Journal of the Mechanical Behavior of Biomedical Materials 85 (2018) 94–101

Contents lists available at ScienceDirect

Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Development of biomimetic *in vitro* fatigue assessment for UHMWPE implant materials

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ARTICLE INFO

Keywords:
Ultra-high molecular weight polyethylene (UHMWPE)
Bioimplants
Environmental fatigue
Process-structure-property relationships
In vitro experiments
FTIR spectroscopy

ABSTRACT

An important research goal in the field of biomaterials lies in the progressive amendment of *in vivo* tests with suitable *in vitro* experiments. Such approaches are gaining more significance nowadays because of an increasing demand on life sciences and the ethical issues bound to the sacrifice of animals for the sake of scientific research. Another advantage of transferring the experiments to the *in vitro* field is the possibility of accurately control the boundary conditions and experimental parameters in order to reduce the need of validation tests involving animals. With the aim to reduce the amount of needed *in vivo* studies for this cause, a short-time *in vitro* test procedure using instrumented load increase tests with superimposed environmental loading has been developed at TUD to assess the mechanical long-term durability of ultra-high molecular weight polyethylene (UHMWPE) under fatigue loading in a biological environment.

1. Introduction

Even though the actual trend in biomaterials is set towards bio-printing and tissue engineering, the fundamental question of mechanical and biocompatibility properties of a biomaterial, and its resistance to degradation and corrosion in aqueous body-similar fluids are always actual (Gilbert Triplett and Budinskaya, 2017). The life reliability of an implant is important when concerning the orthopedic field. Taking into account aging related pathologies such as osteoporosis or arthritis, advancements in implantable materials for joint and bone reconstruction represents a pivotal point for life quality in arthroplasty patients (Kontis et al., 2017; Berrío Valencia, 2012). Polymers represent an ideal choice for the orthopedic implantation in both the biological and mechanical aspects, especially in relation of the bone remodeling and avoidance of inflammation response and stress shielding effect (Frost, 1992; Staiger et al., 2006). In addition to a higher mechanical closeness to bone than metals, some biocompatible polymers display additional attractive properties such as X-ray transparency and low production temperature. Ultra-high molecular weight polyethylene (UHMWPE) possesses chemical and physical properties, including the above listed, that make it attractive as an orthopedic implant (Prever et al., 2009). In addition to that, another point of interest comes from its proven track of biocompatibility both *in vitro* and *in vivo* conditions (Maksimkin et al., 2017a; Senatov et al., 2014a, 2014b, 2015). Concerning the testing of prosthetics, the most important mechanical characteristic in implants undergoing cyclic loading is the fatigue strength as a direct indicator of UHMWPE´s resistance to cyclic loading induced damage.

1.1. State of the art

UHMWPE has been employed in replacements of joints in hips, knees, shoulders, elbows, ankles and spine discs. For the broad use-case, conventional UHMWPE as well as alternative formulations like highly-crosslinked (melted or annealed) or vitamin E-blended UHMWPE have been implemented as an improvement on the wear and mechanical resistance of the devices (Kurtz, 2016). Different methods for the characterization and evaluation of the UHMWPE behavior in a clinical environment, destructive and non-destructive, have been developed during the last forty years. Non-destructive techniques such as optical microscopy, scanning electron microscopy (SEM), energy dispersive spectroscopy and atomic force microscopy are commonly used to evaluate the microstructure-related properties of UHMWPE and its composites. It has to be noted that such testing procedures are seldom used alone, rather as a complement of results obtained on wear, quasi-static and fatigue tests (Furmanski et al., 2009; Gong et al., 2016; Liu et al., 2014; Liza et al., 2011; Patten et al., 2013; Sauer et al., 1996; Sava et al., 2018; Senatov et al., 2014a; Trommer et al., 2015). Notably, microstructure-related properties like crosslinking, oxidation

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https://doi.org/10.1016/j.jmbbm.2018.05.034

Available online 26 May 2018

degradation and crystallinity have been evaluated in commercially available retrieved prosthesis (Furmanski et al., 2009; Liza et al., 2011) as well as in new UHMWPE formulations (Cheng et al., 2017; Gong et al., 2016) by means of FTIR.

Quasi-static mechanical testing has been performed either on their own to evaluate the results of different polymerization and production technologies (Gong et al., 2016; Hofsté et al., 1997; Maksimkin et al., 2017b; Ronca et al., 2012; Senatov et al., 2014b, 2015; Yang et al., 2005), or as a complementary analysis of dynamic loading testing (Ansari et al., 2016a, 2016b; Huang et al., 2014; Ratner et al., 2005; Sobieraj et al., 2013).

Impact testing, more specifically ballistic testing, has been widely performed over UHMWPE and its composites, to investigate the deformation mechanisms after impact mainly through image correlation (Cwik et al., 2016; Hazzard et al., 2017; Karthikeyan and Russell, 2014; Lässig et al., 2015; Shen et al., 2017; Yang and Chen, 2017; Zhang et al., 2015; Zhang et al., 2018).

Tribological evaluations on UHMWPE vary from conventional testing, to the implementation of custom assemblies, in order to simulate physiological movements and contacting. The latter has been achieved *via* custom assemblies or devices, which were used to mimic the kinematic conditions of the actual implants (Patten et al., 2013; Saikko, 2014; Trommer et al., 2015). Other works focused on the assessment of tribological properties using pin-on-disk (Golchin et al., 2017; Liu et al., 2014; Maksimkin et al., 2017a; Oral et al., 2009; Saikko, 2017; Senatov et al., 2014b; Yousef et al., 2017), pin-on roll (Hofsté et al., 1997) or ball-on-plane methodologies (Baena and Peng, 2017; Diaz and Fuentes, 2017; Gong et al., 2016; Saikko, 2014).

