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Dynamic-mechanical properties of a novel composite intervertebral disc prosthesis

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Abstract Over the past years, a tremendous effort has been made to develop an intervertebral disc (IVD) prosthesis with suitable biological, mechanical and transport properties. However, it has been frequently reported that current prostheses undergo failure mainly due to the mismatch between the mechanical properties of the conventional device and the spine segment to be replaced. The aim of the present work was to develop a poly(2-hydroxyethyl methacrylate)/poly(methyl methacrylate) (PHEMA/PMMA) (80/20 w/w) semi-interpenetrating polymer network (s-IPN) composite hydrogel reinforced with poly(ethylene terephthalate) (PET) fibres, and to investigate the static and dynamic mechanical properties. Filament winding and moulding technologies were employed to obtain the composite IVD prostheses with the unique complex structure that is peculiar to the natural IVD. The compressive properties analysis showed the typical J-shaped stress-strain curve which is displayed by natural IVDs. Compressive modulus varied from 84 to 120 MPa, as a function of the strain rate, and stress was higher than 10 MPa. These values are in the range of those of the natural lumbar IVDs. No failure of the prostheses has occurred during fatigue test performed for ten million cycles in physiological solution. Dynamic mechanical tests have confirmed the composite IVD prostheses exhibited appropriate viscoelastic properties.

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Introduction

Low back pain is one of the most common medical conditions in the western world. Intervertebral disc degeneration, due to normal aging or to a pathological process, is a serious disease, affecting many individuals [1, 2].

The major surgical interventions for treating conditions related to the degenerated disc are discectomy, fusion, and total IVD substitution. Whilst these surgical treatments provide relatively good short-term clinical results, their use also alters the biomechanics of the spine, possibly leading to further degeneration of the surrounding tissues and of the discs at the adjacent levels.

Consequently, a preferable solution to a degenerated disc pathology would seem to be an artificial disc substitute, able to mimic the structural properties of the natural IVD.

The structure of the natural IVD, and indeed its biomechanical and transport properties, are unique and very complex. The IVD is a composite structure made up of a nucleus pulposus (translucent gel) surrounded by the annulus fibrosus (lamellar structure) [3]. Superior and inferior to this are two thin layers of vertebral cartilage, which form the endplates. These are characterized by micropores which allow the exchange of water and nutrients [1]. The IVD consists mainly of collagen fibres embedded in a proteoglycan-water gel [4]. The type and orientation of collagen fibres in the IVD have an important influence on how load is distributed. In the disc there is a gradation of collagen type and orientation from annulus to nucleus. From the edge of the disc inwards to the nucleus, the collagen fibres orientation in the concentric lamellae of the annulus fibrosus decreases from an angle of 62–45°, with respect to the spinal axis [5]. It is reported that the mechanical role of the nucleus pulposus is to resist and redistribute compressive forces within the spine, whereas the major function of the annulus fibrosus is to withstand tension [4]. Water is the main constituent of the IVD, and it occupies 65–85% of the tissue volume, depending on age and region.

With age the nucleus loses its gel-like character, due to degradation, dehydration and shrinking. This causes an increase in load concentration on the annulus, leading to its degeneration [1]. There are currently two principal surgical procedures for treating conditions related to the degenerated disc: discectomy and fusion [1]. Although both these approaches produce relatively good short-term clinical results, discectomy and fusion alter the biomechanics of the spine, possibly leading to further degeneration of surrounding tissues and discs at the adjacent levels [6–12]. An alternative solution to a degenerated disc involves the use of an artificial disc substitute [1]. Over the past 40 years, a tremendous effort has been made to develop a suitable artificial disc substitutes to replace the degenerated disc [1, 2, 13, 14]. Artificial discs are intended to restore dynamic and physiological motion of healthy discs, and should theoretically last the lifetime of the patient. There is much controversy concerning what are realistic targets for device lifetime for in vivo testing, and for minimum acceptable clinical lifetimes for artificial replacement discs [15]. It has been estimated that, during the average lifetime, the spine undergoes approximately one hundred million movements [15, 16]. Many studies have demonstrated that the optimum life span is thirty million movements, and ten million movements is considered to be the recommended minimum testing cycle [15, 16]. However, the IVD prostheses on the market to date have been reported frequently to undergo failure, due to wear and degeneration of materials or mismatch between mechanical proprieties of the device and the natural tissue [16].

