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Review

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Polymeric Biomaterials for Medical Implants and Devices

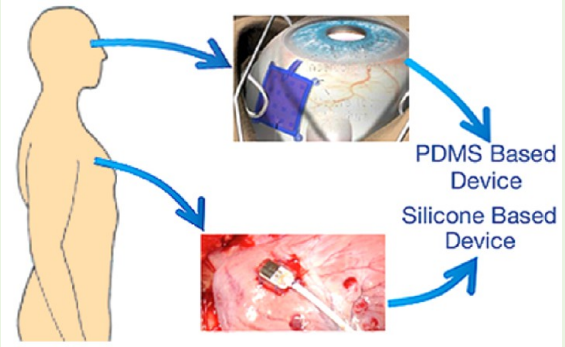
Adrian J.T. Teo,[†] Abhinay Mishra,[†] Inkyu Park,[§] Young-Jin Kim,[†] Woo-Tae Park,*[,‡] and Yong-Jin Yoon*[,†]

[†]School of Mechanical & Aerospace Engineering, Nanyang Technological University, 50 Nanyang Avenue, Singapore 639798

[‡]Department of Mechanical and Automotive Engineering, Seoul National University of Science and Technology, Seoul, Korea 139743

[§]Department of Mechanical Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, South Korea 305701

ABSTRACT: In this review article, we focus on the various types of materials used in biomedical implantable devices, including the polymeric materials used as substrates and for the packaging of such devices. Polymeric materials are used because of the ease of fabrication, flexibility, and their biocompatible nature as well as their wide range of mechanical, electrical, chemical, and thermal behaviors when combined with different materials as composites. Biocompatible and biostable polymers are extensively used to package implanted devices, with the main criteria that include gas permeability and water permeability of the packaging polymer to protect the electronic circuit of the device from moisture and ions inside the human body. Polymeric materials must also have considerable tensile strength and should be able to contain the device over the envisioned lifetime of the implant. For substrates, structural properties and, at times, electrical properties would be of greater concern. Section 1 gives an introduction of some medical devices and implants along with the material requirements and properties needed. Different synthetic polymeric materials such as polyvinylidene fluoride, polyethylene, polypropylene, polydimethylsiloxane, parylene, polyamide, polytetrafluoroethylene, poly(methyl methacrylate), polyimide, and polyurethane have been examined, and liquid crystalline polymers and nanocomposites have been evaluated as biomaterials that are suitable for biomedical packaging (section 2). A summary and glimpse of the future trend in this area has also been given (section 3). Materials and information used in this manuscript are adapted from papers published between 2010 and 2015 representing the most updated information available on each material.



KEYWORDS: *biomedical, packaging, polymer, medical devices, biocompatible, medical implants*

1. INTRODUCTION

Biomedical implants and devices enhance the quality of our lives by extending the functionality of essential body systems beyond their supposed lifespans. Across the medical industry, various implants and devices have been studied and developed for multiple applications in the human body. Ranging from man-made objects that provide physical support, such as knee implants and synthetic blood vessels, to applications that improve functionality of human organs, such as the pacemaker, the central goal of these devices are targeted toward the preservation of human lives. These applications also vary in terms of their placement and positions within the body. Many of these devices are placed in regions of high mechanical stress such as in the joints during bone replacement or in regions of high chemical and electrical activity such as the usage of neuroprosthetics. Placement of each implant or device brings has a different set of requirements in the design and material selections. According to the U.S. Food and Drug Administration, a medical device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article which is used in the diagnosis, cure, mitigation, treatment or prevention of a disease, or intended to affect the structure of any function of the body which does not achieve its primary intended purpose through chemical action within or on the body".[1] The FDA definition does not give a clear segregation on whether the device or implant would be of an active nature or to simply provide a mechanical support. In this paper, these two commonly used terms, "implants" and "devices" are further divided as follows. Implants are objects that do not require any form of power for the device to carry out its expected functions. Devices are objects that require a form of power, which may be chemical or electrical, to produce a reaction to either correct certain bodily functions or to capture information from the body. Examples of implants include knee prosthetics and breast implants, whereas examples of devices include pacemakers and defibrillators. By redefining these terms, there is no clash with their definitions as provided by the FDA, and these redefinitions are simply for simpler categorization of the devices and implants mentioned in this paper.

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Table 1. ISO 10993 Biocompatibility Test Categories[9]

Device Categories			Biological Effect											
Body Contact		Contact duration	Cytotoxicity.	Sensitization	Irritation/Intracuteneous.	Acute Systemic Toxicity.	Subchronic Toxicity.	Genotoxicity	Implantation.	Hemocompatibility	Chronic Toxicity.	Carcinogenicity	Reproductive/Developmental	Biodegradation
Surface Devices	Skin	A	x	x	x									
		B	x	x	x									
		C	x	x	x									
	Mucosal Membrane	A	x	x	x									
		B	x	x	x	o	o		o					
		C	x	x	x	o	x	x	o		o			
	Breached or compromised spaces	A	x	x	x	o								
		B	x	x	x	o	o		o					
		C	x	x	x	o	x	x	o		o			
Externally Communicating Devices	Blood path, Indirect	A	x	x	x	x				x				
		B	x	x	x	x	o			x				
		C	x	x	o	x	x	x	o	x	o	o		
	Tissue/Bone/ Dentin Communicating	A	x	x	x	o								
		B	x	x	x	x	x	x	x					
		C	x	x	x	x	x	x	x		o	o		
	Circulating Blood	A	x	x	x	x		o		x				
		B	x	x	x	x	x	x	x	x				
		C	x	x	x	x	x	x	x	x	o	o		
Implant Devices	Tissue/Bone	A	x	x	x	o								
		B	x	x	x	x	x	x	x					
		C	x	x	x	x	x	x	x		o	o		
	Blood	A	x	x	x	x	x		x	x				
		B	x	x	x	x	x	x	x	x				
		C	x	x	x	x	x	x	x	x	o	o		

[a]A = limited (≤24 h), B = prolonged (24 h to 30 days), C = permanent (>30 days).

In the biomedical field, the high demand for medical implants and devices is expected to increase in the future.[2] An increasing number of implants and devices are being researched and developed for placement under the skin. Implants and devices must maintain their operational capabilities within the biological environment of the body. For implants, this refers to the substrate on which the implant is fabricated. For devices, this refers to the packaging film enclosing the entire device when it is in the body. Implants and devices have different requirements that must be satisfied according to their functionality and region of use in the human body, and each requirement is vital for the survival of the implanted object and comfort of users. The different requirements can be classified into four main categories, including the chemical, mechanical, electrical, and thermal characteristics of the packaging for devices and substrate for implants.[3]

In this paper, although it is understood that there are additional factors that contribute to the successful operation and use of an implant or device, we primarily focus on commercially available synthetic polymeric materials and some of their composites used for medical implants and packaging films for devices. Various synthetic and natural polymers are used in such implants and devices. Many researchers consider natural polymers to have additional benefits over synthetic polymers, such as their biodegradable properties. However, in this paper, we discuss synthetic polymers that are commercially available, as they are readily available as well as generally cost-effective for fabrication. The next subsection discusses the material requirements of implants and devices, including the challenges in packaging medical implants. A list of devices and medical implants registered with the U.S. Food and Drug Administration is given in Table 1, categorized according to the type of medical studies involved. The table also lists different synthetic polymers used for these devices. Next, different polymers are discussed individually and some of the applications of these materials in device packaging films and medical implants are described (section 2). Table 2 and Table 3 compare their general material properties; composites are not included in the list because of the wide variability of compositions used. However, a few composites are mentioned in section 2 with the materials. Section 3 provides give a summary of the materials mentioned and discusses the future development trends.

1.1. Material Requirements for Implant and Device. There are specific requirements that an implant or device must meet for long-term use in the human body. If any of these requirements are not satisfied, the user may experience certain

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Table 2. List of Common Medical Implants under CFR by FDA[16−31]

FDA Category	Common Devices	Synthetic Polymer Material Used
Anesthesiology	• Epidural catheters	• Polyethylene • Polytetrafluoroethylene • Polyamide
Cardiovascular	• Pacemaker • Implantable cardioverter/defibrillator • Left Ventricular Assist Device • Mechanical heart valves • Artificial blood vessels • Catheters	• Polypropylene • Polyethylene • Polytetrafluoroethylene • Polyamide • Polyethyleneterephthalate • Polydimethylsiloxane • Polyhydroxyalkanoates
Dental	• Dentures • Dental Implants	• Polymethylmethacrylate
Ear, nose, and throat	• Cochlear implants • Stapes implants • Nasal implants for nose reconstruction	• Polydimethylsiloxane • Liquid crystal polymer • Silicone • Parylene • Polyethylene
Gastroenterology and urology	• Penile implants • Neurostimulator in sacral nerve stimulation • Foley catheter • Artificial urinary sphincter implant • Hernia or vaginal mesh	• Polydimethylsiloxane • Polyethylene • Polytetrafluoroethylene • Polyamide • Polyhydroxyalkanoates • Silicone • Polypropylene
General and plastic surgery	• Synthetic blood vessels • Breast implants • Cheek, jaw and chin implants • Lip implant • Titanium surgical implants • Hip implant	• Polypropylene • Polyethyleneterephthalate • Polytetrafluoroethylene • Silicone • Polydimethylsiloxane
Hematology and pathology	• Central venous access device • Peripherally Inserted Central Catheter	• Polyethylene • Polytetrafluoroethylene • Polyamide
Neurology	• Implantable Pulse Generator for Deep Brain Stimulation • Neuroprosthetics • Cognitive prostheses • Catheters	• Polyimides • Polydimethylsiloxane • Parylene • Liquid crystal polymers • SU-8 • Polyethylene • Polytetrafluoroethylene • Polyamide • Polyhydroxyalkanoates
Obstetric and gynecologic	• Intrauterine Device (IUD) • Intravaginal Rings • Etonogestrel-releasing Contraceptive Implant • Urogynecologic Surgical Mesh Implants • Fetal micro-pacemaker	• Silicone • Polyurethane • Polypropylene
Ophthalmic	• Dexamethasone Intravitreal Implant • Retinal Prothesis • Artificial Intraocular lens • Glaucoma valve • Fluocinolone Opthalmic Implant • Orbital Implant • Catheters	• Polymethylmetacrylate • Polyethylene • Polytetrafluoroethylene • Polyamide
Orthopedic	• Orthopedic implants	• Polyethylene • Polyether Ether Ketone • Polyhydroxyalkanoates

side effects or even death. Thus, a device must be properly packaged before installation in the human body. Specifically, the word "packaging" in this paper refers to the interfacial material between the human environment and the device throughout the operational period within the body. The packaging acts as a protective layer preventing the movement of waste materials between both the device and the human.

