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ABSTRACT: Sequence-coded polyurethanes were tested as anti-counterfeiting tags for the labelling of methacrylate-based intraocular implants. These sequence-defined oligomers were prepared by solid-phase iterative chemistry using two comonomers allowing formation of a controlled 0/1 binary sequence. Tags with different sequences and chain-lengths were synthesized and tested for lenses labeling. Two main methods were investigated for incorporating the tags in the intraocular implants. In a first approach, they were included *in situ* during the free-radical copolymerization of 2-ethoxyethyl methacrylate and ethylene glycol dimethylacrylate. In another strategy, premade lenses were swollen in a THF solution containing the polyurethane tags and dried. Both approaches allowed successful incorporation of the polyurethane labels in the methacrylate networks. In order to demonstrate this, the tags were extracted from the lenses using a solvent swelling protocol and analyzed by electrospray mass spectrometry. In all cases, the labels were found and their coded sequences could be identified by tandem mass spectrometry sequencing. These results indicate that sequence-coded polyurethane tags represent a valid option for the labeling of implants. Importantly, it was shown in this work that the use of small weight fractions of polyurethane tag (i.e. 0.1-0.4 wt%) do not alter significantly the biocompatibility and transparency properties of the intraocular lenses.

1. Introduction

In recent years, the increasing production of counterfeit products had a major impact on global world's economy and industry. In this context, the need for protecting consumers, entrepreneurs and manufacturers is becoming more and more indispensable, in particular in pharmaceutical industry and, more generally, in biosciences where the health and life of consumers can be endangered by cheap replicas of genuine products.[1-2] As a consequence, a wide variety of anti-counterfeiting technologies has been described and patented over the last decades. For example, the use of nano or molecular identification tags is not only interesting for distinguishing a genuine product from a counterfeit but also for enabling a manufacturer to track production date and batch number of a given product. Such traceability tags may be particularly relevant for labeling drugs, implants, prosthesis and other *in vivo* materials, which have to comply with strict regulations and norms.[3-7] However, in such demanding applications, important parameters such as the biocompatibility and biodegradability of the identification tag have to be taken into account. Yet, the labeling of biomedical products is crucial when problems occur after a long period of *in vivo* use, in particular in the case of health complications and lawsuits.

Among the wide range of concepts that have been suggested for developing anti-counterfeiting materials, the use of sequence-controlled polymers has been recently proposed as an interesting new option.[8] In such polymers, information is stored at the molecular level in the form of a coded monomer sequence that can be read using a sequencing technology.[9-10] DNA is, of course, the archetypal example of a sequence-coded polymer that can be used as identification barcode for product labeling.[11] However, synthetic information-containing macromolecules may also be used for such a purpose.[12-14] Various routes for the preparation of uniform (i.e. monodisperse) sequence-defined polymers have been reported in the literature in recent years.[15-22] and it has been evidenced that these precision macromolecules open very interesting avenues for materials design.[8, 23-29] For instance, our group has described in recent years the synthesis and tandem mass spectrometry (MS/MS) sequencing of different classes of non-natural information-containing polymers including poly(phosphodiesters),[30-31] poly(triazole amide)s,[32-34] poly(alkoxyamine amide)s,[35-38] poly(alkoxyamine phosphodiester)s,[39] and polyurethanes (PUs).[13] The latter class of polymers is particularly appealing for anti-counterfeit technologies since PUs constitute a very well-known class of polymer materials with extensively studied physico-chemical properties.[40] For instance, it was shown in previous works that uniform digitally-encoded oligourethanes, which contain a binary sequence built with two monomers defined arbitrarily as 0 and 1 bits **(Figure 1a)**, can be used as molecular barcodes and blended in low amounts in other polymer materials such as casted polystyrene films and methacrylate-based photo-crosslinked 3D prints.[13] In all cases, the barcodes could be easily extracted from the host polymer matrices and readily identified by MS/MS. Thus, these sequence-coded polymers seem promising for tagging a wide variety of materials and, in particular, biomedical materials since PUs are known to be biocompatible and therefore used in a variety of medical devices ranging from simple catheters to artificial hearts.[41] For instance, PUs constitute the most commonly

used class of materials for blood-compatible devices such as artificial heart valves and arteries. PUs are also used in many other bio-applications such a drug-delivery, surgery and ophthalmology.[42-43]

