solidworks has also been verified with simulation to analyze the functionality after deployment.

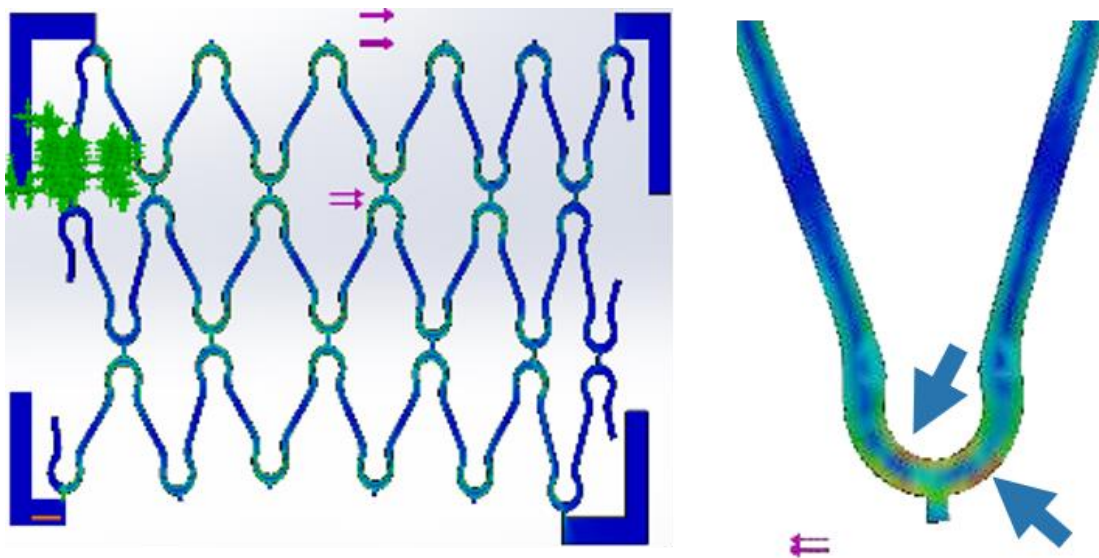


Figure 65: Second iteration design and analysis

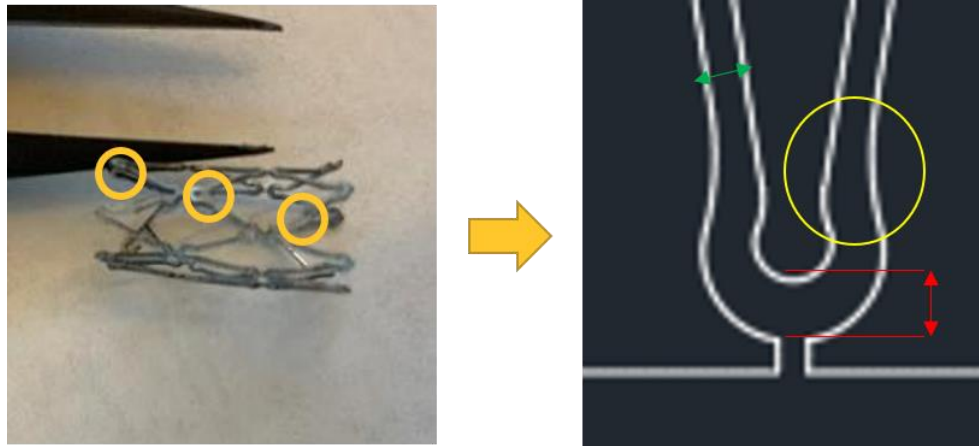


Figure 66: Fracture analysis and design optimization

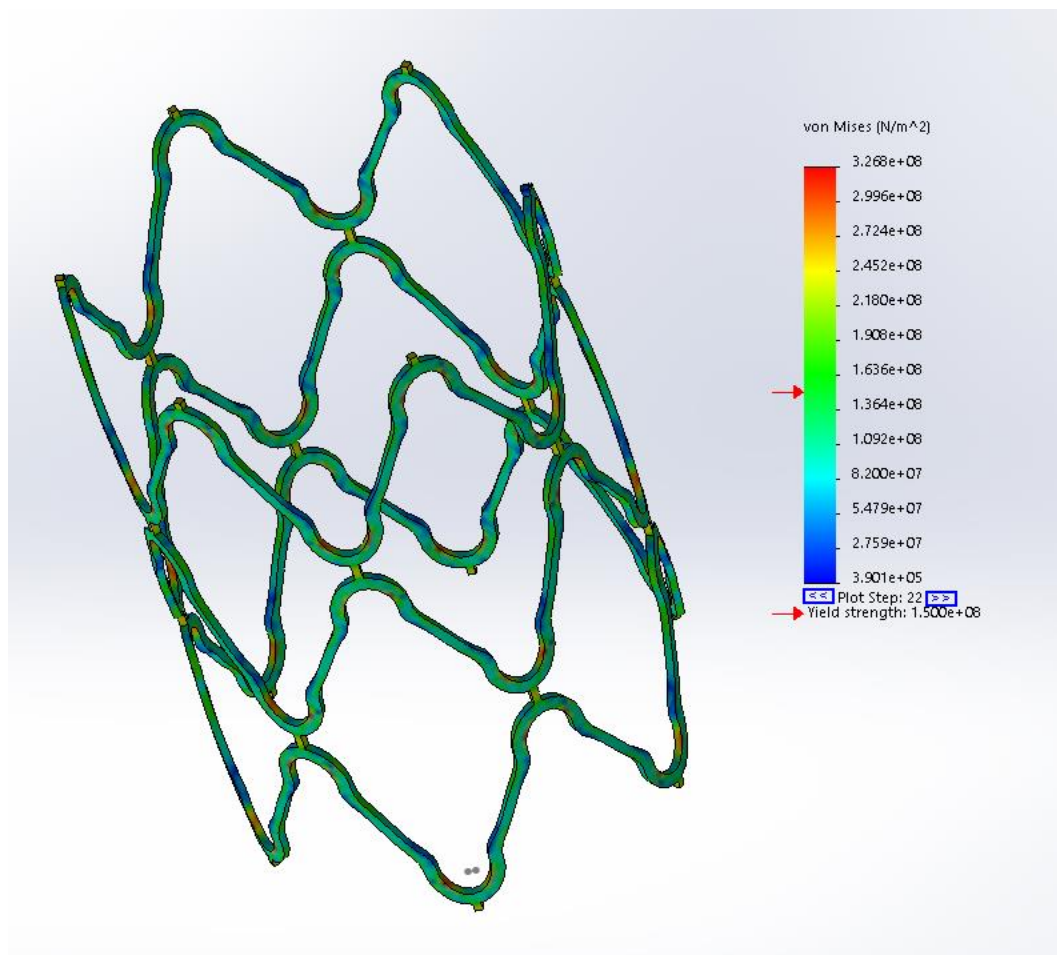


Figure 67: CAD 3D design after expansion simulation

Due to the limitation of Solidworks simulation, a complete expansion could not be performed by simulation. Still, it could insightfully provide suggestions for design optimization and improvement.

Then version 3 was finalized, and the samples were laser cut, as shown in Figure 68 and Figure 69. Although the design has initially added small hooks for the locking mechanism, they did not work well due to the feature resolution. Thus, the specific feature was removed from the laser cut sample. The laser-cut sample was rolled around a steel rod of 3 mm in diameter to form the surface curvature manually, and the supporting structure was removed. In this version, adhesive again was applied for connection, shown in Figure 70.

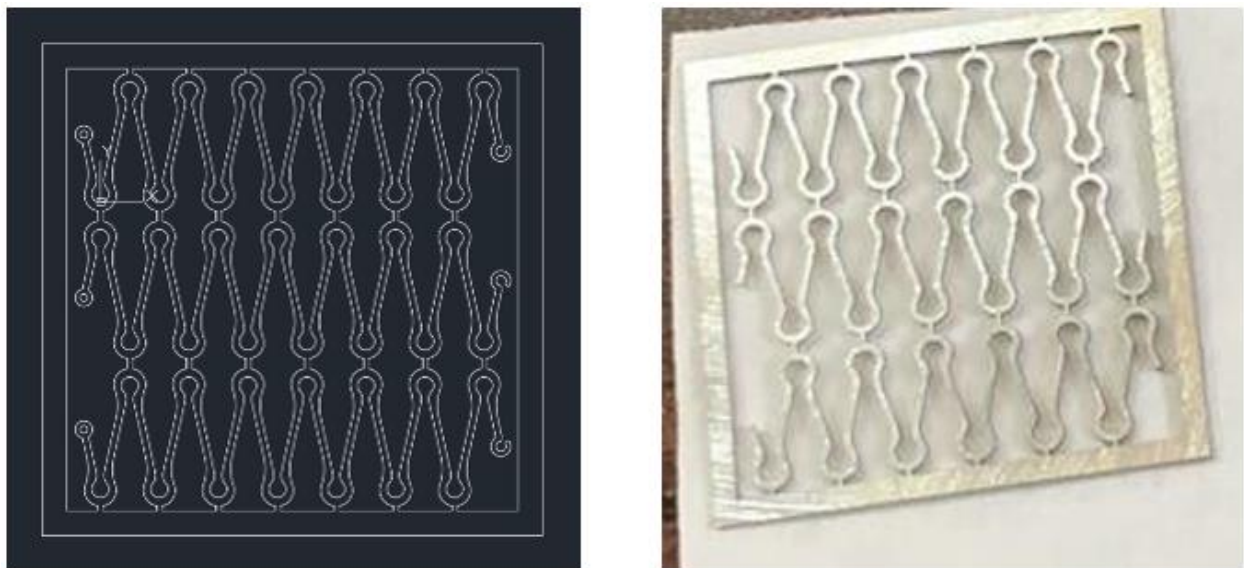


Figure 68: Stent V3 design and laser cut sample

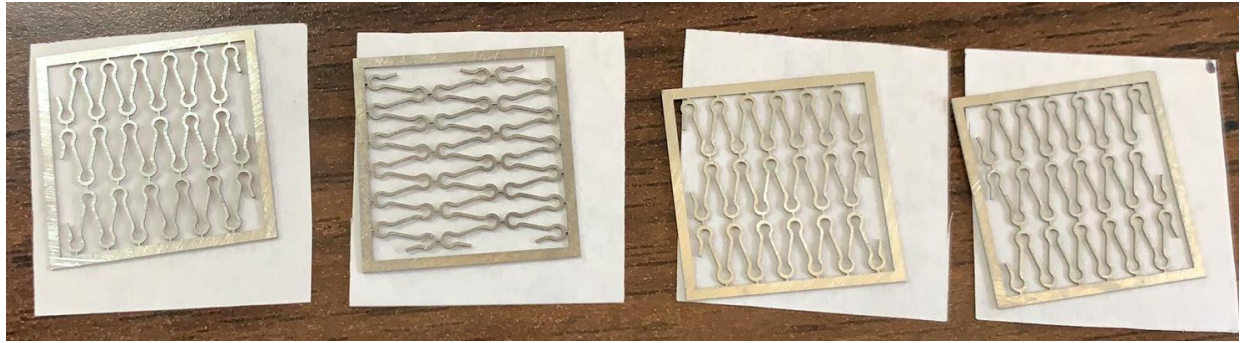


Figure 69: Stent V3 laser cut sample

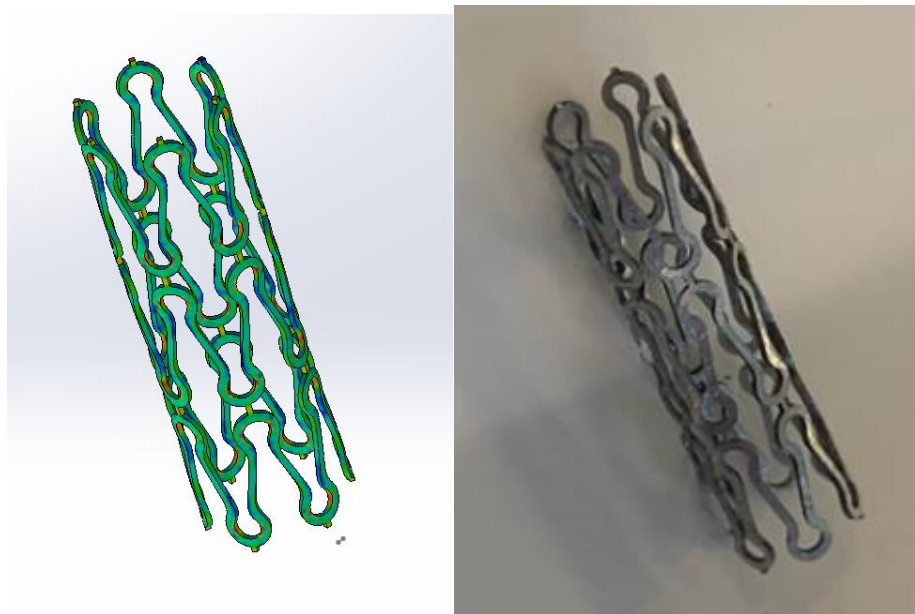


Figure 70: Version 3: Solidwork 3D design and stent prototype

Also, the surface cutting analysis was performed to characterize the surface roughness and the cutting quality under the microscope, shown in Figure 71. Due to the cutting limitation of the laser focus, the cutting surface has shown a smooth section and rough section. Because of the high pattern resolution required, the cutting thickness was decreased, and such rough surfaces were the result out-of-focus laser region.

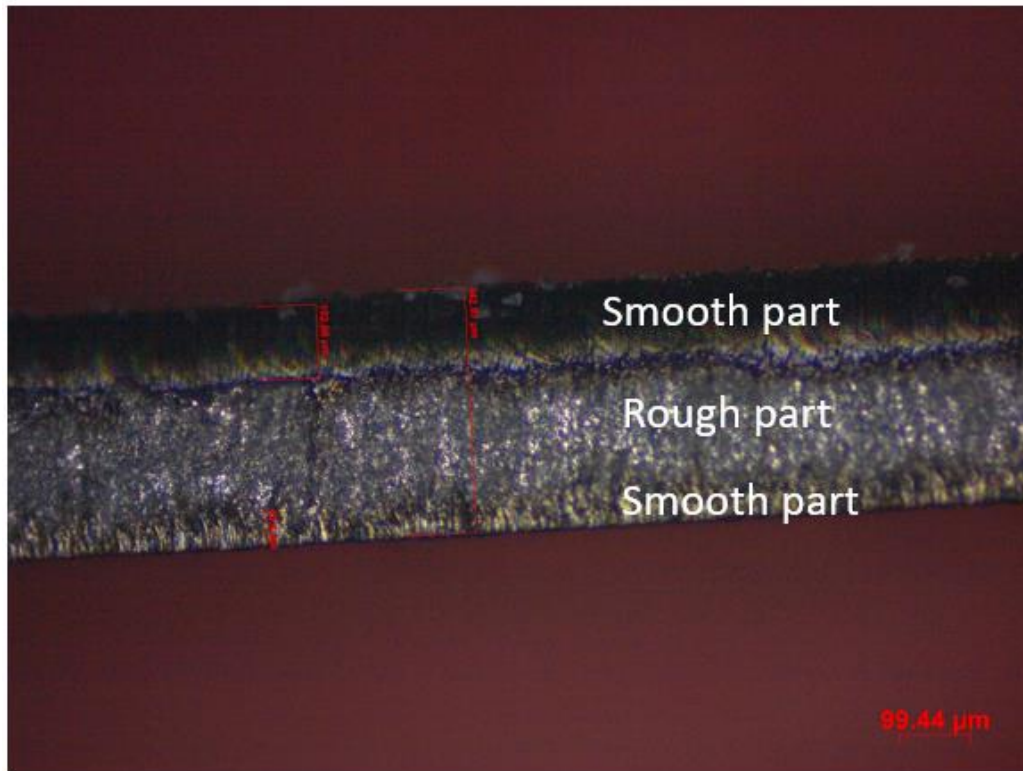


Figure 71: Laser cutting surface roughness

However, by further characterization through SEM, such laser cutting surfaces are acceptable, while no large cracks were observed, shown in Figure 72.

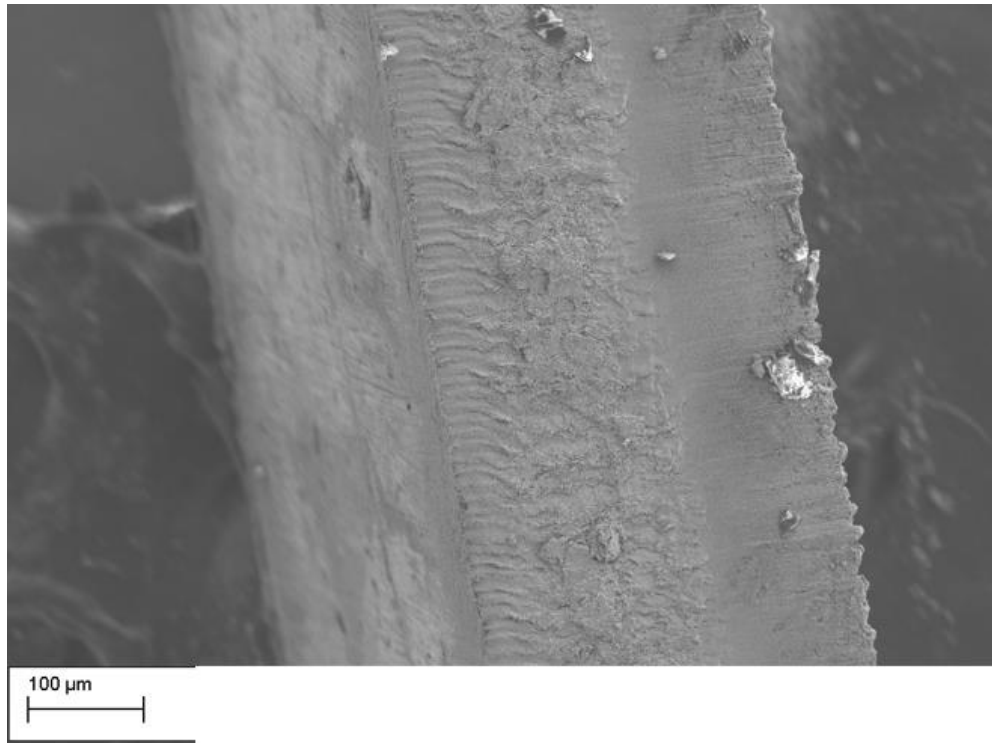


Figure 72: Laser cutting surface characterized by SEM

However, Zn redeposition was found on the surface, shown in Figure 73. Such a thin deposition layer may not affect the property of the material but still required verification in the expansion simulation.

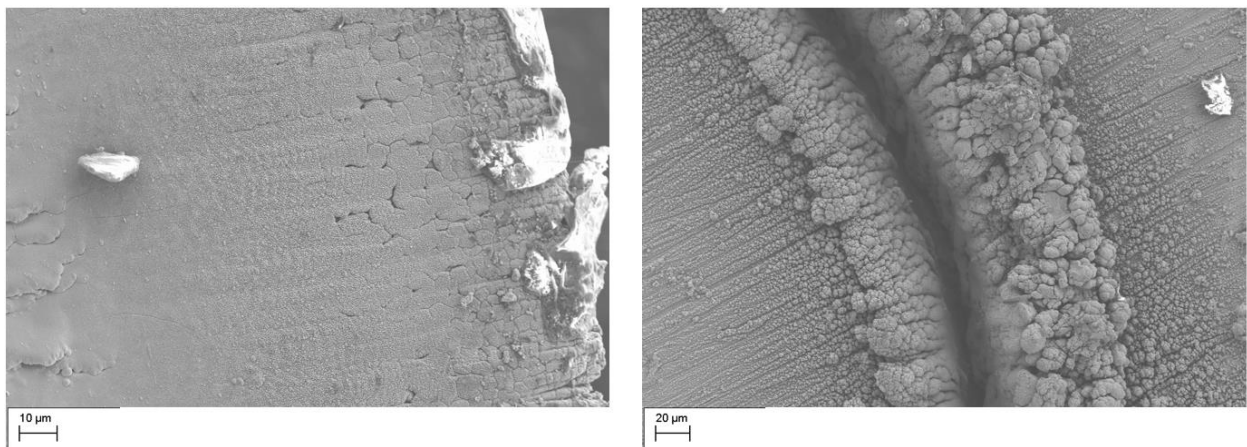


Figure 73: Laser cutting with Zn redeposition on surfaces

In the angioplasty test, the stent was cramped to shrink the size and tightly attached to the balloon, shown in Figure 74. In the actual surgical procedure, the stent will need to go through a sheath and vessel with not resistance for precision implantation. The stent is required to go through the sheath in-and-out smoothly. As measured, the shrunk stent has an outer diameter of 3.4 mm and a length of 1.8 cm.