To enable a foreign object to be implanted into the body of a human, size matters not only during the implantation procedure, but also for the entire duration that the object remains in the body. The size also determines the survivability of the object and the comfort of the user. Thus, the object must be compact to reduce the stress on its surrounding tissues, muscles, and bones where the object has been implanted. The small size of the object also allows minimally invasive procedures to install these devices. Although the reduced size may decrease the structural integrity of more delicate devices, the demand for comfort often outweighs concerns about structural integrity.[4] This creates a higher need for implant substrates and packaging to be equivalent to a thin film covering the entire device.

Regarding mechanical aspects, the packaging must also be able to withstand stresses and shocks, as the human body is in a constant state of motion, and the occasional high and sudden impulses resulting from body exercises and sudden motions. The packaging must be able to endure these forces when the implants are used as additional support or infrastructure for the body to carry out its own regeneration and healing, such as in bone replacement. Additionally, because the implants and devices are constantly experiencing thermal influence from the human body, the packaging must be able to perform its function at body temperature for the required amount of time. Because certain materials denature upon exposure to various temperatures and because creeping can occur after a long period of time, the materials and packaging used for the object must be able to function acceptably within the human body temperature range and survive throughout its duration of operation without undesired or unforeseen mechanical changes.

As described above, implantable devices require electrical inputs to function. As such, electrical insulation is required for the packaging films to ensure the absence of unnecessary electrical interference with the external environment (bones, muscles, etc.). An example is the common pacemaker shown in Figure 1, which has leads that are made using polyurethane. Additionally, certain devices and implants are required to be embedded in areas near electrical signals such as in the brain and spine. Therefore, by using insulation packaging or substrates, no electrical leaks occur to or from the device itself that would either damage the device or pose health risks to the owner.

From the biological perspective, packaging used in devices and substrates for implants must be composed of materials that are bioinert depending on the requirements, and biocompatible with respect to their ability to demonstrate appropriate responses in specific situations as described by Kammula.[6] However, this characteristic depends on the type of material used. With regards to biocompatibility, some basic subdefinitions include that the device materials should not directly or indirectly produce adverse local or system level effects, be carcinogenic, or have adverse reproductive and development effects. Williams derived a new definition of biocompatibility as, "the ability of a biomaterial to perform its desired function with respect to a medical therapy, without eliciting any undesirable local or systemic effects in the recipient, but generating the most appropriate beneficial cellular or tissue response in that specific situation, and optimizing the clinically relevant performance of that therapy".[7] One challenge in the selection of materials for use in these implants or devices is the consideration of the areas in which the materials are being positioned within the body. Different systems within the body contain different kinds of chemicals, have different pH levels, and require different mechanical parameters. Therefore, a material used for a device in a one region of the body may not be used for another device in a different region of the body. This makes the determination of a material for general purposes difficult, and characterization can only be conducted according to specific devices and purposes. Thus, Williams categorized different implants and devices as such, and in this paper, his definitions will be used to describe the biocompatibility of the materials.

There are two different standards used for biocompatibility evaluation of medical devices, the United States Pharmacopoeia (USP) Class VI, primarily used for evaluation of plastics in packaging drugs, and ISO 10993 standard, used for medical

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Table 3. Comparison of Chemical, Electrical, and Thermal Properties of Commercially Available Polymers Used in Medical Implants and Devices[32,33]

		chemical properties		electrical properties			thermal properties				
	unit	solidification shrinkage (%)	water absorption (%)	breakdown potential (kV/mm)	dielectric loss factor (%)	resistivity (Ohm mm^2 /m)	glass temperature (°C)	melting temperature (°C)	specific heat (J/(kg K))	thermal conductivity (W/(m K))	thermal expansion ($\times 10^{-6}$/K)
PVDF	min		0.04	22	0.01	1.00×10^{19}	−40	170	960	0.19	100
	max		0.04	22	0.18	1.00×10^{19}	−40	170	1400	0.19	140
HDPE	min	2	0.01	17.7		5.00×10^{17}	−110	108	1800	0.46	110
	max	4	0.01	19.7		1.00×10^{21}	−110	134	2700	0.52	130
LDPE	min	1.5	0.01	17.7		5.00×10^{17}	−110	125	1800	0.3	150
	max	3	0.02	39.4		1.00×10^{21}	−110	136	3400	0.34	200
PP-copolymer	min	1	0.01	50		1.00×10^{21}	−10	165	1.93	0.12	58
	max	2.5	0.01	65		1.00×10^{21}	−10	165	2	0.22	150
PP-homopolymer	min	0.8		55		5.00×10^{21}	−10	160		0.22	180
	max	2		90		1.00×10^{22}	−10	165		0.22	180
PMMA	min	0.3	0.3	16	0.04	1.00×10^{19}	105		1466	0.17	50
	max	0.8	0.4	30	0.06		105		1466	0.25	90
PTFE	min	3.5		50		1.00×10^{22}	127	327	1000	0.23	100
	max	6		80		1.00×10^{22}	127	327	1000	0.25	100
LCP	min	0.6	0.02	31		1.00×10^{19}		275			50
	max	0.6	0.04	43		1.00×10^{20}		330			50
PU thermoset	min		1.5		0.01				1700		130
	max		1.5		0.04				2100	0.19	200
PA11	min		1.2	30	0.03	1.00×10^{18}	46	190	2400	0.28	110
	max		1.8	30	0.08	1.00×10^{19}	46	190	2400	0.28	120
PA12	min	0.6	1.45	20	0.03	1.00×10^{17}		190	1.17	0.22	80
	max	1.8	1.6	60	0.04	2.50×10^{19}		190	1.2	0.24	100
PA46	min		4	60	0.01	1.00×10^{17}	85	295	2100	0.3	75
	max		4	60	0.35	1.00×10^{18}	85		2100	0.3	75
PA6 cast	min		6.5	35	0.03	1.00×10^{16}	50	215		0.3	70
	max		9.5	35	0.3	5.00×10^{18}	75	220		0.3	100
PA66	min	0.3	3	15.2	0.01	1.00×10^{19}	78	260	1670	0.25	70
	max	2	4	18.5	0.04	1.00×10^{20}	78	260	1670	0.27	100
PA6-3-T	min			35	0.03	1.00×10^{15}			1.6	0.23	80
	max			35	0.04	1.00×10^{15}			1.6	0.23	80
PI	min	1	0.24	22		1.00×10^{21}			1130	0.55	40
	max	1	0.3	22		1.00×10^{21}			1130	0.55	50
PDMS	min	1.06		10	0.013	6.00×10^{18}	150	226	1460	0.15	907
	max	1.94		10	0.013	6.00×10^{18}	150	232	1460	0.15	907
parylene C	min		0.09	220		6.00×10^{16}		290	712	0.084	35
	max		0.09	220		6.00×10^{16}		290	712	0.084	35

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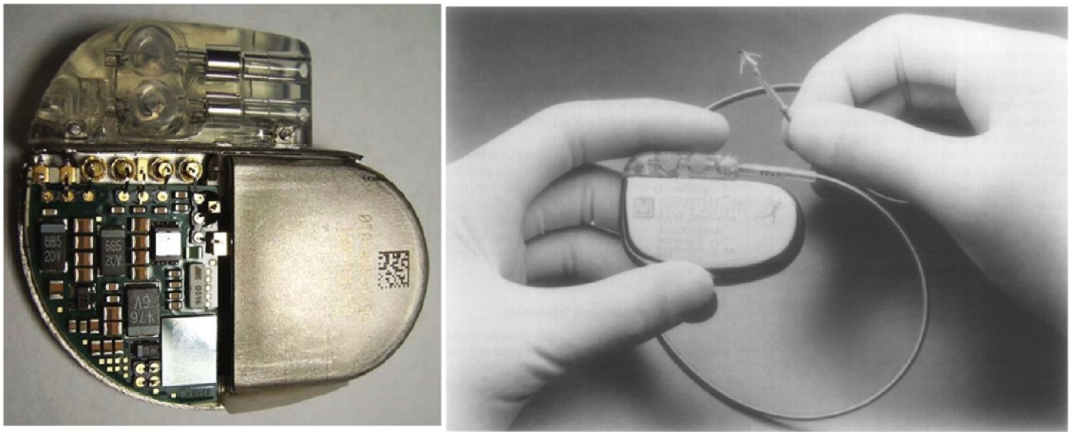

Figure 1. Leads used in pacemakers are made using polyurethane (Medtronic EnRhythm Model P1501DR). Reprinted with permission from refs 3 and 5. Copyright 2009 Springer and 1995 Elsevier.

grade materials and medical devices.[8] The ISO 10993 biocompatibility test categories are given in Table 1, and a short list of materials, as summarized by Joung, that are biocompatible include titanium and its alloys, noble metals and their alloys, cobalt-based alloys, tantalum, niobium, titanium–niobium alloys, nitinol, MP35N, alumina, zirconia, quartz, fused silica, biograde glass, silicon, and some biocompatible polymers that include epoxies, silicones, polyurethanes, polyimides, silicon-polyimides, parylenes, polycyclic-olefins, silicon-carbons, liquid crystal polymers, and benzocyclobutenes.[10] In addition to biocompatibility, the packaging must also provide hermetic sealing, which is airtight sealing to prevent physical components within the device to leak out into the body environment. A standard testing procedure in the clinical devices industry is used to test for this requirement, MIL-STD-883, Method 1014.10. The most common hermeticity test is conducted using a helium leak detector, which is a mass spectrometer designed to analyze helium gas leakage. A series of hermeticity test results for different materials is shown in Figure 2, where the time required for moisture to pass through each material is based on the thicknesses of each material. The graph shows that metals and ceramics are relatively impermeable; however, there are very few materials in these two categories that fulfill the other requirements mentioned previously. Therefore, there is an increased need to examine polymers that are suitable for use as packaging films.

