



Citation for published version:

Hossein Zadeh Zaribaf, F, Gill, R & Pegg, E 2020, 'Characterisation of the physical, chemical and mechanical properties of a radiopaque polyethylene', *Journal of Biomaterials Applications*.

Publication date:
2020

Document Version
Peer reviewed version

[Link to publication](#)

Hossein Zadeh Zaribaf, Fedra ; Gill, Richie ; Pegg, Elise. / Characterisation of the physical, chemical and mechanical properties of a radiopaque polyethylene. In: *Journal of Biomaterials Applications*. 2020. (c) The Copyright Holder 2020. Reproduced by permission of SAGE Publications.

University of Bath

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Characterisation of the physical, chemical and mechanical properties of a radiopaque polyethylene

Fedra P. Zaribaf¹, Harinderjit S. Gill¹, Elise C. Pegg¹

¹ Centre for Orthopaedic Biomechanics, Department of Mechanical Engineering, University of Bath, Bath, UK

Abstract

Ultra-high molecular weight polyethylene (UHMWPE) has a low X-ray attenuation; hence, the performance of the polyethylene implants used for joint replacements cannot be directly investigated using X-ray-based imaging techniques. In this study, the X-ray attenuation of polyethylene was increased by diffusing an FDA-approved oil-based contrast agent (Lipiodol Ultra Fluid) into the surface of the samples, and the suitability of this novel radiopaque UHMWPE for clinical applications was examined. Different levels of radiopacity were created by controlling the diffusion parameters, and the level of radiopacity was quantified from CT scans and reported in Hounsfield units (HU). The physical, chemical and tensile properties of the radiopaque UHMWPE were examined and compared to untreated and thermally treated controls. The results of this study confirmed that for the samples treated at 115°C or less the diffusion of the contrast agent did not significantly alter the crystallinity ($p=0.7$) or melting point ($p=0.4$) of the polyethylene. Concomitantly, the tensile properties were not significantly different from the control samples ($p>0.05$ for all properties). In conclusion, the radiopaque UHMWPE treated for less than 18 hours at a temperature of 115°C or below is a promising candidate for joint replacement applications as it can be identified in a standard X-ray while retaining the tensile properties of clinically used radiolucent UHMWPE.

Keywords: Polyethylene, Radiopaque, Tensile properties, Imaging, Joint replacement

1 Introduction

Ultra-High Molecular Weight Polyethylene (UHMWPE) is the articulating material used in the majority of joint arthroplasties. Clinical studies on joint replacements have showed that on average the revision rate for hip and knee replacements at 14 years is 6% [1]; but despite the overall success of the procedure, the polyethylene bearing can dislocate (3.3% of partial knee replacement failures), fracture (2.2%) and severely wear (4%) [2]. Informed post-operative follow-up and evaluation of the clinical performance of a polyethylene part could lead to early diagnosis of such failures, which would benefit patient outcomes. Currently, the early diagnosis of failure, particularly of all-polyethylene components, can be challenging as the UHMWPE part cannot be identified on standard radiographs [3].

There are a few ways to monitor the position and condition of the polyethylene bearing from post-operative radiographs, but none of these collects the information directly from the polyethylene implant. Some polyethylene prostheses contain radiopaque metallic markers, which are positioned within the bearing; however, the radiopaque marker can increase the risk of polyethylene fracture [5]. Radiopaque markers can aid the identification of some complications such as dislocation and fracture, but not issues such as wear or creep. *In-vivo* wear progression of polyethylene bearings is often inferred from the metallic parts in contact with the polyethylene components [6]. For example, in hip replacements the wear can be calculated based on the total penetration of the femoral head into the acetabular cup on radiographs [7, 8]. Similarly, in knee replacements, to examine the wear, the minimum distance between the femoral condyles and the tibial plateau can be measured [9]. A major limitation of relying on the metallic components to indirectly assess the polyethylene state, is that these measurements require a weight-bearing radiograph, which is often not used clinically, and the calculated wear also includes creep and bearing compression [10]. Furthermore, mild and moderate wear are often difficult to identify as the measurements are often from a single-source X-ray image. The interpretation of a single source

Table 1: The following experiments were conducted to examine the physical, chemical and mechanical properties of radiopaque UHMWPE

Test type	Samples type	Investigated properties
Tensile testing	ISO-572 Annex A 1AB tensile	Tensile properties
Thermal properties (DSC)	Cuboid 10×10×4 mm	Crystallinity and melting point
Oxidation properties (FTIR)	Cuboid 10×10×4 mm	Oxidation
Radiopacity (CT scan)	Cuboid 10×10×4 mm and ISO 1AB tensile	Lipiodol uptake
Gravimetric changes	ISO-572 Annex A 1AB tensile	Lipiodol uptake

radiograph are dependent on imaging angle and the patient position [11], double source radiographs are also an option but relatively few hospitals are equipped with stereo-imaging systems.

The current study investigates the possibility of using a novel radiopaque UHMWPE as an alternative. We hypothesised that the radiopacity can be increased by incorporating an oil based contrast agent (Lipiodol Ultra Fluid) into UHMWPE. Due to the oily nature of the fluid, the contrast agent can be diffused into the polyethylene part using an elevated temperature.