Current synthetic discs, such as the unconstrained mobile-bearing Link SB Charitè III [17] and the constrained Arcoflex [18], have not overcome these problems [16], even though they have demonstrated a high biocompatibility with the surrounding tissues whilst maintaining unrestricted biological mobility. These prosthetic implants usually consist of a polymer core interposed between two metallic plates, and may lead to immobilization or dislocation of the structure [16].

In order to design an alternative intervertebral disc prosthesis with appropriate transport, mechanical and biological properties, the research has been focused on the basic concept of mimicking the natural structure of the disc tissues. The objectives of this current study were, therefore, to engineer and to manufacture a novel fibre-reinforced hydrogel to act as a disc substitute, and to characterize its short- and long-term mechanical properties.

Materials and methods

Preparation of the composite intervertebral disc prosthesis

Poly(methyl methacrylate) (PMMA, average particle size 170 μm, BDH Laboratory Reagent) was dissolved, with stirring at room temperature, in 2-hydroxyethyl methacrylate monomer (HEMA, Aldrich) to form an 80/20 w/w solution. Successively, the initiator azo-*bis*-isobutyronitrile (AIBN, Fluka) (0.1% w/w with respect to HEMA monomer) and the crosslinking agent ethylene glycol dimethacrylate (EGDMA, Aldrich) (0.5% w/w) were added. Poly(ethylene terephthalate) (PET) fibres (1670 dtex, Sofradim, France), impregnated with the reactive solution, were wound helically by winding filament technique on the mandrel having the geometry of the nucleus, until the final size of the disc was obtained; the winding angle was varied from 45–65°. Upon completion of this phase, the wound structure was transferred in a pseudoelliptically shaped Teflon mould and filled with the reactive solution. During this process hydroxyapatite (P205 Plasma Biotal, Tideswell, UK) (30% w/w) reinforcing hydrogel was used for endplate interface (Fig. 1). The system was cured in an oven at 60 °C for 4 h, 70 °C

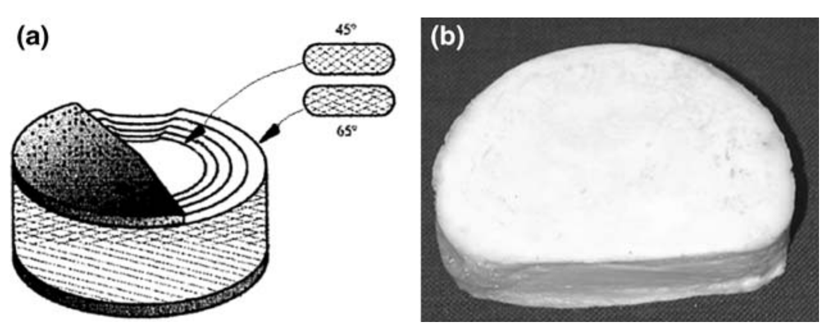

Fig. 1 (**a**) A schematic representation of the fibre-reinforced disc substitute with hydroxyapatite reinforcing hydrogel endplates (**b**) The total intervertebral disc substitute prototype

for other 4 h and then at 80 °C for 12 h to allow a complete polymerization. A post-cure was then performed at 90 °C for 2 h. After cooling, the samples were immersed in a saline bath at 37 ± 0.5 °C for hydration and to remove eventual unreacted monomer.

Mechanical characterization

Compressive properties

Static compressive tests were performed on swollen fibre-reinforced composite hydrogels at different strain rates, ranging from 1 to 10 mm/min, by using a servohydraulic MTS 858 Bionix Test System. Engineering stress and strain were evaluated and compressive moduli were expressed in terms of mean value ± standard deviation.

Compressive creep tests were carried out on swollen samples in a saline bath at 37 ± 0.5 °C by a MTS Bionix 858 Test System. A stress value of 2 MPa was applied and the strain was monitored for 4,500 s. A viscoelastic four-parameter model, which is a linear viscoelastic model and consists of two ideal elastic and two viscous components, was also used to describe the creep response of the fibre-reinforced hydrogel.

The trend of the experimental data was fitted by a four-parameter viscoelastic model using the following relationship between strain and time [19, 20]:

$$\varepsilon(t) = \frac{\sigma_0}{E_1} + \frac{\sigma_0}{E_2}\left[1 - exp\left(-\frac{t}{\tau}\right)\right] + \frac{\sigma_0}{\eta_1}t \quad (1)$$

Creep-fatigue and dynamic-mechanical tests

Creep-fatigue tests were performed on swollen samples in a saline bath at 37 ± 0.5 °C up to 10^7 cycles at 2 Hz with a MTS Bionix 858 test system.

