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Biodegradable sheath-core biphasic monofilament braided stent for bio-functional treatment of esophageal strictures

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ABSTRACT

In this study, a polydioxanone (PDO) and poly(L-lactic acid) (PLLA) sheath-core biphasic monofilament was designed to develop an esophageal stent with improved mechanical properties and controlled biodegradability. The radial force of PDO/PLLA sheath-core stent was 10.24 N, while that of PDO stent was 5.64 N. Deteriorations of tensile strength, elastic modulus and elongation during degradation test were also delayed on PDO/PLLA group. Hyaluronic acid–dopamine conjugate and $BaSO_4$/PDO conjugate coating layers provided improved tissue adhesion strength and reasonable X-ray contrast, respectively. Taken all together, the sheath-core filaments with tissue adhesive and radiopaque properties will be useful in designing esophageal stents.

Introduction

Esophageal stricture generally occurred by malignancies causes dysphagia, malnutrition or even cancer-related death [1,2]. Along with a balloon dilation therapy, stent placement is one of the effective ways to manage esophageal stricture. The esophageal stent has evolved from rigid plastic tube to self-expandable metallic or plastic stent. Although the metallic and permanent plastic stents demonstrated good mechanical properties, they often require removal process, which is very difficult and sometimes causes trauma [3]. Many efforts, thus, have been made to develop biodegradable stent which does not need removal [3–5].

Biodegradable polyesters such as polylactide (PLA), polyglycolide (PGA) and polydioxanone (PDO) have been used for the fabrication of biodegradable-based stents that degrade via hydrolytic processes [6–9]. Among the biodegradable polymers, PDO possesses higher flexibility and biocompatibility [10]. Due to its degradability and biocompatibility, PDO has been widely used as an absorbable suture in a variety of clinical cases [11]. The PDO-based esophageal stents, however, still have several limitations such as low mechanical stability during the degradation [12,13], stent migration due to low tissue adhesion [14] and poor X-ray visibility due to radiolucency [15].

Fabrication of sheath-core filament is one of effective ways to enhance filament strength [16,17]. Poly(L-lactic acid) (PLLA) is FDA-approved synthetic polymer that has been widely used in biomedical fields due to its relatively high mechanical properties, biodegradability, and biocompatibility [8,18–20]. Researches demonstrated that PLLA has higher elastic modulus and lower degradation rate than PDO [12]. The limitations of PLLA for use as esophageal stent are its lack of flexibility due to its brittle nature [21]. Thus, the PDO and PLLA (PDO/PLLA) sheath-core biphasic filament is expected to help to maintain the long-term mechanical integrity of biodegradable esophageal stent while maintaining stent flexibility.

The migration of stent after placement is also one of the major issues of stent procedure, which is more common when the lesion

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is benign [3,22,23]. The dopamine (DA) has been widely utilized as an alternative molecule to dihydroxylphenyl alanine (DOPA), an amino acid of mussel-adhesive proteins, which the major moiety of both molecules is the catechol, dihydroxyphenyl, group. The catechol group can bind strongly with various substrates including ceramics, inorganic and organic surfaces [24,25]. Due to its binding properties, DA has been studied as one of the major components of tissue adhesive biomaterials [26,27]. Despite its superior binding property, poor biocompatibility of the DA remains a problem [28]. The HA is a linear polysaccharide that consists of glucuronic acid and *N*-acetyl-glucosamine. HA is a non-sulfated glycosaminoglycan and can be found throughout the body in the vitreous of the eye and the extracellular matrix of cartilage tissues [29]. Because of its superior biocompatibility and anti-fouling effect, the HA has been widely studied as tissue engineering scaffold [30,31] and a coating material for biomedical applications [31,32]. Although HA has such advantages as a biomaterial, it is not preferably attached to surfaces which do not have proper functional groups. The HA–DA conjugate, thus, has frequently been used to increase biocompatibility and adhesion properties of biomaterial surfaces [28,32].

Placement of stent on a proper site is an important factor of success of stenting procedure. PDO stents, composed of an organic substance, however, were not optimally visible at the X-ray examination. Barium sulfate ($BaSO_4$) is the most commonly used as a contrast agent for gastrointestinal imaging [33] and has been investigated for enhancing the radiopacity of biodegradable vascular stent systems because of its relatively superior biocompatibility and radiopacity.

