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The influence of low-temperature sterilization procedures on piezoelectric ceramics for biomedical applications

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ABSTRACT

Piezoelectric materials are intensively investigated for usage in biomedical applications ranging from *in vivo* sensors and energy harvesters to implants for bone and neural cell stimulation. Besides the high requirements for reliability and low cytotoxicity, implantable materials must be sterilizable without losing their functionality. In this study, we investigate the impact of low temperature plasma sterilization and the associated cleaning routines on the piezoelectric properties of PZT, BCZT and KNN bulk ceramics. The stability of the piezoelectric response strongly depends on the material system, with BCZT ceramics showing the strongest decline in properties. Several factors were identified to contribute to this reduction of the piezoelectric coefficient, the most important being mechanical stress due to sample handling as well as chemical reactions during cleaning, disinfection and sterilization. The study highlights the importance of evaluating the impact of all influencing factors along the pre-implantation handling chain in the material selection process.

1. Introduction

Perovskite-based piezoelectric ceramics are today utilized in many applications like sensors, piezo-motors and ultrasound devices, where their coupling between electrical and mechanical energy is exploited [1]. In recent years, the potential of piezoelectric materials for biomedical applications has become apparent and opened up a rapidly growing, interdisciplinary research field [2–9]. The developmental efforts range from transferring established knowledge on sensing [10], actuating [11] and energy harvesting [12] to the biomedical realm, but aim as well for novel applications such as neural and bone tissue stimulation [13,14].

In the development of any new device and implant material, it is important to not only consider its initial functionality and general non-toxicity, but as well its compatibility with regulatory stipulated pre-implantation routines such as cleaning and terminal sterilization. Guidance on the overall development process is helpfully outlined in ISO 13485:2016. Sterilization is an important process to prevent the transmission of bacteria, viruses and other infectious contaminants such as prions. There are numerous options for terminal sterilization of medical devices and implants, but only some may suit the given device and material. A validated technique must verify that sterilization assurance limits are met for the final product without having deleterious impact on the functional properties of the device or its constituent materials. The American Food and Drug Administration (FDA) divides the methods currently used to sterilize medical devices into three categories; traditional, non-traditional and novel non-traditional [15]. The traditional methods have a long record of reliable use, have been thoroughly studied and from which standards have been developed. Examples are moist (ISO17665–1:2006) and dry heat (ISO 20857:2010), gamma and electron beam radiation (ISO 11137–1:2006) and ethylene oxide gas (ISO 11135:2014) sterilization. Although these methods are known to be efficient, the standards are periodically revised and new methods are being developed because of stricter regulations, new materials and practical limitations. The non-traditional methods encompass ozone and hydrogen peroxide gas plasma sterilization and are methods that do not have recognized standards, but non the less have been cleared by the FDA based on reliable validation studies. Chlorine dioxide, high intensity light or pulse light, microwave radiation, sound waves and ultraviolet light are all novel non-traditional sterilization methods that have not been sufficiently evaluated and thus are not cleared by the FDA [15].

When considering suitable sterilization techniques for piezoelectric materials, one has to be aware of their operating temperature range, which must not surpass the Curie temperature in case the material is of ferroelectric nature. For temperatures higher than the Curie temperature

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the polar characteristics of ferroelectric materials are lost due to a phase transition to a non-polar crystal symmetry and hence the macroscopic piezoelectric effect vanishes. For ferroelectric materials having a low Curie temperature (<100 °C) this is of special importance as it limits the use of traditional heat-based sterilization techniques operating at T > 120 °C.

In this study, the effect of the low temperature hydrogen peroxide gas plasma (LTHPGP) method on the piezoelectric properties of $Pb(Zr,Ti)O_3$ (PZT), $(Ba,Ca)(Zr,Ti)O_3$ (BCZT) and $(K,Na)NbO_3$ (KNN) ceramics is investigated. Both BCZT and KNN are considered promising systems for biomedical applications due to their low cell toxicity [2,5,6,9]. PZT was used as reference material. The sterilization method chosen operates at temperatures below 100 °C and has become a common procedure at clinical facilities due to its practical and safe use. It is comprised of a cleaning and disinfection step prior to the actual sterilization procedure. The impact of both steps on the materials piezoelectric performance has been studied separately with a focus on chemical, thermal, mechanical and time-dependent effects.

2. Experimental

For the synthesis of $Ba_{0.9}Ca_{0.1}Zr_{0.1}Ti_{0.9}O_3$ (BCZT) ceramics samples, powders of $BaCO_3$ (99.98%; Sigma Aldrich, US), $CaCO_3$ (99.0%; Sigma Aldrich, US), TiO_2 (99.99%; Sigma Aldrich, US) and ZrO_2 (99.978%, Alfa Aeasar, US) were used. The powders were dried and mixed in stoichiometric amounts prior to milling for 24 h in 96% ethanol using 5 mm zirconia balls as grinding media. The dried and sieved powder mixture was then pressed into 25 mm diameter disks in a uniaxial press. The disks were calcined in a zirconia crucible at 1300 °C for 2 h using 350 °C/h and 400 °C/h as heating and cooling rate, respectively. The calcined samples were crushed, and the milling, drying and sieving procedure was repeated. The calcined powder was uniaxially pressed into 10 mm diameter disks. Sintering was conducted in Pt crucibles with the samples partially covered in a bed of sacrificial powder. The samples were held at 1400 °C for 6 h using the same heating and cooling rate as for the calcination.

