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X-ray irradiation: an alternative technology to improve vitamin E blended polyethylene properties as orthopedic implant material

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II. Abstract

Total hip arthroplasty is one of the most successful surgical procedures in Germany. Due to the elongation of life expectancy and the success of the procedure, the number of implantations is steadily rising and the age of patients at the time of primary surgery is decreasing. Consequently, an increase in the incidence of revisions is expected in the future. In addition, as a result of the ion release issues the metal-metal-bearings are about to disappear and the highly cross-linked polyethylene to become the gold standard. Rising raw material costs and price pressure on the market make it a challenge to develop better implants at lower manufacturing costs.

The considerable wear resistance improvement through cross-linking by irradiation is clinically established. The most common cross-linking methods are Gamma rays and electron beam (e-beam). Gamma rays are characterized by a low dose rate, which excludes serial irradiation at elevated temperature and promotes in-process oxidation, the main limitation of e-beam is the low penetration depth. With their high penetration depth and a relatively high dose rate, X-rays allow for "warm" irradiation and its beneficial effect on cross-linking and vitamin E stabilization. The aim of this work was to determine, by means of physical, chemical, mechanical and tribological material characterization, the extent to which X-rays are able to improve the properties of polyethylene and offer an alternative to Gamma rays and e-beam.

The positive influence of elevated irradiation temperature on the radiation cross-linking and oxidation resistance of vitamin E stabilized polyethylene, independent of the irradiation source E-Beam or X-rays, was confirmed. Our results supported the hypothesis that, using same base material (GUR® 1020E), same irradiation temperature (100 °C) and dose (80 kGy), different radiation sources, e-beam and X-ray, lead to equivalent physical, chemical, mechanical properties and in vitro wear resistance. It is not known how this oxidative stabilized and X-ray highly cross-linked polyethylene will affect the long term revision rate, but the in vitro results are encouraging.

III. Zusammenfassung

Die Hüftendoprothetik zählt zu den erfolgreichsten chirurgischen Eingriffen Deutschlands. Aufgrund der Verlängerung der Lebenserwartung und des Erfolges des Eingriffes nimmt die Zahl der Implantationen stetig zu und das Patientenalter bei der Erstimplantation ab. Infolgedessen ist mit einer Zunahme der Revisionen in Zukunft zu rechnen. Darüber hinaus, bedingt durch die Ionenfreisetzungsproblematik der Metall-Metall-Gleitpaarungen, ist das hochvernetzte Polyethylen auf dem Weg zum Goldstandard. Steigende Rohstoffkosten und Preisdruck auf dem Markt bringen die Herausforderung, bessere Implantate zu niedrigeren Fertigungskosten zu entwickeln.

Die erhebliche Verbesserung der Abriebfestigkeit durch die Quervernetzung mittels ionisierender Strahlung ist klinisch etabliert. Die gängigsten Vernetzungsmethoden sind die Gammastrahlen und der Elektronenstrahl (E-Beam). Die Gammastrahlen zeichnen sich durch eine niedrige Dosisrate aus, die eine Serienbestrahlung bei erhöhter Temperatur ausschließt und eine Inprozess-Oxidation fördert. Die wesentliche Einschränkung von E-Beam besteht in einer geringen Eindringtiefe. Mit ihrer hohen Eindringtiefe und einer verhältnismäßig hohen Dosisrate ermöglichen die Röntgenstrahlen eine „warm“-Bestrahlung mit ihrer vorteilhaften Wirkung auf die Vernetzung und die Stabilisierung durch Vitamin E. Die Zielsetzung dieser Arbeit war mittels einer physikalischen, chemischen, mechanischen und tribologischen Materialcharakterisierung zu eruieren, inwieweit die Röntgenstrahlung in der Lage ist, die Polyethylen-Eigenschaften zu verbessern und eine Alternative zu Gamma und E-Beam zu bilden.

Der positive Einfluss der erhöhten Bestrahlungstemperatur auf die Strahlenvernetzung und Oxidationsbeständigkeit von Vitamin E stabilisiertem Polyethylen, unabhängig von der Bestrahlungsquelle E-Beam oder Röntgen, wurde bestätigt. Unsere Ergebnisse stützten die Hypothese, dass bei gleichem Grundmaterial (GUR$^{®}$ 1020E), gleicher Bestrahlungstemperatur (100 °C) und Dosis (80 kGy), unterschiedliche Strahlungsquellen E-Beam und Röntgen zu gleichwertigen physikalischen, chemischen, mechanischen Eigenschaften und in-vitro-Verschleißfestigkeit führen. Es ist nicht bekannt, wie sich dieses oxidativ stabilisierte und Röntgenstrahlung-hochvernetzte Polyethylen auf die langfristige Revisionsrate auswirken wird, die in-vitro-Ergebnisse sind jedoch ermutigend.

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V. Abbildungsverzeichnis

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VII. Abkürzungsverzeichnis

GUR®	**G**ranular **U**HMWPE **R**uhrchemie
UHMWPE	**U**ltra **H**igh **M**olecular **W**eight **P**olyethylene
E-Beam	**E**lectron **B**eam (Elektronenstrahl)
z.B.	zum Beispiel
kGy/h	Kilogray pro Stunde
vs.	versus
kGy/s	Kilogray pro Sekunde
mm	Millimeter
ggfs.	gegebenenfalls
X/S	Crosslinks per Scission (Vernetzungen pro Spaltung)
°C	Grad Celsius
wt%	Gewichtsprozent
RT	**R**aum**t**emperatur
CoCr	**Co**balt **C**h**r**omium
DSC	**D**ifferential **S**canning **C**alorimetry
ASTM	**A**merican **S**ociety for **T**esting and **M**aterials
SPT	**S**mall **P**unch **T**esting
OI	**O**xidations**i**ndex
FTIR	**F**ourier **T**ransform **I**nfra**r**otspektrometer
OIT	**O**xidation **I**nduction **T**ime
TVI	**T**rans-**V**inylene **I**ndex
ISO	**I**nternational **O**rganization for **S**tandardization
p-Wert	Signifikanzwert
MPa	Megapascal
µm	Mikrometer
Min	Minuten
mg/mc	Milligramm pro Million Zyklen
mg	Milligramm
mio	Million

1. Einleitung

Ultrahigh Molecular Weight Polyethylen findet seit 60 Jahren Anwendung in der Arthroplastik sowohl der Hüfte, des Knies und des Sprunggelenks als auch der Schulter und der Bandscheibe zur Behandlung der Arthrose. Der Zusammenhang zwischen Polyethylenabrieb und aseptischer Lockerung des Gelenkimplantats bedingt durch Osteolyse wurde zu Beginn der 1980er etabliert [1]. Die schädlichen Effekte der Oxidation auf die Eigenschaften der Polyethylenimplantate, mittels Gamma Strahlungen an Luft sterilisiert wie Versprödung, Delamination und Abriebbildung wurden kurz darauf erkannt. Die Sterilisation unter Schutzgas brachte eine deutliche doch nicht ausreichende Verbesserung [2]. Ab Ende der 1990er Jahre wurde das Quervernetzen durch hochenergetische Strahlungen verwendet, um die Abriebbeständigkeit des Polyethylens merklich zu erhöhen [3]. Die resultierenden freien Radikale, die das Material für Oxidation anfällig machen, wurden mittels einer thermischen Nachbehandlung minimiert. Das Remelting (oberhalb der Schmelztemperatur) beeinträchtigte jedoch die mechanischen Eigenschaften. Das Annealing (unterhalb der Schmelztemperatur) führte lediglich zu einer Reduzierung und nicht zur vollständigen Auslöschung der freien Radikale. Die Einführung von Antioxidantien wie die Zugabe von Vitamin E ermöglichte zeitgleich einen effizienten Oxidationsschutz ohne auf eine thermische Nachbehandlung zurückzugreifen und damit den Erhalt der Materialeigenschaften [4].

1.1. Hintergrund

Mit 239 204 Prozeduren im Jahr 2018 zählt die Hüftendoprothetik zu den häufigsten chirurgischen Eingriffen in Deutschland und zu einem der erfolgreichsten chirurgischen Eingriffe überhaupt [5,6]. Aufgrund der demographischen Entwicklung hin zu einer Verlängerung der Lebenserwartung einerseits und des Erfolges des Eingriffes andererseits nimmt die Zahl der Implantationen stetig zu [7]. Eine hohe Überlebensrate größer 95% nach 10 Jahren [8] und immer noch 58%-78% nach 25 Jahren [9] fördert die Versorgung immer jüngerer Patienten. Letztere sind in der Regel aktiver als ältere und stellen an das Implantatsystem signifikant höhere Anforderungen [10,11] über einen längeren Zeitraum. So wird für Patienten in jüngerem Alter (<65 Jahre) eine erhöhte Revisionsrate nach 10 Jahren beobachtet [12]. Aus diesen Gründen ist mit einer Zunahme der Revisionen mit der Notwendigkeit komplexe Eingriffe bei älteren Patienten durchzuführen in Zukunft zu rechnen. Darüber hinaus ist es absehbar, dass infolge der Freisetzungsproblematik von Metall-Ionen wie Cobalt und Chrom mit lokalen und systemischen adversen Gewebereaktionen, die Metall-

Metall-Gleitpaarungen zunehmend verschwinden und vom hochvernetzten Polyethylen ersetzt werden, welches in Kombination mit Keramikköpfen auf dem Weg zum Goldstandard ist [13]. Jedoch steigen seit 2010 sowohl die Rohstoffkosten (GUR® UHMW-PE) als auch der Preisdruck auf dem Markt kontinuierlich. Die Herausforderung besteht darin fortwährend leistungsfähigere Implantate zu immer niedrigeren Fertigungskosten zu entwickeln, mit dem Ziel die Lebensdauer der Implantate zu verlängern, Revisionen zu vermeiden, damit die Patientenversorgung zu verbessern und die finanzielle Belastung für die Gesundheitssysteme der Länder auf vertretbarem Niveau zu halten. In diesem Kontext eröffnet die Röntgen-Vernetzung unter einem technologischen und wirtschaftlichen Gesichtspunkt bislang nicht beschrittene Wege und Möglichkeiten.

Seit der Einführung von UHMWPE (Ultrahigh Molecular Weight Polyethylene) in der Hüftendoprothetik durch Charnley in den 1960er Jahren wurden die Bemühungen zur Verbesserung der Verschleiß- und Alterungsbeständigkeit ununterbrochen fortgeführt [14,15]. In den 1970er Jahren führte Oonishi [3] die Strahlenvernetzung des UHMWPEs ein. Die Reduzierung der Polymerkettenmobilität durch das dreidimensionale Netzwerk und die Abnahme der Duktilität erhöhten die Abriebbeständigkeit erheblich [16].

Die gängigsten Vernetzungsmethoden basieren auf Gammastrahlen, erzeugt durch den Zerfall von Kobalt-60 und mittels Elektronenstrahl (Electron Beam oder E-Beam) [17]. Als rein physikalischer Prozess zeichnet sich die Strahlenvernetzung im Vergleich zu chemischen Alternativen, die mit Rückständen mit toxischem Potential einhergehen, durch Zweckmäßigkeit und Effizienz aus [18–21]. Limitierungen bestehen heute infolge von unvorhersehbarem Aufstieg der Kobaltpreise, Umweltbelangen wie beispielweise der Unmöglichkeit, die radioaktive Quelle abzuschalten, Nachschubschwierigkeiten und anderen technologischen Nachteilen, wie z.B. der niedrigen Dosisrate der Gammastrahlen (100 kGy/10h vs. 100 kGy/s für E-Beam und 100 kGy/h für Röntgenstrahlung [15,16,22]), ungleichmäßiger Dosisverteilung und geringer Eindringtiefe bei E-Beam (38 mm vs. 450 mm für Gamma und Röntgen [15,16,22]). Aus wirtschaftlichen, technologischen und produktionstechnischen Gründen liegt die Notwendigkeit einer Technologie, die diese Limitierungen überwindet, auf der Hand [15,20,23,24].

Während der Bestrahlung bei hohen bis sehr hohen Strahlendosen (50-10 000 kGy) erfährt das Polyethylen zwei Arten von Modifikationen: Vernetzungen [17,25] und Spaltungen [16]. Bei Polyethylen überwiegen die Vernetzungen [26]. Energiequelle, Dosisrate, Gesamtdosis, Prozessbedingungen "vor, während und nach" der Bestrahlung sowie Temperatur, Umgebung (Luft, Inertgas, Vakuum), Zeit und ggfs. Antioxidantien beeinflussen das Vernetzungen-zu-

Kettenspaltungen-Verhältnis (X/S) [17,21,27–29]. Eine Bestrahlung an Luft mit niedriger Dosisrate führt zu einer längeren Luftexposition. Sie kann die Sauerstoffdiffusion im Polymer begünstigen und die oxidative Spaltreaktion fördern [20,21,30,31]. X/S nimmt ab und die Materialeigenschaften verschlechtern sich [19]. Bei einer höheren Dosisrate entstehen Vernetzungen gegenüber Kettenspaltungen bevorzugt [32], damit wird die Wahrscheinlichkeit eines oxidativen Abbaus reduziert [33]. Diese Zeitabhängigkeit der Sauerstoffdiffusion während der Bestrahlung besteht bei Raumtemperatur, ist aber bei erhöhter Temperatur umso relevanter, da die Wärme die Sauerstoffdiffusion beschleunigt.

In vitro Ergebnisse [34,35] und erste klinische Daten [36–38] lassen eine Verlängerung der Lebensdauer orthopädischer Implantate dank den kombinierten Vorteilen der Vernetzung und Antioxidantienstabilisierung erwarten. Da die Oxidation nicht nur durch die Bestrahlung, sondern auch in vivo eingeleitet wird und das antioxidative Potenzial des Vitamin E begrenzt ist, ist es wünschenswert, dessen Abbau während des Herstellungsprozesses möglichst einzuschränken, um seine Wirksamkeit in vivo zu optimieren und so die Lebensdauer der Prothese zu verlängern. Auf der Grundlage dieser Erkenntnisse entstand im Rahmen der vorliegenden Arbeit die Konzeption und deren Verifizierung die Röntgenbestrahlung als neuen Ansatz zu nutzen, um die beschriebenen Einschränkungen zu überwinden. Mit ihrer hohen Eindringtiefe und einer verhältnismäßig hohen Dosisrate bietet die Röntgenstrahlung Verarbeitungsparameter, die eine Vernetzung bei erhöhter Temperatur ermöglichen und vor frühzeitiger Oxidation der Polyethylen-Implantatkomponenten schützen.

1.2. Zielsetzung und Hypothese

Die Zielsetzung dieser Arbeit war -angesichts der physikalischen und wirtschaftlichen Vorteile der Röntgenstrahlung- zu eruieren, in wieweit sie in der Lage ist, die Eigenschaften von UHMWPE für die Gelenkendoprothetik zu verbessern und eine Alternative zu Gamma und Elektronenstrahl (E-Beam) zu bilden.

Die Hypothese war, dass die Verwendung der gleichen Prozessparameter Dosis (in dieser Studie 80 kGy) und Bestrahlungstemperatur (100 °C) zu äquivalenten Materialeigenschaften führen würde, unabhängig von der benutzten Strahlungsquelle E-Beam oder Röntgen.

1.3. Material und Methoden

1.3.1. Material

Die Proben wurden aus GUR® 1020 UHMW-PE gemischt mit 0,1 wt% (Gewichtsprozent) Vitamin E hergestellt. Im Anschluss zum Sinter- und Temperprozess wurden Stangen aus der Platte geschnitten und mittels Röntgen-Strahlungen vernetzt. Das Material wurde in vier Gruppen aufgeteilt, die sich im Rahmen einer systematischen Versuchsführung durch die absorbierte Dosis und Bestrahlungstemperatur wie folgt unterschieden: 80 kGy, Raumtemperatur (RT): "X (80 kGy)-RT"; 100 kGy, Raumtemperatur: "X (100 kGy)-RT"; 80kGy, 100°C: "X (80 kGy)-warm" und 100 kGy, 100°C: "X (100 kGy)-warm". Als Referenz diente Vitelene® (Aesculap AG, Tuttlingen, Deutschland), ein mit 0,1 wt% Vitamin E stabilisiertes und hochvernetztes (E-Beam, 80 kGy, 100 °C) UHMWPE, welches seit 2012 klinisch eingesetzt wird. Weder das röntgenvernetzte Material noch die Referenz wurden einer thermischen Nachbehandlung unterzogen, da diese die mechanischen Eigenschaften reduziert und sich damit nachteilig auf die Robustheit der Implantatkomponenten im klinischen Einsatz auswirkt.

Für den Verschleißversuch wurden Inlays mit Durchmesser 40 mm und 5 mm Wandstärke aus den fünf Materialien gefertigt und in Plasmafit® Poly Titan-Pfannen Größe 54 (Aesculap AG) gefügt. Die Inlays liefen gegen CoCr (Cobalt Chromium)-Köpfe.

Abbildung 1: *Plasmafit® Poly Titan-Pfanne, Plasmafit® Pfanne mit Vitelene® Inlay, CoCr-Kopf*

1.3.2. Methoden

Die Materialien wurde einer physikalischen, mechanischen, chemischen Charakterisierung und in vitro Verschleißsimulation unterzogen. Die thermischen Eigenschaften wurden mittels Differential Scanning Calorimetry (DSC) nach ASTM F2625, die mechanischen nach

ASTM D638 (monoaxiale Zugfestigkeit), ASTM D256 (Izod-Kerbschlagzähigkeit) und ASTM F2183 (SPT=Small Punch Testing) bestimmt.

Zur Ermittlung der oxidativen Eigenschaften wurden der Oxidationsindex (OI) mittels Fourier Transform Infrarotspektrometer (FTIR) nach ASTM F2102 und die Oxidation Induction Time (OIT) nach ASTM D3895 gemessen. Der Trans-Vinylene-Index (TVI) nach ASTM F2381, der Gelgehalt nach ASTM D2765 und die Vernetzungsdichte wurden zur Charakterisierung des dreidimensionalen Netzwerkes herangezogen.

Die Verschleißsimulation erfolgte nach ISO 14242-1 und -2 für 5 Millionen Zyklen nachdem die Inlays gemäß ASTM F2003 für 2 Wochen künstlich gealtert wurden.

Die Ergebnisse wurden mittels einer einschlägigen statistischen Auswertung auf Signifikanz untersucht. Ein p-Wert kleiner als 0,05 wurde als signifikant angesehen.

1.4. Ergebnisse

Nachfolgend werden einzelne besonders aussagekräftige Ergebnisse dargestellt. Die Ergebnisse sind in den Veröffentlichungen im Anschluss (siehe Kapitel 2, 3 und 4) in vollem Umfang dargelegt.

Die DSC-Messungen ergaben für das warm bestrahlte Material eine geringere Kristallinität als für das Material welches bei Raumtemperatur bestrahlt wurde [Abbildung 2]. Es wurde kein signifikanter dosisabhängiger Kristallinitätsunterschied zwischen 80 und 100 kGy beobachtet.