The sinusoidal compressive load ranged from 200 to 2,200 N, which represents the load on human lumbar IVDs while lying supine and bending position, respectively, for an individual of 100 kg bodyweight. Dynamic-mechanical measurements were also realized in a load control mode at an increasing level of the mean load, ranging from 200 to 2,200 N, using a dynamic amplitude of 100 N; the frequency was scanned from 0.1 to 10 Hz. Creep recovery steps of 8 hours (sleeping time) at 200 N (supine position) were performed after different fatigue cycles (Fig. 2).

Storage modulus (E′) and loss modulus (E″) were calculated according to the following equations:

$$E' = \frac{\sigma_0}{\varepsilon_0}\cos\delta \qquad E'' = \frac{\sigma_0}{\varepsilon_0}\sin\delta \quad (2)$$

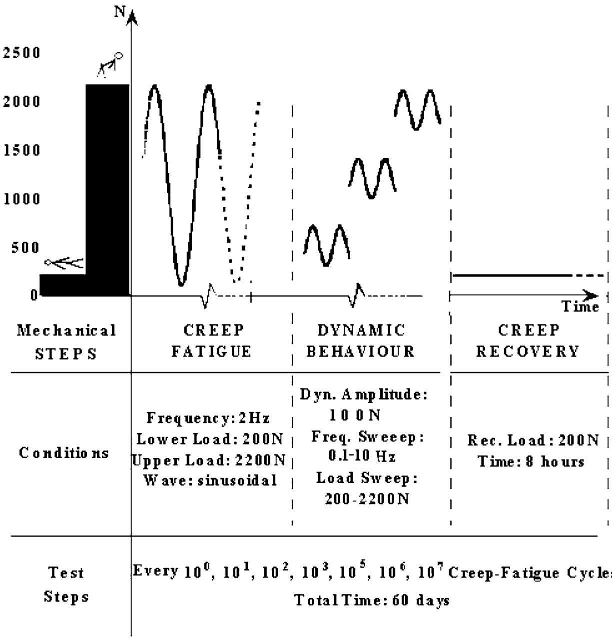

Fig. 2 Load history imposed to the swollen fibre-reinforced hydrogel: creep-fatigue, dynamic-mechanical and creep-recovery tests

Results

Compressive properties

Static compressive properties

Compression tests were carried out up to a load level of 17,000 N without breaking. The stress-strain curves show a toe region which extends up to 0.09 mm/mm, followed by a linear region (Fig. 3).

The toe region is mainly due to the matrix properties and realignment of fibres, which straighten their crimped waveform and reorient themselves in the transverse direc-

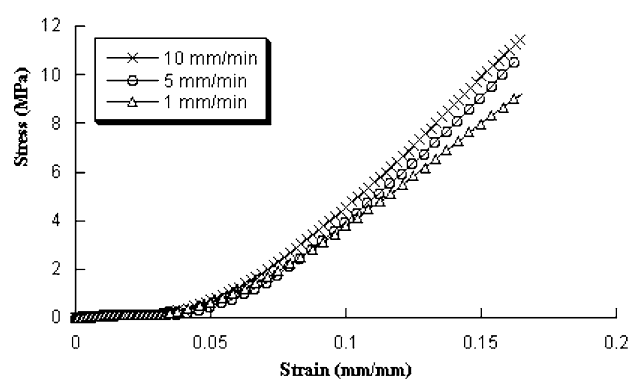

Fig. 3 Compressive stress-strain curves of the swollen fibre-reinforced hydrogel at strain rates of 1 mm/min (Δ), 5 mm/min (o) and 10 mm/min (x)

tion. During the loading process the influence of the fibres sharply increases and the linear region is related to the fibres straightening.

The compressive modulus has been evaluated as the slope of the linear region of the J-shaped curve. Values of compressive modulus of (84.0 ± 9.8) MPa, (102.0 ± 11.0) and (120.0 ± 12.0) MPa have been calculated at strain rates of 1, 5 and 10 mm/min, respectively.

Creep properties

Compressive creep tests have confirmed the time-dependent properties, which had been already demonstrated by the dependence of compressive stress-strain curves on strain rate. Typical strain values varied from 0.069 to 0.12 mm/mm after 4,500 s (Fig. 4). These results were compared to those obtained through compressive creep tests performed on canine IVDs for a stress of 2 MPa [20].