Figure 74: Version 3 stent tightly attached on the ballon

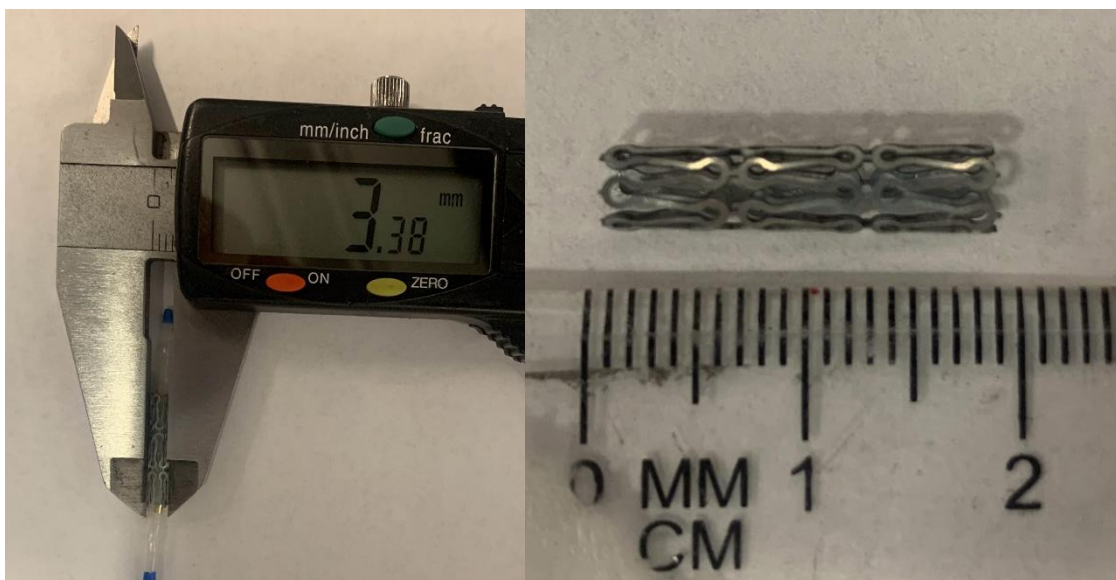


Figure 75: Shrunken stent dimension measurement

Figure 76 indicated the expanded stent by a 10 mm balloon. The stent expanded uniformly to reach a final outer diameter of 10 mm. No strut failure was observed, and recoil is less than 5%. Multiple stents have passed the angioplasty test, shown in Figure 77.

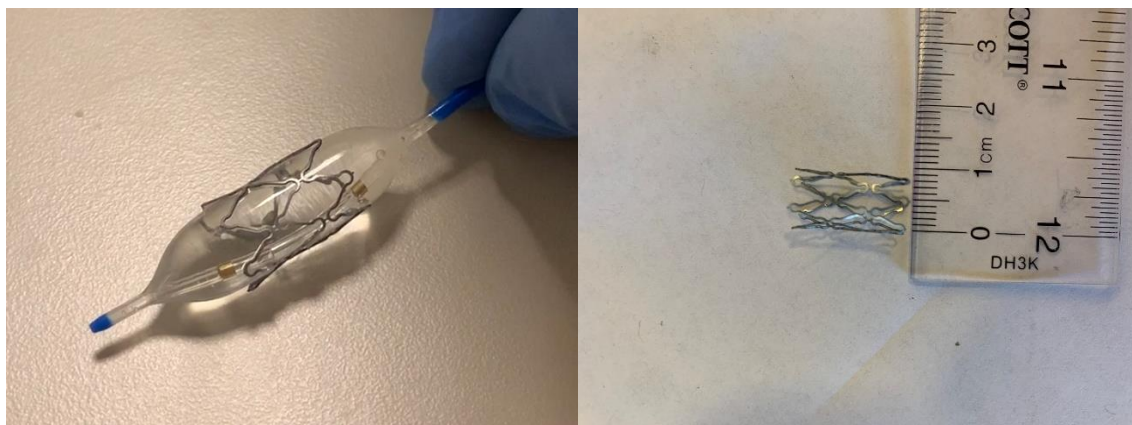


Figure 76: Stent V3 expanded by 10 mm balloon

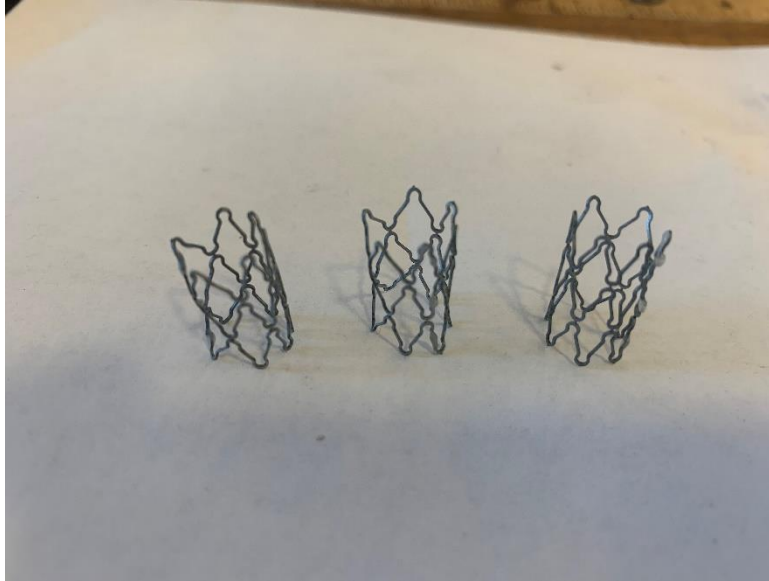


Figure 77: 3 stents showed highly uniform expansion after deployment

Overall, version 3 has performed excellently in deployment simulation outside the human body. Based on this design, a few more improvements will need to be addressed in the future before the *in vivo* implantation. The further improvement includes:

- Reduce the strut size to less than 200 μm . Thinner strut size would apply for various vessel sizes, especially usefully for pediatric patients.
- Substitute biocompatible adhesive with a mechanical locking mechanism. There is no commercial product obtaining high sticking force and biocompatibility so that a locking mechanism would be necessary for later applications.

4.2. Zn-Fe-WC

On the aspect of Zn-based alloy biodegradable material, a grand challenge came out to be the ductility loss due to the introduction of highly brittle intermetallic phases. Alloying is commonly used to strengthen materials, and Zn alloys have been studied to obtain a combination of desired mechanical and biological properties for applications as degradable implant materials [72]. Alloying elements, such as iron (Fe), have been shown to improve the strength significantly, but

at the cost of compromised ductility and corrosion rate. Zn-Fe alloys serve as potential candidates that could provide strengthening while retaining excellent biocompatibility [52, 229]. The alloying element Fe has been evaluated as degradable material that could degrade in the human body with a little-to-no inflammatory response [230]. A low concentration of Fe in as-cast Zn has shown to provide efficient precipitation strengthening, reaching more than 130MPa in ultimate tensile strength(UTS). Additionally, Zn-Fe alloy has shown little sign of anemia from in vivo assessment, and the corrosion rate remained 13 um/year, within the maximum rate of 20 um/year [89, 231]. However, the lack of ductility remains one of the critical limitations of the Zn-Fe alloy system, due to the formation of brittle ξ phase (FeZn_{13}). Previous studies proposed using less than 0.3 wt% Al to suppress brittleness by inhibiting the formation of ξ phase in the Zn-Fe alloys [232, 233]. However, Al can cause chronic cytotoxicity in animals and is not suitable for such biomedical applications [234].

In this part of the study, tungsten carbide (WC) nanoparticles were incorporated into the Zn-2Fe alloy system for strengthening, microstructure modification, and ductility enhancement. The primary purpose of nanoparticles is to enhance the mechanical strength through Orowan strengthening and to modify the ξ phase formation and growth by serving as nucleation sites and grain growth blockers to control the intermetallic microstructure and morphology [145]. These intermetallic phases did not have flat and faceted grain boundaries that commonly initiated the cracks, enabling effective dislocation pinning and simultaneously increasing the strength and ductility [235]. Meanwhile, compared with the Al alloying element, chemically stable WC nanoparticles are generally inert and non-reactive in the human body. Moreover, WC nanoparticles show no acute toxicity to mammalian cell lines [236]. Consequently, WC nanoparticles simultaneously enhance mechanical strength and ductility while maintaining a reasonable

corrosion rate. Overall, this novel Zn-Fe-WC nanocomposite could be used as biodegradable materials for biomedical applications where pure Zn was inadequate.

4.2.1. Fabrication of Zn-Fe-WC

Salt assisted stir casting and ultrasound processing were performed to manufacture the Zn-WC nanocomposite, shown in

Figure 78. An induction furnace was used to melt potassium aluminum fluoride (KAlF_4) at 800°C in a graphite crucible. Bulk Zn pellet (99.9%, RotoMetals) was weighed and added to the crucible. WC nanoparticles (150 nm diameter on average) were mixed with fine KAlF_4 salt powders at a volume ratio of 1:20. This powder mixture was gradually added to the crucible until 8 vol.% WC nanoparticles concentration in Zn was reached. A graphite stirrer was used to mix and effectively incorporate WC nanoparticles (500 rpm, 1.0 hour). Ultrasound processor (Misonix S-400 Ultrasonic Liquid Processor, Nb probe) was used to further homogeneously dispersed the nanoparticles and eliminate molten salt that was trapped in the metal melt. Granular Fe metal pieces (Alfa Aesar, 20 mesh, 99%) were weighed and added to the crucible. The temperature was maintained at 800°C for 20 min, and the metal melt was cast to steel mold. Zn-2Fe-WC samples were post-processed with hot rolling under a thickness reduction of 10:1 at 250°C . Wire-electrical discharge machining (wire-EDM) was used to cut samples to dog-bone shape for the tensile test (ASTM E8/E8M standard sub-size). Tensile tests were carried out using Instron ElectroPlus 1000 mechanical tester at a strain rate of 2 mm/min. 0.2% proof stress was used as yield strength.

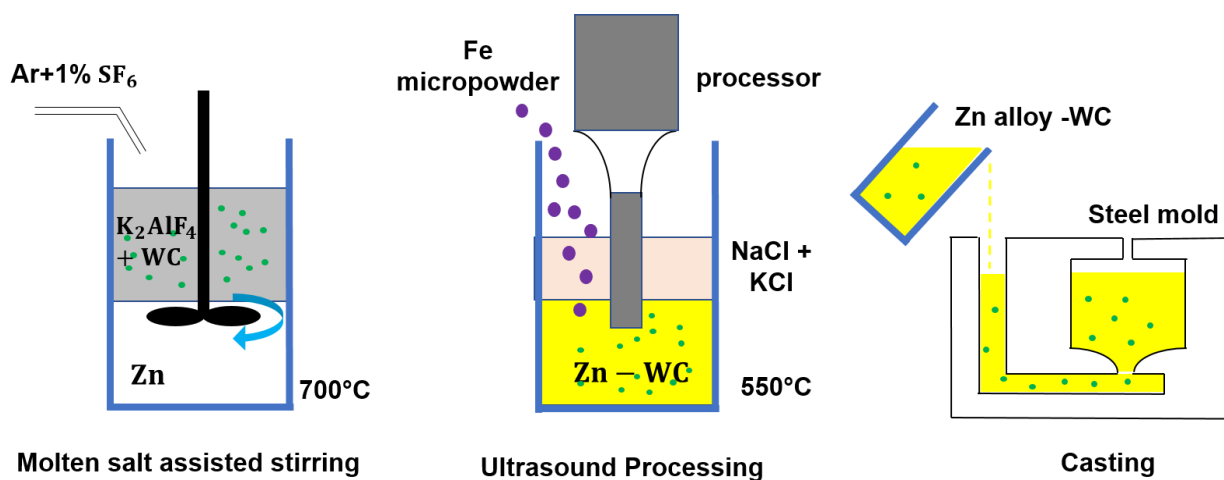


Figure 78: Schematics of Zn-Fe-WC nanocomposite manufacturing.

4.2.2. Microstructure of Zn-Fe-WC

The typical microstructures of Zn-2Fe-WC are shown in Figure 79. Zn-2Fe-8 vol.% WC sample was observed from the SEM before etching, shown in Figure 2(a). Darker phases were the metal matrix, while brighter phases represented the nanoparticle formed pseudo-clusters. A higher magnification SEM image showed the good dispersion of WC nanoparticles within this pseudo-clusters, shown in Figure 2(b). Such a phenomenon was reasonable due to the nanoparticle size effect and wettability between the WC nanoparticles and the molten metal matrix. The corresponding EDS analysis was shown in Figure 80. Furthermore, an etched sample also showed the nanoparticle dispersion in the Zn-rich phase instead of in the $\zeta\text{-FeZn}_{13}$ precipitates, shown in Figure 2(c). Point scanings were performed in different places to indicate that WC nanoparticles preferred to stay in the Zn-rich phase, shown in Figure 2(d). An EDX map scanning has indicated a total WC concentration of 8 vol.% for typical nanocomposite samples.

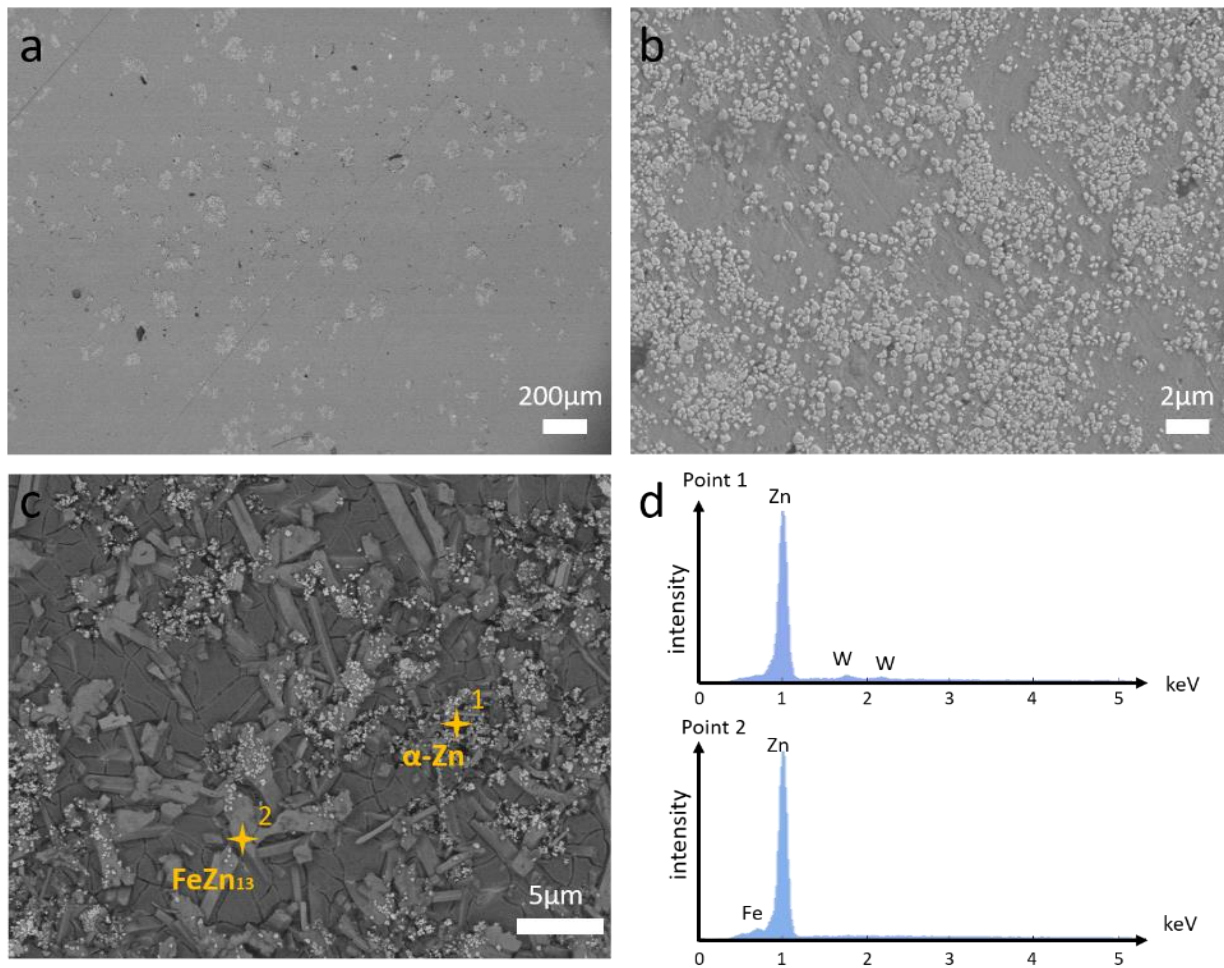


Figure 79: Microstructure of Zn-2Fe-8 vol.% WC. (a) The microstructure image of Zn-2Fe-WC under SEM at low magnification. Brighter phases indicated the high-density nanoparticle pseudo-clusters. (b) The microstructure image of Zn-2Fe-WC under SEM at high magnification, showing the good distribution of WC nanoparticles inside the pseudo-clusters. (c) SEM image of Zn-2Fe-WC after grain etching, showing nanoparticles modified the formation of FeZn_{13} precipitates. (d) EDS point scanning was performed on places shown in (c), indicating nanoparticles were likely to stay in the Zn-rich phase.

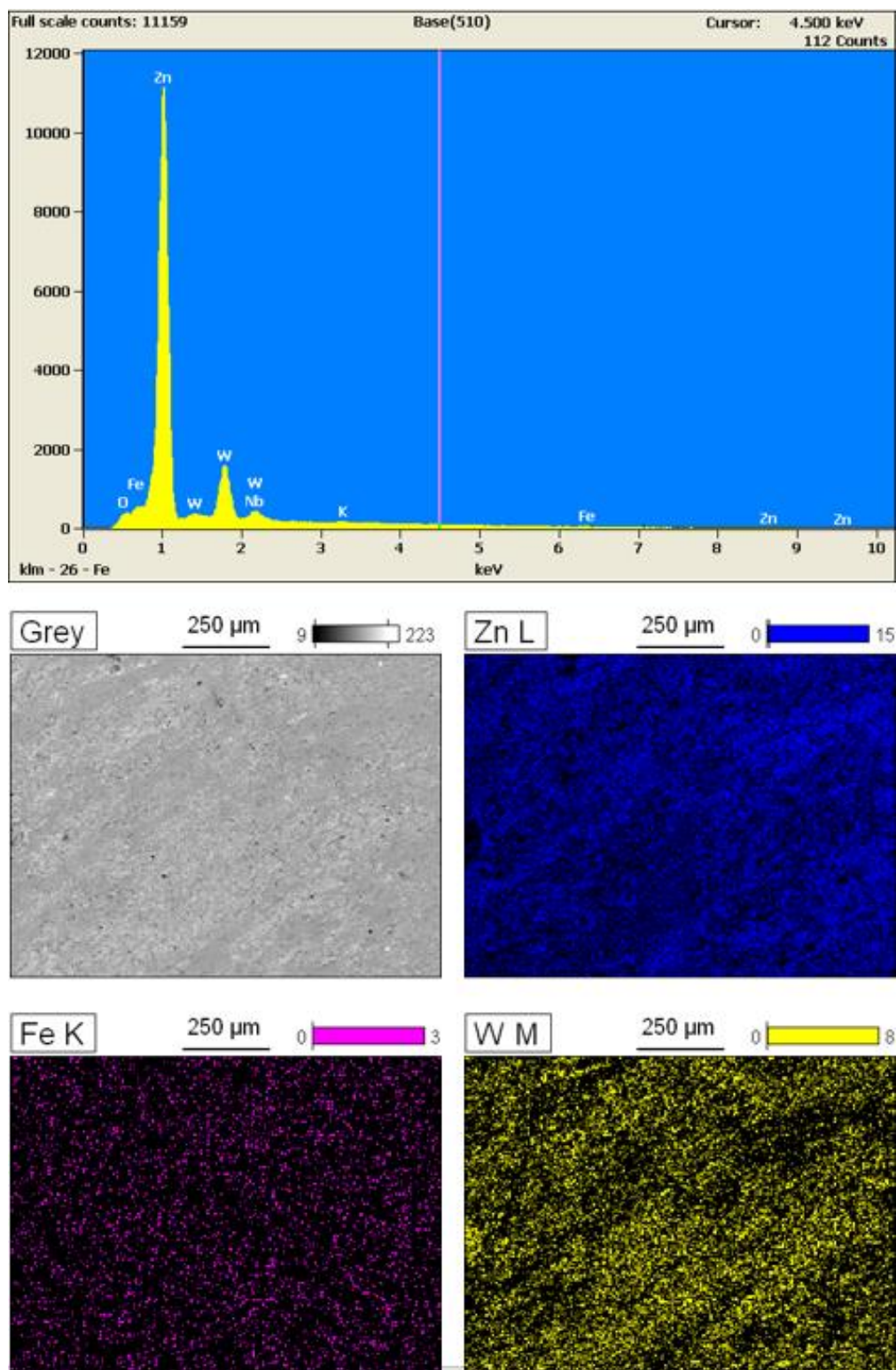


Figure 80: EDS mapping of Zn-2Fe-WC

Grain etchant (20g CrO₃, 5g Na₂SO₄) was applied as an etchant to expose the intermetallic phase for optical microscopy imaging (Zeiss Primotech optical microscopy). The microhardness test was performed by LM 800AT microhardness tester using a load of 200gf with a 10 s dwell time. The as-cast high purity Zn-2Fe and as-cast Zn-2Fe-8vol%WC nanocomposites were prepared by mechanical grinding, alumina nanoparticle polishing, and ion milling polishing for microstructure characterization by scanning electron microscopy (ZEISS Supra 40VP SEM), energy-dispersive X-ray spectroscopy (EDS), and element detection by x-ray diffraction (XRD).