In this context, the present article describes the use of digitally-encoded polyurethanes as molecular tags for the labeling of hydrophobic intraocular lenses. Ophthalmic implants constitute a widespread class of materials that are very often used after cataract surgery.[44] Although very different types of intraocular lenses are used on the market, these materials are often obtained by free radical polymerization of methacrylates. Historically, the first monomer used for the preparation of intraocular lenses was methyl methacrylate but in order to respect recent surgical procedures requiring a very small incision in the corner of the eye to introduce the lens, the methyl methacrylate was quickly replaced by a mixture of hydrophobic and hydrophilic methacrylates that can be homopolymerized or copolymerized to obtain the optimal properties, e.g. high refractive index, flexibility, shape memory and biocompatibility.[45] Despite the fact that important technological progress has been made in this field during the last decades, ophthalmic implants have usually an expiration date and their efficiency decreases with use and time. Therefore, the idea to incorporate a molecular identification barcode directly in the polymethacrylate matrix of intraocular implants is relevant since it should enable product identification after long period of times even if the original packaging is lost or thrown away. In order to illustrate the versatility of this concept, digitally-encoded polyurethanes were incorporated in two different types of lenses. In a first approach, the PU tags were dispersed in a methacrylate solution and included *in situ* in the lenses during molded thermal methacrylate polymerization **(Figure 1b)**. Alternatively, the tags were included in a ready-made commercial implant using a facile swelling/deswelling procedure **(Figure 1c)**. In both cases, the PU-tagged materials were studied by MS/MS sequencing. In addition, the biocompatibility and the transparency of the modified lenses were tested using standardized tests.

