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Development of low frequency (20-100 kHz) clinically viable ultrasound applicator for chronic wound treatment

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Abstract

This paper details the systematic approach used to develop a viable clinical prototype of a therapeutic ultrasound applicator and discusses the rationale and deliberations that led to the design strategy. The applicator was specifically devised to treat chronic wounds and – to the best of the author’s knowledge – is the first truly wearable device with a proven record of reducing healing time, directly translating to a reduction of healthcare costs.

The prototype operates in the kHz (20-100) range of frequencies and uses non-cavitation and non-thermal levels of ultrasound energy. Hence, in the absence of inertial cavitation and temperature elevation, the tissue-ultrasound interaction is considered to be dependent on stable cavitation (if any) and radiation force. The peak acoustic output pressure amplitude is limited to 55 kPa, corresponding to a spatial peak temporal peak intensity of 100 mW/cm². This level of intensity is considered to be safe to apply for extended (up to four hours) periods of time.

The patch-like applicator design is suitable to be embedded in wound dressing. With its light weight (<20g) and circular (40 mm dia) disk shape architecture, the applicator is well suited for chronic wound treatment. A small (n=8) pilot study on the effects of the applicator on diabetic ulcers healing time is presented. The average time to wound closure was 4.7 weeks for subjects treated with the active ultrasound applicator, compared to 12 weeks for subjects treated with a sham applicator, suggesting that patients with diabetic ulcers may benefit from the proposed treatment.

Keywords

Ultrasonically assisted wound healing; kHz range therapeutic ultrasound applicator; Ultrasound/tissue interaction

I. Introduction

THE primary goal of this work was to systematically delineate the process of the design and hardware implementation of the clinically viable ultrasound applicator. The applicator was specifically developed to treat chronic wounds, and – as already reported - successfully used [1] to treat venous ulcers (VUs). In this context, it is appropriate to note that the applicator's array geometry used in [1] was modified (see details in Section II), and the first use of the applicator in diabetic ulcers is described. To gauge the financial burden associated with wound treatment, it is worthy to note that VUs are the most common type of chronic wound, affecting an estimated 600,000 patients in the United States alone [2], and the direct healthcare cost of treating a single VU patient is estimated to be \$16,400 [3]. The treatment of diabetic foot ulcers (DUs) is even more expensive – it costs about \$50,000 [5]. As a reduction of healing time directly translates into a reduction of healthcare costs, a positive clinical outcome would create a substantial societal impact.

Thus, there is a well-defined clinical need for the development of an effective therapeutic approach that could accelerate wound closure, and hence, reduce the cost of healthcare. The availability of such an approach would substantially improve the quality of life of the patients suffering from these debilitating illnesses.

Prior to presenting the considerations that led to the development of the applicator, a concise explanation of the complexity of chronic wound healing is given. Briefly, these wounds fail to follow the normal healing course, which starts with an initial inflammation phase followed by proliferation of new tissue, including the development of blood vessels or angiogenesis; in chronic wounds, the inflammation phase continues, inhibiting healing progress [6].

The current standard of care for chronic ulcers largely consists of regular debridement followed by “passive” treatments that maintain a wound environment that may be conducive to the natural healing process but do not actively promote healing. Debridement is defined as the “removal of necrotic and senescent tissues as well as foreign and infected materials from a wound...[to] decrease in the possibility of limb amputation in patients” [5]. It removes “unhealthy” or necrotic tissue from the wound area by employing inertial cavitation and is usually implemented using commercially available ultrasound devices [7][35]. The ultrasound energy delivered by these debridement systems is difficult to quantify because the relevant field exposure parameters of these instruments are not published. Additionally, these devices are manually held and moved by the operator on or above the wound, a process that is likely to introduce variability in the ultrasound exposure between treatments.

