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Pitch–Catch Phase Aberration Correction of Multiple Isoplanatic Patches for 3-D Transcranial Ultrasound Imaging

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Abstract

Having previously presented the ultrasound brain helmet, a system for simultaneous 3-D ultrasound imaging via both temporal bone acoustic windows, the scanning geometry of this system is utilized to allow each matrix array to serve as a correction source for the opposing array. Aberration is estimated using cross-correlation of RF channel signals, followed by least mean squares solution of the resulting overdetermined system. Delay maps are updated and real-time 3-D scanning resumes. A first attempt is made at using multiple arrival time maps to correct multiple unique aberrators within a single transcranial imaging volume, i.e., several isoplanatic patches. This adaptive imaging technique, which uses steered unfocused waves transmitted by the opposing, or beacon, array, updates the transmit and receive delays of 5 isoplanatic patches within a $64^\circ \times 64^\circ$ volume. In phantom experiments, color flow voxels above a common threshold have also increased by an average of 92%, whereas color flow variance decreased by an average of 10%. This approach has been applied to both temporal acoustic windows of two human subjects, yielding increases in echo brightness in 5 isoplanatic patches with a mean value of $24.3 \pm 9.1\%$, suggesting that such a technique may be beneficial in the future for performing noninvasive 3-D color flow imaging of cerebrovascular disease, including stroke.

Introduction

As the third-leading cause of death in developed nations [1], stroke constitutes a significant public health concern. The impact of stroke diagnosis, treatment, and rehabilitation on the health care systems of developed nations is expected to increase as the population ages [2]. Currently, the clinical state of the art in stroke protocols is to use computed tomography (CT) scans to rule out hemorrhagic stroke [3], [4]. If hemorrhagic stroke can be ruled out within 4.5 h of the onset of stroke symptoms, patients in the United States are eligible to receive intravenous tissue plasminogen activator (tPA), a thrombolytic agent [5], [6].

Although ischemic stroke accounts for 87% of all stroke cases [7], only 1% to 7% of eligible patients actually receive tPA [8]–[10], primarily because the patient is not diagnosed quickly enough or because symptoms are considered to be too mild [11], opening the discussion for alternative means of determining the nature of a stroke. In a 2165-patient study [11], 14.6% of the patients who missed the time window did so because of either the delay in transferring from an outlying hospital or lack of access to the treating hospital. In patients within the time window, an additional 8.9% were not given tPA because of a delay in emergency department referral. These are particular areas in which technology can help improve patient outcomes.

In recent years, transcranial ultrasound imaging has sought to fill this niche as a portable, inexpensive imaging modality, the feasibility of which has been demonstrated in various pre-hospital settings, including ambulances and emergency helicopters, and in remote environments [12]–[16]. Three-dimensional ultrasound is particularly well-suited to

emergency medicine because an operator with limited training has a greater likelihood of capturing clinically useful information within a 3-D volume than within a single 1-D scan or 2-D slice. In addition to diagnosis, transcranial ultrasound imaging may also help in patient screenings and follow-up.

Although ultrasound imaging of the adult brain has been pursued since the 1960s [17], [18], with real-time imaging beginning in the 1970s [19]–[22], the quality—and thus the diagnostic utility—of these images has remained limited by the acoustic properties of the skull. Specifically, within the temporal acoustic window (cortical bone), the skull has a longitudinal velocity of 2327 to 2650 m/s [23], [24], density of 1850 kg/m³ [25], and attenuation of 2.8 dB/cm/MHz [26], whereas soft tissue has a longitudinal velocity of 1540 m/s, density of 1000 kg/m³, and attenuation of ~0.5 dB/cm/MHz. The mismatch in propagation velocities and variations in skull thickness across the transducer aperture result in time shifts to and from each individual element, or phase aberrations, which broaden transmit and receive beams. Differing acoustic impedances produce significant refraction and reflection at skull–soft tissue interfaces. The high level of attenuation in the skull reduces both energy reaching the transmit focus and backscattered energy arriving at the transducer.

Several techniques have been devised for improving the image quality of transcranial ultrasound images, including imaging through known acoustic windows such as the temporal bone window [27], [28], inducing shear-mode conversions at the soft tissue–skull interfaces [29], [30], contrast-specific imaging techniques for both large artery [31], [32] and perfusion imaging [33], [34], and adaptively adjusting probe element delays and/or amplitudes [19], [22], [35]–[43]. Notably, Miller-Jones proposed using a contralateral active source as a correction beacon [36], and Ivancevich *et al.* corrected *in vivo* aberration on a 2-D array using a multi-lag cross-correlation technique [42]. It is now proposed to combine these last two approaches, but taking into consideration the size of the isoplanatic patch (IP) of the aberration within the temporal bone acoustic window to improve image quality throughout an entire 3-D transcranial volume.

The IP—or spatial stability—of an aberrator describes the area over which the aberrator may be corrected using a single arrival time map [44]. The skull has been well modeled by the near-field phase screen model [39]–[43], in which the aberrating layer is assumed to be infinitesimally thin, to lie immediately adjacent to the face of the transducer, and to have an infinite IP. As these assumptions fail, the IP decreases in size. Thus, the thickness of the skull at a given transducer element may be corrected by application of the appropriate equal and opposite time delay. In actuality, the skull has a finite thickness and is separated from the transducer by a few millimeters of extracranial tissues and vessels, resulting in a finite IP. For a phased-array scan, the near-field phase screen assumption begins to fail as scan angle increases from broadside (0°, 0°) to approximately $\pm 16^\circ$ [43], [45], decreasing the potential benefit of phase aberration correction [46]. Applying the appropriate phase correction maps to the appropriate steering angles could improve brightness and contrast in transcranial images over the entire field of view. In this work, the aberrator is assumed to be temporally stable because the skull is rigid and fixed relative to the position of the transducer.

There is not a single, standard definition for the IP; it has been variously defined as the positions in the field over which the point spread function (PSF) increases by 10% [47], aberrators are correlated by 70% to 90% [44], or speckle/target brightness increases [43], [45]. IP size varies depending on the definition used, the scanning system, the correction method used, and on the individual skull [45]. Correction of multiple IPs has been investigated by Liu and Waag in *ex vivo* abdominal tissues [47], and by Fernandez and

Trahey [48] and Dahl *et al.* in the breast [44]. For the cranial bone (temporal acoustic window), two known attempts have been made to measure the size of the IP in angular extent and depth, both using the increasing brightness metric. In the first, Ivancevich measured a two-sided angular extent of 33° in the transverse plane in a casting of a human temporal bone [49], and an angular extent of 9.7° *in vivo* in 2 subjects using a correlation-based correction method. Vignon *et al.* measured $36 \pm 18^\circ$ in *ex vivo* skulls and 33° *in vivo* in a single subject, both in the transverse plane, using a time-reversal mirror correction method (FDORT) [45]. This study also suggested that aberration correction effectiveness in transcranial sector scans might be divided into 3 broad categories of “effective,” “lowly effective,” and “ineffective” as scan angle increases, where “effective” denotes the center 30° of a transcranial sector scan. The IP in a 2-D sector scan is often reported as an azimuthal angle and an axial depth. Because both previous measurements found the axial depth of the temporal bone IP to extend to the entire scan depth (12 cm [49] and 15 cm [45]), an infinite patch size in the axial direction will be assumed.