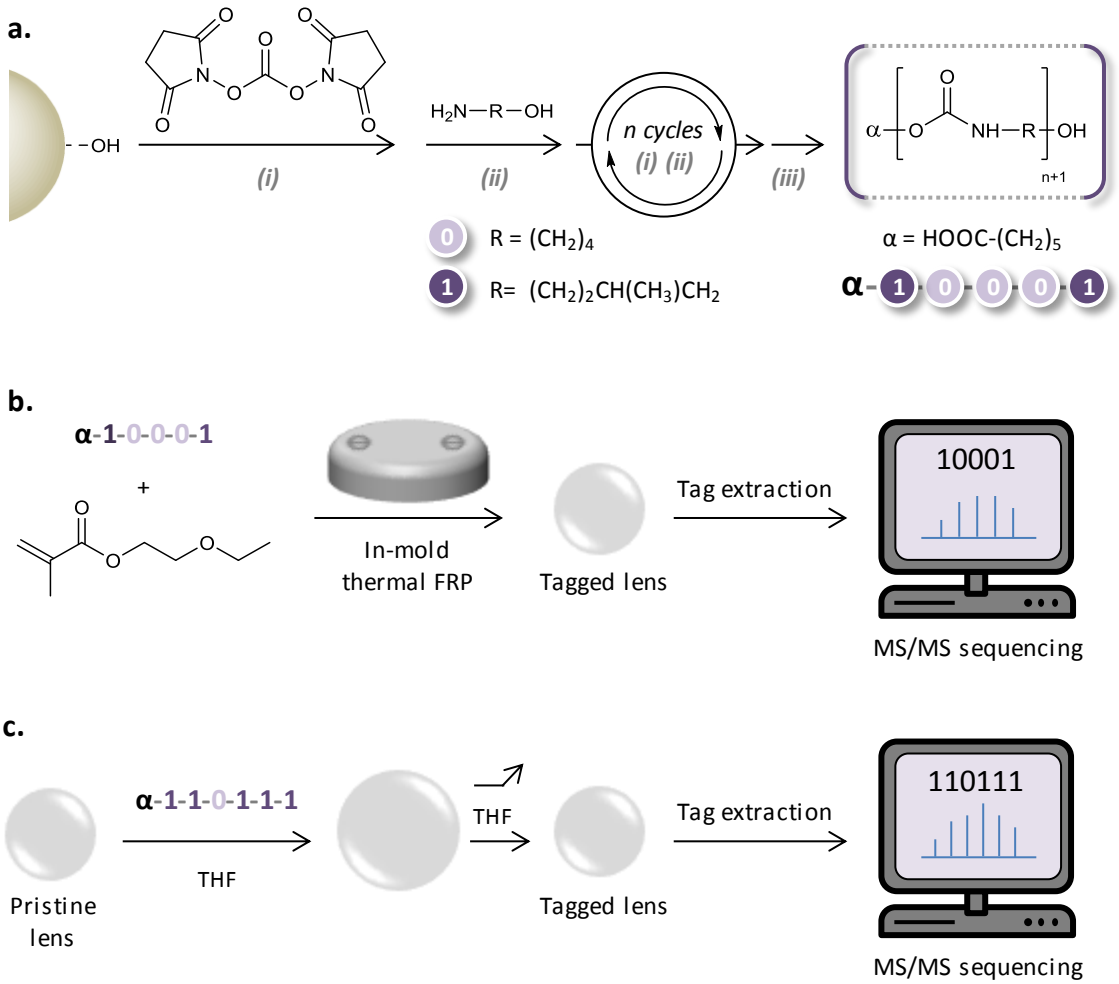

Figure 1. (**a**) General route used for the solid-phase orthogonal synthesis of sequence-coded polyurethanes.[13] Experimental conditions: *(i)* ACN, triethylamine, microwave, 60°C; *(ii)* DMF, triethylamine, RT; *(iii)* Cleavage: TFA/DCM, RT. (**b**) Direct lens-labelling obtained by *in situ* free radical polymerization (FRP) of 2-ethoxyethyl methacrylate in the presence of a polyurethane tag. (**c**) Swelling/deswelling strategy used for the polyurethane-labelling of premade lenses.

2. Experimental part

2.1. Materials

4-Amino-1-butanol (TCI, 98%), 4-amino-2-methyl-1-butanol (TCI, 98%),%), *N*,*N'*-disuccinimidyl carbonate (DSC, TCI, >98.0%), triethylamine (TEA, Merck, >97%), 2-ethoxyethyl methacrylate (EEMA, Sigma-Aldrich, 99%, stabilized with hydroquinone monomethyl ether), ethylene glycol dimethylacrylate (EGDMA, Sigma-Aldrich, 98%, stabilized with monomethyl ether hydroquinone), Luperox® 26 (LC26, Arkema), anhydrous acetonitrile (dry ACN, Sigma-Aldrich, 99.8%), anhydrous dichloromethane (dry DCM, Sigma-Aldrich, ≥99.9%, 40-150 ppm amylene), dichloromethane (DCM, Sigma-Aldrich, ≥99.9%) (Carlo Erba), diethyl ether (Carlo Erba), anhydrous N,N-dimethylformamide (dry DMF, Sigma-Aldrich, 99.8%), N,N-dimethylformamide, (DMF, Sigma-Aldrich, ≥99.0%), tetrahydrofuran (THF, Aldrich, 99%, stabilized with BHT) were used as purchased. Commercial Artis® intraocular lenses were kindly provided by Acrylian (Strasbourg, France). The Wang resin used for sequence-defined polyurethane synthesis was modified with a cleavable linker as described in the literature.[13] Methanol (Fisher Chemical) and ammonium acetate (Sigma-Aldrich) were used as received for mass spectrometry experiments.

2.2. Solid-phase synthesis of sequence-coded polyurethanes

Digitally-encoded polyurethanes were synthesized following a recently-described orthogonal iterative protocol.[13] In brief, these polymers were prepared on a hydroxy-functionalized crosslinked polystyrene resin using the coupling steps shown in Figure 1a. In a first step, the resin (100 mg, 1 Eq.) was reacted for 1h with di(*N*-succinimidyl) carbonate (6 Eq.) in the presence of TEA in dry ACN under microwave irradiation (Monowave 300, Anton Paar, 60°C, 8W). Afterwards, the resin was transferred into a solid-phase extraction tube and washed several times with DMF. In a second step, the activated resin was reacted for 20 min at RT with an excess amino-alcohol (i.e. 4-amino-1-butanol **0**, or 4-amino-2-methyl-1-butanol **1**, 10 Eq.) in the presence of TEA in dry DMF. Then, the resin was washed with DMF, diethyl ether and transferred back to a microwave tube. These two coupling steps were repeated successively a given number of times in order to reach a desired sequence and chain-length. The final polyurethanes were cleaved from the resin using a TFA/CH_2Cl_2 mixture (5:5 v/v). After filtering-off the resin, TFA and CH_2Cl_2 are evaporated under reduced pressure to afford the desired polyurethanes as a white solid.