To further analyze the microstructure modification of Zn-Fe by dispersed WC nanoparticles during the solidification process, optical microscopy images were used to illustrate the microstructure of the precipitates, shown in Figure 81. Since Fe is not soluble in Zn at temperatures below 800K, ζ -FeZn₁₃ precipitates are likely to form during the solidification process and be dispersed homogeneously across the bulk alloy^[11]. Due to the non-uniform energy at different atomic orientation, ζ -FeZn₁₃ precipitates had faceted intermetallic grain boundaries, shown in Figure 3(a) and 3(b). Intermetallic phases commonly grow along the low energy surface [237]. These faceted grain boundaries could be one of the reasons that result in embrittlement and low elongation to failure, which has been demonstrated in Cu [238]. The Zn-2Fe-WC sample has a significantly different microstructure, shown in Fig. 3(c) and (d). The ζ -FeZn₁₃ precipitates, though obtained an average grain size about similar to the reference samples, had non-faceted grain boundaries, which were uncommon for crystalline materials. It can be assumed that the existence of well-dispersed nanoparticles in molten metal could interfere with the solidification during casting by changing the intermetallic grain boundaries from faceted to non-faceted.

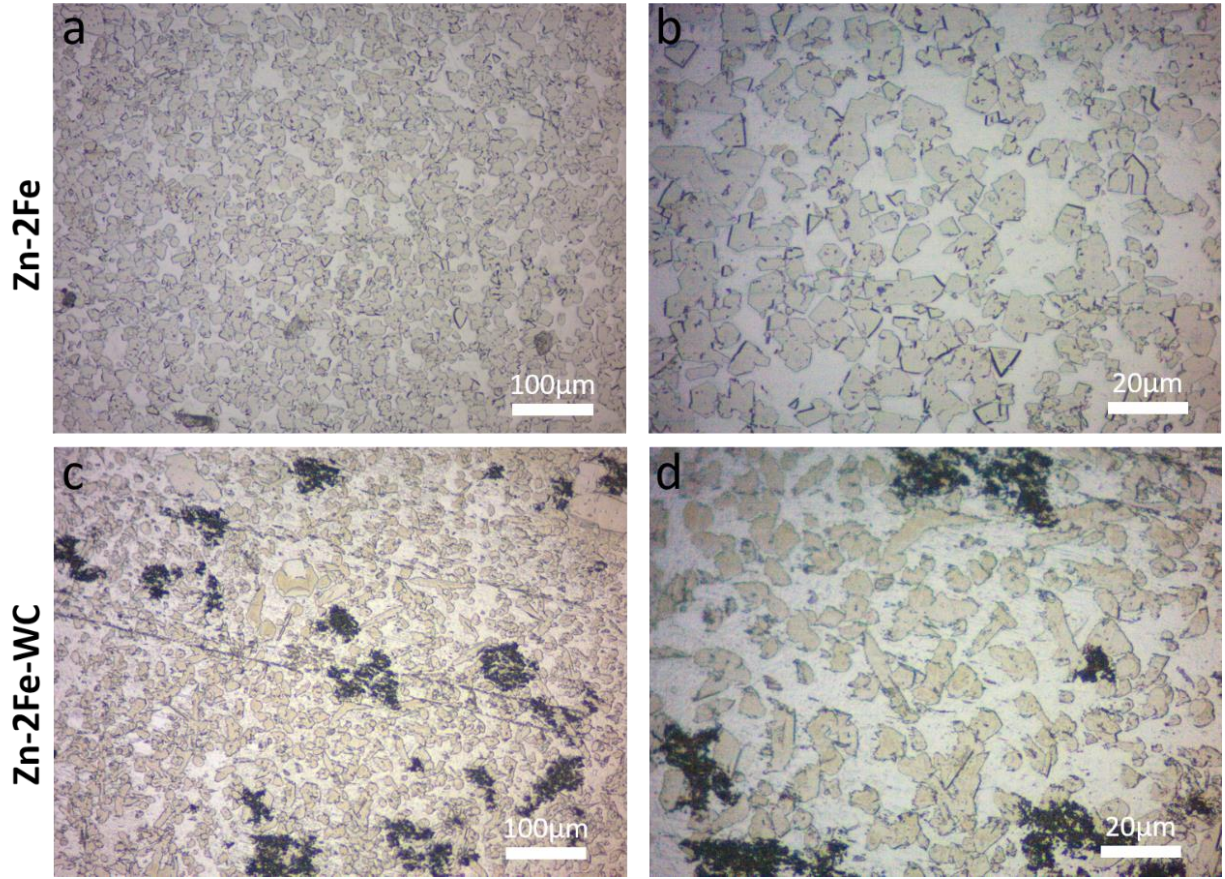


Figure 81: (a) and (b) Zn-2Fe optical images after etching, yellow phases indicated the faceted intermetallic precipitate (ζ -FeZn₁₃). (c) and (d) Zn-2Fe-WC optical images after etching, intermetallic phases showed non-faceted grain boundaries, and the black spots indicated the nanoparticle pseudo-clusters.

According to the Zn-Fe phase diagram and the phenomenon that nanoparticles were rarely found in the ζ -FeZn₁₃ phase, the interaction between WC nanoparticles and the molten metal during the solidification process can be deduced as follows, shown in Figure 82:

- (1) Solid-phase WC nanoparticle was well-dispersed in metal melt before cooling, partially due to the good wettability between molten zinc and WC [132].

(2) Nanoparticles initiate the intermetallic phase formation as nucleation sites. They also encounter the solidification front and modified the microstructure of the ξ - phase by restricting the grain growth.

(3) The zinc matrix solidified as WC nanoparticles dispersed uniformly inside the matrix.

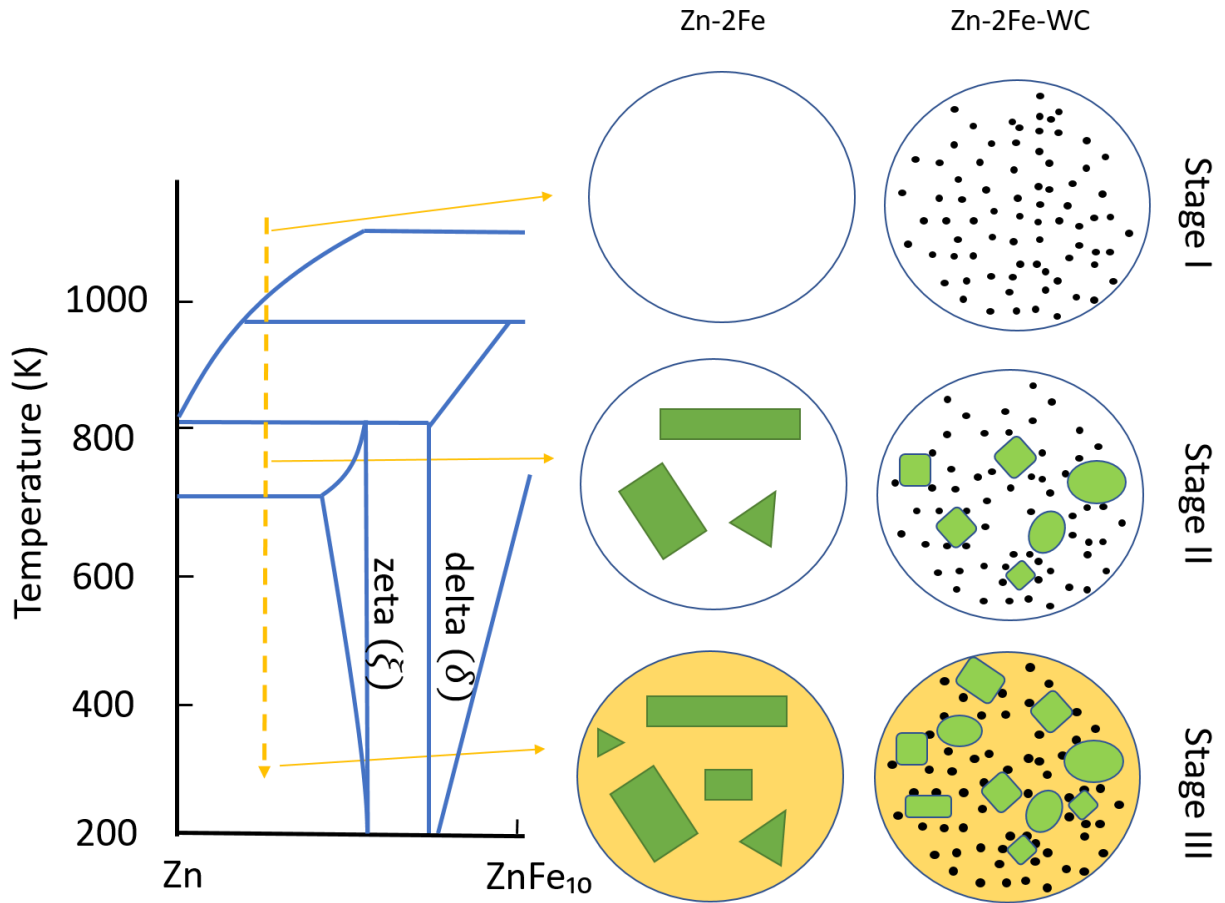


Figure 82: Proposed schematic of the solidification process for Zn-2Fe and Zn-2Fe-WC at stages I-III.

Chemical compositions of the samples were further confirmed through XRD, which detected both samples from 30° to 50°, shown in Figure 83. The intermetallic phases were confirmed to be ξ phase.

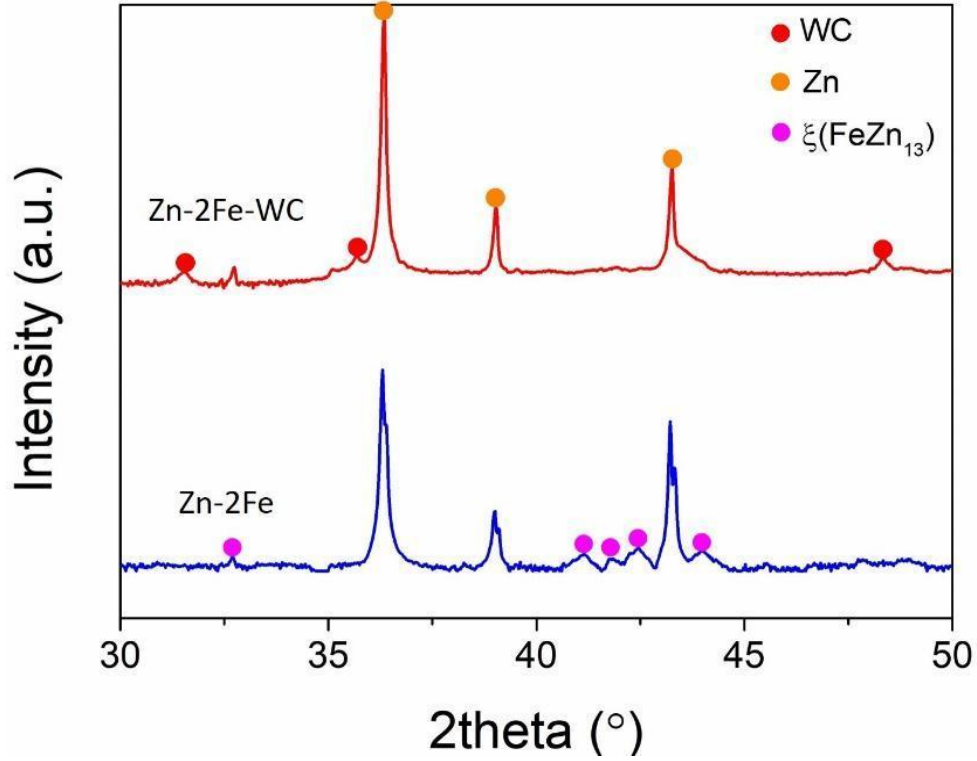


Figure 83: XRD results of Zn-2Fe and Zn-2Fe-WC

4.2.3. Mechanical performance of Zn-Fe-WC

Vickers microhardness of as-cast Zn-2Fe and as-cast Zn-2Fe-WC was characterized using a microhardness tester compared with the pure Zn cast in the same method, shown in Figure 84. 8 vol.% WC nanoparticles primarily existed inside the zinc matrix, enabling the nanoparticle-induced precipitation strengthening [132]. WC nanoparticles with Vickers microhardness larger than 2200HV dispersed inside the material could efficiently impede the dislocation movement to enhance mechanical strength. Thus, in addition to the ξ phase hardening, WC nanoparticles further increase the Vickers microhardness from 47.9HV to 59.3HV.

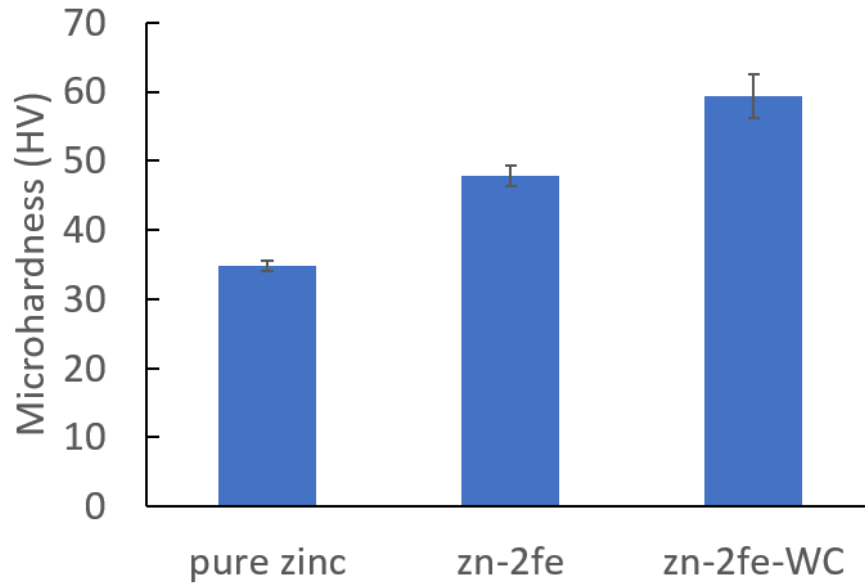


Figure 84: Vickers Microhardness of Zn-2Fe and Zn-2Fe-WC compared with pure Zinc sample ($n=8$).

Tensile testing was performed on Zn-2Fe and Zn-2Fe-WC, and the results are shown in Figure 85. With 8 vol.% WC nanoparticles, the ultimate tensile stress (UTS) and elongation to failure increased from 92.0MPa to 121.1MPa and from 1.4% to 8.6%, respectively. The corresponding fracture surfaces of the specimens are shown in Figure 86. The pure Zn-2Fe sample has a flat fracture surface due to the brittleness of the zeta phase. In contrast, Zn-2Fe-WC had a large amount of WC nanoparticles on the fracture surface, which potentially impedes the propagation of cracks. To further improve the nanocomposite material's mechanical behavior, the hot rolling process was performed on Zn-2Fe-WC. The results showed that the UTS and elongation to failure further increased to 155.8MPa and 15.3%. The improved performance of the hot-rolled (HR) sample suggests a reduction in porosity and improvement in nanoparticle dispersion [152], which enhances both ductility and strength [239].

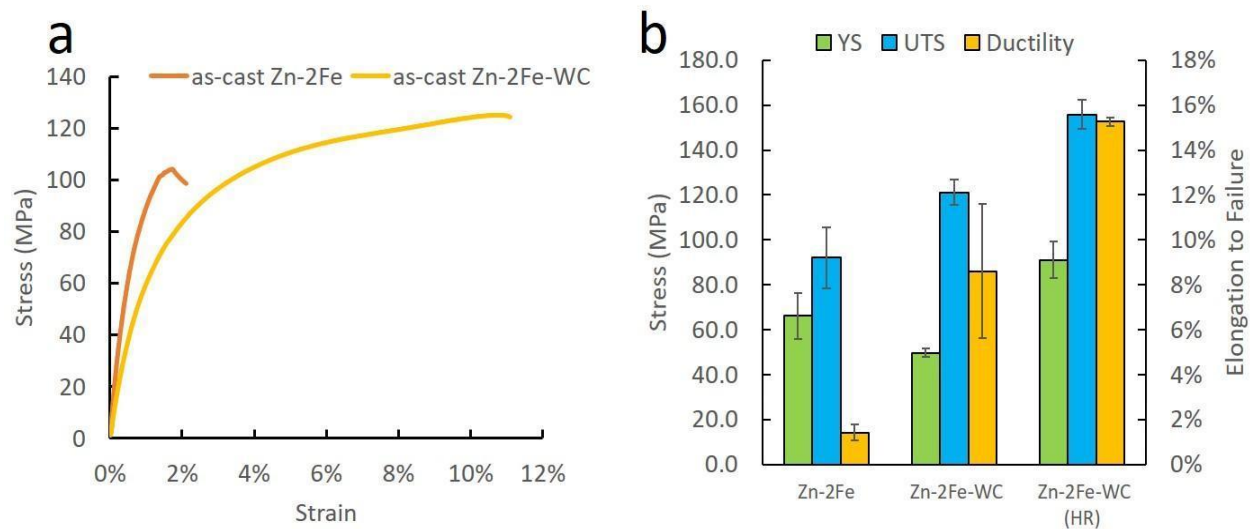


Figure 85: (a) Representative Stress-Strain curve from the tensile test of cast Zn-2Fe, cast Zn-2Fe-WC. (b) Average values of yield strength, ultimate tensile strength, and elongation to failure ($n=3$).