Lipiodol Ultra Fluid (hereafter Lipiodol), also known as ethiodized oil, is an iodised-poppy seed oil which is a pale yellow oily fluid. The fluid changes colour when it is thermally treated. In Lipiodol the carbon-carbon double bond is saturated using iodine; hence the oil can be detected with a standard X-ray. This contrast agent has FDA-approval and is often used in diagnostic and interventional radiography [4, 12, 13]. The density of Lipiodol is 1.28 g/cm and 1 ml of solution contains 480 mg of iodine (37% w/w) [12]. The fluid only contains naturally occurring unsaturated fatty acids [12]. The predominant fatty acid in poppy seed oil (the precursor for Lipiodol) is a triglyceride; the fluid also contains other lipophilic ingredients such as Linoleic acid side chains (60-70%), tocopherols and α -tocopherol (vitamin E).

When considering a new polyethylene, patient safety is paramount, so it is essential that the properties of the new polyethylene are thoroughly investigated to ensure it is equivalent to currently used polyethylene. Other oil-based fluids (e.g. vitamin E) have been incorporated into medical grade UHMWPE and used clinically. The presence of vitamin E led to no significant alteration in the tensile properties of the polymer and improved aging properties, but an increased ductility and creep has been reported [14, 15] and there is potential for similar observations with Lipiodol-infused polyethylene. For vitamin E polyethylene these effects have been mitigated through optimised diffusion protocols including a homogenisation step which leads to more even distribution of vitamin E throughout the part, and γ -irradiation to increase crosslinks in the polymer [17].

The aim of the current study was to examine the effect of Lipiodol on the physical (dimensional and thermal), chemical (crystallinity and oxidation) and mechanical (tensile) behaviour of medical grade UHMWPE (GUR 1050).

2 Materials and methods

The experiments were designed to answer the following questions:

- Do the treatment conditions (temperature and time) correlate with Lipiodol uptake?
- Does the Lipiodol treatment lead to any alteration in the physical properties (weight, colour, dimension melting point, or radiopacity)?
- Does the Lipiodol treatment significantly change the chemical properties (crystallinity or oxidation)?
- Does the Lipiodol treatment lead to any changes in the tensile properties (modulus, elongation at break, ultimate tensile strength)?

2.1 Sample preparation

Tensile test specimens were machined based on ISO-572 Annex A, type 1AB [18]. All the samples were made from un-irradiated medical grade UHMWPE manufactured from GUR 1050 moulded UHMWPE sheets 160 mm square and 4 mm thick from (Celanese, Oberhausen, Germany). A sheet of GUR 1050 was also cut to small cuboids of 10 mm by 15 mm by 4 mm, for oxidation and crystallinity analysis. Table 1 summarises the type of samples used for each experiment (5 repeats for all tests).

Table 2: Treatment conditions and the number (n) of repeats used for each study

Time (h)	Temperature ($^{\circ}\text{C}$)		
	85	105	115
12		n=5	
18	n=5	n=5	n=5
24		n=5	

Table 3: Main bands identified in the FTIR spectrum of Lipiodol.

Peak (cm^{-1})	Functional group
1263 [31]	Phenolic C-O (tocopherols), methyl ester, (C-O-C)
1730 [33]	Ethyl ester (due to starching the carbonyl group)
2900 [21]	Phythyl chains (tocopherols) symmetric (C-H)
3050 [31]	$\nu(\text{C-H})$, $\nu(=\text{CH})$

2.2 Lipiodol diffusion

Samples were immersed into 25 ml of Lipiodol for either 12 h, 18 h or 24 h and a range of elevated temperatures (from 85°C to 115°C) was applied to facilitate the diffusion. Preliminary results [3] showed temperatures above 120°C caused oxidation (supplementary data) and changed the crystallinity of the polyethylene. Therefore, in this study, diffusion temperatures were kept below 120°C . All treatment temperatures were therefore also below the melting point of polyethylene ($135 \pm 2^{\circ}\text{C}$) so preserved the crystalline content [19]. The different combinations of treatment temperatures and times examined are summarised in Table 2. After treatment the samples were allowed to cool down to ambient temperature and wiped with a lint-free tissue to remove any excess Lipiodol from the surface.

Samples held at 105°C for 18 h but not immersed in Lipiodol were used as thermal controls to assess the impact of the Lipiodol treatment independently of temperature. For the tensile tests untreated control samples without thermal treatment were also tested, representing virgin uncrosslinked polyethylene.

2.3 Determination of Lipiodol content from gravimetric change

The weight of all samples was measured using a digital scale (Mettler Toledo XP205, Ohio, US) before and after the treatment. The effect of thermal treatment on the weight of the samples was also recorded. This information was used to calculate the percentage of gravimetric change in the samples due to the absorption of Lipiodol.

