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Layered Superhydrophobic Meshes for Controlled Drug Release

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Abstract

Layered superhydrophobic electrospun meshes composed of poly(ϵ -caprolactone) (PCL) and poly(glycerol monostearate-co- ϵ -caprolactone) (PGC-C18) are described as a local source of chemotherapeutic delivery. Specifically, the chemotherapeutic agent SN-38 is incorporated into a central 'core' layer, between two 'shield' layers of mesh without drug. This mesh is resistant to wetting of the surface and throughout the bulk due to the pronounced hydrophobicity imparted by the high roughness of a hydrophobic polymer, PGC-C18. In serum solution, these meshes exhibit slow initial drug release over 10 days corresponding to media infiltrating the shield layer, followed by steady release over >30 days, as the drug-loaded core layer is wetted. This sequence of events is supported by X-ray computed tomography imaging of a contrast agent solution infiltrating the mesh. *In vitro* cytotoxicity data collected with Lewis Lung Carcinoma (LLC) cells are consistent with this release profile, remaining cytotoxic for over 20 days, longer than the unlayered version. Finally, after subcutaneous implantation in rats, histology of meshes with and without drug demonstrated good integration and lack of adverse reaction over 28 days. The drug release rates, robust superhydrophobicity, *in vitro* cytotoxicity of SN-38 loaded meshes, and compatibility provide key design parameters for the development of an implantable chemotherapeutic-loaded device for the prevention of local lung cancer recurrence following surgical resection.

Graphical abstract

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Introduction

Lung cancer is the most commonly diagnosed cancer and the most common cause of cancer deaths, with more than 1.61 million new diagnoses and 1.38 million deaths worldwide [1]. For the roughly 80,000 patients diagnosed with early-stage (stage I and II) disease each year in the U.S. [2], surgery is the most effective treatment, whereas chemotherapy is the primary treatment for later stage patients [3,4]. Surgeons must remove the cancer while preserving as much lung tissue as possible, particularly in cases where lung function is limited. In these cases, a wedge of tissue is removed including a small rim of lung tissue around the cancer. This results in a “limited margin” between the tumor and the resection line, with a subcentimeter margin correlating with an increased risk of local cancer recurrence [5]. The prognosis of recurrent NSCLC is extremely poor, and surgery to remove recurrent disease is rarely performed due to clinical and technical limitations [4]. Overall, patients with early, staged I or II non-small-cell lung cancer (NSCLC) have a five-year local recurrence rate of 23% [6]. Accordingly, a strategy to prevent cancer recurrence at the surgical margin would benefit thousands of patients annually, as shown by the improved outcomes following the application of brachytherapy seeds along the surgical margin at the time of limited surgical resection. In stage IA NSCLC patients with larger (2–3 cm) tumors, this treatment significantly increased survival following surgery (from 44.7 to 70 months) [7]. However, clinical acceptance of brachytherapy has been limited by the concerns of radiation exposure to health care professionals and the technical and regulatory challenges of this approach [8]. Building off this success, our goal is therefore to design an easy to use, regulatory-friendly, chemotherapeutic delivery system to prevent local recurrence.

We envision the use of a drug-loaded buttressing device that is stapled into the resection margin as the wedge resection is performed using a standard surgical stapler. In order to achieve this goal, the following design criteria are required for the drug-loaded buttressing material: a) elute minimal drug during the first 10 days of wound healing; b) subsequently elute drug over several weeks in order to expose any remaining tumor cells to the drug over several cell cycles; c) be readily processed into a polymeric structure that can be stapled into tissue by the surgeon; and d) not elicit an adverse reaction after implant. We are exploring two potential form-factor solutions for this unmet clinical need – films [9,10] and meshes [11,12]. Both form-factors are composed of hydrophobic, biocompatible, and biodegradable polymers poly(glycerol monostearate-co- ϵ -caprolactone), or PGC-C18, and poly(ϵ -caprolactone), or PCL, to prolong the delivery of anticancer agents. The former represents a cast film of a drug loaded polymer solution on a collagen buttressing material used to prevent air-leaks. In contrast, and as a means to further control drug delivery, meshes are electrospun into a fibrous morphology where the porosity and inherent hydrophobicity create a superhydrophobic material that slows wetting and subsequent drug release. Thus, these meshes offer the potential benefit of being both a lung buttressing material as well as a delivery device to tailored drug release, which can be fabricated in a single processing step.

