Synthesis of degradable poly(L-lactide-co-ethylene glycol) porous tubes by liquid–liquid centrifugal casting for use as nerve guidance channels

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Abstract

Biodegradable nerve guidance channels are advantageous, obviating the need for their removal after regeneration; however, most channels lack the appropriate mechanical properties for soft tissue implantation and/or degrade too quickly, resulting in reduced regeneration and necessitating the need for the design of polymers with tunable degradation profiles and mechanical properties. We designed a series of biodegradable polymeric hydrogel tubes consisting of L-lactide (LLA) and polyethylene glycol (PEG) where both the ratio of LLA to PEG and PEG molar mass were varied. By adjusting the PEG:LLA ratio and the molecular weight of the PEG oligomer we were able to control degradation and mechanical properties of our polymers. By incorporating methacrylate (MA) groups on both termini of the linear oligomers, porous tubes were synthesized with a redox-initiated free radical mechanism during a liquid–liquid centrifugal casting process. The tube wall had a bead-like morphology, as determined by SEM, which was reminiscent of previous porous hydrogel tubes synthesized by the same method. Tubes swelled with degradation to 160 vol\%, or 640 wt\%, and an increased radius calculated at 1.26 times. Those tubes with greater PEG content and PEG molar mass degraded faster than those with greater LLA content, as was expected. Interestingly, the wall morphology changed with degradation to a fiber-like structure and the mechanical properties decreased with degradation. By correlating the accelerated degradation study to a physiologic one, these porous hydrogel tubes were stable for an equivalent of 1.5 months, after which the mechanical properties began to deteriorate. This study demonstrates how porous hydrogel tubes can be designed to meet tissue regeneration criteria by tuning the formulation chemistry and specifically how the ratio of hydrophobic/crystalline LLA and hydrophilic/amorphous PEG impact tube properties.

Keywords: Poly(lactide); Poly(ethylene glycol); Centrifugal casting; Polymer tubes; Nerve guidance channels

1. Introduction

Nerve guidance channels have been used clinically to bridge the gap created in the peripheral nerve after injury. Of the five clinically available channels (or cuffs), four are degradable and of these, two are composed of collagen and two are synthetic, composed of poly-(glycolic acid) [1] and poly(lactide-co-e-caprolactone) [2]. Biodegradable nerve guidance channels are advantageous over their non-degradable analogs, obviating the need for their removal after regeneration. Yet these degradable nerve guidance channels suffer from either premature degradation leading to compression of the regenerated nerve or excessively slow degradation, yielding sharp shards [3–5].

We recently reported the synthesis of poly(hydroxyethyl methacrylate-co-methyl methacrylate) (PHEMA–MMA) hollow fiber membranes using a novel liquid–liquid...
centrifugal casting technique and tested these in vivo as nerve guidance channels [6,7]. While in the initial studies tubes collapsed after 8 weeks of implantation, subsequent studies demonstrated that patent tubes could be achieved in long-term studies for at least 16 weeks where nerves regenerated through synthetic channels similar to those in autograft controls (the current “gold standard”) [8]. Despite these promising results for peripheral nerve injury repair, the PHEMA–MMA channels are non-degradable, necessitating a biodegradable alternative that ideally incorporates acrylate chemistry to facilitate use in the liquid–liquid centrifugal casting technique.

Several linear polyesters derived from aliphatic \( \alpha \)-hydroxy esters have been engineered for a variety of biomedical applications including drug delivery devices, surgical sutures, cranio-maxillofacial fixations, tissue engineering scaffolds and nerve guidance channels [9,10]. High molar mass linear polyesters have been synthesized by ring opening polymerization of cyclic dimers or monomers using Sn(II) 2-ethylhexanoate (Sn(Oct)\(_2\)) at a by ring opening polymerization of cyclic dimers or monomers using Sn(II) 2-ethylhexanoate (Sn(Oct)\(_2\)).

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The following 1H NMR analysis. 1H NMR: \( \delta = 5.26 \) (broad multiplet, 1.0H, \(-O_2C–C(CH_3)–\)), \( \delta = 4.41 \) (broad multiplet, 1.1H, overlap: \(-CH_2–O_2C–CH(CH_3)–\) and \(-O_2C–CH(CH_3)–OH), \( \delta = 3.72 \) (sharp triplet, 3.1H, \(-O–CH_2–CH_2–\)), \( \delta = 1.59 \) (broad multiplet, 4.0H, \(-O_2C–CH(CH_3)–\)).