2.4 Determination of Lipiodol content using FTIR

A thin slice (approximately $200 \mu\text{m}$ thick) was sectioned using a sledge microtome (MSW-106SM, India) from the surface of the samples. A Thermo Scientific spectrometer (Magna 560 IR, Nicolet, Massachusetts, United States) was used to obtain the FTIR spectra in transmission mode. An average of 32 scans was taken for each section from 4000 to 600 cm^{-1} . The Lipiodol concentration was calculated from the areas under the Lipiodol absorbance peak at 1728 cm^{-1} (Figure 1). This peak was assigned to Lipiodol as it was present in all the spectra of pure and diluted solutions of Lipiodol. Peaks between 1730 to 1750 cm^{-1} are due to the ester group (Lipiodol is the ethyl ester of poppy seed oil (Table 3). The exact position of the peak depends on the functional groups attached to the ester group. Lipiodol contains iodine, and the presence of an electronegative group can shift the peak by 15 cm^{-1} [21]. The area under the peaks was compared to the calibration curve made from the known solutions of Lipiodol, and the concentration was calculated using Beer-Lamberts law [21].

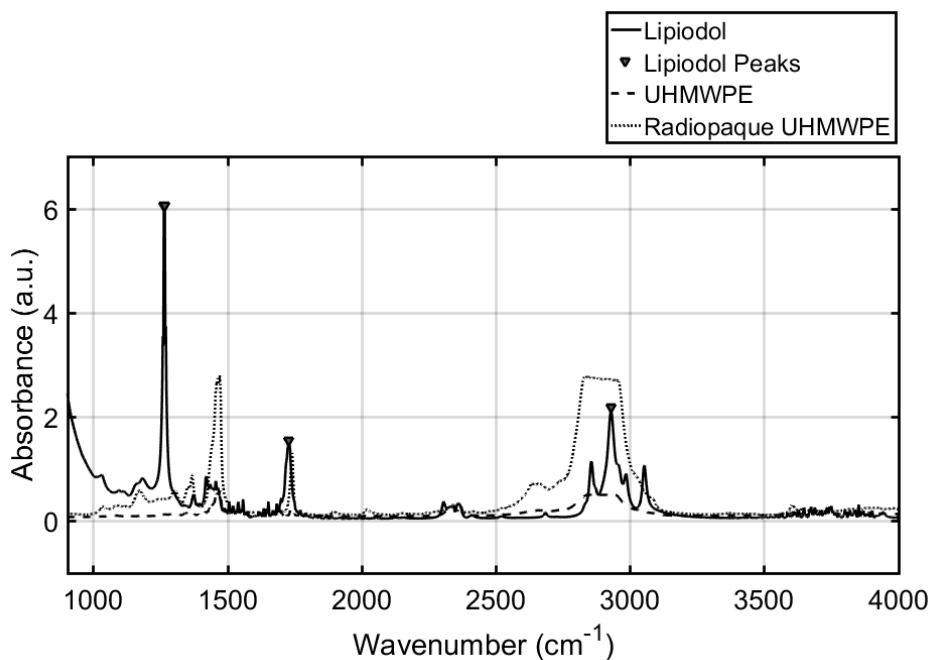


Figure 1: The FTIR spectra of pure Lipiodol, untreated UHMWPE and radiopaque UHMWPE. The peak located approximately at 1730 cm^{-1} indicates the ester group in Lipiodol; this peak can be identified in the Lipiodol and radiopaque UHMWPE spectra.

2.5 Radiopacity measurements

Each sample was imaged using a μ CT scanner (X Tec, XT H 225 ST, Nikon Metrology UK Ltd, Derby, UK); scanning protocols were the same for all samples (162 kV, resolution 0.2 mm). Analysis of the CT data was performed using Simpleware ScanIP (Version 2017, Synopsys, Inc., Exeter, UK). Water, air and untreated polyethylene were used for calibration to calculate the Hounsfield units (HU) [20].

2.6 Melting point and crystallinity measurement

Differential scanning calorimetry (DSC) was used to determine the melting point and the degree of crystallinity of UHMWPE ($n=5$). Approximately 2.0 mg of each sample was taken from the outer surface of the samples and then was analysed (DSC 250, TA Instruments, Delaware, United States). The pan was crimped with an aluminium cover. The testing was conducted from 20°C to 180°C at a heat flow of rate $10^{\circ}\text{C}/\text{min}$ under a nitrogen purge. TA Universal Software (Version 4.5) was used to analyse the data and calculate the degree of crystallinity using the following steps:

- The endothermic peak was integrated from 50°C to 160°C to find the enthalpy of fusion of the sample.
- The enthalpy of fusion obtained was then normalised with the heat of fusion of pure UHMWPE (289 J/g , [23])

2.7 Determination of oxidation using FTIR

The FTIR spectra obtained from the polyethylene slices were also used to calculate the oxidation index according to ASTM F2102 [22]. There are different peaks, which signify the oxidative degradation such as the transvinylene peak at 965 cm^{-1} or carbonyl absorption peak at 1720 cm^{-1} . The oxidation index (OI) is the area under the carbonyl absorption peak divided against the peak due to the methyl stretch at 1396 cm^{-1} [22]. The standard method of calculating the oxidation index requires using the carbonyl peak which is located around the same area as the peak representing the Lipiodol. Hence, we were unable to calculate the oxidation index of samples but to ensure there was no significant oxidation reaction, each spectrum was checked for other oxidation by-products (transvinylene) at 950 cm^{-1} .