2.3. Direct lens labeling by *in situ* free radical polymerization in the presence of a polyurethane tag

The free radical polymerization was performed in a commercial mold (Acrylian, Strasbourg, France) allowing synthesis of a lens-shaped crosslinked methacrylate network. A digitally encoded polyurethane (0.1-0.4%wt as compared to EEMA) was first dissolved in 1 mL of warm THF and then gently mixed in a mixture of 2-ethoxyethyl methacrylate (3 g, 18.96 mmol, 1 Eq.),

the crosslinker EGDMA (0.06 g, 0.303 mmol, 0.02 Eq.) and the radical initiator LC26 (0.03 g, 0.139 mmol, 0,01 Eq.). The mixture was left for 1h in order to avoid the formation of bubbles, poured in the mold and placed in an oven at 55^{o}C for 18 hours. It should be noted that degassing is not strictly necessary in these experiments. After polymerization, the mold was opened and the crosslinked transparent lens was removed from it.

2.4. Labelling of premade lenses using a swelling/deswelling strategy in the presence of a polyurethane tag

The following strategy can be used to label commercial Artis® lenses or non-commercial ones obtained by in-mold free radical polymerization of EEMA. In all cases, the lenses were first swollen in THF for 15 minutes. Afterwards, pure THF was removed and replaced by a solution of a digitally encoded polyurethane in THF (the oligomer was previously dissolved in warm THF). The lens was kept in the solution for 5-8 hours and it was then placed in a closed vial with holes in the cap. Deswelling and drying was performed by letting THF evaporate slowly at RT for approximately two days.

2.5. Polyurethane tags extraction and analysis by electrospray mass spectrometry

Extraction of PU tags from lenses was performed in an ultrasonic bath (10-15 min) and using a methanol solution of ammonium acetate (3 mM). This solution composition was selected to fit requirements for best ionization of PUs in case the extracts could not be diluted prior to ESI-MS. Different experimental conditions were tested, all allowing sufficiently concentrated extracts to be obtained. Either a piece (5-25 mg) or the whole tagged lens (5-25 mg) was immersed in a minimum solvent volume (200-500 µL or 1-3 mL, respectively). So-obtained solutions were perfectly clear and eventually further diluted (1/10 to 1/100, v/v) prior infusion in the ESI source at 10 µL/ min using a syringe pump. High resolution MS and MS/MS experiments were performed using a QqTOF mass spectrometer (QStar Elite, Applied Biosystems SCIEX, Concord, ON, Canada) with the ESI source operated in the negative mode (capillary voltage: -4200 V; cone voltage: -75 V). Ions were accurately mass measured in the orthogonal acceleration time-of-flight (oa-TOF) mass analyzer, using PEG oligomers adducted with an acetate anion (in MS) or the precursor ions (in MS/MS) as internal standards. In this instrument, air was used as nebulizing gas (10 psi) while nitrogen was used as curtain gas (20 psi) and collision gas. Instrument control, data acquisition and data processing were achieved using Analyst software (QS 2.0) provided by Applied Biosystems. PU oligomers (1-2 mg) were dissolved in methanol (300 µL) in an ultrasonic bath (15 min). Samples were further diluted (1/100 to 1/1000, v/v) in a methanolic solution of ammonium acetate (3 mM) and injected in the ESI source at 10 µL/min using a syringe pump.

2.6. Biocompatibility tests

In order to check their biocompatibility, the polyurethane-tagged lenses were tested using the standard ISO 11979-5:2006 procedure that permits to detect extractible additives. First, the

lenses were dried at 60°C ± 5°C under vacuum for 48h in order to remove traces of moisture. Then, a piece a lens of approximately 0.1 mg was weighed and placed in the extraction cartridge of the Soxhlet apparatus. The flask was filled with deionized water (70% of its capacity) and placed in a heated oil-bath to reflux water vigorously. After 4 hours, the water was allowed to cool down to RT and the sample was taken out. The water was concentrated to a final volume of 10 mL and analyzed by UPLC-MS using a Waters apparatus equipped with a PDA and a single quadrupole mass spectrometer (3100 SQ Waters). The measurements were performed on a RP18 column (1.7 µm, 2.1x50 mm) using water with 0.1% of formic acid and acetonitrile with 0.1 % of formic acid as eluents; gradient 95/5 and 5/95 in 5 minutes. Similar results were obtained after direct ESI-MS analysis by infusing water extracts (after a 1/10 dilution in methanol supplemented with 3 mM ammonium acetate) into the ionization source using a syringe pump. The lens piece was left drying for several days and weighed in order to assess its weight loss.

2.7. Transparency test

The lenses were immersed in a black walled aquarium equipped with 220V LED white light and filled with deionized water. The lenses were left at 35°C for 10 days. A Nikon D7100 camera covered with black curtain was placed in a distance of 40 cm from the center of the front glass of the aquarium. Pictures from all the lenses were captured at the same time.