Non-contact, low-frequency (40kHz), low intensity (100–500 mW/cm²) ultrasound applied 3 times per week has been shown to accelerate the healing rate of chronic venous ulcers compared to standard wound care (62% wound size reduction after 4 weeks in treatment group vs. 45% wound size reduction in control group) [8]. This non-contact device delivers acoustic energy to wounds using sterile saline droplets rather than through direct contact, must be operated by trained clinician, and has been shown to significantly decrease the

abundance of *Peptoniphilus* bacteria ($p < 0.01$) and fibrinogen ($p < 0.05$) over time compared to standard care [9].

In contrast to the debridement devices mentioned above, the ultrasound applicator prototype described in this paper is designed to *actively* promote wound healing using low frequency, low intensity ultrasound, similar to the device described in [9], but in a more patient-friendly manner. Rather than requiring the patient to visit a provider 3 times per week, we sought to develop a system that can be safely utilized by patients at home.

As the applicator was intentionally designed to operate below the intensity level (here $< 100 \text{ mW/cm}^2$, spatial peak, temporal peak) that causes inertial cavitation, the healing process can most likely be attributed to non-thermal, non-inertial cavitation effects such as acoustic radiation forces and stable cavitation [10,11]. The successful outcome of the previously reported human pilot studies [1] suggests that ultrasound – acting as external, mechanical stimulus – interrupts the undesirable, prolonged inflammation of tissue; so the healing process can be initiated. Murine 3T3 fibroblasts were exposed to a similar applicator generating identical acoustic output. This ultrasound applicator prototype stimulated proliferation of fibroblasts in comparison with a sham control applicator, suggesting active healing [1].

To ensure that the biological end-point could be linked directly with the quantified ultrasound exposure parameters, a dedicated measurement setup was developed concurrently. Such quantification is essential to link the input stimulus (here, pressure amplitude of 55 kPa) with the healing outcome [1]. Also, the acoustic output measurement system development was considered critical because clinically relevant ultrasound exposimetry discussion is not covered by pertinent international standards such as IEC 60565, which describes calibration of the underwater acoustics hydrophones in the frequency range 0.01 Hz to 1 MHz [12].

In the next section the design considerations are discussed and the final implementation of the ultrasound applicator is described. The following section details the verification of the acoustic output achieved by making use of absolute reciprocity calibration and miniature (1.6 mm dia) hollow cylinder hydrophones. Next, a pilot study in which the ultrasound applicator was tested on patients with diabetic foot ulcers is described. The final section offers conclusions and directions for the possible improvements of the current clinical prototype.

II. Design Considerations

This section described the process of designing the geometry (foot-print) of the applicator and the key acoustic parameters needed to implement the ultrasound exposure matrix that was used in clinical practice.

From this project's inception, safety and efficacy were the two constraints that dictated the design. Recognizing the potential of making the applicator available commercially, it was acknowledged that the device must comply with the FDA requirements for extended (up to 4

hours) exposure periods by operating below the intensity level of 100 mW/cm^2 , spatial peak, temporal peak [4].

A. Physical Design Requirements

Analysis of the safety and efficacy constraints introduced another important consideration; namely that a home-administered treatment is expected to be more effective than treatments that are provided in a clinical environment. This is because at home-administered treatments can be applied more frequently and have better patient compliance than the clinical ones. Chronic wound patients' mobility is often impaired, and they must be transported to the clinic regularly to obtain many wound treatments. An acoustic treatment that is designed for use at a patient's home is expected to have maximum effectiveness, since it will not require frequent burdensome trips to a healthcare provider.

The home-use requirement reinforced the importance of the safety of operation and also suggested a portable physical design of the treatment device, a thin (implemented eventually as less than 10 mm, see Figs 1-3) acoustic applicator. Standard of care requires patients or caregivers to replace wound dressings at least once weekly, so a minimized thickness or patch-like construction would facilitate the applicator to be embedded in a standard dressing used in the current wound care treatment procedure. The ultrasound treatment would occur during this time and a new dressing would be placed on the wound following the ultrasound treatment. An additional benefit of a small applicator for research and development purposes is that it can readily be adapted for use with *in vitro* studies of cultured cells. Such studies – when properly designed [13] – might be helpful to identify the mechanism(s) of interaction between ultrasound and wound tissue that ultimately results in enhanced healing [1]. Knowledge of these biological mechanisms is of importance because it may lead to personalized and customized treatment with associated improvement of patients' quality of life and reduction in healthcare costs.