Creep-fatigue and dynamic-mechanical tests

The results from preliminary dynamic-mechanical tests have shown that both the storage modulus E′ and the loss modulus E″ increase in frequency at different mean load levels (Fig. 5). This is a typical behaviour of rubbery materials. It can be attributable to the rubbery matrix, since in this condition the PET fibres give a poor contribution to the overall viscoelastic behaviour, as long as the load range investigated (200–2,200 N) falls within the toe region of the static stress-strain curve in compression. Moreover, fatigue tests and dynamic-mechanical measurements have evidenced that the storage modulus increases as the number of cycles increases, reflecting a gradual hardening of the composite structure (cyclic hardening) (Fig. 6). The same behaviour has been shown in the whole frequency sweep (0.1–10 Hz).

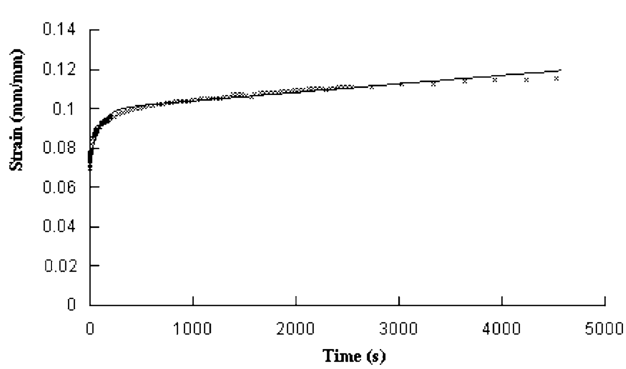

Fig. 4 Compressive creep behaviour of the swollen fibre-reinforced hydrogel for a compressive stress of 2 MPa. Experimental data for a typical sample (x) compared with the four-parameter model (—)

By comparing the creep-recovery responses of the composite structure, a slight difference in terms of strain values can be observed with the increasing number of cycles (Fig. 7).

Discussion

Biological materials are dynamic, complex and multi-functional – characteristics which are difficult to achieve in purely synthetic systems. It was previously believed that artificial biomaterials had to be designed to provide a high strength associated with a high modulus of elasticity at low strain levels. It was attempted to achieve this combination of properties through the use of metals, ceramics and plastics with a relatively high strength as biomaterials [16]. However, in contrast to most artificial materials, soft biological tissues are characterized by a large amount of strain before failure, and they are flexible and tough, showing a high strength. In order to avoid the mechanical mismatch which exists between traditional disc devices and tissues, design of new high performance and multifunctional materials has to proceed by mimicking the structure of the natural materials [21]. This biomimetic approach has been adopted to design a fibre-reinforced hydrogel, which is able to match the mechanical properties of natural IVD and the surrounding tissues.

To satisfy all the requirements for designing an alternative intervertebral disc prosthesis, the use of PHEMA hydrogels was considered in this work, these hydrogels having already been used in a wide variety of biomedical applications because of their biocompatibility, high permeability and high hydrophilicity [22–26]. However, the mechanical properties of these materials in the hydrated state are not sufficient for biomedical applications where high mechanical strength is required [25, 26]. The mechanical properties of polymer hydrogels have been improved by the incorporation of a hydrophobic component, such as poly(caprolactone) (PCL), and polymeric fibres [25–27]. The inclusion of hydroxyapatite and/or calcium phosphate would be beneficial, as these materials are bioactive and can stiffen polymers, as is required for the realization of the endplates.

Different PHEMA-based networks composite hydrogels reinforced with PET fibres have been designed for potential use as total IVD substitutes [28]. These devices have been made by filament winding and subsequently by moulding technology. The mechanical behaviour of PHEMA/PCL semi-interpenetrating polymer networks composite hydrogels reinforced with PET fibres has been investigated [28]. However, PCL is a biodegradable polymer, and its degradation leave voids in the network, undermining mechanical properties. Therefore PMMA, a biostable polymer, was examined and adopted as a replacement for PCL to