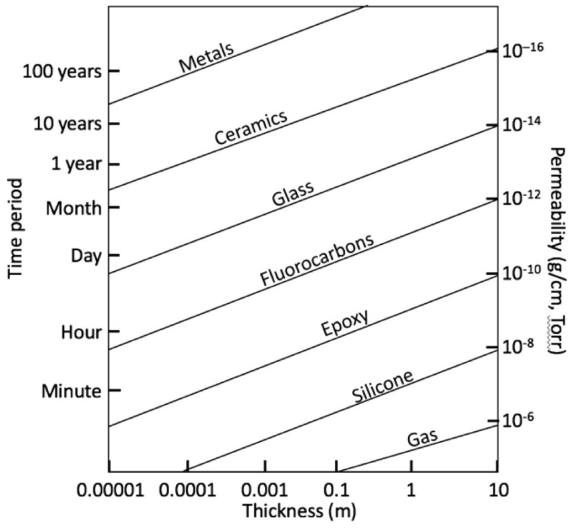

Figure 2. Material-dependent permeability graph as a function of thickness. The time period in this graph shows the approximate time required for water vapor to pass through the layer of material so that the humidity on the interior of the package is 50% of the exterior. Adapted with permission from ref10.

The materials used for packaging are vital to the survivability of the implant or device within the human body environment. In general, these materials include ceramics, metals, polymers, and polymer composites.[11] Ceramics show good biocompatibility, good corrosion resistance, and high compression resistance and density. Some disadvantages of ceramics include brittleness, low fracture strength, low mechanical reliability, lack of resilience, and relatively difficult fabrication. Metals have high strength, ductility and resistance to wear, and high density. In contrast, polymers are available in wide variety of compositions, properties and forms. They can also be fabricated readily into complex shapes and structures. However, not all polymers meet the mechanical demands of certain applications as they can be quite flexible and weak. Polymers may also absorb fluids, swell up, and leach undesirable products depending on the application. When multiple types of polymers are used in cohesion in one thin layer, such as in a polymer composite, the properties of the layer differ compared to their parent materials. However, the composite material simultaneously has a low elastic modulus and high strength with a greater potential for structural biocompatibility compared to the separate parent materials. Corrosion and fatigue failure of metal alloys do not occur, and the release of metal ions is prevented and fracture toughness is increased ceramic materials. Additional advantages of polymer and polymer composites are that they are nonmagnetic and are radio transparent for X-ray radiography and MRI scans.

Sterilization processes may also affect polymer properties, which can result in different outcomes. First, the efficiency of sterilization is determined by the ability to eliminate all kinds of microbes, like viruses, bacteria, fungi and spores.[12] A comparison of methods like steam sterilization, electron beam, and dry heat sterilization have been given by Lerouge with the advantages and limitations of each method mentioned. Effects of these processes could inadvertently cause damage to the polymer itself. With the example of dry heat sterilization, toxic ethylene oxide can be exuded from thin layers of polymer which would cause harm to the body. High temperatures would also

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Table 4. Comparison of Mechanical Properties of Commercially Available Polymers Used in Medical Implants and Devices[32,33]

	unit	bending strength (MPa)	compressive strength (MPa)	density (kg/m^3)	elongation (%)	fatigue failure (MPa)	friction coeficient	impact strength (J/cm)	shear modulus (MPa)	tensile strength (MPa)	yield strength (MPa)	Young's modulus (MPa)
PVDF	min	94		1780	20		0.34	1		50		2100
	max	94		1780	25		0.34	2		57		2900
HDPE	min	20		940	180	18	0.25	0.27	700	20		600
	max	45		965	1000	20	0.3	10.9	800	32		1400
LDPE	min	10		910	600		0.3		100	8	15	200
	max	40		928	650		0.5		350	12	20	400
PP-Copolymer	min	32	38	902	200	24	0.3	0.27	300	30		1100
	max	50	55	906	700	24	0.5	1.1	500	38		1550
PP-Homopolymer	min	20		902	500		0.3	0.27		25	17	800
	max	29		907	800		0.5	1		30	35	1300
PMMA	min	120	83	1170	2	11	0.54	0.16	1700	48		1800
	max	148	124	1200	10	12	0.54	0.27	1700	76		3100
PTFE	min	5	7	2150	350		0.05	1.6	110	25		410
	max	6	8	2200	550		0.08	1.6	350	36		750
LCP	min	150		1070	1.2			0.53		120		10000
	max	300		1070	7			5.3		240		40000
PU thermoset	min			1100	500					20		
	max			1700	500					45		
PA11	min	55		1040	280		0.32		450	47		1100
	max	60		1050	280		0.38		500	47		1400
PA12	min	70		1010	120		0.3	0.5	300	35		1270
	max	85		1020	300		0.4	2	500	55		2600
PA46	min	150		1180	40		0.4		1200	100	30	1000
	max	150		1180	40		0.4		1200	100		3000
PA6 cast	min	115		1135	10		0.36			55		700
	max	135		1155	350		0.43			85		3000
PA66	min	115	46	1130	12	22	0.25	0.48	1100	80		1700
	max	125	86	1150	300	22	0.42	1.5	1200	85		2000
PA6−3-T	min			1120	70					70		2000
	max			1120	150					84		2000
PI	min	100	165	1400	5	20	0.29	2.5		85	73	3100
	max	130	165	1430	7	20	0.29	5		90	73	3100
PDMS	min			970	430				0.203	2.24		360
	max			970	640				0.203	2.24		870
Parylene C	min			1.289	200		0.29			69	3200	2800
	max			1.289	200		0.29			69	3200	2800

cause deformation to occur because of the transition temperature and melting temperature of each material, or even reduced ductility, chalking, and color changes to the material itself. Later developments of sterilization processes have also enabled low temperature sterilization to take place. Hydrogen peroxide, which by itself is a good microbial agent, oxygen, peracetic acid, nitrogen, argon, helium xeon, and neon have been used in gas plasma sterilization.[13] Other methods also include using microwave sterilization and pulsed high intensity light; however, there is not one method that can be used as a general method for sterilization across the medical industry and to narrow down the scope of the paper, the effects of sterilization on each material would not be discussed.

The largest challenge facing the development of medical devices is packaging rather than the materials used as substrates for implants. As mentioned by Najafi et al, the first and most difficult challenge is the size of the implant.[14] This is because as the size of the implant decreases, the technologies available for packaging become more limited. Additionally, the mechanical strength of the packaging film itself is more delicate, and a single scratch may create a tear in the film, destroying the hermetic seal. Uneven surfaces on the device may also cause uneven coating of the polymeric layers, leading to inaccurate predictions of the operational lifespan. Although the thickness of the substrate in implants is also critical, the effects in devices are more pronounced. On the basis of these requirements, the basic requirements can be categorized into operational requirements and material requirements for the device itself.

In this paper, the main focus is specifically on the packaging requirements of biomedical implants and devices. Examples of a few of these latest designs developed by researchers worldwide would also be given. It is also understood that the product design of certain implants and devices would directly affect the biocompatibility and mechanical behavior of the implants and devices, therefore to standardize, the information provided in this paper would not mention such properties arising from these effects. The scope of this paper is limited to the materials, specifically commercially available synthetic polymers, and applications in the biomedical field, not including the different techniques used for packaging and the technology needed for these packaging methods. To be more specific, the materials mentioned in this paper are based on their pure form, without any use of additives, stabilizers, colorants, antioxidants, fillers, etc., unless specifically mentioned like in the case of PDMS,

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which requires a curing agent, additives of carbon nanotubes (CNTs) to form composites, etc.

1.2. Categories of Medical Devices and Implants. The U.S. Food and Drug Administration (FDA) divides the devices into 16 different categories based on the type of medical specialty panels in Title 21 of the Code of Federal Regulations (CFR), Parts 862−892.[15] Of the 16 categories, a list of common medical implants is shown below.

According to their classifications, different polymer groups can be used in multiple systems in the body. It is also relatively difficult to specifically indicate the polymer that works best for each system. A list of all the synthetic polymeric materials in the above categories is given below, together with their material properties (See Tables 3 and 4) and a compilation of their advantages and disadvantages are given in Table 5.

2. MATERIALS

A wide variety of polymers can be used in biomedical implants and device packaging. The ability to specifically modify the final properties of the packaging material to cater to different applications in different parts of the body makes this topic a hotspot in the industry. There are various methods of applying polymers in medical implants and devices. Designers can either use the polymers as a protective coating by itself, as an adhesive to seal off the interface between two materials, or as a substrate for the device itself. For example, implantable sensors that are used to monitor the pH level in the gastrointestinal system requires biocompatibility that prevents corrosion against the acidic juices found in the stomach; thus, the sensor must employ a packaging with high corrosion resistance while also allowing for the transmittance of RF signals. One such device that has been widely used in the industry is the Medtronic Bravo pH System device, where little discomfort was reported by patients who had the device implanted.[68] A layer of epoxy was used to package the device, and the device itself was still well-protected at the end of the testing period of 2 days.

Some combinations of polymers used as adhesives in sealing devices that are used as implants include combinations of epoxy and glass or silicone and glass to encapsulate structures to protect implants from the biological environment. Chang et al. compared these two methods to determine which method would allow for a longer lifetime in the body and found that the combined silicone and adhesion promoter combination provided the longest lifetime; however, the results showed no substantial evidence demonstrating the effects of stress and strain on the packaging itself.[69] Apart from epoxy, there are many other types of commercially available synthetic polymers used, and short descriptions of these are listed below.

2.1. Polyvinylidene Fluoride (PVDF). PVDF is a polymer that is widely used in the medical industry and has been widely characterized by various researchers worldwide. Its nonreactivity makes it a very good material for use in surgical meshes and sutures while its piezoelectric effects make it a suitable material for wound healing (Figure 3); it can also be used as a substrate for sensors.[35−37] However, it is very difficult to find pure PVDF film in biomedical devices used as packaging films because of its disadvantages like its inability to form smooth films and poor adhesion to other materials. Attempts have been made to use PVDF together with other materials to form composites that would have the advantages of both materials. It has also been demonstrated that energy can be harvested from the expansion and contraction of blood vessels through the use of combination nanofibers of PVDF together with graphene in the human body.[70] In another paper, electrical stimulation of cells promoted healing, and based on the combination of the piezoelectric properties of PVDF and the mechanical properties of polyurethane (PU), electrospun scaffolds of PU/PVDF were developed (Figure 4).[71] Recent developments in the use of PVDF have shown various applications for this material. With the current trend in multifunctionality, PVDF can be used as a substrate or sensing material within a single device, such as the device developed by Marques et al.[72] Current fabrication technology requires PVDF to be part of a composite material if it is to be used as a very thin film. Sharma et al. fabricated a 1-μm thin film of PVDF-TrFe, to be used as a piezoelectric pressure sensor via standard lithography processes as an example for future cost-effective batch processing (Figure 4).[73] Given the difficulty in thin film fabrication, greater advancements must be made in PVDF fabrication technology if it is to be used in nanoscale devices, which would be greatly beneficial to the industry.