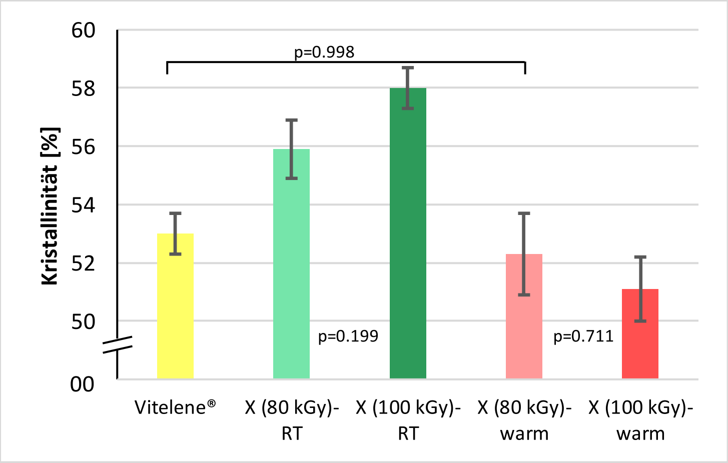

Abbildung 2: *Kristallinität von Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm und X (100 kGy)-warm*

Mit steigender Bestrahlungstemperatur wurde ein Elastizitätsverlust (Streckgrenze) festgestellt ($p<0,001$) [Abbildung 3a]. Eine Dosisabhängigkeit mit Abnahme der Streckgrenze konnte mit zunehmender Dosis ausschließlich bei erhöhter Temperatur beobachtet werden (p=0,007). Eine Temperaturabhängigkeit (p<0,001) und eine Dosisabhängigkeit bei Raumtemperatur (p>0,001) zeigten sich für die Bruchdehnung [Abbildung 3b]. Die Erhöhung der Temperatur ermöglichte eine größere Dehnung, während eine höhere Dosis eine sichtbare Abnahme der Dehnung zur Folge hatte. Der Unterschied zwischen E-Beam (Vitelene®) und Röntgen-Strahlung X (80 kGy)-warm war nicht signifikant (p=0,552).

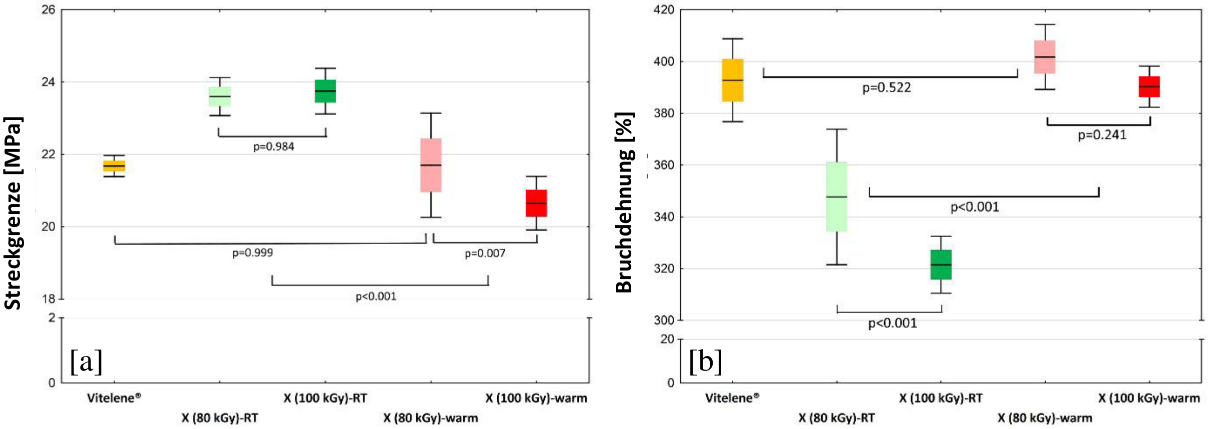

Abbildung 3: *Zugfestigkeit von Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm und X (100 kGy)-warm. [a]: Streckgrenze, [b]: Bruchdehnung.*

Die FTIR-Spektren zeigten niedrige Oxidationsindizes (<0,20), die geringer waren für das warm bestrahlte Material als bei Raumtemperatur (p<0,001) [Abbildung 4].

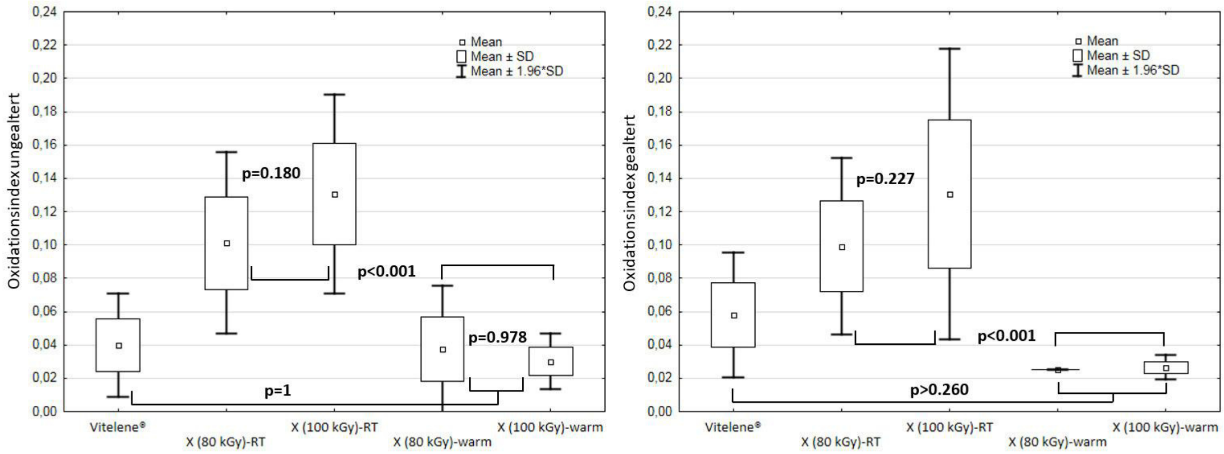

Abbildung 4: *Oxidationsindex der Röntgen-vernetzten Stangen und der Vitelene®-Implantate ungealtert (links) und nach 2 Wochen künstlicher Alterung gem. ASTM F2003 (rechts) nach Entfernung der ersten 100 µm-Randschicht der Stangen. Nachweisgrenze: 0,025.*

Das mit Röntgen warm bestrahlte UHMWPE wies eine fast nicht nachweisbare, sehr geringfügige Oxidation auf. Der OI lag sehr nah an der Nachweisgrenze des Verfahrens von 0,025. Eine leichte Zunahme der Oxidation konnte zwischen 80 und 100 kGy bei Raumtemperatur beobachtet werden, die jedoch nicht statistisch signifikant war (p=0,180 ungealtert, p=0,227 gealtert). Der OI war vor und nach künstlicher Alterung äquivalent. Es wurde kein signifikanter Unterschied (p=1) zwischen E-Beam-Vernetzung warm (Vitelene®) und Röntgen-Vernetzung warm je mit 80 kGy detektiert und damit die Gleichwertigkeit der beiden Materialien für diese Parameter nachgewiesen.

Relativ niedrige OIT-Werte für die Bestrahlung bei Raumtemperatur und teilweise eine große Standardabweichung von bis zu 80% wurden beobachtet [Tabelle 1]. Obwohl die Temperaturabhängigkeit nicht immer statistisch bestätigt werden konnte (ungealtert: p=0,003 zwischen X (80 kGy)-RT und X (80 kGy)-warm; p=0,168 zwischen X (100 kGy)-RT und X (100 kGy)-warm; gealtert: p=0,001 zwischen X (80 kGy)-RT und X (80 kGy)-warm; p=0,534 zwischen X (100 kGy)-RT und X (100 kGy)-warm), war der positive Einfluss der Wärmeeinwirkung während des Bestrahlungsprozesses offensichtlich.

Weder für die Bestrahlung bei Raumtemperatur noch bei warmer Bestrahlung konnte ein dosisbezogener signifikanter Unterschied beobachtet werden (p>0,1).

Tabelle 1: *Oxidation Induction Time von Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm und X (100 kGy)-warm*

	OIT – ungealtert [Min]	**OIT - gealtert [Min]**
Vitelene®	11.3 ± 1.8	10.9 ± 1.2
X (80 kGy) - RT	6.2 ± 3.1	3.7 ± 2.9
X (100 kGy) - RT	5.6 ± 2.9	5.7 ± 0.0
X (80 kGy) - warm	18.8 ± 0.4	12.8 ± 0.6
X (100 kGy) - warm	11.8 ± 5.9	8.4 ± 3.7

Sowohl die Bestrahlungstemperatur als auch die Dosis hatten einen Einfluss auf die Bildung von Trans-Vinylene-Doppelbindungen mit einem höheren TVI bei der „warm“-Bestrahlung und der höheren Dosis [Tabelle 2]. Das mit E-Beam bestrahlte UHMWPE zeigte ebenfalls einen höheren TVI.

Die Ermittlung des löslichen Anteils war nicht imstande zwischen 80 und 100 kGy sowohl bei RT als auch „warm“ [Tabelle 2] zu diskriminieren. Im Gegensetz dazu führte die Erhöhung der Bestrahlungstemperatur zu einem höheren Gel-Gehalt. Es wurde kein Unterschied zwischen E-Beam Vitelene® und Röntgenstrahlung X (80 kGy)-warm beobachtet.

Tabelle 2: *Vernetzungseigenschaften von Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm und X (100 kGy)-warm*

	TVI	**Gel-Gehalt [%]**
Vitelene®	0.053 ± 0.004	99
X (80 kGy) - RT	0.034 ± 0.006	93
X (100 kGy) - RT	0.041 ± 0.006	94
X (80 kGy) - warm	0.042 ± 0.006	99
X (100 kGy) - warm	0.048 ± 0.003	99

Der Verschleißsimulationstest ergab eine Verschleißrate von 11,3 ± 0,7 mg/mc für X (80 kGy)-RT, 7,5 ± 0,3 mg/mc für X (100 kGy)-RT, 5,1 ± 0,8 mg/mc für X (80 kGy)-warm und 2,6 ± 0,1 mg/mc für X (100 kGy)-warm, was einer um 34% (bei RT) bzw. 50% (warm) niedrigeren Verschleißrate für das mit 100 kGy vernetzte Material im Vergleich zu 80 kGy entspricht [Abbildung 5, links]. Ebenso war der Einfluss der Bestrahlungstemperatur auf die Verschleißrate zu beobachten. Wobei hier das warm bestrahlte Material deutlich niedrigere Verschleißwerte aufwies. X (80 kGy)-warm zeigte 55% weniger Verschleiß als X (80 kGy)-RT und X (100 kGy)-warm 66% weniger als X (100 kGy)-RT.

Eine vergleichbare Tendenz wurde für den kumulativen Verschleiß festgestellt: 58,0 ± 2,0 mg für X (80 kGy)-RT, 35,3 ± 2,1 mg für X (100 kGy)-RT, 22,5 ± 4,1 mg für X (80 kGy)-warm und 10,9 ± 0,7 mg für X(100 kGy)-warm entsprechen einem um 39% (bei RT) bzw. 52% (warm) geringeren kumulativen Verschleiß für das mit 100 kGy vernetzte Material im Vergleich zu 80 kGy [Abbildung 5, rechts]. Die Verschleißreduzierung zwischen warmer und RT-Bestrahlung war ebenfalls signifikant und betrug 61% (80 kGy) bzw. 69% (100 kGy).

Mit einer Verschleißrate von 6,9 ± 1 mg/mc und einem kumulativen Verschleiß von 31,9 ± 6,9 mg hatte das E-Beam bestrahlte Vitelene® eine geringere Verschleißrate (39% und 8%) und einen geringeren kumulativen Verschleiß (45% und 10%) im Vergleich zu X (80 kGy)-RT und X (100 kGy)-RT. Der Unterschied zwischen Vitelene® und X (100 kGy)-RT wurde jedoch nicht als statistisch signifikant angesehen (p=0,909 für die Verschleißrate bzw. p=0,770 für den kumulativen Verschleiß). Bei erhöhter Temperatur war es umgekehrt. Die Verschleißrate von Vitelene® war um 35% (p=0,145) im Vergleich zu X(80 kGy)-warm und um 165% im Vergleich zu X (100 kGy)-warm erhöht. Der kumulative Verschleiß von Vitelene® war 42% bzw. 193% höher als X (80 kGy)-warm (p=0,041) und X (100 kGy)-warm (p<0,001).

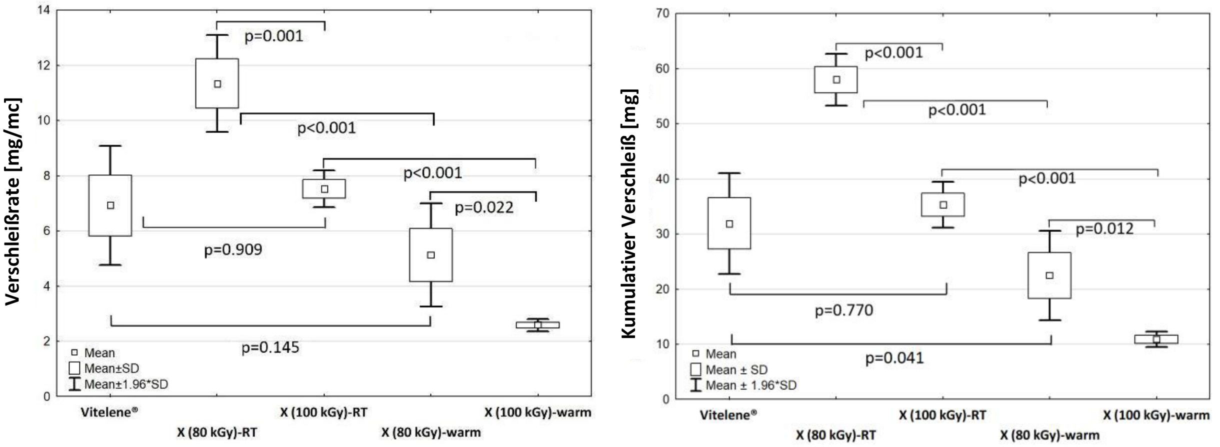

Abbildung 5: *Verschleißrate (links) und kumulativer Verschleißnach 5 Millionen Zyklen (rechts) von Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm und X (100 kGy)-warm*

1.5. Diskussion

Sämtliche Analysen bestätigten unsere Hypothese: sowohl die physikalischen, chemischen, mechanischen als auch die tribologischen Eigenschaften von Vitelene® (E-Beam-80 kGy, warm) waren äquivalent zum X (80 kGy)-warm UHMWPE.

Im Gegensatz zu den Beobachtungen von Premnath et al. [39] konnte keine dosisinduzierte Erhöhung der Kristallinität zwischen 80 und 100 kGy bei gleicher Temperatur (55,9% und 58,0% bei RT und 52,2% und 51,1% "warm") festgestellt werden. Dies war wahrscheinlich auf den relativ geringen Dosisunterschied von 20 kGy zurückzuführen, der jedoch den klinisch relevanten Bereich abbildet.
Die höhere Kristallinität bei RT (55,9 % für 80 kGy und 58,0 % für 100 kGy) im Vergleich zum warm behandelten Material (52,2 % für 80 kGy und 51,1 % für 100 kGy) lässt sich durch ein höheres Kettenspaltungen-Vernetzungen-Verhältnis [21] und das anschließende Kristallwachstum [40] erklären. Darüber hinaus fördert die erhöhte Kettenbeweglichkeit bei erhöhter Temperatur die radikale Rekombination. Die so gebildeten Vernetzungen hemmen das Kristallwachstum und verhindern die Rekristallisation [29,32,39,41–43].

Der mit der Kristallinitätsabnahme einhergehende Elastizitätsverlust (Streckgrenze) [3,44] lag am direkten Zusammenhang zwischen Mikrostruktur und mechanischem Verhalten [40,45,46]. Jeweils die höhere Dosis (100 kGy) und die niedrigere Bestrahlungstemperatur (RT) führten zu einer Senkung der Bruchdehnung. Je höher die Dosis, desto höher die Vernetzung und Steifigkeit und umso geringer die Dehnung und Plastizität [47]. Im Gegensatz dazu sorgte die geringere Kristallinität des warm bestrahlten Materials für eine erhöhte Kriechneigung und plastische Verformung.

Mit Werten kleiner als 0,2 lag der Oxidationsindex weit unter 1, anerkannt als der bisherige Grenzwert worüber sich die mechanischen Eigenschaften von konventionellem UHMWPE dramatisch verschlechtern [2,34,48,49]. Die Erhöhung der Bestrahlungstemperatur zeigte einen positiven Effekt auf die Oxidationsstabilität. Die Literatur liefert hierzu folgende Erklärungen: die Wärme steigert die Kettenmobilität und damit die Rekombination der freien Radikale [45,50] und/oder sie fördert das Aufpfropfen des Vitamin E an das Rückgrat des Polymers und damit die Oxidationsbeständigkeit [45]. Der unveränderte OI vor und nach beschleunigter Alterung wird auf das Antioxidans Vitamin E zurückgeführt. Demnach vermag die beschleunigte Alterung nach ASTM F2003 über 2 Wochen nicht zwischen den getesteten Materialien zu differenzieren. Im Gegensatz zu Oral et al. [51] und Slouf et al. [32] konnte keine erhöhte Oxidation bei erhöhter Dosis festgestellt werden. Dies war wahrscheinlich auf den relativ geringen Unterschied von 20 kGy zurückzuführen.

Die OIT wurde bestimmt, um das antioxidative Potenzial der Werkstoffe unter Bedingungen, welche zum Versagen führen, zu vergleichen. Die große Varianz erlaubte für diese Kenngröße keine zuverlässigen Rückschlüsse auf den Einfluss der Dosis. Die günstige Wirkung der Bestrahlung bei erhöhter Temperatur wurde jedoch bestätigt. Wärme verbessert die Konservierung und das Aufpfropfen des Vitamin E während der Bestrahlung, was möglicherweise zu einer verbesserten Langzeitstabilität führt [35,43,50,52,53].

Der Trans-Vinylene-Index war höher nach „warm“-Bestrahlung als bei Raumtemperatur. Die Wärme bewirkte eine Zunahme der radiolytischen Reaktionskinetik [54–56]. Darüber hinaus wurden bei 100 kGy mehr Trans-Vinylene-Doppelbindungen gebildet als bei 80 kGy, was der Zusammenhang zwischen TVI und Dosis bestätigte [32,56–64]. Eine tendenziell höhere Reaktion wurde für E-Beam (im Durchschnitt, wegen seiner hohen *Dose Uniformity Ratio*) als für Röntgenstrahlen beobachtet. Die Bestrahlungsquelle sowie die absorbierte Dosis, die Dosisrate und die Temperatur beeinflussten die Reaktionskinetik [57,62].