To produce $K_{0.5}Na_{0.5}NbO_3$ (KNN) ceramic samples, raw, spray pyrolyzed powder (Cerpotech, Norway) was milled for 24 h in 100% ethanol. The powder was dried and calcined in an alumina crucible at 650 °C for 5 h using 180 °C/h and 600 °C/h as heating and cooling rate, respectively. Subsequently, the powders were milled, dried, sieved and pressed into pellets using the same procedure as for the BCZT ceramic samples. Pressed pellets were covered in sacrificial powder and were sintered in alumina crucibles at 1125 °C for 2 h using 300 °C/h and 600 °C/h as heating and cooling rate, respectively.

The sintered pellets of both BCZT and KNN were ground from both sides down to approx. 1 mm thickness using 1200 grit SiC paper. Afterwards, they were cleaned in an ultrasonic bath using ethanol for 10 min before they were dried at 100 °C for 24 h. Gold electrodes were deposited on half of each batch of the BCZT and KNN samples (S150B sputter coater, Edwards, UK).

Commercially available lead zirconate titanate (PZT) ceramics of 10 mm diameter and 1 mm thickness were received both with co-fired silver electrodes and without electrodes (PIC151, PI Ceramics, Germany).

An in-house corona discharge single tip electrode setup was utilized to pole the samples. A description of the setup and the poling procedure can be found elsewhere [16].

The piezoelectric coefficient d_{33} of the corona poled samples was measured by the direct method on a YE2730A d_{33} -meter (APC International Ltd., China) applying 0.25 N at 100 Hz. Readings were taken 10 s after sample insertion. Each sample was measured on both sides and the average of the absolute value is given. Samples poled without electrodes were coated with gold electrodes prior to d_{33} measurements.

The time dependent permittivity was measured using a TF Analyzer 2000 piezotester (aixACCT, Germany) using 50 mV/mm amplitude and a frequency of 1 kHz. 25 data points were collected over the course of 24 h.

