Mechanics of Biomaterials for Regenerative Medicine

Yevgeniy Kreinin, Iris Bonshtein, and Netanel Korin

Abstract The mechanical properties of biomaterials play a critical role in designing and developing medical products and selecting suitable materials for various applications. This is particularly important in regenerative medicine, where the biomaterials interact to heal tissues and restore function.

In this chapter, we define diverse types of biomaterials and describe their mechanical characteristics. Conventional methods for measurement of the mechanical properties of biomaterials will be described. The investigation of the mechanical behavior of tissues and biomaterials for regenerative medicine will be discussed, as well as functional biomechanical tests for different applications. At the end, two examples focusing on applications for biomaterials in the cardiovascular area will be presented: (1) An aneurysm embolic hydrogel; (2) A polymeric artificial heart valve.Graphical Abstract

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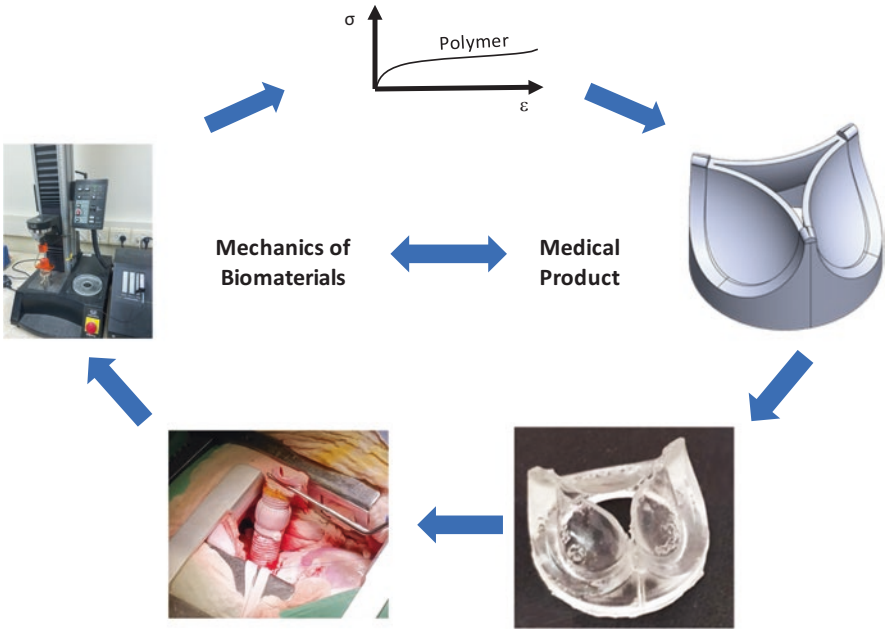

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1 Biomaterials: Classification and Their General Mechanical Properties

Biomaterials are materials designed for biomedical or clinical applications and thus can interact with biological systems for medical purposes. Depending on the nature of the chemical bond, biomaterials can be categorized into four main groups: (i) ceramics, (ii) metals, (iii) polymers, and (iv) hybrids. As these material structures vary by their characteristic chemical bond (covalent, ionic, or metallic), they possess different properties, and thus are utilized for different applications in the body. Another categorization is synthetic or natural biomaterials, where synthetic biomaterials include, for example, metals, ceramics, non-biodegradable polymers, and biodegradable polymers, while nature-derived biomaterials include for example, hyaluronic acid, chitin, cellulose, silk, chitosan, gelatin, and fibrin.

As mentioned above, biomaterials of different classes are characterized by different mechanical properties, *see* Fig. 1. Generally, these mechanical properties are derived by studying the mechanical behavior of materials upon subjecting them to a defined mechanical stimulation. Stress and strain are basic terms used to describe

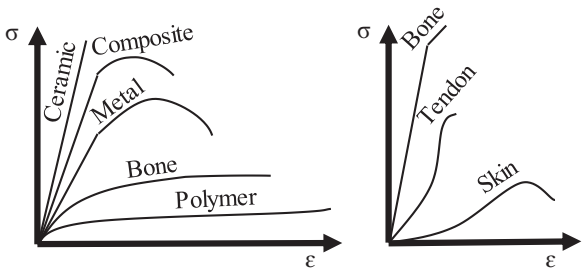

Fig. 1 Material Stress-strain curve, on the left for different materials classes, on the right for different tissues

the behavior of a solid object to external mechanical stimulations. When a force is applied to a material (e.g., a plate made of a biomaterial) the internal forces that resist the externally applied force produce internal local stresses (area normalized forces) within the material, which also cause it to deform and thus the structure of the material undergoes geometrical changes. A measure for the deformation of a solid material is strain, which can be related to the change in a defined length compared to its original unstressed length. Biomaterials of different classes present different stress-strain relationship and are accordingly characterized by different mechanical properties, *see* Fig. 1.