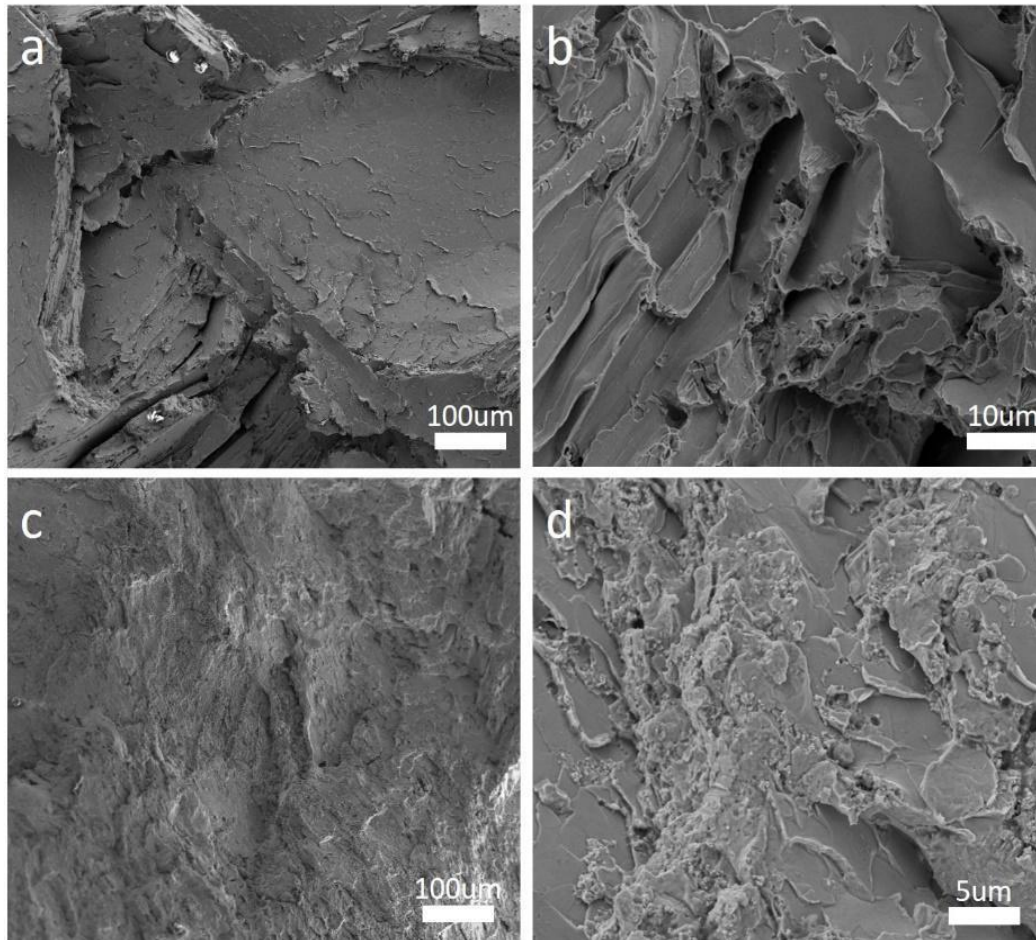


Figure 86: The fracture surface of as-cast Zn-2Fe and as-cast Zn-2Fe-WC are shown in (a, b) and (c, d), respectively

The tensile test data of as-cast Zn-2Fe-WC samples showed a significant ductility improvement, compared with other biodegradable Zn alloys, whose alloying elements include Mg, Ca, Fe, and Sr, as shown in Figure 87. With the addition of WC nanoparticles that homogeneously modify the strengthening intermetallic, the elongation to failure of Zn-2Fe reached more than 8%, exceeding most of the as-cast Zn alloys. The non-faceted morphology of the intermetallic phase is presumed to be the critical factor in improving the ductility. While the Zn-2Fe-WC did not offer a relatively high strength suitable for load-bearing biodegradable implants such as bone plates and cardiovascular stents, this work has shown an effective method to improve ductility for as-cast

zinc alloys, providing a solution for the manufacturing of ductile biodegradable Zn alloys. In the previous work, hot work processing (e.g., hot extrusion and hot rolling) was a necessary procedure to gain ductility due to the HCP atomic structure of Zn. Such processes limited the manufacturing of complex geometries. Laser micromachining was introduced to solve this problem, but the heat-affected zone is a side effect for most commercially available lasers. Thus, this work leveraged the simple casting method for Zn and Zn alloy, which has no geometry restriction and could further broaden the applications of Zn alloys.

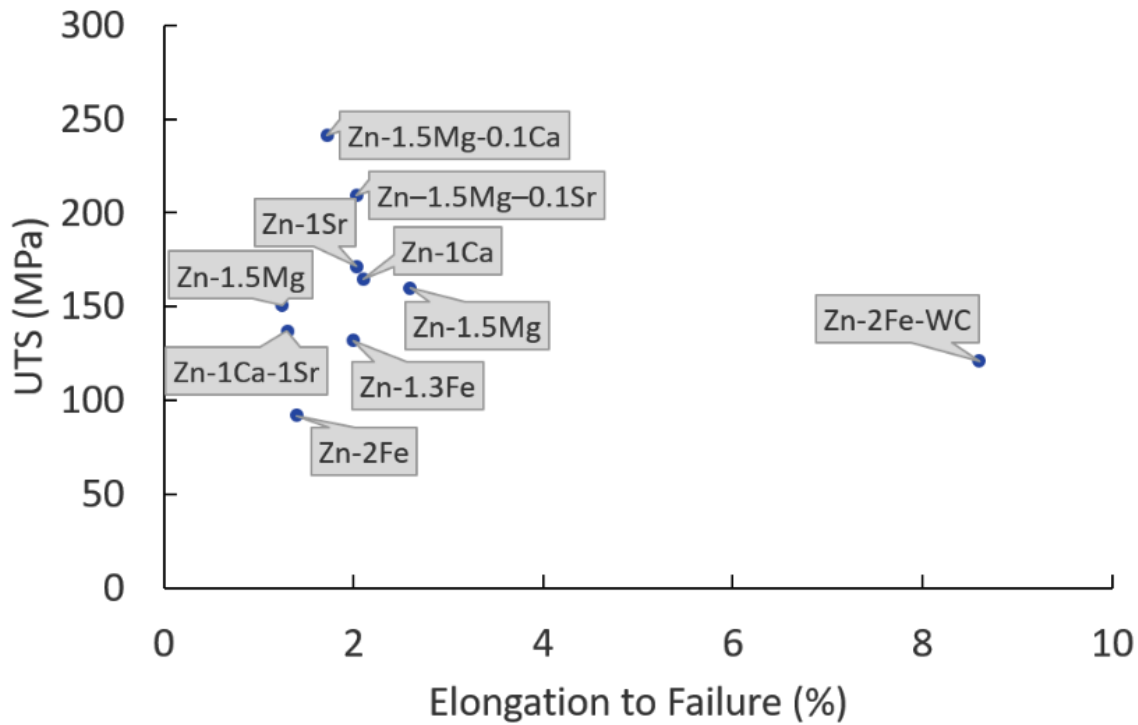


Figure 87: UTS vs. elongation to failure for as-cast biocompatible and biodegradable zinc alloys. As-cast Zn-2Fe-WC stands out due to the significantly improved ductility.

4.2.4. Biodegradability of Zn-Fe-WC

One of the reasons Zn has been extensively studied as a biodegradable implant material is because it has corrosion behavior suitable for many biomedical applications, but alloy elements

have been shown to influence the corrosion behavior. The corrosion resistance of the as-cast Zn, Zn-2Fe, and Zn-2Fe-WC was evaluated by electrochemical analysis [117]. The corrosion rate was calculated from the following equation

$$CR = 3.27 \cdot 10^{-3} \frac{i_{corr}EW}{\rho}$$

where CR is the corrosion rate (mm/yr), i_{corr} is the corrosion current density (uA/cm²), EW is the equivalent weight of the metal, and ρ is the density(g/cm³). No difference in the CR was measured between as-cast Zn, Zn-2Fe, and Zn-2Fe-WC, shown in Table 1. It has been previously reported that Zn-Fe alloys have greater corrosion rates compared to pure Zn due to ξ phase acting as a cathode to the Zn matrix, causing accelerated degradation by microgalvanic effect [89]. Since electrochemical techniques capture the corrosion behavior of a specimen during the narrow window of time over which the measurement was carried out, immersion tests were also carried out to investigate corrosion behavior (Table 2 and Figure 10). In the first week, Zn ion release was the greatest from the samples alloyed with Fe, and the Zn-2Fe samples had the greatest followed by Zn-2Fe-WC; however, by day 14, there was no difference in the cumulative Zn ion release between the 3 different groups. Similarly, the release of Fe from the Zn-2Fe samples was greater than the samples containing the WC nanoparticles in the first 2 weeks, but there was no difference in cumulative Fe ion release after day 14. These results corroborate the electrochemical testing, which found no difference in CR between the pure Zn and the samples alloyed with 2 wt% Fe and 8 vol.% WC nanoparticles. Long-term immersion studies (i.e. 3+ months) and *in vivo* studies are required to elucidate the corrosion behavior of Zn-Fe based nanocomposites and their applicability as a biodegradable implant material. Encouragingly, little-to-no W ions were released after 28 days. Only one sample had measurable levels of W ions, and by day 28, the cumulative release was 2 ng/mm². For elemental W to be detectable, the WC nanoparticles must first escape the bulk

metal and undergo oxidation to release W ions. For biomedical applications, it is more likely that cells will encounter WC nanoparticles over elemental W, and both cytotoxicity and genotoxicity of WC nanoparticles on relevant cell lines are required.

Table 11: Electrochemical analysis data

Sample	Temp	OCP (V _{SCE})	R _p (kΩ cm ²)	i _{corr} (uA/cm ²)	CR (mm/yr)
Zn	37°C	-0.966 (±0.003)	11.978 (±1.269)	0.81 (±0.39)	0.012 (±0.007)
Zn-2Fe	37°C	-0.959 (±0.007)	6.258 (±0.753)	0.82 (±0.16)	0.012 (±0.002)
Zn-2Fe-WC	37°C	-0.977 (±0.022)	5.195 (±3.383)	1.34 (±0.50)	0.020 (±0.007)

OCP: open circuit potential; R_p: polarization resistance; i_{corr}: corrosion current; CR: corrosion rate.

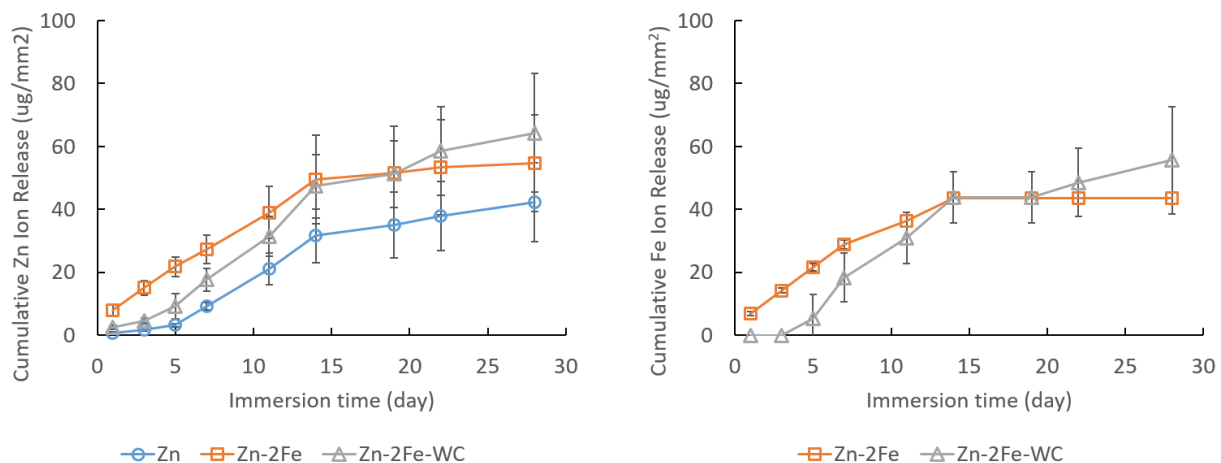


Figure 88: Immersion test result: cumulative ion releases of Zn and Fe after 4 weeks in SBF.

Table 12: Cumulative ion release at day 28 (n=5)

Sample	Temp	Zn (ug/mm ²)	Fe (ug/mm ²)	W (ug/mm ²)
Zn	37°C	42.2 (±12.5)	N/A	N/A
Zn-2Fe	37°C	54.6 (±15.4)	43.6 (±2.0)	N/A
Zn-2Fe-WC	37°C	64.3 (±18.8)	55.6 (±17.1)	0.002 (±0.003)

Chapter V: Nanoparticle enabled fabrication of metal micro/nanowires for medical applications

5.1. Thermal fiber drawing

The thermal fiber drawing process was shown in Figure 89, where a glass-coated metal rod is fed into the high-temperature furnace with a relatively slower velocity v_f . A motor connected rotating wheel vertically beneath the furnace pulls the wire out of the furnace with a faster velocity v_p . Inside the high-temperature heating furnace, since pulling speed is faster than the feeding speed, soft glass tubing shrunk to smaller tubing due to the mass conservation, formed a tapered area, and stretched the metal core to a smaller size. While being drawn out of the furnace, both of the glass tube cladding and metal wires became thinner after solidification. At a steady-state drawing condition, the law of mass conservation gives the conclusion that the diameter of the drawn wire follows the draw-down ratio of velocity, written as:

$$D_{out} = D_{in}/\sqrt{R} = D_{in} \sqrt{\frac{v_f}{v_p}}$$

where D_{in} and D_{out} refers to the feeding and drawing wire diameter correspondingly, and R refers to the draw-down ratio. This drawing tower was built specifically for a heating temperature up to 1600°C, enabling a slowest feeding speed of 10um/s and a fastest pulling speed of 0.7m/s with the largest draw-down ratio of 265. Such setup enabled different material nanowire fabrication including but not limited to Zn, Al, Cu, Ag, Au, and most of their alloys.

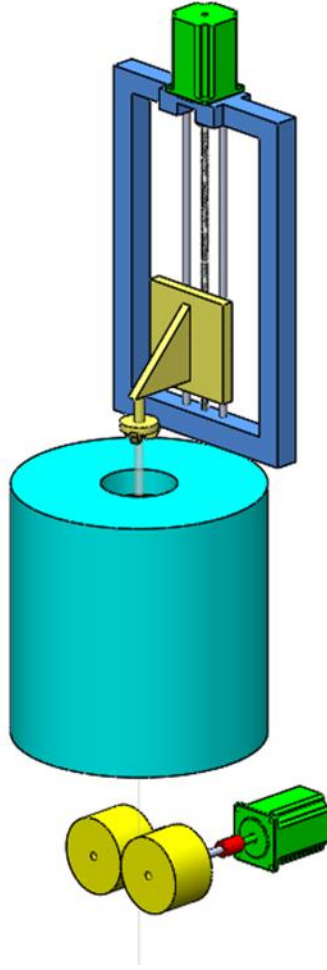


Figure 89: Schematic of thermal fiber drawing tower

5.2. Fluid instability suppression during thermal fiber drawing through dispersed nanoparticles

Tomotika model expresses the dispersion relation of a long cylinder of viscous fluid jet surrounded by another indefinitely long viscous medium [240], where instability was introduced by perturbation-caused equilibrium surface deformation [241], also called varicose perturbation.

Tomotika dispersion relation is defined as:

$$\tau = \frac{1}{i n} = \frac{D_{core} \cdot \mu_{clad}}{\gamma \cdot G\left(x, \frac{u_{core}}{u_{clad}}\right)}$$

$$x = \frac{\pi D_{core}}{\lambda}$$

$$G = \max [(1 - x^2)\Phi\left(x, \frac{u_{core}}{u_{clad}}\right)]$$

where τ is the associate instability growth time, $i n$ is the instability growth rate, D_{core} is the diameter of the core, μ_{clad} and μ_{core} are the viscosities of the core and cladding, respectively, γ is interfacial energy between the core and cladding, λ is the varicosity wavelength, and Φ is a function containing the modified Bessel functions. G is related to the wave vector and the viscosity ratio between the core and cladding. In the equation of Tomotika dispersion relation, the term associated instability growth time (τ) can be generally understood as a measurement of time-lapse in which the core would remain continuous before it is broken into droplets. According to the Tomotika model, which describes the fluid instability in cladding under ideal static conditions (e.g., small motion, no interface slipping, negligible fluid flow and interfacial surface tension as the only normal stress), the instability growth time is related to the core diameter (D), cladding viscosity (μ_{clad}), interfacial energy (γ), and the core fluid viscosity (μ_{core}). The cladding viscosity is a parameter that could be tuned by temperature, which has its upper limit at the glass transition temperature. Moreover, in actual experiments, when drawing at the glass transition temperature, the high viscosity of glass cladding would inhibit the flowability and significantly reduces the productivity and the scalability, which are supposed to be one of the greatest advantages of thermal drawing. Furthermore, additional influential factors of drawing speed and longitudinal stretching force will need to be considered in the actual drawing process for optimization [242]. This model expresses the surface perturbation of the fluid jet as an amplified wave under ideal conditions. Thus, it could essentially guide the thermal fiber drawing for the fundamental optimization of drawing parameters for indefinitely long micro/nanowires. The associate instability growth time represents how fast the continuous liquid core thread breaks into droplets. Optimization of experimental settings, such as drawing speed and temperature, could

successfully produce ultra-long semiconductors nanowires of 10 nm in diameter by thermal drawing, due to their high viscosity and low interfacial energy with cladding [162].

Although Tomotika model has successfully guided the nanowire fabrication of material of high liquid viscosity and low interfacial energy, it also set the boundary for metal nanowire fabrication. There are still great challenges when the scalable production of metal wires below a few hundreds of nanometers in diameter is needed. These are due to the high interfacial energy between molten metals and glass claddings that makes the associated instability growth time too short when the core diameter reaches nanometer scale (Table S1). Especially for metals like zinc (Zn), copper (Cu), silver (Ag), gold (Au), and platinum (Pt) with high melting temperatures, the interfacial energy between the molten metals and glass claddings is 2 to 3 times higher than low-melting metals like tin (Sn) [243], bismuth (Bi), lead (Pb) [182], and indium (In) [244], with polymer claddings, making it significantly more difficult for manufacturing. Figure 90 demonstrates the theoretical calculation of the associated instability growth time with respect to the core material viscosity and interfacial energy, according to the Tomotika model. It argues for the viability of nanowire fabrication using thermal fiber drawing for materials like semiconductors and low melting-point metals. However, since high melting-point metals (e.g., Zn, Cu, Au) have very short associated instability growth times, they could hardly be fabricated as ultra-long nanowires by thermal fiber drawing. The only way to realize high-temperature metal nanowires is bottom-up methods, such as chemical synthesis, which is costly, non-scalable, and difficult to apply for industrial manufacturing.

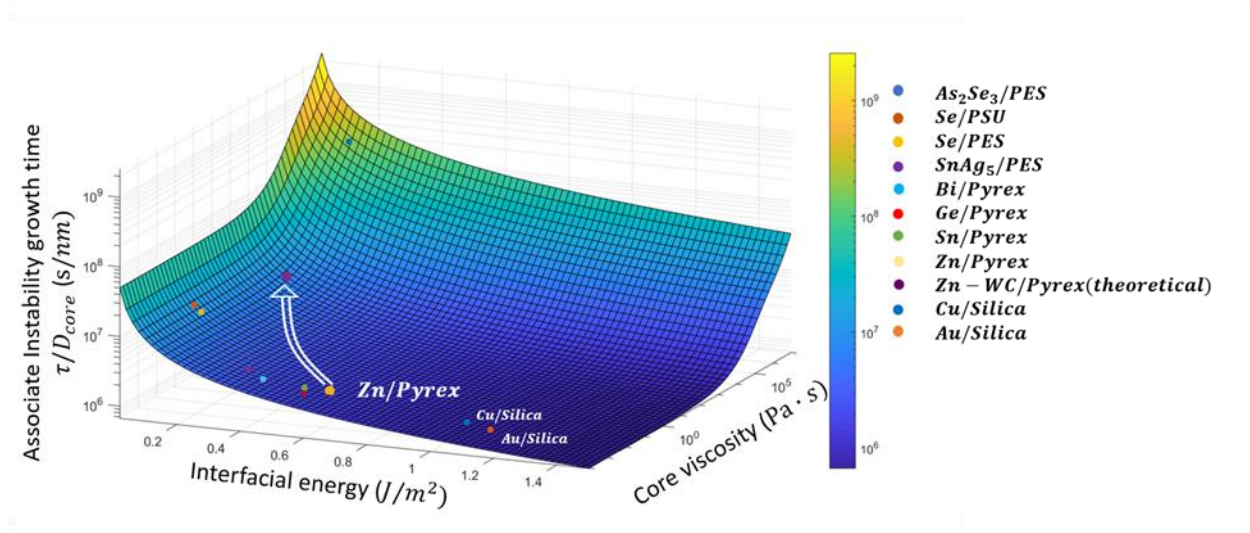


Figure 90: Associated instability growth time vs. core material interfacial energy and viscosity under the condition that the cladding viscosity is $10^6 \text{ Pa}\cdot\text{s}$. Zinc-WC/Pyrex has been demonstrated to enhance the associate instability growth time by adding nanoparticles to the core material for interfacial energy reduction and viscosity enhancement²⁸, making it promising to allow a longer associate instability growth time as indicated by the arrow. High melting temperature metals (Zn, Cu, Au) have been explicitly marked on the graph.

