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Original article

Mechanical properties of a bioabsorbable nerve guide tube for long nerve defects

Propriétés mécaniques d'un guide de repousse nerveuse résorbable pour de longues pertes de substance nerveuses

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Abstract

The mechanical properties of nerve guide tubes must be taken into consideration when they are being developed. We previously reported the feasibility of using 50:50 tubes in a canine 40 mm peroneal nerve defect model, where 50:50 represents the proportion of poly(L-lactic) acid (PLLA) and polyglycolic acid (PGA). The aim of the current study was to show that 50:50 tubes have suitable mechanical properties for repairing long nerve defects. Four types of nerve guide tubes made with PLLA to PGA fiber ratios of 100:0 (i.e. 100% PLLA) (100:0 tube), 50:50 (50:50 tube), 10:90 (10:90 tube), and 0:100 (0:100 tube) were designed and created using a tubular braiding machine. Their mechanical properties were examined in vitro (up to 16 weeks). In compression testing, 50:50 tubes had the highest normalized force value, followed in order by the 100:0, 10:90, and 0:100 tubes up to 8 weeks after immersion. From the point of view of biomechanics and bioresorbability, out of the 4 tube types tested, 50:50 tubes appeared to have the optimal mechanical properties for longer nerve defects.

Keywords: Nerve guide tube; PGA; PLLA; Mechanical properties

Résumé

La fabrication de guides de repousse nerveuse doit tenir compte de leurs propriétés mécaniques. Nous avons rapporté précédemment la faisabilité de tubes 50/50 (50/50 représente la proportion de fibres d'acide poly(L-lactique) [PLLA] et d'acide polyglycolique [PGA]) sur un modèle canin de 40 mm de perte de substance de nerf fibulaire. Le but de cette expérience était de prouver que les tubes 50/50 possèdent bien les propriétés mécaniques adéquates pour réparer les longues pertes de substance nerveuses. Nous avons défini 4 types de guides de repousse nerveuse faits de fibres de PLLA et de PGA dans des proportions de 100/0 de PLLA, 50/50 PLLA/PGA, 10/90 PLLA/PGA et 0/100 de PGA, respectivement. Ils ont été fabriqués avec une machine à tisser tubulaire et leurs propriétés mécaniques ont été étudiées in vitro (jusqu'à 16 semaines). Aux tests de compression, les guides 50/50 présentaient la valeur F la plus haute, suivis par ordre décroissant par les guides 100/0, 10/90 et 0/100 jusqu'à 8 semaines après immersion. D'un point de vue biomécanique et de biorésorption, des 4 guides testés, les guides 50/50 semblaient présenter les propriétés mécaniques optimales pour combler les longues pertes de substance nerveuse.

Mots clés : Guide de repousse nerveuse ; PGA ; PLLA ; Propriétés mécaniques

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1. Introduction

Repair of peripheral nerves has long been a focus of intensive study. In orthopedics or plastic surgery, direct suturing has been a common technique for repairing injured nerves. However, if a nerve defect is longer than 5 mm, it is impossible to directly suture one stump to the other, thus requiring interposition of an autograft [1,2]. Although autografting is now a well-established method, it does not always give satisfactory results [3]. Painful neuroma or numbness may occur at the site where the autograft was harvested. Such donor site morbidity [4,5] can be avoided if an artificial nerve graft is employed.

Much work has been conducted to develop nerve guide tubes [6–8]. Use of a silicone guide tube for repair of nerve gaps less than 10 mm presents little problem [9]. However, for longer nerve defects, it is necessary to employ biodegradable artificial nerve conduits. In general, the ideal artificial nerve conduit should degrade after accomplishing its guiding function. If a tube is initially too fragile mechanically, the tube cannot withstand pressure from the surrounding tissues; conversely, if it is too firm, it can damage the surrounding tissues such as nerve stumps and blood vessels. Biodegradable artificial nerve tubes such as the polyglycolic acid (PGA) hollow tube (Neurotube, Neuroregen, L.L.C., PA, USA) [10] or collagen hollow tube (Neura Gen, Integra life Sciences, Plainsboro, NJ, USA) [11] are commercially available for clinical use. However, their indications are limited only to sensory nerve defects shorter than 30 mm.