Ceramics have the following mechanical characteristics: they are relatively strong (high failure stress), have high mechanical stiffness (high elastic modulus), are brittle (low strain to failure), and possess low toughness (low energy to failure). Bio-ceramics are used in medical devices as rigid materials in applications that include surgical implants for bone and cartilage regeneration or dental and hip prostheses. The main disadvantage of ceramics is their brittleness, which is the tendency of a material to fracture or break without plastic deformation when subjected to stress, particularly under rapid loading or impact. Metal biomaterials have similar high elastic modulus and yield strength; however, they are ductile, allowing them to bear a load and carry plastic deformation without rupturing. Their medical applications are similar in scope to ceramic materials and include bone regeneration and dentistry prostheses.

Natural and synthetic polymers are relativity weak (low resistance to mechanical stress), soft (low modulus of elasticity), ductile (high strain to failure), and tough (high energy to failure). Polymers have been used in bone, cartilage, tendon, and ligament regeneration, among other applications. The advantage of synthetic polymers over natural materials is that they allow to modulate their mechanical properties, and hence can be also used in cardiovascular and bone cements, suture threads, orthopedic screws, and prostheses manufacture.

Natural and synthetic hydrophilic polymers can also form hydrogels, water-soluble polymer networks that can hold a considerable amount of water (>10%) while maintaining their structure. Hydrogels are used in a variety of industries, most notably in the medical field. Although hydrogels are relatively weak, they can withstand large deformations and display complex mechanical behavior. Hydrogels can exhibit both elastic and viscous behavior, which is known as viscoelasticity. The viscoelastic properties of hydrogels are dependent on their composition,

cross-linking density, and water content and can be characterized by their storage modulus, loss modulus, and complex modulus. The mechanical and transport properties of hydrogels, as well as their mass transport properties make them attractive biomaterials for various applications in tissue engineering and regenerative medicine, including drug delivery, wound healing, and hard and soft tissue regeneration [1].

Hybrid biomaterials (a composition of different biomaterials such as natural or synthetic polymers, ceramics, or metals) can have appreciable mechanical strength and hence can be used in hard and soft tissue. This class of material may offer superior mechanical properties compared to non-hybrid materials; however, their design, manufacturing, optimization, and regulations may be more challenging.

2 Mechanics of Biomaterials for Regenerative Medicine and Viscoelasticity

The mechanical properties of a biomaterial for regenerative medicine have a profound impact on the tissue to be treated and can determine the effectiveness of the tissue repair. In most cases for tissue regeneration, the general dogma is that a biomaterial that is optimal to replace a specific tissue should mimic its mechanical properties. The biomaterials need to provide temporary mechanical support as well as serve as a suitable environment for tissue regeneration. Biomaterials that are stiffer than their surrounding tissue can lead to tissue resorption. Thus, the aim is to design the biomaterial to be strong enough to prevent its mechanical failure but soft enough to avoid tissue resorption. Moreover, most tissues are complex structures that contain both liquid (water) and solid and are thus naturally viscoelastic materials. Viscoelastic materials integrate both viscous and elastic mechanical reactions to mechanical loads. The viscous reaction is time and rate dependent, while the elastic reaction is immediate. The time-dependent reaction can be observed, for example, in a creep response whereupon an immediate increase in the load to a new level of stress that remains constant, the instant change in strain (elastic response) is followed by an increase in the strain over time (creep), *see* Fig. 2a. Another effect is stress relation, in which an immediate increase in the strain results in an immediate change in the stress (elastic response) followed by a reduction in the stress over time (stress relaxation), *see* Fig. 2b. Additionally, while purely elastic materials do not dissipate energy when stress is applied and then released, viscoelastic materials do. Thus, the stress-strain curve of a viscoelastic substance shows hysteresis, which implies loss of energy during a stress cycle, *see* Fig. 2c [2]. Moreover, when cyclic sinusoidal stress is applied, a phase lag occurs between the stress and strain. The phase lag, defined by shift angle δ in the response, represents the viscoelastic damping of the material ($\delta = 0$ for elastic material and $\delta = 90$ for pure viscous liquids), *see* Fig. 2c. Additionally, the response to axial stress can be separated to the storage modulus E', which is a measure of the stored

