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ADVANCED TECHNOLOGIES AND POLYMER MATERIALS FOR SURGICAL SUTURES

Edited by
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KARTHIK NAIR

ELSEVIER

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CHAPTER 5

Polymers for surgical sutures

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5.1 Introduction

One of the biggest challenges within the medical practice is the innovation and improvements in technologies for the closure of wounds or sutures [1]. The general technologies comprise physically perforating materials, for example, staples or sutures. These approaches have several limitations and challenges such as the risk of infections [2], cause continues pain, not always effective and in some cases can result in leakage at the site of closure. To overcome these challenges and limitations polymer-based sutures can be employed to hold body tissues together or ligate blood vessels, after a surgery or accidental injury [3]. Depending on the damaged site, specific features are required to withstand the natural conditions of the body, but the utmost property for a suture material is its tensile strength, which can be tailored by the composition and thickness of the yarn. Aside the strength, other important properties to be considered are absorbability, sterility, high knot security, lack of allergic reaction, and ease of handling [4].

In addition to these characteristics of biomaterials, in general, other criteria used for suture selection are based on the properties of the tissues involved, such as the specific healing rate; wound condition and general health of the patient, potential postoperative complications, personal preference and experience of the surgeon, and economic reasons [5,6].

Among the extensive portfolio of materials currently available, synthetic and natural polymers have been the most frequently targeted.

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Over the past millennia, a huge number of suture materials have been developed by scientists and used by physicians, dentists, and veterinarians [7]. Original sutures were made from biological materials, such as silk and gut (made by twisting together strands of purified collagen), but most modern sutures are synthetic, including absorbable (poly(glycolic acid) (PGA), poly(lactide-co-glycolic acid) (PLGA), poly(lactic acid) (PLA), polycaprolactone (PCL), poly(4-hydroxybutyrate) (P4HB) and poly-dioxanone (PDO or PDS)) as well as nonabsorbable polymers (polytetra-fluoroethylene (PTFE), nylon, poly(ethylene terephthalate) (PET), polypropylene (PP), polybutester (copolymer composed of polyglycol terephthalate and polybutylene terephthalate) and poly(vinylidene fluoride) (PVDF)) (Fig. 5.1) [8]. Additionally, stainless steel has also been used as sutures due to its high tensile strength [9], and applied in abdominal wound closure, intestinal anastomosis, hernia repair, sternal closure, and for certain orthopedic procedures [9,10].

Additionally, very recently, Afewerki et al. disclosed the engineering of multifunctional surgical bactericidal nanofibers with tunable mechanical and biological properties comprising the integrated strategy of combining electrospinning-, plasma treatment, and direct surface modification strat-agem [11]. The devised nanofibers were employed in abdominal hernia repair, which showed good biointegration, blood vessel formation, and tissue growth. Furthermore, the nanofibers with their antibacterial

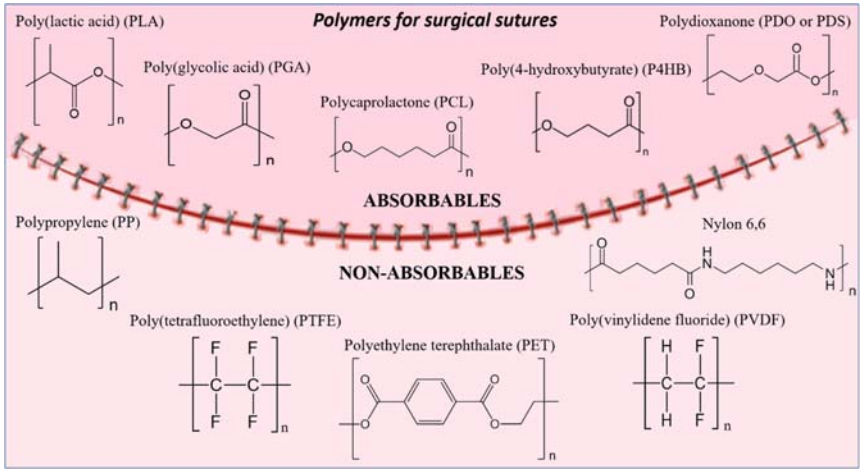


Figure 5.1 Examples of some of the most employed absorbable and nonabsorbable polymers for surgical sutures and their structures.

properties could be a good candidate for the treatment of abdominal hernia repair and prevent any future infections [11].

Sutures are generally categorized by their (i) absorption (nonabsorbable or absorbable), (ii) yarn construction (monofilament or multifilament/twisted/braided), (iii) origin (synthetic or natural), (iv) presence of dye (undyed or dyed to enhance visibility in tissue), (v) presence of coating, to improve biocompatibility or to provide antibacterial property [4], and (vi) thickness, normally called size [7]. Other characteristics that are often considered are the capillarity of the suture, tissue reactivity and the rate of wound healing in the area [12]. Some commercial availably surgical sutures and their properties are summarized and systematic classified based on natural and absorbable, natural and nonabsorbable, synthetic and absorbable, and synthetic and nonabsorbable characteristics in Table 5.1.

The yarn can be constructed by a single filament (called monofilament) or by multiple filaments that can be twisted or braided into bundles (Fig. 5.2). The size of the suture is defined by the United States Pharmacopeia (U.S.P.) ranging from #10 (diameter of 1.2 mm) to #12−0 (diameter of 0.001 mm) [7] (Tables 5.2 and 5.3). The diameter for a given U.S.P. size differs depending on the suture origin (natural or synthetic) and absorbability (nonabsorbable or absorbable). Thicker sutures present higher knot-pull tensile strength and are normally used for orthopedics, while thinner sutures are commonly used for ophthalmic.

Absorbable materials naturally degrade in the body over time and the byproducts are eliminated by urine. The degradation rate depends on the material and can take days or even months. Many synthetic suture polymers are primarily degraded by hydrolysis of their ester bonds [15]. However, natural polymers, such as collagen and silk fibroin, are degraded by catalyzed proteolysis, that is the breakdown of proteins through the hydrolysis of peptide bonds catalyzed by cellular enzymes called proteases [15]. Typically, the biodegradability of polymer sutures is investigated using in vitro assays in which the absorbable suture is immersed in a medium capable of simulating body fluid characteristics, such as phosphate-buffered saline and HANKs' balanced salt solution composed of 8.0 g/L sodium chloride (NaCl), 0.4 g/L potassium chloride (KCl), 0.14 g/L calcium chloride (CaCl), 0.1 g/L magnesium chloride ($MgCl_2$), 0.06 g/L magnesium sulfate ($MgSO_4$), 0.06 g/L potassium phosphate monobasic (KH_2PO_4), 0.06 g/L disodium phosphate (Na_2HPO_4), 0.35 g/L sodium bicarbonate ($NaHCO_3$), 1.0 g/L glucose ($C_6H_{12}O_6$). After a preestablished time interval, the biodegradation behavior can be analyzed by observing the

Table 5.1 Commercially available sutures.