Table 4: Influence of Lipiodol diffusion temperature on Lipiodol uptake and physical properties (mean \pm SD)

Temperature (°C)	Volume change (%)	Weight change (%)	Lipiodol conc. (%v/v)
85	1.6 \pm 0.4	2.0 \pm 1.1	0.9 \pm 0.4
105	6.5 \pm 1.5	4.7 \pm 1.0	5.8 \pm 1.9
115	26.5 \pm 3.1	29.9 \pm 3.5	19.8 \pm 3.6
105-Control	0.1 \pm 1.7	-	0.3 \pm 2.0

2.8 Tensile mechanical testing

Tensile tests were conducted at room temperature (\sim 20°C) in accordance with ISO-527 [18] using an electromechanical test machine (Instron 5965) at a rate of 50 mm/min. The tests were carried out with virgin UHMWPE, thermally treated UHMWPE and Lipiodol treated UHMWPE. Five specimens per condition were tested to obtain tensile modulus (E), 0.2% yield strain, ultimate tensile strength (UTS) and elongation at failure. The raw data were processed by a custom Matlab code (R2012a, Natick, Massachusetts, United States) to extract tensile properties. The calculations were conducted as specified in the standards. The initial displacement (first 10 seconds, equivalent of approximately 0.3% strain) data was measured using a high-speed camera (DFK 33UX290, ImagingSource, Germany).

2.9 Statistical analysis

Sample groups were compared using a Kruskal-Wallis test and multiple pairwise comparisons where applicable; a p-value less than 0.05 was considered statistically significant. Statistical analysis were performed using IBM SPSS software (Version 25, IBM, New York, USA).

3 Results

The physical, chemical, and tensile properties of the radiopaque UHMWPE were examined and compared to untreated controls to investigate the suitability of the radiopaque polyethylene for clinical applications.

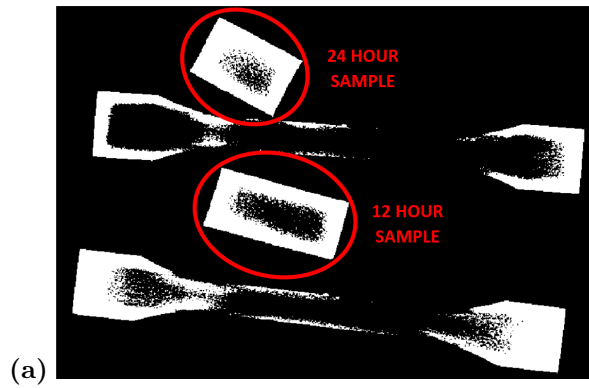
Gravimetric change and infrared spectroscopy were used to estimate the Lipiodol intake (Table 4). The Lipiodol treated samples significantly increased in weight (up to 30%), whereas the weight change of the samples only treated thermally was as low as 0.5%. The Lipiodol concentration measured using FTIR (Figure 1) showed that there was a linear correlation between the Lipiodol concentration and weight change, with a Pearson’s correlation coefficient of 0.983. The lowest amount of Lipiodol detected in the treated samples by FTIR was 0.3% v/v, which was for the samples treated at 85°C, and there was a power relationship between temperature and Lipiodol concentration. A significant alteration was also observed in the dimensions (up to 27% volume increase) of the samples (Table 4, Figure 4), and the colour of the samples changed from white to dark yellow or dark grey, depending on the treatment temperature and duration.

The radiopacity level was increased by the treatment and was directly correlated with Lipiodol intake (Figure 2, Figure 3). X-ray attenuation can be directly correlated with the mass thickness (mass per area), and a linear relationship was seen between the radiopacity level and gravimetric change (Figure 3, Pearson’s correlation coefficient of 0.921).

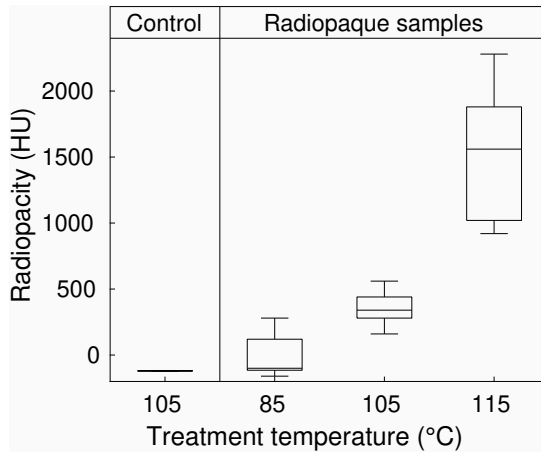
The DSC results found that there was no significant change in the melting point (p=0.4) or the crystallinity (p=0.08) of the radiopaque polyethylene (p=0.4) (Figure 4) indicating no alteration in the thermal properties of polyethylene after the Lipiodol treatment.

The study also investigated the oxidative stability of the samples after the treatment. The FTIR spectra showed the treatment did not cause oxidation in the samples within 24 hours of the treatment. The oxidation index of thermally treated samples were between 0.2-0.4. Based on the current standard [22] oxidation index less than one confirms that the polyethylene is suitable for clinical applications.

The effect of time and temperature on the tensile properties of the radiopaque polyethylene was investigated. The modulus and the 0.2% yield strain of the samples treated at 115°C for 18 hours were significantly lower than the untreated samples (modulus: p=0.01, yield: p=0.04), and there was a reducing trend in the modulus of the samples as the treatment temperature increased (Figure 5c). The correlation coefficient of the line was



(a)



(b)

Figure 2: Treatment with Lipiodol increased the radiopacity of the samples and this was dependent on treatment temperature and time, as demonstrated by a) a CT scan slice through the centre of UHMWPE samples treated at 105°C for 12 h and 24 h; the white regions indicate the presence of Lipiodol, and b) the correlation between Hounsfield unit and treatment temperature.