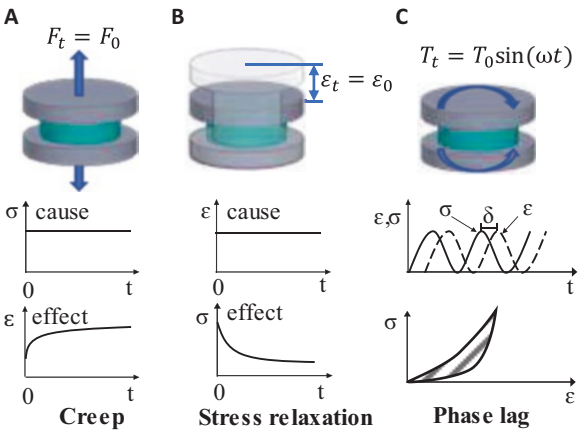

Fig. 2 Characteristics of a viscoelastic material (**a**) creep (**b**) stress relaxation (**c**) phase lag upon cyclic loading and hysteresis during a cycle (bottom graph)

energy, representing the elastic portion, and the loss modulus E" which is a measure of the dissipated energy, representing the viscous portion. Similarly, a shear storage and a shear loss modulus, G' and G'', respectively, can be defined for the case of shear stress and strain. Altogether, viscoelastic materials are characterized by a complex modulus that can be used to describe their dynamic behavior [3].

3 Measurements of the Mechanical Properties of Viscoelastic Biomaterials

To develop biomaterial-based products for regenerative medicine, the basic mechanical properties of the material need to be defined as they critically affect the product's performance. These mechanical characterization measurements are based on applying a defined force to a sample and measuring the resulting deformation, or vice versa. The type of the applied load and deformation can differ based on the type of the instrument and measuring modality. Additionally, mathematical models describing the material's mechanics (constitutive models) are needed to extract the material properties based on the measurements. Furthermore, it is also important to define relevant standards for the measurement conditions and the measurement should be performed in a relevant physiological environment as needed (buffer, temperature, etc.). For example, most biomaterials are designed to function in an aqueous environment, and an aqueous environment may be valuable for hydrogel mechanical response. Below, we briefly describe four basic methods for measuring the mechanical properties of biomaterials, *see* Fig. 3.

Tensile Test: The tensile method is well-established and widely used for measuring materials' mechanical properties. In this method, the material is stretched by applying forces near its ends in opposite directions. The simplest form of tensile testing is uniaxial, where the sample is stretched along one axis. The material

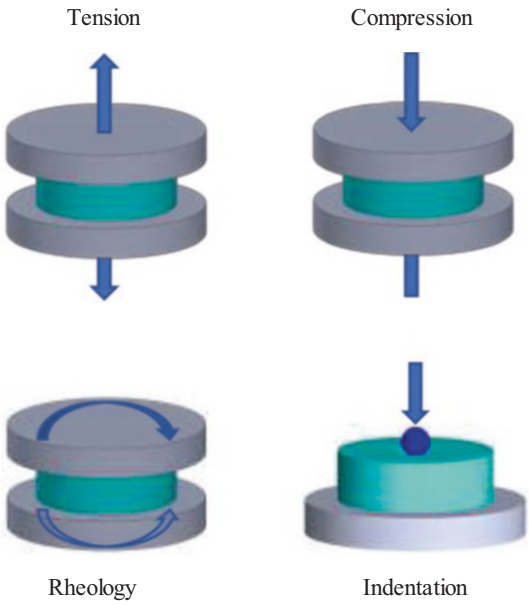

Fig. 3 Different methods for measuring mechanical properties of biomaterials

specimens are prepared in a dumbbell or dog-bone shape. Since usually, biomaterial specimens are hydrated and soft, it is not easy to grip them properly for tensile testing. Once the clamped biomaterial specimen is stretched at a uniform deformation rate up to a certain level of strain, the relationships between the deformation and stress can be extracted and its elastic modulus can be calculated (for elastic solids). Temporal changes can also be tracked to evaluate viscoelastic behavior and properties, such as in creep and stress relaxation experiments.