Superhydrophobicity is a property of several natural materials such as lotus leaves, water strider legs, and gecko feet [13,14]. These surfaces possess micrometer and/or nanometer features, resulting in roughness that magnifies their hydrophobic character by creating an energetically unfavorable increase in liquid-air surface area before wetting. If the apparent

contact angle (θ^*) exceeds 150, the materials are commonly called superhydrophobic [13]. When roughness is increased sufficiently, the air-liquid interface is stabilized, which inhibits or stops wetting, and the material enters what is known as the Cassie-Baxter state. Superhydrophobic materials are useful in applications such as non-fouling coatings, low-drag surfaces, and microfluidics [15–25]. In our case, we are interested in 3D bulk structures (i.e., meshes) composed of layers of electrospun fibers that are superhydrophobic throughout. In contrast to most other approaches [26] to superhydrophobic materials, our design does not depend on indefinite maintenance of the Cassie-Baxter state; instead it is designed to be metastable with a controlled wetting rate where fibers in the core release drug once wetted.

Control of drug release from a porous superhydrophobic material has been demonstrated in earlier papers [11,12] from our group using SN-38 and CPT-11, and by the Lynn group using hydrophilic small molecules TMR and 2-ABI [27]. Layered electrospun meshes have been designed for sequential and delayed drug release, but without intent to use superhydrophobicity as a means of control [28,29]. Building off of these results we are evaluating layered superhydrophobic material for controlled drug release. As drug release will be dependent on wetting, we hypothesized that by controlling the superhydrophobic metastable state the rate of wetting will be controlled (and thus drug release). In this study we report the design, fabrication, and evaluation of layered electrospun polymeric meshes containing a chemotherapeutic agent within the fibers of a central core layer surrounded by layers of unloaded fibers. This design was intended to slow initial drug release, while later providing robust delivery of local chemotherapy. In this study we employ a chemotherapeutic agent that has proved difficult to deliver in traditional formulations due to low aqueous solubility: 7-ethyl-10-hydroxycamptothecin (SN-38). SN-38 is the active metabolite of irinotecan, which is used clinically in the treatment of colon, rectal, and lung cancer but is 1000 fold less active than SN-38 [30–32]. Specifically, we describe the fabrication of layered meshes, the resistance to mesh wetting as measured by X-ray CT imaging, the elution of a sustained and controlled amount of SN-38 in saline and serum solutions under both static and agitated conditions, the cytotoxic activity against lung cancer cells *in vitro*, and the results from a 28 day subcutaneous implant biocompatibility study. Finally, we discuss these results in relation to our drug-device design requirements, the potential limitations of this system, and propose solutions for further testing.

Materials and Methods

Please see the Supplementary Information section for complete details on materials, methods, mesh fabrication, and characterization. For each mesh layer, thickness vs. time was calibrated immediately beforehand by electrospinning a mesh for a known time and measuring thickness. Fiber diameters ranged from 1.4 to 5.3 μm , as detailed in Table S1. The meshes were named as shown in Table 1.

Results and Discussion

As discussed below, our approach to locally tuned chemotherapeutic delivery, with the ultimate goal of preventing local tumor recurrence, entails using a triple-layered electrospun

mesh containing an inner drug core with two outer non-drug layers. The resultant control of the wetting rate of the mesh leads to a marked delay in drug release with prolonged kinetics. Given that the average doubling times of rapidly growing NSCLC tumors are reported to be between 46 and 181 days [33–36], it is important that cell-cycle specific drugs such as SN-38 are present for many weeks in order to prevent local growth of any occult tumor cells. Further, low local drug concentrations resulting from systemic chemotherapy are correlated with higher cancer recurrence [37], highlighting the need to increase drug concentration locally via the use of an implantable drug loaded device at the resection margin. Therefore, as a proof of concept for our studies utilizing these superhydrophobic meshes, we have chosen to target 60 days of chemotherapeutic delivery using SN-38 as a model drug. We begin with a discussion of mesh fabrication, characterization, and wettability, followed by drug release from layered and non-layered meshes under static and dynamic conditions in the presence of saline or saline with serum, the cytotoxicity of these meshes *in vitro*, and, finally, the *in vivo* response of these meshes after implantation.