New nerve guide tubes are currently being developed for the reconstruction of longer nerve defects. However, such studies are still in the experimental stage in animal models [12]. Ideally, a biomaterial should alter its mechanical properties as a function of the functional requirements during degradation. For example, biodegradable surgical suture made of PGA, such as Dexon (DAVIS + GECK, NJ, USA), maintains its burst strength for 8 weeks, and is completely resorbed in 3 months [13]. If a device requires a longer functional lifespan, a different resorbable material is used. For example, screws for internal fixation of bone fractures are made of poly (L-lactic) acid (PLLA). These screws need to stabilize the fractured segment for 4 months to allow rigid bone union, and then the screws themselves are resorbed in 8 months [14].

We previously reported on the feasibility of 50:50 tubes (PLLA:PGA = 50:50) in a canine 40 mm peroneal nerve defect model [15]. The aim of the present study was to show that 50:50 tubes have suitable mechanical properties for repairing long nerve defects.

2. Material and methods

2.1. Tubes

Four typical types of artificial nerve tubes were prepared by braiding together poly(L-lactic) acid (PLLA) with polyglycolic acid (PGA). The PLLA fiber was a monofilament (average molecular weight: 130,000; crystallinity: 50 to 60%; diameter: 200 μm) and the PGA fiber was a multifilament consisting of 26 PGA monofilaments (DEGRIX^{TM}, Mitsui Fine Chemical Co. Ltd., Tokyo, Japan; average molecular weight: 150,000; crystallinity: 56%; diameter: 17.4 μm). Four kinds of complex tubes made from PLLA and PGA fibers braided in various proportions were prepared: PLLA:PGA ratio of 100:0 (100:0 tube), PLLA:PGA ratio of 50:50 (50:50 tube), PLLA:PGA ratio of 10:90 (10:90 tube), and PLLA:PGA ratio of 0:100 (0:100 tube).

The PLLA and PGA fibers were placed in a tubular braiding machine with 48 spindles (Maruchu Co. Ltd., Kyoto, Japan). Each spindle held one PLLA fiber or four PGA fibers. A Teflon tube with an outer diameter of 4 mm (equivalent to the inner diameter of the nerve guide tube) was inserted as a mandrel at the center of the spindles, where the fibers converged to braid. One end of the fibers was held at the top of the mandrel and pulled upwards. The other end of the fibers from the spindles was then pulled to the center of the braiding machine, all of the other spindles circulating clockwise around the mandrel and the remaining spindles circulating counterclockwise. The porosity of the tubular structure could be controlled by changing any of several parameters, including the braiding angle, the number of fibers in a bundle, and the number of fiber bundles. Table 1 summarizes the sample code, the ratio of PLLA and PGA fibers, the outer diameter of the tube, the PLLA interval (indicating the distance between PLLA fibers along the length of the tube), the braiding angle and the pore size. Fig. 1A–D shows macroscopic views of the four nerve tubes and the appearance of the tubes by scanning electron microscopy (SEM).

2.2. In vitro degradation

The four types of tubes were immersed in 30 ml phosphate-buffered saline (PBS) at 37 °C and pH 7.4; the solution was replaced with fresh PBS every week [16]. Tubes were taken out after 1, 2, 4, 8, 10, 12, 14 and 16 weeks, and their mechanical properties were evaluated ($n = 8$ for each type at each time point). Stiffness was evaluated during compression and tensile testing; SEM was used to discern the microscopic surface features (Fig. 2A–D).

2.3. In vitro mechanical testing

A tensile tester (RTM-250, Orientec, Tokyo, Japan) was used to test the stiffness of the tube during compression. Parallel plates with diameters of 8 cm (upper plate) and 10 cm (lower plate) with a load cell of 10 kg were employed in compression mode (Fig. 3A). All mechanical testing was carried out in ambient air at room temperature with a crosshead speed of 1.0 mm/min. Each test was completed within 3–4 min, to ensure minimal water evaporation during the tests. Specimens (sample outer diameter 4 mm) were compressed from the sides. The resulting force and displacement data were captured on a chart recorder [17].

The elasticity of the tubes in the axial direction was examined using the same apparatus as the one used for compression tests. For tensile tests, the measurements were carried out in ambient