Compression Test: Another similar and well-established method for materials elasticity measurement is the compression test method, which is most relevant for testing biomaterial in applications where compression is the main loading modality. In this method, biomaterial samples are usually prepared in a disc form and compressed using a controlled force while their deformation is measured, *see* Fig. 3. Then the applied force and resultant biomaterial deformation are converted to compressive stress and strain. For linear elastic materials, the elastic modulus of the material specimen can be determined from the slope of the obtained stress-strain curve. Temporal changes can be tracked to evaluate viscoelastic behavior and properties.

Rotational Rheometery: A rotational rheometer is a laboratory device that is frequently used to measure how fluids or viscoelastic materials (e.g., hydrogels and polymers) "flow" or react in response to applied oscillating rotation/torque that produces shear forces, *see* Fig. 3. A biomaterial specimen is placed between the top and base plates of the rheometer, it is then slightly compressed to ensure its stable interaction and the top plate oscillates at a desired frequency and shear

strain. As the specimen is twisted and undergoes shear deformation, it exerts a resistant shear force on the oscillating plate. The rheometer simultaneously measures the rotational motion and the applied torque. Based on these measurements at different frequencies and amplitudes, it is possible to measure the complex shear, shear storage, shear loss moduli, and loss angle (G, G', G', δ), *see* Fig. 2c [4].

Indentation test: In this method, a material is locally indented at a single point to a predetermined displacement depth while measuring the reaction force required to cause the indentation, *see* Fig. 3. The displacement can be measured via a tip gauge or using optical-based measurements. A force-displacement curve is used to calculate the elastic modulus of the material. This approach allows local measurements within a specimen and can be performed at different scales [4]. This method also can be done in specimens that are difficult to grip for tensile or compressive mechanical testing, allows relatively small volumes of material (micro\nanoscales), and can be performed in a specific area of interest within a specimen and on multiple different locations in the material's surface [5].

4 Functional Mechanical Tests for Different Biomaterial Applications

In addition to the standard mechanical tests of the biomaterial, every tissue/biomedical application has unique properties that must be considered and tested as per its application. Thus, functional mechanical tests are important for evaluating the performance of biomaterials in designated applications as well as for standardized testing for approval of the treatment/device. The choice of test will depend on the specific application of the biomaterial and the properties that need to be evaluated.

For example, in the case of soft-tissue adhesives, the shear adhesion can be measured by the lap shear test, which is used to evaluate the shear strength of a bond between two materials. Specimens are pulled in a direction parallel to the bond line. The maximum force that the bond can withstand before it fails is recorded as the lap shear strength. A standard test method for strength properties of tissue adhesives via lap-shear by tension loading has been defined (ASTM F2255-05). The standard is intended to provide a mean for comparison of the adhesive strengths of tissue adhesives intended for use as surgical adhesives or sealants on soft tissue [6].

Another example for functional mechanical tests is such tests performed for vascular grafts, which include burst pressure, compliance, and suture retention tests. The standard that defines these tests is the standard for cardiovascular implants – tubular vascular prostheses (ISO 7198:2016). Burst pressure is a critical parameter for vascular grafts as the graft needs to endure physiological hemodynamic pressures. The burst pressure test measures the greatest pressure before graft failure. Compliance tests measure the geometrical 3D change of a graft as a function of the change in the vessel's internal pressure. Compliance mismatch between the host

vessel and vascular graft can lead to serious pathological events such as intimal hyperplasia and vessel occlusion. The graft should also have enough strength to endure the forces applied by sutures without failure. This is tested by suturing a graft that was cut in its middle, sutured back together, and then pulled at a constant rate until it fails. The maximum tensile force that it can withstand is the suture retention strength [7].

Other widely used mechanical tests also include wear tests, fatigue tests, and bending tests, among others. Wear test measures the resistance of a biomaterial to wear and tear. It is commonly used for testing the durability of materials used in joint replacements and dental restorations. Bending tests are used to measure the resistance of a biomaterial to bending forces. It is commonly used for testing the strength of orthopedic implants such as plates, screws, and rods. For orthopedic implants and dental materials, fatigue test is a common test that measures the resistance of a biomaterial to repeated loading over time. Generally, there are many other mechanical tests suitable for different applications, and thus, the choice of the biomaterial and the product design should address these tests and standards [8].