The foot-print of the device was decided considering the trade-off between the full tether-free wearability, the typical wound area to be treated, and the electrical and acoustic requirements (discussed below). It was recognized that the applicator must produce adequate, spatially uniform pressure amplitude distribution for a minimum of 15 or 45 minutes (clinically proven treatment time [1] while battery powered). These trade-offs were reconciled through extensive modeling [14] and resulted in the (10 mm thickness and 40 mm dia) disk-shape device (Fig 1).

The applicator architecture shown in Fig.1 lends itself for patch-like design that could be embedded in wound dressing and - as discussed in the following – it also influenced the choice of frequency of operation.

B. Acoustic Design Requirements

The choice of frequency of operation and other acoustic output parameters such as pressure amplitude and rate of delivery of ultrasound exposure emerged as a result of examination of the reports describing tissue healing process at conventional (1-3 MHz) therapeutic ultrasound frequencies [15], and the results of laboratory *in vitro* experiments performed at 20 kHz [1].

A systematic literature review suggested that ultrasound at frequencies in the tens of kHz range is beneficial to wound healing [16, 17]. This frequency choice was also reinforced by the data published in [18], which 20 kHz planar ultrasound had a greater effect on membrane permeability (cell model) than 1 MHz and 1.6 MHz ultrasound [18]. These findings were further supported by a similar experiment published by Sundaram, Mellein, Mitragotri [17]; they reported that exposure to 20-100 kHz range frequency ultrasound caused increased fibroblast membrane permeability (critical to wound healing process).

The consideration presented above led to decision of the setting the resonance frequency of the applicator between 20 and 100 kHz. The final determination to make use of 20 kHz operating frequency was reached by examining the outcome of the *in vitro* experiments [1], which indicated that the frequency of 20 kHz was most effective in activating fibroblast cells. These cells are responsible for initiating the production of collagen; an indispensable component of the wound healing process. No attempts were made to further lower this frequency as the corresponding wavelength of 75 mm appeared to have adequate penetration to stimulate wound bed tissue by promoting wound contraction, angiogenesis, collagen deposition, and re-epithelialization.

As mentioned previously, early in the design process it was decided to ensure the complete safety of the device through implementation of non-thermal and non-cavitation mode of operation. In such mode, the ultrasound exposure should not lead to temperature elevation exceeding 1 deg C or the onset of inertial cavitation [19]. The possibility that the applicator might cause inertial cavitation was eliminated by limiting acoustic output pressure amplitude of the device to be 55 kPa and experimental verification.

Two independent tests confirmed that the applicator operating at 20 kHz with a pressure amplitude of 55 kPa does not produce inertial cavitation. The first test used aluminum foil to show pitting if inertial cavitation was present. This was done with axial distance between the foil and the surface of the applicator minimized (< 1mm) and filled with deionized water to closely mimic clinical treatment. The second test used a hollow cylinder hydrophone [16] coupled to an HP 8535A Spectrum Analyzer to display the cavitation spectrum. This technique allowed both stable and inertial cavitation events to be detected. Stable cavitation manifests itself by generation of subharmonics and odd multiples, whereas inertial cavitation is characterized by white noise produced by the imploding of microbubbles with a diameter on the order of microns [23, 24]. In both experiments, the prototype discussed showed no signs of inertial cavitation. The temperature test was completed by inserting miniature thermocouple (HI98509-Checktemp@1C Pocket Thermometer) into the less than 1 mm water gap and monitoring its output for 300 minutes. The maximum temperature variation observed was less than 1 deg C.

