Published in final edited form as:

Ultrasonics. 2013 February ; 53(2): 511–517. doi:10.1016/j.ultras.2012.09.005.

Finite Element Static Displacement Optimization of 20–100 kHz flexural transducers for fully portable ultrasound applicator

Christopher R. Bawiec¹, Youhan Sunny¹, An T. Nguyen¹, Joshua A. Samuels¹, Michael S. Weingarten², Leonid A. Zubkov¹, and Peter A. Lewin¹

¹School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, Pennsylvania 19104

²Drexel University College of Medicine—Surgery, Philadelphia, Pennsylvania 19102

Abstract

This paper focuses on the development of a finite-element model and subsequent stationary analysis performed to optimize individual flexural piezoelectric elements for operation in the frequency range of 20–100 kHz. These elements form the basic building blocks of a viable, untethered, and portable ultrasound applicator that can produce intensities on the order of 100 mW/cm² spatial-peak temporal-peak (I_{SPTP}) with minimum (on the order of 15 V) excitation voltage. The ultrasound applicator can be constructed with different numbers of individual transducer elements and different geometries such that its footprint or active area is adjustable.

The primary motivation behind this research was to develop a tether-free, battery operated, fully portable ultrasound applicator for therapeutic applications such as wound healing and non-invasive transdermal delivery of both naked and encapsulated drugs.

It is shown that careful selection of the components determining applicator architecture allows the displacement amplitude to be maximized for a specific frequency of operation. The work described here used the finite-element analysis software COMSOL to identify the geometry and material properties that permit the applicator's design to be optimized. By minimizing the excitation voltage required to achieve the desired output (100 mW/cm² I_{SPTP}) the power source (rechargeable Li-Polymer batteries) size may be reduced permitting both the electronics and ultrasound applicator to fit in a wearable housing [1].

Keywords

Low frequency (<100 kHz) ultrasound transducers; design optimization; finite element analysis; therapeutic ultrasound; wearable ultrasound patch

Introduction

In the previously published paper by our research team [1] the implementation of an early clinically relevant ultrasound applicator prototype, designed with the preliminary results of the proceeding modeling procedure, was described along with the motivation leading to the specific design parameters such as frequency range (20–100 kHz), acoustic output (100 mW/cm² I_{SPTP}), geometry (flat, < 10 mm thickness), lightweight (< 100 g), and Li-Polymer

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

battery (15 V) operation. For the convenience of the reader the motivation is saliently summarized below and the seminal papers related to the applications considered, namely wound healing and transdermal drug delivery, are pointed out. Furthermore, the pioneering work of Pennsylvania State University scholars on the flexural transducer design (Newnham, Tressler, Dogan et al. [2–5]) which formed the basis on which the optimization modeling was performed is acknowledged and the difference between the optimized applicator design described here and the cymbal transducers developed by the Pennsylvania State University research team is analyzed in more detail.

This paper focuses on the development of a finite-element model and its subsequent stationary analysis performed to optimize individual flexural piezoelectric elements for operation in the frequency range of 20–100 kHz. These elements form the basic building blocks of a viable, un-tethered, and portable ultrasound applicator (examples shown below in Figs. 1-d and 1-e) that can produce intensities on the order of 100 mW/cm² spatial-peak temporal-peak (I_{SPTP}) with minimum (approximately 15 V) excitation voltage. The ultrasound applicator can be constructed with different numbers of individual transducer elements and different geometries such that its footprint (10×10 mm to 60×60 mm or more) and active area is adjustable. As already mentioned, the primary motivation behind this research was to develop a tether-free battery operated ultrasound applicator for therapeutic applications such as wound healing and non-invasive transdermal delivery of both naked and encapsulated drugs [6–9]. The most promising results were reported in [9], where 20 kHz ultrasound pulsed with 20% duty-cycle at intensity levels less than 100 mW/cm² was employed in successful, *in vivo* transdermal insulin delivery, with a similar albeit bulky and non-portable ultrasound assisted delivery system.