In addition to wavefront aberration, other mechanisms of degradation in transcranial ultrasound imaging include mode conversion [50], [51], refraction [37], multiple scattering [25], attenuation [52], and nonlinearity. Of these phenomena, aberration is the only one which may be compensated for in the course of conventional delay-and-sum beamforming. Because a clinical ultrasound scanning system assumes a constant longitudinal propagation velocity (typically $c_{\text{tissue}} = 1540$ m/s) when computing both transmit and receive delays for focusing and steering, the introduction of a layer having different velocity ($c_{\text{skull}} \approx 2327 \pm 90$ m/s at 1.97 MHz [23]) results in a broadening of the imaging system’s point spread function (PSF). Because signals are summed partially out of phase both at transmit foci and during receive beamforming, the wavefront coherence diminishes, resulting in decreased speckle and point target brightness, enlargement of axial and lateral resolution, and decreased contrast.

Numerous techniques for aberration estimation and correction have been proposed [39], [44], [47], [49], [53]–[74]. The work of Trahey *et al.* explores phase correction techniques for phase screen aberrators and delineates the need for 2-D phase aberration correction to accurately estimate and correct aberrators containing high spatial frequencies [44], [53]–[57]. Specifically, Nock *et al.* describe the need for different delay update profiles at different angles because of a finite IP [58]. Following these efforts and those of Flax and O’Donnell [59] and Liu and Waag [60], our lab has previously implemented phase aberration correction on a 2-D array using both multi-lag least-mean-squares cross-correlation [59], [60] and speckle brightness [58], [61] correction algorithms [39], [49]. Optimization of a coherence metric has also demonstrated success, especially for the case of an offset phase screen [62], [63]. Propagation path effects in aberration estimation and correction in the absence of a point target using statistical methods have been investigated by Waag and Astheimer [64], Astheimer *et al.* [65], and Tillet *et al.* [66].

The time-reversal mirror technique [67] has demonstrated success at focusing through aberrating layers [68]–[72] by addressing the aberration problem as a complex filtering operation, allowing variation of both amplitude and phase with frequency and more fully addressing the various degradation phenomena described previously. The basic principle is that the matched filter producing optimum SNR is the time reversal of the received signal. Ng *et al.* have examined the closely-related phase conjugate filters, which correct distortions in phase spectra without modifying magnitude spectra [55], [73]. Inverse filters attempt to take this one step further by eliminating both phase and magnitude distortions, but are often non-realizable and amplify noise at frequencies for which the operator being inverted (i.e., aberration or other distortion operation) has a small response. This is typically addressed by regularization via singular value decomposition and by applying inverse filters only over

selected band-limited regions [73]–[75]. For each individual frequency, it is possible to compute the number of physically relevant singular values given imaging system characteristics; then, only these singular vectors are inverted [74], [75].

Vignon *et al.* [40] and Tanter *et al.* [74] have demonstrated an inverse filtering technique suitable for correcting skull-induced distortion using a linear array and the pitch–catch geometry proposed by Miller-Jones [36]. An inverse filtering approach more fully measures all mechanisms of image degradation, including aberration by the near skull, path-dependent aberration, and path-dependent attenuation, although when applied to skull aberrations, it uses a phase screen assumption in approximating the propagation operator as a diagonal matrix [40]. However, the cost of implementing this approach on a 2-D array is significant, requiring a fully programmable transmitter and access to the RF signal for each element, a difficult proposition at a time when many manufacturers have moved toward digitization and partial beamforming in the probe handle [76], [77]. In this work, it is assumed that aberration effects from the first skull transit are small relative to aberration effects resulting from the second skull transit, because wave divergence and path-dependent effects tend to average out any initial aberrations, whereas aberration effects caused by the second skull transit are directly measured immediately after they occur.

Previously, we have demonstrated an experimental system capable of acquiring, registering, and fusing two contrast-enhanced transcranial ultrasound volumes (Fig. 1) with a 7 dB increase in SNR resulting from reduced cable lengths [78], [79]. This work takes advantage of the beacon provided by this geometry to add phase aberration correction to this diagnostic ultrasound brain helmet. The existing state-of-the-art is improved upon in the following ways: 1) correcting on a coherent, high-amplitude source reduces the error in arrival time maps for 3-D transcranial aberration correction compared with speckle-based corrections, and 2) utilizing each 2-D array to transmit multiple steered wavefronts allows estimation of multiple arrival time maps, where each map can be used to correct a different group of image lines within the phased array volume (i.e., a different IP). Previous attempts at transcranial phase correction have assumed an infinite IP size, causing a decrease in image brightness at the edges of a 2-D sector or 3-D volume [45]. By updating imaging delays to correct for skull inhomogeneities and partially restore lost resolution and contrast throughout two entire 3-D volumes, we hope to aid in the emergence of transcranial ultrasound as a rapid, effective diagnostic alternative for cerebrovascular imaging.

II. Methods

A. Scanning System

Experiments were performed using the Volumetrics Model 1 scanner (Volumetrics Medical Imaging, Durham, NC), a real-time 3-D ultrasound system using 16:1 parallel receive processing [80], [81]. This system has 256 transmit channels and 256 shared transmit/receive channels. A 2-D phased array transducer on this system typically transmits 256 broadened beams in succession. For each transmit beam, 16 receive beams are formed from echoes arranged in a 4×4 pattern centered on the transmit beam. The transmit beam spacing is 4° in a typical $64^\circ \times 64^\circ$ scan, enabling frame rates of up to 30 volumes/s.