Table 5. Advantages and Disadvantages of Materials

	Advantages	Disadvantages
PVDF[34-37]	• Chemically inert • Good material stiffness and strength • Strong piezoelectric effect • Good biocompatibility • High resistance to hydrolysis	• Unable to form smooth films • Low thermal stability • Poor adhesion properties to other materials.
Polyethylene[22, 38-39]	• Good chemical resistance • Material mechanical properties modifiable according to molecular weight • Low melting temperature • Lightweight • Quick drying characteristics • Porous HDPE has good biocompatibility, good elasticity, and strong anti-infective properties	• Has a 'plastic' feel to skin • Low ability to be dyed • High friction coefficient
Polypropylene[40-42]	• Non-toxic, • Has two forms, copolymer and homopolymer, with different mechanical strengths • High melting point, • Good dielectric properties	• Non-degradable • Semi rigid material which can cause local discomfort in patients • Not confirmed if fully biocompatible
PMMA[16, 43-48]	• Mechanically strong • Lightweight • Poor thermal and electrical conductivity • Acceptable biocompatibility • Radiolucency	• High curing temperature • Does not support osseointegration of the structure with other structures
Silicone[28, 49-54]	• Chemically Inert • Low toxicity • Good biocompatibility • Good electrical insulation, • Low thermal conductivity, • Thermal stability, • High gas permeability, • Hydrophobic.(context dependent) • PDMS ○ Clear ○ Non-flammable • Parylene ○ Good conformity ○ Able to provide thin layer of coatings (1-2μm) with low friction coefficient	• Long term effects not studied • High coefficient of friction • Soft (prone to damage during implantation) • Size and swelling • PDMS ○ Hydrophobic (context dependent) ○ Propensity for protein absorption ○ Possible contamination of cyclic silicone monomer • Parylene ○ Low mechanical strength, ○ Weak adhesion, ○ High moisture absorption rate ○ Low life-expectancy
Polyurethane [28, 50, 55]	• High durability, • High toughness, • Good biocompatibility and hemocompatibility • Good biostability • Low coefficient of friction • Low water permeability	• Environmental stress cracking • Degradation of the material in vivo • Metal ion oxidation
Polytetrafluoroethylene [50, 56]	• Chemically inert • Mechanically strong • Electrically inert • Hydrophobic	• Stiff • Susceptible to damage from traction when lead migrates • Has insulation microdefects
Polyamide (Nylon)[39-40,57-59]	• Causes minimal tissue reactivity • Has long-lasting tensile strength and high elasticity • Have temperature-varying electrical properties. • Moisture absorbent • Able to prevent bacterial transmission	• Moisture permeability • Poor heat sealability • High friction coefficient
Polyimide [60-62]	• Good chemical resistance, • Good mechanical and electrical properties • Low creep • High tensile strength • Flexible, can be folded into compact module for restricted spaces • Constant dielectric constant over wide frequency range with low loss tangent • Stable over wide range of temperatures. • High heat resistance, • High light transmittance for a wide range of wavelengths • Certain polyimides are biocompatible upon interaction with blood	• High moisture absorption
Liquid Crystal Polymer [63-65]	• Chemically inert, • High mechanical strength and durability • Resistant to fire • Low moisture absorption • Able to fabricate thin layers • Flexible and easily conform to difficult shapes • Good MRI capability	• Composite film has poor adhesion to flexible substrates
CNT [66-67]	• Electrically conductive in specified orientation and insulative in another • Good mechanical and surface properties, • Mechanically strong with high tensile modulus and elastic modulus • Good bonding strength with metal substrates with good packing density	• Has concerns over cytotoxicity • weak against shearing between adjacent shells • easily compressed because of their hollow structure

2.2. Polyethylene (PE). Polyethylene can be categorized according to its molecular weight, e.g., low-density polyethylene (LDPE) and high-density polyethylene (HDPE), which can be used in different applications based on their characteristics. As molecular weight

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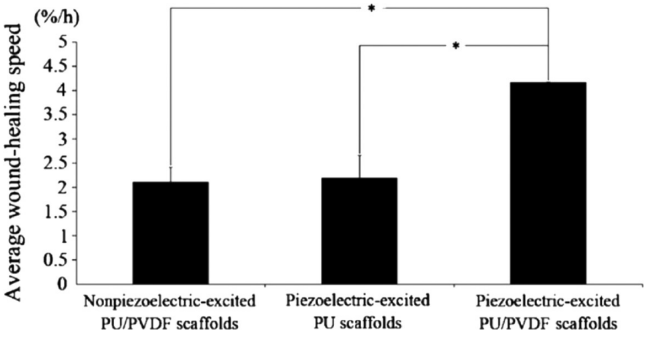

Figure 3. Comparison of average wound healing speed using different scaffolds. Reprinted with permission from ref 71. Copyright 2012 Elsevier.

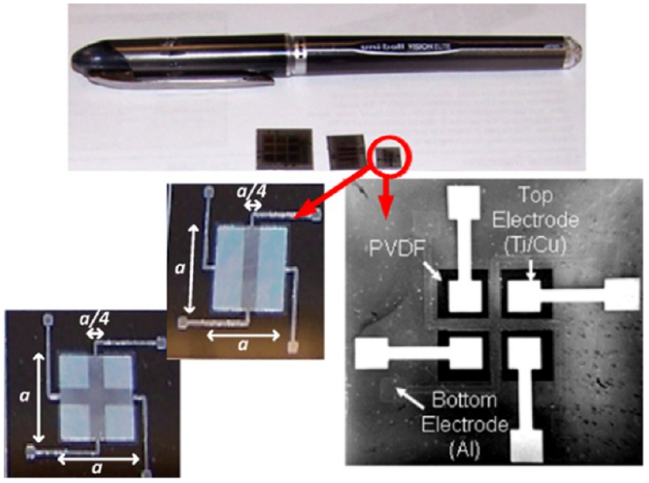

Figure 4. Fabricated pressure sensor showing dimensions using PVDF-TrFe thin film. Reprinted with permission from ref 73. Copyright 2012 Elsevier.

increases, material strength also increases while elasticity decreases. In a previous study, the process of fabricating medical implants using PE from the resin stage to final product stage was described.[74] The details of the characterization and procedures are described for ultrahigh molecular weight polyethylene.

The effectiveness in using PE for total hip anthroplasty have found that ceramic-polystyrene couplings demonstrated lower facture rates and lower audible component-related noise as compared to traditional ceramic−ceramic couplings.[75] Additionally, the ceramic-polystyrene did not show reduced osteolysis, and thus did not show high statistical differences. However, PE components may be treated to reduce osteolysis.[76] Zhou et al. also found that porous HDPE showed good biocompatibility, good elasticity, and strong anti-infective properties, and used this material for rhinoplasty surgery (Figure 5).[22]

Surface modification of PE-related materials have also been conducted to improve various properties for different applications. An example is the modification of ultrahigh molecular weight PE (UHMWPE) using laser radiation to modify the surface roughness and wettability of samples.[77] This method enables the surface roughness of the material to be reduced to 1.7 ± 0.5 μm using a 532 nm wavelength laser. Optimal bone bonding to the implant surface was observed at approximately 1 μm. Cools et al. also used atmospheric pressure plasma technology to treat the surface of PE implants for increased adhesion to commonly used PMMA bone cement.[78] The paper also showed atomic force microscopy images of the effects of plasma polymerization on the surface, making the surface smoother and more desirable (Figure 6). Upon exposure of high concentration of monomer flow, the PMMA structure became incorporated into the deposited monomer film, thus smoothing the surface.

2.3. Polypropylene (PP). Polypropylene, similarly to PE, is a thermoplastic polymer that can also be altered according to its density and categorized into its copolymer and homopolymer constituents, where the major difference is the strength of the material (Table 2). PP has been widely used as surgical mesh to reinforce weakened tissues while also acting as a scaffold for fibro-collagenous tissues to grow on the mesh itself and has mainly been applied in urogynecology to treat stress urinary incontinence and pelvic organ prolapse.[42] Recently, numerous studies have examined its use in other parts of the body, such as for implant-based breast reconstruction.[79] However, for this application, there is some disagreement regarding the use of PP materials. Zheng et al.[80] described that the use of such implants induces an inflammatory response contributing to a poorer healing process. In contrast, Moalli et al. found that these inflammatory responses were unavoidable processes in healing carried out by the body and thus PP meshes should continue to be used.[24] In fact, the use of PP should be supported, as these meshes have a low potential for carcinogenesis in the human body. It is still uncertain whether PP is fully biocompatible because of controversy in the use of PP hernia meshes.[42] PP has also been used together with titanium to produce a mesh with a thinner capsular contracture, which is a major complication in implant-based breast reconstruction. It is also a good material that can be used for supportive soft tissue structure (Figure 7).[81] PP has also been used as a blood oxygenator membrane in the past; however, there were many instances of immune system responses by the body. Thus, a variety of methods have been employed to surface-treat the PP membrane to improve blood compatibility.[82] Other materials have also been found to show better results than PP membranes.[83] Thus, it is believed that polypropylene is a good material but has limitations for use as a biomedical implant because of biocompatibility issues. Further research

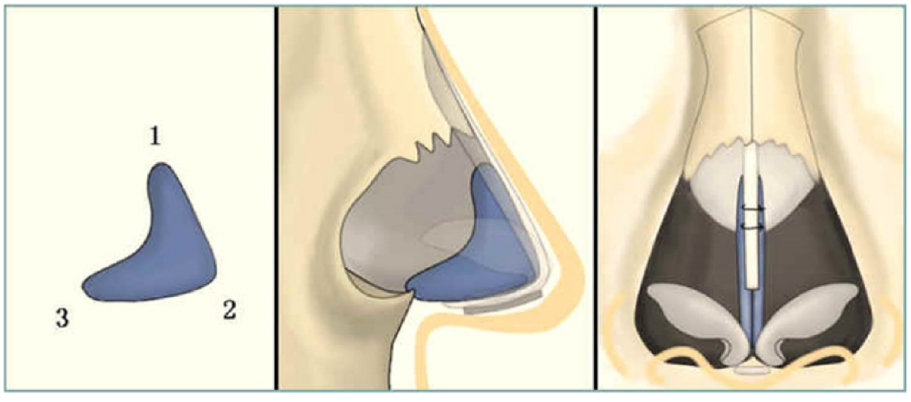

Figure 5. Schematic diagram of PE implant (left) and positioning of implant in nose during rhinoplasty(right). Mechanical properties of PE material has enabled low level of complications after surgery. Reprinted with permission from ref 22. Copyright 2014 Springer.