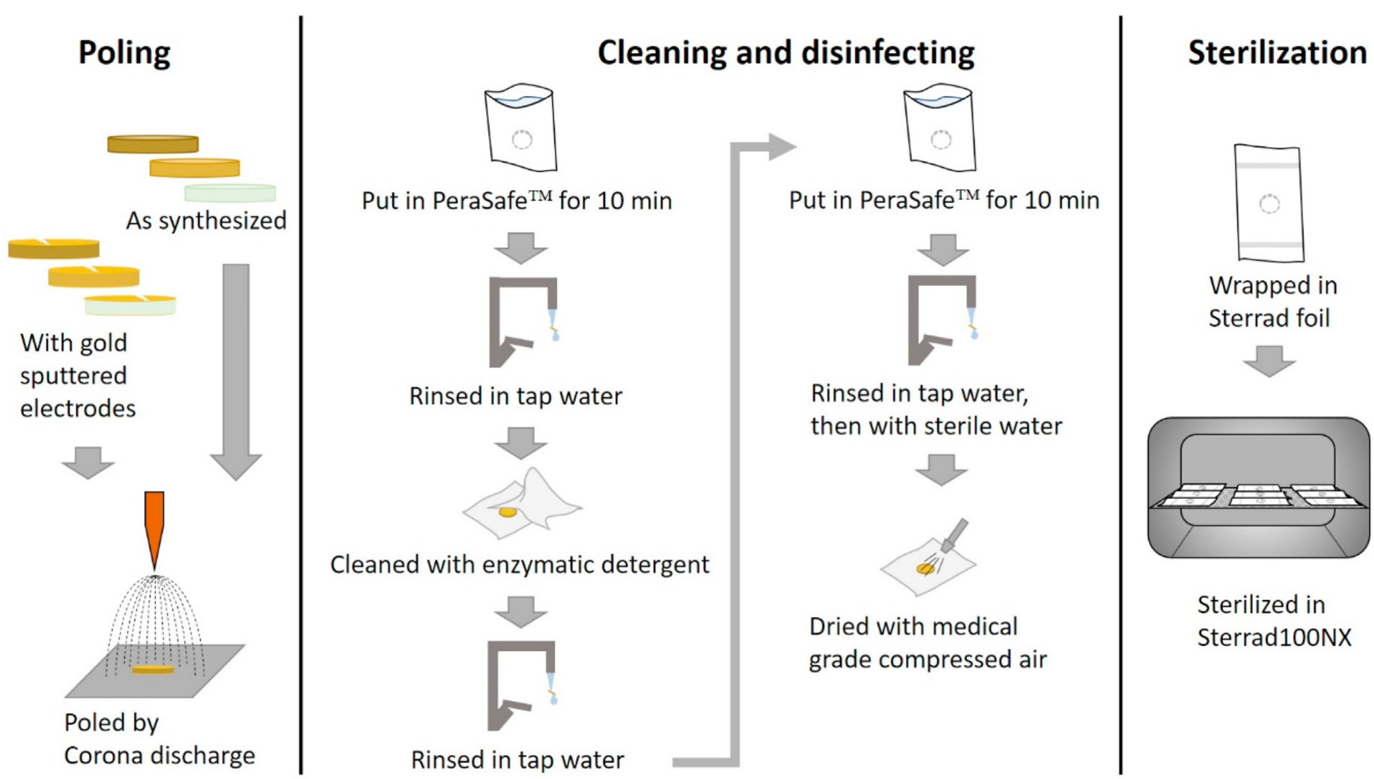

Fig. 1. Flowchart of the sample preparation and the following cleaning, disinfecting and sterilization process.

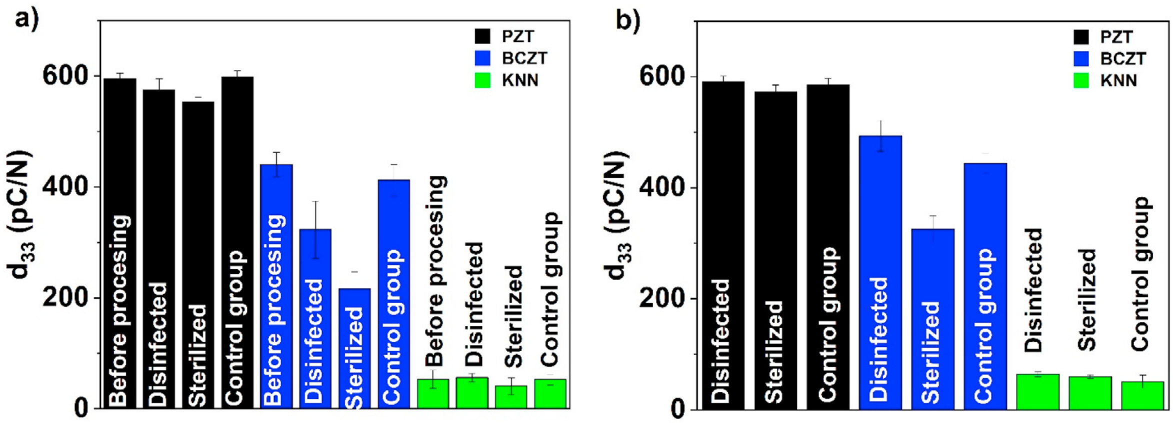

Fig. 2. Impact of disinfection and sterilization on the piezoelectric coefficient of PZT, BCZT and KNN ceramics for a) samples with electrodes and b) without electrodes. The results show the average of 15 samples "Before processing" and the average of 5 for all other data points. Also, note that the category "Disinfected" covers the samples that underwent both the cleaning and disinfecting procedure (Fig. 1).

Temperature dependent permittivity measurements were performed using the same instrument with a 3 V/mm amplitude and 1 kHz frequency (TREK 610 E, Advanced Energy, US). The temperature was ramped from room temperature to 110 °C with a heating rate of 2 °C/min.

AC-conductivity was determined using a Novocontrol Dielectric Measurement System (Novocontrol, Germany). Measurements were conducted at room temperature using an electric field of $0.5V_{rms}$/mm and a frequency range from 10^{-2} Hz–10^{5} Hz.

Contact angle measurements were performed on non-electroded samples using a Drop Shape Analyzer (Krüss DSA 100, Germany). Prior to the first measurements the samples were polished using 4000 grit SiC paper and cleaned in an ultrasound bath for 10 min followed by heat treatment at 400 °C for 1 h in a conventional furnace. Five measurements were performed on each side of each pellet after poling and repeated after the sterilization procedure.

The steps of the full sterilization procedure are shown in Fig. 1. Both electroded samples and non-electroded samples were corona poled prior to the procedure. Cleaning and disinfecting contained the steps described in the following: the pellets were submerged in a solution of Rely + On™ PeraSafe (Lanxess, Germany) and kept submerged for 10 min before rinsed in tap water. Then they were manually cleaned with enzymatic detergent (SumaMed enzyme, Lilleborg, Norway), rinsed in tap water and submerged a second time in PeraSafe for 10 min. After that the samples were rinsed in tap water and then with sterile water before they were dried using medical grade compressed air. For sterilization, the samples were wrapped individually in Sterrad foil and sterilized using the Sterrad NX (Sterrad®, Advanced Sterilization Products (ASP), Johnson & Johnson) standard program. In the sterilization process the wrapped specimens are placed in a chamber that is evacuated prior to exposure to a hydrogen peroxide vapor. After the vapor has entered into all available space, an electromagnetic field is switched on (50 kHz at 500 W) to sublimate the peroxide into a cold plasma consisting of electrons, UV light and reactive species such as hydroxyl and atomic oxygen radicals. The maximum temperature measured inside the chamber during the cycle did not exceed 50 °C. After the reaction, the active components recombine forming oxygen and water and the system is ventilated. The full cycle is repeated once to ensure effective sterilization.