To enable simultaneous real-time 3-D imaging with two 2-D arrays, the scanner's channels and its 4096 image lines have been split equally between two matrix arrays so that two $64^\circ \times 64^\circ$ pyramidal volumes may be acquired simultaneously. Each matrix array has 128 transmit elements and 128 shared transmit/receive elements. As before, for each transmit beam, 16 receive beams are formed from one of the two transducers. However, transmit beam separation has now doubled in the elevation direction, so transmit beams in each $64^\circ \times 64^\circ$ volume are now spaced at 4° in azimuth and 8° in elevation. An alternative design approach

would maintain beam density while decreasing frame rate by a factor of 2; however, this is not advantageous for color flow imaging and is not a realistic implementation on this parallel processing system. Four slices from two probes are displayed in real time: one azimuth and one elevation slice from each transducer, corresponding to coronal and transverse planes in transtemporal imaging [Fig. 2(a)]. The operator uses a trackball control to select any four slices in either volume for display. Although custom transducers were designed for this system [79], limitations in bandwidth and inter-element uniformity compared with commercially manufactured transducers rendered the jitter errors in aberration estimates too high for this study. For this reason, all experiments were performed using commercial (Volumetrics) sparse 2-D arrays having inter-element separation of 0.35×0.35 mm and remapped by a custom printed circuit board to allow for dual simultaneous 3-D imaging [82]. Each sparse matrix array has 128 elements with an aperture diameter of 6.6 mm [Fig. 2(b)], producing a -6 -dB pulse-echo beamwidth of 5.5 mm at a depth of 70 mm [78]; studies were performed with echo at 2.5 MHz and Doppler at 1.8 MHz. For phantom studies, transducers were aligned to face one other across the phantom or water tank with zero tilt between them unless otherwise noted. For human imaging, transducers are held in place by a modified non-imaging transcranial Doppler head frame (Mark III, Spencer Technologies Inc., Seattle, WA) which allows both arrays to be positioned and fixed within the temporal acoustic windows.

B. Cramér–Rao Lower Bound

Phase aberration correction techniques may be divided into two categories: those that correct on a beacon signal or point target, and those that do not. The beaconless techniques rely on speckle signals, backscattered echoes from subwavelength scatterers having random positions and amplitudes. These received signals are subject to the van Cittert–Zernicke theorem, which states that the mutual coherence Γ_{AB} of two stationary signals A and B at locations x_1 and x_2 on the aperture decreases with increasing spatial distance across the aperture in a manner proportional to the autocorrelation of the aperture [83], [84]:

$$\Gamma_{AB}(x_1, x_2) = R(x_1 - x_2), \quad (1)$$

where R is the autocorrelation of the aperture.

The success of correlation-based correction techniques, such as those proposed by Flax and O'Donnell [59] or Liu and Waag [60], depends on the amount of jitter present in the aberration estimate. The Cramér–Rao lower bound (CRLB) describes the lower bound on the jitter—or the minimum standard deviation between the true (Δt) and estimated ($\hat{\Delta t}$) time delay—for correlation-based time delay estimators [85], and is given by

$$\sigma(\Delta t - \hat{\Delta t}) \geq \sqrt{\frac{3}{2f_0^3 \pi^2 T (B^3 + 12B)} \left(\frac{1}{\rho^2} \left(1 + \frac{1}{\text{SNR}^2} \right) - 1 \right)}, \quad (2)$$

where f_0 is the center frequency, B is the -6 -dB bandwidth, T is the window length, ρ is the correlation coefficient between the two signals, and SNR is the signal-to-noise ratio. The correlation between two partially coherent signals is less than 1, leading to an increase in jitter errors as coherence between the signals decreases from 1. In theory, echoes received from a coherent source remain correlated across the entire aperture, and therefore provide an ideal signal to estimate phase errors. The dual-array configuration of the proposed system can be used to generate a coherent, high-amplitude source, ensuring that both ρ and SNR remain high, and thus reducing jitter to diagnostically useful levels.

A tissue-mimicking phantom (Model 539, ATS Laboratories Inc., Bridgeport, CT) was used to measure the mean correlation coefficient of the received channel signals from an active source. The transducer separation was 17 cm for this experiment, which is larger than the diameter of the typical human head.

C. Aberration Estimation and Computation of Delay Updates

Implementing adaptive imaging on any clinical system poses a considerable challenge given frame rate considerations and limited transmit control capabilities, although some successful implementations have been achieved [39], [48], [56], [86]–[90]. The presented approach uses two matrix arrays, each of which sequentially transmits a series of unfocused waves at varying steering angles to serve as beacons. These data are used to compute multiple arrival time maps, each of which is used to correct the time delays of a subset of image lines.

For each beacon wave, transmit elements were fired with the desired phasing on one array to produce either a steered or an unsteered unfocused wave. Single-channel RF data were acquired on the opposing array and digitized on an adjacent PC at 25 MHz (PDA14, Signatec Inc., Corona, CA). These signals were filtered axially [finite impulse response (FIR) band-pass filter, 60% bandwidth (BW)] and laterally [91] (FIR low-pass, cutoff at 75% of spatial Nyquist), then the direction of arrival (DOA) was estimated by determining the look direction (θ, φ) which maximizes received power:

$$[\theta_0, \varphi_0] = \arg \max_{\theta, \varphi} \left\{ \sum_z \left[\sum_{\theta} \sum_{\varphi} f(z, \theta, \varphi) \right]^2 \right\}, \quad (3)$$

where f is the received wavefield and $[\theta_0, \varphi_0]$ is the optimum look direction.

DOA estimation was performed using an iterative coarse-to-fine approach starting at -35° to 35° in 5° increments and ending with step sizes of 0.67° in both θ and φ . Received data f was then steered to $[\theta_0, \varphi_0]$. DOA estimation is necessary because the orientations of the two transducers are selected based on the imaging region of interest and the individual's temporal bone windows, and thus may be tilted with respect to one another. By steering to the direction of maximum power, large steering components are removed, allowing aberrations—which are small in magnitude (rms) relative to steering components—to be detected and corrected. DOA estimation has previously been used in speckle-based aberration correction to steer toward the dominant scatterer [91].

Phase aberrations were estimated using a multi-lag least squares estimation technique [56]. This estimation algorithm is performed by computing the normalized cross correlation between all element signals within a specified spatial lag. This provides multiple estimates of the time delays between pairs of elements, producing an overdetermined system of equations, described by

$$\mathbf{D} = \mathbf{M}\mathbf{T}, \quad (4)$$

where $\mathbf{D}$ is an $m \times 1$ vector containing the positions of maximum correlation coefficients and $\mathbf{M}$ is the $m \times n$ model matrix. This system is approximately solved using linear least squares [60], producing the $n \times 1$ vector of arrival time estimates:

$$\mathbf{T} = (\mathbf{M}^T \mathbf{M})^{-1} \mathbf{M}^T \mathbf{D}. \quad (5)$$

The least squares solution ensures phase closure, or that the arrival times on any closed path on the aperture sum to zero.