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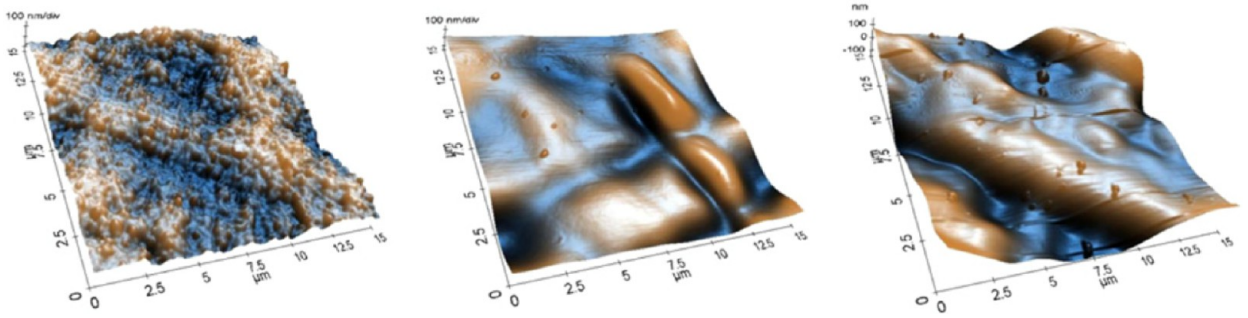

Figure 6. Effects of plasma polymerization on PE at exposure time intervals of 1, 3, and 5 min, respectively. Reprinted with permission from ref 78. Copyright 2014 Elsevier.

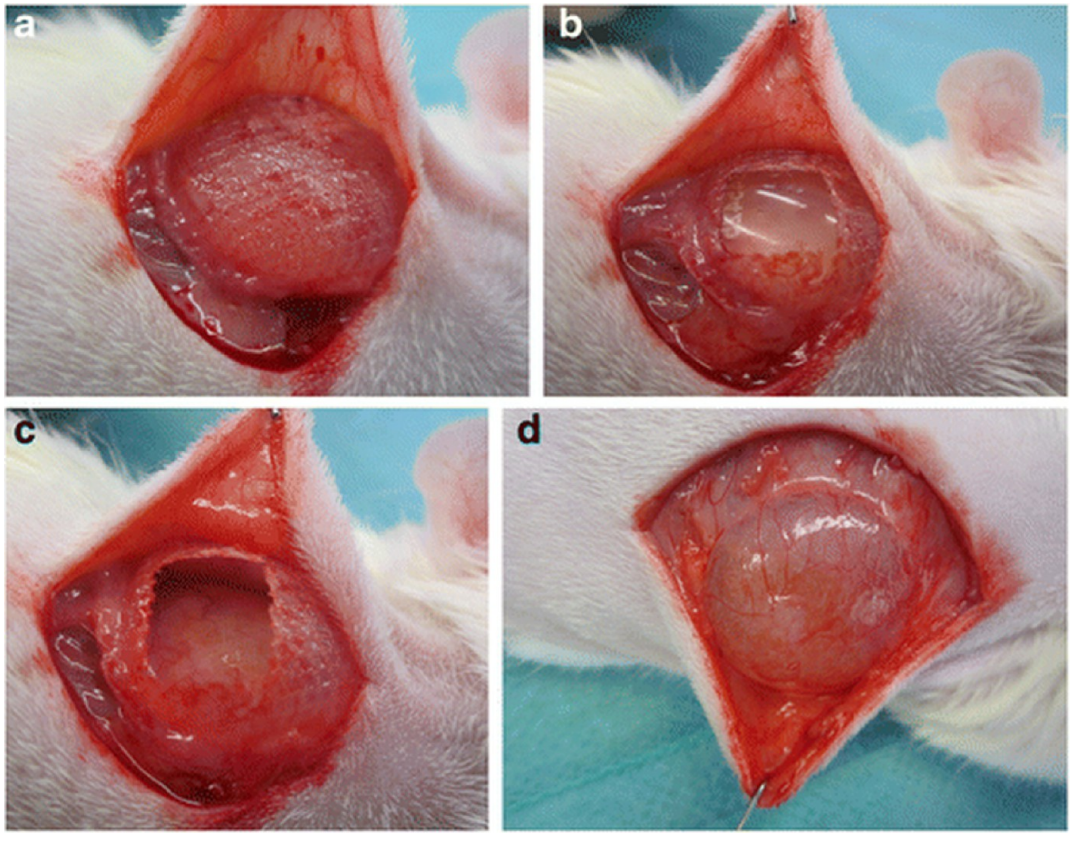

Figure 7. (a−c) Titanium-coated polypropylene mesh-covered implant with visible structure and (d) textured implant protected by mesh after mesh was removed. Reprinted with permission from ref 81. Copyright 2014 Springer.

on surface treatments should be carried out on the material surface to improve its biocompatibility before use in the human body. One such surface modification process that has been used on the PP membrane surface is graft polymerization using PEG.[82,84]

2.4. Poly(methyl methacrylate) (PMMA). PMMA has been used in various medical implants such as in intraocular lens, rhinoplasty, and cranioplasty (Figure 8), and as bone cement in total joint replacements.[16,44−47] However, PMMA does not support osseointegration of the structure with other structures with which it comes in contact, reducing its applicability. Hence, Goncalves et al. developed two different formulations to induce calcium phosphate layer growth on the surface of the cement discs to promote osseointegration.[85] Porous PMMA space maintainers have also been developed for use in patients who experience damaged or loss of craniofacial tissues and bones for which repair is not possible.[86] These space maintainers can also provide support to the surrounding tissues, potentially aiding in soft tissue healing around the damaged structure. One major failure mode in bone cements using PMMA is fatigue and deterioration of the interfaces between cement-bone and cement-implant, resulting in further issues such as mechanical failure and instability. Improvements have also been attempted using a variety of materials including stainless steel or titanium alloy reinforcements, ultrahigh molecular weight polyethylene, or even Kevlar to reduce the peak temperature for cement polymerization, reducing tissue necrosis.[11] Prototypes for centrifugal blood pumps have also been fabricated using PMMA because of the ease of fabrication using laser-cutting technology, low costs incurred, and the potential for use in future implantation; however, few studies have examined the actual implantation of these devices.[87]

Tissue growth for PMMA orbital implants has also been tested, and results showed that fibrovascular ingrowth of tissues from surrounding orbital tissues in the eyes could be achieved with no signs of infection.[88] Intraocular lenses have also been developed using PMMA, and the results showed that the chromatic difference of focus values were similar to the physiological values measured in young eyes. With the advancement of 3D printing, PMMA has been increasingly used in patient-specific biomedical applications in the fabrication of porous

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Figure 8. PMMA fabrication for cranioplasty using 3D printing, with (A) the 3D printer, (B) the prefabricated mold, and (C) the resultant PMMA cranial piece with the mold. Reprinted with permission from ref 46. Copyright 2012 Korean Neurosurgical Society.

customized freeform structures.[89] The diverse methods of application and usability of PMMA suggests that PMMA should be further examined to provide additional solutions to current problems that are unique to individuals.

2.5. Silicones Parylene and PDMS. Silicones are inert compounds used in a variety of forms and applications. Silicone implants have been used in laryngeal surgeries to overcome issues such as unilateral vocal fold paralysis that causes incomplete glottis closure and vocal impairment, as well as an encapsulant material in implants (Figure 9). Studies examining these implants have demonstrated improvement in the vocal function of patients.[90] Surgeries to adjust human aesthetics have also widely used silicon products, which were found to be safe with low infection rates.[91−93] Silicone was studied to be the most reliable for long-term encapsulation in the body compared to epoxy resin and polyurethane coatings because of their lower surface energy and smoother topography.[94] These features also prevent cells and molecules from being absorbed by the polymer itself. There were also fewer defects observed on the silicon surface, indicating better protective functions.

Two derivatives of silicone that are commonly used in biomedical implants include parylene and polydimethylsiloxane (PDMS). Parylene is commonly used as a packaging material in implanted neural prostheses;[95,96] among its variants, parylene C is the most commonly used for implants. Parylene has also been used as packaging material for long-term implantable electronic devices,[97] retinal stimulation arrays,[53] and intraocular microactuators. Luo et al. reduced the thickness of the packaging film to 0.25 μm to avoid having a large effect on the output of the device (Figure 10).[21] Parylene has been shown to be effective for use as a packaging material; however, researchers must still take into context the disadvantages of using this material as mentioned in Table 5.

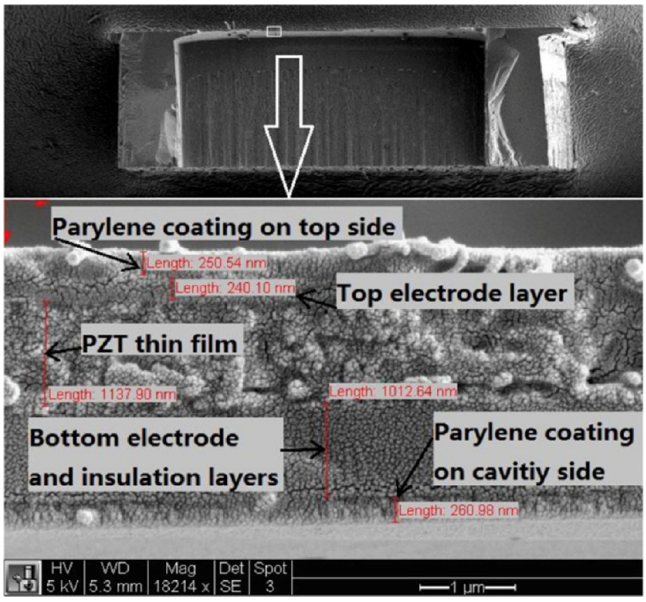

Figure 10. Cross-sectional view of PZT diaphragm packaged with parylene. Reprinted with permission from ref 21. Copyright 2013 Elsevier.