It is well established that bubble formation, growth, and dynamics are governed by the viscosity of the host medium, [26] and the inertial cavitation threshold increases with increasing viscosity. The viscosity of deionized water at 20° C is about 8.9×10^{-4} Pa·s [26] so no cavitation activity is expected to take place in the wound coupling medium – Aquagel, which exhibits a viscosity that is 3 orders of magnitudes higher (0.25-0.75 Pa·s) [25].

Having assured the safety of the device by limiting the acoustic output pressure amplitude to

55 kPa, the rationale behind the efficacy of the proposed treatment assumes that radiation force and stable cavitation with its induced microstreaming and associated stresses would be sufficient to stimulate the wound healing process. Acoustic radiation forces are mechanical stresses caused by acoustic energy interacting directly with cells, while stable cavitation indirectly induces mechanical (shear) stress by causing acoustic streaming [27]. This streaming represents a steady state fluid flow induced by time variable ultrasound energy [28]. Rooney et al. [29] demonstrated that acoustic radiation forces and steady state streaming associated with the possible (microns) size bubble can be induced at frequencies and pressure amplitude similar to those considered here. Although the biological mechanisms by which ultrasound affects wound healing are not well-characterized, there is evidence that angiogenesis (the creation of new blood vessels) plays a role in ultrasound-assisted wound healing [30], and that mechanical forces, such as the shear stress from fluid flow, can enhance angiogenesis [31, 32].

C. Choice of Principle of Operation

The selection of the desired frequency and the long-term plan mentioned above to embed the design in the wound dressing necessitated a major re-thinking of the transducer architecture and departure from the conventional piezoelectric ceramic design.

This was essential because conventional (half-wavelength thickness vibration PZT ceramic) applicator design for a frequency of 20 kHz would require a piezo-element with a thickness of about 10 cm. Moreover, minimization of spurious resonances would suggest aspect ratio between the ceramic disk diameter and the thickness to be about 10. With typical PZT ceramic density on the order of 7000 kg/m^3 and material volume (cylinder of 10 cm height and diameter of 100 cm) of 0.079 m^3 , the resulting weight would be close to 549 kg. Even if available, an element this large would not only be bulky, but would require hundreds of volts for excitation (requiring a heavy (10 kg+) Power Amplifier, such as e.g. ENI 300.). Such an applicator would not be appropriate for wearable design [33, 14]. Hence, the conventional design was deemed to be unacceptable for clinical wound treatment.

The subsequent critical review of the literature (well documented in [12]), and stressing the pioneering contributions of Professor Newnham's team at Materials Research Lab, Penn State University [20-22], suggested a flexural transducer design. The piezoceramic (PZT) disc is capped at both sides by "dome-like" shaped metal caps, which are firmly glued to the PZT ceramic using an adhesive. This adhesive introduces specific displacement boundary conditions to deliver maximum displacement amplitude with the lowest possible excitation voltage. The principal architecture of the flexural, single element 20 kHz ultrasound applicator developed for chronic wound treatment is shown in Fig. 2.

It is instructional to concisely describe the principle of operation of the transducer of Fig. 2. Each single transducer element uses a piezoelectric ceramic positioned between two metal end caps, offering a spatial intensity distribution at the axial distance of 1-2 mm that ensures the wound tissue is exposed to uniform ultrasound field [14]. The transducer maximizes the perpendicular displacement amplitude with minimum electrical excitation applied to the piezoelectric disk.

The design of (Fig. 2) represents practical implementation of mechanical displacement amplifier, which translates 2 MHz ultrasound waves into 20 kHz output at the desired pressure amplitude (55 kPa; i.e. 100 mW/cm^2 , I_{sptp}). The triangle design of the applicator (Fig. 1), was introduced to optimize the area of wound tissue stimulation. The requirement for the uniform spatial cross-section of the pressure amplitude was achieved by connecting triangle configuration of single element transducers electrically in parallel (see Fig. 3).

Detailed analysis of the design was prepared by Youhan Sunny [14], who has shown that the optimization process requires detailed consideration of the following parameters: the radius and thickness of the PZT disk, the base and apex radius, and finally cavity depth and thickness.