	Material	Brand/Company	Yarn construction	Coating	Antibacterial property
Natural and absorbable	Plain gut	CP medical	Twisted	–	No
	Plain gut	Atramat, Internacional Farmacéutica	Twisted	–	No
	Chromic gut	CP medical	Twisted	Treated with a chromic salt solution	No
	Chromic gut	Atramat, Internacional Farmacéutica	Twisted	Treated with a chromic salt solution	No
Natural and non-absorbable	Linen	LIN, Peters surgical	Twisted	–	No
Synthetic and absorbable	PLGA (polyglactin 910)	Coated Vicryl, Ethicon (Johnson & Johnson)	Braided or monofilament	PLGA (polyglactin 370) and calcium stearate	No
	PLGA	Coated Vicryl rapide, Ethicon (Johnson & Johnson)	Braided	PLGA (polyglactin 370) and calcium stearate	No
	PLGA with triclosan	Coated Vicryl plus, Ethicon (Johnson & Johnson)	Braided	PLGA (polyglactin 370) and calcium stearate	Yes
	PLGA	Polysorb, Covidien, Medtronic	Braided	PLGA and calcium stearoyl lactylate	No
	PLGA	Velosorb, Covidien, Medtronic	Braided	PLGA and calcium stearate	No
	PGA	Visorb synthetic, CP medical	Braided	PCL and calcium stearate	No
	PGA	Bondek plus, Teleflex	Braided	Polycaprolactone copolyglycolic acid	No
	PGA	OPTIME, Peters surgical	Braided	–	No
	PGA-PCL	Atramat, Internacional Farmacéutica	Monofilament	–	No
	PGA-PCL with triclosan	MONOCRYL PlusAntibacterial, Ethicon (Johnson & Johnson)	Monofilament	–	Yes
	PDS	Monodek, Teleflex	Monofilament	–	No
	PDS	PDSII, Ethicon (Johnson & Johnson)	Monofilament	–	No
	PDS with triclosan	PDS plus antibacterial, Ethicon (Johnson & Johnson)	Monofilament	–	Yes
	P4HB	Monomax, B. Braun	Monofilament	–	No

Synthetic and non-absorbable	PTFE	Cytoplast, Osteogenics biomedical	Monofilament	–	Yes
	PVDF	PREMIO, Peters surgical	Monofilament	–	No
	Nylon6,6	Teleflex	Monofilament	-	No
	Nylon6,6	Trelon, B. Braun	Braided	Silicone	No
	Nylon6,6	Supramid, B. Braun	Pseudomono-filament	Polyamide 6	No
	Nylon6,6	CARDIONYL, Peters surgical	Monofilament	–	No
	Silk	Teleflex	Braided	Wax	No
	Silk	Mersilk, Ethicon (Johnson & Johnson)	Braided	Beeswax	No
	PP	CP medical	Monofilament	–	No
	PP	Perma Sharp, Hu-Friedy manufacturing company	Monofilament	–	No
	PET	DemeBond™, DemeTech Corporation	Braided	–	No
	PET	Polydek, Teleflex	Braided	PTFE	No
	PET	Ethibond Excel, Ethicon (Johnson & Johnson)	Braided	–	No
	Polybutester	Novafil™, Medtronic	Monofilament	–	No
	Stainless steel	Medtronic	Monofilament	–	No
	Stainless steel	ACIER, Peters surgical	Monofilament	–	No

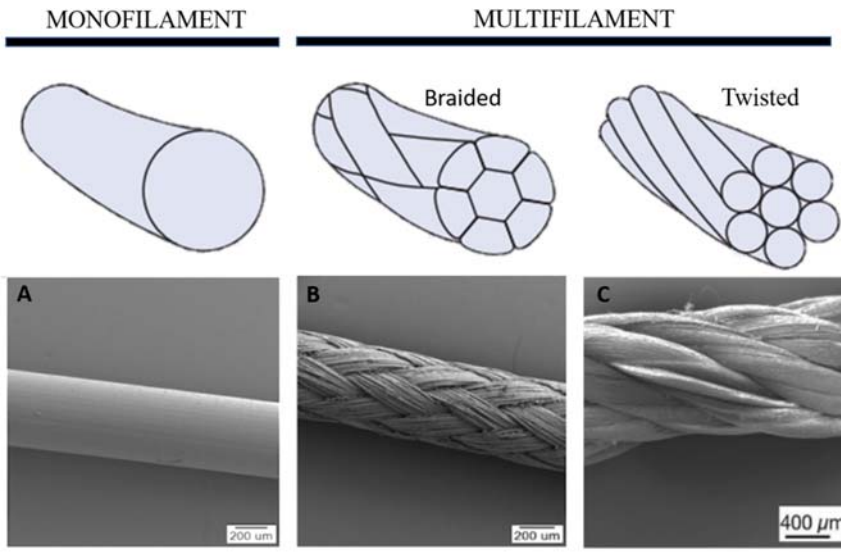


Figure 5.2 Structure of monofilament and multifilament sutures. SEM micrographs of (A) monofilament PDO suture, (B) braided PGA suture, and (C) twisted PDO suture. *(Reproduced with permission Copyright: © 2018 Ercan et al. and Copyright: © 2020 Rashid et al., licensed under A creative Commons Attribution License (CC BY) [13,14].)*

changes in the surface morphology of the sutures by scanning electron microscopy and by determining the degradation rate from measuring the suture weight loss during the process [5,16]. Absorbable sutures are normally applied in internal body tissues, with the exceptions of stressful internal environments, such as heart or bladder, where nonabsorbable sutures are normally preferred. Nonabsorbable materials are also commonly used for skin wound closure, where the sutures can be removed after a few weeks [17].

Polymers used for surgical suture are often recognized as foreign materials within the body, trigging a host of immune response and leading to inflammation [4]. In this context, to minimize potential risks to patients, it is essential that the biocompatibility of sutures have to be evaluated. Although it is not possible to generalize which biocompatibility tests should be performed, since the test depends on the material, type of device and, mainly, the application, the International Organization for Standardization (ISO) provides a series of guidelines that can assist in selection of the most appropriate assay. The ISSO 10993, which has the general title of "Biological evaluation of medical devices," consists of a set of standardized tests

Table 5.2 List of absorbable suture size as defined by the United States Pharmacopeia (U.S.P.).

	Collagen suture		Synthetic suture	
U.S.P. size	**Diameter range (mm)**	**Knot-pull tensile strength (N)**	**Diameter range (mm)**	**Knot-pull tensile strength (N)**
12–0			0.001–0.009	–
11–0			0.010–0.019	–
10–0			0.020–0.029	0.24
9–0	0.040–0.049	–	0.030–0.039	0.49
8–0	0.050–0.069	0.44	0.040–0.049	0.69
7–0	0.070–0.099	0.69	0.050–0.069	1.37
6–0	0.10–0.149	1.76	0.070–0.099	2.45
5–0	0.15–0.199	3.73	0.10–0.149	6.67
4–0	0.20–0.249	7.55	0.15–0.199	9.32
3–0	0.25–0.339	12.2	0.20–0.249	17.4
2–0	0.35–0.399	19.6	0.25–0.299	26.3
0	0.40–0.499	27.2	0.30–0.399	38.2
1	0.50–0.599	37.3	0.40–0.499	49.8
2	0.60–0.699	44.2	0.50–0.599	62.3
3	0.70–0.799	57.8	0.60–0.699	71.5
4	0.80–0.899	68.6	0.60–0.699	71.5
5			0.70–0.799	–

to assess biocompatibility that comprise, for example, in vitro assays as tests for cytotoxicity (ISO 10,993–5) [18], and in vivo assays as well (ISO 10993–10) [19]. Usually, multifilament and absorbable suture materials are more reactive than monofilament and nonabsorbable sutures [12]. Additionally, the yarn itself can be a vehicle for bacterial contamination, and therefore, increasing the chances of a surgical site infection [20]. Here again, multifilament sutures are more likely to contribute to the wicking of bacteria and fluids into the wound, due to the capillary action [21]. Although the multifilament sutures present higher tissue reactivity and capillarity, they display better handling characteristics [12].

Furthermore, bioactive materials that can enhance suture function and capability have been at the forefront of suture technology. Alshomer and

Table 5.3 List of nonabsorbable suture size as defined by the United States Pharmacopeia (U.S.P.).