2.8. Accelerated microvacuole test

The lenses were immersed in a bottle filled with deionized water that was closed and placed in an oven at 45±1 °C for 24 hours. Afterwards, the lenses were transferred to another bottle filled with water. The bottle was placed in a closed box made from expanded polystyrene. The temperature in the box and in the water was 37±1 °C and a B1 series microscope equipped with a Nikon D7100 camera was placed next to the bottle at the same temperature. After 2.5 hours, each lens was observed through the microscope and several photos were captured from the entire surface.

3. Results and discussion

Sequence-coded polyurethanes were used as readable barcodes for the traceability and anti-counterfeiting labeling of intraocular implants. These sequence-defined oligomers were synthesized by stepwise orthogonal solid-phase synthesis as shown in Figure 1a.[13] Two successive coupling steps are used in this strategy to form uniform polyurethanes. In a first step, a resin-immobilized alcohol function is reacted with *N*,*N*'-disuccinimidyl carbonate in order to form an activated succinimide carbonate mono-adduct on the solid support. This reactive function is then selectively reacted in a second step with the primary amine function of an amino alcohol building block to afford a hydroxy-functional carbamate unit. These two consecutive steps can be repeated a certain number of times until a desired chain-length is reached.[13] In order to form readable binary sequences, two amino alcohols building blocks, namely 4-amino-1-butanol and 4-amino-2-methyl-1-butanol, were used and set as coding moieties **0** and **1**,

respectively. After synthesis, the sequence-coded polyurethanes are cleaved from the resin and purified. Depending on the amount of information that should be stored in a barcode, coded sequences may be of different size. Thus, five polyurethanes, with different lengths and sequences, were studied in this work as shown in Table 1. All these polymers were characterized by high-resolution electrospray ionization mass spectrometry (HR-ESI-MS), which indicated in all case formation of uniform polymers **(Table 1 and Figures S1-S5)**. Furthermore, the coded sequences were examined by tandem mass spectrometry (MS/MS), which confirmed that the expected sequences were obtained in all cases **(Figures S1-S5)**. As indicated in a previous publication, the MS/MS sequencing of sequence-coded polyurethanes is remarkably easy when a negative ionization mode is used.[13]

Table 1. HR-ESI-MS characterization of the sequence-coded polyurethanes that were tested as barcodes in the present work.

	Sequence	**Yield (%)**	m/z_{th} [a]	m/z_{exp} [a]
PU1	α-0-0-0-1	88	605.3403	605.3403
PU2	α-0-0-1-0	60	605.3403	605.3399
PU3	α-1-0-0-0-1	87	734.4193	734.4191
PU4	α-1-1-0-1-1-1	100	891.5296	891.5286
PU5	α-0-0-1-1-1-1-1-0	77	1121.6562	1121.6557

[a] Theoretical and experimental *m/z* values found by ESI-MS for deprotonated molecules $[M-H]^-$.

The incorporation of the sequence-coded polyurethane in intraocular implants was then tested. As discussed in the introduction, one of the interesting advantages of polyurethanes is that their physico-chemistry and miscibility with other polymer materials is well-documented in the literature.[46] In the present case, the intraocular implants are covalently crosslinked networks obtained by free-radical (co)polymerization of polar methacrylates. Thus, two main routes were studied in this work for lens-labeling **(Figure 1)**. In the first approach, the polyurethane tags were incorporated *in situ* during network formation **(Figure 1b)**. Although various methacrylates can be used to prepare intraocular implants, 2-ethoxyethyl methacrylate was investigated in the present work as a model monomer and ethylene glycol dimethylacrylate was selected as a bifunctional crosslinker. The polymerizations were initiated by a peroxide initiator Luperox® 26 and were performed in bulk at 55°C in a commercial mold that gives a lens-shape to the formed networks. In order to select the best conditions for lens preparation, a series of model experiments was first performed in the presence of different amounts of crosslinker EGDMA ranging from 1-6 wt% as compared to EEMA (data not shown). These experiments evidenced that the use of 2 wt% of EGDMA is optimal for obtained defect-free intraocular implants. Above that number, the crosslinked poly(2-ethoxyethyl methacrylate) (*c*-PEEMA) lenses may contain pronounced defects such as wrinkles and sometimes white lumps. Below that number, the lenses may become brittle and fragile when swollen in a good solvent like THF. Thus, this optimized amount of EGDMA was used in all further polymerizations conducted in the presence of the

polyurethane labels. However, initial attempts to incorporate the tags *in situ* during the thermal copolymerization of EEMA and EGDMA were unsuccessful. In bulk conditions, the polyurethane labels were found to be poorly soluble in EEMA and therefore lenses with tiny macroscopic defects were obtained.