Mesh Fabrication and Characterization

The meshes were prepared by electrospinning chloroform:methanol solutions of PCL and various mixtures (0, 10 or 30 wt%) of PGC-C18 (Figure 1A). For drug-loaded layers, SN-38 was dissolved in the polymer solution at 1 wt% to polymer and the three layers of mesh (two empty shield layers and one drug load core layer) were fabricated in a continuous manner. The structure of a representative layered mesh is shown in Figure 1B. Scanning electron microscopy shows the drug-loaded PCL layer (slightly thicker fibers) between two shield layers of 30% PGC-C18 on left and right. The two compositions (unloaded and drug loaded) are co-electrospun for 15 seconds between layers to minimize delamination. The apparent contact angle of the different mesh formulations as measured with deionized water is shown in Figure 2, where the upper points (solid symbols) indicate advancing contact angles which increases as a function of more PGC-C18 content and smaller fiber diameter. The lower set of points (open symbols) denotes the receding angles, and a similar trend is observed. The vertical lines represent the difference between the two angles, hysteresis, which decreases with higher PGC-C18 content. Hysteresis is caused by “asymmetry of wetting and dewetting and the irreversibility of the wetting – dewetting cycle” [13], and greater values indicate a less robust Cassie-Baxter state.

Drug Release into Saline and Serum Solutions

The first set of drug release studies tested the effect of shield layer thickness on SN-38 release. A 90- μ m thick core of PCL (PCL₉₀ core) with SN-38 was layered between shield layers of 10% PGC-C18 of varying thickness. As shown in Figure 3, increasing the thickness of 10% PGC-C18 afforded a decrease in drug release rate. The bare core layer (in blue) has an initial burst release of ~25% within 24 hours and complete release occurred within ~20 days. Layering the core between unloaded 75 μ m meshes does not considerably change this timing. Unloaded shield layers that were 150 μ m thick extended the time of SN-38 release to ~50 days (Figure 3). Wetting with ethanol at 80 days did not cause any increased release, indicating that the mesh was wetted and the majority of drug had released. With 300 μ m thick layers on either side of the drug-loaded core, there was still metastable

air that could be displaced with an ethanol treatment after 100 days of immersion (at the black arrows), as indicated by the resultant increase in drug release.

Next, the effect of shield layer polymer composition was examined while keeping thickness constant. The same PCL₉₀ core loaded with SN-38 was layered between 150- μ m thick unloaded meshes of either pure PCL, or PCL blended with 10% or 30% of PGC-C18, a hydrophobic dopant, as shown in Figure 4. The bare core and 10% data are the same as in Figure 3. Unloaded layers of PCL only extended release marginally, but if the shield layer fibers were composed of 10% PGC-C18, the release profile was extended to ~40 days. Increasing the dopant percentage to 30% PGC-C18, yielded <10% release over 100 days. Subsequent wetting of the mesh with ethanol and submersion into the aqueous solution resulted in an immediate burst release of drug. These results further demonstrate that readily releasable drug was retained within the mesh for a prolonged period of time, but release is delayed by the inhibition of wetting.

To better model the physiological milieu and the presence of serum on the drug release profiles, we submerged the drug loaded meshes in 10% fetal bovine serum (FBS) and measured the drug release over time, as shown in Figure 5. Serum proteins, such as albumin, are known surfactants and are expected to both increase the wetting rate and also increase drug solubility. The media was changed to ensure sink conditions with SN-38, which was maintained below 3.6 μ g/mL, which is 10% of the reported solubility in PBS [38]. We tested the same meshes as before (PCL-PCL₉₀-PCL, 10-PCL₉₀-10, and 30-PCL₉₀-30) with 150 μ m thick shield layers surrounding a 90 μ m thick PCL core loaded with 1 wt% SN-38. The layered PCL mesh released SN-38 the most rapidly with the addition of serum roughly doubling the release rate (see Figure S2 for a plot of rates). Approximately 30% of drug was released within 24 hours with drug release completed within ~10 days. This increase in rate is likely a result of surfactant absorption on the mesh and increased mesh wetting rate as immersion in 10% serum decreases the advancing contact angle reduces from 151° to 134° after 15 minutes, then to 106° after one hour. Replacing the outer layers with a 10% PGC-C18 blend increased the hydrophobicity enough to prevent the initial burst release and extend release by a few extra days. However, changing the shield layer composition to 30% PGC-C18 prevented any detectable drug for the first two days, with less than 10% drug release, despite the presence of serum, during the next 11 days. A more rapid release subsequently occurred that resulted in complete release of drug within ~30 days.

We next tested the effects of mechanical agitation to further simulate stresses that might occur after implantation. The meshes were incubated in a 10% FBS solution that was subjected to energy input in the form of constant agitation at 200 rpm. Both static and oscillating pressures have been shown to increase the wetting rate of superhydrophobic materials. [39,40] This frequency is in the range of the murine respiration rate, [41] (though higher than human respiration rate of ~12/min [42]) and the displacement (~3 cm radius) is greater so the acceleration is greater than is likely to be experienced *in vivo*.