Next, the receiving transducer became the transmitter and the opposing transducer became the receiver on which aberration was estimated, producing an additional 128 delay updates which were used to update both transmit and receive delays for the shared elements of the second array. A total of 256 delay updates were computed for the two transducers and passed to the scanner, updating the transmit and receive delays of all shared elements. Central transmit elements cannot be updated because there is no data from which to estimate the aberrator adjacent to these elements. Although most of the improvement in phase correction arises from correcting receive delays [92], an additional gain of a few decibels might be realized if all transmit delays could be updated. Model matrix $\mathbf{M}$ is typically pre-computed for a specified spatial lag between elements (3 mm in this work).

To correct aberrations in a phased array image, we propose using the contralateral matrix array to transmit a series of steered unfocused waves. Each steered unfocused wave acquisition is used to compute a unique map of delay updates for the receiving array as described. Multiple maps are then passed to the scanner, with each map updating the delays only in the section of the imaging volume corresponding to the steering angle of the transmitted wave used to generate that map (Fig. 3).

D. Algorithm Testing and Validation

The single-IP approach described in Section II-C was validated using electronic near-field aberrators. To compare pitch-catch aberrator detection with previous pulse-echo detection, six 75-ns RMS aberrators (three for each transducer) were created for each of 3 correlation lengths: 1.3, 2.7, and 5.4 mm full-width at half-maximum (FWHM). The two matrix array probes were positioned facing one another across a water tank with side-viewing membrane panels. Each of the 18 aberrators was measured 3 times using the described approach, and the detected and applied aberrators were compared for each trial.

To validate direction of arrival estimation and subsequent steering of the received wavefront f , facing transducers in the water tank were again used. Six 75-ns (3 for each transducer), 2.7-mm FWHM aberrators were tested for each of four relative transducer alignments: $(0^\circ, 0^\circ)$, $(0^\circ, 5^\circ)$, $(0^\circ, 10^\circ)$, and $(0^\circ, 15^\circ)$. The estimated arrival time map was used to correct the pulse-echo imaging delays, and the brightness of a 3-D image of a pin in the water tank was assessed before and after correction three times for each aberrator.

E. Evaluation of Steered Transmit Waves as Correction Beacons

The received channel data must be partially uncorrelated *between* different steering angles to correct multiple IPs, yet should remain highly correlated *within* a single steering angle for accurate estimation of arrival time using the multi-lag least-mean-square error approach. In the case in which multiple acquisitions produced highly-correlated data, then only a single IP would be corrected, and this technique would default to the 1-IP case. Inter-element correlation and inter-steering angle correlation were tested by placing two aligned transducers on either side of a tissue-mimicking phantom (separation of 17 cm, Model 539, ATS Laboratories Inc.) in the presence of an aberrating layer (skull casting, $c \approx 2300$ m/s). Channel data were acquired on each probe using the other as a beacon for 5 proposed steering angles: $(0^\circ, 0^\circ)$, $(0^\circ, -15^\circ)$, $(0^\circ, 15^\circ)$, $(-15^\circ, 0^\circ)$, and $(15^\circ, 0^\circ)$ for 9 unique aberrators by moving the aberrator with respect to the transducer between acquisitions. was measured both as a function of spatial distance within a single steering direction and as a function of varying beacon steering angle.

F. Temporal Bone IP

IP size was estimated using the following method. One transducer was placed against a casting of a human temporal bone immediately adjacent to a water tank containing a row of 1-cm-spaced copper wires at a depth of 6 cm. The second transducer was placed on the opposite side of the water tank. The aberrator was estimated and corrected in the manner described in Section II-C using an unsteered unfocused wave. The corrected volume was saved and processed offline to determine the angles over which target brightness increased. The angle of each wire target was determined within each saved volume. Two-dimensional measurements were made in the transverse direction using 4 different transducer positions on 2 unique bone castings. IP size was not measured in the coronal direction at this time, so for the purposes of this work coronal IP patch size was assumed to be the same as in the transverse direction.

Using measured ($31.8^\circ \pm 15.9^\circ$, Section III-D) IP values and IP values from the literature, we subdivided the $64^\circ \times 64^\circ$ volume acquired by each transducer into 5 patches: a center patch measuring $32^\circ \times 32^\circ$, top and bottom patches each measuring $16^\circ \times 32^\circ$, and left and right patches each measuring $32^\circ \times 16^\circ$ (Fig. 4). Each $16^\circ \times 16^\circ$ corner has been ignored in this work, although in previous work in which an infinite IP was assumed the entire volume was corrected [93]. Each patch has been corrected using an unfocused wave fired by the opposing transducer that was steered in the direction of incident echoes contributing to image lines in that particular patch. All active elements are used to provide adequate energy in the steering direction. Steering angles were chosen to be 15° , small enough to fall well within the $\sim 30^\circ$ critical angle and yet large enough to correct a phased array sector out to $15^\circ + 32^\circ$ (see Section III-D) $+ 15^\circ = 62^\circ$ based on the mean measurement of the IP for this system.

G. Physical Aberrator Correction and Color Flow

For flow experiments, two transducers were positioned over the side-viewing silicone rubber windows of a water tank at a separation of 18 cm. Physical aberrators were applied to the proposed system using two unique polymer castings of the human temporal bone. One bone casting was placed in front of each array and a 3-mm-diameter tube was held in a U-shape using a custom fixture located above the water tank. Seltzer water was made to flow continuously through the tube at approximately 50 cm/s, and fused flow renderings were assessed for pre- and post-correction volumes. For 7 different aberrators, 10 volumes in time were acquired for each case: aberrated, 1-IP corrected, and 5-IP corrected. The three cases were compared on the basis of the number of color flow voxels above a common threshold and on color flow variance.

When performing phantom experiments, the physical setup remained stationary between trials. The only exception to this is that scatterers in the tube moved from one acquisition to the next, as in any flow experiment. Because flow experiments must be performed sequentially on this modified clinical system, statistics of these trials will be reported.

H. Offline Processing, Registration, and Fusion

Saved volumes were processed on an offline computer, where they were scan converted, averaged in time, registered and fused into a single 3-D visualization in Mat-lab (The MathWorks Inc., Natick, MA). Rigid registration was performed in the frequency domain using the finite Fourier transform (FFT)-based phase correlation technique [94]. Then, each volume was normalized and the two optimally transformed volumes were summed in place. We have previously presented rigid registration of two transcranial ultrasound volumes and discussed associated challenges in [79]. Offline processing required approximately 2.5 min.