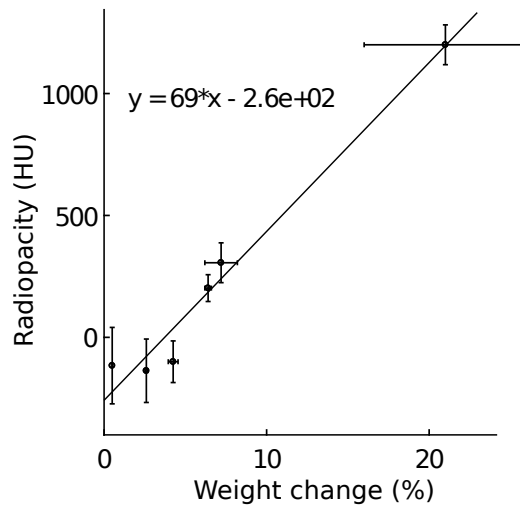


Figure 3: The level of radiopacity linearly correlated with gravimetric changes ($R^2=0.921$)

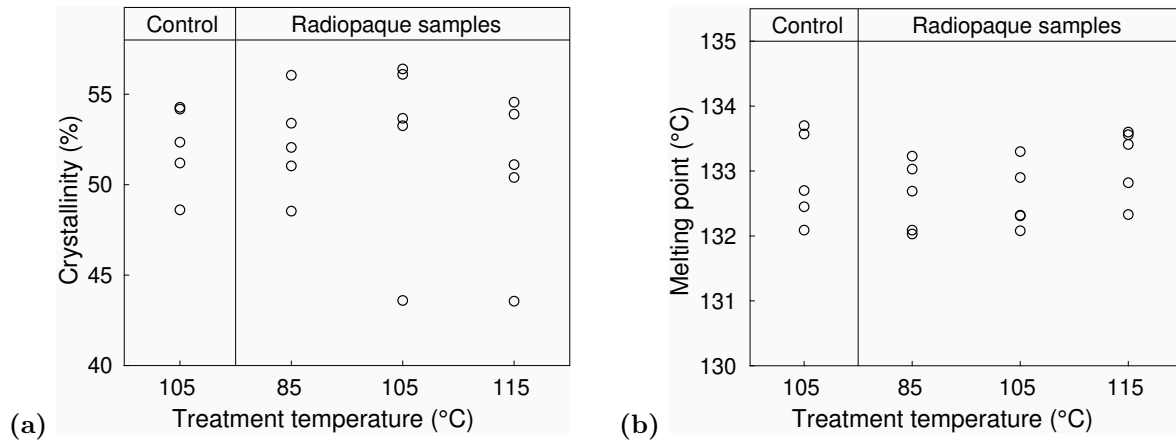


Figure 4: No significant change was observed in a) the crystallinity ($p=0.08$) or b) the melting point ($p=0.4$) of the treated samples compared to the untreated controls.

-0.9, which suggests a negative monotonic correlation between the modulus of the samples and the concentration of Lipiodol. The elongation at failure increased with temperature at a rate average of 30% (Figure 5g). The effect of the treatment duration on the tensile properties was also examined. As Figure 5f shows, the ultimate tensile strength of the samples increased significantly at 24 hours ($p=0.046$). The other tensile properties of polyethylene (elongation at failure $p=0.052$, yield $p=0.15$ and modulus $p=0.09$) of the samples were not affected significantly by the treatment duration.

4 Discussion

This study investigated a novel UHMWPE for medical applications, which has a significantly higher radiopacity than conventional polyethylene. The increased radiopacity was due to the presence of an FDA approved radio-contrast agent called Lipiodol, which is an iodised oil. Thermal treatment is necessary for the diffusion and to obtain enough Lipiodol throughout a component to be able to identify the part in a radiograph. However, the thermal treatment can potentially alter the part dimensions, crystallinity and tensile properties [25]; Hence, to ensure patient safety, it is crucial to prevent any significant alteration in the material and mechanical properties of this novel radiopaque polyethylene. This study fully characterised the physical, chemical and mechanical properties of the novel UHMWPE. It was important to distinguish between changes due to temperature and those due to the Lipiodol treatment, so heat treated control samples were used.

The degree of the crystallinity is one of the most important properties of UHMWPE as it directly influences the tensile properties of the part. The thermal treatment can alter the crystallinity [25]; a reduction in the degree of crystallinity causes a higher risk of oxidation and oxidative failure, while an increase of degree of crystallinity increases the brittleness of the polyethylene, and makes the polyethylene part less suitable for load-bearing applications [27]. The results of this study found that none of the treatment conditions altered the studied thermal properties of UHMWPE. This agrees with studies on vitamin E incorporated UHMWPE (the only other example of an oil-infused medical polyethylene) which showed no difference in crystallinity after treatment [16].