2.3. Synthesis of methacrylate terminated LLA–PEG [B]

As shown in Scheme 1, LLA–PEG oligomers [A] were reacted with anhydrous methacryloyl chloride (MAC) to yield MA-terminated LLA–PEG (MA–LLA–PEG) [B]. To a 100mL round bottom flask equipped with a stir bar were added 15 mL dichloromethane (DCM), 34.4mmol free hydroxyl of LLA–PEG and 6.7 mL triethylamine (TEA). The mixture was gently heated, allowing the mixture to melt, stirred for 3 min and then purged with \( N_2 \) gas after which 6.62mL of MAC was added dropwise over 2–4 min while the round bottom flask was cooled in an ice/salt bath at \(-4\) °C. The flask was cooled for an additional 5 min, after which it was transferred to a silicon oil bath and heated at 50 °C under reflux with stirring for 24 h under \( N_2 \). The resulting product was purified by filtration (using Whatman 4.25cm #1 filter discs) under reduced vacuum to remove the solid TEA salt and washed with DCM two times. Excess DCM was removed by rotary evaporation at 45 °C under reduced vacuum. The solvent-free oily product was precipitated three times in cold hexane followed by rotary evaporation at 60 °C under reduced vacuum. Dried MA–LLA–PEG was a yellow viscous liquid with a yield of 95% and 75% substitution of end groups as analyzed by \(^1\)H NMR. For example, MA–LLA–PEG200:1 had the following \(^1\)H NMR: \( \delta = 6.22 \) (sharp singlet, 0.3H, \(-O_2C–C(CH_2)–\) = CH(Z–H)), \( \delta = 5.66 \) (sharp singlet, 0.3H, \(-O_2C–C(CH_2)–\) = CH(E–H)), \( \delta = 5.17 \) (broad multiplet, 1.0H, \(-O_2C–C(CH_2)–\) = CH(Z–H)), \( \delta = 4.34 \) (broad multiplet, 1.1H, overlap: \(-CH_2–O_2C–CH(CH_3)–\) and \(-O_2C–CH(CH_3)–OH), \( \delta = 3.67 \) (sharp triplet, 3.1H, \(-O–CH_2–CH_2–\)), \( \delta = 1.53 \) (broad multiplet, 4.0H, \(-O_2C–CH(CH_3)–\)).

2.4. Polymerization of MA–LLA–PEG porous tubes

To a 10mL glass vial were added, 1 g of MA–LLA–PEG, 2.0mL of \( H_2O \) and 1.942mL of \( N \)-methyl pyrrolidone (NMP). Ten microlitres of freshly prepared 1mL stock solutions of 10wt% ammonium persulfate (APS) and 10wt% sodium metabisulfate (SMBS) in water were added.
to the MA–LLA–PEG solution. The polymerizing mixture was mixed and then injected, via a 5mL syringe equipped with a 2μm filter, into a septa-sealed cylindrical glass tubular mould (internal diameter of 3.4mm) as previously described for HEMA–MMA polymeric tubes [6]. The glass mould was inserted into a horizontally mounted drill chuck (Arrow Engineering Co. Inc.) and spun for 6h at 2500rpm, yielding the crosslinked polymer [C] of Scheme 1. After the polymerization was complete, the septa were removed and the porous tubes were removed from the glass moulds. The tubes were washed three times with hexane and water and allowed to swell in H₂O for 1 week in a 5mL vial.

Table 1
Trans-esterification reagents and amounts

<table>
<thead>
<tr>
<th>Index</th>
<th>PEG</th>
<th>Molar ratio LLA/PEG</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>MW 200</td>
<td>MW 400</td>
</tr>
<tr>
<td>PEG200 2:1</td>
<td>615.0μL</td>
<td>2/1</td>
</tr>
<tr>
<td>PEG200 4:1</td>
<td>307.5μL</td>
<td>4/1</td>
</tr>
<tr>
<td>PEG400 2:1</td>
<td>1.23mL</td>
<td>2/1</td>
</tr>
<tr>
<td>PEG400 4:1</td>
<td>615μL</td>
<td>4/1</td>
</tr>
</tbody>
</table>

2.5. Processing PLLA control tubes by centrifugal casting

In a 100mL round bottom flask, 20mL of 10 wt% stock solution of PLLA in dioxane was prepared by gently heating and mixing by vortex. A 1mL aliquot of this solution was injected via a syringe into a similar cylindrical glass tubular mould (ID = 3.5mm) that had been capped with two rubber septa. The glass mould was inserted into a similar horizontally mounted drill chuck and spun at 3000rpm at −20°C for 20 min. The glass mould was removed from the drill, the septa removed and the frozen PLLA was extracted at 8°C in cold water for 1 day. The following day, extracted tubes were removed and placed in a glass vial filled with phosphate buffered saline (PBS).