I. Human Scanning Procedure

The operator began by placing a matrix array probe on each temporal acoustic window of the subject. The scanner's real-time display was used to qualitatively maximize image brightness and to locate anatomical markers, such as the lesser wing of the sphenoid bone. Once positioned, the transducers were fixed in place and two 3-D volumes were acquired. A modified non-imaging transcranial Doppler head frame was used to hold the transducers in place (Mark III, Spencer Technologies). Next, the pitch-catch RF data was acquired and processed for each transducer as previously described. The 256 delay updates were passed to the scanner via UDP datagram and used to update the transmit and receive delay tables of the system. The two phase-corrected 3-D volumes were then acquired. For a single-IP correction, the delay between data acquisition and resumption of scanning was just under 1 min. Of this, 23 s were the result of updating delays, a limitation for this particular system, which has bus and processing speeds of 20 MB/s and 100 MHz, respectively. For a 5-IP correction, the delay update period was approximately 2.5 min.

The system is designed for *in vivo* use rather than collecting experimental data, and it functions by performing either one or five measurements of aberration, then updating delays. After an update, it is then possible to acquire *in vivo* real-time 3-D volumes indefinitely as long as the transducers—which are fixed in place—do not move. Delay maps can only be updated before real-time scanning; it is not possible to retroactively update saved volumes of data with new delay maps, because this is a clinical system that only can only save volumes of envelope-detected data. For human scanning, repeated acquisitions of pitch-catch data guard against subject motion.

We have scanned two human volunteers without contrast agent, a healthy 64-year-old male (subject 1) and a healthy 27-year-old male (subject 2). Typical 3-D Doppler settings include a 4-cycle pulse and an ensemble length of 7, producing a frame rate of approximately 3 frames/s. The Doppler pulse sequence follows that of Jensen [95], in which echo and Doppler pulses are interleaved.

The VMI on-screen display showed a mechanical index of 1.2 and a thermal index of 0.1. Subject 1 was scanned only before and after a 5-IP correction, whereas subject 2 was scanned before correction, after a 1-IP correction, and after a 5-IP correction.

III. Results

A. Cramér–Rao Lower Bound

Mean correlation between nearest neighbor elements using unaberrated, unsteered data was $= 0.966 \pm 0.022$. Correlation remained sufficiently high for larger spatial lags, decreasing to only 0.906 for elements separated by 3 mm. Using measured data, a CRLB of 7.8 ns was computed. Previous results using this scanner reported a mean of 0.838 ± 0.041 on unaberrated speckle data, yielding a CRLB of 19.3 ns at 2.5 MHz [39].

B. Electronic Aberrators

As expected, residual error for pitch-catch corrections decreased substantially compared with pulse-echo techniques at all correlation lengths [Fig. 5(a)] [43]. Mean residual error for pitch-catch was 11.2 ns. Additionally, steering the data to the direction of maximum power, then correcting aberration produced an increase in target brightness in pulse-echo images for all tilts up to 15° , the largest angle tested [Fig. 5(b)]. In most cases, brightness increased by approximately 20% with DOA. Without DOA, the system confuses aberration and steering. This indicates that the planar tilt may be removed for physical tilts between the transducers of up to 15° . These results are discussed further in Section IV.

C. Evaluation of Steered Unfocused Wave as Transmit Beacon

In Fig. 6, inter-element correlation for a steered wavefront decreased more rapidly and had larger standard deviations than in the unsteered case, but for 15° steering, the mean was 0.919 for elements within 1 mm and 0.863 for elements within 3 mm, indicating that accurate arrival time estimation is possible, though perhaps it is advisable to include only shorter lags when estimating the aberration map in these cases. In the case in which only random scatterers are available in the medium, correlation is expected to decrease rapidly with spatial distance, as shown in Fig. 6(a). In the presence of a point target in the medium, in theory, correlation is expected to remain constant with distance, although in practice there is some decrease, as seen in Figs. 6(b) and 6(c). Here, we have observed that in practice, correlation at a relatively large distance (3 mm) remains high even for steered unfocused waves.

The results of a typical steering angle comparison are presented in Fig. 7. They suggest that in a tissue-like medium with an aberrating layer, propagation path differences between different transmit angles are significant enough that correlation remains below ~ 0.8 over most of the aperture. For 9 aberrators, mean correlation between a channel receiving an unsteered beacon signal and one receiving a 15° steered signal was 0.788. Examination of these maps reveals that in some isolated spatial locations the aberrator was highly correlated, whereas over most of the aperture, steering the transmit beacon from $(0^\circ, 0^\circ)$ to 15° off-axis in any direction produced channel data which was poorly correlated between these steering angles, which indicates that correcting multiple IPs is necessary. In instances where the steered data are highly correlated with the unsteered data, the resultant phase maps will be nearly identical and the benefit of multi-IP correction over single-IP will be negligible.

In the presented work, the wavefront received by the receiving array crosses the same region of skull even as angle of incidence varies; however, the finite thicknesses of the skull and extracranial tissues cause the near-field phase screen model to break down. Different propagation paths through an aberrator of finite thickness produce multiple measurements of the aberrator which may then be used when forming the image.

D. Temporal Bone IP

Average measured IP size was $31.8^\circ \pm 15.9^\circ$, which provided us with an estimate of patch size for this specific scanner, aperture, and correction technique. This was similar to the previous measurements [45], [49] and allowed us to proceed with designing a multi-patch correction system with a 32° IP dimension in azimuth and elevation.

E. Physical Aberrator Correction and Color Flow

Dual transducer corrections of color flow volumes for physical aberrators produced an increase in CF voxels above a common threshold for both transducers in 5 of 7 aberrators for the 1-IP correction and 6 of 7 aberrators for the 5-IP correction. Of the 6 successful 5-IP corrections, 5-IP correction produced more CF voxels above the common threshold than 1-IP correction in 5 cases. Mean increase in CF voxels above a common threshold was 25.4% for 1-IP correction and 92.0% for 5-IP correction. Mean decrease in color flow variance for all voxels inside the CF gates was 4.9% for 1-IP correction and 10.0% for 5-IP correction. The improvement in image quality for a single correction may be seen the 3-D renderings of Fig. 8. From one frame to the next, scatterers move between different IPs, thus Doppler magnitude increases when going from single to multi-patch correction because moving scatterers were better detected in the side patches (because of increased SNR). These scatterers subsequently move into the central patch.

F. In Vivo Imaging

Results from imaging subject 1 are shown in Fig. 9. For each of the two transducers, an axial and a coronal echo slice and a 3-D rendered view are shown both before and after performing a 5-IP correction. In the four corrected echo slices, an increase in speckle brightness may be observed, even at the volume edges, indicating an increase in coherence. Brightness increase in sphenoid bone targets is also observable, particularly in the renderings in the last row. This subject's right window appears to be more favorable than the left. Limited success was observed in consistently visualizing color flow on this subject's left side. The following four figures provide additional information on this correction. For the unsteered cases, the estimated angle between probes *in vivo* was typically 1° to 2° .