Der Extraktionstest bestätigte die Hochvernetzung aller Materialien. Der Gelanteil bis zu 99% der warm bestrahlten Gruppen führte auf eine geringe Kettenspaltung und/oder eine in einer Käfigreaktion stattfindende Rekombination der freien Radikale während des Quellens in Xylol zurück [65]. Darüber hinaus sorgte das Aufpfropfen des Vitamin E auf das Rückgrat des UHMWPEs für eine verminderte Mobilität, somit für eine geschwächte Reaktionskonkurrenz und förderte womöglich die Rekombination der freien Radikale zur Bildung von Quervernetzungen [35]. Im Gegensatz zur Literatur wurde kein Anstieg des Gel-Gehalts mit der Dosis beobachtet [66].

Sowohl die Erhöhung der Dosis als auch der Bestrahlungstemperatur führten zu einer geringeren Verschleißrate, wobei die Temperatur einen größeren Effekt hatte [Abbildung 5]. Beide führten zu einer stärkeren Vernetzung. Das dreidimensionale molekulare Netzwerk hemmte die molekulare Ausrichtung, die Bildung von Fibrillen und förderte eine bessere Adhäsions- und Abriebfestigkeit [4,67–72]. Der Verschleißversuch bestätigte die Beobachtungen von Oral et al. [35] und Popoola et al. [52], dass aus der Bestrahlung bei erhöhter Temperatur von Vitamin-E stabilisiertem Polyethylen eine verbesserte Verschleißbeständigkeit resultiert. Die Ergebnisse des kumulativen Verschleißes legen die Hypothese nahe, dass verglichen mit dem E-Beam die Röntgenvernetzung unter erhöhter Temperatur die Abriebfestigkeit unter Berücksichtigung der gegebenen Parameter weiter verbessert.

1.6. Fazit

Der maßgebliche Beitrag der Quervernetzung zur Verbesserung der Verschleißbeständigkeit von UHMWPE [17,57,58,76,87-91] und die Notwendigkeit einer dauerhaften Stabilisierung gegen den oxidativen Abbau in vivo sind weitestgehend wissenschaftlich anerkannt [48,54]. Bislang wurde der optimale Prozess nicht gefunden, der zu höchstem Abriebwiderstand bei gleichzeitig bestmöglichen mechanischen Eigenschaften und hoher Langzeit-Alterungsbeständigkeit führt. Die Materialeigenschaften hängen von zahlreichen Parametern wie Gesamtdosis, Dosisrate, Bestrahlungstemperatur und -atmosphäre, Energiequelle, thermische Nachbehandlung, Antioxidans, thermische Geschichte und anderen ab, die jeweils die supramolekulare Struktur des UHMWPEs beeinflussen und damit die Komplexität der vielfältigen Einflussfaktoren auf die Materialentwicklung veranschaulichen. In dieser Studie wurde eine alternative Vernetzungstechnologie „die Röntgenstrahlen" im Vergleich zu E-Beam bewertet. Die Wirkung der Bestrahlungstemperatur (RT vs. 100°C) wurde als vorherrschend gegenüber der Dosis herausgefunden, wobei der Dosisgradient klinisch-anwendungsbezogen und damit relativ gering war (80 vs. 100 kGy). Auch der positive Einfluss der erhöhten Bestrahlungstemperatur auf die Strahlenvernetzung und auf die Oxidationsbeständigkeit von Vitamin E stabilisiertem UHMWPE, unabhängig von der Bestrahlungsquelle E-Beam oder Röntgen, wurde bestätigt.

Unsere Ergebnisse stützen die Hypothese, dass bei gleichem Grundmaterial (GUR® 1020E), gleicher Bestrahlungstemperatur (100 °C) und Dosis (80 kGy), unterschiedliche Strahlungsquellen, E-Beam und Röntgen, zu gleichwertigen physikalischen, chemischen, mechanischen Eigenschaften und in-vitro-Verschleißbeständigkeit führen. Es ist nicht bekannt, wie sich dieses oxidativ stabilisierte und Röntgenstrahlung-hochvernetzte Polyethylen auf den klinischen Langzeitverlauf auswirken wird, die vorliegenden in-vitro-Ergebnisse sind jedoch sehr ermutigend.

1.7. Eigenanteil

Die Doktorandin konzipierte das Design der Studie, wertete die Ergebnisse aus und interpretierte sie. Sie verfasste die 3 Publikationen in vollem Umfang und verantwortete sowohl die Einreichung als auch den gesamten Review-Prozess.

Die Ko-Autoren führten die Versuche, die statistische Auswertung der Ergebnisse und das kritische Korrekturlesen vor Einreichung durch.

2. Erste Veröffentlichung

Equivalent mechanical properties of X-ray and E-beam cross-linked vitamin E blended ultrahigh molecular weight polyethylene

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ORIGINAL RESEARCH REPORT

Equivalent mechanical properties of X-ray and E-beam cross-linked vitamin E blended ultrahigh molecular weight polyethylene

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Abstract

The influence of X-ray cross-linking compared with electron beam cross-linking on the mechanical and thermal properties of UHMWPE blended with 0.1 wt% vitamin E was investigated. Two X-ray doses (80 and 100 kGy) and two irradiation temperatures (RT: room temperature; 100 °C: warm) were considered. The reference was Vitelene® a vitamin E stabilized UHMWPE cross-linked with 80 kGy e-beam at 100°C. Uniaxial tensile and small punch testing were conducted. The Izod impact strength and the thermal properties were determined. The yield, ultimate tensile strength and elongation were 21.7 MPa, 48 MPa, and 393% for Vitelene® and 21.7 MPa, 47 MPa, and 402% for X (80 kGy)-warm, respectively. The peak load, ultimate displacement, and work to failure accounted for 63 N, 5.7 mm and 331 mJ for Vitelene® and 65 N, 5.6 mm, and 322 mJ for X (80 kGy)-warm respectively. The Izod impact strength of Vitelene® amounted to 81 kJ/m^2, that of X (80 kGy)-warm to 82 kJ/m^2. Crystallinity of both was 52%. The melt temperature of Vitelene® was 140 °C, that of X (80 kGy)-warm 139°C. In conclusion, using the same irradiation temperature (100 °C) and dose (80 kGy), the different radiation sources e-beam and X-rays resulted in equivalent thermal and mechanical properties.

KEYWORDS

hip prosthesis, mechanical characterization, thermal properties, vitamin E stabilized UHMWPE, X-ray cross-linking

1 | INTRODUCTION

Ultrahigh molecular weight polyethylene (UHMWPE) was introduced in the hip arthroplasty in the 1960s by Sir John Charnley (Charnley, 1970). Since that time, its use as an orthopedic implant material and the effort to improve its wear performance and aging properties went on and on (Berejka, Cleland, & Walo, 2014; Chapiro, 2002; Clough, 2001; International Irradiation Association, 2011; Kashiwagi, 2012). In the 1950s, Charlesby discovered that the thermal, chemical, and aging properties of polyethylene can be enhanced by radiation cross-linking. It was followed by a wide range of industrial applications (Chmielewski, 2006). Twenty years later Oonishi (Oonishi, Takayama, & Tsuji, 1992) introduced the irradiation cross-linking to improve the wear resistance of UHMWPE hip arthroplasties. The reduction of polymer chain mobility and the decrease in plasticity obtained by cross-linking have proven to augment the friction resistance of UHMWPE considerably (Makuuchi & Cheng, 2012).

The most current cross-linking methods are gamma rays generated by the decay of Cobalt 60 and beta rays or electron beam (e-beam) (Lewis, 2001). Due to economic reasons such as unforeseeable prices of Cobalt, environmental issues like the impossibility to turn off the radioactive source, difficulties like supply and other technological drawbacks such as low dose rate for gamma rays and low penetration depth for e-beam respectively, the need for a technology, which overcomes these limitations is noticeable (Clough, 2001; International Atomic Energy Agency, 2008; International Irradiation Association, 2011; Mizera et al., 2012). X-rays, which provide a homogeneous cross-linking in a relatively short time, seem to offer an alternative solution (Cleland, 1993). While only limited dimensions up to 40 mm can be irradiated by means of e-beam, whole rods could be cross-linked by X-rays. This would provide real manufacturing and economic advantages.

In the 1980–1990s, the first X-ray facilities were developed and found application in the sterilization of medical devices. New powerful X-ray radiation sources opened unexplored fields of polymer processing (Chmielewski, Haji-Saeid, & Ahmed, 2005). In 2004, Greer et al. disclosed a work evaluating amongst others the influence of the irradiation source on the mechanical resistance of UHMWPE (Greer, King, & Chan, 2004). They investigated merely gamma rays and e-beam. Except an article by Park et al. appeared in 2007 where X-rays are mentioned beside gamma rays, electron beam and microwave as radiation source to radicalizing UHMWPE side chains, for cross-linking and to improve its tribological properties (Park & Lakes, 2007), the authors are unaware of further literature about the concrete use of X-rays to enhance the UHMWPE stability as a joint replacement material.

This article was dedicated to examine the particular influence of X-ray cross-linking in comparison with e-beam cross-linking on the mechanical and thermal properties of UHMWPE mixed with 0.1 wt% (weight percent) vitamin E. Two different doses and irradiation temperatures were considered. The hypothesis was that at same absorbed dose and irradiation temperature both cross-linking technologies will lead to similar mechanical and thermal properties.

2 | MATERIALS AND METHODS

2.1 | Materials

The specimens were made of GUR® 1020 blended with 0.1 wt% vitamin E. After consolidation and annealing, bars were cut from the sheet and submitted to X-ray radiation cross-linking (10 MeV, Rhodotron TT300, X-Ray mode). The material was split into four groups distinguished by absorbed dose and irradiation temperature, respectively, as follows. 80 kGy, room temperature (RT): “X (80 kGy)-RT”; 100 kGy, room temperature: “X (100 kGy)-RT”; 80 kGy, 100°C: “X (80 kGy)-warm” and 100 kGy, 100°C: “X (100 kGy)-warm”. Vitelene® (Aesculap AG, Tuttlingen, Germany), highly cross-linked (e-beam, 80 kGy at 100°C), vitamin E (0.1 wt%) blended UHMWPE was taken as reference. We focused on UHMWPE irradiated below the melting point, as treatments above the melting point have deleterious effects on the mechanical properties.

No further postirradiation thermal treatment was performed neither for the X-ray cross-linked material nor for the reference.

2.2 | Methods

Subsequently, the thermal and mechanical properties of all five groups were determined.

Differential scanning calorimetry (DSC) gives essential information about the thermal properties of UHMWPE, which help understand its mechanical performance. Crystallinity and melting

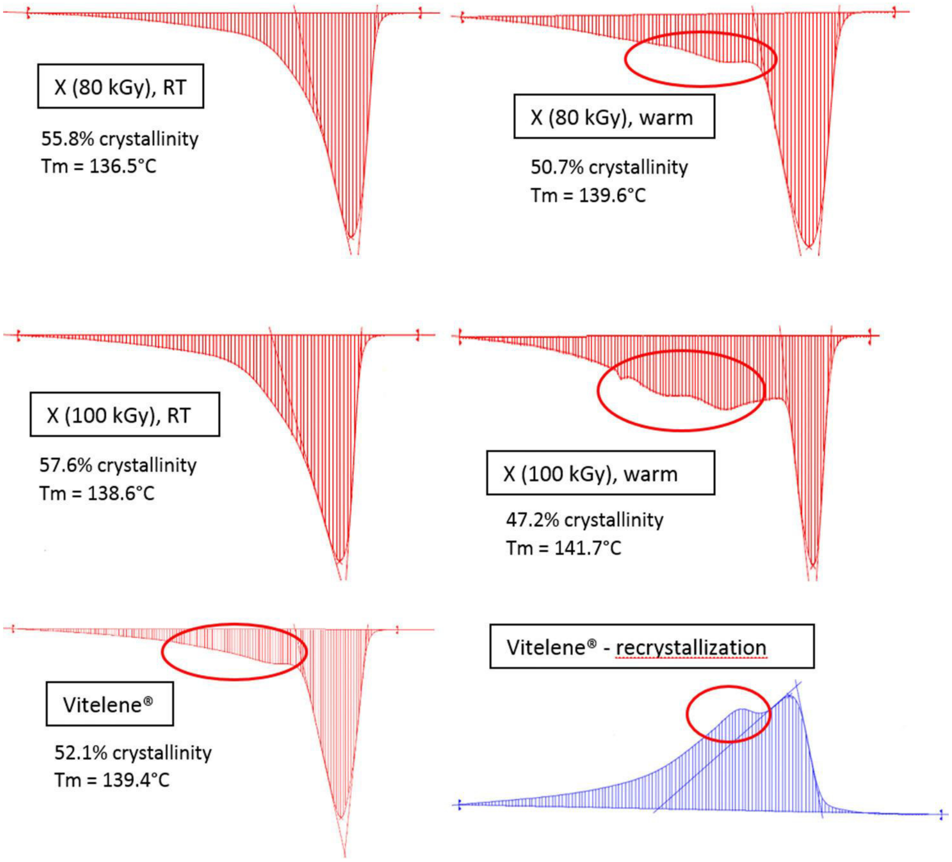

FIGURE 1 Exemplary Differential scanning calorimetry curves — First heating (red)/Recrystallization (blue) — Presence of multiple melting/recrystallization peak for warm irradiated material (circled in red)

temperature were measured according to ASTM F2625 with three samples. Uniaxial tensile testing was carried out according to ASTM D638. Yield stress, ultimate tensile stress (UTS), and elongation at break (EAB) were calculated for each material. Moreover, Izod impact strength (IIS) according to ASTM D256 and bidimensional tensile resistance by so-called small punch testing (SPT) according to ASTM F2183 were ascertained. The small punch test as multiaxial loading provides extended understanding of the mechanical behavior at large deformation, which is more directly related to the clinical performance than uniaxial testing does (Edidin & Kurtz, 2001). Peak load (PL), ultimate load (UL), ultimate displacement (UD), and work to failure (WTF) were assessed. The number of test specimens was $n \geq 4$ according to the ASTM guidelines.

TABLE 1 Influence of the dose on the thermal and mechanical properties of 0.1 wt% vitamin E blended X-ray cross-linked UHMWPE at room temperature

	C [%]	T_m [°C]	Yield [MPa]	UTS [MPa]	EAB [%]	IIS [kJ/m^2]	PL [N]	UL [N]	UD [mm]	WTF [mJ]
X (80 kGy)-RT	55.9 ± 1.0	137.6 ± 1.0	23.6 ± 0.3	48 ± 2	348 ± 13	81 ± 2	74 ± 1	90 ± 1	4.6 ± 0.1	253 ± 4
X (100 kGy)-RT	58.0 ± 0.7	138.7 ± 0.1	23.8 ± 0.3	48 ± 2	321 ± 6[a]	71 ± 3[a]	72 ± 1[a]	93 ± 3	4.6 ± 0.1	255 ± 18

[a] Differences between the two materials statistically significant according to a *t*-test ($p < 0.05$).

TABLE 2 Influence of the dose on the thermal and mechanical properties of 0.1 wt% vitamin E blended X-ray cross-linked UHMWPE at 100°C

	C [%]	T_m [°C]	Yield [MPa]	UTS [MPa]	EAB [%]	IIS [kJ/m^2]	PL [N]	UL [N]	UD [mm]	WTF [mJ]
X (80 kGy)-warm	52.3 ± 1.4	139.1 ± 1.7	21.7 ± 0.7	47 ± 1	402 ± 6	82 ± 3	65 ± 0	94 ± 2	5.6 ± 0.2	322 ± 21
X (100 kGy)-warm	51.1 ± 1.1	141.6 ± 1.1	20.7 ± 0.4[a]	37 ± 1[a]	390 ± 4	81 ± 2	62 ± 1[a]	92 ± 3	6.4 ± 0.3[a]	368 ± 27[a]

[a] Differences between the two materials statistically significant ($p < 0.05$).

TABLE 3 Influence of the processing temperature on the thermal and mechanical properties of 0.1 wt% vitamin E blended X-ray cross-linked UHMWPE with 80 kGy

	C [%]	T_m [°C]	Yield [MPa]	UTS [MPa]	EAB [%]	IIS [kJ/m^2]	PL [N]	UL [N]	UD [mm]	WTF [mJ]
X (80 kGy)-RT	55.9 ± 1.0	137.6 ± 1.0	23.6 ± 0.3	48 ± 2	348 ± 13	81 ± 2	74 ± 1	90 ± 1	4.6 ± 0.1	253 ± 4
X (80 kGy)-warm	52.3 ± 1.4[a]	139.1 ± 1.7	21.7 ± 0.7[a]	47 ± 1	402 ± 6[a]	82 ± 3	65 ± 0[a]	94 ± 2	5.6 ± 0.2[a]	322 ± 21

[a] Differences between the two materials statistically significant ($p < 0.05$).

TABLE 4 Influence of the processing temperature on the thermal and mechanical properties of 0.1 wt% vitamin E blended X-ray cross-linked UHMWPE with 100 kGy

	C [%]	T_m [°C]	Yield [MPa]	UTS [MPa]	EAB [%]	IIS [kJ/m^2]	PL [N]	UL [N]	UD [mm]	WTF [mJ]
X (100 kGy)-RT	58.0 ± 0.7	138.7 ± 0.1	23.8 ± 0.3	48 ± 2	321 ± 6	71 ± 3	72 ± 1	93 ± 3	4.6 ± 0.1	255 ± 18
X (100 kGy)-warm	51.1 ± 1.1[a]	141.6 ± 1.1	20.7 ± 0.4[a]	37 ± 1[a]	390 ± 4[a]	81 ± 2[a]	62 ± 1[a]	92 ± 3	6.4 ± 0.3[a]	368 ± 27[a]

[a] Differences between the two materials statistically significant ($p < 0.05$).

TABLE 5 Table recapitulating the thermal and mechanical properties of 0.1 wt% vitamin E blended UHMWPE with 80 kGy cross-linked by X-ray "X(80 kGy)-warm" in comparison with E-beam "Vitelene®"

	C [%]	T_m [°C]	Yield [MPa]	UTS [MPa]	EAB [%]	IIS [kJ/m^2]	PL [N]	UL [N]	UD [mm]	WTF [mJ]
Vitelene®	52.5 ± 0.4	139.4 ± 0.1	21.7 ± 0.1	48 ± 1	393 ± 8	81 ± 1	63 ± 0	89 ± 5	5.7 ± 0.7	331 ± 64
X (80 kGy)-warm	52.3 ± 1.4	139.1 ± 1.7	21.7 ± 0.7	47 ± 1	402 ± 6	82 ± 3	65 ± 0[a]	94 ± 2	5.6 ± 0.2	322 ± 21

[a] Differences between the two materials statistically significant ($p < 0.05$).

2.3 | Statistics

To differentiate the mechanical and thermal performance between the five material groups, an analysis of variance was carried out ($p < 0.05$) followed by a post hoc test (Scheffe-Test, $p < 0.05$). Prior to analysis, the normal distribution (p–p plots) and the homogeneity of variance (Levene Test) were verified (Statistica R13, TIBCO Software Inc.). A p-value less than 0.05 was considered as significant.