We hypothesized that agitation would increase wetting due to contact angle hysteresis, as agitation advances the contact line that is then pinned to the fibrous topology [43,44]. The meshes are designed to stabilize entrapped air only temporarily, and to be wetted and release

drug over time. Again the same 30-PCL₉₀-30 mesh was tested, and agitation markedly increased the release rate, requiring ~25 days for drug release under static conditions but only ~15 days with agitation as shown in Figures 6 and S2. To assess whether drug delivery could be prolonged under these more aggressive conditions, we tested the hydrophobic mesh with 30% PGC-C18 in all three layers (30-30₃₀₀-30). A thicker core mesh layer was selected to contain a greater amount of SN-38 in anticipation of the forthcoming *in vitro* cell assay studies. As seen in Figure 6, comparison of the 30-30₃₀₀-30 and 30-PCL₉₀-30 formulations demonstrated significantly slower release with the more hydrophobic core layer with SN-38 release prolonged to ~40 days in FBS with agitation. As expected both layered meshes released drug more slowly than the un-layered 30% core. Unexpectedly however, the change to a 30% PGC-C18 core layer reduced the overall release to about 60% of loading, compared to complete release from the PCL core. Incomplete drug release from PCL is reported, and is more common with lower molecular weight and more crystalline polymers [45]. In our case, the PCL is much higher molecular weight and likely less crystalline than the PGC-C18, which will entrap the drug possibly until the polymer itself is degraded.

To assess the rate at which the core wets (and thus initiation of drug release) based on the hydrophobicity on mesh, the infiltration of aqueous media into the different layers of 30-PCL₃₀₀-30 and 30-30₃₀₀-30 electrospun meshes was directly imaged using contrast-enhanced micro computed tomography (μ CT). The addition of unloaded layering slowed the infiltration of the aqueous solution into the drug-loaded core of either mesh but, as shown in Figure 7, the more hydrophilic PCL core wetted fully in about a week whereas the mesh composed entirely of 30% PGC-C18 (i.e., 30-30₃₀₀-30) wetted the slowest, requiring nearly a month to become fully wetted. Since the drug was present only in the core layer and a fiber can only release drug after it wets, the core wetting was rate limiting for overall drug release. Accordingly, we further analyzed the CT imaging data to gate for extent of core wetted at each time. The results in Figure 8 indicated that the drug-loaded core layer exhibited a delay in wetting with both formulations, but the 30% PGC-C18 core remained virtually dry for nearly two weeks. Comparing this wetting release to the SN-38 release shown in Figure 6, we find good agreement between the wetting of the core and the release of drug. It should also be noted that this wetting rate is much greater than that in PBS alone using very similar meshes [46].

***In Vitro* Anti-Cancer Efficacy**

Next we evaluated the cytotoxicity of SN-38-loaded 30-30₃₀₀-30 layered meshes and 30₃₀₀ core unlayered meshes by incubating the meshes with Lewis Lung Carcinoma (LLC) cells in serum-containing media. When not exposed to cells, the meshes were subjected to sink conditions in agitated cell culture media containing 10% serum, a more rigorous test than typical cell culture conditions. As shown in Figure, the SN-38-layered mesh maintains cytotoxicity for at least 20 days, much longer than the unlayered mesh. This confirms the cytotoxic potential of superhydrophobic, layered meshes against lung cancer cells with superior performance compared to unlayered meshes. The time that unlayered and layered meshes remain cytotoxic (~15 and ~30 days respectively) is remarkably similar to the time for complete wetting of the core as shown in Figure 8.