Two examples of mechanics in biomaterials application are: (1) a hydrogel embolic agent for brain aneurysms; (2) a polymeric artificial heart valve.

Study Case 1: Photopolymerizable Hydrogels for the Treatment of Brain Aneurysms [9]

Main goal: To develop injectable photopolymerizable hydrogels designed to treat brain aneurysms by selectively filling the entire aneurysm space allowing a complete separation of the aneurysm from the parent vessel.

The biomaterial: Photopolymerizable polyethylene glycol dimethacrylate (PEGDMA) hydrogels.

The mechanical requirements: Crosslink fast enough within a few minutes, swell pressure that will not damage the tissue, similar mechanics as the native tissue, fill the aneurysm, stay stable within the aneurysm.

Material Mechanical tests: Compression test, swelling pressure test.

The functional mechanical tests: Stability and fatigue tests when placed in an in vitro aneurysm model subjected to physiological flow in a perfusion system.

Background: Cerebral or intracranial aneurysms (IAs) are abnormal focal dilations of an artery in the brain caused by a weakened area in the wall of a blood vessel. The risk of IAs is that they may rupture or burst, leading to bleeding in the brain (hemorrhagic stroke). This can cause severe brain damage or even death.

Aneurysm embolization treatment is a minimally invasive procedure used to treat a cerebral aneurysm. During the embolization procedure, a catheter is used to introduce embolic material into the aneurysm. This aids in preventing blood from entering the aneurysm and reduces the risk of bleeding.

Guglielmi detachable coils (GDC) composed of a platinum alloy were the first embolization devices approved by the FDA for occlusion of aneurysms. While metallic coil embolization is minimally invasive and has replaced, in most cases, the high-risk strategy of open surgical clipping, it still has its limitations, such as partial occlusion and recurrence. Synthetic polymers like n-butyl cyanoacrylate (n-BCA)

and Onyx (based on polyvinyl alcohol, PVA) and natural polymers like calcium alginate have been studied as potential embolic agents for aneurysms, however, none have yet been successfully translated into the clinic. Locally injectable hydrogels have the potential to be used as embolic agents in endovascular therapy and could provide an improved environment for vessel repair. These hydrogels can be delivered to the aneurysm in liquid form through a catheter and can solidify under various stimuli, such as temperature or pH changes. This approach may enable more accurate and targeted aneurysm blocking without causing any harm to the surrounding tissue or blood vessels. Moreover, using hydrogels, the cavity can be potently filled completely, which can be valuable for irregularly shaped aneurysms and wide-neck aneurysms, *see* Fig. 4.

An example of such an approach is a study exploring light-induced photopolymerization to form PEGDMA hydrogel in aneurysm cavities. Hydrogels belong to the soft biomaterials group and have low stiffness but offer controllable mechanical properties and swelling capacity. Swelling is defined as the ability of the material to absorb water and expand. The hydrogel swelling needs to be just enough to completely fill the aneurysm cavity, without occluding the parent vessel. Also, it must not exert too much pressure against the aneurysm wall, since aneurysms may rupture when the wall stresses exceed tissue strength. In general, the hydrogel's compliance, mechanical strength, and elasticity need to be comparable to those of the parent artery.

Since mechanical properties and swelling capacity are controlled by the molecular weight of PEGDMA and its concentrations, three different molecular weights at various concentrations of the polymer were investigated. The swelling capacity was tested in two modes: free swelling in phosphate-buffered saline (PBS) or confined swelling (where the sample is exposed to the solvent just at the neck of the aneurysm in the in vitro model). After 1 month, the weight and volume swelling ratios were calculated. The results show that increasing the polymer molecular weight or concentration led to an increase in the swelling ratio, in both the free and confined swelling modes and that the free swelling was higher than the confined swelling.