U.S.P. size	Diameter range (mm)	Knot-pull tensile strength (N)		
		Class I[a]	Class II[b]	Class III[c]
12−0	0.001−0.009	0.01	–	0.02
11−0	0.010−0.019	0.06	0.05	0.20
10−0	0.020−0.029	0.194	0.14	0.59
9−0	0.030−0.039	0.424	0.28	0.68
8−0	0.040−0.049	0.59	0.39	1.08
7−0	0.050−0.069	1.08	0.59	1.57
6−0	0.070−0.099	1.96	1.08	2.65
5−0	0.10−0.149	3.92	2.26	5.30
4−0	0.15−0.199	5.88	4.51	8.04
3−0	0.20−0.249	9.41	6.47	13.3
2−0	0.25−0.299	14.1	10.0	17.6
0	0.30−0.399	21.2	14.2	33.3
1	0.40−0.499	26.7	17.8	46.7
2	0.50−0.599	34.5	24.9	57.8
3 and 4	0.60−0.699	47.8	36.1	89.3
5	0.70−0.799	60.4	–	112
6	0.80−0.899	71.4	–	133
7	0.90−0.999	88.6	–	156
8	1.00−1.099	–	–	178
9	1.100−1.199	–	–	201
10	1.200−1.299	–	–	224

[a]Class I: suture composed of silk or synthetic fibers of monofilament, twisted, or braided construction where the coating, if any, does not significantly affect thickness.
[b]Class II: suture composed of cotton or linen fibers, or coated natural or synthetic fibers where the coating affects thickness.
[c]Class III: suture composed of metal wire.

coauthors have defined bioactive sutures as "*biomaterials that are engineered to have controlled tissue interaction to optimize wound/defect healing, in addition to their essential function in tissue approximation*" [4]. Beyond their traditional function, bioactive sutures play a major role as a vessel to host and delivery drugs (e.g., antimicrobial-, anti-inflammatory-, and anesthetics drugs), growth factors (e.g., vascular endothelial growth factor (VEGF), recombinant human growth/differentiation factor-5 (rhGDF-5), and recombinant human platelet-derived growth factor-BB (rhPDGF-BB)), active nanoparticles (silver and bioglass (BG)), peptides (RGD (arginine-glycine-aspartic acid) and polylysine), proteins (intracellular adhesion molecule 1

(ICAM-1), fibronectin and fibrinogen), and cells (mesenchymal stem cells, osteoblasts, tenocytes, and embryonic stem cells) to traumatic sites [4].

Besides, the need for surgical procedures has increased over the time due to worldwide aging population, which has boosted the search for innovative and high performance materials in suture technology [22]. The market for surgical sutures is dominated by the global leading enterprises like Johnson & Johnson, Medtronic, Covidien, Teleflex, CP Medical, Peters Surgical, DemeTech, Samyang Biopharmaceuticals, B. Braun, Internacional Farmacéutica, among others. Johnson & Johnson has been a pioneer in wound healing, ever since the company created the world's first mass-produced sterile sutures made of either gut or silk in 1887, and kept innovating with the release of antibacterial sutures containing triclosan in 2003 [23]. The purest form of triclosan (IRGACARE MP) is a broad-spectrum antimicrobial agent that prevents bacteria from congregating on the suture, reducing the risk of developing a surgical site infection by almost a third [24].

5.2 Types of polymeric surgical sutures and their applications

5.2.1 Natural polymers

5.2.1.1 Gut

Gut, also known as catgut, is made of twisted collagen fibers usually harvested from beef tendon or from the intestine of sheep, cattle or goats [25]. There are two types of gut used for suture: (i) plain gut, composed of collagen slender strands woven together and further precision grounded to form a suture with uniform diameter, and (ii) chromic gut, when treated with a chromic salt solution promote the crosslinking of the collagen fibers. The chromic gut presents reduced tissue reaction, enhanced tensile strength and higher resistance to body enzymes, thus slowing down the absorption process [26]. The two types of sutures naturally degrade in the body catalyzed by proteolysis, with complete absorption after 90 days for chromic suture and 70 days for plain gut suture. Common uses of these suture materials include general closure, ophthalmic, orthopedics, obstetrics/gynecology, gastro-intestinal tract surgery, urology, and bowel anastomosis. When selecting a suture, its tensile strength, knot strength, handling property, and degradation rate should be taken into account, aside the tissue characteristics such as reactivity, wound healing rate and mechanical

properties [22]. Every specific application has its essential requirements for sutures and will highly depend on the properties of the suture, this kind of information and possible applications of the sutures can be found in the manufacturer instructions.

5.2.1.2 Silk

On the contrary of gut, silk is regarded as a nonabsorbable material according to the U.S.P. definition, because complete biodegradation requires approximately 2 years [15,27]. Silk suture is primarily composed of silk fibroin, that is a natural protein produced by the domestic silkworm *Bombyx mori*, and it is bioinert and relatively inexpensive [28]. Compared to collagen and PLA, silk fibroins have better mechanical properties like strength and toughness [27]. It is commonly coated with wax for easy pull out and applied for skin closure, gastrointestinal, cardiovascular surgery, plastic surgery, ophthalmic, and neurological procedures [29]. Silk suture has high capillarity, and should be avoided in contaminated wounds [12]. In this context, Jo and coauthors have reported the modification of silk sutures with 4-hexylresorcinol (4HR), which is a well-known antiseptic agent, to incorporate antimicrobial property and to achieve biodegradability [15]. In this study, silk sutures containing 12 wt.% of 4HR were compared to untreated silk (Woorhi Medical) and PLGA sutures (coated Vicryl, Ethicon (Johnson & Johnson)). The incorporation of the 4HR increased the expression of matrix metalloproteinase (MMP) in RAW264.7 cells, such as MMP-2, -3, and -9, which can digest a wide spectrum of proteins including silk fibroin. As a result, only 59.5% of the 4HR-silk suture remained after 11 weeks, which was similar to the results obtained for the PLGA degradation (56.4% remained), on the other hand, very different from the residual amount of bare silk suture (91.5% remained). In addition to displaying biodegradation rate similar to PLGA suture, the 4HR-treated silk also exhibited antimicrobial activity against six pathogens (*Staphylococcus aureus* (*S. aureus*), *Streptococcus sanguinis* (*S. sanguinis*), *Actinomyces naeslundii* (*A. naeslundii*), *Streptococcus gordnonii* (*S. gordnonii*), *Escherichia coli* (*E. Coli*), *and Actinomyces odontolyticus* (*A. odontolyticus*)) as evidenced by inhibition zone assay [15]. Moreover, silk sutures have been also modified with peptides [30], BG [31] and silver ions (Ag^{+}) [31,32]. Kardestuncer et al. demonstrated the ability of silk-RGD to stimulate human tenocyte adhesion, proliferation, and differentiation, with the aim of achieving faster and stronger interaction at the tendon to bone interface after tendon reconstruction surgery [30]. Besides, Blaker and coworkers have investigated the

use of Ag^+ containing BG (AgBG) as a coating for silk suture (Mersilk, Ethicon (Johnson & Johnson)) [31]. *In vitro* assay through immersion in simulated body fluid (SBF) solution confirmed the bioactivity of the AgBG-silk suture, with the formation of bonelike hydroxyapatite after only 3 days of immersion. Another attempt to modify silk suture with Ag^+ has been proposed by De Simone et al., who developed an effective and low-cost antibacterial silver coating by implementing an innovative photochemical deposition process [32]. The sutures were dipped in the silver solution and then exposed to UV radiation, which produced silver clusters on the surface of the suture. The silk suture containing Ag^+ presented significantly inhibited microbial colonization, with reduction of 81% on *S. aureus* and 78% on *E. coli*, and only slightly affected fibroblasts viability (82% cell viability compared to 91% of untreated suture) [32].