However, the treatment with Lipiodol caused an overall increase in the ductility of polyethylene which was identified by a reduction in the modulus and an increase in the region of ductile deformation in the stress-strain curve (increased elongation at break) [28]. This alteration was not seen in the control samples treated only with temperature, indicating that the Lipiodol is cause of these alterations. Many studies have correlated changes in ductility to changes in crystallinity, recrystallisation or the molecular weight of the polymer [23, 30], however, as mentioned; there was no evidence of alteration of these properties. A similar plasticising effect has been reported for vitamin E polyethylene, and has been explained by alterations in the crystal structure of polyethylene in the presence of an oil. Oral et al. [29] reported that the pressure-temperature phase diagram of polyethylene is altered by the presence of vitamin E [29]. The crystalline regions formed in the hexagonal phase are less dense than those in orthogonal phase; this allows greater mobility and diffusion of chains in a specific direction leading to changes in the crystalline structure, and hence the mechanical properties without changing the degree of crystallinity. Oral et al. demonstrated that this effect can be mitigated through irradiation-induced crosslinking [26]; a similar approach may be successful for the radiopaque polyethylene.

The ultimate tensile strength (UTS) of polyethylene was found to be unaffected by the treatment temperature

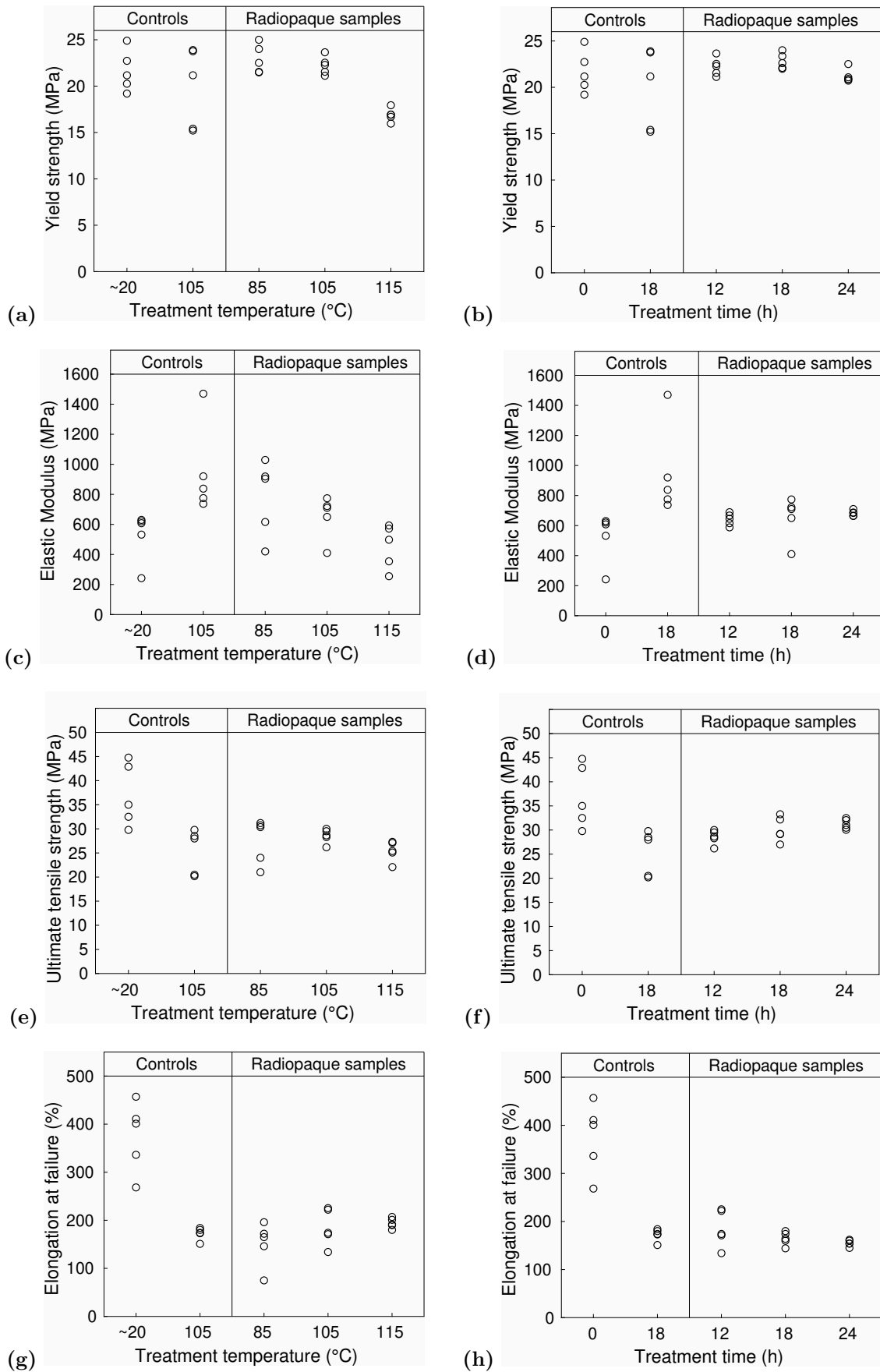


Figure 5: The temperature of the treatment changed the modulus at 115°C ($p=0.013$) and yield strength ($p=0.04$) but the ultimate tensile strength (UTS) ($p=0.24$) and elongation at failure ($p=0.1$) of the samples were not statistically different. The treatment duration, however, changed the material properties only when the duration exceeded 24 hours (modulus ($p=0.093$), UTS($p=0.02$)). No changes were observed in the yield ($p=0.159$) and elongation at failure ($p=0.2$).

and duration. This is encouraging as it has been proven that a reduction in UTS indicates the reduction of the fatigue resistance [28]. However, the fatigue properties of this radiopaque polyethylene still need to be investigated and is planned as part of future work.