According to the abovementioned conditions and limitations, there is a theoretical solution to the feasibility of the metal nanowire scaled fabrication method, by using nanoparticles to change the viscosity and interfacial energy (surface tension) intrinsically. Thus, nanoparticles can tackle the long-standing fluid instability issue and stabilize the varicose perturbation. In this study, thermally stable tungsten carbide (WC) nanoparticles were incorporated in zinc to manufacture Zn-WC nanocomposite as the core material, and borosilicate was used as the cladding materials. According to the past studies on the metal matrix nanocomposites and their viscosities and surface tensions, representative equations can be found as follow [245, 246]:

$$\frac{\mu_{\text{eff}}}{\mu_0} = \frac{1}{1 - 34.87(d_p/d_f)^{-0.3}\varphi^{1.03}}$$

$$\frac{\gamma_{\text{eff}}}{\gamma_0} = -3.7344\varphi + 1$$

where, μ_{eff} , μ_0 and γ_{eff} , γ_0 are respectively the viscosities and interfacial energies of molten nanocomposites and pure molten metals, d_p is the nanoparticle size, d_f is the metal atom size and ϕ is the nanoparticle volume concentration. Although such equations can only generally presume the viscosity/surface tension modification according to the nanoparticle concentration, it still provides a systematic understanding of how nanoparticles could overall increase the associate instability growth time and help on realizing the scale-up fabrication of high-temperature metal nanowires. Figure 91 has shown the results of the associated instability growth time related to Zn-WC nanoparticle concentration and operating temperature through the Matlab calculation.

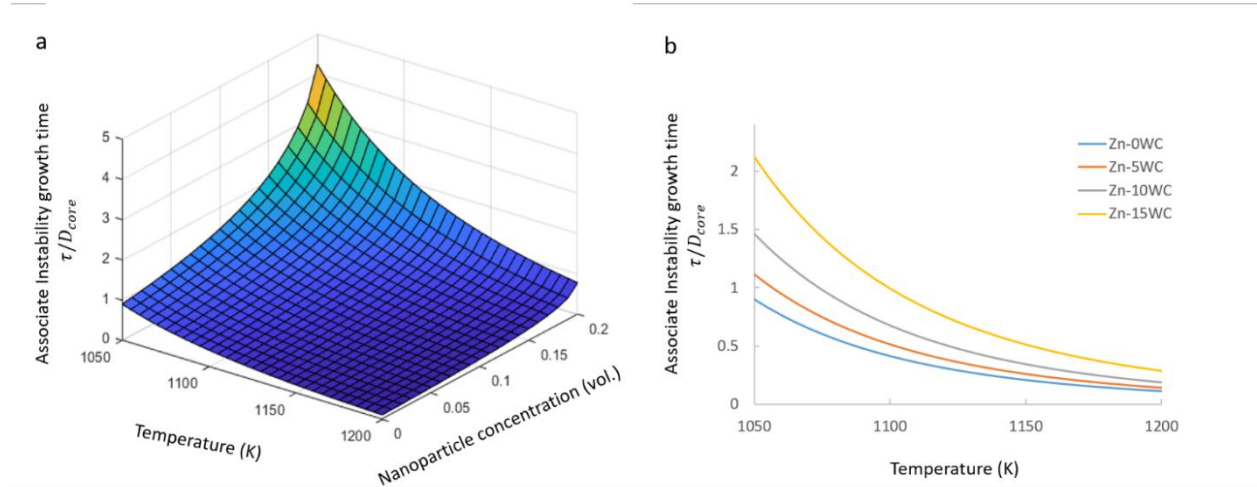


Figure 91: (a) Theoretical associate instability growth time of Zn-WC nanocomposite as the core material in Pyrex glass cladding, with respect to temperature and nanoparticle concentration by Tomotika model. (b) The associate instability growth time vs. drawing temperature. At a typical drawing temperature of 1100K, 15 vol.% nanoparticles efficiently enable the fluid instability control.

Traditionally, the only viable method to enable fluid stabilization of varicose perturbation is by tuning the drawing temperature. While lowering the temperature could enhance the viscosity of cladding material, it prohibits fiber drawing at high speed. By applying Zn-WC nanocomposite

as the core in thermal fiber drawing, the associate instability growth time could be significantly increased in theory.

5.3. Cu/Ag wire

This part has shown the silver-copper alloy (AgCu) reinforced by tungsten carbide (WC) (AgCu_{40} (wt. %)-WC) was manufactured by a stir casting method utilizing a nanoparticle self-dispersion mechanism, and nanocomposite microwires were successfully fabricated using the thermal drawing method. Ag-Cu matrix nanocomposite microwires could also be applied as filler materials in brazing, especially between metals and ceramics, since nanoparticles could enhance the filler performance, and the additional ceramic composition could enhance the wettability between fillers and ceramic base materials [247, 248].

5.3.1. Fabrication method

The schematic of the experimental setup for stir casting is shown in Figure 92a. Pure Ag and Cu bulk samples were weighed and melted together in a graphite crucible within a furnace at 1100°C under the protection of argon. After both metals were melted, the furnace temperature was set to 950°C to maintain the alloy in the liquid state. Then, a 3-blade steel stirrer (BN coated) (Caframo Pitched Blade, Model A511) was placed right above the metal melt surface. WC nanoparticles were pre-mixed with sodium chloride (NaCl), and potassium aluminum fluoride (KAlF_4) powders at a volume ratio of 2:9:9. After the powder mixture was loaded with the metal melt, the mechanical stirrer was turned on at 300 rpm for 30 minutes. The furnace was maintained at 950°C for another 30 minutes to evaporate most of the molten salts. The metal melt was then cast and cooled down to room temperature.

Molten salt assisted stir casting has already been demonstrated as a concrete method in nanocomposite incorporation [249]. Such a method created a vortex in both molten metal and molten salts, accelerating the liquid flow to expedite the nanoparticle self-incorporation.

The purposes of using molten salt include:

- Extra protection of the metal from oxidation
- The effective dissolving of the surface oxide to prevent from blocking the nanoparticle incorporation pathway
- Avoiding contamination due to the low density of the molten salt
- Enhance the incorporation efficiency while, within a three-material system, WC nanoparticles preferred to merge into the liquid that obtained lower interfacial energy (e.g., molten Ag) for systematic energy minimization and stabilization

AgCu₄₀-WC nanocomposite ingot was melted in an alumina crucible under argon protection and then solidified to rods of 2.0mm in diameter after the nanocomposite melt was sucked into fused silica tubes by a vacuum pump. The nanocomposite rods were then taken out by mechanically breaking the fused silica tubes before they were inserted into borosilicate glass tubes (Corning Pyrex), which have an inner diameter of 2.0 mm and an outer diameter of 6.5 mm. The glass tube was sealed under vacuum using an oxygen/propylene torch, to serve as the preform for thermal drawing. After the preform was drawn in a furnace, multiple drawn-out fibers were inserted into another borosilicate tubes for the following drawings. The diameter of the nanocomposite core reduced from 2.0mm to 200um, 60um, and 6um subsequently. The schematic of the experimental setup is shown in Figure 92b and c. The furnace temperature during the drawing process was set to be 850°C, where nanocomposite was melted, and the borosilicate

glasses maintained a relatively high viscosity around 10^7 Pa·s, which was suitable for thermal drawing.

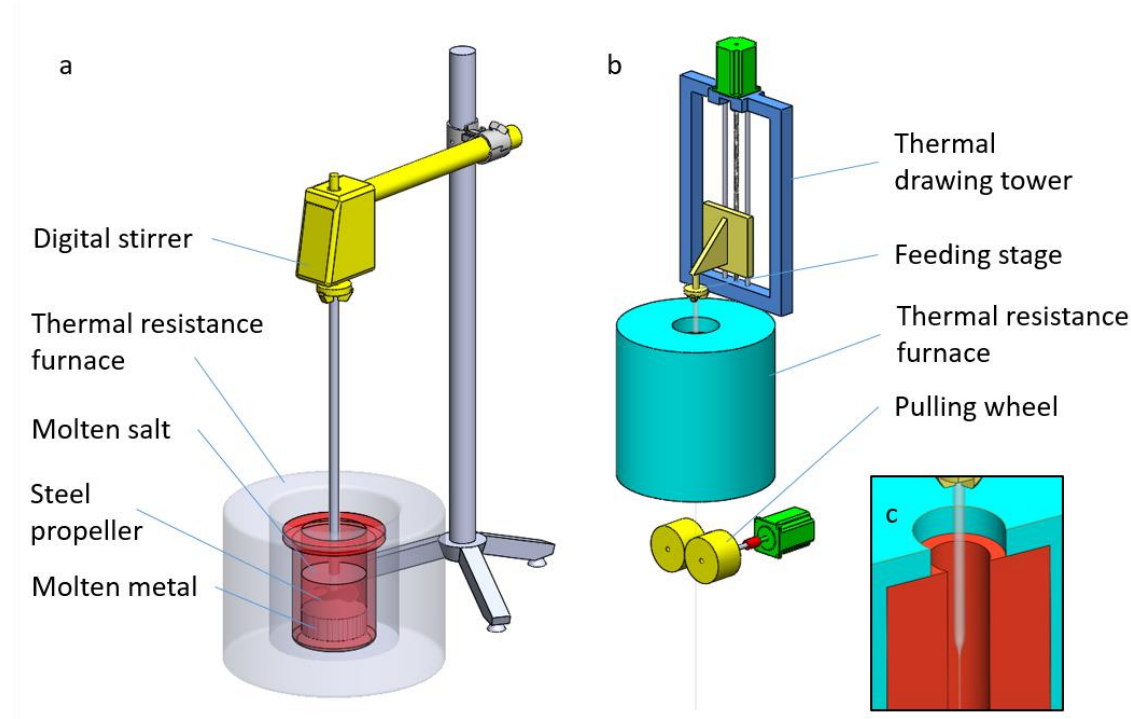


Figure 92: Schematic drawings of (a) the nanocomposite incorporation process using stir casting and (b) the thermal fiber drawing process. (c) illustrates the schematic that the metallic wire with glass cladding shrinks to a smaller size during the thermal fiber drawing.

5.3.2. Results

AgCu₄₀ with 10 vol. % WC and 22 vol. % WC nanocomposite samples were prepared by stir casting process assisted by molten salt. The scanning electron microscopy (SEM) in the backscattering mode was used to study the nanocomposite samples. The nanoparticle dispersion of AgCu₄₀-10 vol. % WC indicated a certain degree of pseudo-dispersion, as shown in Figure 93a. In the area of highly concentrated areas, the nanoparticles are still dispersed, as shown in the magnified image Figure 93b. The corresponding light intensity analysis image was shown in Figure 93c. Images of AgCu₄₀-22 vol. % WC were shown in Figure 93d-f. The relatively bright phase represented an area of high WC nanoparticle concentration, and the dark phase represents

an area of much lower WC concentration. ImageJ was used to analyze image intensity that could quantitatively indicate the comparison of nanoparticle dispersion between these two samples. Higher intensity variation, denoted by the standard deviation, represented a higher possibility of the appearance of “microclusters,” implying AgCu₄₀-10 vol. % WC obtained a pseudo-dispersion. Furthermore, nanoparticle size distribution was studied by analyzing the SEM images using ImageJ, shown in Figure 93g and h. The nanoparticle size distribution was reasonable, indicating that no severe agglomeration and sintering happened during the incorporation.

Grain structures were analyzed on AgCu₄₀-22 vol.% samples and AgCu₄₀ sample after applying etchant (ammonium hydroxide (NH₄OH) and hydrogen peroxide (H₂O₂)) on the polished surface. The grain structure of the pure AgCu₄₀ sample was shown in Figure 93i. Given that Ag and Cu have limited miscibility with each other, AgCu₄₀ obtained a majority of bilayer eutectic phase and Cu-rich phase. During the solidification process, the Cu-rich phase nucleated and grew at the first stage when the alloy cooled down, and the eutectic phase grew along with the Cu-rich phase. However, in the nanocomposite solidification process, the Cu-rich phase growth was restricted by the nanoparticle. Therefore, the grain size of the copper-rich phase reduced from 16.3μm to 5.2μm, shown in Figure 93j. Afterwards, the nanoparticles were pushed to the solidification front, and the nanoparticles affected the solidification of the eutectic phase by blocking the directional growth. Thus, SEM images revealed that the eutectic phase embodied most of the nanoparticles and the grain structure altered from organized bilayer dendrite to randomly and disorderly oriented. The microstructure transformation and grain refinement could contribute to the changes in mechanical strength and electrical conductivity. The characterization of the eutectic grain could not be entirely analyzed because nanoparticles interfered with the observation of the grain boundaries.

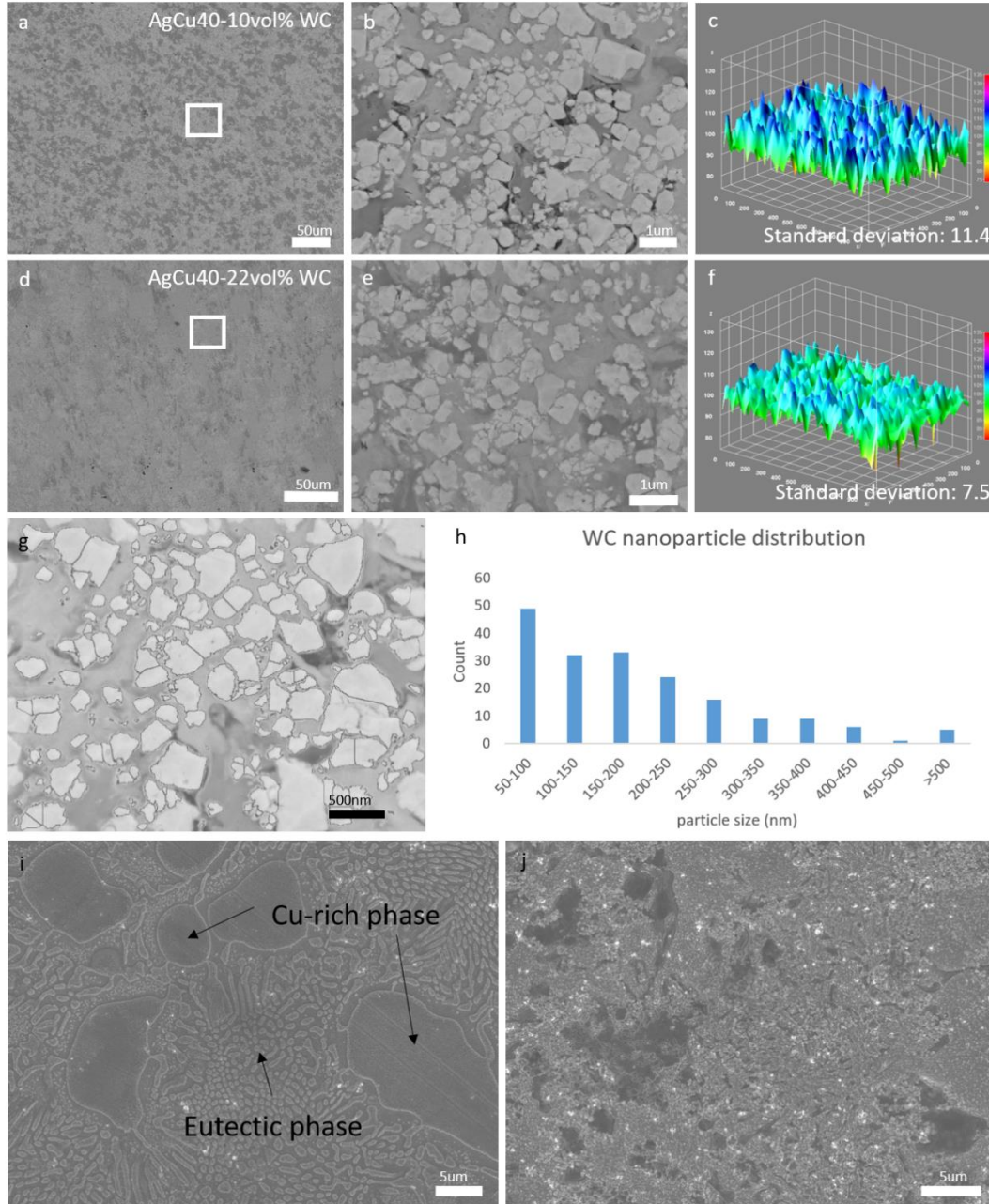


Figure 93: Microstructure analysis of AgCu40-WC nanocomposite. (a),(b),(d),(e) showed the SEM images of WC nanoparticle self-dispersion in metal matrix for nanocomposite bulk samples of 10 vol% WC (a,b) and 22 vol% WC (d,e). (c) and (f) are the image intensities of (a) and (d), where 22 vol% sample, with smaller standard deviation, obtains better nanoparticle dispersion. (h) showed the overlay image after image processing by ImageJ for WC nanoparticle size distribution analysis(g). (i) and (j) showed the grain structure analysis between pure alloy samples and nanocomposite samples.

Vickers microhardness of AgCu₄₀ nanocomposite samples was obtained under the condition of 200gf for 10s. *Figure 94a* showed the microhardness of the nanocomposites for different nanoparticle concentrations, compared with the pure Ag and pure Cu samples manufactured in the same casting method. AgCu₄₀ - 22vol.% WC raised the microhardness from 90HV to 147HV, and the result also showed that the Vickers microhardness linearly increases with the nanoparticle concentration. The microhardness curve indicated that WC nanoparticles contributed to high hardness (more than 50% enhancement), refined grain structure, and nanoscale precipitates.

Furthermore, the electric conductivity test was performed by *CDE ResMap 178 4-point probe* on nanocomposite thin sheets, as shown in *Figure 94b*. The electrical conductivities of AgCu₄₀-10 vol. % WC and AgCu₄₀-22 vol. % WC are 19.7±1.0% and 20.1±2.5% IACS, respectively. The result suggested that the conductivity of the nanocomposites decayed in a near exponential trend with the nanoparticle concentration, which mainly due to the interfacial energy difference at the AgCu₄₀ matrix-WC nanoparticle boundaries, associated with the different free electron energy levels and different electronic band structures [250-252]. Because nanoparticles restricted the grain growth, there were more grain boundaries in the nanocomposite, thus increasing the possibility of electron scattering at the grain boundary, thus showing a decreased electrical conductivity.

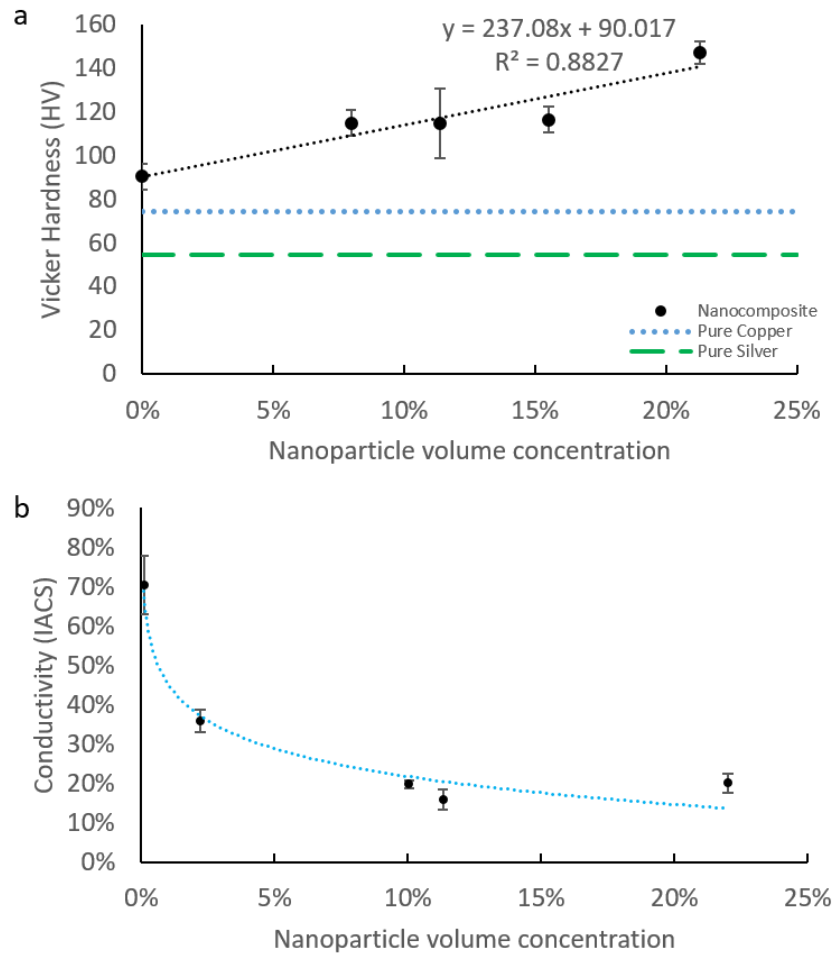


Figure 94. (a) Microhardness vs. nanoparticle concentration in volume percent. (b) Electrical conductivity vs. nanoparticle concentration in volume percent.