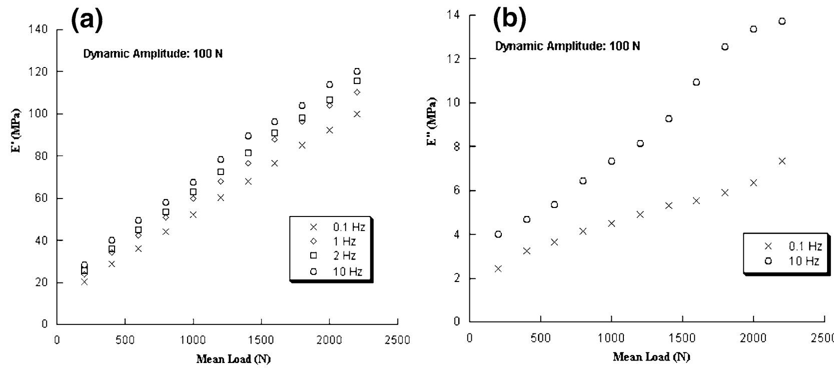

Fig. 5 Dynamic-mechanical properties of the swollen fibre-reinforced hydrogel in the compressive load range (200–2,200 N) with a dynamic amplitude of 100 N. (**a**) Storage modulus E′ versus mean load at 0.1 Hz (x), 1 Hz (◇), 2 Hz (□) and 10 Hz (o) (**b**) Loss modulus E″ versus mean load at 0.1 Hz (x) and 10 Hz (o)

improve the mechanical behaviour of the hydrophilic composite structures. Research has since principally focused on the design, manufacturing and mechanical characterization of PHEMA/PMMA semi-interpenetrating polymer networks composite hydrogels, reinforced with PET fibres. Although different forces—compression, tension, shear—act on the motion of the spine segment, it is possible to assume that, in normal daily life, the loads transferred through the IVD are mainly compressive [29]. This suggested performing static and dynamic compressive tests as preliminary characterization of the designed composite structures.

The compressive J-shaped stress-strain curve obtained for the composite hydrogel (Fig. 3) is typical of soft biological tissues, such as articular fibrocartilage and intervertebral discs, and the initial upward concavity indicates a relatively high flexibility at low strain levels [16]. Despite the high flexibility, with attendant low modulus and hence high compliance, high compressive strengths can be achieved, as shown by the compressive stress-strain curve.

The values of compressive modulus obtained are consistent with those of the lumbar IVDs. Compressive tests performed on composite hydrogels at a strain rate of 5 mm/min showed a modulus of 102.0 MPa and previous studies on canine IVDs have demonstrated that at the same strain rate, the modulus in the linear region increases by a factor of 3 over the length of the spinal column, spanning from 32.0 MPa at C2-C3 level to 115.0 MPa at L6-L7 one, in terms of mean values [30].

A similar observation can be made regarding the extension of the toe region (0.09 mm/mm), which extends to approximately 0.10 mm/mm in natural IVDs [30]. The rate dependence of mechanical properties of the fibre-reinforced hydrogels manufactured is shown by the change of mean values of compressive modulus (from 84.0 to 120.0 MPa) with increasing strain rate, similar to natural

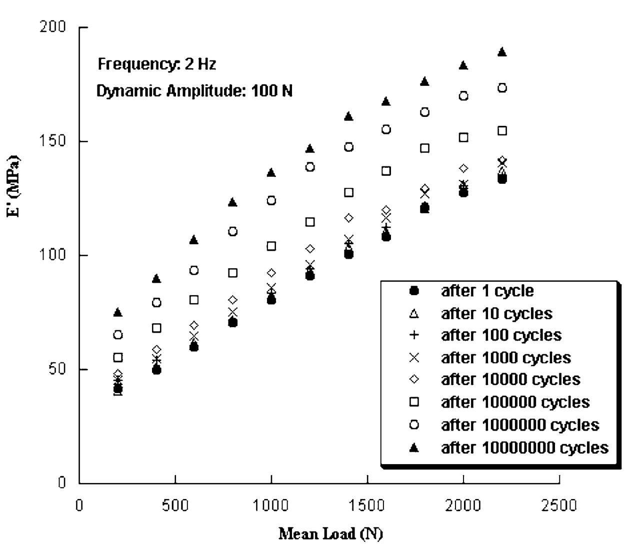

Fig. 6 Creep-fatigue and dynamic-mechanical analysis performed on the swollen fibre-reinforced hydrogel according to the load history imposed as reported in Fig. 2. Storage modulus E′ versus mean load at a frequency of 2 Hz after a different number of cycles