Another common silicone derivative would be polydimethylsiloxane (PDMS). PDMS has been used in pacemakers, blood pumps, mammary prostheses, catheters, shunts, cochlear implants, esophagus replacements, and packaging material for implantable electronic devices and sensors.[28,53,54] Pirmoradi et al. recently developed an implantable MEMS device that was fabricated using PDMS for direct on-demand drug delivery to a human eye for treating ocular posterior segment diseases such as diabetic retinopathy.[99] The basic idea was based off a similar device fabricated by Ronalee et al. in 2009, which consisted of a reservoir to store the drug and a valve that controlled the release of the drug (Figure 12).[100] The drug was delivered to the human eye upon magnetic excitation through the PDMS membrane, which had a laser-drilled aperture of 100 × 100 μm^2. Results did not show any infections or significant leakages of the drug using the PDMS packaging or PDMS membrane and the ex vivo application was successful. PDMS has also been successfully applied as an array substrate for neuronal culture, showing potential for the creation of flexible and biocompatible microelectrode array implants (Figure 11).[101]

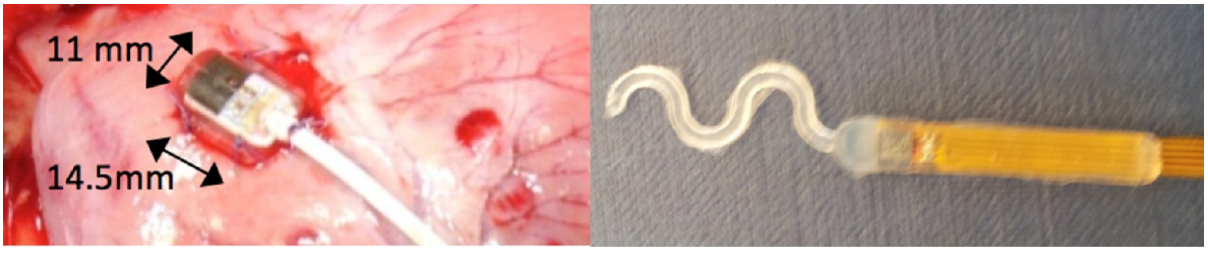

Figure 9. (Left) Prototype sensor by Imnes with silicone encapsulation sutured to heart surface. (Right) Silicone-encapsulated sensor with polyamide flexible cable. Reprinted with permission from ref 98. Copyright 2012 IEEE.

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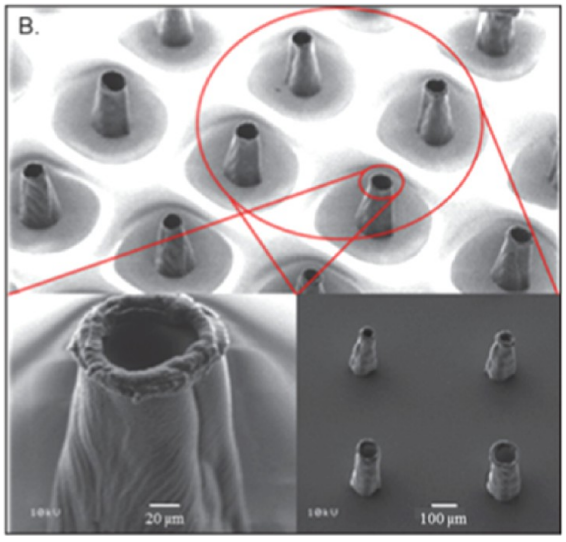

Figure 11. SEM image of 63-electrode polypyrrole post array fabricated on PDMS substrate. Reprinted with permission from ref 101. Copyright 2012 IEEE.

Although PDMS and silicone implants have been widely used, multiple articles have raised concerns regarding the use of silicones, which have been found to be disseminated to the lymph nodes and other parts of the body. Concerns have also been raised related to the overall failure of silicone implants.[102] Overall, silicones have been widely used in medical implants and were shown to provide structural support for various device applications; however, this material is relatively delicate when used as a bulk material and their long-term effects have not been evaluated. Accelerated lifetime tests have been conducted in the past, but few studies have reconfirmed or re-evaluated the findings.

2.6. Polyurethane (PU). PU has been used in a wide range of implants and can also be easily modified to fit different biomedical applications. However, PU can be affected by chemical attacks in vivo, resulting in the degradation of the material. When handled correctly, this degradation can be used to facilitate the growth of new tissues.[28] It was also found that PU had lower water permeability, which can be further reduced by introducing low concentrations of isopropyl myristate (Figure 13).[103] Baj-Rossi et al. found that the epoxy-enhanced PU membrane developed retained enzyme activity for up to 35 days; upon implantation in mice for 30 days, the membrane improved the integration of the sensor with its surrounding tissue with low inflammation levels.[104] PU breast implants show very low rates of capsular contracture.[105,106] PU foam has also been employed as packing material after mucosal trauma, where there was normal mucosal healing in the PU foam and less inflammation was observed compared the use of an absorbable gelatin sponge,[107] A nonporous composite was also developed comprising of mineralized allograft bone particles and biodegradable PU binder.[108] It was found that these composites have high strength and were osteoconductive, making them suitable for weight-bearing applications. The properties can also be modified to suit different applications. This demonstrates that there is high potential for these composites to be used in bone tissue engineering in the future. Thermoplastic PU also shows good potential when incorporated with PDMS for use in implants because of its good surface and thermo-mechanical and biocompatible properties;[109] however, this material is relatively new and few studies have examined the properties of thermoplastic PU.

A recent study by Sowa-Söhle et al. investigated the safety and antimicrobial efficacy of thermoplastic PU, and MG-Ag-PU composites were found to have a reduced lag phase of bioactivity compared to normal Ag-PU composites, as the Mg components enabled faster Ag ion release.[110] PU nanocomposites have also been successfully prepared using a biobased hyper-branched PU and iron(III) oxide nanoparticles, which displayed magnetic behavior with enhanced biodegradation, biocompatibility, antimicrobial properties, and shape recovery effects as compared to the original.[111] This material may thus be used as a thermally and magnetic-controlled smart biomaterial for various applications in the medical industry to overcome traditional limitations.

2.7. Polytetrafluoroethylene (PTFE). PTFE has another commonly used trade name, Teflon, which was developed by DuPont Co. Zhang et al. were among the few researchers to successfully use PTFE as a substrate for a high-frequency surface coil for MRI and spectroscopy.[112] However, it was found that PTFE did not adhere well to metals and very low stability after exposure to γ radiation and could not be used for certain procedures such as gamma sterilization.[113,114] An expanded polytetrafluoroethylene (e-PTFE) covered biliary metal stent, developed to overcome tumor ingrowth and treatment of benign biliary structures, was compared with a silicone-covered stent and another PU-covered stent.[115] it was found that the e-PTFE was less biodurable in the 6-month testing period because the stents were

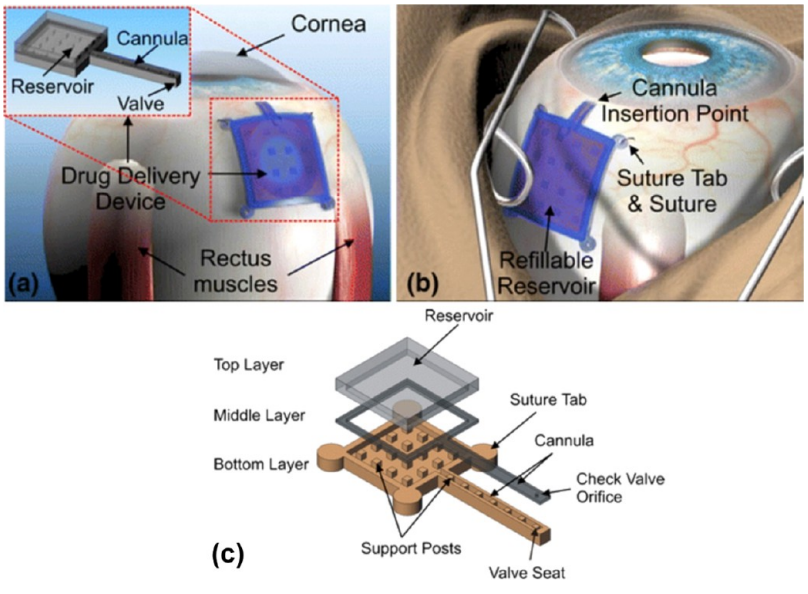

Figure 12. (a, b) Illustration for placement of PDMS device. (c) Expanded view of layers within the device. Reprinted with permission from ref 100. Copyright 2009 Springer.

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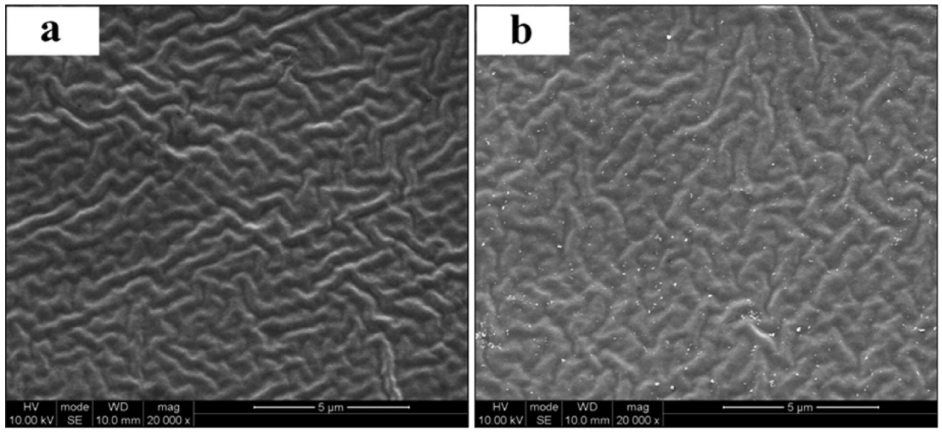

Figure 13. SEM images showing surface of IPM modified PU (a) before and (b) after 10 days in 40 mL of bovine serum albumin and phosphate buffer solution. Reprinted with permission from ref 103. Copyright 2010 MDPI.