For nanoparticle redistribution analysis, nanocomposite fibers from 3 consequent thermal fiber drawings were polished from the side surface. AgCu₄₀-10 vol.% WC was used to produce the microwires, while the viscosity of AgCu₄₀-22 vol.% WC was too high for thermal drawing. Images obtained from SEM (Figure 95) show nanoparticle pseudo-dispersion and redistribution during consequent thermal drawing processes. The pseudo-dispersion zones of high WC nanoparticle loading were well-distributed after the first drawing and divided into smaller pseudo-dispersion zones after the second drawing. The diameter reduction did not significantly influence nanoparticle

dispersion inside the microclusters. However, when nanocomposite wire was reduced to 6 μ m, smaller than the average size of microclusters, a new phenomenon was observed. The microclusters were aligned in the microwire and constrained by the glass cladding, forming a bamboo shape with non-uniform diameters. The primary reason for the node structure was the high viscosity of the pseudo-dispersion zones when the microwires were reduced to 5 μ m. The local viscosity could be even larger than that of the glass cladding at the drawing temperature. Therefore, the nanocomposite core could not shrink along with the glass cladding. Further drawing to submicron size would not guarantee the continuity of the metal wire due to the pseudo-dispersion zones. These problems could be potentially solved through further research using nanoparticles of smaller size and better dispersion.

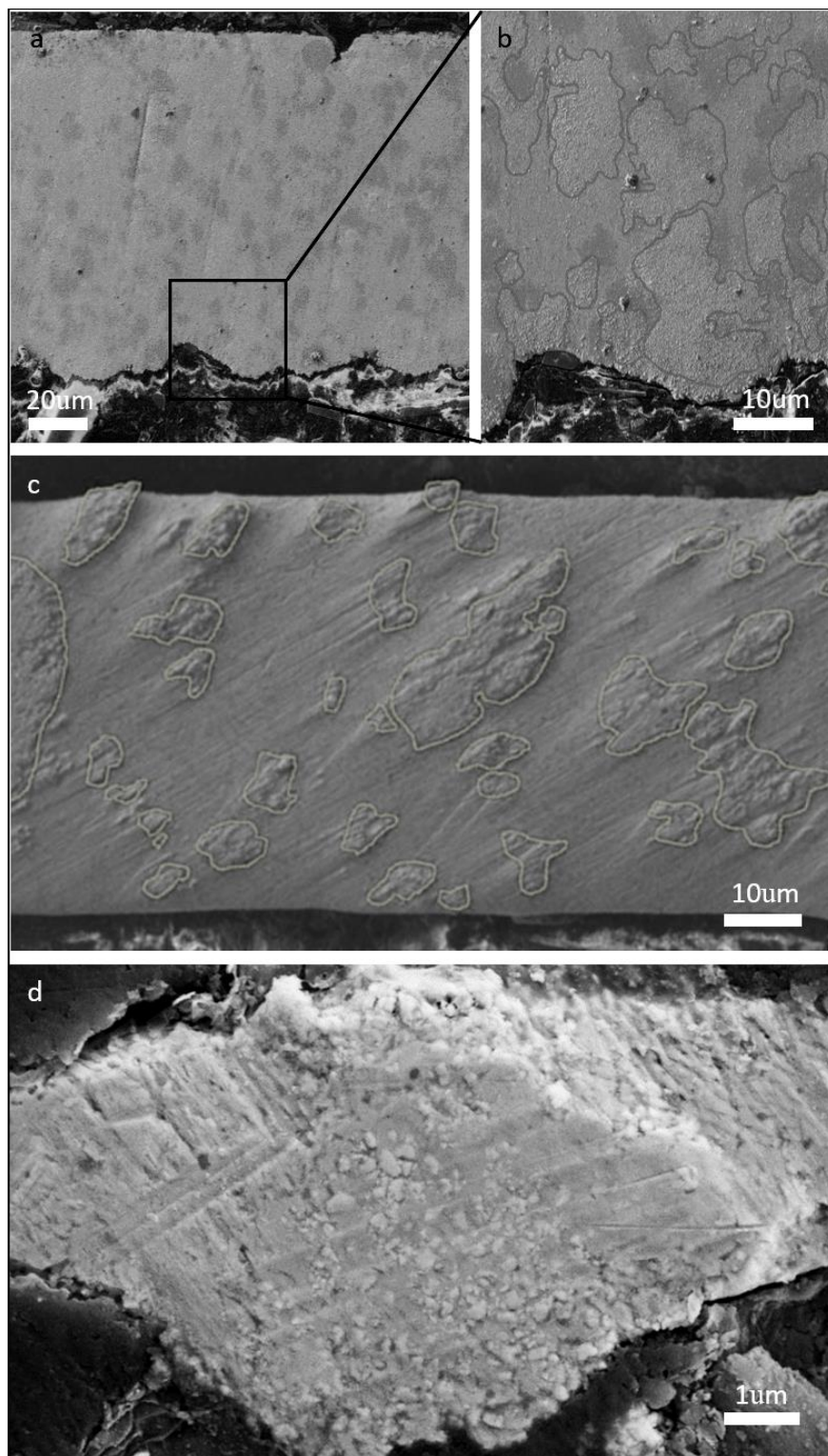


Figure 95. Microclusters of dense dispersed nanoparticle distribution after subsequent drawings. Corresponding nanocomposite microwires have diameters of 200 μ m(a and b), 60 μ m(c), and 5 μ m(d).

Tensile testing by *Q800 DMA TA Instrument* was performed to measure the mechanical properties of the AgCu₄₀- 10 vol. % WC nanocomposite microwires (60um in diameter) obtained from the second drawings, compared with AgCu₄₀ microwires produced in the same method, shown in *Figure 96*. The mechanical properties were also illustrated in *Table 13*. The strain rate was set to $4 \times 10^{-4} \text{ s}^{-1}$ in the tensile test. AgCu₄₀-10 vol. % WC microwires offered an ultimate tensile strength of $353 \pm 35 \text{ MPa}$, while only 203MPa for the pure AgCu₄₀ microwire sample. Furthermore, the nanocomposite microwires maintained an elongation of $5.2\% \pm 1.1\%$, similar to that of the pure alloy samples. From the results of tensile testing, the nanocomposite microwire obtained an improved ultimate tensile stress (UTS) without losing its ductility. The strength improvement could be contributed to the Orowan strengthening, the grain structure alternation, and grain refinement. However, defects on the microwire surface, owing to the mismatch of the thermal expansion coefficient between metal and glass, and inhomogeneous nanoparticle dispersion could affect the results and weaken the strengthening effect, making the strength of the nanocomposite microwires smaller than the actual value.

The mechanical result implied that nanocomposite microwires are promising to be utilized as bio-probes and biosensors, owing to its mechanical strength and conductivity. Compared to the current application of tin (Sn) with polymer cladding as the bio-probes [172], where Sn only obtain an electrical conductivity of 15% IACS and tensile strength of 220MPa, AgCu₄₀-10 vol. % WC has better mechanical strength and higher electrical conductivity. Furthermore, bare microwires could be used without structural support to enhance the quality of received signals.

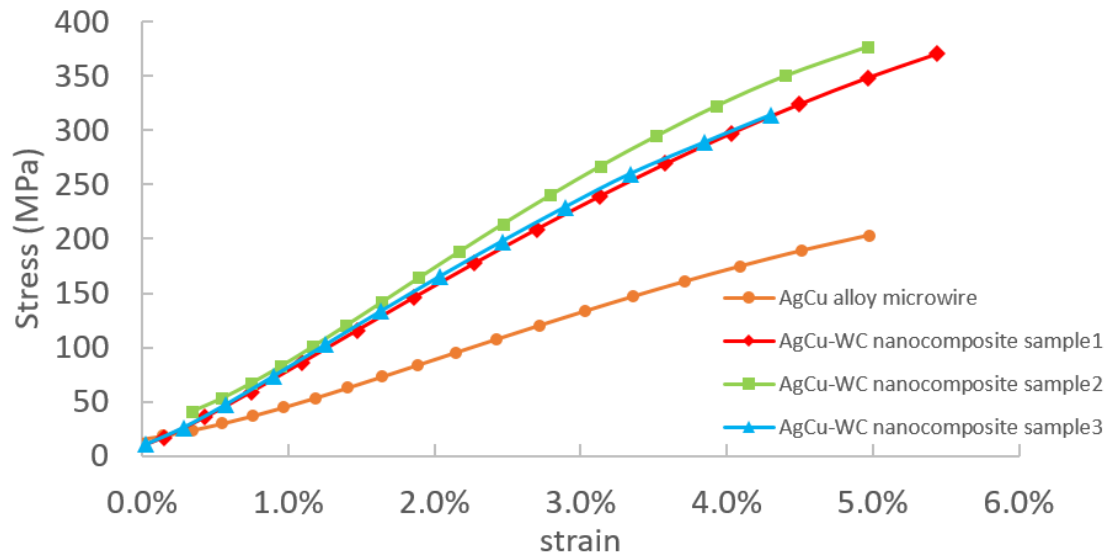


Figure 96. The result of tensile testing of nanocomposite microwires (AgCu_{40} -10 vol. % WC) and AgCu_{40} microwires

Table 13: Mechanical properties of the AgCu_{40} - 10 vol. % WC and AgCu_{40} microwires

	$\text{AgCu}_{40\text{wt.\%}}- 10 \text{ vol. \% WC}$	$\text{AgCu}_{40\text{wt.\%}}$
Ultimate tensile stress (MPa)	354 ± 35	203
Ultimate tensile strain	$5.2\% \pm 1.1\%$	5.0%
Yield stress (MPa)	280 ± 21	185
Microhardness (HV)	115 ± 16	90 ± 6

The self-dispersed WC nanoparticles remarkably improve the performance of AgCu_{40} alloy and provide opportunities for functional devices. However, there is still space for improvement in the process, and further research is needed.

5.4. Ag wire

Ag has been widely known as a useful metal for an abundance of applications, which include but not limited to electronics, energy devices, brazing and soldering, chemical synthesis, photography, antimicrobial, nontoxic medical products, and jewellery and silverware. Ag is also one of the most functional materials, due to its excellent resistance to corrosion and oxidation, and it has the best electrical and thermal conductivity among all metals. Ag micro/nanowires have been investigated for decades on the applications of conductive electronic devices. Tremendous research on Ag for decades found it challenging to enhance its strength while maintaining its prominent properties, such as ductility, conductivity, and chemical stability.

Metal matrix nanocomposite appeared to be an enlightening solution since the particle strengthening effect becomes remarkable when the particle size scales down to nanometers, and the interaction between nanoparticles and dislocation stands out [253]. It is well known that most of the particle incorporation methods see the challenge that the homogenous dispersion of nanoparticles is not achievable due to the poor wettability between the nanoparticle and metal matrix, inducing nanoparticle agglomeration and, consequently, overall non-uniform properties. Another challenge is that, due to the lack of efficient incorporation methods, most metal matrix nanocomposite encountered nanoparticle concentration limitation, unable to reach a high nanoreinforcement concentration [254]. Furthermore, Ag has rarely been studied as the matrix in nanocomposite due to the lack of suitable nanoreinforcements, and only a very limit amount of research has conducted Ag matrix nanocomposite manufacturing, using carbon nanotubes (CNT)[255], alumina (Al_2O_3)[256], and silicon carbide (SiC)[256] as the reinforcement. However, due to the dispersion issue, additional process, such as extrusion, was required to reach a better

homogeneity, not only making the nanocomposite fabrication method non-scalable but also damaging the malleability and ductility.

In this part of the work, Ag-WC nanocomposite with a homogeneous dispersion of high-loading (31 vol.%) nanoparticles was fabricated using a scalable and straightforward molten salt assisted stir casting method. It realized the self-dispersion to reach an extremely high concentration with no porosity and contamination. Molten salt assisted stir casting successfully enabled high concentration nanoparticle self-incorporation into the Ag matrix [202, 257] while prohibiting surface oxidation. Afterwards, melt pressing using a hydraulic press could further enhance the nanoparticle concentration to as high as 31 vol. %, while maintaining the dispersion homogeneity. Due to the nanoparticle precipitation and grain refinement, Ag-WC nanocomposites have been characterized and have shown an increasing trend on microhardness and a decaying trend on electrical conductivity. A fundamental understanding of the nanoparticle self-incorporation and self-dispersion will be discussed, followed by the results that Ag-WC nanocomposite has selectively modified its intrinsic properties, especially mechanical behavior.

5.4.1. Fabrication method

The salt assisted stir casting method followed the procedure as followed: First, the pure Ag bulk material was prepared and placed in a graphite crucible. Then, the crucible was heated up above the Ag melting temperature (961°C) inside an electric resistance furnace, with argon (Ar) gas protection. After Ag was melted, a 3-blade steel stirrer was placed right above the molten metal surface, preparing for mechanical mixing. Meanwhile, powder mixture containing WC nanoparticles (150nm, US Research Nanomaterials Inc.), sodium chloride (NaCl), and potassium aluminum fluoride (KAlF₄) powders at a volume ratio of 2:9:9, was loaded slowly into the crucible. The stirrer was turned on and tuned to 300 rpm for 30 minutes while the furnace temperature was

maintained at 1050°C. The metal melt was then taken out of the crucible and cooled down to room temperature under argon flow protection. After removing the white bulk salt on the top of the sample, the bulk metal matrix nanocomposite was successfully manufactured.

To further enhance the nanoparticle concentration, melt pressing was applied by a hydraulic press to improve the nanoparticle dispersion efficiency. The nanocomposite sample was placed in a graphite crucible with a graphite plate covering the top. The hydraulic press applied forces through the alumina pressing rod to the graphite plate when the induction furnace heated the nanocomposite sample to 1050°C with Ar protection. There was a very tiny gap (~1mm) between the graphite plate and the crucible allowed liquid metal squeezing out. The pressure was set to a maximum of 30 MPa to prevent breaking the graphite crucible. The high concentrated nanocomposite was very viscous so that only the low concentration part could be squeezed out through the fine gap. The very viscous part, which has highly concentrated nanoparticle left underneath the graphite plate, can be collected after cooling down to room temperature. The experimental demonstration was shown in Figure 97.

Steel blade stirring was designed for incorporation and dispersion efficiency. Because the interface between Ag melt and molten salt obtains a certain degree of surface tension, which was dominant in the nanoscale phenomenon, nanoparticles were easily trapped at the interface and took a long time to penetrate the surface. To solve this issue, mechanical stirring on an interface could sufficiently provide energy to support nanoparticle incorporation, accelerating the incorporation process and enhancing efficiency.

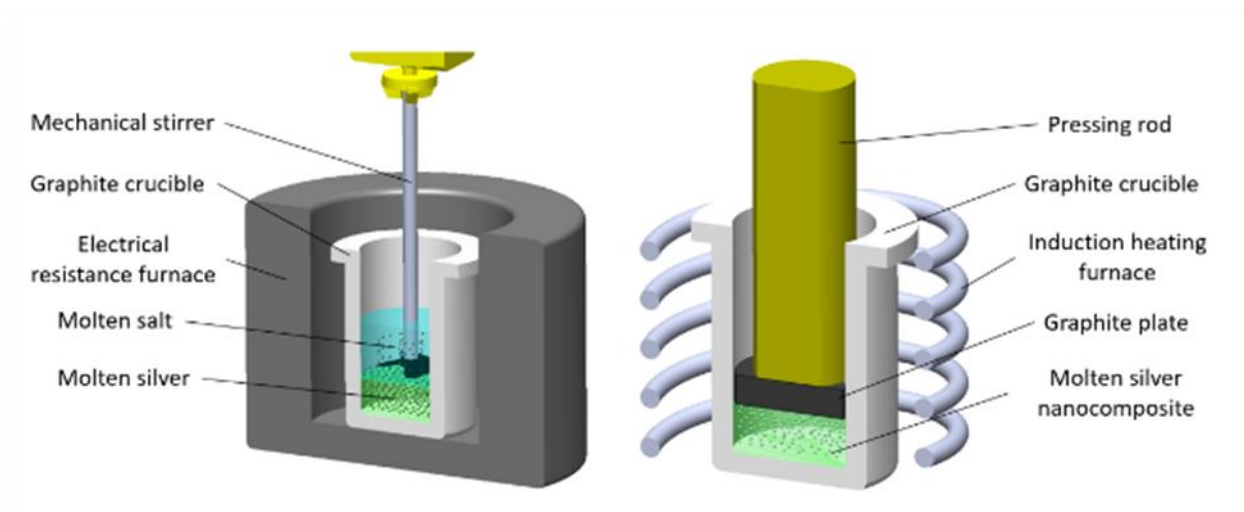


Figure 97: Experimental setup of salt assisted nanoparticle incorporation (a) and melt pressing using a hydraulic press (b).

5.4.2. Results

Ag-WC nanocomposite sample was ground and polished by SiC grinding paper and Al_2O_3 powders for characterization under Scanning Electron Microscopy (SEM) for microstructure analysis. Figure 98 showed the representative microstructure of Ag-WC samples of 8 vol.%, 15 vol.%, and 31 vol.% nanoparticle incorporation under SEM in backscattering mode. The brighter phase represented the WC nanoparticle, and the dark phase represented the Ag metal matrix. Low nanoparticle concentration samples indicated relatively non-homogeneous nanoparticle dispersion where “pseudo-dispersion” was observed, shown in Figure 98a-d. Pseudo-dispersion referred to the phenomenon that WC nanoparticles formed “microclusters,” where the nanoparticles are still separate from each other, in the samples. However, after using the melt pressing method to increase the nanoparticle concentration, the dispersion became homogenous without agglomeration and sintering, shown in Figure 98e-f. Further element characterization of the Ag-31 vol.% WC sample was carried out by energy-dispersive x-ray spectroscopy (EDX) characterization, including the EDX mapping of Ag and W, under the condition of 12.0 kV accelerating voltage and 22.0-degree

take-off angle, indicating significantly high W concentration as well as showing no porosity or salt contamination, illustrated in Figure 99.