Table 2. Description of the tagged implants prepared and studied in this work.

	Labeling strategy	**Type**	**Label**	**Loading (wt%)**
L1	*in situ*	*c*-PEEMA	PU1	0.1[a]
L2	*in situ*	*c*-PEEMA	PU2	0.1[a]
L3	*in situ*	*c*-PEEMA	PU3	0.4[a]
L4	*in situ*	*c*-PEEMA	PU4	0.3[a]
L5	Swelling	Artis®	PU1	0.4[b]
L6	Swelling	Artis®	PU2	0.3[b]
L7	Swelling	Artis®	PU4	1.2[b]
L8	Swelling	*c*-PEEMA	PU5	0.14[b]

[a)] For tagged lenses prepared by an *in-situ* approach, the loading value represents the weight fraction PU/EEMA. [b)] For tagged lenses prepared by a swelling/deswelling approach, the loading value corresponds to the weight fraction PU/THF.

To solve this problem, the coded oligomers were first dissolved in a small quantity of warm THF that was afterwards mixed with the reaction medium (THF/EEMA 1:3.1 v/v). In these conditions, defect-free transparent tagged lenses were obtained **(Table 2)**. Yet, the incorporation of polyurethane labels in the *c*-PEEMA networks could potentially lead to unwished property changes. Thus, the optical and biocompatibility properties of the polyurethane-loaded implants were studied and compared to those of pristine samples. First of all, a standard transparency test was performed **(Figure 2)**. In this test, the tagged and non-tagged lenses were placed in water for several days under intense white light exposure. Non-optimal lenses usually show intense opacity after such a treatment as shown in the reference scale of Figure 2. However, tagged *c*-PEEMA lenses remain overall transparent, thus suggesting that the polyurethane label do not affect significantly the optical properties of the materials. Weak whitening was observed in some samples but these defects were not more pronounced than in pristine *c*-PEEMA lenses. Perhaps more importantly, a microvacuole test was performed **(Figure S6)**. It is well-known that microvacuole-induced glistening effects may significantly impair the properties of (meth)acrylate-based intraocular implants.[47-48] Figure S6 compares optical microscopy images that were taken for the **PU1**-loaded lens **L1** and for a pristine *c*-PEEMA lens after performing the accelerated microvacuole test. It appears clearly that the presence of polyurethane tags does not influence the diameter and number of observed microvacuoles, thus confirming further that the small amounts of incorporated labels do not alter significantly the optical properties of the implants. Furthermore, an ISO test was done in order to verify the biocompatibility of the tagged-lenses. The aim of this test is to detect traces of monomer, tag or other contaminants that may leak out of the lenses when exposed to aqueous environment and thus lead to eye irritation

or other harmful effects. In brief, the lenses were immersed in boiling water for some hours in order to extract potential contaminants and the water was afterwards analyzed by UPLC-MS. The polyurethane labels could not be detected in any cases after performing this test, thus suggesting that *(i)* the label is not leaching out of the lenses in aqueous environment or *(ii)* that it was no incorporated at all in the lenses. The latter scenario was discarded by the mass spectrometry analysis of the tagged lenses. In order to extract the polyurethane labels from the *c*-PEEMA networks, the lenses were placed for 10 minutes in a methanolic solution of ammonium acetate. In all cases, the polyurethane labels were detected by ESI-MS analysis **(Figure 3a and Figures S7-S9)**. Furthermore, the MS/MS analysis of the found oligomers allowed unequivocal decryption of their coded binary sequences **(Figure 3b and Figures S7-S9)**. These results indicate that the polyurethane labels retain their molecular integrity after formation of the network by free radical polymerization and also suggest that they are predominantly physically entrapped in the *c*-PEEMA networks. Perhaps more importantly, mass spectrometry data confirm that the sequence-coded polyurethane barcodes can be stored in biomedical implants and that the information that they contain can be easily recovered.