To investigate the influence of the different steps in the sterilization procedure on the piezoelectric performance, each composition batch was split into three sub-batches of 5 samples each. One batch underwent only the "Cleaning and disinfecting" part, another batch was subjected to both "Cleaning and disinfecting" and "Sterilization" (Fig. 1), while the last batch was used as control group and was not subjected to any treatment.

3. Results and discussion

The impact of the disinfection and sterilization procedure on the piezoelectric performance of the three compositions investigated is shown in Fig. 2. The corresponding values are given in Table 1. Fig. 2 a) displays the results for samples that were electroded during the whole procedure. It can be seen that the PZT ceramics experience only a small reduction of the piezoelectric coefficient, both after the disinfection only as well as after the additional sterilization step. The control group shows

Table 1
Mean d_{33} values and corresponding errors of the data plotted in Fig. 2.

d_{33} (pC/N)	Before processing	Error (+/-)	Disinfected and cleaned	Error (+/-)	Sterilized	Error (+/-)	Control	Error (+/-)
w/ electrodes								
PZT	595	11	575	21	553	9	598	11
BCZT	441	22	323	51	217	30	413	28
KNN	53	17	56	7	41	15	53	10
w/o electrodes								
PZT	N.A.	-	591	11	572	13	585	12
BCZT	N.A.	-	493	28	326	24	444	19
KNN	N.A.	-	64	4	60	3	51	12

no degradation of the piezoelectric performance over time. A comparable, yet strongly amplified trend was observed for the BCZT ceramics. It is evident that the piezoelectric coefficient drops about 25% for each of the consecutive steps of the process. The control group shows slightly reduced d_{33} values on average, but still within the error margin with the measurements taken before processing. The piezoelectric performance of the KNN ceramics was rather low to begin with. One can observe a lower average d_{33} value after the sterilization process, but the parameter varies still only within the error margins.

Fig. 2 b) displays the results of a comparable study but conducted with samples that were not electroded during the poling, disinfection and sterilization procedure. This scenario is relevant as no electrodes are needed when these materials are used *in vivo* e.g. as hard tissue implants for cell stimulation. As such, it must be clarified if the change in surface material as well as electric boundary conditions have an influence on the stability of the piezoelectric performance. For PZT, one can observe that the d_{33} values are more stable throughout the procedure compared to their electroded siblings, with only a slight reduction in d_{33} after the sterilization procedure.

This trend is similar for the BCZT ceramics. While there is a significant reduction in d_{33} of about 27% after sterilization compared to the control group, the piezoelectric response appears more stable compared to the electrode counterparts, where a reduction of about 48% was observed. It must be pointed out that for the BCZT ceramics the electroded sample batch was on average thicker than the sample batch without electrodes. As the conditions during corona discharge poling were the same for both batches, it is expected that better dipole alignment is achieved for the sample batch without electrodes. This is reflected in the overall higher d_{33} values compared to the electroded sample batch. The KNN samples display again only minor changes within the error margins.

The comparison of electroded and non-electroded samples highlights first of all that it is feasible to pole samples equally well using the corona technique independent of the presence of electrodes [16]. This is a great advantage for biomedical applications where piezoelectric materials are supposed to be in direct contact with living tissue. Furthermore, the observed differences indicate that the overall poling state is more stable in the non-electroded case under the same external stimuli. Within thin film research, the changes in electrostatic boundary conditions as induced by the presence and absence of electrodes have been associated with variations of built-in electric fields that significantly influence the stability of the poling state and as such the piezoelectric characteristics [17]. While the influence of electrode material on switching kinetics and piezoelectric response of bulk ceramics is considered to be negligible [18], the electric boundary conditions (e.g. open circuit vs. closed circuit conditions) can still determine the long-term stability of the poling state and its susceptibility towards external stimuli. Samples subjected to mechanical load under open circuit conditions were found to exhibit more stable strain response compared to similar samples kept under closed circuit conditions [19]. The difference in electric boundary conditions imposed by the presence or absence of electrodes might therefor be the reason for the observation of a more stable polarization state of the non-electroded samples.

From the results in Fig. 2 it is clear that the sterilization procedure affects the piezoelectric response of the investigated compositions in a similar way but to a different extend. While PZT and KNN ceramics show only slight changes to their initial piezoelectric performance, BCZT ceramics experience a significant change of this parameter. The continuous reduction of d_{33} with each handling step highlights furthermore that not only the sterilization procedure in itself is critical to the materials performance, but that other factors seem to be relevant as well.