***In Vivo* Integration**

Meshes with and without SN-38 were implanted subcutaneously in rats to monitor tissue integration and foreign body response, a key step prior to evaluating *in vivo* efficacy. The meshes were the same 30–30₃₀₀–30 composition that was evaluated in the previous studies. A control group receiving an equivalent dose of SN-38 was also performed, where the animals received a subcutaneous injection of SN-38. Meshes were explanted 28 days after implant, embedded and stained with Masson's trichrome. The polymeric mesh dissolved during the histology processing but the outline of the mesh can be seen in the subcutaneous tissue (Figs. 10 and 11). The rectangular margins suggested that unloaded or SN38-loaded meshes were able to maintain their shape and stay in a fixed position throughout the 28 day *in vivo* drug release process. There was also evidence of disperse extracellular matrix growth throughout the mesh suggesting complete wetting of the material by 28 days (Fig. 10). Cellular ingrowth was observed near the margins of the mesh without drug (Fig. 11), with a few cells within the disperse extracellular matrix throughout the mesh (not shown), altogether indicating that the mesh was hospitable for cell growth after wetting. Both meshes showed similar and low levels of fibrosis. These results were consistent with reports of biocompatibility of electrospun PCL-based meshes [47,48]. Notably, there was no perturbation of surrounding subcutaneous tissues and subjacent muscle that was observed in the injection controls (Figure S5–S6). There was also no evidence of a chronic inflammatory reaction, suggesting that drug release from the mesh will not be entrapped within a reactive fibrotic capsule. In contrast to the unloaded and SN-38 loaded meshes, the animals that received SN-38 alone showed fibrosis and myolysis at the injection site (Supplementary Figures S5–S6).

Returning to the design criteria outlined in the introduction, we have been largely successful in achieving the stated aims. The layered architecture enabled a lower drug release initially (9±6% released at 9 days) followed by a more rapid release (to 49±3% at 29 days). The composition of the shield layer can also be used to further control drug release rate. The meshes retain the flexible electrospun form with its ability to hold staples after deployment using a cutter-stapler (Figure 12 and Supplementary Figures S3). Finally, the histology results showed no adverse reaction to mesh implantation and minimal inflammation.

These proof-of-concept studies are a significant first step towards characterizing and understanding superhydrophobic biomaterials for drug delivery. First, the cytotoxicity was not as prolonged as may be desirable for clinical use, so we are considering strategies to increase drug loading, employ more effective drugs than SN-38, or to further stabilize the air-liquid-mesh interface to extend release. Second, *in vivo* drug release studies need to be performed to determine if the *in vitro* models are adequate models. Third, *in vivo* efficacy studies are required but these will likely be performed using a subcutaneous lung cancer resection model, as an orthotopic model is not practical given the surgical procedure. Fourth, though the histology results are promising, the host response to the mesh may be different when implanted in lung tissue given the differences in vascularity and tissue types between the two locations. Finally, the duration of Cassie-Baxter state maintenance after implantation needs to be determined as an understanding of the wetting rates are crucial to the development of this drug delivery platform.

Conclusions

In summary, we have developed superhydrophobic, layered meshes that provide controlled release of chemotherapeutics in the presence of serum and agitation conditions. Multi-layered meshes of various thicknesses, fiber diameters, and polymer compositions are prepared using the electrospinning technique, and we can confine the chemotherapeutic to the central core layer. Building off of the idea to control the metastable state of the superhydrophobic material, we extend total drug release time by layering drug within a central layer that provides a delay before initial drug release. We demonstrate through imaging and release studies that the non-wetted Cassie-Baxter state persists for a prolonged and tunable period of time, though not indefinitely under rigorous conditions, and that drug release closely follows wetting of drug-containing layers. We show the tunability of drug release kinetics from this system by varying polymer hydrophobicity, drug content, and thickness of each layer. The extended *in vitro* cytotoxicity results support this release profile and confirm the utility of the layered structure. Finally, histology after implantation shows the unloaded and SN-38 loaded meshes do not elicit an adverse response over 28 days.

The results presented here advance both basic and translational research. Superhydrophobic materials possess unique properties, but maintaining the Cassie-Baxter state indefinitely is rarely possible, so instead exploiting the metastability of that state as shown in this study presents an opportunity for additional control of drug release from polymeric devices. In so doing, these superhydrophobic meshes provide a local drug source with a robust and tunable means of controlling drug loading, sequence and rate of release. Localized drug delivery has and will continue to have an impact on patient care and the treatment of early stage lung cancer is one area where device ideas, such as described herein, may provide optimized drug dose and duration while minimizing systemic side effects. These results provide a proof of concept for a new mode of drug delivery to prevent local lung cancer recurrence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

A) PGC-C18 and PCL polymer structures. B) SEM image of the edge of a sectioned layered mesh, 30–30₃₀₀–30. The central layer is SN-38 loaded PCL, between non-drug-loaded shield layers of 30% PGC-C18. Scale bar is 500 μm. Inset, the advancing contact angle on the shield layer (151.0°).

Figure 2.