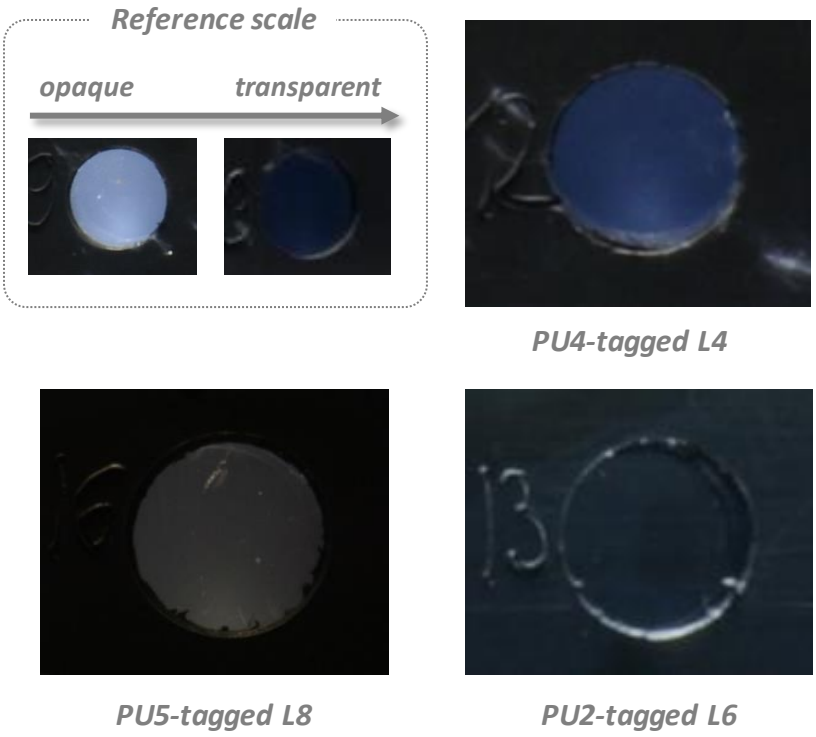

Figure 2. Transparency tests performed for samples **L4**, **L6** and **L8** that was loaded by swelling with **PU4**, **PU5** and **PU2** respectively. The reference scale on the left shows typical opacity of poor and optimal model lenses. The bluish/non-bluish color of the images depends on the

distance between the water-immersed lenses and the camera and should not be interpreted as a sign of opacity.

In order to demonstrate further the versatility of this concept, a swelling/deswelling approach was also tested for lens labeling **(Figure 1c)**. As shown in Table 2, this strategy can be applied to *c*-PEEMA lenses but also to other types of methacrylate-based implants such as commercial Artis® lenses. In this approach, the lenses are simply swollen in THF and afterwards exposed to a THF solution containing a polyurethane label. After some hours, the THF-swollen lenses were dried in order to entrap the labels in the networks. It is important to note that this drying process should be performed slowly since fast drying may result in cracks and even complete breakage of the fragile lenses. The modified lenses were also subjected to optical and biocompatibility tests. Transparency and microvacuole tests evidenced formation of highly transparent materials **(Figure 2 and Figure S6)** and suggested that the swelling/deswelling approach is probably even more suitable than the *in situ* approach, although it should be considered that polyurethane-loading is probably about four times lower when the labels are incorporated by swelling rather than by *in situ* polymerization. On the other hand, traces of the polyurethane labels were detected by UPLC-MS after performing the biocompatibility tests. These findings are probably due to the fact that the polyurethane labels are not only incorporated inside the methacrylate networks but also physically adsorbed on the external surface of the lenses after THF drying. In order to solve that problem, the surfaces of the loaded lenses were first cleaned by immersion in hot water and afterwards rinsed with clean water. The cleaned up lenses were subjected to the biocompatibility test again and no polyurethane leakage could be detected anymore. All the lenses tagged via the swelling/deswelling procedure were also analyzed by MS and MS/MS **(Figure 3 and Figure S10)**. As shown in Figure 3b, the polyurethane tags were efficiently extracted from the lenses and sequenced by MS/MS.