In Fig. 10, the *in vivo* measured arrival time maps from subject 1 are presented for both transducers. Note that these maps show only aberration, after steering has been removed. Although some correlation between maps acquired with different unfocused wave steering angles is visible, unique aberrators appear to have been measured at different steering angles. Fig. 11 shows the aberrator FWHM correlation lengths and rms strengths for each IP. The colors indicating different IPs correspond to the pyramid in Fig. 4(b). Correlation lengths were comparable to those previously reported for the skull [42]–[45]. Aberration was relatively strong in this subject, although within previously published ranges [45].

Fig. 12 presents intra-channel correlation between data acquired with different transmit steering angles and is analogous to the phantom correlation maps shown in Fig. 7. Mean correlation coefficients were 0.652 and 0.702 for the left and right transducers, respectively—lower than the phantom measurement of 0.788. Lack of significant spatial trends in Fig. 12 suggests that acquired data represent unique IPs based on the spatial correlation definition of the IP [44]. Finally, Fig. 13 gives the increase in brightness on a per-IP basis from this correction. In general, correction of stronger aberrators (Fig. 11) yields greater brightness improvement, as expected. Brightness increases in outer patches were not significantly below those in the center, indicating that the decreased SNR in steered beacon acquisitions did not yield an unacceptably high number of jitter errors.

Fig. 14 shows three volume renderings from subject 2, which demonstrate the impact of single-IP and multi-IP correction on 3-D echo + color flow transcranial imaging. These renderings depict blood flow in both internal carotid arteries near the base of the skull and were registered using common color flow voxels as described in Section II-G. Table I shows the increases in mean echo brightness and number of visible color-flow voxels for multi-patch *in vivo* corrections on the two subjects. Note that when averaged over an entire volume, mean brightness may not improve for a single-IP correction because of the limited IP. Mean echo brightness increase for 4 *in vivo* corrections (2 windows on each of 2 subjects) was $24.3 \pm 9.1\%$. For the two subjects, mean variance of the color flow data decreased by 16.7%. Qualitatively, observed segments of contiguous blood flow in the internal carotid arteries lengthen after correction.

IV. Discussion

A. Timing Constraints

Pitch-catch phase aberration correction of multiple IPs in 3-D demonstrated consistent improvements in color flow imaging in a controlled experiment (tube in water tank) and has also produced improvements *in vivo*. For future *in vivo* scanning, it is important to note that the time limitation (the delay update period of 2.5 min) is not a fundamental limitation, but a limitation of this particular system, caused primarily by the scanner's bus speed and the time required to write the delay updates.

Although this system utilizes 128 channels on each array, it is conceivable that a system with a much higher channel count might be able to reliably perform *in vivo* 3-D color flow imaging without the use of microbubble contrast agent. However, access to digitized channel data is required to perform the proposed methods and is generally unavailable on modern 3-D clinical systems because of partial beamforming in the probe handle [76]. If these data were accessible, the requisite operations for the presented approach (cross-correlation, linear algebra, filtering) could reasonably be performed onboard a clinical scanner. The physical limit on the time for acquiring data to correct MIPs is simply:

$$t_{\text{acq}} = \frac{MNz}{c}, \quad (6)$$

where M is the number of independent steering angles for which data are acquired, N is the number of averages, z is the separation between the beacon and receiving arrays, and c is the medium propagation velocity. For example, acquiring sets of channel data to correct 5 IPs with no averaging and a transducer separation of 14 cm requires 0.45 ms. Therefore, the downtime required to calibrate the scanning system for emergency patients is extremely short. If a second array were to be added to an existing system to be used solely as a transmit beacon (i.e., it would not be able to form images), it would require only triggering from the scanner and the pulsing circuitry necessary to produce a small number of steered planar wave fronts.

B. Steered Transmit Wavefronts

The transmitted pressure fields for unsteered and steered ($15^\circ, 0^\circ$) unfocused waves at a distance of 14 cm were simulated using Field II (Fig. 15) [96], indicating that SNR will be reduced in the steered cases due to significant energy away from the central axis of the receiving array, with the peak pressure at approximately 4 cm. The pressure at the receiving array for steered transmits is approximately -20 dB down in this ideal case, though aberration will lead to a broader distribution of energy. In spite of this low SNR, it has still been possible to locate a steered wave and correct aberration in both tissue-mimicking phantom and *in vivo* cases. In the future, this could be addressed by either transmitting a defocused rather than a flat wavefront or by steering to angles smaller than 15° . Simulations indicate that transmitting a steered, de-focused wave may increase the transmitted pressure by approximately 6 dB at the receiving array relative to a steered, unfocused wave (Fig. 15). It should be noted that this affects only the SNR of aberrator estimation, not of the image itself. This increase in SNR and the corresponding increase in σ would be expected to yield a decrease in the CRLB (2) of 2.7 ns relative to the value presented in Section III-A (7.8 ns). In the presented technique, there needs only be sufficient energy—whether plane or edge waves—received in each distinct propagation direction such that the CRLB is low enough to accurately estimate aberration with a mean RMS of 61 ns.

C. Direction of Arrival Estimation

The electronic aberrators used in this testing are 75 ns rms. This is a slightly stronger aberrator than would be expected to be observed *in vivo*, as other researchers have found a mean rms of 60 ns in 12 skull samples [45]. Use of this stronger aberrator allows for direct comparison with previous correction techniques, which also used 75-ns aberrators, and facilitates estimation and correction, providing a best-case scenario for testing.

As seen in Fig. 5(b), there is a noticeable notch in the correction efficacy of the approach when the two arrays are positioned at $(0^\circ, 5^\circ)$ relative to one another. We believe this to be the result of ambiguity between aberration and a strong off-axis scatterer (active source in this case). This is not expected to be a significant problem *in vivo*, because for arbitrary

probe placement to maximize image quality, relative probe angles are expected to be much larger than 5° , where steering is relatively easy to distinguish from aberration. The optimum approach would be to have transducers positioned at $(0^\circ, 0^\circ)$, because this would maximize SNR and ensure no ambiguity between tilt errors and aberration, but this is difficult to achieve for *in vivo* imaging given human skull geometry and anatomical variations between individuals. Because both transducers are fixed against the surface of the head, it is important to note that the relative angle between the two transducers is not the same as the angle at which the transmitted wavefront is incident on the skull, which is the angle that was discussed earlier in regards to the stripe artifact and critical angle concerns. It is also worth noting that refraction of the beams at the skull plays a role in transcranial ultrasound. Although this may impact image quality and registration, it should have a minor role on direction of arrival estimation for the purpose of estimating higher order aberrators.