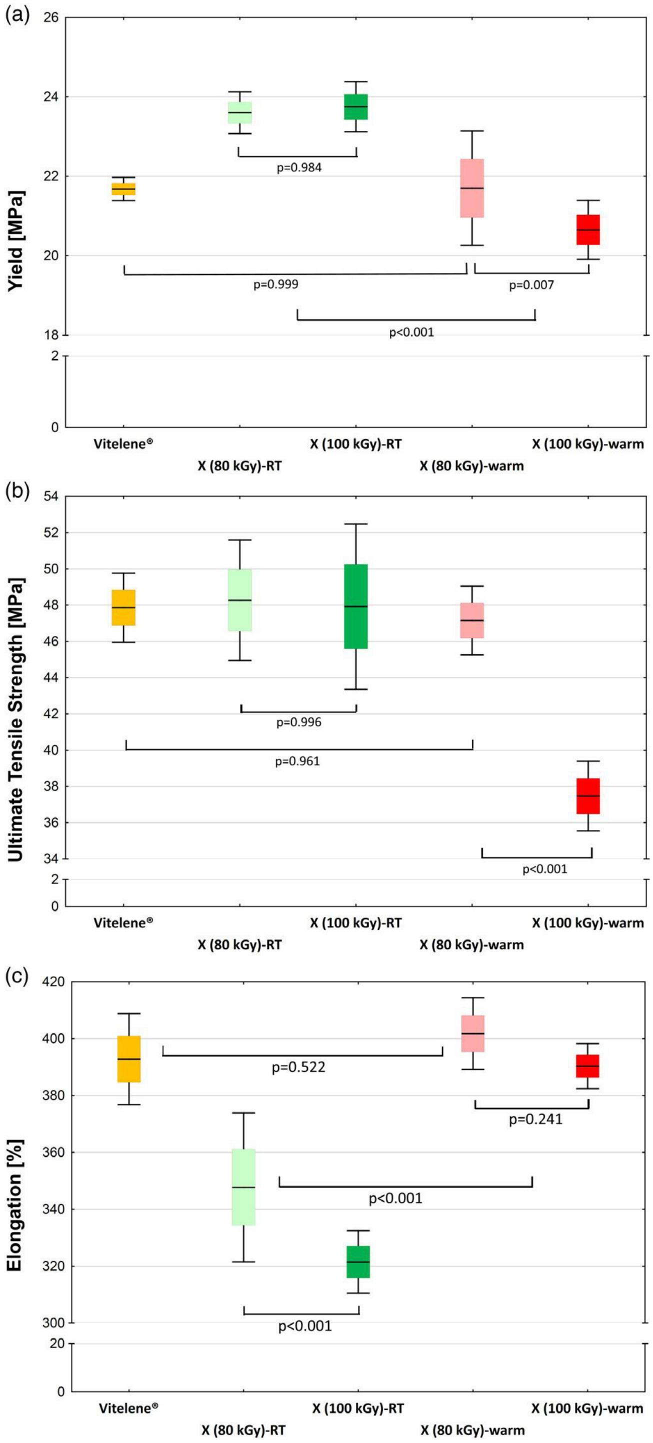

FIGURE 2 Tensile properties for Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy-warm), and X (100 kGy)-warm

3 | RESULTS

3.1 | Differential scanning calorimetry

DSC's measurements revealed a lower crystallinity (C) for warm irradiated UHMWPE compared to material processed at room temperature (Tables 3 and 4; Figure 1).

A second peak could be observed before the main peak on the first heating and on the recrystallization curve of all warm irradiated materials (Figure 1). This indicates the influence of the irradiation temperature on the crystalline structure of the cross-linked UHMWPE. The Vitelene® recrystallization curve is representative for the warm processed materials.

No significant dose-related change of crystallinity could be seen between 80 and 100 kGy (Tables 1 and 2). No tendency and no statistical difference depending on dose or temperature could be identified for the melting temperature (Tables 1–5).

3.2 | Tensile strength

A loss of elasticity (yield) and ultimate strength with rising temperature has been found (Figure 2). Dose dependence could be observed only warm with decrease of yield and UTS with increasing dose. Moreover, the ultimate tensile strength dropped to an unexpected low amount with increasing absorbed dose at elevated irradiation temperature (Table 2). Temperature dependence ($p < 0.001$) (Tables 3 and 4) and dose dependence at room temperature ($p < 0.001$) (Table 1) of the elongation could be noticed. Increasing the temperature allowed for a higher elongation, whereas increasing the dose was followed by a lower elongation. In contrast to yield and ultimate tensile strength, the dose dependence of the elongation at elevated temperature was not significant ($p = 0.241$).

No significant difference between e-beam and X-ray cross-linking was seen (Table 5).

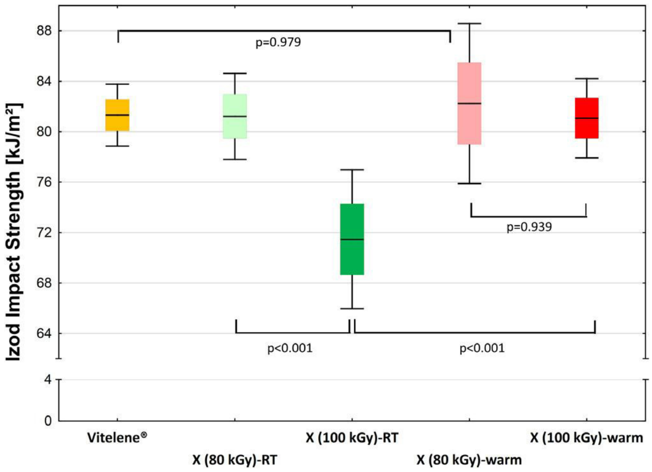

FIGURE 3 Izod impact strength for Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy-warm), and X (100 kGy)-warm

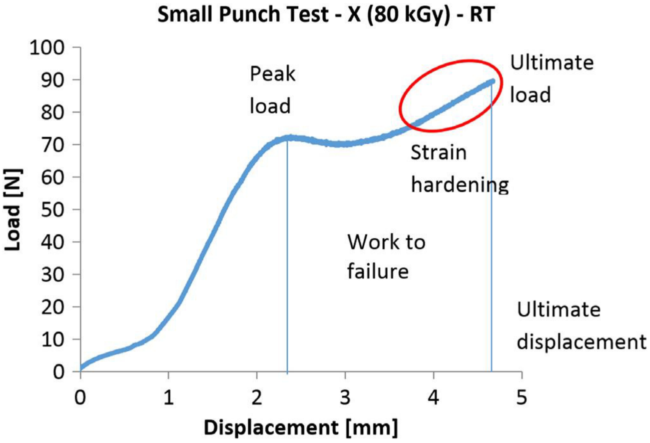

FIGURE 4 Representative load–displacement curve of X-ray cross-linked UHMWPE

3.3 | Izod impact strength

There was a dose dependence at room temperature ($p < 0.001$) (Table 1; Figure 3) but no dose dependence for the warm irradiation ($p = 0.939$) (Table 2). Temperature influence was observed only at 100 kGy ($p < 0.001$) (Tables 3 and 4) and no difference of the radiation type at 80 kGy ($p > 0.950$) (Table 5).

3.4 | Small punch testing

Every small punch test sloop showed a typical cross-linked profile with a strain hardening (Figure 4; Figure 5).

Except for Vitelene® and X (100 kGy)-warm ($p = 0.169$) every peak load result [5a] was found to be significantly different from each other by the statistical analysis ($p = 0$ to $p = 0.019$). However, tendencies were recognizable: influence of the irradiation temperature with a reduction of the peak load at enhanced temperature (Tables 3 and 4) and dose dependence with a reduced peak load at enhanced dose (Tables 1 and 2; Figure 5a). For the ultimate load [5b], it was the opposite: there was no statistically significant difference between the groups ($p = 0.366$ to $p = 0.999$). Neither dose (Tables 1 and 2) nor irradiation temperature (Tables 3 and 4) influence could be noticed.

The ultimate displacement [5c] was influenced by the dose at elevated temperature ($p = 0.035$) (Table 2) with higher strain at

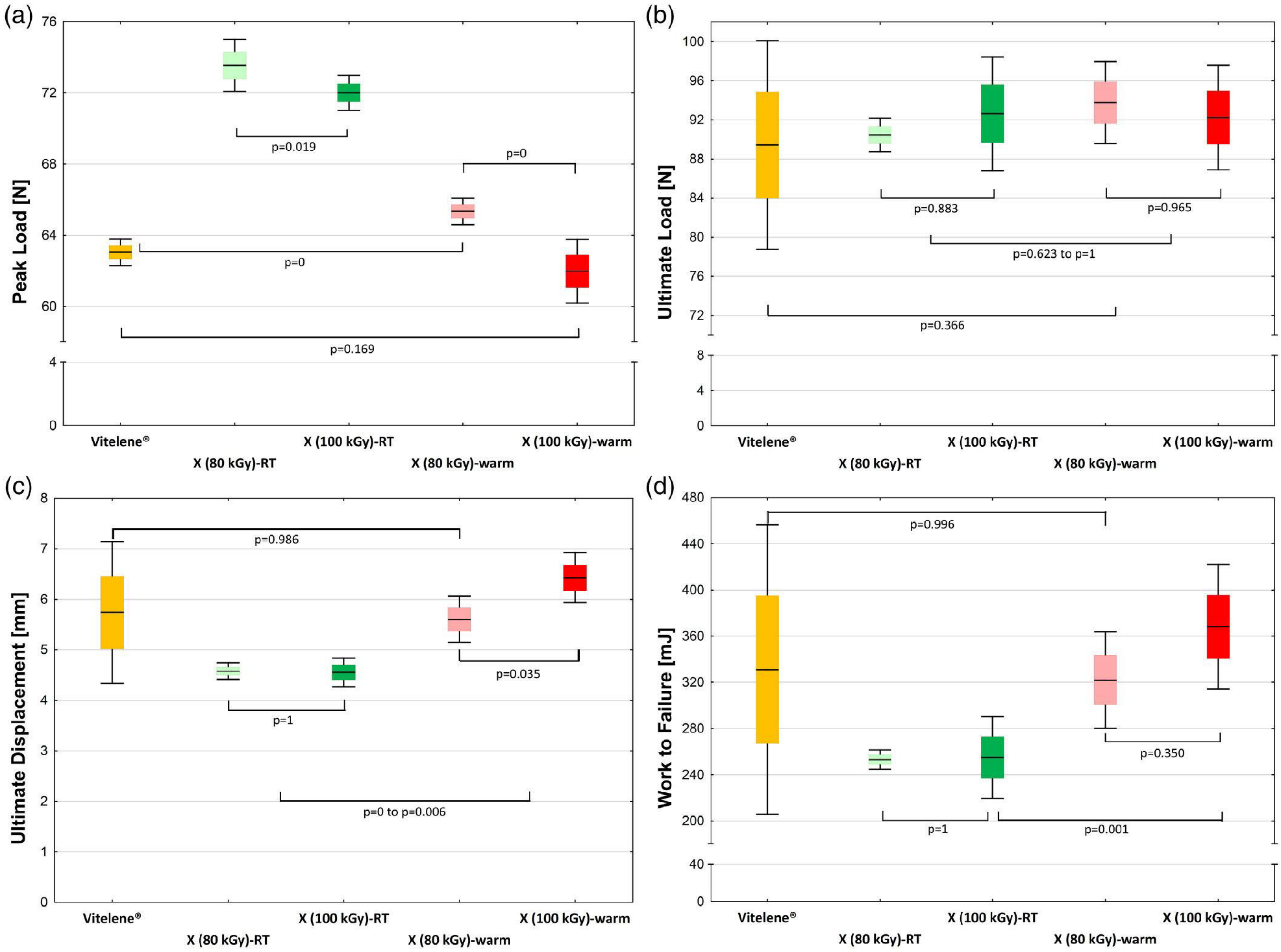

FIGURE 5 Small punch testing for Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm, and X (100 kGy)-warm

100 kGy than at 80 kGy but was not influenced by the dose at room temperature (*p* = 1) (Table 1). A significant increase of 22% (at 80 kGy) and 41% (at 100 kGy) of the ultimate displacement could be noticed for the warm irradiation (*p* = 0.006 for X (80 kGy)-RT vs. X (80 kGy)-warm and *p* = 0 for X (100 kGy)-RT vs. X (100 kGy)-warm).

The work to failure [5d], also seen as a measure for "toughness" (Edidin, 2015), did not show any relevant dose dependence (*p* = 0.999 at RT and *p* = 0.350 "warm"). The influence of the temperature was statistically significant only for 100 kGy (*p* = 0.065 for 80 kGy and *p* = 0.001 for 100 kGy), with the toughness rising with increasing irradiation temperature (Tables 3 and 4).

Vitelene® and X (80 kGy)-warm displayed similar peak load, ultimate load, ultimate displacement, and work to failure (Table 5).

4 | DISCUSSION

The aim of this study was the comparison of the mechanical and thermal properties of X-ray and e-beam highly cross-linked vitamin E blended UHMWPE taking into consideration absorbed dose and irradiation temperature. The hypothesis was that at same dose and same temperature the material properties would not differ significantly regardless of whether the cross-linking occurred with e-beam or with X-rays.

To the author's knowledge, this is the first work that investigated the influence of X-ray cross-linking on vitamin E blended UHMWPE properties in comparison with e-beam cross-linking.

4.1 | Limitations

This work is subjected to several limitations. First, we examined solely two doses in the same range. Second, the influence of the vitamin E content on the mechanical properties was not considered. But, no influence was observed in the literature (Bracco, Bellare, Bistolfi, & Affatato, 2017) when comparing vitamin E UHMWPE with virgin UHMWPE. Third, a restricted number of tests were performed whereas the following investigations could help enhance the understanding of the relationship between the microstructure and the bulk mechanical and thermal properties as described in the literature:

- Small angle X-ray scattering (interlamellar spacing), wide angle X-ray scattering (crystallinity), J-integral (strain energy release rate) (Malito et al., 2018). The determination of the lamellar thickness, lamellar length, and cross-link density could be helpful to understand the influence of radiation method on material changes, as these may govern the fatigue behavior and toughness of the material (Medel, Pena, Cegonino, Gomez-Barrena, & Puertolas, 2007).
- Density as it influences the stiffness (International Atomic Energy Agency, 2008).
- Effect of aging on the material mechanical properties and morphology.
- True stress–strain evaluation as it provides more information at large deformations to describe the basic material properties (Kurtz, Manley, Wang, Taylor, & Dumbleton, 2002; Pruitt, 2005).

However, this is justified by the fact that the aim of our study was to focus primarily on the clinical application of UHMWPE and not to conduct fundamental research in materials science.

4.2 | Differential scanning calorimetry

The DSC analysis confirmed our hypothesis: crystallinity and melt temperature of Vitelene® (e-beam-80 kGy, warm) and X (80 kGy)-warm were found to be equivalent.

In contrast to Premnath (Premnath, Bellare, Merrill, Jasty, & Harris, 1999) observations, no dose induced increase of the crystallinity between 80 and 100 kGy at same temperature (55.9% and 58.0% at RT and 52.2% and 51.1% "warm") could be noticed. This was probably due to the relatively small dose difference of 20 kGy.

The ascertained melting temperatures (Tm) of approximately 139°C are consistent with the literature (Premnath et al., 1999). Although the difference was not statistically confirmed (*p* = 0.147), the observed increase of *Tm* with dose at elevated temperature (139.1°C for 80 kGy vs. 141.6°C for 100 kGy) might be associated with the slow cooling, which favors the gradual thickening of existing lamellae as *Tm* reflects the size and the perfection of the crystals. This phenomenon is also described as a result of annealing (Medel et al., 2007). The molecular rearrangements following cross-linking affect the thermal properties: cross-links increase with dose, what disturbs the melting of the crystals and shifts the melting point upwards (Premnath et al., 1999).

During irradiation even below the melt temperature (the smallest lamellae begin to melt already at temperatures of 60–90°C (Kurtz, 2015)) cross-linking occurs mostly in the amorphous phase but affects the crystal structure and the lattice parameters as well (Ancharova et al., 2017). The higher crystallinity at RT (55.9% and 58.0%) in comparison to the warm irradiated material (52.2% and 51.1%) can be explained by a higher rate of chain scissions (Hemmerich, 2000) related to cross-links followed by additional crystallization: rearrangements (Premnath et al., 1999), thickening of the lamellae, improvement of crystals perfection, and creation of new crystal morphologies (Medel et al., 2007). Moreover, the increased chain mobility at elevated temperature promotes the radical recombination. The cross-links thus formed inhibit crystal growth and prevent recrystallization (Chiesa, Moscatelli, Giordano, Siccardi, & Cigada, 2004; Oral & Muratoglu, 2011; Premnath et al., 1999; Shen, McKellop, & Salovey, 1996; Slouf et al., 2008; Slouf et al., 2009). As a consequence of the more intensive cross-linking only smaller and more imperfect lamellae can fit in the tight molecular arrangement. It results in an inhomogeneous polymer network (Lewis, 2001; Shen et al., 1996) and lower crystallinity. This structural change is illustrated by the presence of a shoulder or multiple crystallization peaks and a larger melting temperature range (Choudhury & Hutchings, 1997; Premnath et al., 1999) as observed on the DSC plots (Figure 1), which corresponds to a polyphasic morphology characteristic for high irradiation temperatures (Chen, Boose, & Yeh, 1991; Muratoglu & Harris, 2001).

The loss of crystallinity can result in the deterioration of some tensile properties (George, Ngo, & Bellare, 2014) as there is a direct relationship between microstructure and mechanical behavior (Medel et al., 2007; Mizera et al., 2014; Oral, Christensen, Malhi, Wannomae, & Muratoglu, 2006). The cross-linking process is associated with concomitant decrease of tensile properties and ductility as well (George et al., 2014; Gomoll, Wanich, & Bellare, 2002; Hemmerich, 2000; McKellop, Shen, Lu, Campbell, & Salovey, 1999; Muratoglu et al., 1999; Muratoglu & Harris, 2001; Oral et al., 2006; Park & Lakes, 2007; Pruitt, 2005; Slouf et al., 2008).

4.3 | Tensile strength

Vitelene® and X (80 kGy)-warm exhibited equivalent tensile characteristics. This outcome supported our hypothesis (Table 5).

The results of the mechanical characterization were in the same range as reported in the literature (Freedman, 2012) and confirmed the correlation between yield strength and crystallinity with decreasing yield concomitant to the loss of crystallinity. The yield stress of X (100 kGy)-RT was 23.8 MPa, its crystallinity 58.0%, these of X (100 kGy)-warm were 20.7 MPa and 51.1%, respectively (Kurtz et al., 2002; Medel et al., 2007). Not only the bulk crystallinity but also the crystal morphology matters (Sobieraj & Rimnac, 2009): the thicker the lamellae and the more perfect the crystals, the higher the yield stress (Medel et al., 2007). In contrast, absorbed dose had little effect on yield stress (Chiesa et al., 2004).