Sessile water contact angles versus polymer blend and fiber diameter. As measured using the Tangent 2 fitting algorithm, the upper filled points represent the advancing contact angle, the lower open points the receding contact angle, and the length of the connecting lines is the hysteresis. Generally, as more PGC-C18 is doped in, the contact angles increase and hysteresis decreases. Error bars indicate standard deviations, with $n > 15$ fibers for diameter and $n = 3$ meshes for contact angles.

Figure 3.

SN-38 release into static PBS with varying shield layer thickness. Drug was loaded in a 90- μ m thick PCL core and thickness of the surrounding 10% PGC-C18 shield layer was increased. Black arrows indicate wetting with ethanol. Error bars represent the standard deviation of $n=5$ for each group.

Figure 4.

SN-38 release into static PBS as a function of shield chemistry, with a 90 μ m thick PCL core and 150 μ m thick shield layers. Wetting with ethanol at the black arrows caused an immediate drug release in the more hydrophobic 30-PCL₉₀-30 mesh. Error bars represent the standard deviation of n=5 for each group.

Figure 5.

Drug release into static 10% FBS from layered meshes with 90 μm PCL cores and 150 μm thick shield layers. The air layer in the 30-PCL₉₀-30 meshes is no longer stable over 100 days due to the lowered media surface tension, but is instead metastable and releases over about 25 days. Error bars represent the standard deviation of $n=5$ for each group.

Figure 6.

Drug release into agitated 10% FBS. Release is faster again than in static FBS solution. A layered mesh with a more hydrophobic, 30% PGC-C18 core (30–30–30) releases much more slowly than the 30-PCL-30, and the un-layered core releases quicker than both. The derivatives of these data are shown in Figure S2. Error bars represent the standard deviation of $n=5$ for each group.

Figure 7. Infiltration of a serum and contrast agent (purple) solution into two meshes while air (red) is displaced. Top, 30-PCL₃₀₀-30 exhibits rapid wetting of the more hydrophilic PCL core layer. Bottom, 30-30₃₀₀-30 exhibits uniform wetting from the outside in a delayed fashion due to the constant bulk hydrophobicity. The scale bars each indicate 1.0 mm.

Figure 8.

Wetting rate of the core in the triple layered mesh as determined from the μ CT imaging data. While both meshes exhibited an initial delay in wetting, the more hydrophobic 30% PGC-C18 core was not appreciably infiltrated for the first 10 days. Error bars represent the standard deviation of $n=3$ for each group.

Figure 9. Viability of LLC cells after exposure to SN-38-loaded layered and un-layered meshes, as measured by the MTS assay. Error bars represent the standard deviation of n=5 for each group.

Figure 10. Histological section of an SN-38-loaded mesh ($92 \mu\text{g}/\text{cm}^2$, 1 cm^2) after 28 days of implantation, stained with Masson's trichrome. A diffuse ingrowth can be seen within the mesh structure, surrounded by mild fibrosis. The scale bar is $200 \mu\text{m}$.

Figure 11. Histological section of the lateral edge of an unloaded 30% PGC-C18 mesh, 28 days after implantation, stained with Masson's trichrome (200x, scale bar is 50 μm). Fibrotic reaction was similar or slightly increased compared to that of an SN-38 loaded mesh shown in Figure 10. The arrow indicates the area of largest cell ingrowth.

Figure 12.
SEM images of a layered mesh after fixing with a cutter-stapler, showing a staple. The scale bars are 200 μm .

Table 1

Names, compositions, and thicknesses of selected meshes are presented. The subscripts refer to core layer thicknesses in micrometers, and number, for example, 30 refers to a polymer blend of 30% PGC-C18 with 70% PCL by mass. The complete listing with contact angles and fiber diameters is shown in Table S1.

Mesh Name	Core	Shield
PCL ₉₀ core	90 µm PCL	none
PCL-PCL ₉₀ -PCL	90 µm PCL	150 µm PCL
10-PCL ₉₀ -10 (75 µm)	90 µm PCL	75 µm 10% PGC-C18
10-PCL ₉₀ -10	90 µm PCL	150 µm 10% PGC-C18
10-PCL ₉₀ -10 (300 µm)	90 µm PCL	300 µm 10% PGC-C18
30-PCL ₉₀ -30	90 µm PCL	150 µm 30% PGC-C18
30 ₃₀₀ core	300 µm 30% PGC-C18	none
30-30 ₃₀₀ -30	300 µm 30% PGC-C18	150 µm 30% PGC-C18
30-PCL ₃₀₀ -30	300 µm PCL	150 µm 30% PGC-C18