The mechanical properties of the hydrogels were assessed using a compression experiment. Hydrogel samples at different swelling times in PBS were compressed to a strain of 50% under a constant speed. Load and displacement were measured, and the elastic modulus was extracted by linear regression of the stress-strain curve. The failure stress and strain were defined as the highest stress and strain that a hydrogel experienced before breaking upon being gradually compressed to a strain of 80%. The compliance of the hydrogel was evaluated under pressures between 80

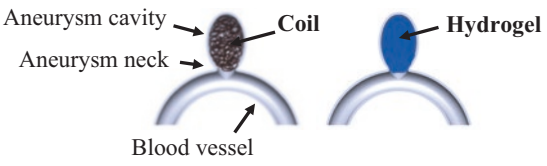

Fig. 4 Schematic showing embolization of brain aneurysms via coils (left) and hydrogel (right)

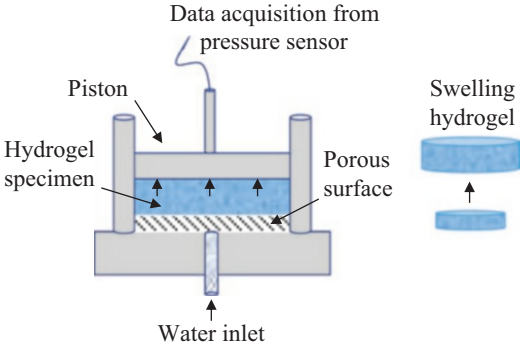

Fig. 5 Measurement tool to determine the swelling pressure under confined conditions

and 120 mm Hg to determine how easily the hydrogel may deform in response to physiological systolic blood pressures.

The swelling pressure was measured as the pressure exerted by swollen hydrogels under confined compression conditions using a piston [10], *see* Fig. 5.

To allow the hydrogel samples to expand, the chamber was filled with PBS. The load was then measured while maintaining a constant displacement until a steady state was reached. The swelling pressure was determined as the highest measured pressure during this test.

It was found that the molecular weight and concentration of the polymer affect the mechanical properties of the hydrogels. In general, increasing the molecular weight or concentration of a polymer increases both the swelling pressure and the compressive elastic modulus while decreasing its compliance under physiological pressure. Eventually, the performance of the hydrogel was evaluated using an in vitro brain aneurysm model filled with the hydrogel and connected to a flow system that applied physiological flow. Compression tests were performed on the hydrogel before and after 1 month in the model, and the surface profile of the hydrogels was studied via 3D laser scanning microscopy. The hydrogels sustained 5.5 million cycles, and no noticeable weight loss of the implant nor protrusion or migration of the polymerized hydrogel into the parent artery was observed.

These investigations revealed that photopolymerizable PEGDMA hydrogels with a molecular weight of 6 kDa and a concentration of 15% exhibited mechanical properties and compliance comparable with the natural aneurysm tissue, as well as provide a modest swelling volume and pressure and, therefore can potentially be used as a biomaterial for intracranial aneurysm treatment or repair.

Study Case 2: Aortic Polymeric Artificial Heart Valve [11]

Main goal: To develop an implantable polymeric aortic trileaflet prosthetic heart valve.

The biomaterial: Polystyrene-b-polyisobutylene-b-polystyrene triblock copolymer with about 30 wt. % polystyrene (SIBS30).

The mechanical requirements: Similar mechanical properties as a human biological aortic heart valve. To enable catheter implantation and physiological flow as well as long-term durability.

Material mechanics tests: Tensile tests, fatigue testing, and dynamic creep.

The functional mechanical tests: Hydrodynamic in vitro test under human physiological conditions (according to ISO 5840:2005 prostatic heart valve performance standards).

Background: Nowadays, approximately 4% of individuals over the age of 65 suffer from aortic stenosis (AS) resulting from calcific aortic valve disease, with an associated mortality of more than 50%. The solution to heart valve failure is implantation of prosthetic heart valves (PHVs) to replace the diseased valve. Today's PHVs are comprised of biological xenografts (tissue) valves, which are implanted via a transcatheter replacement procedure (TAVR), or mechanical valves made of pyrolytic carbon that are surgically implanted. Although these PHVs are effective, there are still unaddressed issues where biological valves deteriorate over time (<10 years) while mechanical valves require chronic anticoagulation, which may lead to bleeding complications. Polymeric heart valves can potentially offer improved durability compared to biological valves and improved hemocompatibility compared to mechanical valves [11]. Thus, there is an interest in studying and developing polymeric PHVs that could provide improved clinical outcomes and can be implanted via a transcatheter procedure.