2.6. Equilibrium water content of MA–LLA–PEG films

The identical polymerization mixture described for the porous tubes was used to prepare the MA–LLA–PEG films, which were used to measure equilibrium water content (EWC): 500μL of the polymerizing mixture was injected into a 10mL glass vial and further mixed for 3 min. After 24h, the polymerization was complete and the polymer film was washed...
three times with 5 mL of H₂O. Film samples were placed in 20 mL vials filled with PBS and allowed to equilibrate in PBS for 1 week.

2.7. Characterization of polymer films and tubes

Films were characterized for EWC. Tubular constructs were characterized for morphology, mechanical properties, and degradation. The tube wall morphology was characterized using the Hitachi S-570 and S-2500 scanning electron microscopes (SEM) using 20 kV acceleration voltage. The tubes were sectioned radially and longitudinally with a razor blade, mounted on SEM stubs with conductive carbon cement and gold coated for 45 s prior to analysis.

The EWC of films was measured after swelling them in PBS at pH 7.4 for 1 week after which the films were removed, blotted gently to remove the surface water and weighed to obtain wet mass. The wet films were freeze dried for 3 d after which their dry mass was measured. The EWC was calculated according to the equation

\[
\text{EWC} = \left( \frac{m_\text{w} - m_\text{d}}{m_\text{w}} \right) \times 100\% ,
\]

where \( m_\text{w} \) is the wet mass and \( m_\text{d} \) is the dry mass of the polymer films. All groups were tested using single factor ANOVA and post hoc t-test (\( p < 0.05 \)).

The mechanical properties of the tubes were tested by transverse compression in a mechanical tester based on a previously developed in vivo–in vitro force-displacement correlation model [7]. The tubes were equilibrated at 37°C in a water bath prior to and during testing. The tube’s resistance to mechanical force (mN) was measured as a function of vertical displacement of the tubes apex (displacement, mm). Sample length and wall thickness were recorded using a calliper and SEM, respectively. The force exerted by the tube was divided by the tube length and wall thickness in order to normalize for differences. Normalized force was plotted against % compression (% reduction in vertical diameter). Tube mechanics were also followed as a function of degradation time.

An accelerated degradation test was used to assess the degradation behaviour of the tubular constructs. Using PLLA as an internal control allowed us to correlate accelerated degradation at 70°C to what it would be at 37°C. Synthesized tubes were cut into ~5 mm lengths and allowed to equilibrate in a pH 7.4 PBS solution for 1 week after which they were removed and weighed for initial mass (\( m_\text{i} \)). Vials were sealed and heated to 70°C for 28 d during which they were characterized by mechanical testing and wet (\( m_\text{w}/m_\text{i} \)) and dry (\( m_\text{d}/m_\text{i} \)) masses. The pH was monitored throughout the degradation study with a digital pH meter and the media replaced every 1–3 days to ensure that the pH was constant at 7.4±0.2.

3. Results

Poly(dimethacrylate PEG di/tetra-LLA) was synthesized as porous tubes by polymerization under centrifugal forces according to Scheme 1 from triblock oligomers of MA–LLA–PEG–LLA–MA with molar ratios of LLA:PEG of 4:1 or 2:1 and PEG molar mass of 200 or 400 g/mol.

3.1. Equilibrium water content

Polymer films were compared by EWC because polymer tubes can trap water in the lumen, thereby complicating the interpretation of otherwise straightforward data. As observed in Fig. 1, the EWC of both MA–LLA–PEG200 2:1 and MA–LLA–PEG400 2:1 films was significantly greater than those films with LLA:PEG ratios of 4:1 (\( p < 0.05 \)), reflecting the greater hydrophilicity of the higher LLA content for mutation. Furthermore, a significant EWC difference was achieved between PEG200 and PEG400 formulations of similar LLA ratios, indicating increased hydrophilicity of the higher molecular weight PEG formulations. EWC was greatest for MA–LLA–PEG400 2:1 and least for MA–LLA–PEG200 4:1 with an EWC of 68.5% and 37.5%, respectively.