5.2.2 Synthetic and absorbable polymers

The most explored absorbable polymers for sutures applications are PGA, PCL, and PLA, and their blends. They present less associated tissue inflammation than the silk and plain or chromic catgut [12]. Their mechanical strength and rate of hydrolytic degradation can be controlled by the blend composition and by altering their physical properties, such as their molecular weights, degree of crystallinity and glass transition temperature (T_g) [33].

5.2.2.1 PGA-PCL blend

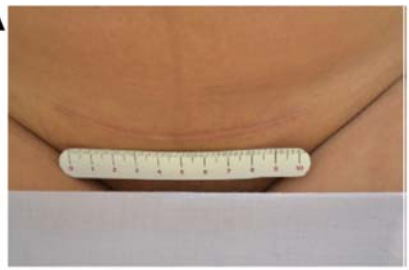
The combination of PGA with PCL at 75:25 ratio, named poliglecaprone 25 or PGC25, is extensively applied for human and veterinary use, in general as soft tissue approximation and/or ligation [34]. It presents an excellent handling property (flexible and easy to tie), smooth tissue passage, lower incidence of infection and trauma due to smooth surface, higher strength compared to catgut, and total absorbability after 110 days by hydrolysis process. De Lima and coworkers compared the PGC25 (Monocryl, Ethicon (Johnson & Johnson)) with a nonabsorbable suture composed of nylon (Mononylon ETHILON, Ethicon (Johnson & Johnson)) as intradermal suture for skin closure in women undergoing their first cesarean section, which was removed after about 7–10 days [35]. The cesarean is the most frequent surgery in women, and its esthetic outcome is a constant concern [36]. This clinical trial was performed with 60 women undergoing their first cesarean section, and 6 months after the operation the authors took photographs of the scars and evaluated the hypertrophy, color, and

width [35]. The scars from patients treated with PGA-PCL were significantly less hypertrophic, thinner, and had more acceptable color, demonstrating that the intradermal suture with PGC25 for skin closure after cesarean incision provides better esthetic outcome (Fig. 5.3) [35].

5.2.2.2 PGA-PLA blend

Another important type of suture material is obtained by the combination of PGA with PLA. For example, the coated Vicryl suture (Ethicon (Johnson & Johnson)) is composed of a copolymer made from 90% PGA and 10% PLA, known as polyglactin 910, and coated with polyglactin 370 (copolymer of 30% PGA and 70% PLA) and calcium stearate [37,38]. The coated Vicryl is usually braided, but a monofilament version is also available for use in ophthalmic practice [39–41]. An equivalent material is produced by Medtronic, named Polysorb and composed of 10% PGA and 90% PLA, with a coating of glycolide and ε-caprolactone [42,43]. Both Vicryl and Polysorb decomposes in 56–70 days within the body, and they are

A



C

Width			
		Nylon	PLG 25
Evaluator 1	Mean	2.88	2.01
	SD	0.40	0.34
	Median	3.00	2.00

B

Groups							
		Nylon			PLG 25		
		Hypertrophy	Coloring	Brands	Hypertrophy	Coloring	Brands
E1	Mean ± SD	3.19 ± 0.85	2.88 ± 0.95	1.00 ± 0.00	2.10 ± 1.05	2.27 ± 1.03	1.00 ± 0.00
	Median	3	3	1	2	2	1
E2	Mean ± SD	2.23 ± 1.03	1.69 ± 0.68	1.00 ± 1.00	1.34 ± 0.61	1.59 ± 0.73	1.00 ± 0.00
	Median	2	2	1	1	1	1
E3	Mean ± SD	2.15 ± 1.08	2.08 ± 0.80	1.00 ± 0.00	1.41 ± 0.78	1.93 ± 0.80	1.00 ± 0.00
	Median	2	2	1	1	1	1
E4	Mean ± SD	2.31 ± 1.12	2.73 ± 0.78	1.00 ± 0.00	1.70 ± 0.93	2.45 ± 0.78	1.00 ± 0.00
	Median	2	3	1	1	2	1

Figure 5.3 (A) Photo of the scar. (B) Value of the hypertrophy and scar staining: GI (Nylon) and GII (PLGA). (C) Values of the scar width for GI (Nylon) and GII (PLG 25). G1: Group 1; GII: Group 2; SD: Standard Deviation; E (1–4): Evaluators. *(Reproduced with permission Copyright: © 2020 Lima et al., licensed under A creative Commons Attribution License (CC BY) [35].)*

designated for soft tissue approximation and ligation applications [43–45]. There is also a faster absorption version of these types of sutures, called coated Vicryl rapide (total absorption in 42 days) and Velosorb (40–50 days). These are indicated for use in soft tissue approximation where only short term wound support is required, such as ophthalmic surgery and skin closure, particularly in pediatric surgery, episiotomies, circumcision, and closure of oral mucosa [46]. Vicryl suture has been extensively modified with different types of coatings to improve the biocompatibility [31,47–49]. Cummings and coworkers have coated Vicryl suture with rhPDGF-BB, using a dip-coating process in rhPDGF-BB solution for 30 min followed by air-drying, to repair tendon injuries, which showed a noticeable increase in tendon tensile strength [47]. A burst release of rhPDGF-BB from the sutures was observed after the first hour of incubation, followed by a continuous and gradual release of growth factor through 48 h. In a similar work, Dines et al. coated Vicryl suture with rhGDF-5/gelatin and demonstrated its beneficial effect on rat tendon fibroblasts [48]. The author also used a dip-coating process to coat the suture, and here approximately 95% of the rhGDF-5 release occurred within 24 h, followed by complete release by 48 h. Another attempt to improve bioactivity was performed by Boccaccini et al., using 45S5 Bioglass coating deposited by a slurry-dipping technique [49]. A stable slurry was prepared by dissolving 47 wt.% Bioglass particles in water, and used to coat the Vicryl suture by immersion during 3 min. Following immersion, the samples were dried at room temperature in a humid atmosphere to avoid microcrack formation on the coating. The adhesion strength of the coating or the release of Bioglass particles was not quantitatively determined; however, the high bioactive character of the composite suture was confirmed by the formation of hydroxyapatite crystals after 7 days of immersion in SBF solution. On the other hand, as vide supra mentioned, Blaker et al. silver-doped bioactive glass powder (AgBG) to coat Vicryl, and confirmed the formation of bonelike hydroxyapatite on the coated suture after only 3 days of immersion in SBF solution [31].