The design shown in Fig. 3 enables delivery of low-frequency ultrasound through a fully wearable ($<20 \text{ g}$, $<1 \text{ cm}$ thickness), untethered transducer that is powered with rechargeable 12V lithium ion batteries [14] and overall weight of 200 grams so that a patient's mobility is not restricted during therapy. As already noted, such transducer design also has the potential to be integrated into existing wound dressings without degrading the ultrasound dose delivered. Also, the ultrasound driving unit and applicator design lend itself for possible future improvements. The relatively thin ($<10 \text{ mm}$) profile of the applicator (see Figs 1 and 2) embedded in the compression dressing would allow multiple wounds to be treated simultaneously.

D. Design Summary

As mentioned earlier, the acoustic design specifications of the ultrasound applicator describe here include frequency of operation of 20 kHz and an acoustic peak pressure amplitude of 55 kPa corresponding to the spatial peak- temporal peak intensity of 100 mW/cm^2 . The applicator was activated by bipolar, 12 Vpp, 20 kHz tone burst with a duty cycle of 50%. A pulse repetition frequency of 25 Hz and operation at 50% duty-cycle were implemented to maximize the life of the battery.

The quantitative methodology designed to determine field distribution and absolute values of the acoustic output parameters (frequency, intensity, etc.) of the ultrasound applicator shown in Fig. 4 is presented in the next section.

III. Acoustic Performance

The quantitative methodology designed to determine field distribution and acoustic output parameters (frequency, intensity, etc.) was implemented using two hollow cylinder type hydrophones [34]. Both hydrophones are commercially available (B&K model 8103 and Reson Model 4032) and exhibit relatively uniform receiving frequency response (uV/Pa). Their absolute sensitivity versus frequency response was determined by implementing three transducers reciprocity setup. The set up uses driver electronics to activate a hydrophone as used a transmitter and a Tektronix oscilloscope (model TDs 2022) to monitor received free-field signals from the two receivers located equidistant from the B&K 8103 hydrophone used in transmitter mode. The electrical current of this (transmitting) hydrophone is recorded

(using the same Tektronix oscilloscope) as a voltage drop across the precision resistor inserted in the ground wire.

The key parameters needed to obtain absolute values of receiving (direct) and transmitting (inverse) conversion coefficients include the transfer impedance and reciprocity parameter [35]. Once these parameters were determined, the absolute values of (end-of-cable) receiving voltage [V/Pa] and transmitting voltage sensitivity [Pa/V] of the hydrophones were calculated.

For hydrophones used in this work to measure the acoustic output of the ultrasound applicator shown in Figs 1 and 3, the overall calibration uncertainty was determined to be 10% or about 1 dB, which is typical when performing underwater hydrophone calibrations [35].

once calibrated the hydrophones were used to monitor the applicators' performance prior to clinical use. To emulate as closely as possible the conditions at which the wound tissue was exposed in clinical practice the measurements were performed at the distance of 2.5 mm (Fig. 4).

IV. Human Subjects Testing

As reported previously [1], the ultrasound applicator was successfully used in a pilot study of venous ulcers, where subjects who received the treatment for 15 minutes per week showed statistically faster ($p < 0.03$) rate of wound closure than subjects who received sham treatment. As a follow up to this study, a pilot study of diabetic foot ulcers was conducted using the ultrasound applicator described above. In this section, the design of the pilot study is briefly described, followed by a summary of the results.

The study was conducted at the Drexel University Wound Healing Center, and all study procedures were approved by the Drexel University IRB. Ten patients with diabetic foot ulcers were recruited. All patients had to be between the ages of 18-80 years, have an ulcer on the foot or ankle secondary to diabetes for at least 2 months, have an ulcer size of approximately 1 cm² or greater, and no known allergies to Tegaderm (the sterile polyurethane wrapping that was used to cover the ultrasound applicators during use). After enrollment in the study, patients were randomly assigned to either the treatment group ($n=5$) or the sham (control) group ($n=5$). The pilot study was single blind (i.e. the researcher administering the treatment knew whether the patient was being given the treatment or sham, while the patient was not). A double-blinded randomized controlled trial is currently in progress (see Acknowledgements).