The aim of this study was to develop novel biodegradable esophageal stent with enhanced strength as well as controlled degradation, tissue adhesion strength, and radiopacity. To achieve these goals, PDO/PLLA sheath-core biphasic monofilament for the improved mechanical stability was developed and further functionalized with HA and DA (HA–DA) conjugate and $BaSO_4$ for enhanced tissue adhesion and radiopacity, respectively. The radial force of PDO/PLLA sheath-core braided stent was compared to PDO stent. In addition, further investigations including

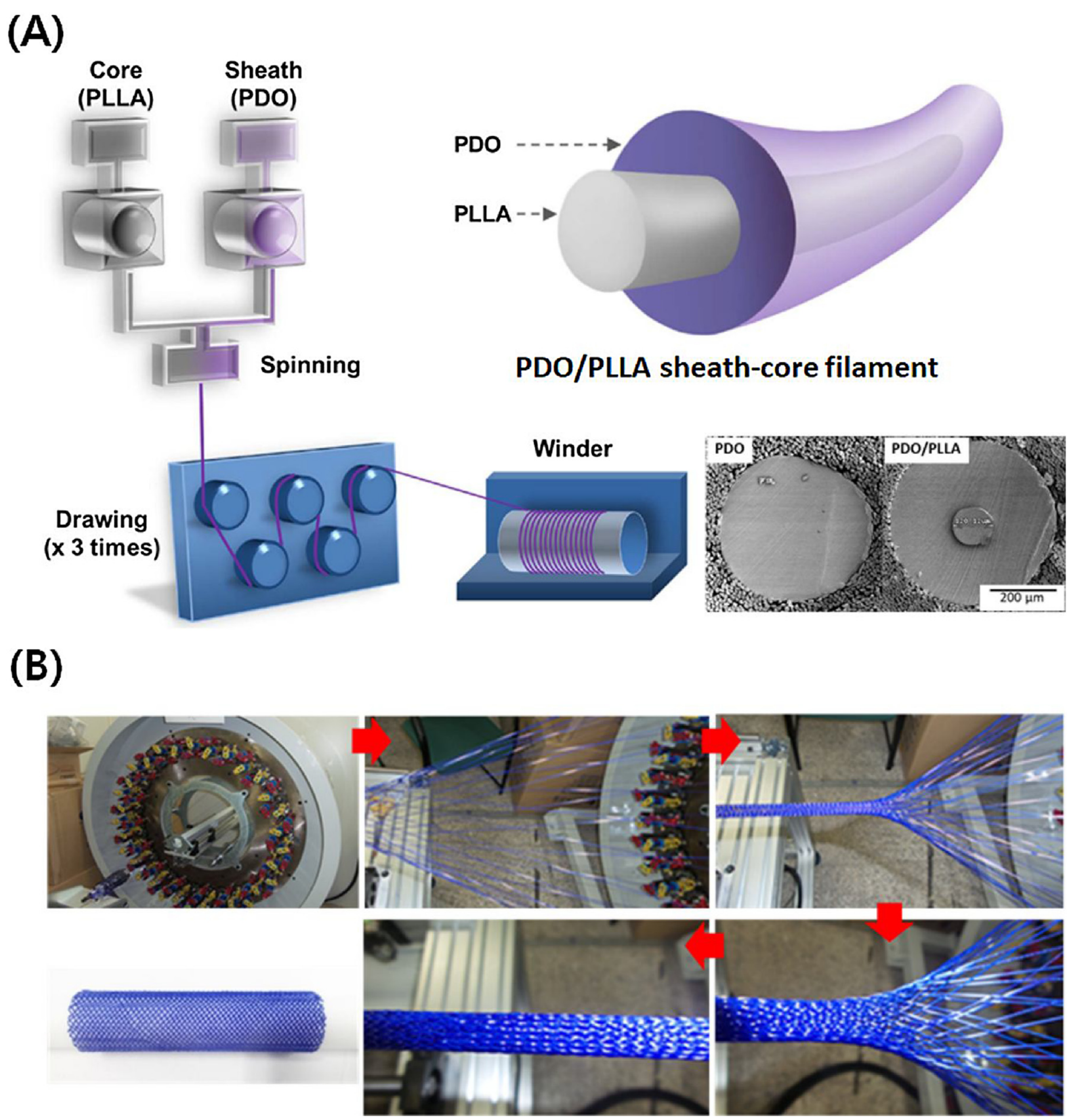

Fig. 1. Schematic diagram of synthesis processes of (A) melt-spun PDO/PLLA sheath-core monofilament and (B) monofilament braided stent.

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