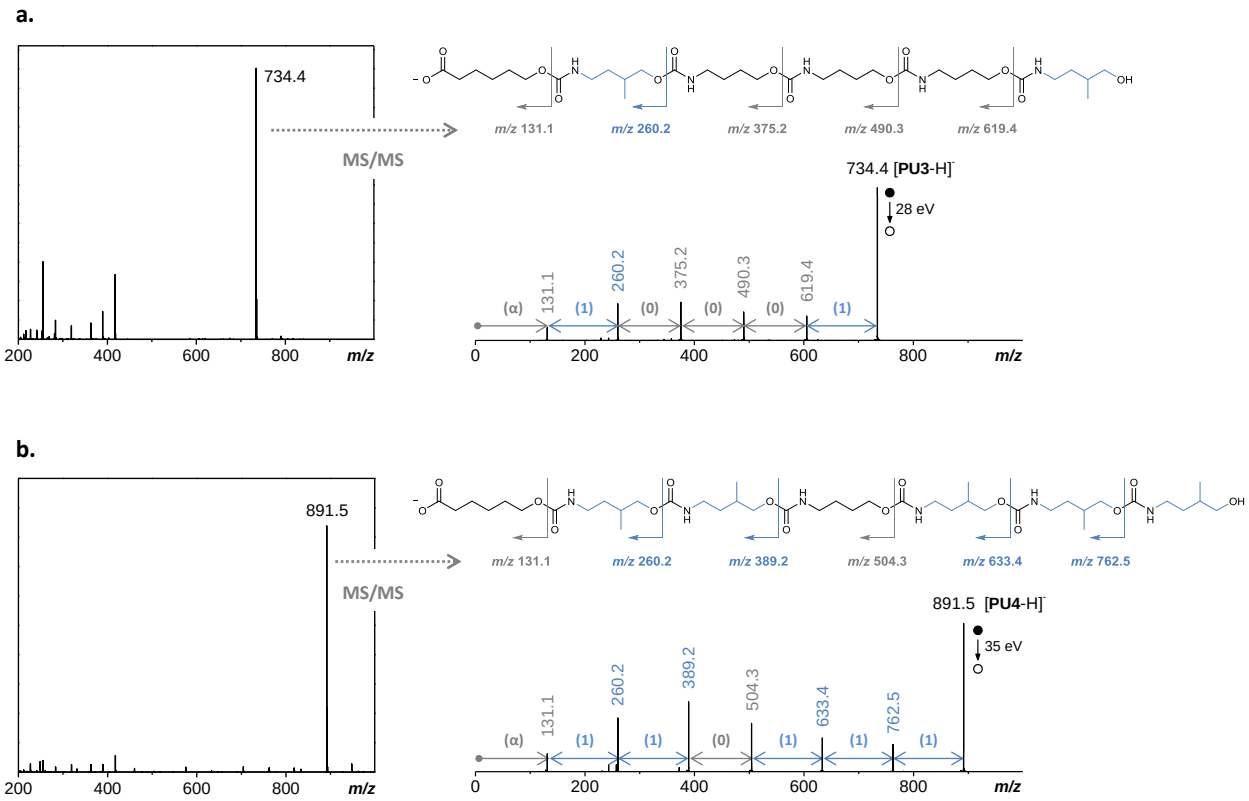

Figure 3. ESI-MS (left) and MS/MS (right) characterization of polyurethane tags extracted from (**a**) sample **L3** prepared by free-radical polymerization of 2-ethoxyethyl methacrylate in the presence of **PU3** and (**b**) from the Artis® intraocular lens **L7** that was loaded with **PU4**.

4. Conclusion

Methacrylate-based intraocular implants were labeled with small amounts of sequence-coded polyurethanes that can be used as traceability and anti-counterfeiting barcodes. Two different strategies were investigated for incorporating the sequence-defined oligomers in the lenses. In a first approach, the label was included *in situ* during the formation of the crosslinked methacrylate network. In an alternative strategy, the polyurethane barcode was included in a premade lens using a simple THF swelling/deswelling procedure. Both approaches led to the successful preparation of polyurethane-tagged intraocular implants. In all cases, it was verified that the incorporation of the polyurethane barcodes does not modify drastically the optical properties of the lenses and also does not lead to significant aqueous release of contaminants that could be potentially irritant or harmful to the eyes. Furthermore, it was demonstrated that the polyurethane tags can be easily extracted from the lenses and characterized by mass spectrometry. In particular, their coded sequences can be easily deciphered by MS/MS, thus opening interesting opportunities for traceability and anti-counterfeit labeling of intraocular implants. Yet, it should

be noted that only short model sequences were studied in the present work. For real industrial applications, longer barcodes containing a higher amount of information may be needed. Furthermore, before thinking about biomedical use, the toxicity of these new PUs oligomers shall also be carefully assessed. Nevertheless, this first proof-of-concept underlines the relevance of these materials for implant tagging. More generally speaking, sequence-coded polyurethane barcodes could be relevant for labeling a wide range of biomaterials and biomedical devices.

Supporting Information

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