Table 6. Strength Tests for e-PTFE, Silicone, and PU[115]

	e-PTFE		silicone		PU	
duration of stents left in bile (months)	tensile strength (N/mm)	tear strength (N/mm)	tensile strength (N/mm)	tear strength (N/mm)	tensile strength (N/mm)	tear strength (N/mm)
0	184.7	179	35.3	56.3	26	45.2
1	158	158.8	39.3	65.3	26.8	41
2	161.2	153.4	38	61.8	18.1	23.9
4	83	140.3	24.8	56.3	11.9	16.7
6	55	127.5	21.4	42.9	7.7	7.5

constantly exposed to bile (Table 6). Nevertheless, e-PTFE showed a greater tendency to form a biofilm during the test, providing efficient protection from antibacterial agents and phagocytic cells.[116] PTFE-coated catheters are also commonly used to drain urine after surgeries and have recently been used as controls in further research to reduce infections.[117] Microporous PTFE catheter balloons have also been used to deliver drugs to target tissues in the body.[118] PTFE introducer sheaths were also coated on metallic stents used for palliative treatment of unresectable malignant esophageal strictures. Compared to PU membranes, PTFE membranes were associated with less frequent tumor ingrowth.[119]

2.8. Polyamide (PA). Polyamides are macromolecules with repeating units linked by amide bonds. PAs can be both naturally occurring and synthetic; however, only synthetic PAs are described in this review. The most common form of PA used in biomedical implants and devices is nylon, which is often used as a material for fibers in composites to increase the mechanical strength of the composite, as suture materials, and in dentures production;[120,121] however, they are rarely used as material for packaging films. Rather, PA composites have been found to be safe for use in bone formation scaffolds and are more commonly used as nanofillers to improve the mechanical attributes of composite materials.[122,123]

Nylon has also has been recently tested with a series of other materials to study microbial contamination and showed the lowest contamination compared to other materials (Figure 14).[59] This shows that nylon has the ability to prevent bacterial transmission. Nylon and some of its composites, such as glass fiber nylon, can be easily fabricated using 3D printing facilities.[124]

2.9. Polyimide. Polyimides can be classified into many different groups based on their polymer chains, types of hydrocarbon residues, and functional groups in the polymer chain. These properties determine their physical properties and possible applications. However, polyimides are still commonly found in the medical industry as encapsulation and insulation materials for medical devices. A series of tests were conducted in another study to determine the long-term survivability of three commercially available polyimides.[125] The results showed no decrease in tensile properties when the materials were placed in phosphate-buffered saline for over 20 months at room

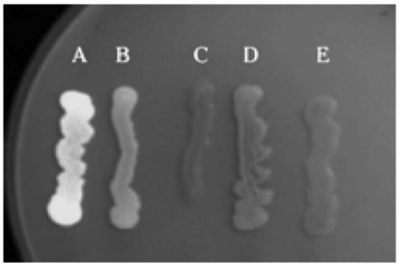

Figure 14. Microbial migration of *Staphylococcus epidermidis* along (A) polyethylene fiber, (B) polyurethane, (C) nylon, (D) polypropylene, (E) silk. Experimental results reveal that nylon had the lowest microbial migration among all. Reprinted with permission from ref 59. Copyright 2013 Marsland Press.

temperature and at 60 °C, justifying their use within this period. Apart from its mechanical properties, PI also has high light transmittance for a wide range of wavelengths, making it attractive for use in optoelectronic devices. Studies found that PI film conditions did not significantly affect the optical transmission values over a wide spectral wavelength range of 420 to 920 nm.[126] Making use of this characteristic, an implantable LED array was developed for obtaining electrocortigram recordings for the control of a brain machine interface.[127]

Polyimide sensors were previously developed for sensing in a wide range of biomedical applications such as deep brain recording and stimulation as well as for contact lens pressure sensors. Hasenkamp et al. recently developed a polyimide-based MEMS strain-sensing device to investigate artificial knee implants and Forchelet et al. developed a polyimide-metal composite MEMS strain-sensing device;[128,129] however, the packaging of their devices still required the use of epoxy to bond the surface-mount connectors to the contact pads (Figure 15). Polyimide was also used as a protective sheath,[130] as it provides suitable protection and can be custom-fabricated with micro apertures to accelerate diffusion of gas during sterilization of the device leads. Polyimides have also been combined with PDMS for use as a substrate for a flexible subdural electrode array in neural recordings.[131]

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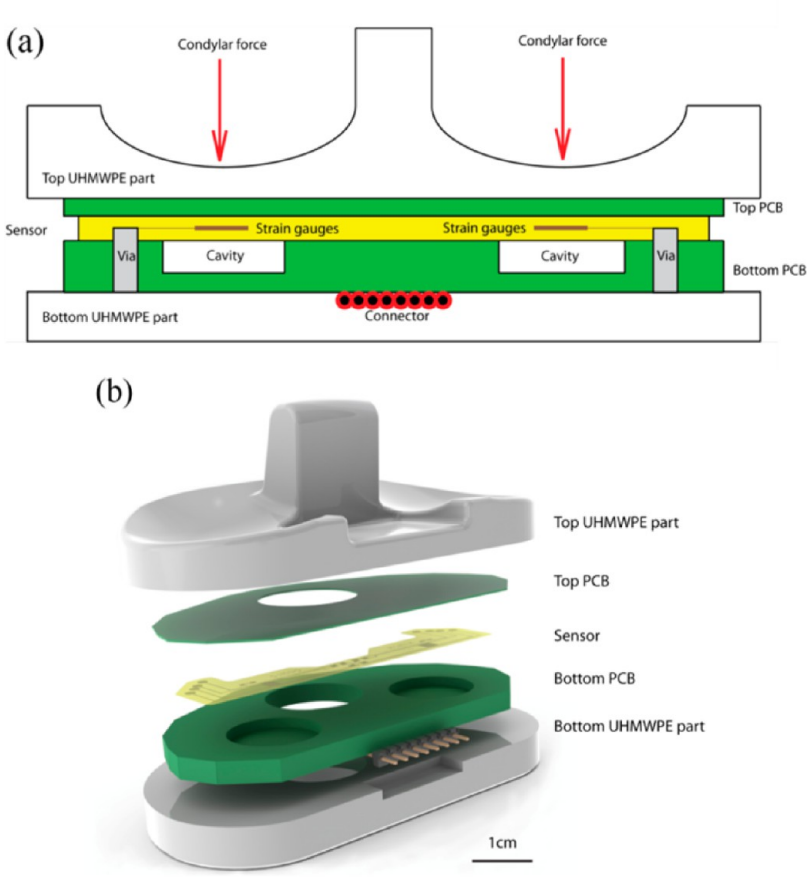

Figure 15. (a) Schematic diagram of prosthetics with polyimide strain gauge. (b) Expanded view. Reprinted with permission from ref 129. Copyright 2014 MDPI.

2.10. Liquid Crystal Polymer (LCP). Liquid crystal polymers have one of the highest Young's Modulus and impact strength in the list of materials in Table 3. LCPs are also very attractive for use in microwave frequency electronics. Recent studies have shown an increasing interest in the use of LCPs as biomaterials for various implants and devices, such as retinal and neural prosthetic implants. The RF characteristics of the devices were also unaffected by this thin film.[132] It was also found that using LCP not only as an encapsulating film but also as a substrate enabled the development of a multilayered planar coil for delivering power and data to devices. Another example recently developed is a neuroprosthetic device using encapsulation via thermoforming and fusion bonding of thin films of LCP, where it was found that this material had very low leakage current through the LCP encapsulation during a period of 300 days in in vitro accelerated soak tests.[27] In another study, it was observed that the LCP packaging for retinal implants affected the pixel density and the device was able to restore user facial recognition and reading functions because of the higher pixel resolution.[133] LCPs have also been used in the development of a flexible electrode array in rats to study neurological diseases and to study brain functions in vivo.[134] LCPs were also used in the fabrication of 3D cubic antennas for future microwave packaging for higher performance circuits and higher compactness in the devices.[61] In using LCP for cochlear implantable devices, Kim et al. showed that the material had good MRI compatibilities and suggested that these LCP packages reduced the size of the cochlear device and were useful for further studies of the auditory perception mechanism (Figure 16).[65] Hwang et al. also demonstrated an in vivo radio frequency-integrated circuit used for wireless communication that was encapsulated by an ultrathin silicon-based LCP (Figure 17).[135]

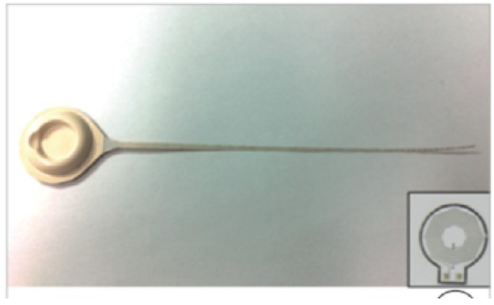

Figure 16. LCP-based cochlear implantable device prototype with inset showing 1 cm diameter LCP-based planar cooper coil for power and data transmission. Reprinted with permission from ref 65. Copyright 2012 Korean Society of Otorhinolaryngology-Head and Neck Surgery.