The mechanical test results had unusually high variation in properties such as UTS and yield; this was noticeable for the untreated control samples as well as the treated radiopaque samples. A possible explanation is the anisotropic properties resulting from compression moulding; the samples were cut from a small moulded sheet (160 mm by 160 mm) and greater crystalline alignment will occur at the edges [32] causing inhomogeneity in the sample set. Although the variability is high, the results for the control samples without thermal treatment are consistent with that published for uncrosslinked UHMWPE [?].

It was also observed that there was a significant dimensional change in the Lipiodol treated samples. Some of this change could be attributed to the release of residual stresses from the previous manufacturing steps (e.g. moulding), but the samples treated only with temperature showed 0.1% increase indicating dimensional changes from residual stress were comparatively minor. One possibility is that the majority of the swelling observed is due to the accumulation of Lipiodol in the surface of the samples. In the similar cases (diffusion of vitamin E) an extra homogenisation process was added to allow the oil to move from the surface throughout the sample which reduces a small part of the dimensional change [26]. Provided this expansion is known, and it can be taken into account during the design of an implant or additional machining stage added after treatment to meet required tolerances.

Finally, we acknowledge the limitations of this work. The results of this study cannot be directly compared with other studies. This because the mechanical properties of polyethylene is controlled by molecular weight, crystal alignment and the uniformity of the resin powder during the consolidation [30], hence changes in the mechanical properties cannot be immediately attributed to any alteration in material structure caused by the contrast agent [23]. Furthermore, micro-dogbone (ISO-572- Annex A) samples were used for this study and some studies have suggested that smaller test samples can lead to size-dependent properties.

5 Conclusion

This study has demonstrated that it is possible to significantly increase the radiopacity of medical grade polyethylene through the diffusion of iodised oil, enabling improved implant follow-up of joint replacement complications such as dislocation and wear. The optimal treatment conditions were when the polyethylene was immersed in iodised oil at 105°C for 18 hours; which resulted in a radiopacity of approximately 500 HU with no significant change in crystallinity, melting point, tensile strength, yield, elongation at failure or oxidation, when compared with standard untreated polyethylene. However, the iodised oil caused a plasticising effect at temperatures and times in excess of the optimum conditions (increased elongation and decreased modulus) highlighting the importance of careful selection of treatment conditions; it may be possible to mitigate these effects through crosslinking. In summary, the radiopaque polyethylene has shown promising mechanical properties for joint replacement applications. To further assess the safety of this novel material for medical applications, future work will examine the influence of longer term loading (fatigue and creep) and aging of the polyethylene in in vivo conditions.

Acknowledgements

Authors would like to acknowledge Celanese for providing the medical grade polyethylene, Mrs Clare Ball for their technical supports, and Prof Michael Whittlesey from the Department of Chemistry (University of Bath) for access to their equipment.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship or publication of the article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and publication of this article: This project was supported by the University of Bath through the University Scholarship Research Allowance funding scheme.