The treatment protocol was similar to the one described previously [1]. Patients were treated with each an active ultrasound applicator or a sham applicator for a period of 15 minutes during their weekly visits to the wound clinic. First, sterile acoustic gel was placed directly on the wound (Aquasonic 100). Next, the ultrasound applicator was wrapped with a sterile Tegaderm plastic coating, and then placed directly on the gel and over the wound. To secure the device, medical tape was placed over the device and adhered to the skin. The device (active or sham) was turned on for 15 minutes, and then shut off and removed from the

patient. All patients, regardless of treatment group, received standard wound care throughout the study, which included weekly debridement, offloading, and moist wound dressings as prescribed by the physician.

Two patients, one from the active treatment group and one from the sham group, did not complete the study and were lost to follow up. All of the remaining 8 patients' wounds healed during the study, and the time to complete wound closure (in weeks) was recorded for each patient. The average number of weeks to closure was 4.67 for patients treated with the active ultrasound applicator, while the average weeks to closure for sham-treated patients was 12 ($p < 0.05$, Student t-test), as shown in Figure 5 below. The difference in the initial wound sizes across the two groups was not significant ($p = 0.61$).

Although the sample size was small with only four wounds per group, these results suggest that patients with diabetic foot ulcers may benefit from treatment with low frequency, low intensity ultrasound. Wounds that were treated with the active ultrasound device closed approximately 3 times faster than sham-treated wounds, thereby requiring approximately 8 fewer weeks of treatment (on average) than sham-treated wounds.

It is difficult to directly compare the outcomes of this pilot study to the results of other ultrasound wound treatment studies [38] because each study involved different ultrasound parameters, treatment times, exposure rates, and wound etiologies. For example, the Vianna-Pompeo (VIP) ultrasound protocol [38] treated wound of mixed etiology three times per week using a combination of relatively high intensity (0.2 to 1.0 W/cm²) ultrasound for debridement and somewhat lower intensity (0.1 to 0.5 W/cm²) ultrasound as an adjunctive therapy, and found 2 of 12 treated wounds healed completely within a 12 week period. In contrast, this study describes the use of low-intensity (<0.1 W/cm²) ultrasound to treat diabetic foot ulcers for 15 minutes once per week, and all four ultrasound-treated wounds healed within 12 weeks.

Although therapeutic ultrasound has shown active wound healing through ultrasound debridement using MIST therapy [37], reducing bacteria in the wound biofilm [37], and increasing fibroblast proliferation [1], mechanism of this healing is still unknown [39]. It is plausible that therapeutic ultrasound affects macrophages, the key biologic regulator of inflammation [40]. It is well established that macrophages are critical to the wound healing process by generating growth factors that promote fibroblast proliferation and angiogenesis [41]. The generation of these factors may be dependent on the polarization of M1-like (pro-inflammatory) macrophages to M2-like (anti-inflammatory) macrophages [41]. Low intensity (30 mW/cm²) pulsed (1.5 MHz) ultrasound pulsed at 1 kHz has been shown to activate the RhoA mechanotransduction pathway in macrophages and increase macrophage phagocytosis [42], which is a characteristic of pro-healing M2 macrophages [43]. Additionally, macrophages increase gene expression of pro-healing growth factors VEGF and TGF-beta in response to mechanical stimuli in the form of low-intensity (30-100 Hz) vibrations [44] and exhibit mechanotransduction pathways that are necessary for M2 polarization [45].