Furthermore, Johnson & Johnson has also launched a version of Vicryl with antibacterial property (coated Vicryl Plus) [50], nevertheless recent findings on triclosan toxicity [51] and triclosan-resistance bacteria have raised potential concerns over the use of this strategy [52]. As an alternative, silver nanoparticles (AgNPs) have been used to coat Vicryl suture through layer-by-layer deposition [53]. The silver nanoparticle solutions were prepared by photo-induced reduction under UV lamp of silver nitrate in

dilute solution of polymethacrylic acid. The deposition of the nanoparticles layer was intercalated with a poly-diallyl dimethylammonium chloride (PDADMAC) solution to immobilize the AgNPs onto the suture. After 20 deposition of each layer, the coated sutures were allowed to dry overnight. *In vitro* antibacterial assay against *E. coli* showed a significant growth inhibition from the silver coated suture. Moreover, immunohistochemistry in the intestinal anastomosis model and burst pressure measurement in healed anastomosis confirmed less inflammatory, cell infiltration and better mechanical properties. Another strategy to impart antibacterial property comprises the use of cefotaxime sodium (CFX-Na), a third generation antibiotic with broad spectrum, but this alternative was tested for PLA suture [54]. Pure PLA fibers fabricated by single-phase electrospinning were compared with PLA/CFX-Na nanofibers obtained by blend electrospinning and with PLA/CFX-Na core—sheath nanofibers fabricated by coaxial electrospinning. For fiber preparation, the PLA was dissolved in 2,2,2-trifluoroethanol (TFE) and the CFX-Na was dissolved in water. For the fabrication of core—sheath nanofibers the solutions were injected separately, while for blend nanofiber suture the CFX-Na solution was mixed with the PLA solution. An in vitro study indicated that CFX-Na release from both the composite nanofibers consisted of a low initial burst release followed by a sustained and slow release over a prolonged period of time. The core—sheath suture exhibited a relatively constant rate of drug release over a much longer duration, due to the presence of drug trapped deep inside the core layer. An inhibition zone experiment showed that both PLA-CFX-Na sutures had favorable antibacterial properties against *E. coli* and *S. aureus* when compared to pure commercial PLA suture. Additionally, Obermeier and coworkers have investigated the use of chlorhexidine (the golden standard in oral antiseptics) as an alternative to triclosan [55]. The authors coated a commercial braided suture made of PGA (Gunze) with chlorhexidine, using two types of fatty acids (palmitic or lauric acid) to optimize the drug release. The coating solutions were prepared by dissolving the fatty acids and chlorhexidine in ethanol, and posteriorly the sutures were immersed in these solutions and placed on a thermo-shaker for 2 min at 35 °C and 150 rpm and finally dried for at least 2 h. The coated sutures showed an initial fast elution of chlorhexidine and a subsequent continuous slow drug release over 96 h, with 70% release of chlorhexidine carried by lauric acid and 46% release for palmitic acid, both at drug content of 33 μg/cm, showing that the palmitic acid lead to a slower drug release over time (Fig. 5.4A and B). Both samples presented

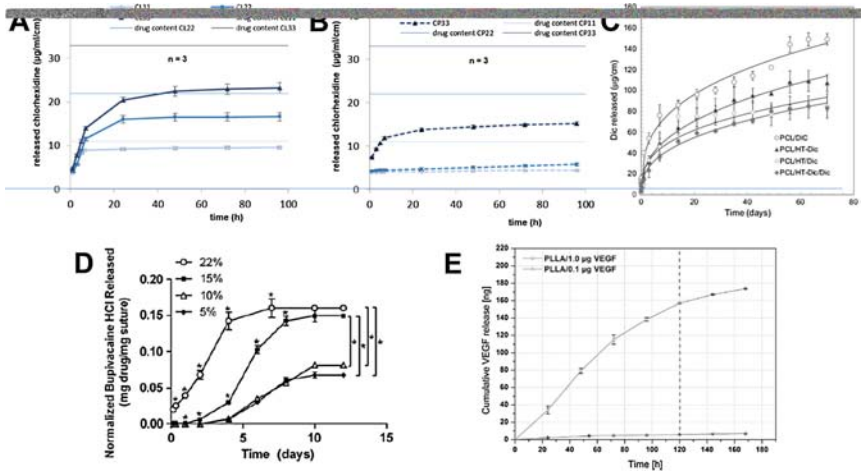


Figure 5.4 Chlorhexidine release from PGA suture using (A) lauric acid and (B) palmitic acid as drug carrier. (C) Diclofenac release from PCL suture using hydrotalcite as carrier. (D) Bupivacaine release from PLGA suture. (E) VEGF release from PDS suture. *(A) and (B) Reproduced with permission Copyright: © 2014 Obermeier et al. licensed under A creative Commons Attribution License (CC BY) [55]. (C) Reproduced with permission Copyright: © 2014 Catanzano et al. licensed under Elsevier by Ref. [56]. (D) Reproduced with permission Copyright: © 2012 Weldon et al. licensed under Elsevier by Ref. [57]. (E) Reproduced with permission Copyright: © 2014 Bigalke et al. under Acta Materialia Inc [58].)*

high antimicrobial efficacy against *S. aureus* for up to 5 days, and acceptable cytotoxicity levels [55]. A different drug carrier was reported by Catanzano et al., who used synthetic hydrotalcite (magnesium/aluminum (Mg/Al) hydroxycarbonate) for the sustained delivery of the antiinflammatory drug diclofenac in PCL sutures [56]. Although a significant reduction in tensile strength (breaking stress of 190 MPa, compared to 400 MPa for pure PCL), the PCL-hydrotalcite-diclofenac suture presented controlled release over 55 days (Figure 5.4C), and reduction of inflammatory responses. Another example of a controlled release system was presented by Weldon and co-authors, who fabricated PLGA sutures with the local anesthetic bupivacaine using the electrospinning technique [57]. It was noted that the sutures released their entire drug payload over the course of 12 days, mitigating the need for postoperative opioid analgesics (Fig. 5.4D).

5.2.2.3 P4HB

Furthermore, P4HB is a homopolymer of 4HB and presents a chemical structure similar to PGA and PCL, differing only by the number of methylene groups (1, 3, or 5) in the polymer backbone (Fig. 5.1) [59].

Similar to PGA and PCL, P4HB degrades by hydrolysis of the ester bonds, producing 4HB that is quickly metabolized and eliminated via the Krebs cycle. However, unlike PGA and PCL, P4HB belongs to a diverse class of biopolyesters called polyhydroxyalkanoates (PHAs) that are produced naturally by microorganisms [60]. The Monomax suture (B. Braun) was the first commercial P4HB product to be launched, and it is indicated for closure of the abdominal wall [59]. P4HB sutures are exceptionally strong, retaining approximately 50% of its initial tensile strength after 12 weeks, and substantially degrades in 1 year [61]. Williams et al. have shown that P4HB monofilament are 35% stronger than PDS suture (PDSII, Ethicon (Johnson & Johnson)) and 16% stronger than PP suture (Prolene, Ethicon (Johnson & Johnson)) [59]. In addition, P4HB suture has the highest pliability of any commercially available monofilament absorbable suture, and present excellent knot strength and security [62].

5.2.2.4 PDS

Additionally, PDS is a homopolymer of p-dioxanone, introduced in 1984 by Ethicon (Johnson & Johnson) [61]. PDS is a colorless, crystalline, and biodegradable polyester. It absorbs slowly over a period of 6–7 months, and it is best suited for use in general orthopedic surgery, pediatric cardiovascular surgery, ophthalmic, general, subcuticular, and fascia closure applications. Bigalke et al. coated PDS suture (PDSII, Ethicon (Johnson & Johnson)) with VEGF/PLA blend [58]. For the coating deposition, PLA and VEGF were separately dissolved in chloroform and then mixed together to achieve PLA/VEGF coatings containing 0.1 and 1 μg of VEGF. An in vitro release study showed for the PLA/VEGF-coated suture material with higher VEGF load a 18% release within 5 days, while the lower VEGF loaded-suture presented 9% release within the same period (Fig. 5.4E). The PLA/ VEGF(1 μg)-coated suture lead to improved cell viability in vitro and enhanced angiogenesis and vascularization in vivo [58].