The flexural transducer elements that were optimized in this work were originally proposed by Newnham [3] in 1991 and were analyzed by Tressler in his comprehensive PhD Thesis [5]. They were selected for displacement optimization in this work because they are capable of operation in the frequency bandwidth that is of interest here and their geometry lends itself well for fabrication of a flat (< 10 mm) patch-like applicator that can be driven by a battery operated power source [1]. The interest in 20–100 kHz frequency range stems from the extensive analysis of data published by Mitragotri and colleagues in Dr. Langer's laboratory at MIT [10–14]. Review papers [10] and [12] investigated the research trends of therapeutic uses of ultrasound and low frequency (20–100 kHz) is cited as the preferred frequency range in transdermal delivery. In [11], the therapeutic effects of low frequency ultrasound (~20 kHz) on tissue, related to drug delivery, were investigated *in vitro* and the results reported indicated that transdermal delivery enhancement effects were up to 1000 times greater at 20 kHz than those observed at higher (1–3 MHz) frequencies [11]. The proposed mechanism of action of this enhancement in [11] was ascribed to stable cavitation: stable oscillations of micron sized bubbles at the surface and within the stratum corneum led to the disordering of the lipid bilayers. Later publications by Mitragotri and his colleagues [13, 14] have also concluded that cavitation plays a critical role in *in vitro* sonophoresis, however, in these [13, 14] inertial not stable cavitation was proposed as the sonoporation mechanism. The conclusions of [11] were considered of importance for this work because they also established that the enhanced delivery was achievable at relatively low intensity levels (12.5 to 225 mW/cm² I_{SPTA}) and a frequency of 20 kHz. Such intensity levels can be produced using the applicator modeled here and they are considered safe even at prolonged (up to 250 minutes) exposure [15].

More recent analysis of ultrasound assisted transdermal drug delivery presented in [16] theorized that provided nuclei of air voids exist in the stratum corneum they can undergo stable cavitation and grow due to rectified diffusion, creating channels for drug transport [16]. The experiments leading to this conclusion were performed at a frequency of 20 kHz

with an intensity of 1–5 W/cm², which is an order of magnitude higher than the intensity proposed here. A similar mechanism which does not require the existence of air voids suggested mechanical disruption within the lipid bilayers themselves [17] enabling enhanced transport through the stratum corneum. The proposed ultrasound device investigated here, which is lightweight (< 200 g) and portable (unlike the applicators used in the above [10–14, 16] research), is not only capable of enabling drug delivery [7–9] but it also has applications in wound healing [6]. The mechanical energy supplied by ultrasound (with as little as 2 mW/cm² [18]) has been shown to have an effect on cellular activity resulting in, for example increased collagen synthesis, angiogenesis, and nitric oxide levels, all of which accelerate the wound healing process [6].

In order to experimentally verify the model proposed here several early prototypes of the flexural transducer were fabricated with geometric dimensions and material properties that were determined by finite element analysis to have fundamental resonance frequencies on the order of 20 kHz.

As already noted, the early (clinically applicable) prototype described in [1] was fabricated using the preliminary results of the model described below. As discussed in the following, there are several geometric parameter combinations that can produce a specific resonance frequency and in order to minimize power requirements, it was necessary to determine the geometry that would result in the largest displacement amplitude for a given excitation voltage. By minimizing the power requirements it was possible to reduce the battery size required to operate the device, thus reducing the overall weight of the applicator. In the next subsection the basic FEA (COMSOL) implementation principles are reviewed. The review is given to aid in providing the background for understanding the fundamental limitations of the FE modeling.

Finite Element Analysis

FEA can be defined as a method which, utilizing computer software, allows numerical solving of complex partial differential equations that are used to describe the physical behavior of a modeled system. FEA employs a system of points, referred to as nodes, which are generated by a grid (mesh) that represents the geometry of a system. This modeled system can then be analyzed after the appropriate assignment of material properties and boundary conditions and a prediction on the behavior of the overall system can be obtained. As noted above, the structure being modeled is divided into a mesh of many elements, intersections of these elements are referred to as nodes and the analysis is run on each of the element's nodes for the entire model. As also mentioned earlier, the FEA of the flexural transducer used in the ultrasound applicator described here was performed using COMSOL Multiphysics software package version 4.2 with the MEMS and Acoustic modules. The selection of COMSOL was arbitrary but version 4.2 allowed all of the parameters of interest to be considered. Specifically, COMSOL version 4.2 offers different types of analysis options for piezoelectric device simulations including eigenfrequency, frequency domain, stationary, and time-dependent analyses. In the work reported here, eigenfrequency analysis was carried out in order to determine the resonance frequencies of the flexural transducer and frequency domain studies were used to compare the reactance spectra plots with both those available in the literature [4] and those obtained experimentally from the fabricated prototypes [1]. After experimental verification, stationary and eigenfrequency analyses were performed in order to optimize the applicator design. Optimization is defined here as the largest possible displacement amplitude achievable for a given geometry and material combination for a given voltage applied at a specified frequency. In the following the FEA (COMSOL) procedure is outlined in more detail.