3.2. Polymer tube degradation mass loss

The accelerated degradation behaviour of the MA–LLA–PEG tubes was compared to that of a control PLLA tube in order to relate accelerated degradation to that expected under physiologic conditions. Both dry and wet mass changes were recorded as a function of degradation time. As shown in Fig. 2(A) the dry mass of all polymers decreased with time with MA–LLA–PEG400 2:1 showing the fastest degradation followed by MA–LLA–PEG400 4:1, MA–LLA–PEG200 2:1, MA–LLA–PEG200 4:1 and then PLLA which had the slowest degradation behaviour. This degradation
behaviour was expected because higher molar mass PEG400 can attract and bind more water molecules than PEG200, resulting in greater water absorption and thus faster degradation of the LLA ester crosslinks. Furthermore, lower ratios of LLA:PEG of 2:1 are less hydrophobic than LLA:PEG of 4:1, further enhancing hydrolytic degradation. The centrifugally cast PLLA tube degraded the slowest with over 80% mass remaining at 14 days because it is the most hydrophobic of the polymers tested, which limits water penetration and hydrolytic degradation. Dry mass loss was greatest during the first 7 days where 24%–50% of the original mass was lost. While the rate of degradation decreased between 7 and 28 days, by 28 days, the mass was 10%–20% of the original mass for all samples, except PLLA which degraded to 50% of its original mass. At 8 weeks the polymers had completely degraded and dissolved into the PBS. During the degradation study, the tubes were observed until day 7 after which the degraded tubes lost their structure yet could still be easily removed and weighed until day 28.

As observed in Fig. 2(B) all of the MA–LLA–PEG polymers showed an increase in wet mass up to day 14, reflecting polymer swelling during degradation, after which the mass began to reduce. The trend in increased wet mass mirrored that observed in decreased dry mass and reflects the relative hydrophilicity of the polymeric tubes tested. The greatest mass increase was observed for MA–LLA–PEG400 2:1 followed by MA–LLA–PEG400 4:1, MA–LLA–PEG200 2:1, MA–LLA–PEG200 4:1 and then PLLA which showed no measurable wet mass increase or swelling. While some water may have been trapped in the tube lumen during these measurements, every effort was made to minimize this. Moreover, any trapped water would have been inconsequential to the change in mass observed and the conclusions derived therefrom.

3.3. Polymer tube mechanical stability during degradation

Mechanical properties of the tubular constructs were followed as a function of degradation time with normalized force readings recorded for fixed displacement values of both 20% vertical compression (D20) and 35% vertical compression (D35) along the tube’s horizontal axis. Force values were recorded over the first 7 days of the degradation study while the tubular structure was maintained for all constructs. All force–displacement curves exhibited an initial linear behaviour (to approximately 45% vertical displacement) followed by an exponential rise of normalized force as a function of transverse compression. A previously developed non-biodegradable PHEMA–MMA tube [6], the elastic modulus of which was similar to that of a spinal cord tissue, was tested at the same displacement values and used as a control for the normalized force. Displacement of 35% compression was used because we had previously observed a tube collapse of 35% in vivo [7]. It was also interesting to investigate whether the newly developed degradable tubes could match the mechanical response of the PHEMA–MMA at a smaller displacement value in the linear range while exhibiting significant force. Thus the 20% displacement was chosen. Fig. 3 shows characteristic degradation induced weakening behaviour for both D20 and D35. At \( t = 0 \), all MA–LLA–PEG tubes (except MA–LLA–PEG400 2:1) exerted a 2 times larger force at D20 and 3–4 times larger force at D35 than that exerted by the PHEMA–MMA tube, indicating their potential applicability as nerve guidance channels in spinal cord transection injuries. As degradation progressed, the forces exerted by all biodegradable tubes decreased. At 3 days of accelerated degradation (roughly equivalent to 1.3 months of physiological degradation), the forces measured at both D20 and D35 for polymeric tubes were approximately 25–33% lower than that of the PHEMA–MMA tube. Mechanical properties of the biodegradable tubes continued to decrease until day 7 at which only a very minimal mechanical response was
measured with forces ranging from 12% to 25% of the PHEMA–MMA tube. By day 7 of the accelerated degradation study (roughly equivalent to 3 months of physiological degradation), all of the MA–LLA–PEG tube formulations were indistinguishable by mechanical forces. At time 0, PLLA tubes had a D20 normalized force of $10.65 \pm 2.03 \text{g/mm}^2$ and a D35 normalized force of $14.37 \pm 1.98 \text{g/mm}^2$. During the accelerated degradation, all PLLA tubes were crushed prior to 20% compression and thus no values could be recorded for D20 or D35.