Degradation of piezoelectric properties is usually described under the collective terms “ageing” and “fatigue” [20]. Whereas ageing is related to a spontaneous loss in functional performance with time under external equilibrium conditions, fatigue is characterized as a decrease in functionality during operation where a cyclic mechanical or electrical load is applied. In the present case, the samples were subjected to a number of different measurements and handling routines, meaning that various factors have to be considered to clarify the origins of the observed degradation.

The core question of the present investigation is how the disinfection and sterilization processes influence the piezoelectric performance and several sources for degradation have been identified: chemical reactions of the sample surfaces with the disinfecting agents and/or the sterilization plasma, mechanical pressure applied during the handling of the samples, elevated temperature during the sterilization procedure and simply the effect of time. In the following, we will address these factors one by one.

4. Ageing at room temperature

A reduction of piezoelectric performance is observed in some materials even without any electrical or mechanical stimulus, e.g. they age over time [20]. Ageing is commonly associated with the presence of defect dipoles or a high number of oxygen vacancies that tend to compensate the internal depolarization fields and pin domain walls. Both for the commercial PZT ceramic investigated as well as for non-doped KNN ceramics no reports on ageing behavior are available. However, acceptor-doped $BaTiO_3$ has been one of the core materials for ageing studies and BCZT ceramics were reported to display property degradation due to ageing as well [21]. The influence of time on the piezoelectric properties can be seen from a comparison of the piezoelectric coefficient before processing with its control group (Fig. 2). The ageing time between the initial measurements of the electroded samples (“before processing”, Fig. 2 a)) and after the sterilization procedure (“control group”) was two days. Whereas both PZT and KNN show no variation in their piezoelectric response as expected, the BCZT ceramics developed a reduction of the piezoelectric performance of about 7.4% during this time period. This could indicate a contribution of ageing, however, the change observed in Fig. 2 falls within the error margins of the measurement.

To get a better picture of the influence of time on the property stability of the BCZT ceramics, the permittivity of a freshly poled, electroded ceramic sample was measured at certain time points over the course of a day (Fig. 3). Permittivity was investigated in this case as it can be measured with a better resolution compared to the piezoelectric coefficient and as such lower electric fields can be used minimizing the influence of the measurement procedure. A continuous change in permittivity up to 8.2% was observed over the measurement period. One can see indications for a leveling of the permittivity for the longest times

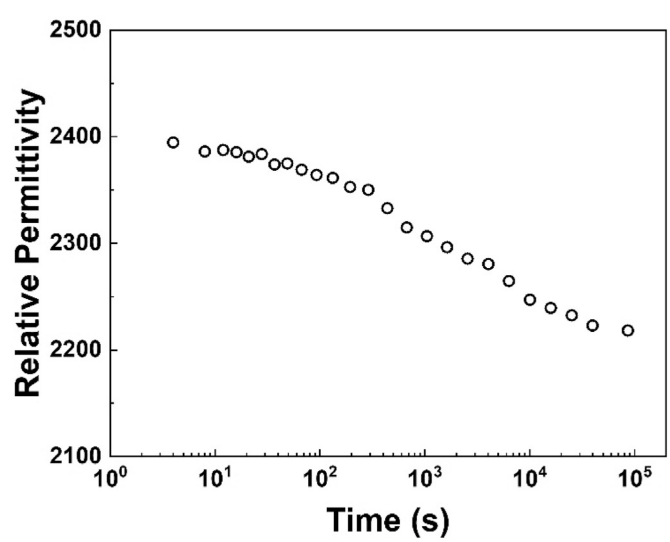

Fig. 3. Time dependent relative permittivity used to estimate the effect of ageing in BCZT ceramics.

points in Fig. 3. However, long term ageing measurements show significant reduction of the piezoelectric response for more than 30 days [22]. It should be noted that ageing processes in general can degrade piezoelectric properties over very long timeframes of months and years [23, 24]. This highlights the importance to investigate and control this material behavior within applications.

5. Chemical interactions

To monitor changes to the surface chemistry introduced by the disinfection and sterilization procedure, the wetting angle before and after these two steps was recorded for the non-electroded samples (Fig. 4). In addition, the measurement would be a first indicator for the materials suitability for biomedical purposes, as liquid interaction with biological tissue is of high importance for successful implantation [25]. For the PZT ceramics, the wetting angle is around 70° before the sterilization procedure and drops to about 50° afterwards. The reduction in wetting angle after plasma treatment is expected, as plasma cleaning is a standard procedure to improve the wetting angle of substrates before the deposition of thin films and coatings [26]. In contrast to PZT, both BCZT and KNN show only small changes of the average contact angle after the samples were subjected to the disinfection and sterilization routine. This might indicate that other factors than cleaning the surface from adhered species play a role.