The goal of this work was to develop and verify a practically convenient (fastest simulation time) finite element FEA model that would enable optimization of 20–100 kHz ultrasound flexural transducers such as those reported recently in [1]. Although COMSOL is capable of simulating mechanical systems dynamically using harmonic or time based analysis, the analysis presented here was performed based on stationary and eigenfrequency simulations as opposed to dynamic FE modeling.

This was done intentionally to reduce computation time and to limit the designs considered to those which resulted in the eigenfrequencies that were of potential interest for future dynamic studies. Approximately 100 thousand different design variations were analyzed, and the time needed for running both a stationary and an eigenfrequency analysis on each variation was averaged to approximately 30 seconds each, i.e. total computational time (Intel Quad-Core processor with 24 GB of RAM) used was over 30 straight days. For comparison, a well-designed harmonic (dynamic) analysis would require the analysis time of a minimum of 15 times longer translating to over 450 days of continuous computation time with our current resources). More specifically, whereas the dynamic analysis is capable of yielding the absolute value of the displacement amplitude for a given excitation voltage produced by the ultrasound applicator [1], it requires a relatively long simulation time. Consequently, the static analysis combined with time effective iterative approach was chosen as it allowed all relevant design parameters (listed and discussed in the following) to be examined within a substantially shorter (~2 months) time frame.

The outcome data of the static analyses were utilized to fabricate the early applicator prototypes [1], which operated at 20 kHz and with merely 15 V excitation were capable of producing the desirable, considered safe [15] acoustic output of 55 kPa or about 100 mW/cm² I_{SPTP} . This 15 V is an order of magnitude lower than that reported earlier [5, 9] and permitted tether-free ultrasound applicator design.

To gain additional understanding into the applicator optimization process, the static analysis was supplemented using eigenfrequency analysis, which allowed identification of the preferred resonance frequencies in air. In the fabricated prototype [1], the air measured resonance frequency was shifted downward due to the mass loading effect of embedding epoxy [19]. The prototype design described in [1] exhibited resonance frequency equal to about 37 kHz in air – the resonance frequency of the final, epoxy embedded applicator of [1] was measured acoustically to be about 20 kHz. The exact analysis of the influence of the epoxy on the optimization process is outside the scope of this work and will be presented separately in a future publication.

FEA Procedure

The three-dimensional exploded view of a single flexural element used in the ultrasound applicator is shown in Fig. 1-a. It is rotationally symmetric about its center line and therefore lends itself well to two-dimensional axis symmetric modeling. Accordingly, two-dimensional axisymmetric modeling was chosen as it allowed the high (1000 fold more time consuming) computational cost associated with three-dimensional modeling to be eliminated. The components of the applicator that were considered in the systematic, step-by-step analysis can be divided into three broad categories: piezoelectric materials, adhesive epoxy, and shaped metal caps. The physical properties of the metal and the piezoelectric materials that were modeled were taken from COMSOL's material library. The adhesive epoxy material properties were obtained from the technical data sheet (Stycast 2741 LV / Catalyst 15 LV, Emerson and Cuming) and the thickness was fixed to be 20 microns. The reason for choosing this epoxy type was based on earlier published data [5]; Tressler suggested that the thickness of the bonding epoxy between the metal cap and the PZT

ceramic was approximately 20 microns. For this study the type of adhesive epoxy was not varied due to the difficulties of finding both suitable epoxy alternatives and determination of the bonded epoxy material properties. Accordingly, only the metal caps and piezoelectric elements were evaluated as far as variable material parameters and geometry were concerned. All of the piezoelectric disk material types that were analyzed in the models were of the lead zirconate titanate ceramics (PZT) family (see PZT modeling section) and were poled in the thickness direction.

The metal caps that were fabricated and modeled in this work were chosen to have the same overall radial dimensions as the PZT disks. Due to manufacturing design constraints, (which required adequate bonding surface area for the metal caps to adhere to the PZT), in the simulations, the base radius of the shaped metal cap (Fig. 1-a) was modeled such that there was at least a 1 mm ring of bonding surface between the PZT disk and the metal cap (bonding epoxy width). The metal cap apex radius was modeled such that the difference between the apex radius and the base radius was at least 1 mm and this was done to ensure that the metal cap retained a “truncated cone” shape (Fig. 1-a) which was required for the desired flexural motion [5].