5.2.3 Synthetic and nonabsorbable polymers

5.2.3.1 Nylon

Nylon is a generic designation for a class of polyamides, composed by repeating units linked by amide bonds, similar to the peptide bonds in proteins. Nylon 6,6 (nylon six to six, nylon 6/6 or nylon 66) and nylon six are the two most common for textile and plastic industries [63]. Nylon 6,6 is synthesized by polycondensation of hexamethylenediamine and adipic acid, forming the chemical structure presented in Fig. 5.1. Polyamides

sutures are usually composed by Nylon 6,6, producing nonabsorbable, smooth, tough and elastic sutures, that generate minimum tissue reactivity. On the other hand, their knot security is poor, and multiple throws are required to properly close a wound [12]. They are commonly used in both human and veterinary medicine for general and skin closure, cardiovascular, ophthalmic, and neurological procedures. Li and coauthors have modified commercially available nylon sutures (Supramid, B. Braun), consisting of a core of polyamide 6,6 and a sheath of polyamide 6, focusing on improved delivery of growth factors for tendon repair application [64]. The authors swollen the fibers into a methanol/calcium chloride ($CaCl_2$) solution and then freeze-dried to generate micrometer-sized pores in the sheaths, that efficiently loaded rhPDGF (disulfide-linked dimers consisting of two 12.0−13.5 kDa polypeptide chains) using fibrin as a carrier material (Fig. 5.5). PDGF has been successfully used to assist tendon healing due to its ability to promote chemotaxis and mitogenesis of mesenchymal cells, enhancing the collagen organization and vascularity [64]. The PDGF-nylon sutures presented sustained release of the growth factor without compromising their mechanical properties, and supported the proliferation of human mesenchymal stem cells (hMSCs).

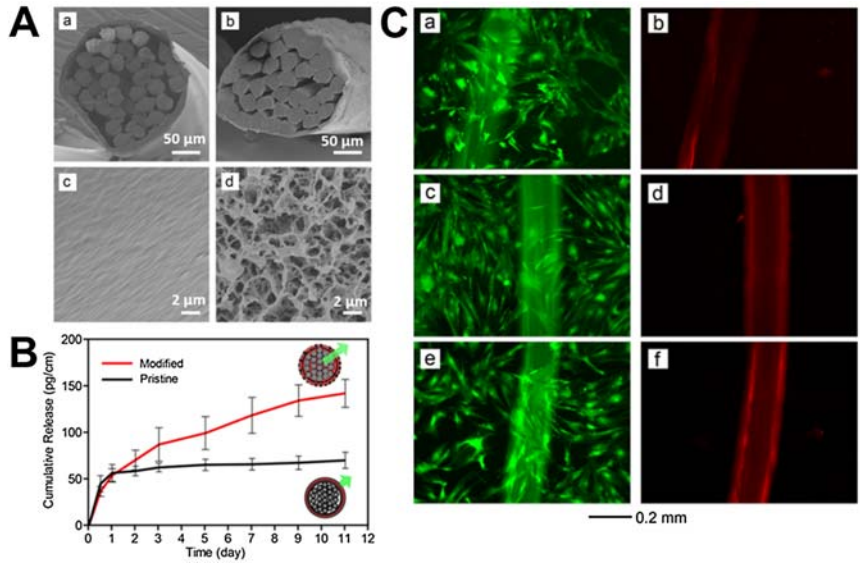


Figure 5.5 (A) SEM images of the pristine (a, c) and modified (b, d) nylon sutures. (B) *In vitro* release of PDGF from the modified nylon suture. (C) Live/dead staining of hMSCs after culture for 72 h on the (a, b) pristine, (c, d) modified, and (e, f) PDGF-loaded suture. *(Reproduced with permission Copyright: © 2016 Li et al. [64].)*

5.2.3.2 PP

Moreover, PP sutures have been used in all surgical branches, especially cardiovascular surgery [65] orthopedics [66], traumatology (tendons) [67], ophthalmology [68] and plastic surgery [69]. They present smooth texture, elasticity, nonporous surface, low tissue reactivity, and no capillary effect, suited for stitches in infected wounds. In comparison to nylon, PP suture has better knot security and pulls smoothly through tissues [12].

5.2.3.3 PET

Additionally, PET sutures, commonly called polyester suture, are commonly used for cardiovascular surgeries [70], general closure [71], ophthalmic [72] and neurological procedures [73]. PET suture has low tissue reactivity, good handling characteristics, high tensile strength, and knot security. It can be uncoated or coated with PTFE or polybutylene. The coating allows for tissue passage with less friction and minimizes capillarity [12]. Yao and coworkers have investigated the use of PET sutures (Ethibond Excel, Ethicon (Johnson & Johnson)) coated with poly-*L*-lysin, intercellular cell adhesion molecule 1 (ICAM-1) and bone marrow—derived stem cells (BMSCs) for tendon repair [74]. *In vivo* assays showed a statistically greater load to failure level in repaired tendon of rats with cell seeded sutures compared to controls.

5.2.3.4 Polybutester

Polybutester is a newer type of polyester composed of a copolymer of polyglycol terephthalate and polybutylene terephthalate. The commercial suture based on polybutester is known as Novafil (Medtronic) and presents hydrophobicity, elasticity, flexibility, fray resistance, and excellent knot security [75]. Compared to nylon, Novafil is less stiff, has a lower memory, and has greater elasticity, as a result, Novafil is capable to accommodate wound edema, reducing suture marks and cut-throughs [12]. In general, it is employed for soft tissue approximation and/or ligation [76], including use in cardiovascular, skin closure and ophthalmic surgery. Pasternak et al. have coated the Novafil suture with doxycycline, which is a substance associated with the inhibition of MMPs [77]. MMPs normally present high activity around sutures inserted into tendon, resulting in tissue breakdown. The coating was applied using plasma treatment, followed by incubation with fibrinogen and doxycycline. The Achilles tendon of rats treated with polybutester-doxycycline suture showed improved suture holding capacity and force of failure [77].

5.2.3.5 PVDF and PTFE

Furthermore, polymers containing fluorine atoms, such as PVDF and PTFE, have also been used to produce sutures [78]. They are physiological inert, soft, smooth, with excellent knotting properties, easy to handle, and do not present capillary effect [79]. PVDF is used in all surgical branches, including cardiovascular surgery, orthopedics [80], traumatology (tendons) [81], plastic [82] and ophthalmologic surgery [83]. PTFE is commonly used for dental bone grafting and implant procedures where a soft monofilament suture is desirable. PTFE has the advantage of preventing bacterial wicking into surgical sites [84].

5.3 Tissue adhesive polymers as suture candidate

Another class of next-generation materials for various suture applications overcoming some of the limitations with traditional staples and sutures are surgical glues or adhesives [85]. These polymers offers great advantages such as being easy to use, able to prevent leakage of fluids, facile application, no requirements for removal, avoiding needlestick injury, and minimal tissue damages [86]. Within this framework, some traditional tissue glues used in clinics are for instance, fibrin sealant (e.g., Tissel) [87], cyanoacrylate based glues (e.g., Histoacryl and Dermabond) [88] and protein based glues (e.g., BioGlue) [89]. However, limitation such as lack of controllable practicability, challenges in their use for minimally invasive procedures, lack on demand activation and controllable adhesion properties have been observed for these clinically approved surgical glues [90]. Therefore, scientist have put dedication and effort to advance these needs and overcome some of the challenges highlighted above [91]. In this context, Annabi et al. disclosed the employment of highly elastic human protein based sealant comprising of the light sensitive methacryloyl modified tropoelastin (MeTro) [92]. The material demonstrated successful in vivo lung sealing in rat models with low toxicity and controllable degradation. Moreover, the crosslinking could be controlled by the light activation, thus simplify its translational and practical application. Here, Lang et al. also disclosed a hydrophobic light-activated adhesive for minimally invasive repair of vessels and heart defects [93]. The poly(glycerol sebacate urethane) based polymer was converted to a patch after crosslinking, which demonstrated strong wet adhesion (after 5 s of UV light exposure) with about 275% stronger adhesion than fibrin sealant. *In vivo* experiments on a beating heart of a pig (onto the interventricular septum) and carotid artery defect demonstrated the superior