The UTS values obtained in this study (48 MPa) were consistent with the literature (46 MPa) (Oral et al., 2006; Oral & Muratoglu, 2011). It is a trade-off of chain scission, cross-linking, and crystallinity. For one thing, the chain scission mechanism reduces the molecular weight and the strength of the polymer, and then again the outcome of cross-linking is mostly an initial increase in tensile strength (Hemmerich, 2000). The deterioration of the mechanical properties at higher irradiation temperature is the result of the loss of crystallinity (Makuuchi & Cheng, 2012). The relatively low UTS of X (100 kGy)-warm (38 MPa) could be due to the presence of fusion defects in the test specimens (Oonishi, Tsuji, & Kim, 1998). However, it appears little probable because the yield and elongation at break were not especially affected.

The elongations at break measured in this study (320–400%) were much higher than reported in the literature for highly cross-linked UHMWPE lying between 230 and 280% (Bistolfi, Turell, Lee, & Bellare, 2009; Bracco & Oral, 2011; Chiesa et al., 2004; Malito et al., 2018; Oral et al., 2006; Pruitt, 2005), although 330% could be achieved with the WIAM processing as well (Muratoglu & Harris, 2001). Irradiation source and resin playing an important role might be possible reasons (Greer et al., 2004; Zaribaf, 2018): most of the investigators used GUR® 1050 basis resin cross-linked with gamma-rays, while we worked with GUR® 1020 irradiated with X-rays (the reference with e-beam). In addition, gamma rays have a more deleterious impact than e-beams because of the enhanced oxidative chain scission responsible for increased material embrittlement (Hemmerich, 2000).

The elongation retention rose with increasing dose (Hemmerich, 2000) as observed for the material irradiated at RT (348% for 80 kGy vs. 321% for 100 kGy). The higher the dose the higher the cross-linking and material stiffness, the lower the strain and plasticity (Baker, Bellare, & Pruitt, 2003).The creation of a three-dimensional network by cross-linking with subsequent loss of polymer chain mobility reduces the deformation in the amorphous region (Medel et al., 2007; Sobieraj & Rimnac, 2009). The increased scission/cross-linking ratio (S/X) for “RT” could lead to decreased elongation as well. Increased crystallinity might also be responsible for enhanced brittleness, greater resistance to plastic deformation, decreased elongation and toughness (Kurtz, Manley, et al., 2002; McKellop, 1995) and higher resistance to creep deformation (Bistolfi et al., 2009).

Due to their lower crystallinity, the warm irradiated materials were more susceptible to creep and plastic deformation. Moreover, the higher ductility of X (80 kGy)-warm compared with X (80 and 100 kGy)-RT at equivalent UTS was associated with a lower rise of stress with increasing deformation or reduced stress hardening rate. The lower crystallinity after warm processing and different entanglement density (to be determined) could be an explanation (George et al., 2014).

4.4 | Izod impact strength

The results of the Izod impact strength measurement sustained our hypothesis, since Vitelene® and X (80 kGy)-warm exhibited equivalent toughness characteristics (Table 5).

As rim fractures in case of malposition or impingement of hip polyethylene inserts have been reported (Bracco et al., 2017; George et al., 2014; Oral et al., 2006) particular attention has to be paid to the material toughness. The statement that impact strength decreases as the polymer becomes more brittle with increased dose (Hemmerich, 2000) could be verified only at RT. Increasing the dose is detrimental to the toughness resistance as it reduce the plasticity in the cross-linked material (Baker et al., 2003; Medel et al., 2007). The higher crystallinity and risen chain scissions accompanied by lower molecular weight with increasing dose might contribute to the loss of impact strength at RT. At 100°C, the influence of the dose (80 kGy vs. 100 kGy) was negligible. The effect of energy supply (100°C) on the microstructure compensated the dose augmentation and achieved comparable S/X.

As X (80 kGy)-RT and X (100 kGy)-RT had a relatively elevated crystallinity, it could be expected they would exhibit a higher resistance to fatigue crack (Bistolfi et al., 2009; Bracco & Oral, 2011). However, in opposition to several reports (Gomoll & Wanich, 2001; Lewis, 2001; Medel et al., 2007; Oral et al., 2006; Oral & Muratoglu, 2011; Pruitt, 2005) the focus of this study was not the long-term fatigue resistance and fatigue crack propagation of the material. Although it would be of interest to gain greater insight in the material by determining the delta K inception value and the J integral fracture toughness, it was not crucial for the considered materials, because fatigue resistance is predominantly affected by post-irradiation thermal treatment, which does not apply to this work. Furthermore, structural material fatigue and delamination occur mainly in knee arthroplasty, which is subjected to relatively high stresses (Gomoll & Wanich, 2001; Grupp et al., 2017; Grupp, Kaddick, Schwiesau, Maas, & Stulberg, 2009) and are less of concern in hip arthroplasty.

4.5 | Small punch testing

The SPT supported our hypothesis as well, as Vitelene® and X (80 kGy)-warm exhibited equivalent multiaxial tensile characteristics (Table 5).

The absence of a ductile drawing phase indicated the relatively brittle behavior of cross-linked UHMWPE (Chiesa et al., 2004). Moreover, a strengthening of the material during larger strain deformation due to the orientation of chain molecules and lamellar crystals was observed. The crystalline phase was responsible for the yield strength whereas the strain hardening was the result of the amorphous region with cross-linking and entanglement density.

No significant dose dependence was observed in our study. The gradient of 20 kGy between the two investigated doses was probably too low to produce measurable and significantly different effects. However, a comparable influence of the temperature as seen for the uniaxial tensile properties was observed. The higher crystallinity at RT led to higher peak load, decreased strain hardening, and lower work to failure. The lower crystallinity resulted in more ductility, higher ultimate displacement and toughness. The significant increase in the ultimate displacement noticed for the warm processing was probably the result of the rearrangement of the molecules during the warm cross-linking, which allowed for more strain hardening and resulted in a rise of the toughness as well.

Our values were logically higher than those of post irradiation heated material whose crystallinity dropped (Chiesa et al., 2004). In contrast to Asano et al. (2007), neither peak load increase nor work to failure rise were observed with dose augmentation. Also, the ultimate displacement did not decrease with increasing dose. The irradiation temperature might have played a more crucial role than the dose in the interaction of chain scission, cross-linking, and crystallinity as Asano et al. irradiated at room temperature. Not the dose alone but also the thermal history of the material is determining the mechanical behavior and the thermal treatment has been proved to be beneficial to the ductility (Edidin & Kurtz, 2001).

4.6 | Synthesis

Our findings corroborated Cleland statement that independent of the energy source (e-beam, gamma- or X-rays), the physical and mechanical properties of the irradiated material are similar since the radiations generate secondary electrons as ionizing product (Cleland, 1993), with the limitation that we had a single reference dose.

In this study, increasing the temperature had more impact on the material properties than augmenting the dose. The temperature changed the thermal history and affected the crystal perfection and crystallinity. Both, the dose influencing the cross-link density and the thermal processing influencing the crystallinity, are key predictors of the mechanical properties of UHMWPE (Kurtz, Villarraga, et al., 2002). UHMWPE is a complex material and its properties are possibly transitory and dependent on functional loading and environmental conditions (Sobieraj & Rimnac, 2009).

5 | CONCLUSIONS

Up to now, it was not possible to determine the optimal processing, which may lead to maximal wear resistance while keeping the best mechanical properties and aging stability. The material characteristics depend namely on numerous parameters like total absorbed dose, dose rate, irradiation temperature and atmosphere, energy source, post irradiation thermal treatment, oxidative stabilizer, thermal history and others, each of them affecting the supramolecular structure of UHMWPE.

This study showed the prevalence of the processing temperature impact (RT vs. 100°C) over the dose impact, whereby the dose gradient was relatively low (80 vs. 100 kGy).

Our findings supported the hypothesis, that using same basic material (GUR® 1020E), irradiation temperature (<Tm) and dose (80 kGy), different radiation sources e-beam and X-rays would lead to equivalent thermal and mechanical properties.

Finally, further investigations like oxidative stability and wear resistance will be needed to confirm these first results.

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CONFLICT OF INTEREST

The authors are employees of Aesculap AG Tuttlingen, a manufacturer of orthopedic implants.

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3. Zweite Veröffentlichung

Influence of Irradiation Temperature on Oxidative and Network Properties of X-ray Cross-linked Vitamin E Stabilized UHMWPE for Hip Arthroplasty

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Research Article

Influence of Irradiation Temperature on Oxidative and Network Properties of X-Ray Cross-Linked Vitamin E Stabilized UHMWPE for Hip Arthroplasty

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Previous studies have shown that increased cross-link density, reduced free radicals, and increased antioxidant grafting resulting from electron-beam irradiation at elevated temperatures improved the wear performance and the oxidative stability of vitamin E blended UHMWPE. The current study explores the impact of elevated irradiation temperature on vitamin E blended UHMWPE using X-ray. We hypothesize that the effects of temperature would be similar to those observed after electron-beam irradiation due to the relatively high dose rate of X-rays. Two X-ray doses of 80 and 100 kGy and two irradiation temperatures, that is, room temperature and 100°C were considered. The reference was Vitelene®, a vitamin E stabilized polyethylene cross-linked with 80 kGy by e-beam at 100°C. Oxidation index and oxidation induction time, as well as cross-link density, gel fraction, and *trans*-vinylene index, were determined, as the oxidative and network properties are decisive for the long-term implant performance. Gel fraction and oxidation induction time were significantly improved subsequently to warm irradiation in comparison with the material irradiated at room temperature. In conclusion, X-ray irradiation at elevated temperatures resulted in an increase of cross-linking and oxidative resistance of vitamin E stabilized polyethylene comparable to those of e-beam irradiated UHMWPE.

1. Introduction

It is clinically established that the creation of a three-dimensional polymer chain network by means of cross-linking increases the wear resistance of polyethylene orthopedic implants considerably [1, 2]. Radiation cross-linking is characterized by convenience and efficiency in comparison to chemical alternatives. It has the major advantage that no chemical adjuvant like a catalyst or special environmental factors like pressure or temperature is needed to perform the reaction: it makes chemical reactions in a solid polymer at room temperature possible. As a pure physical process, it does not lead to residues of alien substances with toxic potential, which is essential when using it for implantable medical devices [3–6].

During irradiation at high to very high radiation doses (50–10,000 kGy), the polyethylene undergoes two types of modification: cross-linking corresponding to the creation of a spatial network through the connection of macromolecular chains to each other [7, 8] and detrimental changes: scissions [2]. In polyethylene, cross-linking prevails over scissioning [9]. Energy source, dose rate, absorbed dose, processing conditions "prior to, during, and after" irradiation, as well as temperature, environment (air, inert, vacuum), time, and the presence of additives in the polymer influence the recombination ratio cross-linking/chain scission [5, 7, 10–12].

Electron-beam (e-beam) exhibits a reduced penetration capacity, whereas Gamma ray exhibits a low dose rate [13, 14]. Ionization radiation in air at low dose rate requires longer treatment time. The greater exposition to air can facilitate the diffusion of oxygen in the polymer and stimulate the oxidative scission reaction [5, 6, 15, 16]. The proportion of scission to cross-linking rises and deterioration of the material properties is intensified [3]. A higher dose rate of irradiation preserves the material for oxidative degradation [17] and promotes cross-linking over chain scission [18]. This time dependence of oxygen diffusion during irradiation exists at room temperature but is even more relevant at elevated temperature, as heat promotes oxygen diffusion.

Based on these insights the authors used X-ray irradiation as a new approach to overcome the described limitations. Shortly after X-rays and their ability to penetrate matter have been discovered by W. C. Röntgen in 1895 [19], their effect on biological, physical, and chemical material properties was identified. One of the first medical applications was the X-ray tubes for blood irradiation. The dose needed for diagnostic and therapeutic purposes amounts 0.01–10 Gy, whereas industrial applications require up to multiple kilo-grays [19, 20]. With its high penetration depth and a moderate dose rate, X-ray offers optimized processing parameters which allow for warm irradiation and for preserving from early oxidation as e-beam does.

The objective of this study was to evaluate the influence of the irradiation temperature on the network properties (*trans-vinylene* index, gel content, degree of cross-linking) and the oxidative behavior virgin and after accelerated aging (oxidation and oxidation resistance via oxidation induction time) of vitamin E stabilized UHMWPE (ultrahigh molecular weight polyethylene) cross-linked using X-rays as a new irradiation source in comparison with e-beam. The hypothesis was that an elevation of the irradiation temperature would have similar effects on the aforementioned material properties after cross-linking whether by X-ray or by state-of-the-art e-beam irradiation.

2. Materials and Methods

2.1. Materials. The specimens were made of GUR® 1020 blended with 0.1 weight percent vitamin E. After consolidation and annealing, $60 \times 60 \times 200$ mm bars were cut from the sheet and submitted to X-ray radiation cross-linking. The material was split into four groups distinguished by absorbed dose and irradiation temperature, respectively, as follows: 80 kGy, room temperature (RT) "X (80 kGy)-RT;" 100 kGy, room temperature "X (100 kGy)-RT;" 80 kGy, 100°C "X (80 kGy)-warm;" 100 kGy, 100°C "X (100 kGy)-warm." Prior to irradiation the bars were introduced in an insulation box and preheated below the melting point in an oven. Temperature and cooling kinetics were determined on the occasion of preliminary tests to ensure a minimum of 100°C during the complete X-ray irradiation process. The test bars were cross-linked by means of X-ray with a double-sided irradiation of each 20 kGy at a dose rate of 0.26 kGy/s. The X (80 kGy) specimens were subjected to four runs, the X (100 kGy) to five runs. The absorbed dose was determined during a pretest thanks to alanine dosimeters.

Vitelene® (Aesculap AG, Tuttlingen, Germany), a highly cross-linked (electron-beam, 100°C, 80 kGy with a 10 MeV-Rhodotron®), vitamin E (0.1%) blended polyethylene available on the market as part of a hip joint prosthesis was taken as reference.

No further postirradiation thermal treatment was performed.

2.2. Methods

2.2.1. Oxidative Characterization. To determine the oxidative properties of X-ray and e-beam cross-linked vitamin E stabilized polyethylene, the Oxidation Index (OI) and the Oxidation Induction Time (OIT) were determined. Accelerated aging according to ASTM F2003-02(2015) was performed in order to compare the oxidation resistance and oxidation potential of the different materials.

The OI was measured with a Fourier Transform Infrared (FTIR) spectrometer by dividing the area of the carbonyl absorptions (>C=O) centered near 1720 cm^{-1} by the area of the normalization peak (C-H absorptions) centered near 1370 cm^{-1} according to ASTM F2102-17.

X-ray specimens were obtained from bulk material. Slices were cut from the surface at depths 0, 100, 200, and 500 μm from two opposite faces. We limited the measurement to 500 μm because in agreement with our experience no significant oxidation could be observed for vitamin E blended polyethylene over this depth even after accelerated aging. Vitelene® serial implants were halved and sliced. A line scan was recorded across the sample towards the surface at 100 μm increments to a depth of 3 mm. The maximum oxidation index was collected.

As OIT correlates with antioxidant efficacy, it was used to compare the oxidative resistance of the tested materials. The OIT measurements were performed with a differential scanning calorimeter according to ASTM D3895-14. The polyethylene samples were taken from the surface and were heated under a nitrogen atmosphere up to 200°C. After that, the atmosphere was switched to oxygen. The time until the exothermal degradation began was recorded.

2.2.2. Network Characterization. The following analyses provide information about radiolytic events occurring during the irradiation of polyethylene like the formation of *trans*-vinylene unsaturations and cross-linkings.

At first, the *trans*-vinylene index (TVI) was determined with a FTIR spectrometer by calculating the ratio of the area of the absorption peak centered on 965 cm^{-1} to the area of the normalization peak centered on 1370 cm^{-1} according to ASTM F2381-10. The yields of *trans*-vinylene radiolytic unsaturations are proportional to the number of cross-links formed [21, 22]. The TVI is a reliable indicator of dose level [12, 23].

Second, the gel and soluble fraction of each material were determined gravimetrically according to ASTM D2765-16. When submitted to radiation emanating from a reactor, polyethylene forms an insoluble gel [13, 24] which gives information about the fraction of long molecules which are entangled and/or cross-linked [12]. During the extraction in xylene the soluble part of the network is extracted whereas the cross-linked is not. The specimens were weighed (m_i), immersed and refluxed for 12 hours in boiling xylene. Afterwards, they were dried and weighed (m_f) another time. The soluble fraction (w_{soluble}) in % mass was calculated as follows:

$$w_{\text{soluble}} = 100 \times \frac{\left(m_i - m_f\right)}{m_i}. \quad (1)$$

The gel fraction (w_{Gel}) in % mass was calculated as follows:

$$w_{\text{Gel}} = 100 - w_{\text{soluble}}. \quad (2)$$

Third, the degree of cross-linking or the number of moles of cross-links per unit volume has been determined as an instructive method in understanding the relative cross-link density between different materials [25]. Direct determination is impossible because it cannot be distinguished between the physical and the chemical cross-links [12, 26]. The swell ratio (ρ) was determined gravimetrically from the absorbed xylene weight divided by its density (0.75 g/cm^3) after immersion at 130°C for 2 hours.

$$\rho = \frac{\left(V_s + V_x\right)}{V_s}, \quad (3)$$

with V_s = initial volume of the specimen as the result of its initial weight divided by its density d assumed to be 0.935 g/cm^3, and V_x = volume of the absorbed xylene as the difference between the final xylene-swollen and the initial weight of the specimen divided by the density of xylene (0.75 g/cm^3).

The cross-link density (v_d) was indirectly calculated based on the determination of the swell ratio and the Flory network theory [27]

$$v_d = -\frac{\ln\left(1 - (1/\rho)\right) + (1/\rho) + \left((1/3) + (5/9\rho)\right)/\rho^2}{136\left(\rho^{-1/3} - (1/2\rho)\right)}. \quad (4)$$

The molecular mass between cross-linking (Mw) was determined as follows:

$$\text{Mw} = \frac{d}{v_d}. \quad (5)$$

For every test n was ≥3, except for the gel fraction $n = 1$.

2.3. Statistics. To differentiate the network and oxidative characteristics between the five material groups, an analysis of variance ANOVA was carried out ($p < 0.05$) followed by a post hoc test (Tukey's HSD-Test, $p < 0.05$).

Prior to analysis, the normal distribution (p-p plots) and the homogeneity of variance (Levene Test) were verified (Statistica R13, TIBCO Software Inc.). A p value of less than 0.05 was considered significant.

3. Results

3.1. Oxidative Characterization

3.1.1. Oxidation Index (Figure 1). The FTIR spectra revealed low oxidation indices (<0.20), less oxidation for warm irradiated polyethylene than for the material processed at room temperature ($p < 0.001$). The X-ray warm irradiated materials showed little to no significant oxidation (their OI level was very close to the limit of quantification 0.025). A light increased oxidation could be observed between 80 and 100 kGy at room temperature, but it was not found to be statistically significant ($p = 0.180$ virgin and $p = 0.227$ aged). The OI level was equivalent before and after accelerated aging. No significant difference between e-beam 80 kGy warm (Vitelene®) and X-ray cross-linking 80 kGy warm was seen ($p = 1$).

The FTIR analysis of the feedstock surface exhibited an oxidation index up to four times higher than that of the subsurface (Figure 2).