Concerning biosimulative conditions, some studies tackled the issue implementing bovine calf serum as simulated body fluid (SBF), showing positive effects on friction and wear rates (Diaz and Fuentes, 2017; Patten et al., 2013; Sava et al., 2018; Trommer et al., 2015; Yousef et al., 2017).

Regarding fatigue behavior, some studies have been performed using tension-tension sinusoidal stress control (Huang et al., 2014; Ratner et al., 2005; Sobieraj et al., 2013), compression stress (Lockard et al., 2016) as well as a cantilever rotating beam rig with a frequency of 3 Hz and load ratio, R = −1 (Sauer et al., 1996). From the revised fatigue related works, only few were performed under biosimulative conditions, using either bovine calf serum (Lockard et al., 2016) or a phosphate buffered saline bath (Sobieraj et al., 2013) as SBF. Fatigue behavior of UHMWPE was also tested using compact tension specimens, to measure the fatigue crack propagation. These samples were loaded with sinusoidal waves, at a frequency of 5 Hz and a stress ratio of R = 0.1 to check the influence on fatigue strength of notch geometries and the effectiveness of additives like vitamin E or procedures like irradiation or crosslinking (Ansari et al., 2016a; Oral et al., 2009).

Despite wide orthopedic implementation of UHMWPE during the last four decades, culminating in the development of standardized testing coded in the ISO and ASTM norms, the existence of said norms does not guarantee an adequately representation of the necessary biosimulative conditions for an *in vitro* characterization (ASTM, 2003).

Among all the reviewed methods no study has been found combining fatigue behavior analysis and non-destructive microstructural examinations, performed under biosimulative conditions. The current work proposes the combination of the aforementioned methods for a quick and more effective estimation of the material behavior in an *in vivo* environment. A novel technique for the rapid determination of fatigue strength, namely Load Increased Tests (LIT), was combined with non-destructive investigation techniques as Fourier Transform Infrared absorption spectroscopy (FTIR) and Computed Tomography (CT) in order to provide a swift and reliable testing strategy for the improvement of UHMWPE characteristics in clinical applications.

2. Materials and methods

2.1. Specimen manufacturing

UHMWPE powder (molecular weight of $5{\cdot}10^6$ g/mol, PJSC "Kazanorgsintez", Russia) was used for the fabrication of UHMWPE bulk samples. Thermopressing of UHMWPE powder was carried out under pressure of 70 MPa and temperature of 180 °C (Maksimkin et al., 2017b).

For the mechanical characterization, a specimen geometry was chosen based on DIN EN ISO 604, which standardizes the determination of quasi-static compressive properties of plastics, and DIN EN ISO 3167, which presents multipurpose specimen geometries for plastics. The processing of the bulk material into a rectangular prism ($10 \times 10 \times 4\ mm^3$) was performed at TUD. Subsequently, specimens' surfaces were polished with a polishing disk (2000 grit) in order to minimize surface roughness.

2.2. Mechanical testing

2.2.1. Environmental fatigue

As mentioned in the introduction, in order to characterize the intended application of UHMWPE as implant material for arthroplasty the material's fatigue degradation behavior was assessed *in vitro* applying cyclic mechanical loading with a superimposed chemical solution in suitable conditions (Klein and Walther, 2017). This procedure is subsequently referred to as environmental fatigue.

The solution, a simulated body fluid (SBF), was produced according to Table 1 in order to properly mimic human blood plasma (Kokubo et al., 1990). The biomimetic properties of the testing environment were rendered even more similar to an implantation site by ensuring the tempering of the SBF at 37 °C for the duration of the fatigue assessment.

The determination and evaluation of the fatigue characteristics of the UHMWPE bulk material was performed *via* Load Increase Tests (LIT), which enable the evaluation of the general fatigue behavior of a material in a relatively short time and furthermore the determination of a first disproportionality material response within one load step (Walther, 2014). Previous studies at TUD have shown the successful implementation of this method for composite structures (Huelsbusch et al., 2017; Myslicki et al., 2017; Scholz et al., 2016). Furthermore, in order to separate the effects of mechanical loading and a degradative environment, LIT were performed at room temperature (RT) without superimposed SBF. The tests were performed on a servo-hydraulic testing system with an axial-torsional load unit ($F_{max,axial} = \pm 25$ kN, $M_{max,torsional} = \pm 200$ Nm, MTS 858, Berlin, Germany), see Fig. 1. Custom compression dies were designed and manufactured at TUD in order to fit the present hydraulic clamps of the servo-hydraulic testing system and to enable the application of an already existing corrosion cell. A corrosion resistant X5CrNi18-10 (AISI 304, 1.4301) alloy was chosen as dies material in order to prevent a corrosive degradation by SBF.

In Fig. 2 the schematic of LIT (a) is shown together with the related material response (b). Details of the LIT test procedure are given in (Walther, 2014). During LIT, specimens were subjected to a compression-compression load of R = 10 and a sinusoidal load-time function

Table 1
Concentration of relevant ions in human interstitial fluid. Adapted from (Kokubo et al., 1990).

Ion concentration (mmol/l) or (mM)							
Interstitional fluid/ Simulated body fluid (SBF)	Na^+ 142.0	K^+ 5.0	Ca^{2+} 2.5	Mg^{2+} 1.5	$(HCO_3)^-$ 4.2	Cl^- 147.8	$(HPO_4)^{2-}$ 1.0