performance of the adhesive material under highly dynamic and wet environment. Recently we have seen the increase interest in bioinspired tissue adhesives, in particular, the mussel-inspired wet adhesion [94,95]. In this context, Mehdizadeh et al. devised citrate based strong wet bioadhesive based on the mussel mimicry strategy [96]. The adhesive polymer was designed by the combination of citric acid, polyethylene glycol (PEG) and dopamine. Through a 2-component injection procedure, the polymer and the oxidizing solution (sodium periodate), the crosslinking of the polymers could be promoted, which provided successful sutureless wound closure. *In vitro* adhesion tests comparing the devised adhesive material with the clinical employed fibrin glue demonstrated 2.5−8.0-fold stronger wet tissue adhesion strength. Moreover Liu et al. presented a moldable bioadhesive made of nanosilicate laponite [97] and dopamine modified-PEG [98]. Due to the ability of the composite to undergo auto-oxidation rendered from the dopamine moiety, the material initially underwent reversible cross-linked network and eventually a more compact gel through covalent bonding. These unique abilities presented a material that could fit as moldable sealant to any shape, besides the nanocomposite hydrogel could be injected through a syringe, simplifying its application [98].

In 2018, a study comparing the cyanoacrylate glue performance with conventional sutures in the closure of inguinal hernia skin incisions on randomized control trials was reported [99]. The authors concluded that the tissue adhesive was superior, while both the procedures presented similar safety. Another study compared Histoacryl with suture in the repair of knee meniscal tears, where the biomechanical evaluation demonstrated a better performance from the adhesive material [100]. However, despite that a large number of reports have been disclosed presenting a huge number of new adhesive biomaterials and their proof of concept applications, very few have ended up as clinical products [101]. Hence, overcoming the translational barriers of tissue adhesives is one of the greatest challenges within this research field. Here, Taboada and coauthors, very recently presented a beautiful review on how to overcome the translational barriers of tissue adhesives [102]. The authors highlighted some important aspects to consider when designing translational adhesive materials such as clearly understanding the target tissue surface and environment, the long-term performance, and consideration of the regulatory and development pathways at early stage [102].

5.4 Challenges with current technologies

Surgical sutures play a crucial role in the success of surgical treatment, and the increase in the number of surgical procedures performed worldwide has led to a consequent increase in the demand for better suture materials [103]. The search for a perfect, ideal suture material has been ongoing for decades and, in all likelihood, will continue in the future, since the current technologies employed in rejoining injured tissue after surgery such as surgical sutures and staples encounter several challenges and limitations [1]. In addition to conceivably inducing damages in the surrounding tissue of the surgery site and some cosmetic challenges, there are potential risk for infections [13] and leakage that could be devasting and cause substantial problems [104]. Recently, Ananda et al. reported a comparative study between the use of skin suture, staples, and adhesive glue for surgical skin closure [105]. The authors concluded that staples were the fastest option, while the adhesive glue provided the best outcomes with regard to less postoperative pain, improved cosmetics, and more cost-effective. Although recent advances have increased the effectiveness of sutures, most of the progress can be attributed to technological advances focused on the field of materials science, especially polymeric sutures [5]. Indeed, polymers, natural or synthetic, absorbable or nonabsorbable, have significant potential and, over the years, through the improvement of materials, such as changes in composition, surface alteration and polymer blend, several sutures have been created with excellent physical and mechanical properties [106]. Interestingly, it is undeniable that the sutures currently available for clinical use has been evolving significantly regarding the manufacturing techniques and applicability; nevertheless, little has been advanced to increase the therapeutic properties of the suture itself [4].

5.4.1 Bioactive sutures

Current efforts are focused on the development of suture materials that have improved mechanical properties, but with additional features, emphasizing biologically active sutures. Bioactive materials that can enhance suture function and capability have been at the forefront of suture technology nowadays [4]. Therefore, the strategy of sutures developed as a yarn of biocompatible material only to mechanically bring the tissues together is over, but instead a multifunctionality approach is of great interest [107]. Moreover, antibacterial sutures have been a historic milestone in the development of novel sutures with additional features [108]. After several

years of research and development, the first antibacterial suture available for clinical use, VICRYL Plus by Johnson & Johnson (coated polyglactin 910 with triclosan) was approved in 2002 by the Food and Drug Administration (FDA), helping to reduce the risk of infections at the surgical site [4]. However, even though antimicrobial effectiveness has been extensively researched including other methods such as the incorporation of agents into the suture (e.g., chlorhexidine and octenidine) and AgNPs treated sutures, the applications of bioactive sutures are not limited to antimicrobial activity [53,109–112]. The drug release from the suture (drug delivery suture) can be used to deliver a high drug concentration at the wound area from a wide variety of drugs with potential anesthetic, antiinflammatory, and antineoplastic activity [4,57,113,114]. However, there are several challenges that need to be overcome with drug eluting sutures in order to make them translational and sustainable, such as controlled and sustained drug release, thus avoiding burst release and toxicity to the tissues [114,115].

Prior work on the delivery of bioactive growth factors, the delivery has mainly been focused on coating the surface of a suture with the bioactive compound. Nevertheless, disadvantages with this strategy includes, the limited number of bioactive agents that can be loaded into the suture, which is restricted to a thin coating layer [116]. Further limitation is the quick release (burst release) of a large portion of the agents within the first few hours after implantation [64]. In order to obtain a sustained and controlled release, a recent strategy has been the use of carriers, such as inorganic clays (magnesium and aluminum hydroxycarbonates) [56,117], fatty acid [55], and fibrin [64].

Moreover, the tissue engineering and regenerative medicine strategies have contributed to further transforming the vision of the suture from solely a yarn of biocompatible material, to a biologically active medical device with the aim of not only being a material to mechanically close the sutured wound and prevent infections [110]. For this purpose, cells have been incorporated within the suture material [118]. The main objective of cell seeded biological sutures is to increase the number of healthy cells at the injured site to accelerate the tissue regeneration and repair [119]. Although several types of cells have been evaluated (e.g., osteoblasts and tenocytes) [4], the stem cells have been highlighted for this application and have shown great potential, both pluripotent embryonic cells [120], adipose-derived stem cells [121], and mesenchymal stem cells [122]. However, some challenges regarding the use of this technology with current methods

remain unresolved. Among the main limitations are the low rate of cell retention at the site, the challenges in targeting cells to a specific region, the time required to expand a cell population and problems associated with genetic mutations of the cells during culture [110].

5.4.2 Smart sutures

Another considerably promising advancement within the area of sutures is the development of smart sutures [123]. This new class of sutures is based on responsive polymers capable of significantly altering their properties under small physical or chemical stimuli [124]. Through shape memory selfknotting and tightening sutures, this type of suture can allow suturing of difficult tissues and wounds, where access is strictly limited. In this context, Lendlein and Langer were the first to introduce the concept of shape memory polymer in sutures applications [125]. The authors developed a smart degradable polyurethane suture that underwent spatial transformation according to temperature. The material had a temporary shape below a critical temperature and acquired a permanent shape at a higher temperature. Thus, after the suture was applied to the site and the temperature increased, the suture material decreased in size, creating a knot with adequate tension in the surrounding tissue [125]. Other intelligent sutures were developed following these principles, in which the suture can be loosely connected in wounds with its temporary shape, and with appropriate stimuli (such as heat, light, solution and applied magnetics or electric field) the suture recovers its original state and forming the knot automatically (selftightening knots) [106,126]. In addition to conformational changes, smart sutures can be used for controlled release of drugs and bioactive agents. Both exogenous stimuli (magnetic fields, ultrasound, electric and light fields) and endogenous stimuli (such as pH, temperature and mechanical load) can be used to control the release of drugs from bioactive sutures for each patient [110]. However, although this study demonstrates that smart sutures have the potential to change when stimulated by physiologically relevant environments, the generation of clinically useful and biologically safe materials still remains a challenge [127].