An important aspect of the FEA study was the assignment of appropriate structural and electrical boundary conditions. Three structural boundary conditions were considered, one that fixed the model about its rotational axis, another that was applied along the horizontal center of the PZT disk (prohibiting rotational movement), and finally, the one ensuring “free” movement everywhere else. The electrical boundary conditions were implemented by placing a voltage terminal on the top and a ground terminal on the bottom surface of the PZT disk, respectively.

As pointed out earlier, in order to verify the model the initial finite element analysis was performed with the same geometric dimensions and materials as those reported in [4]. The analysis presented in [4] was performed using a different FEA software (ANSYS) and the comparison of the eigenfrequencies obtained using COMSOL and ANSYS corroborated the validity of the analysis applied. Further verification of the model was obtained by comparing simulated and experimental data. More specifically, the eigenfrequencies and the reactance spectra were modeled using the COMSOL software for a selected geometry, piezoelectric material, and adhesive epoxy. Next, the prototype, similar to the one described in [1], was fabricated and tested using AIM 4170C antenna analyzer (Array Solutions, Sunnyvale, Texas USA). The experimental and simulated results compared well (to within 5%); this agreement was deemed sufficient to confirm the validity of the model.

Once the COMSOL model was verified, stationary and eigenfrequency analysis was performed on the flexural transducer model. As already noted, the ultimate goal of the simulation was to determine the geometry and material components providing maximum pressure amplitude at a given frequency while using minimum voltage excitation. The results presented below pertain to a design that operates at 20 kHz. This frequency was initially chosen because it is the only frequency that was successfully used *in vivo* for transdermal non-invasive insulin delivery in piglets [9], however optimization results were also obtained for prototype designs operating at 100 kHz. A frequency range (20 – 100 kHz) was investigated in order to have multiple designs such that the applicators’ clinical treatment efficacy (in relation to the frequency) could have been evaluated and optimized. In the following the results of analysis of the geometric and material parameters of the metal caps and the PZT are presented. The geometric parameters of interest (Fig. 1-a), which included those of the PZT disk (thickness and radius) and the metal cap (thickness, base radius, apex radius, and cavity depth), were also examined. Analyses on the FEA model were performed varying all of the aforementioned geometric dimensions for both stationary

and eigenfrequency analysis. The PZT type and the metal cap material were initially investigated for a constant geometry in order to determine their effects on the model simulation such that they could remain constant during the subsequent analyses. After the modeling components were analyzed and set to be PZT-5H for the piezoelectric ceramic and brass for the metal end caps, the geometric parameters of interest were varied to obtain the optimized design (see modeling section for more details on material selection). For the stationary studies a maximum axial displacement amplitude was determined at the center of each metal cap with 100 V applied. The voltage choice for this modeling was arbitrary as the results scale linearly with the applied voltage (the final fabricated prototype operated with 15V excitation [1]). The modeling results are presented in the next section.

Modeling Results

Below are detailed descriptions of the influence of each parameter's geometry and material influence on the design optimization.

Piezoelectric material type and thickness

There are many different types of piezoelectric materials that are both naturally occurring and man-made. Of these materials only piezoelectric ceramics that were commercially available, relatively inexpensive, and easy to procure are analyzed here. Thus, PZT ceramics that were commercially available with relatively short lead times (< 2 months) were analyzed. It is conceivable that recent advances in composite ceramic and single crystal ultrasound transducers could potentially provide a more optimized design alternative than the PZT ceramics described here [19–21]. However, as 1–3 composite PZT ceramics and single crystals are relatively expensive and difficult to procure they were not analyzed in the course of this work. Also, due to a recent directive in the European Union attempting to phase out lead usage [22], lead-free ceramics that are currently under development [23] could potentially replace PZT ones; again, they were not investigated here.

In order to determine the ideal PZT type it was necessary to examine the electromechanical properties of the PZT ceramics. The piezoelectric ceramic manufacturers provide data sheets for the standard PZT types that they make along with explanations of the material properties. As the displacement amplitude is primarily dependent upon the values of the d_{33} and d_{31} coefficients [2], PZT-5H was chosen as the PZT ceramic that was used in the analysis presented. Although PZT-4 and PZT-8 are the commonly accepted transmitter type ceramics PZT-5H was found to be better suited (higher displacement for a given voltage) for this low-intensity (100 mW/cm^2) flexural transducer application.