As an example, to explore such valves, a study was performed on the design and performance of a polystyrene-b-polyisobutylene-b-polystyrene triblock copolymer with about 30 wt. % polystyrene (SIBS30) TAVR polymeric valves.

First, to study the basic mechanical properties of the polymer, such as elastic moduli, yield stress, ultimate stress, and maximal strain, tensile testing was performed by using an Instron® tensile machine according to the ASTM D 638 standard. These are essential mechanical tests for materials to be used in catheter implantation. To find the viscoelastic dynamic modulus, SIBS30 specimens were subjected to a stress-controlled sinusoidal oscillation with varied cyclic loading frequencies of the stress levels. An important mechanical test for materials to be used in PHV is a fatigue test which measures the material durability when subjected to intense cyclic loading. Fatigue testing on SIBS30 was carried out using an Instron® instrument. Once the material's properties were defined, the design of the PHV was done in an iterative process that combined simulations followed by functional experiments [12], *see* Fig. 6.

Based on anatomical data, a TAVR 3D computer-aided design (CAD) model was created using CAD software, *see* Fig. 6 left upper picture. To study the functionality of the design, a dynamic computer simulation was performed using the Finite Element Analysis (FEA) method, *see* Fig. 6 right upper picture. For this purpose, the mechanical data of the tested SIBS30 polymer was integrated into the simulation data. Finally, the valve's stress and hemodynamic parameters were simulated under normal physiologic aortic pressures to show its functionality in silico. Following this analysis step, a functional polymeric TAVR model was produced via a molding method. To test the produced SIBS30 TAVR prototype under physiological

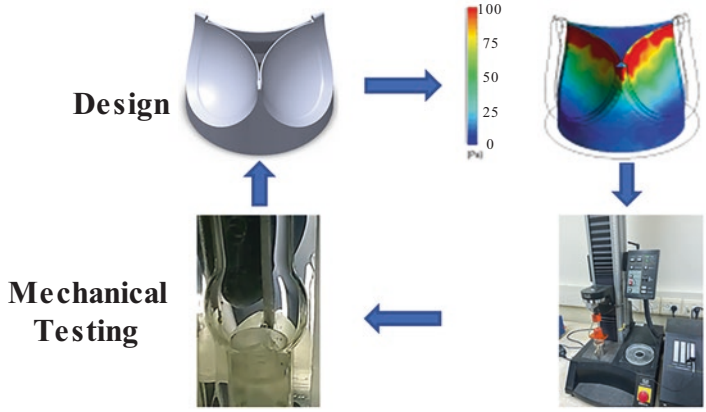

Fig. 6 Schematic representing the polymeric PHVs development process which includes mechanical analysis and polymer mechanical testing, CAD modeling, FEA simulations and in vitro functional tests

conditions and compare it to the computer simulation results, in vitro hydrodynamic testing was conducted in a Vivitro left heart simulator (LHS), as per ISO 5840:2005 prostatic heart valve performance standards. The LHS can simulate precise physiological pressure and flow waveforms, *see* Fig. 6 bottom section. The transvalvular pressure gradient, regurgitation, energy loss, and effective orifice area were recorded and analyzed optically and by an electromagnetic flow meter [11].

Results of the study showed that proper design and leveraging advances in material science can be instrumental in developing a functional polymeric valve that may potentially serve as a PHV.

5 Summary and Future Prospective

In this chapter, we briefly reviewed the mechanical properties of biomaterials, presented measurement techniques, and discussed the pivotal role these properties play in the design of new medical products. We succinctly also presented two examples highlighting the integrative process in designing new medical products/therapeutic procedures while integrating material science and material mechanics.

We believe that recent advances in manufacturing, which include bioprinting, will offer new opportunities to improve medical products as well as produce complex structures that would possess better mechanical properties. Moreover, bioprinting and new fabrication modalities require a better understating of the biomaterials' mechanical properties, both for optimizing the fabrication process and developing a new product with superior mechanical properties. Additionally, the ability to integrate cells in printed tissue-engineered products would require further

expanding our understanding of biomechanical processes and materials that combine living and artificial components and allow us to propose new approaches for disease treatment.