3.1.2. Oxidation Induction Time. First of all, relatively low values for irradiation at room temperature and to some extent a large standard deviation of up to 80% were observed. The reason for these findings might be the fact that most of the samples for the measurement were taken out of the surface of the feedstock and others out of a cut face. The surface has been subjected to high thermal and mechanical stresses during manufacturing what was responsible for increased degradation (Table 1).

Although the temperature dependence could not be always statistically confirmed (virgin: $p = 0.003$ for 80 kGy, $p = 0.168$ for 100 kGy, aged: $p = 0.001$ for 80 kGy, $p = 0.534$ for 100 kGy, between room temperature and warm irradiation, respectively), the positive influence of heat supply during irradiation processing was obvious.

No dose-related significant difference could be observed neither for irradiation at room temperature nor for warm irradiation ($p > 0.1$).

3.2. Network Characterization. Table 2 gives a summary of the results of the network characterization.

3.2.1. trans-Vinylene Index. Both the irradiation temperature and the dose were found to affect the amount of *trans*-vinylene unsaturations with higher TVI for warm irradiation and increased dose. UHMWPE irradiated with e-beam exhibited higher TVI as well (Figure 3, Table 2).

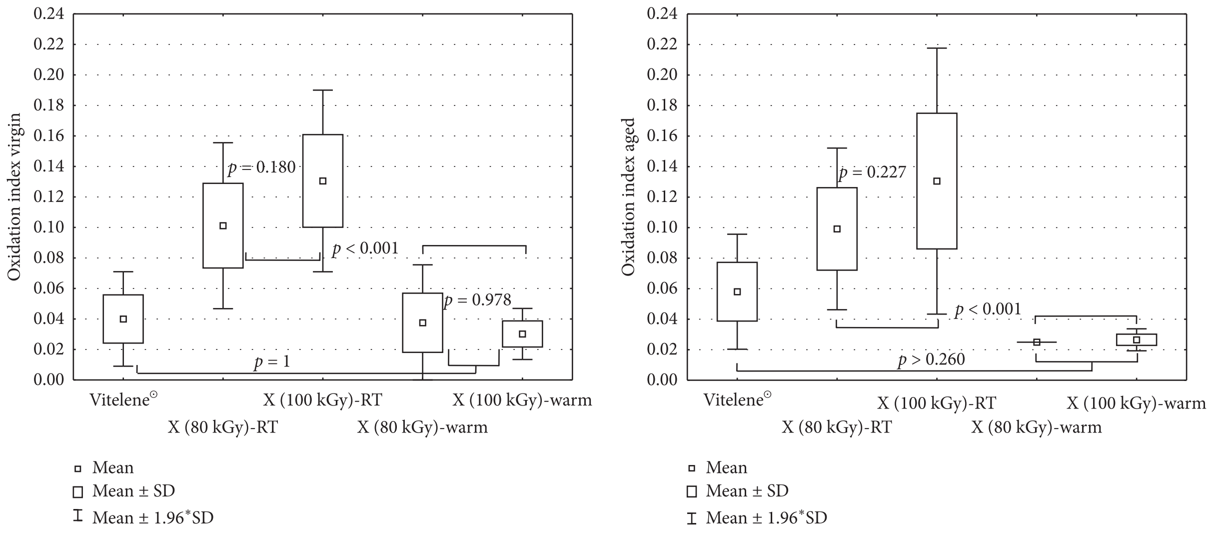
3.2.2. Gel Fraction. The data in Table 2 show that the difference between samples irradiated at 80 kGy and 100 kGy was almost negligible concerning the solubility measurement. In contrast, enhancing irradiation temperature led to a higher insoluble fraction of the polymer.

No difference was seen between e-beam and X-ray.

3.2.3. Degree of Cross-Linking. Except between Vitelene® and X (80 kGy)-warm ($p = 0.015$) the differences between cross-link densities were not statistically significant ($p = 0.143$ to 0.999). However, a slight increase could be observed with a higher dose. Neither the irradiation temperature nor the radiation source seemed to substantially affect the cross-link density.

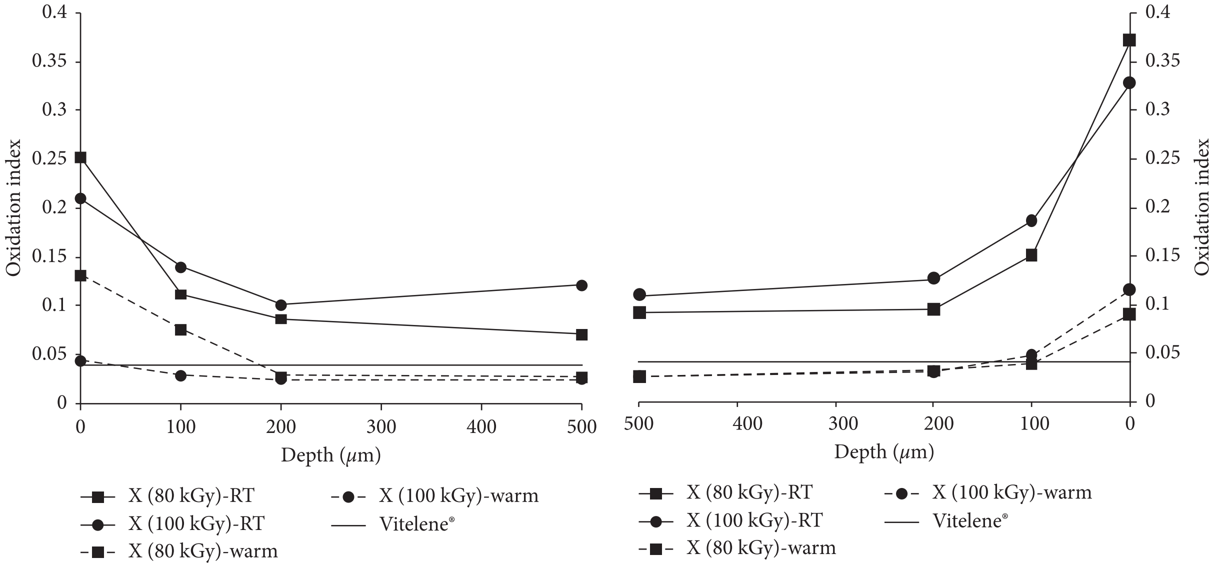
4. Discussion

The objective of this study was to evaluate the influence of the irradiation temperature on the network properties



(a) (b)

Figure 1: Oxidation index of Vitelene® implants, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm, and X (100 kGy)-warm, virgin (a) and after accelerated aging (b) according to ASTM F2003 for 2 weeks after elimination of the first 100 μm of the feedstock. Limit of quantification (LOQ): 0.025.



(a) (b)

Figure 2: Surface oxidation of the X-ray cross-linked UHMWPE feedstock and of the Vitelene® implants, both virgin. (a) Subsurface OI measured from one side of the test bar. (b) Subsurface OI measured from the opposite side of the test bar. LOQ: 0.025.

(TVI, gel content, degree of cross-linking) and the oxidative behavior virgin and after accelerated aging (oxidation and oxidation resistance via OIT) of vitamin E stabilized UHMWPE cross-linked using X-rays as a new irradiation source in comparison with e-beam. The hypothesis was that an elevation of the irradiation temperature would have similar effects on the aforementioned properties after cross-linking whether by X-ray or by state-of-the-art e-beam irradiation.

Table 1: OIT of Vitelene® implants, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm, and X (100 kGy)-warm, virgin and after accelerated aging according to ASTM F2003 for 2 weeks.

	OIT-virgin (min)	OIT-aged (min)
Vitelene®	11.3 ± 1.8	10.9 ± 1.2
X (80 kGy)-RT	6.2 ± 3.1	3.7 ± 2.9
X (100 kGy)-RT	5.6 ± 2.9	5.7 ± 0.0
X (80 kGy)-warm	18.8 ± 0.4	12.8 ± 0.6
X (100 kGy)-warm	11.8 ± 5.9	8.4 ± 3.7

Table 2: Network properties of Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm, and X (100 kGy)-warm.

	TVI	Gel content (%)	Cross-link density (mol/dm^3)	Mw between cross-links (g/mol)
Vitelene®	0.053 ± 0.004	99	0.195 ± 0.007	4800 ± 173
X (80 kGy)-RT	0.034 ± 0.006	93	0.179 ± 0.006	5222 ± 190
X (100 kGy)-RT	0.041 ± 0.006	94	0.183 ± 0.012	5133 ± 355
X (80 kGy)-warm	0.042 ± 0.006	99	0.172 ± 0.005	5450 ± 157
X (100 kGy)-warm	0.048 ± 0.003	99	0.180 ± 0.009	5213 ± 257

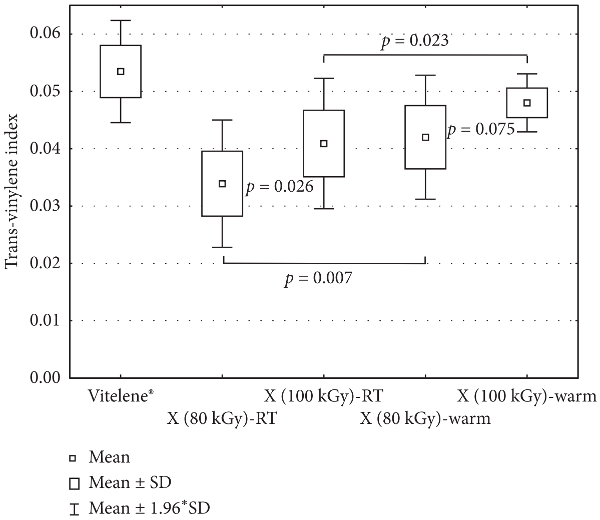


Figure 3: *trans*-vinylene unsaturations of Vitelene®, X (80 kGy)-RT, X (100 kGy)-RT, X (80 kGy)-warm, and X (100 kGy)-warm.

4.1. Limitations. This work is subjected to some limitations.

First, we investigated only 2 irradiation doses in the same clinically relevant range. For this reason, the real influence of the dose could not be systematically analyzed.

Second, our in vitro aging model did not reproduce all the mechanisms involved in initiating and propagating oxidation in vivo like mechanical stress, cyclic loading, and influence of lipids (squalene) [28–34].

Third, cross-linking density was determined below the melt temperature. The crystalline phase did not vanish completely. Therefore, not only the persisting cross-links in the amorphous phase were considered but also other physical bonds like entanglements and crystals. Rheological characteristics in the melt could give more information about the real cross-link density [12].

As accentuated by Premnath et al. [35], the determination of the cross-link density according to Flory–Rehner expression for swollen cross-linked networks is not possible since the irradiation cross-linking carried out in the solid state does not take place homogeneously but preferentially in the amorphous region [7, 18]. Therefore, our measurement serves only as a comparison of the different materials.

Fourth, since the oxidative degradation of polyethylene is mostly due to long-lived radiation-induced free radicals particularly those trapped in the crystalline phase, an Electron Spin Resonance analysis could help predict the oxidation kinetic. At last, the FTIR determination of hydroperoxides, which are intermediate oxidation products, could have been carried out as a measure of oxidation potential [36].

The focus was the evaluation of X-rays versus e-beam at elevated temperatures to cross-link UHMWPE implant material. Further investigations would be of scientific interest but beyond the scope of the current study.

4.2. Oxidative Characterization

4.2.1. Oxidation Index. The OI levels were in the same range (<0.2) as reported in the literature for XLPE stabilized with vitamin E [33, 37, 38] and far below 1 which was considered to be the limit associated with the degradation of mechanical properties for conventional polyethylene [39–42]. However, to what extent this threshold applies for highly cross-linked polyethylene is unknown.

The FTIR analysis confirmed our hypothesis: OI of Vitelene® (β-80 kGy, warm) and X (80 kGy)-warm were found to be equivalent ($p = 1$). The presence of vitamin E and the elevated irradiation temperature may explain why in contradiction to Wannomae and Muratoglu [43] no detrimental effect of X-ray irradiation on the oxidation resistance of the material was observed. Elevation of the irradiation temperature was shown to be useful against oxidative degradation. Several reasons are possible: the heat increases the mobility of the chains and promotes the free radical decay [28, 29] and/or the heat may favor the chemical bonding of the vitamin E to the polyethylene chains during irradiation which prevents loss of oxidation resistance [28]. The similar OI before and after 2 weeks accelerated aging is attributed to the presence of the antioxidant vitamin E. The accelerated aging according to ASTM F2003 for 2 weeks was not able to generate a difference between the materials.

The high oxidation level (up to 0.6) on the surface layer of the X-ray irradiated feedstocks in air was attributed to immediate oxidative degradation, also in the presence of vitamin E [12, 18, 33, 44, 45]. Oxygen is able to diffuse within about 0.5 to 2 mm the polyethylene surface [21, 31]. Dissolved oxygen reacts with the free radicals even in the presence of a small amount of antioxidant (0.05–0.1%) [12, 28, 33, 34, 46–49]. Furthermore, the degradation of vitamin E at higher temperatures can occur [50] and the low vitamin E concentration could not prevent completely the surface oxidation during processing. The oxidation cascade is hindered as vitamin E gives hydrogen to the free radicals and the further oxidation of the material is prevented.

In contrast to Oral et al. [30] and Slouf et al. [18], no raised oxidation with increased dose could be noticed. This was probably due to the relatively small dose difference of 20 kGy.

As oxidative degradation remains ongoing in vivo and in the long-term [15, 29, 30, 33, 39, 51–53], a manufacturing method that allows for optimal preservation of the antioxidant is highly desirable.

4.2.2. Oxidation Induction Time. OIT was determined to compare the antioxidative potential of the materials.

The values were in the same range as mentioned in the literature [54]. The large variance did not permit any reliable conclusions about the role of the dose. However, the beneficial effect of irradiation at increased temperature was confirmed. Heat improves vitamin E preservation and grafting during irradiation. This would probably result in increased long-term stability [29, 50, 52, 53, 55]. Furthermore, a stabilizing activity of the α-tocopherol derivatives could amplify the effect [56]. In contrast to the findings of Wannomae et al. no deleterious effect of the X-ray irradiation on the antioxidative potency was asserted [43]. Although the reliability of this measurement is controversially discussed particularly for low OIT values (<15 minutes) [57], this method is described to be helpful for assessing and ranking the antioxidative potential of antioxidant-containing UHMWPEs [54, 58]. As the test is conducted under very harsh conditions which absolutely do not correspond to in vivo aging, it serves exclusively the material comparison and a correlation with the clinical behavior remains to be established.

4.3. Network Characterization

4.3.1. trans-Vinylene Index. The yield of *trans*-vinylene unsaturations was higher for warm irradiation than for irradiation at room temperature. It can be interpreted such that the temperature increases the radiolytic reactions kinetics [23, 59, 60].

Furthermore, more *trans*-vinylene units were formed at 100 kGy than at 80 kGy confirming their augmentation with increasing the absorbed dose [18, 33, 60–67].

We observed a tendentially higher response for e-beam (on average, because of its high dose uniformity ratio) than for X-ray. The irradiation source affects the reaction kinetics as well as the dose rate, the absorbed dose, and the temperature [33, 65].

4.3.2. Gel Fraction. The extraction test verified that all the materials were highly cross-linked. As a gel fraction of 75% is typically reached after sterilization with 25–35 kGy [54] higher doses lead systematically to gel fractions between 90% and 100% making the differentiation of the materials based on this parameter difficult. However, some tendencies could be seen.

The gel fraction up to 99% for the warm irradiated groups indicated that only little chain scissioning occurred or that the radicals created during irradiation recombined in a cage reaction during swelling in xylene [68]. The higher gel content at elevated temperature can be explained by the reduced mobility of vitamin E due to greater grafting. This reduces the reaction competition and promotes the recombination of the free radicals to form cross-links [53]. In contrast to the literature, no increase of gel content with dose was observed [69]. Vitelene® and X (80 kGy)-warm exhibited equivalent gel content supporting our hypothesis.

4.3.3. Cross-Link Density. In opposition to the literature [23, 26, 53, 59, 61, 64, 70–73], no significant influence of dose and temperature ($p > 0.05$) was noticed. One reason for this discrepancy might be the error in the measurement of the swollen mass which increases as the swell ratio decreases [35]. Another reason might be the fact that the cross-link density was determined at 130°C, whereby the melting range of UHMWPE extends from 50°C to 160°C [54]. In this way, much more short chains and entanglements still remain and bias the determination of the cross-link density.

As the cross-link density is directly related to the wear behavior of UHMWPE [70, 74], particular attention should be paid to the result of the oncoming wear simulation tests.

5. Conclusion

It is currently accepted that the combined advantages of cross-linking and stabilization with a suitable antioxidant lead to an extension of the lifetime of orthopedic implants. However, oxidation is initiated not only as a result of irradiation but is induced in vivo as well. Taking into consideration that vitamin E has a limited potency, it is worthwhile to prevent its degradation during the manufacturing process in order to prolong its efficacy in vivo and in this way further increase the longevity of the prosthesis.

Our study confirmed the positive effect of the elevated irradiation temperature on the radiation cross-linking and on the oxidation resistance of vitamin E stabilized UHMWPE, independently of the irradiation source e-beam or X-ray.

Data Availability

The results of the measurements or the data used to support the findings of this study are included within the article (Figures 1–3 and Tables 1 and 2).

Additional Points

Statement of Significance. Two important topics when considering the clinical relevance of the study are the cross-link density and the long-term oxidative stability. The cross-link density is directly related to the wear resistance. Oxidation promotes chain scission and reduces the yield of cross-linking. Although its clinical effects and impact on implant revision are still unclear especially for cross-linked UHMWPE, the resistance to oxidation allows the wear and mechanical properties to be maintained in the long run. Therefore, it is necessary to pay particular attention to the influence of the irradiation conditions of X-ray as a quite new cross-linking method on the aforementioned material properties.

Conflicts of Interest

The authors are employees of Aesculap AG Tuttlingen, a manufacturer of orthopedic implants.

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In Vitro Wear Performance of X-ray Cross-Linked Vitamin E Blended Polyethylene

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ABSTRACT

The most common radiation cross-linking methods are electron-beam and Gamma-irradiation. Gamma-irradiation has a very low dose rate and e-beam serious penetration limitations. X-ray exhibits an excellent penetration capacity with a moderate dose rate. The objective of the study was the investigation of the wear behavior of vitamin E blended Ultrahigh Molecular Weight Polyethylene highly cross-linked by X-ray as an alternative cross-linking technology. We hypothesized that using same dose and irradiation temperature the wear behavior would be equivalent regardless of the radiation source.

Hip wear simulation was performed with five different polyethylene acetabular inserts articulating with 40 mm diameter cobalt-chromium heads. Two X-ray doses of 80 and 100 kGy and two irradiation temperatures each, i.e. room temperature and 100 °C, were considered. The reference was Vitelene®, a vitamin E stabilized polyethylene cross-linked by e-beam with 80 kGy at 100 °C. The inserts were subjected to artificial aging for 2 weeks prior to test.

Increasing both the dose and the irradiation temperature led to an improved wear performance.

X-ray showed the ability to improve the wear resistance of polyethylene in the same range as e-beam, as both are ionizing irradiation.