In Figs. 16–18, we present experimentally measured wavefronts without (Fig. 16) and with electronic aberration in a water tank (Fig. 17), and *in vivo* (Fig. 18). The coarse-to-fine localization approach described in Section II-C is visible here, as resolution increases from 5° to 0.67° moving toward the direction of maximum energy. These delay maps may be displayed during scanning and update in real time as the search region is reduced and step size is refined, verifying localization of the beacon. In analyzing these maps, the effects of steering and aberration on the transmitted beacon wavefronts may be observed. Specifically, although aberration alone degrades the quality of the wavefront (Fig. 17), there is little impact on the direction of the steered wavefronts. *In vivo*, the discrepancies between expected and measured angles of arrival are expected to arise primarily as a result of probe placements (optimized for imaging rather than aligning the two probes). There are also effects caused by refraction at multiple interfaces; previous studies indicate an angular shift of the beam by 1.5° to 3° may be expected when steering a beam at an angle of 15° through a poly(methyl methacrylate) plate used to mimic the skull [37].

D. Correction of Multiple IPs

Although image brightness increased by approximately 25%, this 2 dB improvement is less than the expected improvement of 7 dB resulting from decreasing cable lengths [79]. However, it should be noted that this ~ 2 dB improvement is incremental—it could be added to the 7 dB resulting from decreasing cable lengths.

For subject 1, mean correlation coefficients were 0.652 and 0.702 for the left and right transducers, respectively. Because these *in vivo* values were well below those for the physical aberrator with the phantom (Fig. 7) and below the IP definition proposed by Dahl and Trahey (aberrator correlation of at least 0.7 and perhaps as high as 0.9 [44]), these results suggest that further subdivision of the volume into an increased number of smaller IPs may be desirable; however, as discussed, more time is required when more IPs are corrected [increasing M in (7)]. Also, we assumed the IP to be as large in the coronal direction as in the transverse direction. The IP is most likely smaller in the coronal direction given that the window is smaller in this direction [98], although this cannot be concluded from the observed results.

The aberrator RMS values presented in Fig. 11 are quite high for some patches, meaning the effects of aberration correction are larger and more noticeable than in a subject with a weakly aberrating window. This makes sense given the relatively high attenuation in this subject, because attenuation and aberration are often coincident phenomena in the skull [99].

V. Summary

Having previously demonstrated simultaneous dual-probe real-time 3-D transcranial ultrasound imaging, we have now shown proof of concept of a pitch-catch approach to correct skull-induced aberrations in these pulse-echo images, even for arrays tilted at arbitrary angles. Furthermore, we have also presented the first attempt at *in vivo* correction of multiple IPs in the skull, and have observed increases in echo brightness in all corrected regions of two simultaneously-acquired 3-D volumes with a mean value of $24.3 \pm 9.1\%$. In phantom experiments, color flow voxels above a common threshold have also increased by an average of 92%, whereas color flow variance decreased by an average of 10%, suggesting that such a technique may be beneficial for performing noninvasive 3-D color flow imaging.

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Biographies

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Stephen W. Smith (M'91) was born in Covington, KY, on July 27, 1947. He received the B.A. degree in physics (summa cum laude) in 1967 from Thomas More College, Ft. Mitchell, KY; the M.S. degree in physics in 1969 from Iowa State University, Ames; and the Ph.D. degree in biomedical engineering in 1975 from Duke University, Durham, NC. In 1969, he became a Commissioned Officer in the U.S. Public Health Service, assigned to the Food and Drug Administration, Center for Devices and Radiological Health, Rockville, MD, where he worked until 1990 in the study of medical imaging, particularly diagnostic ultrasound and in the development of performance standards for such equipment. In 1978, he became an adjunct associate professor of radiology at Duke University Medical Center. In 1990, he became an associate professor of biomedical engineering and radiology, and

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Dr. Smith is cofounder of Volumetrics Medical Imaging. He has served on the education committee of the American Institute of Ultrasound in Medicine, the executive board of the American Registry of Diagnostic Medical Sonographers, the editorial board of *Ultrasonic Imaging*, and the Technical Program Committee of IEEE-UFFC. He was co-recipient of the American Institute of Ultrasound in Medicine Matzuk Award in 1988 and 1990 and co-recipient of the IEEE-UFFC Outstanding Paper Award in 1983 and 1994..

Fig. 1. Probe placement for proposed transcranial imaging system using two 2-D arrays positioned at temporal bone windows. This system has previously been used to acquire the contrast-enhanced (Definity) 3-D volume shown at right [79].

Fig. 2.

(a) Volume interrogated during a typical transtemporal 3-D ultrasound examination. Coronal and transverse plane views are displayed simultaneously. A steerable Doppler beam is also shown in gray. Two such volumes are acquired simultaneously with this system. (b) Transmit and receive apertures used for each array in this system are shown; each element is 0.35 mm square.

Fig. 3.

Proposed scheme for correction of multiple isoplanatic patches in a phased array sector scan. Each arrow indicates a propagation direction of an unfocused wave aligned with the patch of the same color.

Fig. 4.

Definitions of update regions for (a) single-isoplanatic patch (IP) and (b) multi-IP correction of a single $64^\circ \times 64^\circ$ volume. In the multi-IP case, each color indicates the use of a unique delay map to update image lines within this portion of the volume. Traditionally, the center (red) IP has been used to update an entire phased array volume or sector scan, as in (a). In this work, the outer $16^\circ \times 16^\circ$ corners were ignored in both cases.

Fig. 5.

(a) Electronic aberrator residual error for full-width at half-maximum (FWHM) correlation lengths of 1.3, 2.7, and 5.4 mm for static and moving target cross-correlation (CC) and static and moving target speckle brightness (SB) [43] are compared with pitch-catch (static) cross-correlation (white bars). Mean residual for pitch-catch is 11.2 ns; the Cramér-Rao lower bound is 7.8 ns. (b) Fractional point target brightness increase in pulse-echo 3-D images with varying angle between transducers with (black) and without (red) direction of arrival estimation and steering. Off-axis brightness increased by approximately 20% with direction of arrival (DOA). Each data point is the average of testing 6 different aberrators.

Fig. 6.

Plots of inter-element correlation versus lateral distance across the receive aperture of a sparse 2-D array for (a) random scatterers according to the van Cittert–Zernicke theorem for both the aperture used in this work (solid line) and that of [39] (dashed line). For the case of a coherent source such as in this work, the van Cittert–Zernicke theorem predicts $\rho = 1$ across the entire aperture. However, propagation path differences cause ρ to decrease slightly across the aperture, as seen in (b) the case of an unsteered transmitted beacon wave measured with a tissue-mimicking phantom and skull casting, and in (c) the case of a transmitted beacon wave steered to 15° off-axis with tissue-mimicking phantom and skull casting; (c) is the average result of steering 15° off-axis in all four directions.