2.11. Carbon Nanotube (CNT) Composites. CNTs are widely suggested for use as biomedical packaging films due to its unique electrical, mechanical and surface properties, which can enable it to improve the functionality of its devices. Carbon nanotube composites are by far the strongest materials used in this category with high tensile strength and elastic modulus. However, they are relatively weak against shearing between adjacent shells and are easily compressed because of their hollow structure. Buckling occurs under compressive, bending, and torsional stresses.[67] CNTs also display superconductivity characteristics along their specific axis when combined with zeolite as a composite.[136,137] A composite of poly(lactic acid) and CNT was also used to develop a degradation monitoring system to study the degradation of biodegradable polymers (Figures 18 and 19),[138] and Li et al. examined CNT composites used in scaffolds for bone tissue engineering.[139] In one of the studies, it was discovered that although there is no direct correlation between the primary dimensions of carbon nanomaterials among materials and biocompatibility, some studies have shown that smaller or shorter CNTs are more biocompatible than

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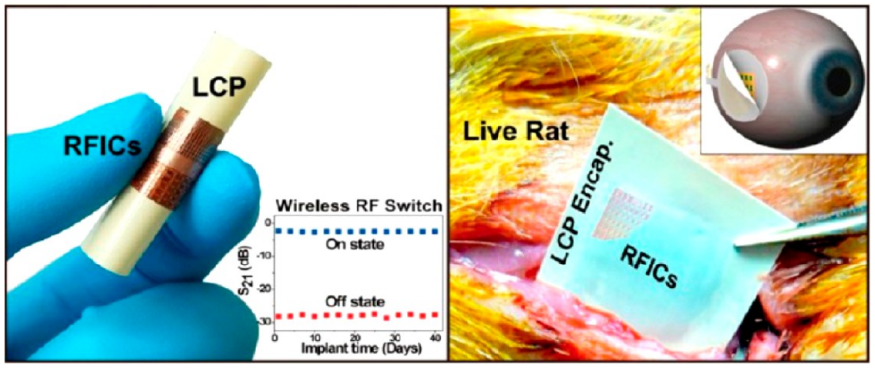

Figure 17. LCP-encapsulated radio frequency integrated circuits tested in a rat. Reprinted with permission from ref 135. Copyright 2013 American Chemical Society.

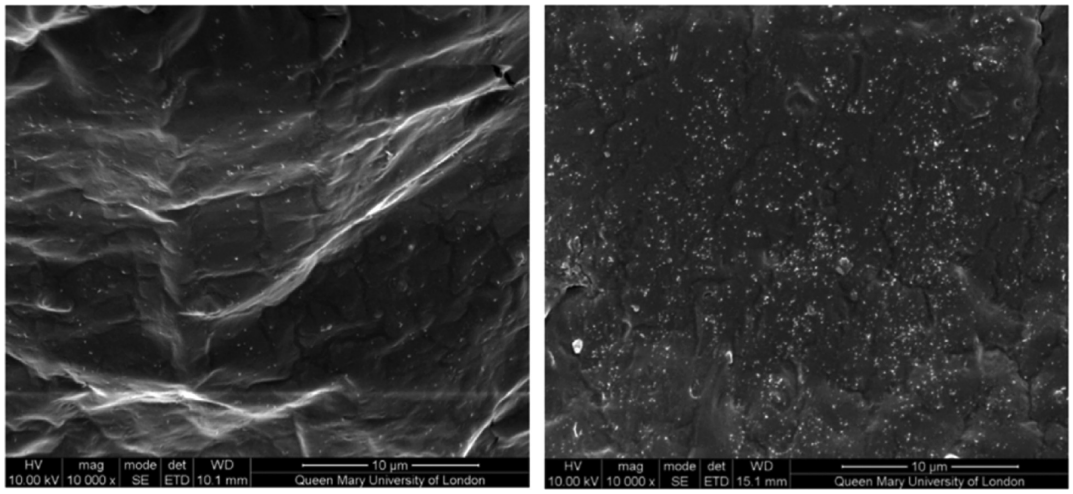

Figure 18. SEM images of PLA/0.5 wt % CNT (left) and PLA/5 wt % CNT (right) showing good dispersion of CNT and low aggregation for both composites. Reprinted with permission from ref 138. Copyright 2013 Elsevier.

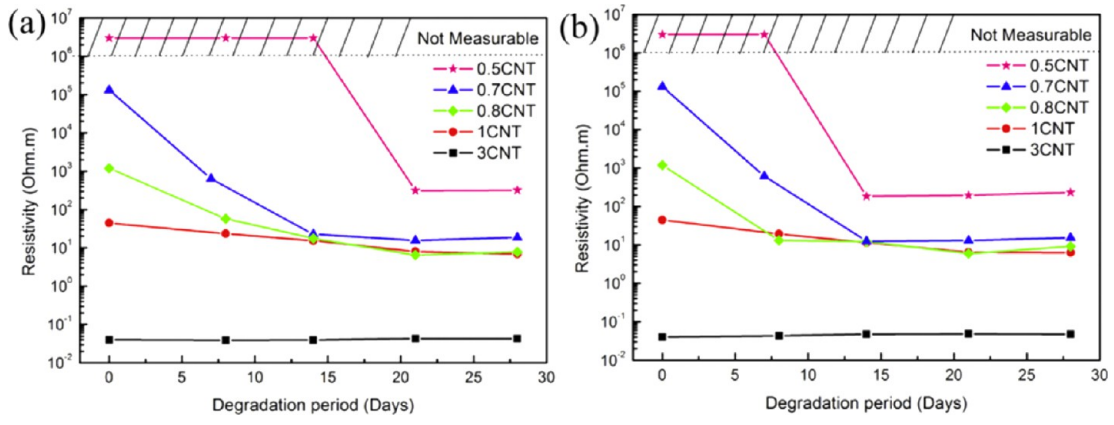

Figure 19. Change in resistivity during degradation for different % wt of CNT in water (left) and phosphate-buffered solution (right). Reprinted with permission from ref138. Copyright 2013 Elsevier.

larger CNTs.[140] CNT composites can be coated on metals to give excellent porosity and packing density within the films itself, reducing the ionization of the metal encapsulated. Li et al. found that CNTs are useful as high load-bearing orthopedic implants and can promote the precipitation and materialization of hydroxylapatite in such coatings.[66] CNT coatings were also found to allow an electrically conductive fibrous surface layer for its interfaces. A cement coating composite comprised of PMMA/CNT/high-load HA was developed and optimized and was found to induce calcium phosphate layer growth on the surface of cement discs with increased cell viability and low apoptosis.[85] Extensive spread over the disc surface was also observed.

In 2013, Chen developed a composite film comprised of poly(3,4-ethylenedioxythiophene) and multiwalled carbon nanotube (PEDOT/MWCNT) to coat microelectrode arrays to improve the neural interface between the device and the human environment.[141] A higher charge storage capacity and charge injection limit were observed compared to gold electrodes and PEDOT-coated electrodes. The use of CNTs in biomedical packaging have enabled higher detection, connectivity, and conductivity within the body. This may result in

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higher input signals for sensors in the body, allowing for the higher sensitivity of medical devices.

3. SUMMARY AND FUTURE TRENDS

Recent studies have focused more on composites rather than using individual materials in biomedical implants and devices in the field of synthetic materials. It is difficult to distinguish which material functions best for different applications. This review discussed the general categorization of medical implants and devices and the types of materials that have been used, as well as the latest studies and developments in the research industry on different materials and composites. Some of the more interesting materials include polyimide sensors that can be used in neural optoelectronics, polyurethane nanocomposite with iron(III) oxide nanoparticles that have magnetic properties, and the materials that can be 3D printed. With the introduction of rapid prototyping techniques like 3D printing, the demands for unique implants can be met. There is also an increasing number of studies examining liquid crystal polymers and carbon nanotube composites to further enhance their packaging films, as these materials are relatively easy to fabricate and have good mechanical and electrical properties. Researchers have yet to carry out in vivo characterization experiments and conduct comparison studies of these materials in vivo. Concurrently, many are also gradually developing new composites that would meet the unique biocompatibility and mechanical requirements of each different region in the body. It is safe to conclude that pure synthetic polymeric materials have already attained their peaks in terms of usage for medical implants and devices. The current trend observed in this field is in the combination of different materials to produce composites that would either provide more suitable mechanical strength and flexibility or provide new functionality, like the usage of CNT. Similarly, the research trend for MRI-safe implanted medical devices is also growing because of the increasing needs of the global population.[142,143]

Additionally, the concern of biodegradability is increasing as nondegradable implants experience issues like stress shielding, wear debris, and may require surgical removal after usage. By having polymers that can degrade in the body and reduce the reliance on the implant itself, while encouraging the growth and self-supportability of the muscle or bones around the implant, a more comfortable and efficient healing process can be achieved. For example, biodegradable bone implants are being examined for this purpose.[144] Such concerns regarding biodegradable materials include not only their mechanical strength, but also the time required for degradation and the waste products produced upon contact with the human body. Another material that is of good mention would be silk. Silk fibroin polymers are biological in nature, however there has been research on production of synthetic silk for the biomedical industry's use in medical devices.[145] Biodegradable silk has been used as suture material for centuries and silk fibroin films have been observed to have good attachment to mammalian cells.[146] As such, they have been used for improvement of cell attachment and also as composites for bone formation.[147,148] Algarrahi et al.[149] made use of bilayer silk fibroid scaffolds in onlay esophagoplasty in rats and have observed that these scaffolds promoted formation of innervated, vascularized epithelial and muscular tissues within implantation sites. This goes to show that silk has the potential to speed up healing processes.

A new aspect of biomedical devices would be in the area of shape memory, where materials are able to deform according to a set of certain characteristics when triggered by an external stimulus. These smart materials are able to be designed according to specific applications and are highly advantageous for minimally invasive procedures.[150] In this aspect, mechanical properties of the material would be of great concern. Currently, there are many synthetic polymers that have been used as material for such "smart devices", like polyurethane shape memory polymer, polytetrafluoroethylene, polyacrylonitrile, etc.[151,152] To date, there are still many challenges in using shape memory polymers as medical implants and devices, like for example the fabrication of polymer fibers and multiple stimulus of polymers, thus only having a few commercialized products available in the market.[153] However, given that there is an increasing need for minimally invasive procedures, it is believed that there would be more focus in this area of shape memory polymers, which would lead to further breakthroughs.

The future for synthetic polymeric materials in the medical industry appears to be promising given the wide attention it is receiving because of the global emphasis on healthcare. Apart from that, works are still ongoing in the development of greater functionality of devices and implants, like in the areas of biodegradability and MRI safety. Combinations of materials as composites are essentially endless given the wide range of materials that are compatible with one another. New composites are constantly being developed worldwide, including compositions between natural and synthetic polymers that have the potential to provide mechanical functions that are similar to the human body structure. Fabrication technology employing the use of such polymeric materials is also improving, enabling fast and cheap fabrication of unique parts, opening the doors for a wider range of applications. In retrospect, what was once known to cause permanent dysfunction has been reduced to limited disability with greater comfort because of the development of various medical devices and implants. This has been a huge milestone for the biomedical industry. By continuing to progress in this area of synthetic polymeric materials, this pursuit for enhancement of the quality of lives can finally be achieved.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: yongjiny@ntu.edu.sg.
*E-mail: wtpark@seoultech.ac.kr.

Notes

The authors declare no competing financial interest.

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