References

- [1] National-Joint-Registry. Annual reports. 14th Annual Report, National Joint Registry for England, Wales, Northern Ireland and the Isle of Man, 2017.
- [2] van der List JP, Zuiderbaan HA, Pearle AD. Why do medial unicompartmental knee arthroplasties fail today?. *The Journal of Arthroplasty* 2016; 31(5): 1016-1021.
- [3] Zaribaf FP. Medical-grade ultra-high molecular weight polyethylene: past, current and future. *Mater Sci Tech* 2018; 34(16): 1940–1953.
- [4] Ho S, Lau WY and Leung WT. In vitro assessment of Lipiodol-targeted radiotherapy for liver and colorectal cancer cell lines. *Brit J Cancer* 2000; 82(2): 497.
- [5] Pegg EC, Murray DW, Pandit HG et al. Fracture of mobile unicompartmental knee bearings: A parametric finite element study. *P I Mech Eng H* 2013; 227(11): 1213-1223.
- [6] Ebramzadeh E, Sangiorgio SN, Lattuada F et al. Accuracy of measurement of polyethylene wear with use of radiographs of total hip replacements. *J Bone Joint Surg Am* 2003; 85(12): 2378–2384.
- [7] Seehaus F, Emmerich J, Kaptein BL, et al. Dependence of model-based RSA accuracy on higher and lower implant surface model quality. *Biomed Eng Online* 2013; 12(1): 32.
- [8] Livermore J, Ilstrup D, Morrey B. Effect of femoral head size on wear of the polyethylene acetabular component. *J Bone Joint Surg Am* 1990; 72(4): 518–528.
- [9] Gill HS, Waite JC, Short A, et al. In vivo measurement of volumetric wear of a total knee replacement. *Knee* 2006; 13(4): 312–317.
- [10] Bevill SL, Bevill GR, Penmetsa JR et al. Finite element simulation of early creep and wear in total hip arthroplasty. *J Biomech* 2005; 38(12): 2365–2374.
- [11] Fukuoka Y, Hoshino A and Ishida A. A simple radiographic measurement method for polyethylene wear in total knee arthroplasty. *IEEE T Rehabil Eng* 1999; 7(2): 228–233.
- [12] Durand-Fontanier S, Simon A, Duroux JL et al. Lipiodol ultra-fluid: an antitumor agent-in vitro study. *Anticancer Res* 1999; 19(5B): 4357–4361.
- [13] Idée JM and Guiu B. Use of Lipiodol as a drug-delivery system for transcatheter arterial chemoembolization of hepatocellular carcinoma: a review. *Crc Cr Rev Oncol-Hem* 2013; 88(3): 530–549.
- [14] Oral E, Malhi AS, Wannomae KK et al. Highly cross-linked ultrahigh molecular weight polyethylene with improved fatigue resistance for total joint arthroplasty: recipient of the 2006 Hap Paul Award. *J Arthrop* 2008; 23(7): 1037–1044.
- [15] Mori A, Sakuramoto I, Tomita N et al. Mechanical behavior of UHMWPE when mixed with vitamin E. *Transactions of the 47th Annual Meeting of the Orthopaedic Research Society* 2001;.
- [16] Bracco P and Oral E. Vitamin E-stabilized UHMWPE for total joint implants: a review. *Clin Orthop Relat R* 2011; 469(8): 2286–2293.
- [17] Jacobson K. Oxidation of ultra high molecular weight polyethylene (UHMWPE) part 1: Interpretation of the chemiluminescence curve recorded during thermal oxidation. *Polym Degrad Stabil* 2006; 91(9): 2126–2132.
- [18] International Organization for Standardization I. 527-1,Plastics – Determination of tensile properties – Part 1: General principles, 2012.
- [19] Narkis M, Raiter I, Shkolnik S et al. Structure and tensile behavior of irradiation-and peroxide-crosslinked polyethylenes. *J Macromol Sci Phys* 1987; 26(1): 37–58.

- [20] Scholz MS, Blanchfield JP, Bloom LD et al. The use of composite materials in modern orthopaedic medicine and prosthetic devices: a review. *Compos Science Technol* 2011; 71(16): 1791–1803.
- [21] Sinclair RG, McKay AF, Myers GS et al. The Infrared Absorption Spectra of Unsaturated Fatty Acids and Esters. *J Am Chem Soc* 1952; 74(10): 2578–2585.
- [22] ASTM. 2102-01 Standard guide for evaluating the extent of oxidation in ultra-high-molecular-weight polyethylene fabricated forms intended for surgical implants. *Annual book of ASTM standards: Medical Devices; Emergency Medical Services* 2001; 13: 1680–1683.
- [23] Kurtz SM. UHMWPE biomaterials handbook: ultra high molecular weight polyethylene in total joint replacement and medical devices. Chapter 9. *Academic Press* 2009.
- [24] Renò F and Cannas M. UHMWPE and vitamin E bioactivity: An emerging perspective. *Biomaterials* 2006; 27(16): 3039–3043.
- [25] Slouf M, Synkova H, Baldrian J et al. Structural changes of UHMWPE after e-beam irradiation and thermal treatment. *JJ Biomed Mater Res B* 2008; 85(1): 240–251.
- [26] Oral E, GodleskiBeckos C, Ghali BW et al. Effect of crosslink density on the high pressure crystallization of UHMWPE. *J Biomed Mater Res B* 2009; 90(2): 720–729.
- [27] Bédoui F, Diani J, Régnier G et al. Micromechanical modeling of isotropic elastic behavior of semicrystalline polymers. *Acta Mater* 2006; 54(6): 1513–1523.
- [28] Kurtz SM, Rinnac CM, Pruitt L et al. The relationship between the clinical performance and large deformation mechanical behavior of retrieved UHMWPE tibial inserts. *Biomaterials* 2000; 21(3): 283–291.
- [29] Oral E, Beckos CAG, Lozynsky AJ et al. Improved resistance to wear and fatigue fracture in high pressure crystallized vitamin E-containing ultra-high molecular weight polyethylene. *Biomaterials* 2009; 30(10): 1870–1880.
- [30] Edidin AA, Villarraga ML, Herr MP et al. Accelerated aging studies of UHMWPE. II. Virgin UHMWPE is not immune to oxidative degradation. *J Biomed Mater Res* 2002; 61(2): 323–329.
- [31] Zagonel GF, Peralta-Zamora P, Ramos LP et al. Multivariate monitoring of soybean oil ethanolysis by FTIR. *Talanta* 2004; 63(4): 1021–1025.
- [32] Kurtz SM. UHMWPE biomaterials handbook: ultra high molecular weight polyethylene in total joint replacement and medical devices. Chapter 2: From Ethylene Gas to UHMWPE Component: The Process of Producing Orthopaedic Implants. *Academic Press* 2015.
- [33] Carrin-Prieto P, Silva-Castro I, Ramos-Silva M et al. Vibrational analysis and thermal behavior of salvia hispanica, nigella sativa and papaver somniferum seeds. *Pharmacogn J* 2017; 9(2): 157-162.