Significance: Highly cross-linked polyethylene has been established and taken over 80–100% of polyethylene usage in Total Hip Arthroplasty [1–3]. The goal is to retain its mechanical properties, oxidative stability and superior wear resistance over time, which is crucial in order to reduce the incidence of periprosthetic osteolysis and increase the service time over the second implantation decade [4]. Vitamin E stabilized polyethylene has been successfully introduced showing very good results at 5 years [5–7]. X-ray irradiation stands out by its worthwhile characteristics like high penetration capacity and moderate dose rate which extend the treatment possibilities of polyethylene and the preservation of its properties in the long term.

1. Introduction

Cross-linking is the formation of a three-dimensional (3D) insoluble polymer network (ASTM D-883). Creation of bonds between molecular polymeric chains and forming 3D structures improve some product performances such as mechanical, corrosive and thermal stability. Cross-linking for industrial purposes with radiation is achieved mainly by electron-beam [8–10] and has been used for 70 years in various applications such as modifying wire and cable, shape memory products and foams. Later the ionizing radiations were implemented in the manufacturing of medical devices like hydrogels and ultrahigh molecular weight polyethylene (UHMWPE) implants [11–13]. The 3D cross-linked network created during irradiation enhances particularly the wear resistance and the clinical outcome of UHMWPE acetabular inserts for total hip replacement [14–25]. Meanwhile, the use of highly cross-linked polyethylene (XLPE) is clinically established [26–32]. It is foreseeable that due to the issue of ion release and metallosis the metal-on-metal bearings in hip arthroplasty will be replaced by metal- or ceramic-on-cross-linked polyethylene which is on the way to becoming the Gold Standard [33].

Cross-linking is achieved mostly by irradiation. UHMWPE has to undergo post radiation thermal treatment to quench the free radicals sprouted during irradiation, which could lead to oxidation and early implant failure. Annealing -below the melting point- does not eliminate completely the free radicals. Remelting -above the melting point- has a deleterious effect on the mechanical properties. During the last decade the addition of an antioxidant like vitamin E which enables effective oxidation prevention without thermal treatment and concomitantly the

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conservation of the mechanical properties over time, found a wide acceptance in the implant fabrication [25].

There are two main sources of ionizing radiations available: Gamma irradiation (Cobalt 60) and Beta irradiation (electron beam). X-ray (conversion of accelerated electrons) remains an oncoming technology. All sources differ in several manners. First, the penetration depth depending on current and power (e-beam and X-ray), and material density is in the range of about 38 mm, 450 mm and 450 mm for a material with unit density [34] for e-beam, Gamma ray and X-ray respectively [35,36]. Second, the dose repartition is more uniform for Gamma-ray and X-ray with an exponential attenuation for Gamma- and X-ray and finite range attenuation for e-beam [35]. Third, their dose rate vary considerably in the order of 100 kGy/s, 100 kGy/10 h and 100 kGy/h for e-beam, Gamma ray and X-ray, respectively [35,36]. Radiation technologies with higher dose rates are preferable because they lead to a predominance of cross-links over chain scissions [37]. The balance between penetration depth and dose rate, the power activity (on-off) and the supply difficulties (e.g. Co60) make braking X-ray irradiation (bremsstrahlung) a valuable alternative to the electron beam and radioactive isotopes [12].

Cross-linking influences not only the wear resistance of the polymer but also numerous of their other mechanical, physical and thermal characteristics. Often, the improvement of the wear resistance is accompanied by the deterioration of other relevant properties. Starting resin, fabrication method, environmental conditions under which radiation occurs (e.g. atmosphere, temperature) [38,39] and cross-linking process were identified as variables which affect the in vivo wear behavior of UHMWPE [40]. The stabilization and the sterilization method are able to alter significantly the material performance as well. Up to now, the ideal cross-linking process has not been found. The challenge remains to discover the optimal processing parameters [20].

To the author's knowledge the wear behavior of X-ray cross-linked polyethylene has not been ascertained before. This work was designed to establish whether or not X-ray could be taken into account as alternative technology to e-beam and Gamma-irradiation for cross-linking polyethylene. The focus was the investigation of the wear behavior of X-ray cross-linked vitamin E stabilized UHMWPE. The study sought to elucidate the influence of dose and temperature during irradiation on the wear resistance. We hypothesized that using same dose and irradiation temperature the wear behavior would be equivalent independently of the radiation source.

2. Materials and Methods

2.1. Materials

The specimens were made of GUR® 1020 stabilized with 0.1 wt% vitamin E as a blend. After consolidation and annealing, 60 × 60 × 200 mm bars were cut from the sheet and subjected to X-ray radiation cross-linking. Inserts were turned from the cross-linked bars, packaged and sterilized by ethylene oxide. The material was split into four groups distinguished by absorbed dose and irradiation temperature respectively as follows: 80 kGy, room temperature (RT = 20 °C) "X (80 kGy)-RT"; 100 kGy, room temperature "X(100 kGy)-RT"; 80 kGy, 100 °C "X(80 kGy)-warm"; 100 kGy, 100 °C "X(100 kGy)-warm". Vitelene® (Aesculap AG, Tuttlingen, Germany), a highly cross-linked (electron beam, 80 kGy with a 10 MeV-Rhodotron®, at 100 °C), vitamin E (0.1 wt%) blended polyethylene available on the market as part of a hip joint prosthesis was taken as reference. None of the inserts underwent any post irradiation thermal treatment. They differ exclusively in the cross-link method. The tests were performed with the largest (40 mm diameter) and thinnest (5 mm) inserts available in the system to constitute a worst case configuration as the wear of polymer bearings in hip arthroplasty is related to the diameter and thickness of the insert [41,42]. Prior to test the polyethylene inserts were subjected to 5 bars oxygen at 70 °C for two weeks according to ASTM F2003–02 in order to include the influence of aging in the evaluation of the wear behavior. A titanium Plasmafit® Poly Cup size 54 (Aesculap AG, Tuttlingen, Germany) was taken as acetabular cup. To complete the worst case cobalt chromium (CoCr) femoral heads (taper 12/14) were chosen for the articulation, as they produce more wear compared to ceramic heads [43].

2.2. Methods

The acetabular inserts with an inner diameter of 40 mm made of the four described X-ray ($n = 3$) and of the e-beam ($n = 6$) cross-linked polyethylene groups were tested on a customized 6 + 2 (loaded soak controls) stations servohydraulic hip simulator (Endolab GmbH, Thansau, Germany) with kinematic and load patterns according to ISO 14242-1:2014(E) for 5 million cycles (mc) at a frequency of 1 Hz in diluted newborn calf serum with a protein content of 30 g/l and incubated at 37 °C. Following accelerated aging the inserts were soaked in the test medium until the incremental mass change over 24 h was < 10% of the previous cumulative mass change (Vitelene® 13 days, X-RT 27 days, X-warm 41 days) in order to achieve fluid saturation according to ISO 14242-2:2016(E). The loaded soak controls were subjected only to axial load. The wear of the remaining specimens was determined gravimetrically in relation to the loaded soak controls.

The measurement of the gravimetrical changes was performed after 0.5, 1, 2, 3, 4 and 5 million cycles. The polyethylene wear was calculated as the difference of the initial insert weight and its weight after wear simulation. The weight was corrected taking into account the fluid absorption of the axially loaded soak control insert. The wear rates were calculated as per ISO 14242-2 using the least squares linear fit relationship between the net mass loss after 5 million cycles and the number of loading cycles (5 million) excluding the zero time point.

The articulation surface and the back side of the polyethylene inserts underwent an optical analysis after 5 million cycles using a digital microscope (VHX-5000, Keyence Corporation, Osaka, Japan) with a 30-fold magnification for the former and a 20-fold magnification for the latter.

The geometrical alterations due to creep and wear after 5 million cycles were assessed by means of a 3D measuring machine (UMM850, Carl Zeiss AG, Oberkochen, Germany) in a tactile measuring mode (1500 points per scan). The geometrical changes were displayed vertically to the transversal plane of the polyethylene inserts with a pseudo-color mode. The uni-axially loaded soak controls exhibited a creep deformation which was responsible for the initial three dimensional changes [41,42]. The creep was subtracted from the overall deformation to obtain the linear wear. For each insert the deformation was calculated as the mean value of the color range at the deepest position.

2.3. Statistics

To determine the wear amount and the wear rates an analysis of variance ANOVA was carried out ($p < .05$) followed by a post hoc test to differentiate between the five material groups (Tukeys HSD-Test, $p < .05$). Prior to analysis, the normal distribution (p-p plots) and the homogeneity of variance (Levene Test) were verified (Statistica R13, TIBCO Software Inc.). A p value < .05 was considered as significant.

3. Results

The gravimetrical wear of the X-ray irradiated materials and of Vitelene® as clinically established reference showed a linear progression [Fig. 1].

The wear simulation test revealed a wear rates of 11.3 ± 0.7 mg/mc for X(80 kGy)-RT, 7.5 ± 0.3 mg/mc for X(100 kGy)-RT, 5.1 ± 0.8 mg/mc for X(80 kGy)-warm, and 2.6 ± 0.1 mg/mc for X (100 kGy)-warm respectively, corresponding to a 34% (at RT) and 50%

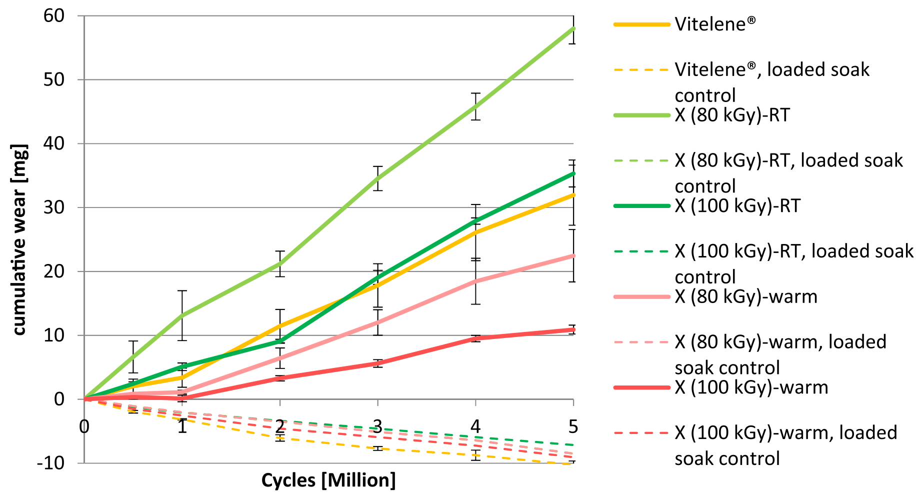

Fig. 1. Gravimetric wear of each material group.

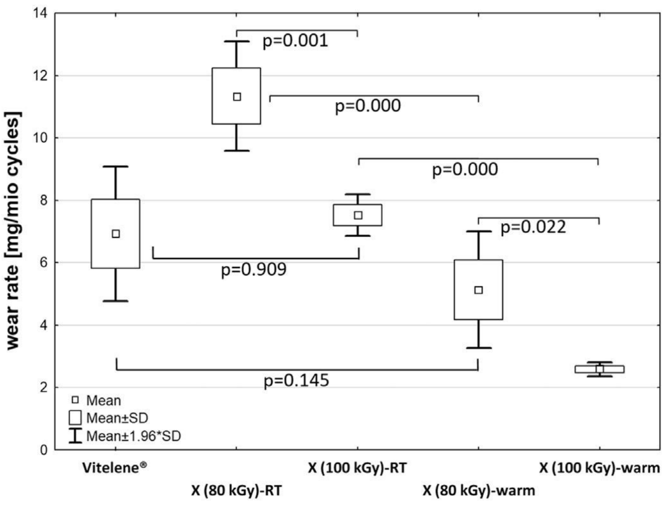

Fig. 2. Wear rate of the four X-ray cross-linked UHMWPE groups in comparison with the e-beam irradiated Vitelene® as clinical established reference. The wear rates were calculated as per ISO 14242-2 using a least squares linear regression between 0.5 and 5 million cycles.

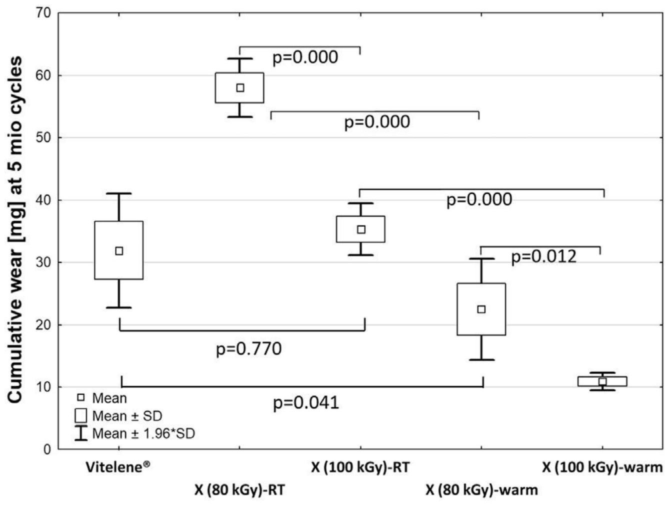

Fig. 3. Cumulative wear of the four X-ray cross-linked UHMWPE groups in comparison with the e-beam cross-linked Vitelene®. Both increasing the dose and enhancing the irradiation temperature led to reduced wear.

(warm) lower wear rate for the material cross-linked with 100 kGy compared to 80 kGy. A similar observation could be made with the irradiation temperature with less wear for the warm irradiated material. X(80 kGy)-warm exhibited 55% less wear than X(80 kGy)-RT and X (100 kGy)-warm 66% less than X(100 kGy)-RT respectively [Fig. 2].

Considering the cumulative wear [Fig. 3] a comparable tendency was seen with 58.0 ± 2.0 mg for X(80 kGy)-RT, 35.3 ± 2.1 mg for X (100 kGy)-RT, 18.5 ± 3.0 mg for X(80 kGy)-warm, and 10.9 ± 0.7 mg for X(100 kGy)-warm respectively, corresponding to a 39% (at RT) and 41% (warm) lower cumulative wear for the material cross-linked with 100 kGy compared to 80 kGy. The wear reduction between warm and RT irradiation amounted over 68%.

With a wear rate of 6.9 ± 1 mg/mc and a cumulative wear of 31.9 ± 6.9 mg e-beam irradiated material Vitelene® had a lower wear rate (64% and 9%) and cumulative wear (82% and 11%) in comparison with X(80 kGy)-RT and X(100 kGy)-RT. However, the difference between Vitelene® and X(100 kGy)-RT was not considered to be statistically significant (p = .909 for the wear rate and p = .770 for the cumulative wear respectively). At elevated temperature it was the opposite: the wear rate of Vitelene® was increased by 26% (p = .145) compared to X(80 kGy)-warm and by 63% compared to X(100 kGy)-warm. The cumulative wear of Vitelene® was 42% and 66% higher than X(80 kGy)-warm (p = .041) and X(100 kGy)-warm (p = .000) respectively [Fig. 1-3].

The volumetric wear rate was calculated as the quotient of the gravimetric wear and the density of UHMWPE (0.940 g/mm^3). For the volumetric wear per year we assumed 1.76 million gait cycles performed per year for an average patient [44] [Table 1].

Third body wear was not observed on the CoCr heads. The macroscopic analysis of the inserts following testing showed neither cracks nor pitting or delamination of the gliding surface. The machining marks remained apparent on the articulation surface of the uni-axially loaded soak controls. The wear simulated specimens exhibited two zones: a polished area and an unworn area where the machining marks were still visible [Fig. 4].

Table 1
Volumetric wear per million cycles and per year.

	Volumetric wear [mm^3/mc]	Volumetric wear [mm^3/year]
Vitelene®	6.8 ± 1.0	12.0 ± 1.7
X(80 kGy)-RT	12.3 ± 0.5	21.7 ± 0.9
X(100 kGy)-RT	7.5 ± 0.4	13.2 ± 0.8
X(80 kGy)-warm	4.8 ± 0.9	8.4 ± 1.6
X(100 kGy)-warm	2.3 ± 0.2	4.1 ± 0.3

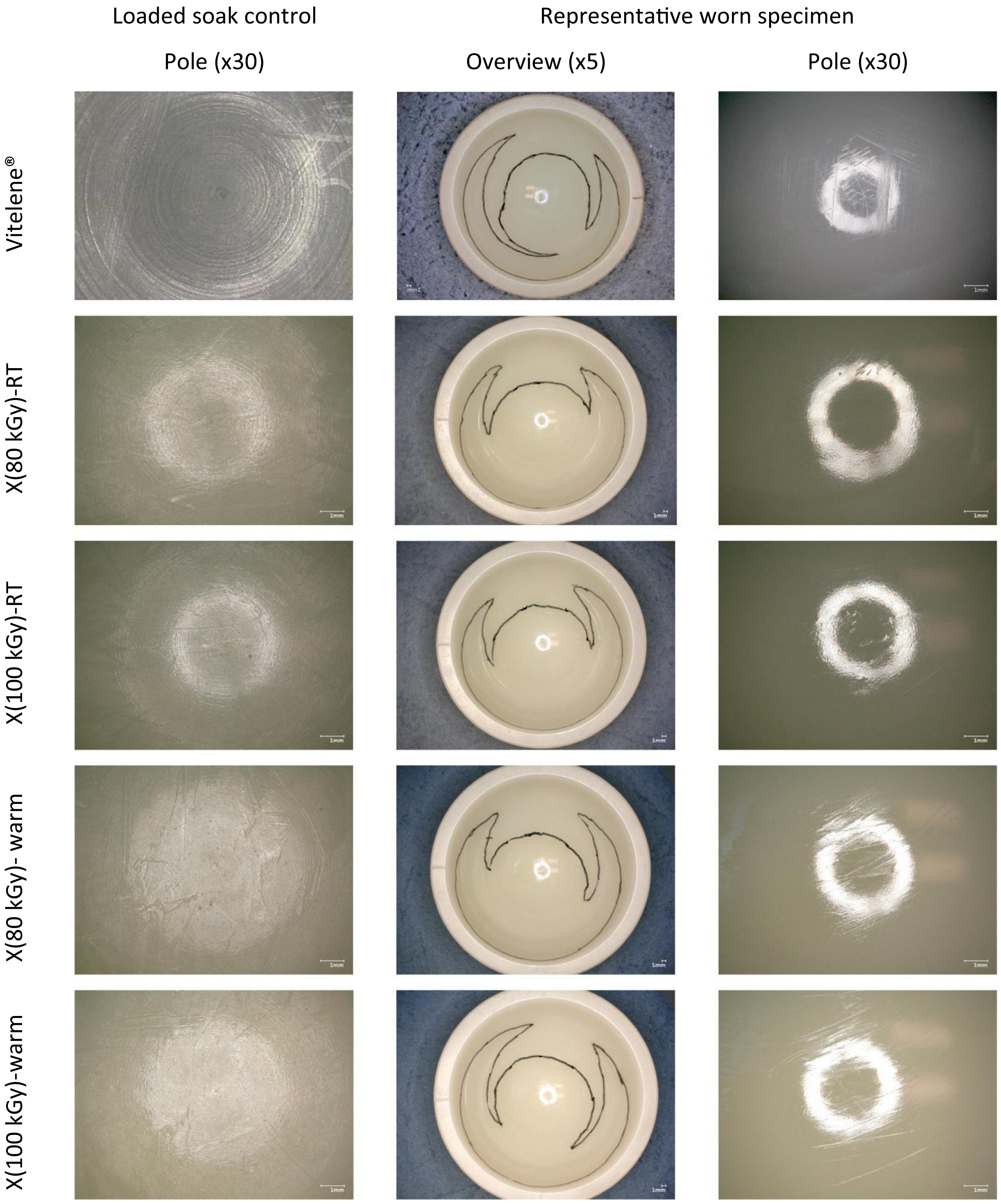

Fig. 4. Articulation surface of the loaded soak control (left) exhibiting the machining marks and of one representative worn specimen after 5 million cycles. Overview (center) showing the two zones (polished into the black line and machining marks outside the black line) and the polished pole area (right).