V. Conclusions

The step-by-step process delineating the design of the hardware implementation of the first-generation therapeutic ultrasound prototype intended for treatment of chronic wounds was presented. The patch-like applicator was intentionally designed to operate at relatively low frequency of 20 kHz and with acoustic output limited to 100 mW/cm² (Spatial Peak, Temporal Peak). The device is currently being used in successful treatment of human patients for chronic ulcers and is fully wearable, lightweight (<20g) and Li-ion battery powered. The possibility of using this early, non-cavitation, non-thermal prototype as a tool for pre-clinical studies, including non-invasive drug delivery is also considered [14]. Although the current prototype is clinically acceptable, the next prototype model is being developed to further optimize the electroacoustic efficiency of the device (including new generation of lightweight batteries as they enter the marketplace), fabrication yield, ergonomics, and programmable timer for timed treatments. In addition to chronic wound treatment and noninvasive drug delivery it is expected that the prototype described might be useful as a potential tool for neurostimulation of different body parts, including brain as 20 kHz wave should penetrate skull with minimum attenuation of the ultrasound energy. The possibility of using this device in activation of brain tissue appears to be conceivable in view of the recent reports [34]. These reports describe the feasibility study performed in the frequency range 440 kHz – 670 kHz and intensity of about 500 mW/cm² *in vivo* in rat brain tissue. Lastly, it is anticipated that the wearable ultrasound applicator may also be used for general neural stimulation, such as neuropathy that is prevalent as the undesirable side-effect of chemotherapy treatment.

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Leonid Zubkov , Ph.D., DSc is currently a research professor in the School of Biomedical Engineering, Science and Health Systems at Drexel University, Philadelphia. Before arriving to the USA in 1998, he worked at the Optical laboratory of the Department of Physics at St. Petersburg University in Russia as a Professor of Physics. His major research interests included application of molecular light scattering, Mie scattering spectroscopy, and interferometric methods to investigation of fundamental problems of phase transitions in liquids, liquid crystals and suspensions. In the course of his work he discovered for the first time the coherent light scattering in liquid crystals and observed fluctuations of non-ordinary beam when it propagates through mono liquid crystal in real time. At the University of Pennsylvania, he created several modifications of Diffuse Near Infrared Spectroscopy (DNIRS) medical devices based on the diffuse photon density wave (DPDW) method. He also assembled diagnostic instruments based on Diffuse Correlation Spectroscopy (DCS) method for blood flow measurements in human tissue. Several variations of DNIRS devices designed by him are being used successfully in the U. Penn Hospital for breast tumors and brain stroke detection research, and at the Hahnemann Hospital of Drexel University for research of healing in diabetic wounds and venous leg ulcers. One version of the DNIRS device was licensed by Emunamedica, LLC in 2009 for commercialization as a wound healing monitor. Previously, he worked at the University of Pennsylvania Department of Physics, and was a Professor of Physics at St. Petersburg University. He received his Ph.D. and D.Sc. in Physics from St. Petersburg State University. His research interests involve using diffuse optical methods to address medical problems.

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awarded several patents in the field of ultrasound and has authored or co-authored over 240 scientific publications, most of them on topics in ultrasound and is co-editor of *Ultrasonic Exposimetry* (CRC Press, 1993), a landmark book in the field. His current interests are primarily in the field of biomedical ultrasonics including the design and testing of piezoelectric transducers and sensors, power ultrasonics, ultrasonic exposimetry, tissue characterization using nonlinear acoustics, biological effects of ultrasound, applications of shock waves in medicine and image reconstruction and processing.

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For additional information please visit: <http://drexel.edu/biomed/faculty/core/LewinPeter>

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Fig. 1.
Ultrasound Applicator: Triangular Element Array model

Fig. 2. Flexural design – (*left, center left*) – measured diameter (1.6 cm) and thickness (1 mm) of PZT disc. (*Right*) fully assembled transducer element with PZT disc and flexural brass caps.

Fig. 3.
Clinical applicator with black housing box for driving electronics powered by 12V Lithium
– Ion rechargeable battery

Fig. 4. (*left*) Clinical testing fixture. (*Right*) The needle hydrophone (Reson 4038) is adjusted using the thumb-nuts to a position 2.5 mm below the applicator transmitting surface

Fig. 5. Average Weeks to Full Closure for Diabetic Ulcers (DU). This graph shows that treated diabetic ulcers healed approximately 3 times faster than non-treated diabetic ulcers.