The cleaning and disinfection step subjects all samples to a commercial sterilization agent, an enzymatic detergent as well as water. This procedure can potentially damage the electrodes as well as influence the chemical composition on the surface of the samples. To test the influence of the cleaning/disinfection step on the electronic properties, AC-conductivity was measured before and after each step (Fig. 5). After disinfection the samples exhibit a significant increase in conductivity at frequencies of 10^4 Hz and below. The increase in conductivity can not be explained by a deterioration of the electrode as in that case a reduction in σ' would be expected. Furthermore, the property change is spread over a broad frequency range, rather indicating a change in the bulk properties. It has been reported for several piezoelectric materials with perovskite structure that release of A-site cations occurs easily in contact with water-based solutions and the literature suggests that a B-site terminated surface is created [27–29]. Furthermore, significant changes in the surface microstructure of bulk BT ceramics after one day of immersion in water have been observed [30]. Even though the whole cleaning and disinfection procedure is completed in less than an hour, it can be expected that significant dissolution has occurred during this step, leaving the surface structure altered both in terms of surface chemistry and local morphology. The cation field strength (Z/r^2, with Z being the cation valency and r being the ionic radius), which is typically used to describe the stability of glass networks [31], has been suggested as an indicator for the stability of a cation within the perovskite structure as well [28]. For the A-site cations present in the investigated systems, the cation field strength ranks them in the following order: $K^+<Na^+<Ba^{2+}<Pb^{2+}<Ca^{2+}$. The Pb cations are stronger bound in the crystal structure compared to the main A-site cations of the other two systems. This supports the observation that the PZT surface chemistry is the least affected by the cleaning/disinfection procedure and follows the expected reduction in wetting angle. For BCZT and KNN ceramics surface chemistry and topography might have been altered through the loss of A-site cations, counteracting the expected reduction in wetting angle. The leaching of A-site cations from ceramic powders is commonly described to stop as soon as a B-site terminated surface is reached [28]. However, for bulk ceramic samples continuous changes in microstructure were observed at least up to 7 days in contact with water [30]. Continuous leaching of Ba ions will lead to the creation of point defects in the affected surface layer of the samples, which can be the origin of the observed increase in conductivity. To further investigate the role of the electrode and bulk properties, the samples were re-sputtered with an additional layer of gold. Fig. 5 clearly shows that this procedure restores the electric properties of the sample, e.g. the conductivity decreases to the original values. A reduction in conductivity after application of another layer of gold is not likely. However, the process of making new electrodes includes the removal of the sputtered gold and the sample surface from the rim of the sample. Assuming that the change in conductivity originates from the electric properties of the sample surface that was altered during disinfection, it becomes clear that removal of this surface layer from the sample rim disrupts the continuous conductive layer, which is reflected in the reduction of conductivity after the new electrodes were applied.

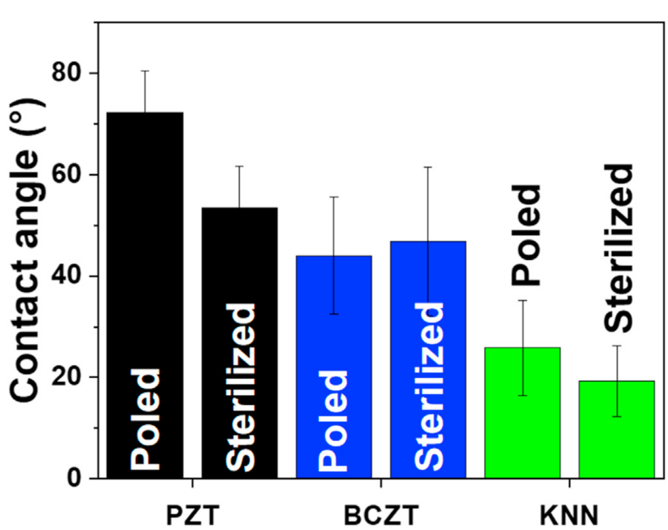

Fig. 4. Wetting angle of PZT, BCZT and KNN ceramics after poling and after sterilization. Five measurements were performed on each side of each pellet and the average is plotted.

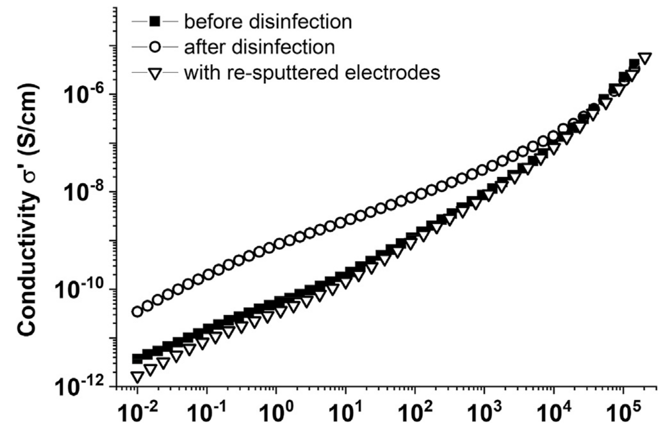

Fig. 5. Frequency dependent AC-conductivity of BCZT measured before and after disinfection as well as after an additional layer of gold electrode was applied.