The geometry of the PZT disk (thickness and radius) also determines the achievable displacement amplitude. As shown in Fig. 2 the displacement amplitude is inversely proportional to the PZT disk thickness for a given PZT disk radius. For example with a 10 mm radius PZT disk lowering the thickness from 3 mm to 0.5 mm results in a 4 fold displacement amplitude increase from approximately $3 \mu\text{m}$ to $12.5 \mu\text{m}$. Although the results of modeling show that 0.25 mm thickness would further increase the displacement amplitude 0.5 mm thick disks were chosen to minimize the tradeoff between fragility (due to the brittle nature of the PZT) and mechanical compliance of the ceramic material.

Metal cap materials

Influence of different metal cap materials on relative displacement amplitude compared for a constant geometry is shown in Fig. 3. A constant geometry (PZT disk radius: 6 mm, base radius: 5 mm, apex radius: 1 mm, cavity depth: 0.2 mm, cap thickness: 0.125 mm) was chosen for display of the analysis although other geometries were also analyzed and the trend was found to be similar for all of the metals considered. For the modeling condition

shown in Fig. 3 the maximum displacement amplitude was obtained for aluminum, however in the following analysis brass was used. This was because the availability of brass and the relative ease of cutting and shaping the metal cap for experimental prototypes.

Metal cap cavity depth and thickness

The cavity depth in Fig. 4 is defined as the distance between the PZT ceramic face and the apical planar region of the shaped metal cap (shown in Figure 1-f). The displacement amplitude depends on the cavity depth for a given PZT radius and metal cap thickness and facilitates up to a three-fold increase in displacement amplitude for a given PZT radius. For example in Fig. 4-a for a PZT radius of 10 mm there exists a peak in maximum displacement amplitude which was found to be $12+ \mu\text{m}$ at a cavity depth of approximately 0.175 mm. The graphs (Figs. 4-a and 4-b) of cavity depth versus displacement amplitude illustrate that the maximum displacement amplitude appears at different cavity depths depending upon the thickness of the metal cap that is used. The maximum displacement amplitude was obtained for dimensions of approximately 0.175 mm cavity depth for metal cap thickness of 0.125 mm and approximately 0.325 mm cavity depth for metal cap thickness of 0.25 mm (the remaining geometric dimensions were fixed – see Fig. 4 for details). Inspection of Figs. 4-a (metal cap thickness 0.125 mm) and 4-b (metal cap thickness 0.25 mm) reveals that with increasing thickness of the metal cap the cavity depth that is necessary for maximum displacement also increases. It is worthy of noting that decreasing metal cap thickness from 0.3 mm to 0.125 mm results in increasing of the displacement amplitude (Fig. 5). The analysis performed indicated that 0.125 mm thick metal caps were most practical for use in the prototype fabrication [1] because the sheets of 0.125 mm are commercially available. Also, the machining of the shaping die that was used for their fabrication was simplified.

Metal cap base and apex dimensions

In addition to the PZT disk radius, the base radius of metal cap influences the displacement amplitude. As shown in Fig. 6, with increasing metal cap base radius (modeled from 2 to 9 mm) the maximum displacement amplitude also increases (from approximately 0.8 to $12+ \mu\text{m}$, respectively). The plots in Fig. 6 overlap indicating that the metal cap base radius plays a more dominant role in comparison with the influence exerted by the PZT disk radius. For instance, if the metal cap base radius were fixed at 2mm, with all other parameters constant, the maximum displacement amplitude would be within 5% for all PZT disk radii varying from 3 to 10 mm. In Fig. 6 the apex radius was kept constant at 1 mm whereas the base diameter was varied from 2 to 9 mm (always ensuring that it was 1 mm less than the PZT disk radius). As previously mentioned, the reason for keeping the outer radius a minimum of 1 mm less than the PZT disk radius was to ensure that an adequate bounding surface was available for the adhesive epoxy to be applied during manufacturing. Also, the choice for making the apex radius always 1 mm smaller than the base radius was to maintain the desired flexural motion which requires the metal cap to retain a “truncated cone” shape. Fig. 7 depicts the influence of apex radius on the displacement amplitude and shows that the maximum value is dependent upon the PZT disk radius. For the 10 mm and 3 mm disks the apex radius providing the maximum displacement is 2.25 mm and 0.75 mm, respectively. However, as seen in Fig. 7, there is less than 5% change in the maximum displacement amplitude as long as the apex radius is less than half of the base radius. This is most clearly seen with the 10 mm PZT disk radius in Fig. 7 where there is a near horizontal trend in displacement amplitude from 0.1–4.5 mm metal cap apex radius dimensions.