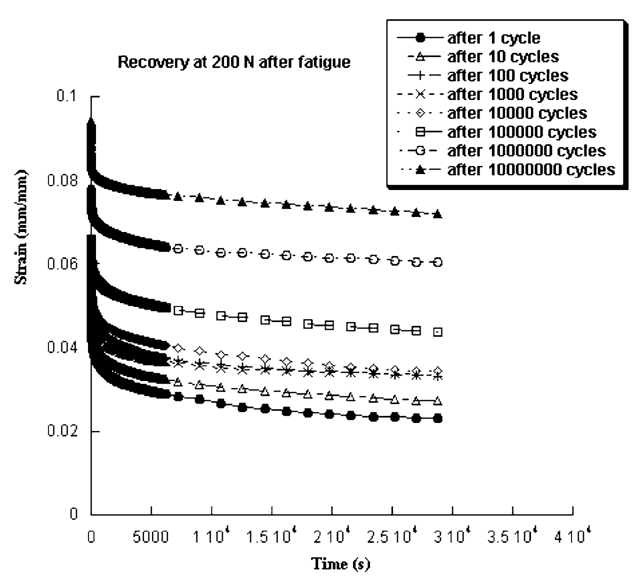

Fig. 7 Creep-recovery behaviour at different number of cycles performed on the swollen fibre-reinforced hydrogel, according to the load history imposed, as reported in Fig. 2

canine IVDs [30]. However, the strain rate does not dramatically affect the extension of the toe region, again as in the natural structure. Consequently, similar to natural IVDs, the time-dependence of mechanical properties of the composite hydrogels seems to be stress- rather than strain-dependent.

Like soft biological tissues, IVDs exhibit viscoelastic behaviours such as stress-relaxation and creep [31]. These show the ability of the natural structures to attenuate the stress concentration when they are strained, and to limit rapid deformations when they are subjected to high stresses [31].

The results of tests on the prostheses have shown that creep is rapid at the outset, gradually levelling off over time (Fig. 4). Comparing creep responses of the composite structure to those of natural IVDs [20], the fibre-reinforced hydrogel has shown a flatter creep curve and hence a higher dimensional stability, resulting in smaller strain values at creep. The differences observed are probably due to the higher water content of natural IVDs and to the mode of testing, which does not consider the flow of water through the surfaces, as would occur between two adjacent vertebrae.

Even though a four parameter viscoelastic model properly fits the experimental data obtained from creep tests performed on composite hydrogels and natural IVDs [20], this model cannot address physical mechanisms responsible for time-dependent behaviour in complex hierarchical systems such as those mentioned above. The main reason of using a four-parameter model instead of a three-parameter one is that it takes into account an irreversible component of deformation [19, 20].

The evaluation of compressive modulus, strength and creep behaviour are important, however the knowledge of the long-term properties are crucial to define design parameters. Because of non-linear stress-strain curves in compression, the viscoelasticity of the fibre-reinforced hydrogel cannot be interpreted through the simple theory of linear viscoelasticity. Consequently, dynamic-mechanical tests have also been carried out at an increasing level of mean (or static) load ranging from 200 to 2,200 N, and after differing numbers of cycles.

The results from fatigue tests have shown a high long-term performance, since the fibre-reinforced hydrogel underwent ten million cycles without failure, which corresponds to the recommended minimum conditions [15, 16]. This is also supported by the fact that values of compressive storage modulus do not drop with increasing the number of cycles, indicating that no structural failure occurred (Fig. 6). Furthermore, the ability of the composite device to recover the strain can be readily recognized in the creep-recovery curves (Fig. 7), which show a high mechanical stability after fatigue test. However, the main future of the proposed composite structure is that by varying the composition of the hydrogelic matrix, the winding angle and the amount of the PET fibres, it is possible to modulate the hydrophilicity and the mechanical properties of the composite structure, in order to optimize its properties at different locations in the spinal column.

Conclusions

The proposed approach has allowed the design and preparation of devices characterized by a softer and more hydrophilic inner part, which emulated the nucleus, and a harder and less hydrophilic outer fibrous part, which played the role of the annulus.

The compressive stress-strain behaviour of natural IVDs has been reproduced by the composite structure, while dynamic-mechanical measurements have suggested that the complex viscoelastic behaviour of the disc tissues can be emulated by selecting the suitable matrix and an opportune design of the composite structure. Creep-fatigue tests have shown endurance, resistance to long-term compressive creep and a high dimension stability.

The results suggest that the use of fibre-reinforced composite hydrogels as IVD prostheses provides devices able to combine both the appropriate transport and mechanical properties, which are important features of an IVD prosthesis.

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