3.4. Polymer tube wall morphology change during degradation

As observed in Fig. 4 with representative SEM micrographs, the tube wall morphology changed during the accelerated degradation study. The pore size was observed to gradually increase as the MA–LLA–PEG polymer tube degraded. Furthermore the bead-like structure observed for all MA–LLA–PEG tube walls at $t = 0$ progressively changed to a fiber-like structure between days 5 and 7. As shown in Fig. 5, a similar increase in pore size was observed for PLLA tubes during degradation; however, no other morphological changes were obvious.

4. Discussion

LLA–PEG oligomers have been previously synthesized with stannous octanoate or zinc powder catalysis, which are effective yet potentially toxic [23]. To overcome this limitation, we used H$_3$PO$_4$ to catalyze the ring opening oligomerization of cyclic LLA by PEG diol. The high yields (>95%) coupled with the nearly complete reaction of LLA and PEG allowed MAC coupling without first purifying the LLA–PEG oligomer. MAC reaction with LLA end groups resulted in 75% substitution which was sufficient for the formation
of crosslinked polymeric tubes by redox initiated free radical polymerization in rotating cylindrical moulds. The swelling behaviour observed in aqueous solution confirmed the network formation as did the insolubility of the MA–LLA–PEG tubes in organic solvents.

Unlike other more conventional tube processing methods, such as dip-coating, casting or extrusion which have a dense wall morphology when prepared with, for example, PLLA, our tubes were porous and had a beaded wall morphology, similar to tubes previously synthesized with PHEMA–MMA [6] by a similar liquid–liquid centrifugal casting technique. The beaded wall morphology reflects the mechanism of phase separation of the growing polymer chain during polymerization where monomer swollen crosslinked polymer beads separated from the aqueous phase. Because these “beads” are denser than the water in which they are polymerized, they are pushed to the periphery and form a coating along the inner lumen of the cylindrical glass mould. The resulting porous structure is advantageous in terms of both diffusion and degradation. For application as nerve guidance channels, it is well established that porous polymeric tubes perform better than non-porous equivalents [24] because they allow for facile diffusion of nutrients across the tube wall which is critical for cell survival and regeneration. Similarly, porous structures should provide better release of potentially cytotoxic acidic degradation products than densely packed structures. While porous PLLA tubes can be prepared by extrusion combined with, for example, particulate leaching, the processing is more complicated, not scaleable and difficult to reproduce [25]. The porosity of nerve guidance channels should be sufficient for nutrient diffusion yet limit cell infiltration. Given the inclusion of non-cell adhesive PEG in the polymer formulation and the lack of cell infiltration in clinically used PGA mesh nerve guidance channels [26], it is unlikely that cells will penetrate these MA–LLA–PEG tubes.

The swelling behaviour of MA–LLA–PEG films was examined in terms of the chemical composition of the backbone. The EWC increased with PEG molar mass and decreased with LLA content, reflecting the hydrophilic nature of PEG and hydrophobic nature of PLLA.

In order to use these newly formed porous hydrogel tubes as nerve guidance channels, we had to first investigate their in vitro degradation behaviour. Given that previous studies have demonstrated partial tube collapse over time, it was important to understand not only mass loss with time, but also change in compressive modulus as a result of degradation and to correlate these with changes in tube wall morphology. By using PLLA as an internal control, we were able to correlate accelerated degradation at 70 °C and pH 7.4 to that at physiological conditions of 37 °C and pH 7.4 for MA–LLA–PEG polymeric tubes. By comparing the degradation that we observed for PLLA at 70 °C to that observed in a previously published study at physiological conditions [27], we estimated that 1 week of accelerated degradation corresponded to 3 months of physiological degradation. Notwithstanding that molar mass and geometry affect the degradation profile, this estimate is still applicable. This in vitro comparison provided us with a good perspective on expected degradation in vivo where PLLA has been shown to degrade in 24 months [27].