A minimal amount of wear occurred on the backside of the polyethylene inserts. Only small scratches due to the insertion in and removal out of the corundum blasted titanium cups could be seen. The machining marks were always visible [Fig. 5].

Compared to Vitelene® the initial plastic deformation of the X-ray cross-linked polyethylene was low. The geometrical changes reflected to a limited extent the findings of the gravimetrical and volumetric wear [Fig. 6, Table 2].

For the annual linear wear we assumed 1.76 million gait cycles performed per year by an average patient [44].

4. Discussion

Little or no attention has been paid to X-ray as cross-linking technology so far. The aim of this study was to gain knowledge on the impact of dose and irradiation temperature on the wear behavior of vitamin E blended polyethylene cross-linked by X-ray. The hypothesis was that irradiation source e-beam or X-ray would not affect the wear behavior of the material when processed with same dose and at same temperature.

4.1. Limitations

This study is subjected to limitations. One is the small sample size. Due to the time consuming simulator testing only three specimens per material were tested. However, the obtained results enabled to distinguish between the irradiation method, the dose levels and irradiation temperatures. Also the accelerated aging according to ASTM F2003 could not reproduce all the mechanisms involved in oxidation [23,45–49], thus this simulator testing took predominantly the mechanical wear into account but did not reproduce the chemical alteration [50]. Moreover, we did not analyze the amount and the impact of

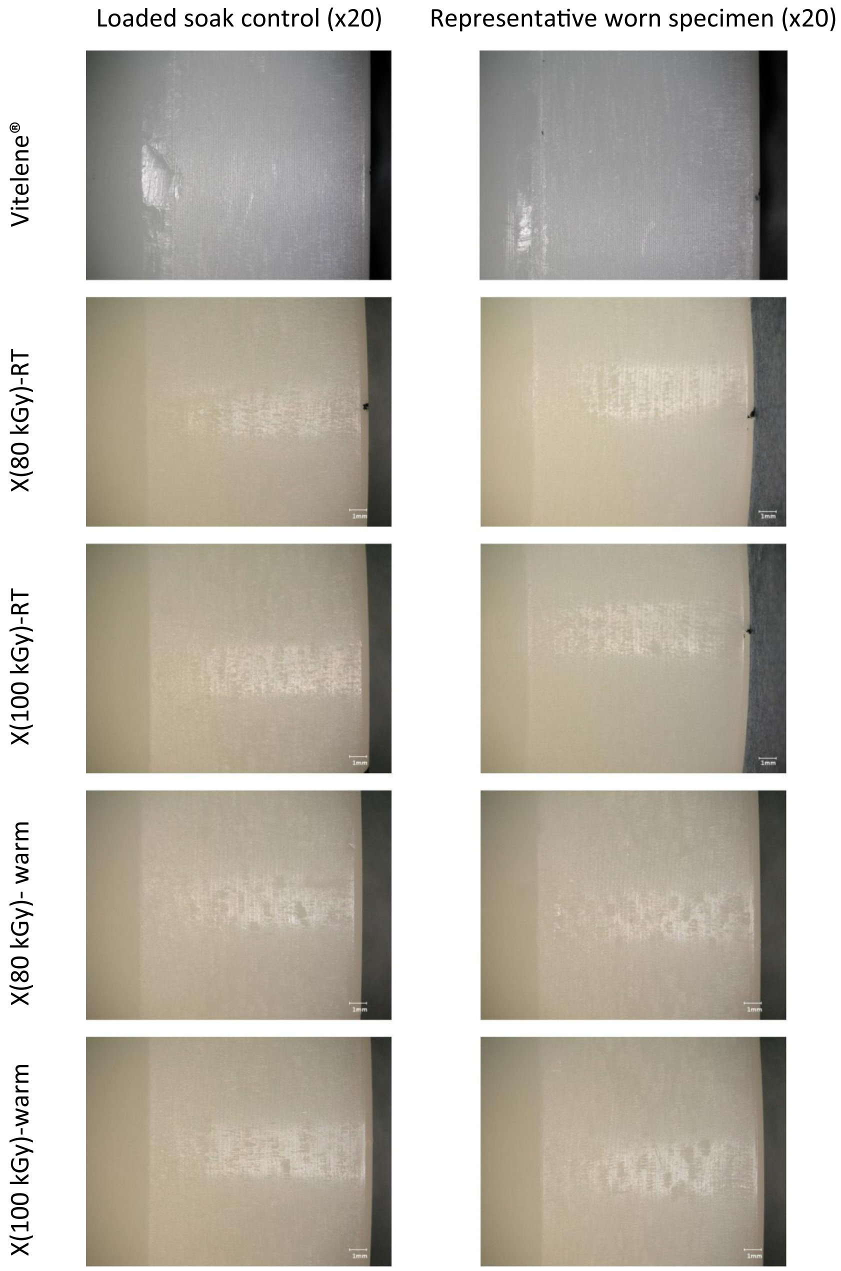

Fig. 5. Backside of the loaded soak control (left) and of one representative tested specimen after 5 million cycles (right) all showing the machining marks and some scratches due to insertion and removal out of the corundum blasted inner surface of the titanium cup.

adsorbed lipids from the serum which are described to strongly (+13–53%) affect the gravimetric measurement of wear [51]. These findings have to be confirmed by further investigations, for example with third-body abrasive wear tests, analysis of the damage modes and particle analysis.

4.2. *Wear behavior*

Although simulator testing is well accepted to determine the wear performance of acetabular inserts, the comparison with the literature was difficult. Most of the trials used Ø36 mm heads and there was a broad distribution of wear rates probably due to variations in wear testing method including lubrication, insert design, analysis and evaluation methods.

The linear course of the gravimetrical wear [Fig. 1] attested an unobtrusive running-in phase where the weight loss due to wear steadily prevailed over the medium intake. Our results (2.6–11.3 mg/mc) were comparable to the findings of the literature (1.0–8.9 mg/mc for Ø36 mm heads) [23,52–54]. Furthermore, we observed a reduction of wear rate and cumulative wear of the X-ray irradiated materials with 100 kGy in comparison with 80 kGy independently of the irradiation temperature (room or 100 °C). Increasing absorbed dose led to more cross-linking, the three dimensional molecular network inhibited the molecular alignment, the formation of fibrils and promoted a better adhesive and abrasive wear resistance [17,19,25,41,55–57]. In other words changes at the molecular level might have influenced the wear behavior [58]. Closer unspecified cross-linked fraction, more entangled amorphous region and lower crystallinity of the warm irradiated material as shown in a previous study [59] might have contributed to the reduction of wear [25,37,57,60–62]. These results have to be considered with caution because the simulator allowed for an optimal positioning of the inserts whereas it is much more difficult to implant

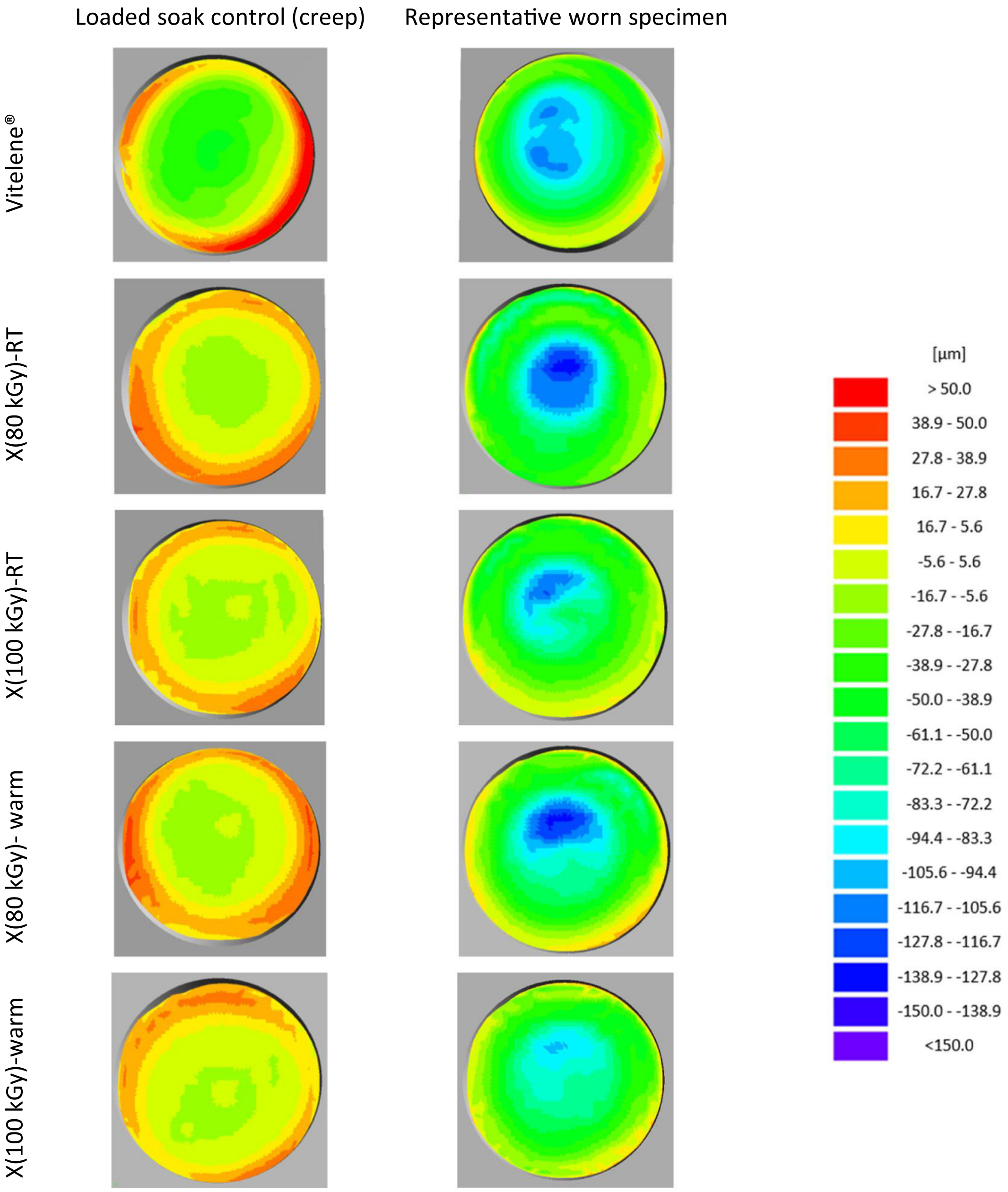

Fig. 6. Three dimensional geometrical change of the loaded soak control "creep" (left) and of a representative specimen "creep and wear" (right).

the cup exactly in the load direction in vivo. An eccentric position would alter the conformity of the articulation and the contact mechanics conducting to higher penetration rates [50].

Concerning the volumetric wear, the X-ray XLPE showed results (2–12 mg/mc corresponding to 4–12 mm^3/year) consistent with the literature. Fisher et al. [53] measured 9.5 mm^3/mc with a Ø36 mm CoCr head, Johnson et al. [52] 2.2–5 mm^3/mc as a function of insert thickness (1.9–7.9 mm) and a Ø36 mm CoCr head as well. Oparaugo et al. [63] highlighted the direct correlation among volumetric wear rates, incidence of osteolysis and revision rates in total hip arthroplasty.

Table 2
3D geometrical changes of the inserts. The deformation corresponds to the deepest area in the cavity. As discussed later, this optical investigation gives a punctual indication about the wear pattern, but is not absolutely representative of the average linear wear.

	Creep [µm] (loaded soak control)	Total deformation [µm]	Wear [µm] (= Total deformation minus Creep)	Linear wear per million cycles [µm/mc]	Linear wear per year [µm/year]
Vitelene®	44.5 ± 0.0	114.9 ± 5.7	70.4 ± 5.7	14.1 ± 1.1	24.8 ± 2.0
X(80 kGy)-RT	11.2 ± 0.0	142.6 ± 8.5	131.5 ± 8.5	26.3 ± 1.7	46.3 ± 3.0
X(100 kGy)-RT	11.2 ± 0.0	118.6 ± 6.4	107.4 ± 6.4	21.5 ± 1.3	37.8 ± 2.3
X(80 kGy)-warm	11.2 ± 0.0	126.0 ± 12.8	114.8 ± 12.8	23.0 ± 2.6	40.4 ± 4.5
X(100 kGy)-warm	11.2 ± 0.0	96.3 ± 6.4	85.1 ± 6.4	17.0 ± 1.3	30.0 ± 2.3

They found that a wear rate of 0–80 mm^3/year rarely led to osteolysis. Kurtz et al. [21] reported a radiographic wear rate of 0.05 mm/year in clinical series as well, corresponding to a volumetric wear rate of 30 mm^3/year for a 28 mm femoral head, making osteolysis very unlikely. Therefore our in vitro findings can be considered to be promising.

It was assumed that the backside wear as observed by Braun et al. which was several times lower than published values of articulating wear [64] and the wear induced through insertion and removal of the inserts was negligible and affected all inserts in the same way so that it did not influence the final result.

The linear wear of the X-ray cross-linked polyethylene inserts (30.0–46.3 mm/year) fell within the same range reported in literature for XLPE: 18.5–95 µm/year [65–67]. Despite worst case configuration in this study with large diameter (Ø40 mm), thin inserts (5 mm) which are known to have inferior wear resistance [41,42] and accelerated aging, the X-ray cross-linked polyethylene achieved in all cases a linear wear rate $<$ 50 µm/year. Dumbleton et al. [68] reported that osteolysis is almost absent at wear rate below 50 µm/year when testing 22–32 mm diameter bearings and proposed a practical wear rate threshold of 100 µm/year, confirmed by Glyn-Jones et al. [69], conscious that larger diameters would lead to more volumetric wear for the same linear penetration. Hence, a transfer to clinical finding has to be done very carefully. Moreover, the determination of the linear wear corresponded to the deepest point of the wear zone and was not representative for the overall surface wear. The 3D geometrical analysis gave an order of magnitude of creep and cumulative geometric head penetration, but seemed not to be adequate to strictly discriminate between the tested materials. However, a consistency of the in vitro and in vivo linear wear after 5 years implantation of the Vitelene® inserts can be noticed: the wear simulated inserts exhibited a linear wear rate of 24.8 µm/year [Table 2] and a linear wear rate of 2–43 µm/year was reported after 5 years in vivo by means of a virtual Computer Assisted Design-based wear analysis using the RayMatch® Software [5].

The irradiation temperature and the dose have been found to affect significantly the wear behavior of the vitamin E blended cross-linked polyethylene, with the temperature having a bigger effect than the dose [Figs. 2 and 3]. Both, increasing the dose and enhancing the irradiation temperature led to reduced wear rate. This outcome corroborated the observations of Oral et al. [70] and Popoola et al. [71] that irradiating vitamin E blended polyethylene at elevated temperature resulted in improved wear resistance. In a former study (unpublished results) we showed a superior oxidative resistance of polyethylene cross-linked by X-ray at elevated temperature. As the preservation of the wear and mechanical behavior depends on oxidation [23,72], a good performance of this material over time can be confidently expected but still needs to be proved.

Several studies [19,56,73,74] recommend a dose of 100 kGy to achieve optimal wear performance, oxidation resistance, mechanical properties and vitamin E preservation. The efficiency of vitamin E as antioxidant has been proven [75] and its presence seemed not to have any deleterious effect on the wear resistance [76]. Our results indicated that vitamin E stabilized polyethylene warm irradiated by X-ray at 80 kGy provided a valuable trade-off. The cross-linking attenuation due to the vitamin E could be compensated by elevating the irradiation temperature. In addition, increasing irradiation temperature promotes the vitamin E grafting onto the polyethylene backbone [70] and seems to be able to reduce the frictional torque [71].

Patients receive a joint implant even earlier and as reported by the Australian National Joint Replacement Registry [1–3] young patients ($<$ 65 years old) experience an increased revision risk. As the latter are rather more active, their implants are subjected to more gait cycles per year [77,78]. Depending on the activity intensity the implants could also be exposed to higher loads over a longer time especially when the patients practice high-impact sports like tennis, football or alpine skiing [79,80]. The requirements to the wear resistance in the long term are correspondingly increased [4,81–83]. Each new modification should enhance or at least not worsen the wear resistance of polyethylene as wear remains the main cause of hip joint implant revision [52,69,84–86].

5. Conclusion

The predominant contribution of cross-linking to the improvement of the wear resistance of polyethylene [17,57,58,76,87–91] and the necessity to warrant a long lasting stabilization against oxidative degradation in vivo are well recognized [48,54]. In this study an alternative cross-linking technology was assessed. It could be shown that X-ray cross-linking at elevated temperature is able to improve the wear resistance of vitamin E blended UHMWPE as well as e-beam cross-linking at elevated temperature did. It is unknown how this oxidative stabilized and X-ray highly cross-linked polyethylene will affect the revision rate, but the in vitro results are encouraging. The finding concerning the wear rate of Vitelene® and X(80 kGy)-warm confirmed our hypothesis that using same absorbed dose and irradiation temperature, e-beam and X-ray will lead to equivalent wear ($p = .145$). However, the results concerning the cumulative wear did not ($p = .041$). They supported the possibility that X-ray cross-linking would further increase the wear resistance of UHMWPE versus e-beam.

Declaration

Competing interests: the authors are employees of Aesculap AG Tuttlingen, a manufacturer of orthopedic implants.

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Ethical approval

Not required.

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6. Veröffentlichungsliste

Originale Forschungspublikationen

1. **Mulliez MA**, Schilling C, Grupp TM. Equivalent mechanical properties of X-ray and E-beam crosslinked vitamin E blended ultrahigh molecular weight polyethylene. J Biomed Mater Res. 2020;1–10. https://doi.org/10.1002/jbm.b.34552
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4. Grupp TM, Holderied M, **Mulliez MA**, Streller R, Jäger M, Blömer W, Utzschneider S (2014), Biotribology of a vitamin E stabilised polyethylene for hip arthroplasty – influence of artificial ageing and third-body particles on wear. Acta Biomaterialia Vol. 10, pp. 3068-3078 doi.org/10.1016./j.jactbio.2014.02.052

Vorträge

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Poster

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