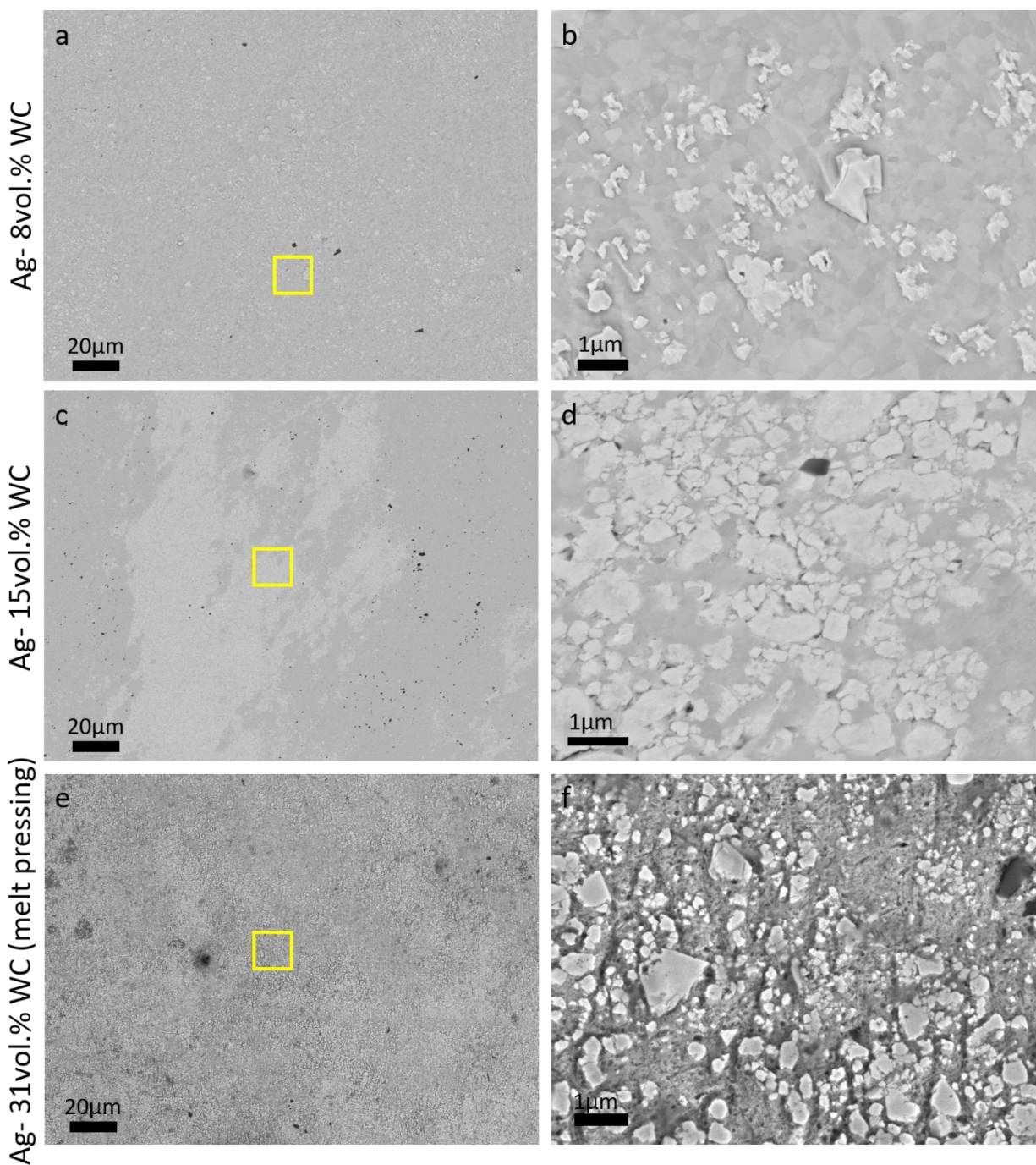


Figure 98: SEM images of Ag-WC nanocomposite samples with different nanoparticle concentration and the corresponding magnified images: (a) and (b) Ag-8 vol.% WC, (c) and (d) Ag-15 vol.% WC, (e) and (f) Ag-31 vol.% WC

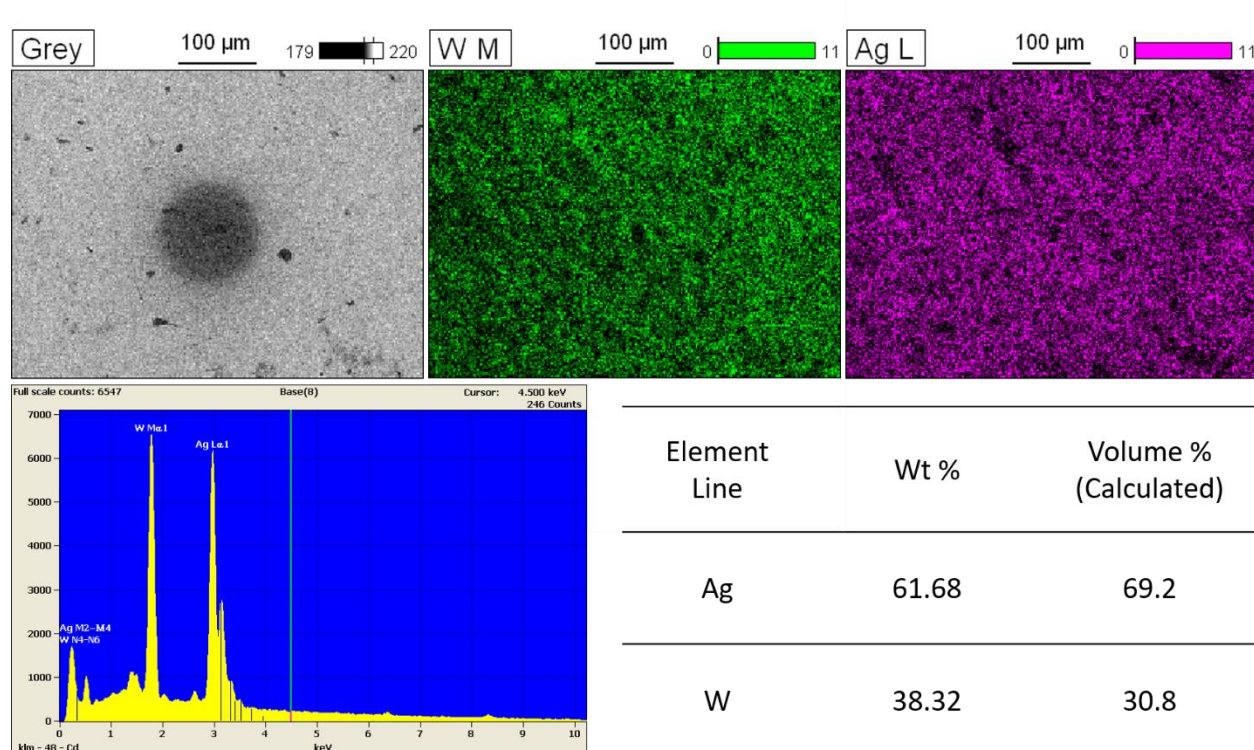


Figure 99: EDX analysis of Ag-31 vol. % WC illustrated the detection of tungsten (W) element and Ag element

The corresponding grain refinement effect was also measured on samples prepared by using etchant ammonium hydroxide (NH_4OH) and hydrogen peroxide (H_2O_2) to clean the surface. The incorporation of nanoparticles, even for the low concentration samples (Ag-8vol.% WC), significantly refined the grain approximately from a few millimeters to 200 nanometers, shown in Figure 100. Higher nanoparticle concentration, though, could further refine the grain, did not reduce the grain size as significantly.

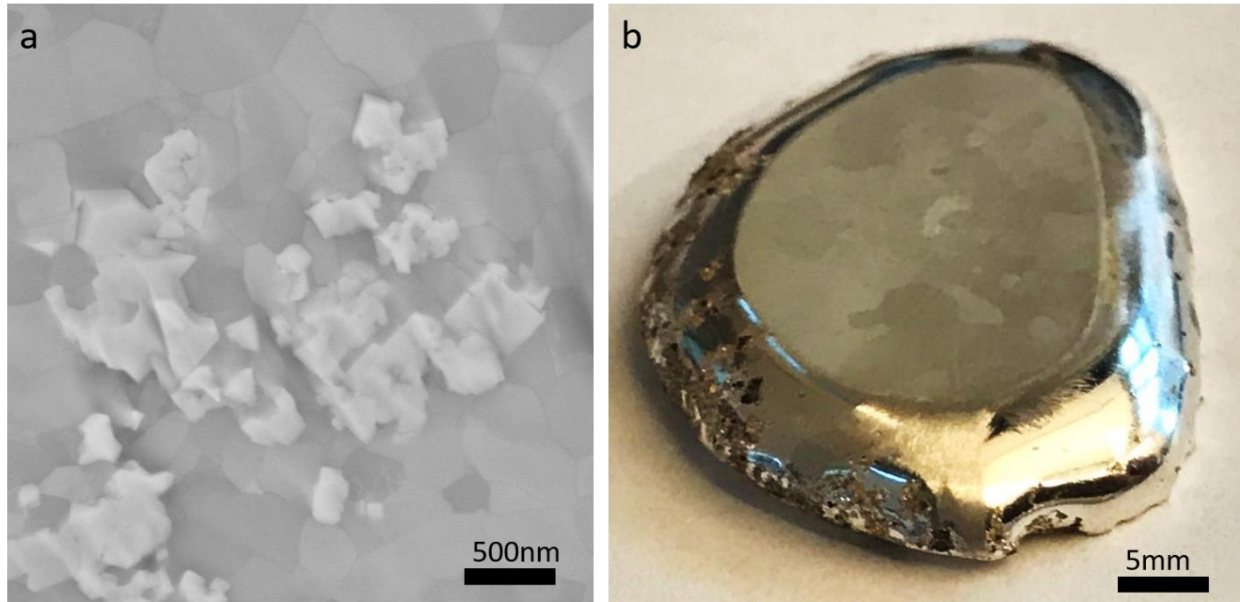


Figure 100: Images of (a) Ag-8 vol. % WC and (b) pure Ag samples grains produced by similar casting method and cooling condition.

Vickers microhardness test was performed on pure Ag and Ag-WC nanocomposite samples of different concentrations, using the standard testing condition (200gf, 10s) by *Microhardness tester LM 800AT*, shown in Figure 101. The nanocomposite sample of 22 vol. % nanoparticle raised the microhardness from 59.4HV to 137.6HV, following an increasing trend corresponding to the nanoparticle concentration. The near-exponential microhardness curve indicated that the microhardness enhancement of more than 200% could be contributed to the combination of nanoparticle precipitation and grain refinement.

Similarly, the electric conductivity test was performed on *CDE ResMap 178 4-point probe* to estimate the conductivity of nanocomposites. Samples were cut and polished to thin sheets around 500μm. The actual conductivity of Ag-WC nanocomposites produced by molten salt assisted stir casting shown an exponentially decaying trend, where 10 vol.% of WC nanoparticles incorporation could result in the conductivity reduction to around 30% IACS. Conductivity data for higher

nanoparticle concentration was not obtained because large samples of the highly concentrated nanocomposite were not fabricated in this research.

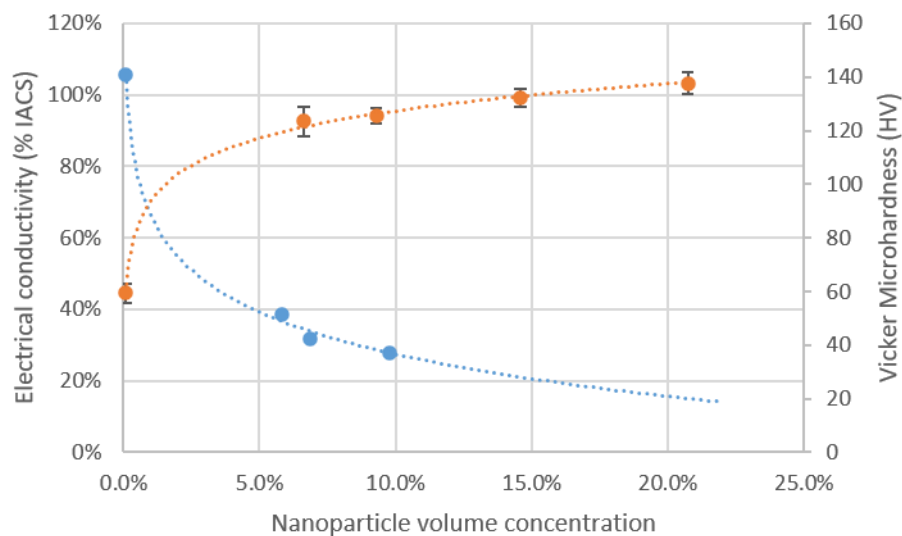


Figure 101: Electrical conductivity (left y-axis) and Vickers microhardness (right y-axis) of Ag-WC nanocomposite versus nanoparticle volume concentration

Ag microwire was also fabricated by thermal fiber drawing, shown in Figure 102.



Figure 102: Optical microscopy image of Ag microwire by thermal fiber drawing

5.4.3. Discussion

It has been the first time utilizing the good wettability between WC and Ag to initiate a self-incorporation of as high as 31 vol. % WC nanoparticles into the Ag matrix with porosity-free, sintering-free, contamination-free, and homogeneous dispersion microstructure.

Firstly, this work pioneers in using WC as the nanoreinforcement to enhance the mechanical properties of the Ag metal matrix successfully. It has also broadened the selection of nanoreinforcement to the Ag matrix, while WC particle was traditionally used to reinforce copper and copper alloy matrix [258]. A small contact angle ($\sim 40^\circ$) of molten Ag on the WC substrate at high temperature (e.g., 1050°) indicates a relatively small interfacial energy [259]. Thus, during the incorporation, the small interfacial energy could stabilize the nanoparticle self-dispersion by

the nanoparticle self-stabilization mechanism [127, 245]. Nanoparticle dispersion was enabled by the balance between particle-particle van der Waals attraction and the nanoparticle-molten metal surface tension. The homogeneous nanoparticle dispersion could be explained by the fact that a high energy barrier prevents nanoparticles from agglomeration. Thus, it became possible to produce Ag-WC nanocomposite with a high volume loading of nanoparticles (31 vol.%) with uniform dispersion and no aggregation.

Secondly, compared with other methods for Ag matrix composite fabrication, the molten salt assisted stir casting method is convenient and straightforward without extra high-energy post-processing. The entire incorporation process was simple, and the nanocomposite was produced by casting with few porosities. The nanocomposite produced from this method is valuable for the fundamental understanding of WC nanoparticle interaction in molten Ag. It should be noted that such a method left plenty of space for further property enhancement using rolling and forging, due to the high malleability.

Significant Vickers microhardness enhancement is the result of not only the nanoparticle strengthening effect but also the grain refinement during the solidification. Nanoparticles could effectively interact with the solidification front by blocking the solidification growth to refine the grain, leading to the better the mechanical strength. The near exponential decay in electrical conductivity concerning the nanoparticle volume concentration could be due to the boundary scattering as the dominant factor for Ag-WC nanocomposite. The nanoparticles have introduced significant electron scattering at the Ag-WC interface, while the incorporation of nanoparticles has also significantly reduced the grain size to induce more grain boundaries to the nanocomposite.

5.5. Zn-WC nanowire

Because of the need for degradable metal nanowire, this part of the work introduces the fabrication of Zn-WC nanowire and the characterization.

5.5.1. Bulk Zn-WC nanocomposite fabrication

Powder compaction was used for bulk material fabrication. WC nanoparticles (with an average size of 150 nm) and Zn powders (50 μm) were first mixed by a mechanical shaker (SK-O330-Pro) at 300 RPM for an hour. The powder mixture was loaded to a cylindrical stainless-steel mold with an inner diameter of 2 cm, followed by cold compaction using a hydraulic press (Carver laboratory press, Fred S Carver Inc.) with 58 kN force to obtain Zn-10WC (vol.%) pellets. The Zn-WC nanocomposite pellets were then placed in an alumina crucible and were melted in an electric resistance furnace under Argon (Ar) and Sulfur hexafluoride (SF_6) gas flow at 450 $^{\circ}\text{C}$ to disperse nanoparticles and eliminate porosity.

5.5.2. Zn-WC nanocomposite thermal drawing preform

Molten Zn-WC nanocomposite was then sucked into a 30 cm-long borosilicate glass tube (inner diameter: 1mm, and outer diameter: 6.5 mm) by a vacuum pump to make the thermal drawing preforms. The 30 cm-long preforms were finally fabricated through sealing both ends under vacuum by a high-temperature torch.

5.5.3. Zn-WC nanocomposite thermal drawing procedure and parameters

The Zn-WC nanocomposite preform was fed into an electric resistance furnace with a constant feeding speed (v_f). The temperature of the furnace was set to 820 $^{\circ}\text{C}$ (1093 K), which is an optimized temperature to obtain the most suitable cladding viscosity ($10^{6.6}$ Pa·s) for thermal drawing, after considering the softening point of borosilicate glass and the metal core - furnace temperature difference. The heated preform in the furnace was narrowed down when the

temperature increased above the softening point, and the fiber was further pulled down at a constant speed (v_p) by a motor-connected wheel. In a steady-state, the diameter of the drawn-out fiber is determined by the draw-down ratio D_r :

$$D_r \equiv \frac{v_f}{v_p} = \left(\frac{d_p}{d_f} \right)^2$$

where v_f , v_p , d_p and d_f are the fiber pulling speed, the preform feeding speed, the diameter of a preform, and the diameter of a drawn fiber, respectively. After the first drawing, the metal-in-glass fiber was collected and was inserted into another borosilicate glass tube, working as the preform for the next thermal drawing cycle. During the second drawing process, layers of glass cladding could merge, forming a thicker cladding. The thermal drawing parameters were recorded in Table 14.

Table 14: Thermal fiber drawing parameters and dimensions of preform/drawn wires

Cycle	Preform core diameter (μm)	Preform cladding diameter (mm)	Feeding speed (mm/s)	Pulling speed (mm/s)	Drawn-down ratio (D_r)	The expected core diameter of drawn wires (μm)	Drawing temperature (°C)
1	1000	6.5	0.1	19.6	196	71	820
2	71	5.5	0.1	40	400	3.55	820
3	3.5	5.5	0.1	40	400	0.178	820

5.5.4. Zn-WC nanowire characterization

The fiber was firstly mounted vertically on epoxy and polished to expose the metalcore. Then, the cross-section was characterized under SEM at low excitation energy, while using focused ion

beam (FIB) etching to peel off a thin layer on the top to prevent any polishing powder residues from interfering with the characterization. For characterization of bare wires, a combination of HF wet etching and AOE oxide etching (STS MESC Multiplex AOE, SPTS Technologies Limited, 90 minutes) was performed. Due to the chemical reactivity of Zn, nanowires can barely be taken out of the borosilicate cladding massively by any scalable etching method to dissolve the glass claddings. Thus, AOE etching was utilized to slowly remove the glass cladding residues after hydrofluoric acid (HF) wet etching (35 minutes, 49% aqueous). The bare Zn-WC nanocomposite nanowires were finally exposed for characterization under SEM.

Drawn fibers were characterized by optical microscopy and SEM for thickness and continuity verification. Nanocomposite wires within borosilicate glass cladding after each thermal fiber drawing cycle were fixed in epoxy, and the cross-sectional surfaces were cut and polished, followed by 20nm-thick Pt deposition for optical microscopy and SEM characterization. Focused ion beam (FIB) was used to further cut and polish the cross-sectional surface of the nanowire after the third drawing for wire diameter measurement. The diameter of nanocomposite micro/nanowires were measured, which decreased from 70 μm (Figure 103a, b) cross-sectional SEM images of Zn-WC nanocomposite nanowires after the first drawing (65 μm). (c, d) after the second drawing (5.8 μm). (e, f) after the third drawing (170nm). (g) EDX line scanning of Zinc-WC nanowire on the cross-section in (f).a and b) to 6 μm (Figure 103c and d) and eventually to 171nm (Figure 103e and f) after three cycles of thermal fiber drawing. EDS line scanning was performed further to confirm the intensity of element Zn across the nanowire, showing that Zn-WC nanocomposite wire reached a diameter of 171nm (Full-Width-at-Half Maximum) in Figure 103g.