Operating Frequency

The last parameter considered for device optimization was frequency of operation. Only designs that had their first eigenfrequency within 10% of the desired frequency of operation

(i.e. 18–22 kHz for 20 kHz applicator and 90–110 kHz for the 100 kHz applicator) are displayed in Fig. 8 and Table 1. In the final prototype implementation mass loading effects of the potting epoxy can shift the resonance frequency by much more than 10%; as noted earlier in [1] the shift in resonance frequency from 37 kHz in air down to 20 kHz once the prototype was embedded in epoxy was observed. It was determined experimentally that the resonance frequency was dependent upon the volumetric combination of the multi-component epoxy (Spurr's epoxy). Spurr's epoxy was selected here due to its proved performance in other piezoelectric ultrasound transducer designs (such as the composite transducer described in [19]) and the ability to adjust its "hardness". The influence of epoxy "hardness" on acoustic output and resonance frequency of the fabricated prototype is being investigated and the results will be presented in an upcoming publication.

Figure 8 displays a single, yet representative, example demonstrating the dependence of the resonance frequency on the geometric dimensions of the flexural transducer as a function of the cavity depth. Resonance frequency analysis was run concurrently with stationary analysis on all of the models analyzed. The models that generated resonance frequencies at 20 and 100 kHz were then selected and compared to determine the geometry that produced the maximum displacement amplitude at those frequencies. Although several geometries were capable of generating 20 and 100 kHz resonance frequencies, the specific dimensions shown in Fig. 8 produced the maximum displacement amplitudes at both 20 and 100 kHz.

For the 20 kHz design the FEA analysis indicated that the maximum displacement amplitude condition requires PZT disk radii to be at least 6 mm (6 to 10 mm radii were modeled here) with metal cap geometric dimensions of: base radius from 4.75 to 5.25 mm, an apex radius from 1.5 to 2.0 mm, and a cavity depth from 0.25 to 0.30 mm. For the described metal cap geometric dimensions the PZT disk radius had less than 5% effect on the displacement amplitude from 6 to 10 mm, however, when the radius became less than 5 mm the peak displacement amplitude started to decline. In Fig. 8 the dimensions that were selected show just a single geometry ensuring optimal displacement (see also Table 1) and for a given frequency of operation (20 and 100 kHz) the displacement amplitude at those geometries was in the top 5% of the amplitudes for all the models investigated. For the 100 kHz design the optimal dimensions were determined to be 3 to 5 mm for the PZT disk radii with a metal cap base radius between 2 and 2.25 mm, a metal cap apex radius between 0.5 and 0.75 mm, and a cavity depth from 0.225 to 0.325 mm. Again, the PZT disk radius had less than a 5% effect on the displacement amplitude for 3 to 5 mm PZT disk radii when the metal cap was fixed at the above mentioned geometric dimensions, and smaller PZT disk radii were not modeled. As indicated in Fig. 1-d the ultrasound applicator is primarily operated as arrays of elements and therefore the smallest PZT disk radius that could produce the desired displacement amplitude at the desired frequency should have been chosen, however due to commercial availability of the PZT disks as well as the machining tools, the experimental verification of the prototype described in [1] used PZT disks having 6.35 mm radius (1/2" diameter).

Conclusions

Systematic step-by-step finite element analysis leading to the optimization of a clinically relevant prototype for ultrasound assisted chronic wound healing and transdermal drug delivery applications was described. The results of this research provide guidelines for optimization of the applicator design examined and indicate that consideration of the ceramic properties may further improve its performance. Additional (slightly less than 10 %) improvement could also be achieved if brass is replaced with aluminum (see Fig. 3). As noted earlier it is conceivable that replacing conventional PZT materials with PZT composites or single crystals could further enhance the applicator's acoustic output. Also, in

light of the recent developments in lead-free piezoelectric ceramics [23], it is plausible that medical devices may require the incorporation of these ceramics in the future [22]. As these ceramics' electromechanical parameters are in general lower than those of PZT ceramics, future studies might be needed to determine the effect of lead-free ceramics on the ultrasound applicator's acoustic output.

Acknowledgments

This work was partially supported by the NIH grant 5 R01 EB009670 and NSF Grant 1064802. Also, prematurely departed, Dr. Nadine Barrie Smith, Department of Bioengineering, Pennsylvania State University is sincerely thanked for sharing her experience with similar devices and generously donating testing transducers, which substantially accelerated the process of optimization described in this work.