The creation of a conductive surface layer is as well supported by the differences observed for electroded and non electroded samples (Fig. 2). Electroded samples with a conductive surface layer correspond to a "closed circuit" configuration, in which the piezoelectric properties are destabilized, because the conductive layer allows charges to flow from one electrode of the sample to the other. For samples that did not have electrodes during the disinfection and sterilization procedure, the electrodes were applied afterwards and the more conductive rim of the samples was removed. The lack of highly conductive electrodes during the treatment and the removal of the conductive connection between the electrodes during measurement, makes these samples less susceptible to external stimuli and their piezoelectric response more stable [19].

6. Elevated temperature during sterilization

Already small changes in temperature can alter the piezoelectric response of a material. One reason can be the variation in ageing dynamics as discussed in the previous paragraph, another can be the alteration of the poling state due to proximity to a phase transition temperature. Subjecting piezoelectric samples to a thermal cycle across a phase transition temperature between two polar phases or between a polar and non-polar phase (Curie temperature T_C) can alter their piezoelectric response significantly. The plasma sterilization procedure utilized is a low temperature sterilization technique. The temperature was monitored at various locations within the sterilization chamber throughout the process and did not exceed 50 °C at any time. For both PZT and KNN ceramics no influence on their piezoelectric response is expected due to this temperature variation, as the PZT ceramics have a Curie temperature of $T_C = 250$ °C [32], while KNN ceramics show a phase transition between two polar phases around 220 °C and $T_C = 420$ °C [33]. The situation is different though for BCZT ceramics. Thermal cycling of a different BCZT ceramics across orthorhombic-tetragonal phase transition revealed a reduction of the piezoelectric coefficient of 40% for only 30 thermal cycles [34]. For the present composition a polar-to-polar phase transition is observed at 59 °C and the Curie temperature upon heating is found to be 102 °C (Fig. S1 – Supplementary). While the Curie temperature upon cooling can occur 5–10 °C lower compared to the one observed during heating [35], it is significantly above the maximum operating temperature during sterilization. However, due to the proximity of the operating temperature to the polar-to-polar transition, the exposure to 50 °C has to be considered as one cause for the degradation of the piezoelectric properties. The BCZT ceramics were therefor subjected to a heat treatment at 50 °C for 1 h, which is comparable to the maximum temperature and duration during the sterilization treatment. The piezoelectric coefficient is not reduced due to this heat treatment, highlighting that the proximity of the maximum temperature during sterilization to the polar-to-polar phase transition does not deteriorate the poling state and the piezoelectric performance (Fig. S2 - Supplementary).

While the overall chamber temperature should not have affected the piezoelectric properties, another source for local changes in sample temperature must be taken into account. In the present plasma sterilization process reactive species are created from an H_2O_2 gas, with the decomposition of H_2O_2 being highly exothermic. Both $BaTiO_3$ and gold have been reported as catalysts for this reaction [36,37]. This reaction could facilitate a local increase of the sample surface temperature above the average temperature of 50 °C within the chamber, as well as local temperature fluctuations due to the multi-cycle nature of the sterilization process. A local increase of the sample temperature would facilitate the depolarization of the samples as indicated by the drop in d_{33} values in Fig. 2. Furthermore, it is possible that the charged species created during the H_2O_2 decomposition will interact with the sample surfaces and influence the poling state. The correlation between surface adsorbates and local piezoelectric performance has been a subject of study mostly for the interaction with humidity [38–40], showing that adsorption is strongly determined by the polarization orientation of the samples. For both BT and PZT thin films it has been shown that irreversible changes of the surface chemistry can be induced through adsorption of hydroxyl groups that in some cases lead to a non-switchable surface layer. However, bulk properties of these thin films have been reported to be un-affected in their switching characteristics [40]. Characterization of the AC-conductivity after sterilization revealed the same characteristics as observed after the disinfection and cleaning step (Fig. 5). It is, therefore, not expected that further variations in surface chemistry are the cause for the observed changes in the piezoelectric coefficient (Fig. 2).