In this study the impact of morphology and hydrophilicity were examined in terms of the degradation profile of MA–LLA–PEG polymeric tubes where crystallinity and hydrophobicity increase with LLA content whereas amorphous content and hydrophilicity increase with PEG molar mass and content. With these divergent properties in mind and the importance of water–polymer interaction for hydrolytic degradation, it is clear that the degradation rate increased with PEG molar mass and decreased with LLA concentration, as was observed for change in dry mass over time. For PLLA, both crystallinity and hydrophobicity reduced water contact and infiltration, thereby accounting for the slower degradation profile.

The changes observed in wet mass complemented those observed for dry mass and corroborated the findings of greater water–polymer contact with increased PEG content and molar mass. It is well known that hydrogels swell with degradation [28,29] and thus it was not a surprise that the wet mass increased up to day 14 due to swelling and then decreased at day 28 due to polymer degradation. The swelling behaviour is accentuated here by both the accelerated degradation and the morphology of the polymer tube wall which allows facile diffusion of water into the bulk structure. It is important to note, however, that although maximum mass swelling reached nearly 640 wt%, maximum volumetric swelling at that same time-point (where the polymer had degraded to nearly 25% of its original mass) was only 160 vol% or 1.6 times its initial shape. Assuming that the volume varies quadratically with the radius, the radial swelling was calculated to be only 1.26 times, suggesting that the swelling observed would not significantly impact nerve regeneration during polymer degradation.

For ultimate use as nerve guidance channels, these polymeric tubes are compelling because they are porous, degradable to non-toxic products and have a degradation profile greater than 6 months under physiologic conditions which is concomitant with the time-scale of peripheral nerve regeneration [1]. However, peripheral nerve grafts have failed for numerous reasons, one of which is premature loss in mechanical stability [1]. To gain greater insight into how these MA–LLA–PEG
tubes would perform, we followed their mechanical integrity during degradation. Force measurements at 20% and 35% of initial diameter may be indicative of the tube’s in vivo performance. The forces exerted by the tube during compression of 20% and 35% decreased for all tubes reflecting decreased mechanical integrity during degradation. The most rapid loss of strength was observed for the MA–LLA–PEG400 2:1 tubes which also had the fastest mass loss. While all of the MA–LLA–PEG polymeric tubes initially had greater mechanical strength than PHEMA–MMA tubes (that have been implanted), all tubes lost this mechanical strength early in degradation. By 3 days of accelerated degradation (corresponding to 1.5 months of physiological degradation), the mechanical response decreased dramatically (and below that of PHEMA–MMA) suggesting that these tubes alone are insufficient for use as peripheral nerve guidance channels. However, the liquid–liquid centrifugal casting technique allows for the facile inclusion of, for example, reinforcing coils, which increase the overall strength of the tubes [8] and may be worth pursuing here.

The rapid decrease in mechanical properties cannot be explained by mass loss alone but requires morphological changes of polymeric tube walls to be examined in more detail. As shown in Fig. 4 with SEM micrographs for MA–LLA–PEG400 2:1, where the most striking changes were observed likely due to the fastest degradation, both the pore size increased and the morphology changed from a bead-like to a fiber-like morphology. The increase in pore size correlates with the loss of mechanical strength and increase in water content of the tubes, thereby accounting for the swelling behaviour observed. The bead to fiber morphology change has not been observed before and may reflect a swelling-induced coalescence of beads concomitant with swelling which would enlarge the pores.

5. Conclusion

The chemical composition of MA–LLA–PEG impacts changes in physical properties of the resulting polymer. Changing the ratios between hydrophilic and hydrophobic segments of the oligomeric backbone led to changes in the EWC, microstructure and the mechanical properties of the tube. The unique ability to tailor physical and chemical properties of a polymer by slightly varying the chemistry of the backbone opens the possibility of engineering a polymer for a particular application prior to its synthesis. Properties obtained from selective synthesis allowed us to design an oligomeric ether–ester-based polymer as a tubular construct for nerve repair. Similar engineering approaches can aid in the development of polymers for other biomedical applications.

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References