5.4.3 Biomimetic sutures

Since an ideal bioactive suture should stimulate a regenerative response in the tissue, it is crucial to consider the native tissue environment in which the suture will be applied. The cells within the tissue detect and

respond to the nanoarchitecture in the native extracellular matrix (ECM) and, therefore, biomimetic materials that resemble the original ECM architecture is also another strategy inherited from tissue engineering concept, which has been applied in the development of novel sutures [110,128]. Here, a trend in tissue engineering is the application of nanotechnology to produce biomimetic scaffolds with dimensions at the nanoscale that is the same scale as the native ECM. Scaffolds composed of nanofibers have high porosity, high surface/volume ratio, promote better cell adhesion and proliferation and facilitate the transport of nutrients and oxygen during regeneration. In addition, the fibers are at the same scale as the size of the ECM components, allowing to simulate the original environment and allowing the cells to behave similarly to native tissue cells [129,130]. In this context, the electrospinning has proven to be a powerful tool for the manufacturing of polymeric nanofibers for tissue engineering application, since it is a simple, low-cost, versatile method capable of forming nanostructured scaffolds [131–134]. Despite these advantages of the electrospun nanofibers, little has been related to their applications as tissue sutures. This is because the nanofibers obtained through electrospinning are generally in nonwoven form, which leads to poor mechanical performance [135]. However, electrospinning does have several unique advantages in providing mechanical functionality and for the production of composite nanofibers, unlike any other processing technology [133,136].

5.4.4 Translation of basic discoveries in clinical applications

Another challenge with current technologies of sutures is their clinical evaluation. There is a need to conduct detailed preclinical studies and evaluate the long-term safety and efficacy in human trials on these emerging sutures, in particularly with novel materials. Moreover, a recent review revealed that many of the sutures currently in use, even though they have been available for decades, have never been clinically evaluated [110].

Furthermore, the regulatory question is also an important challenge to overcome regarding new suture material technologies [137]. Most suture research and development efforts have been focusing on modifying sutures made of materials already approved by the FDA, for example by modifying the surface or by different combinations of these materials. This strategy is probably employed in order to smoothly simplify and promote the fast approval of the new suture materials. Hence, the development of biomaterial sutures completely different from those commercially available and

approved by the FDA has been very rare. One reason as mentioned above could be that completely new suture materials that do not have a substantially equivalent predecessor approved by the FDA can be considered as a Class III device, and in that case, a Premarket Approval would be required. The purpose of a PMA is to provide adequate safety and efficacy information for a new material, which requires extensive preclinical and clinical testing, increasing the regulatory burden and cost, and resulting in longer development times [138]. In the case of bioactive sutures containing pharmacological substances, they are automatically classified as a high risk Class III medical device independent of the primary suture material, which also adding extra complexity to the regulatory approval process [139].

5.5 Future perspective and remarks

One of the aims in the field of polymeric surgical sutures is to advance materials design providing polymers with the desired properties (e.g., biocompatible, biodegradable, high performer and stable), thus simplifying its use and at the same time promote its mission. This would provide surgeon with easy to use and conduct technologies which are safer and less stress to the tissue, thus avoiding current invasive technologies (e.g., sutures, staples or clips) [140]. In the context of simplicity, an in situ deposition approach of nanofibers via solution blow spinning has been presented [141]. The ease of the technology was demonstrated in the direct deposition in various surgical piglet models such as lung resection, intestinal anastomosis, liver injury, and hernia. These experiments showed successful blocking of the bleeding and leakage in the injury and the quick formation of the protective fiber layer (less than 1 min). Moreover, the development of novel materials has also led to the invention of polymers with the ability to promote healing of tissues and regeneration [142]. Further, remarks on future ideal surgical polymer, they should display multifunctionality and also overcome current challenges and limitation such as potential microbial infection [143], fluid leakage, poor cosmetic, poor healing, and ideally "one fits all," thus suitable for a wide range of surgical applications and in minimally invasive procedure. All these characteristics should ideally be incorporated without trade-off any of the vital properties (biocompatible, stable, sufficient mechanical property etc.). We believe that the future holds great promise in the advancement and invention of the perfect polymeric

surgical sutures; nevertheless, to turn the vision into reality, a better understanding of the tissue, its microenvironment and behavior is vital. A couple of examples have already been presented in this chapter, where smart materials (ability to respond to physiological and external stimuli and change their properties) are believed to play a crucial role in this quest providing improved treatments [126]. Despite, that we have seen the increase inventions the last decades, of new polymeric materials as surgical sutures, little is known about their long-term performance and stability. Therefore, we should not rush into translating novel discoveries from basic research into clinics without understanding its long-term safety, biocompatible and stability, in particularly with novel chemistries and structures. Nevertheless, the advancement can also be elevated where new polymeric smart sutures with the ability to monitor the healing and detect potential defects in the injured environment and surrounding will be designed, thus preventing any future infections or failure.

5.6 Conclusion

Natural and synthetic polymers have been used as surgical suture to hold body tissues together or ligate blood vessels, after a surgery or accidental injury. Among the large portfolio of biomaterials, synthetic polymers such as PGA, PLA, PCL, P4HB, and PDO are currently the most employed as absorbable suture, and synthetic polymers including nylon, PP, PET, polybutester, PVDF, and PTFE as nonabsorbable suture. The development of bioactive sutures enabled to enhance the biocompatibility with tissues and also to display additional functions such as antimicrobial, antiinflammatory, and anesthetics properties. Another improvement was achieved by the use of smart polymers capable of significantly altering their properties under small physical or chemical stimuli. Recently, sutures have been replaced by polymeric based tissue glues, which are easier to use and provides minimal tissue damage. Although bioactive, smart, and adhesive polymers are promising for the field, there are still some challenges for clinical application.

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WOODHEAD PUBLISHING SERIES IN BIOMATERIALS

This book presents current advances in the design, development, and application of surgical sutures.

Key Features:

- Depicts recent advances in both the therapeutic effects of polymer-based sutures, as well as the various manufacturing techniques employed in the production of sutures.
- Offers an interdisciplinary approach, covering material properties and engineering technologies, as well as an understanding of the biological properties of sutures, such as suture/body interactions.
- Comprehensive coverage allows both experienced researchers in the area and new entrants (such as clinicians) to learn more about this important topic.

Polymeric materials offer a high level of versatility due to the range of applications possible within the biomedical and clinical fields—including wound closure—particularly in comparison to metals or ceramics. These specialized materials also allow for a diverse array of therapeutic effects. Although there have been advances in improving polymeric materials for surgical sutures, there is little information available regarding improving the therapeutic value of sutures and advanced technologies used to implement this improvement. This book provides thorough coverage on suture materials with improved mechanical and therapeutic properties that can improve the quality of life; chapter topics include drug-releasing kinetics of sutures, shape memory polymer sutures, and future trends.

This book is a useful resource for academics and researchers in the materials science and biomedical engineering fields, as well as professionals in biomaterials and biotextiles development, and clinicians looking to learn more about suture material properties and suture/body interactions.

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