Fig. 7.

Maps of maximum correlation coefficient on a per-channel basis after removal of steering components for two typical aberrators using a tissue mimicking phantom and physical aberrator (skull casting). Each ring represents a correlation on channel data received on the aperture (Fig. 2). Within each map, the center ring is always 1 (autocorrelation of unsteered beacon signal channel data); the top, right, bottom, and left maps depict that same unsteered beacon data correlated with data acquired using a $(0^\circ, 15^\circ)$, $(15^\circ, 0^\circ)$, $(0^\circ, -15^\circ)$, and $(-15^\circ, 0^\circ)$ steered beacon, respectively. Each channel is correlated with the same channel, but for a different steering angle of the transmitted wave. For these 9 aberrators, the average correlation between a channel receiving an unsteered beacon signal and one receiving a 15° steered signal is 0.788. This is well below the inter-element correlation coefficient of 0.863 at a lag of 3 mm for 15° steered data or 0.919 at the same lag for unsteered data (Fig. 6).

Fig. 8.

(a) Experimental setup (not to scale) for flow measurements in a water tank in the presence of two physical aberrators. Actual probe-to-tube distance was approximately 6 cm. (b) Registered, fused rendering without aberration correction. (c) Rendering acquired when a single phase map is used to correct the entire 3-D volume. (d) Rendering acquired when five phase maps are used to correct appropriate regions of the 3-D volume.

Fig. 9.

The first two rows show aberrated (columns A and C) and corrected (columns B and D) orthogonal echo slices acquired simultaneously by transducers positioned over the right (columns A and B) and left (columns C and D) temporal bone windows of subject 1. Corrected volumes utilize the five-isoplanatic patch (IP) correction scheme; single-IP corrections were not performed on this subject. Mean brightness increases resulting from aberration correction were 21.2% and 24.2% for the left and right volumes, respectively. The bottom row displays the corresponding 3-D rendering of echo and color flow data. Orientation for these renderings is the same as the top axial row of images. Blood flow shown is the C5 segment of the internal carotid artery. Brightness increases are most easily observed in the edges of the right transducer coronal slice and in the central target (sphenoid bone) of the left transducer. The distance between white tick marks at the edge of sectors is 1 cm.

Fig. 10.

Estimated arrival time maps for the five isoplanatic patches (IPs) used to perform the *in vivo* correction of Fig. 9. Steering components have been removed from these maps. Negative values indicate thick portions of the skull, as incoming signals arrived earlier than the mean arrival time ($t = 0$).

Fig. 11. Correlation lengths (top row) and rms aberrator strength (bottom row) for the subject 1 correction (Fig. 9) are shown for each isoplanatic patch (IP).

Fig. 12.

Channel data from the center isoplanatic patch (IP) was cross-correlated after the removal of steering components with the four outer IPs to produce these maps using the *in vivo* data used to perform the correction of Fig. 9. Mean correlation coefficients were 0.652 and 0.702 for the left and right transducers, respectively.

Fig. 13.

Increases in mean brightness of echo data by isoplanatic patch for left and right transducers for the *in vivo* correction on subject 1 (Fig. 9). Overall mean brightness increases were 21.2% for the left transducer and 24.2% for the right transducer.

Fig. 14.

Three volume renderings of echo (gray) and color flow (red) for subject 2 demonstrating the benefits of multi-IP correction. (a) The uncorrected aberrated image. (b) Although single-isoplanatic patch (IP) correction increases the number of color flow voxels at the center of the scan, brightness of echo data and supra-threshold color flow voxels decrease near the edges of the volume (top and bottom of the figure). (c) Performing a 5-IP correction improves this loss of information at volume edges. (d) An anatomical reference is shown for both the echo and color flow data in the region of interest, where internal carotid arteries enter the base of the skull. The top images are photographs of a human skull casting. The bottom image is coronal slice of an illustrative magnetic resonance angiogram (MRA). Original MRA image (d) was produced by Ofir Glazer, Biomedical Engineering Department, Tel Aviv University, reproduced with permission of the author.

Fig. 15.

Two-dimensional slices through the peak of three-dimensional Field II simulated wavefronts are presented for unfocused wave (red line) and two experimental focusings. A focusing scheme with a virtual point source 5 cm behind the array (dashed black line) yields the greatest pressure increase at the receiving array (indicated by black rectangles), approximately 6 dB, though its side lobes will be subject to the aforementioned effects of probe placement and refraction [97]. An inverse focusing scheme, or spherical law defocusing on the opposing skull, yields the most spatially uniform pressure field (dotted green line) [40]. Energy distributions are expected to be broadened in the presence of aberration and multiple reflections (Figs. 16–18).

Fig. 16.

Results of a typical direction of arrival estimation for (a) un-steered and (b) steered wavefronts. In this control case, two arrays were aligned across a water tank and direction of arrival is accurately measured as $(0^\circ, 0^\circ)$ for the unsteered case and $(15^\circ, 0^\circ)$ for the steered case using the described coarse-to-fine approach.

Fig. 17.

Results of a typical direction of arrival estimation for (a) un-steered and (b) steered wavefronts in the presence of aberration. In this experimental case, two arrays were aligned across a water tank and direction of arrival is accurately measured as $(0^\circ, 0^\circ)$ for the unsteered case and $(15^\circ, 0^\circ)$ for the steered case using the described coarse-to-fine approach in the presence of a 75-ns rms electronic aberrator.

Fig. 18.

Two *in vivo* pitch-catch measured wavefronts using the cross-skull probe placement of Fig. 1 for (a) unsteered and (b) steered wavefronts. The coarse-to-fine approach reduces the size of the search region by 20% for each of 10 iterations, with each successive search region centered about the direction of maximum energy. For a steered map, SNR is lower, as discussed in Section-IV-B. In these examples, the maximum energy for the (a) unsteered case is found at $(-0.5^\circ, -0.6^\circ)$ and for (b) the steered case, it is found at $(9.8^\circ, 1.2^\circ)$.

TABLE I

Summary of Data for Two Human Subjects Using Transducer A or B.

	<u>Subject 1 5-IP correction</u>		<u>Subject 2 1-IP correction</u>		<u>Subject 2 5-IP correction</u>	
	A	B	A	B	A	B
Mean echo brightness increase (%)	21.2	24.2	-1.24	7.54	36.7	15.1
Number of color flow voxels increase (%)	90.8	8.51	3.85	-15.1	162	539