Questions

Question 1: Which of the following materials is not mechanically suitable for use as a bone tissue repair and regeneration:

(a) Synthetic polymers
(b) Ceramics
(c) Natural polymers
(d) Metal

Explanation: Natural polymer are relativity weak (low resistance to mechanical stress), soft (low modulus of elasticity) while bone tissue repair requires stronger materials.

Question 2: For tissue repair, it is advised that the biomaterial will be:

(a) Much stiffer than the target tissue
(b) Much softer than the target tissue
(c) With similar stiffness to the target tissue
(d) The stiffness of the biomaterials is not important

Explanation: In most cases for tissue regeneration, the general guideline is that a biomaterial that is optimal to replace a specific tissue should mimic its mechanical properties. Biomaterials that are stiffer than their surrounding tissue can lead to tissue resorption. Thus the biomaterial needs to be strong enough to prevent its mechanical failure but soft enough to avoid tissue resorption.

Question 3: Which test can be used to directly derive the elastic Modulus of a material?

(a) Fatigue test
(b) Tensile test
(c) Stress-controlled sinusoidal oscillation test
(d) Aging test

Explanation: The elastic modulus of a material can be derived from the slope of the stress-strain curve obtained via a tensile test.

Question 4: Which sentence about viscoelastic materials is false:

(a) Viscoelastic materials show hysteresis while elastic materials do not
(b) Viscoelastic materials show creep behavior
(c) Viscoelastic materials show stress relaxation
(d) Elastic materials are stiffer than viscoelastic materials

Explanation: Viscoelastic materials show hysteresis, creep, and stress relaxation. However, viscoelastic material can be also stiffer than soft elastic materials.

Question 5: Creep experiment is an experiment where:

(a) Constant strain is applied, and the force changes over time are measured.
(b) Cyclic force is applied, and the strain is measured over time
(c) Constant force is applied, and the strain is measured over time
(d) Cyclic strain is applied, and the force is measured over time

Explanation: A creep response occurs when a material that is subjected to a force exhibits a continuous increase in the strain over time (creep). Thus in creep experiments a force is applied and the strain is measured over time.

Question 6: The potential advantage of using hydrogels over coils for the treatment of intracranial aneurysms according to study case 1 is:

(a) Hydrogels have high stiffness
(b) Its feasibility to be delivered through a catheter
(c) Its ability to completely fill the aneurysm cavity
(d) Being a synthetic material

Explanation: While coils have high mechanical stiffness, they cannot completely fill the aneurysm cavity whereas hydrogels can be used to completely fill the cavity.

Question 7: The mechanical properties of the hydrogels can be controlled by their concentrations, according to study case 1 with the increasing of their concentration:

(a) Both the elastic modulus and the compliance increased
(b) The elastic modulus increased while the compliance decreased
(c) The elastic modulus decreased while the compliance increased
(d) Both the elastic modulus and the compliance decreased

Explanation: Result in the experiments performed in the study showed that as the hydrogel concentration increased (there is more polymer in it) the hydrogel became stiffer.

Question 8: Compared to mechanical prosthetic heart valves and biological valves, polymeric valves may offer:

(a) Improved durability compared to the biological valve and improved hemocompatibility compared to mechanical valves
(b) Improved durability compared to the mechanical valve and improved hemocompatibility compared to biological valves
(c) Improved durability compared to both of them
(d) Improved hemocompatibility compared to both of them

Explanation: Biological valves deteriorate over time whereas mechanical valves require chronic anticoagulation. Polymeric heart valves can potentially offer

improved durability compared to biological valves and improved hemocompatibility compared to mechanical valves.

Question 9: Functional mechanical tests for vascular grafts include:

(a) Creep experiments of the material
(b) Rotational rheometer tests
(c) Burst pressure, compliance, and suture retention tests
(d) A nano-indentation tests

Explanation: Creep, rotational rheometery, and indentation experiments can be used to characterize the material properties but are not functional mechanical tests. Burst pressure, compliance, and suture retention tests are functional mechanical tests used for testing vascular grafts.

Question 10: According to the material stress-strain curve, which type of the biomaterial suit for skin regeneration:

(a) Ceramic
(b) Polymer
(c) Metal
(d) Composite

Explanation: The skin is a highly deformable tissue whereas ceramics; metals and composite materials are not ductile enough to serve for skin regeneration. Polymers and polymeric hydrogels are ductile materials that can deform substantially.

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