References

1. Sunny Y, et al. Optimization of un-tethered, low voltage, 20–100 kHz flexural transducers for biomedical ultrasonics applications. *Ultrasonics*. 2012; 52(7):943–948. [PubMed: 22513259]
2. Dogan A, et al. Tailoring the performance of ceramic-metal piezocomposite actuators, [] cymbals'. *Sensors and Actuators A: Physical*. 1998; 65(2–3):228–237.
3. Newnham, RE.; Xu, QC.; Yoshikawa, S. Transformed stress direction acoustic transducer. Google Patents, Patent ID 4,999,819. 1991.
4. Tressler J, et al. Finite element analysis of the cymbal-type flextensional transducer. *IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control*. 1998; 45(5):1363–1369.
5. Tressler, JF. Capped ceramic underwater sound projector :The 'Cymbal'. The Pennsylvania state University; 1997.
6. Ennis WJ, et al. Current Status of the Use of Modalities in Wound Care: Electrical Stimulation and Ultrasound Therapy. *Plastic and Reconstructive Surgery*. 2011; 127(1):93s–102s. [PubMed: 21200278]
7. Huang SL. Liposomes in ultrasonic drug and gene delivery. *Advanced Drug Delivery Reviews*. 2008; 60(10):1167–1176. [PubMed: 18479776]
8. Miller DL, et al. Overview of Therapeutic Ultrasound Applications and Safety Considerations. *Journal of Ultrasound in Medicine*. 2012; 31(4):623–634. [PubMed: 22441920]
9. Park EJ, Werner J, Smith NB. Ultrasound mediated transdermal insulin delivery in pigs using a lightweight transducer. *Pharmaceutical research*. 2007; 24(7):1396–1401. [PubMed: 17443398]
10. Mitragotri S. Healing sound: the use of ultrasound in drug delivery and other therapeutic applications. *Nature Reviews Drug Discovery*. 2005; 4(3):255–260.
11. Mitragotri S, Blankschtein D, Langer R. Transdermal Drug Delivery Using Low-Frequency Sonophoresis. *Pharmaceutical research*. 1996; 13(3):411–420. [PubMed: 8692734]
12. Ogura M, Paliwal S, Mitragotri S. Low-frequency sonophoresis: Current status and future prospects. *Advanced Drug Delivery Reviews*. 2008; 60(10):1218–1223. [PubMed: 18450318]
13. Tezel A, Mitragotri S. Interactions of inertial cavitation bubbles with stratum corneum lipid bilayers during low-frequency sonophoresis. *Biophysical journal*. 2003; 85(6):3502–3512. [PubMed: 14645045]
14. Tezel A, Sens A, Mitragotri S. Investigations of the role of cavitation in low-frequency sonophoresis using acoustic spectroscopy. *Journal of pharmaceutical sciences*. 2002; 91(2):444–453. [PubMed: 11835204]
15. AUIM. Statement on Mammalian In Vivo Ultrasonic Biological Effects. 2008. <http://www.aium.org/publications/statements.aspx>
16. Lavon I, et al. Bubble growth within the skin by rectified diffusion might play a significant role in sonophoresis. *Journal of Controlled Release*. 2007; 117(2):246–255. [PubMed: 17197050]
17. Krasovitski B, et al. Intramembrane cavitation as a unifying mechanism for ultrasound-induced bioeffects. *Proceedings of the National Academy of Sciences*. 2011; 108(8):3258.
18. Lai J, Pittelkow MR. Physiological effects of ultrasound mist on fibroblasts. *International journal of dermatology*. 2007; 46(6):587–593. [PubMed: 17550557]

19. Gururaja T, et al. Piezoelectric composite materials for ultrasonic transducer applications. Part I: Resonant modes of vibration of PZT rod-polymer composites. *IEEE Trans Sonics Ultrason SU*. 1985; 32(19985):481–498.
20. Anton S, Erturk A, Inman D. Bending strength of piezoelectric ceramics and single crystals for multifunctional load-bearing applications. *Ultrasonics, Ferroelectrics and Frequency Control*, *IEEE Transactions on*. 2012; 59(6):1085–1092.
21. Sherlock N, Meyer R Jr. Modified single crystals for high-power underwater projectors. *Ultrasonics, Ferroelectrics and Frequency Control*, *IEEE Transactions on*. 2012; 59(6):1285–1291.
22. COMMISSION DIRECTIVE 2011/37/EU. Official Journal of the European Union. 2011. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:085:0003:0007:EN:PDF>
23. Hejazi M, Jadidian B, Safari A. Fabrication and evaluation of a single-element Bi (0.5) Na (0.5) TiO (3)-based ultrasonic transducer. *IEEE transactions on ultrasonics, ferroelectrics, and frequency control*. 2012; 59(8):1840.