7. Exposure to mechanical pressure

It is quite striking that both PZT and KNN ceramics are only slightly affected by the disinfection/sterilization procedure, while BCZT ceramics show a drastic reduction of their piezoelectric performance. One difference in basic characteristics of these material systems is the lower Curie temperature and the related lower coercive field of BCZT compared to the other two compositions [16]. BCZT ceramics are electromechanically “soft”, meaning that they are easy to pole, as indicated by the low coercive field, but their susceptibility towards external stimuli makes them as well prone to be depoled. It has been reported that application of mechanical pressure in the range of 50 MPa can induce a reduction of the piezoelectric response by 80% [41]. The coercive stress for similar compositions was found to be 10 MPa, but significant changes to the dielectric properties occur already below this stress value [42]. Mechanical stress is applied in the present experimental procedure in two ways: 1) during the direct measurement of the piezoelectric coefficient, 2) during the manual handing of the samples in the disinfection/sterilization step. In the first case, a force of 0.25 N is applied to the samples using a pin-on-disc electrode configuration, with a pin diameter of 1 mm. This equals an applied pressure of about 3 MPa, which is close to range for which de-poling of BCZT samples has been reported. The influence of this type of measurement on the piezoelectric coefficient can as well be seen in Fig. 6 d_{33} significantly decreases already in the first few seconds of stress application and after 90 s of measurement a reduction of 22.5% is observed.

For the case of the impact of manual handling, the exact load applied to the samples depends on many factors. Assuming the simplest case that the samples are lightly picked up with thumb and index finger and no other force was applied, a rough estimate of 30–40 kPa pressure can be obtained [43]. The actual pressure during manual handling can be assumed to be higher, e.g. manual handling with standard lab tweezers could subject samples to high focal stresses on contact. Even though these stresses might not reach values close to the coercive stress, Fig. 6 clearly shows that application of mechanical pressure way below the coercive stress can cause significant degradation of the piezoelectric response. Furthermore, the electric boundary conditions can have a significant influence on the stability of the piezoelectric response towards mechanical loading [19]. Samples subjected to mechanical stress under open circuit conditions, as it is the case for a sample with low conductivity in a non-conductive medium, show less depolarization compared to samples in closed circuit conditions, as resembled by leaky samples or immersion in conductive media. This indicates that manual handling in water as it occurs during the cleaning and disinfection step can facilitate depolarization. This effect is amplified when electrodes are applied to the samples and charges can easily be re-distributed over the whole sample surface. Furthermore, the cleaning and disinfection procedure might lead to the development of a surface layer with higher conductivity than the bulk, rendering samples with electrodes more conductive in the subsequent measurements and as such more susceptible to the applied mechanical loads. In the case of non-electroded samples, the conductive layer formed on the rim of the samples was removed in the process of applying electrodes before the measurements, thus creating a less conductive state that is beneficial to retain the piezoelectric response. For future implant design, BCZT compositions with higher coercive stress, as found for compositions with purely tetragonal structure, are considered to be more suitable to retain the piezoelectric response throughout the different handling steps. Furthermore, streamlining handling procedures implementing gloved hand handling and usage of rubber-tipped tweezers, could mitigate parts of the observed property degradation.

8. Conclusion

The aim of this investigation was to characterize the impact of a plasma sterilization procedure, commonly used in hospitals, on the piezoelectric performance of BCZT and KNN ceramics. These are promising candidates for use in bioactive hard tissue implants. The stability of the piezoelectric response was found to be strongly dependent on the material system, with KNN ceramics and the PZT reference system being

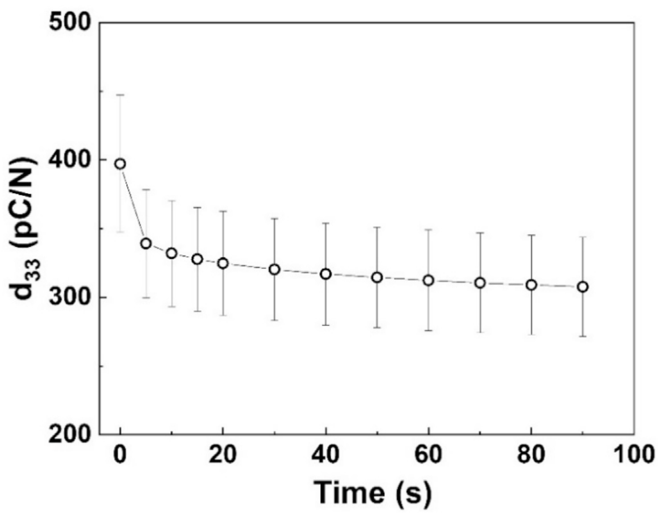

Fig. 6. Piezoelectric coefficient of BCZT ceramics as a function of exposure time to the mechanical stimulus in the d_{33}-meter.

largely unaffected by the procedure. In contrast, a significant and adverse reduction of the piezoelectric response was observed for the BCZT system. Several factors were identified to contribute to the property degradation of BCZT: ageing, modification of the surface chemistry and topography during cleaning, depoling due to local heating of the sample related to H_2O_2 decomposition as well as application of mechanical stresses during handing and measuring. BCZT ceramics are more susceptible to these factors than the other systems investigated due to their lower chemical stability and their inherent electromechanical softness. This study clearly highlights the importance of accounting for all factors that may lead to adverse impacts on piezo-active materials' functionality. Terminal sterilization and surgical handling are two essential areas that must be considered early on in developing piezo-ceramic candidates for orthopedic implant applications.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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