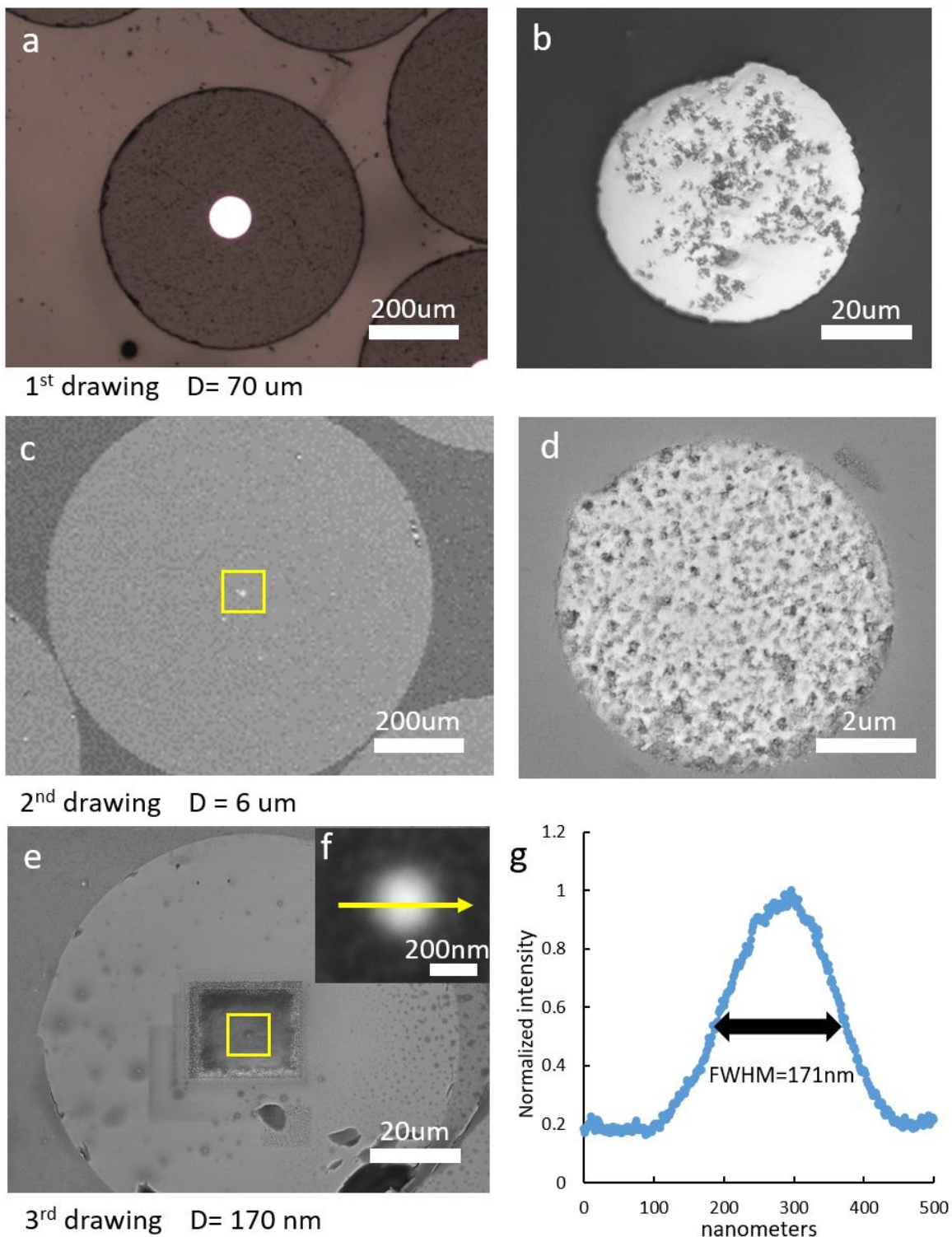


Figure 103: (a, b) cross-sectional SEM images of Zn-WC nanocomposite nanowires after the first drawing ($65 \mu\text{m}$). (c, d) after the second drawing ($5.8 \mu\text{m}$). (e, f) after the third drawing (170 nm). (g) EDX line scanning of Zinc-WC nanowire on the cross-section in (f).

Although optical micrographs cannot measure the nanowire diameter due to the resolution limit, it could still be utilized to verify the continuity of the 170nm Zn-WC nanocomposite wire, as shown in Figure 104a and b. In order to expose the bare nanowire, a small piece of such nanowire preserved in glass cladding sitting on silicon wafer went through an anisotropic oxide etching, removing all cladding glass except those directly underneath the nanowire. SEM images from the top view and isometric views are shown in Figure 104c-f. WC nanoparticles could be observed on the nanowire, where most of them are separated and partially exposed to the surface. The nanocomposite nanowire was also cut at the position where WC nanoparticle sits on the wire, using the FIB for cross-sectional atomic analysis by TEM (Figure 104g). Zn and WC crystalline phase and their corresponding images obtained from fast Fourier transform were shown in Figure 104h-m.

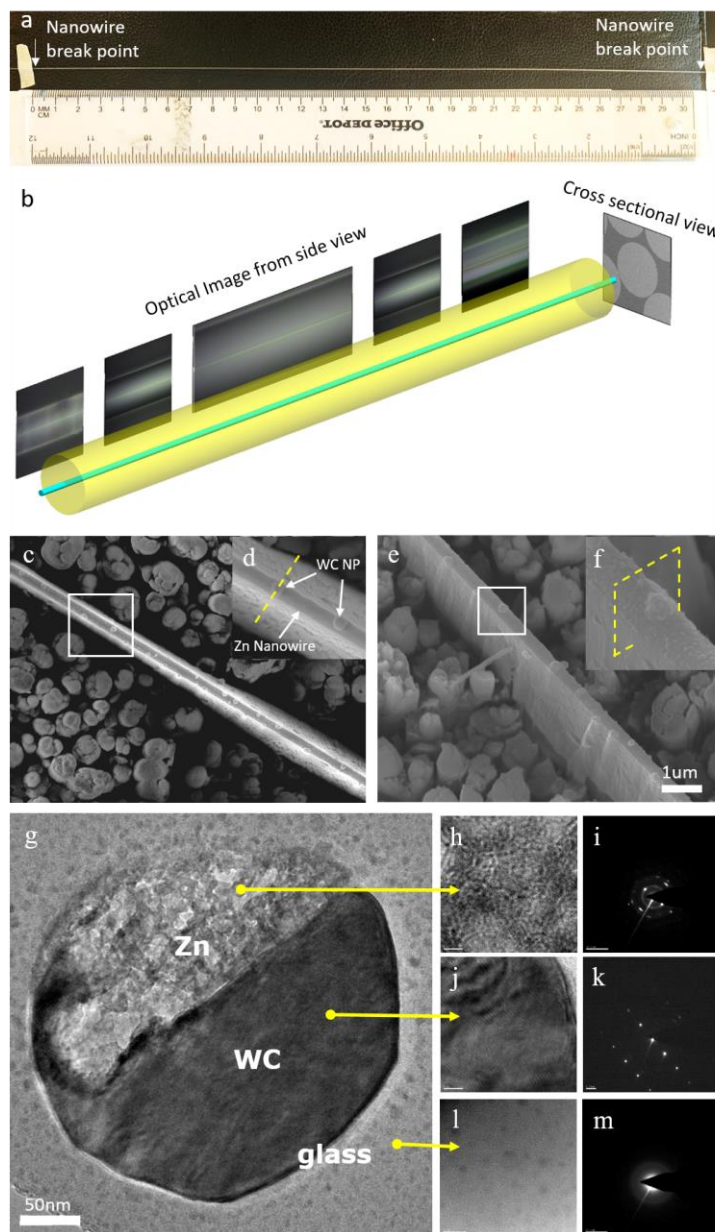


Figure 104: Characterization of Zn-WC ultrafine/nanowires. (a) 31cm long Zn-WC nanowire measured by a ruler. (b) Demonstration of the characterization of nanowire continuity optical microscope. Top view (c) and isometric view (e) of Zn-WC nanocomposite nanowire after AOE deep etching through SEM, and (d) and (f) are the corresponding magnified images. (g) TEM characterization of the cross-sectional samples shown in (d) and (f) by the dashed line. (h), (j) and (l) are the TEM image of high magnification for zinc, WC nanoparticle, and surrounding Pyrex glass, respectively (Scale bar 1nm). (i), (k) and (m) are the corresponding images from fast Fourier transform.

As benchmarked in Figure 105 with metal nanowires manufactured by various methods including thermal fiber drawing, electrospinning, and laser drawn-cast process, the nanocomposite nanowire demonstrated in this work exhibits a record-high aspect ratio of 1.8×10^6 . Data from the literature have been specified in Table 15. Further note that this even exceeds that of metal nanowires produced by chemical synthesis [260-262], which has been one of the most reliable methods for metal nanowire fabrication to date.

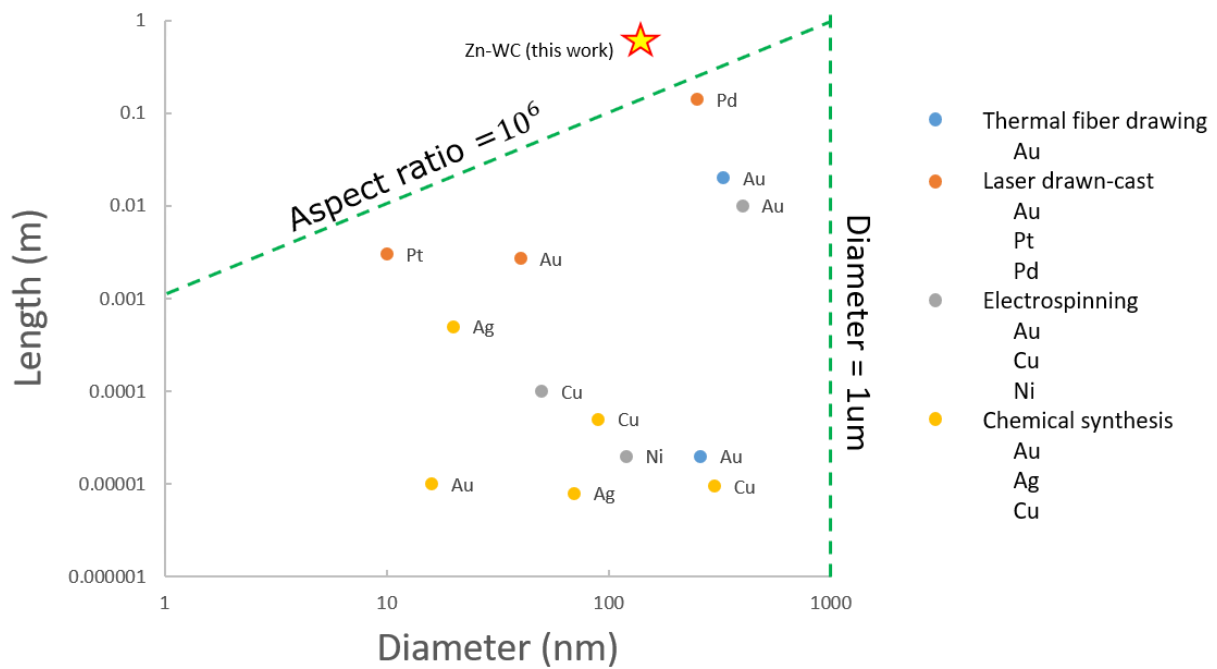


Figure 105: Nanowire manufacturing methods, including thermal fiber drawing, electrospinning, laser drawn-cast process, and chemical synthesis and our works

Table 15: Nanowire manufacturing methods and results from this work and the literature.

	Core material	Cladding	core diameter	length	reference
Thermal fiber drawing	Au	Fused silica	260 nm	20 μ m	[181]
laser drawn-cast	Pd	Fused silica	250nm	140mm	[263]
	Pt	Quartz	10nm	3mm	[189]
	Au	Quartz	40nm	2.7 mm	[189]
electrospinning	Cu	N/A	50-200nm	100 μ m	[190]
	Au	N/A	400nm	10mm	[191]
	Ni	N/A	120nm	>20 μ m	[264]
chemical synthesis	Ag	N/A	70nm	8 μ m	[265]
	Cu	N/A	90-120nm	40-50 μ m	[260]
	Au	N/A	16-66nm	10 μ m	[261]
Nanoparticle controlled thermal fiber drawing	Zn-WC	Pyrex	170nm	31mm	This work

5.6. Nanoparticle Pinning Effect to Overcome Fluid Instability at Nanoscale

Theoretically, ultra-long nanowires could not survive due to fluid instability intrinsic to the conventional thermal drawing process. When the size of metal ultrafine/nanowires and nanoparticles approach the same order of magnitude, the equations involving nanoparticles-modified viscosity and interfacial energy will break down because the nanoparticle dispersion could no longer be assumed homogeneous. Therefore, the existence of high aspect ratio nanowires, as demonstrated in this work, should result from effect(s) other than substantiated control of fluid instability.

One possible reason for the nanoparticle-enabled instability control is the nanoparticle pinning effect based on phenomena observed in the exposed Zn-WC nanowires:

- WC nanoparticles exist on the interface between the metal core and the cladding, instead of being embedded inside the metalcore. This phenomenon could be due to the extremely high viscosity and low flowability at the local area that squeezes the nanoparticles out of the molten metal threads during the thermal fiber drawing process, even though molten Zn wets WC well.
- WC nanoparticle is homogeneously distributed along the nanowire without agglomeration or sintering. The experimental measurement of nanoparticle-to-nanoparticle distance is 631nm. Theoretically, when nanoparticles of 150nm in diameter are evenly distributed long the zinc nanowire with a diameter of 170nm, the inter-particle spacing is about 769nm, which matches the measured inter-particle distance well.

Such phenomena could induce a pinning effect and reduce the instability wavelength, thus effectively suppressing the fluid instability during drawing. The pinning effect describes the phenomenon where nanoparticles on the nanowire surface act like “permanent nodes” for the varicose perturbation waves. In this case, WC nanoparticles adhered to the zinc-glass surface would act as nodes for the varicose perturbation. The distance x_i between the nanoparticles at the interface could sufficiently define the viable wavelength that:

$$x_i = n\lambda/2$$

$$n = 1, 2, 3, \dots$$

More nanoparticles exist on the zinc-glass surface results in the existence of nodes so that these randomly distributed nanoparticles could individually affect the wavelength according to

$$\lambda = \frac{2x_i}{n_i} = \frac{2x_1}{n_1} = \frac{2x_2}{n_2} = \frac{2x_3}{n_3} \dots$$

Nanoparticles, thus, could sufficiently modify the varicose perturbation wavelength to a minimal value. This phenomenon, in turn, would help to obtain a much smaller G value, ultimately increasing the associated instability growth time. This pinning effect utilizing nanoparticles as nodes hence helps to stabilize the thin metal thread longer to overcome the fluid instability during thermal fiber drawing. The theoretical demonstration of the nanoparticle pinning effect was shown in Figure 106.

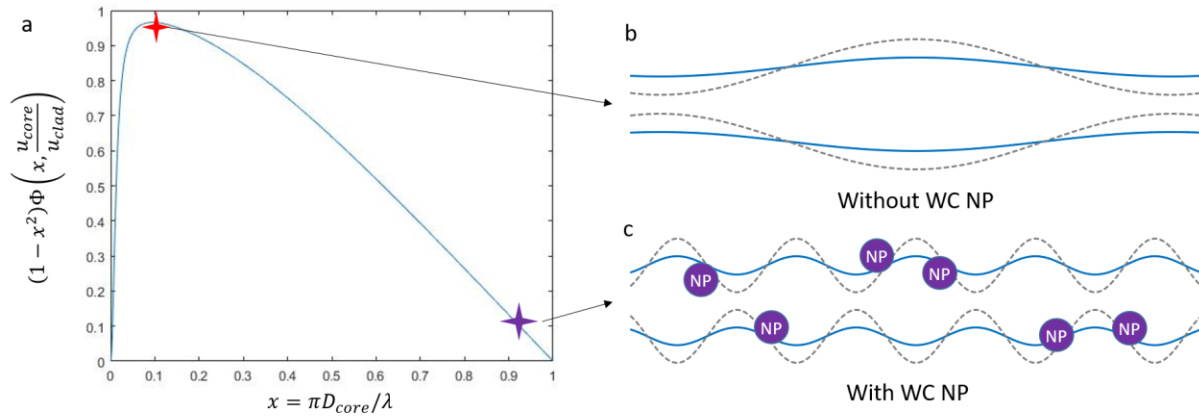


Figure 106: Nanoparticle pinning for instability control (a) Plot of function G for the actual viscosity ratio at 950 °C. (b) and (c) are the demonstration varicose perturbation waves with and without nanoparticles. The long-wavelength corresponds to large G value and short associate instability growth time, and the short wavelength with nanoparticle pinning as nodes refers to small G value and relatively long associate instability growth time.

Chapter VI: Summary

This work has studied the nanoparticle particle effects on metals for biomedical applications. By demonstrating the Zn-WC nanocomposite system and its unprecedented properties, this work provided an innovative material for bioresorbable stents. Zn-based nanocomposites are proposed as a new material for biomedical applications since nanoparticles can introduce strengthening effect and thermal stability. The major achievement of this study is summarized below:

This study has firstly achieved the fabrication of Zn matrix nanocomposite fabrication using molten salt assisted stir casting and ultrasound processing while realizing homogeneously dispersed nanoparticles. This method has proposed a scalable, highly efficient, and cost-effective method for Zn-WC nanocomposite fabrication by far. Nevertheless, the material properties have been significantly enhanced with 90% and 200 % increment in UTS and YS, respectively, with less than 5 vol.% WC nanoparticles. Furthermore, it has first shown the phenomenon of increasing strength with not elongation reduction because of the highly uniform nanoparticle dispersion. The in vitro electrochemical test and immersion test has proven a suitable degradability for the cardiovascular stents while indicating no toxic ion releasing during the degradation.

Furthermore, this work detailedly analyzed the WC nanoparticle interaction with Zn and Zn alloy matrix in the aspect of microstructure and mechanical properties. WC nanoparticles could efficiently enhance the mechanical strength by Orowan strengthening and grain refinement. In addition, nanoparticles generally serve as the nucleation sites for intermetallic formation during the solidification due to the higher energy at the nanoparticle interface. Specifically, for the system of Zn-Mg-WC, WC nanoparticles have deflected and guided the intermetallic formation and growth to alter the intermetallic morphology. Thus, the corresponding mechanical performance of Zn-Mg was altered correspondingly. Zn-Mg-WC has been proven to have a significantly improved

thermal stability with anti-aging property, while the ductility was enhanced for Mg with 0.2-0.6 wt.%. Overall, the nanoparticle has been proven as an agent for intermetallic modification for better ductility. The prototype of a bioresorbable stent was successfully fabricated using this material and was proven to be functional in the angioplasty (deployment) testing, awaiting in vivo biological characterization.

Additionally, by utilizing the enhanced viscosity and decreased surface tension of molten Zn-WC, ultralong metal nanowire was fabricated by thermal fiber drawing to break the fundamental limit of the fabrication capability. Nanoparticles were also proven as a surface modifier to stabilize the liquid instability during the fabrication process. A 170nm Zn nanowire with an aspect ratio of 1,800,000 was fabricated in this study, realizing a world record for metal wire fabrication.

Chapter VII: Future work

7.1. A systematic study on Zn-Mg-WC system and additional Zn alloy matrix nanocomposite systems

Although this work has performed mechanical analysis on Zn-Mg-WC with Mg concentration from 0 wt.% to 0.7 wt.%, a systematic study on Mg concentration will need to be addressed in the future. Furthermore, a more detailed intermetallic formation and growth process will need to be further characterized using advanced technique, e.g., in-situ X-ray.

This work has only been investigated in pure Zn, Zn-Mg, and Zn-Fe systems with effect from WC nanoparticles. Zn-Li system will also need to be studied because it also has an age-hardening effect. Apart from the mechanical properties of the innovative nanocomposite material, other properties will need to be thoroughly studied in the future, such as the degradable mechanism and the biocompatibility.

7.2. Hot extrusion of Zn nanocomposite

In this work, the current fabrication method excluded the hot tube extrusion due to the lack of commercial machines. However, according to the industrial requirement, the fabrication using standard tube extrusion methods would be more suitable for large scale fabrication, and the fabrication procedure could be easily standardized. Even though the principles of work hardening are similar between hot rolling and hot extrusion, there are minor differences between microstructure and the corresponding mechanical performance. Scifacturing lab has already performed Al matrix nanocomposite fabrication using extrusion, obtaining highly equiaxial grain structure and homogeneous nanoparticle dispersion. In the future work, hot tube extrusion is required for stent fabrication followed with tube laser cutting.

7.3. In vivo studies in animal models

This work has indicated the feasibility of Zn matrix nanocomposite as biomaterials and initiated prototype fabrication. The next step would be a thorough material optimization and in vivo biological characterization on animal models. Although the materials studied in this work showed no harmful response from in vitro experiments and received positive responses from cell culture, in vivo experiments to evaluate the response from animal models would be more critical. The biological response from animal models could indicate the degradation mechanism and determine the material toxicity. Furthermore, it would guide material composition optimization for the final product.

7.4. Investigation in other biodegradable applications

Apart from the bioresorbable stent, Zn-based nanocomposites have potentials in related implant applications, e.g., biodegradable bone plates and screws. For applications with high strength requirements, creep resistance would stand out as another important property for evaluation. Based on the review of the literature, nanocomposite would enhance the creep resistance by the Zenner effect by pinning the grain boundaries. A thorough study on creep behavior will need to be carried out to understand the fatigue-resistant enhancement mechanism.

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