Stationary finite element analysis (COMSOL) of flexural transducers enabling low voltage operation.

Displacement optimization of flexural transducers for therapeutic applications.

Low frequency (<100 kHz), Low intensity (~100 mW/cm²), low profile ultrasound applicator.

Several therapeutic applications (wound healing and transdermal drug delivery), due to small size and portable operation

Figure 1.

a) Three-dimensional exploded view of a single flexural element used in the ultrasound applicator (also shown in d). b) Two-dimensional axisymmetric model with mesh used in FEA analysis. c) Two-dimensional axisymmetric model with applied voltage excitation showing normalized displacement (displacement shown is not to scale). d) Ultrasound applicator prototype [1] (3×3 array configuration – dimensions of $55 \times 55 \times 8$ mm). e) Photo showing applicator prototype being worn on the forearm (2×2 array configuration – dimensions of $35 \times 35 \times 8$ mm). f) Top-half two-dimensional slice of single flexural element used to facilitate interpretation of the results shown in Figs. 2–8 (here the cavity depth is shown as an example, see also Fig. 4).

Figure 2.

Influence of PZT disk thickness varying from 3 to 0.25 mm on relative displacement amplitude for PZT disk radii varying from 3 to 10 mm. As mentioned previously, the metal cap base radius was modeled such that its maximum value was always 1 mm less than that of the PZT disk (See text for details).

Figure 3.

Influence of different metal cap materials on relative displacement amplitude compared for a constant geometry (PZT disk radius: 6 mm, base radius: 5 mm, apex radius: 1 mm, cavity depth: 0.2 mm, cap thickness: 0.125 mm).

Figure 4.

Influence of metal cap cavity depth on the relative displacement amplitude for PZT disk radii varying from 3 to 10 mm for metal cap thickness of a) 0.125 mm and b) 0.25 mm. These graphs show that the maximum displacement amplitude peak shifts from approximately 0.175 mm cavity depth for metal cap thickness of 0.125 mm to approximately 0.325 mm cavity depth for metal cap thickness of 0.25 mm. Also shown is the overall effect of metal cap thickness on the displacement amplitude; the maximum displacement amplitude increases from 4.5 μm with a metal cap thickness of 0.25 mm to over 12 μm with a metal cap thickness of 0.125 mm.

Figure 5.

Influence of metal cap thickness on relative displacement amplitude for PZT disk radii varying from 3 to 10 mm. This figure summarizes the data obtained for metal cap thickness ranging from 0.3 to 0.125 mm for a PZT radius varying from 3 to 10 mm. To facilitate the fabrication process 0.125 mm thickness was chosen to be the thinnest metal cap modeled.

Figure 6.

Influence of metal cap base radius on relative displacement amplitude for PZT disk radii varying from 3 to 10 mm. To facilitate fabrication and ensure adequate bonding surface for the adhesive epoxy the metal cap base radius was modeled such that its maximum value was set to be 1 mm less than the radius of the PZT disk. The above results indicate that the displacement amplitude was controlled primarily by the metal cap base radius and not by the PZT disk radius (see text for further explanation).

Figure 7.

Influence of metal cap apex radius on relative displacement amplitude for PZT disk radii varying from 3 to 10 mm. In order to ensure flexural motion the metal cap needs to retain a “truncated cone” shape, therefore the metal cap apex radius was always set to be at least 1 mm less than the metal cap base radius.

Figure 8.

Resonance frequency vs. cavity depth of transducers with various PZT disk radii varying from 3 to 10 mm. PZT with radii of 3 to 5 mm (a) were modeled with geometric dimensions for the metal cap base and apex radii of 2 and 0.75 mm, respectively, whereas PZT disk radii of 6 to 10 mm (b) have fixed metal cap base and apex radii of 5 and 1.75 mm, respectively. The stars on lines a and b represent the optimal flexural transducer design geometry at the frequencies considered here (i.e. 20 and 100 kHz).

Table 1

Dimensions for manufacturing an optimized flexural transducer element operating at 20 and 100 kHz.

	PZT Dimensions (mm)		Metal Cap Dimensions (mm)			
Resonance Frequency	Radius	Thickness	Base Radius	Apex Radius	Cavity Depth	Thickness
20 kHz	6–10	0.5	5	1.75	.275	0.125
100 kHz	3–5	0.5	2	0.75	.075	0.125