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(54) **Title**: AN ULTRASOUND TRANSCEIVER AND CONTROL OF A THERMAL DAMAGE PROCESS

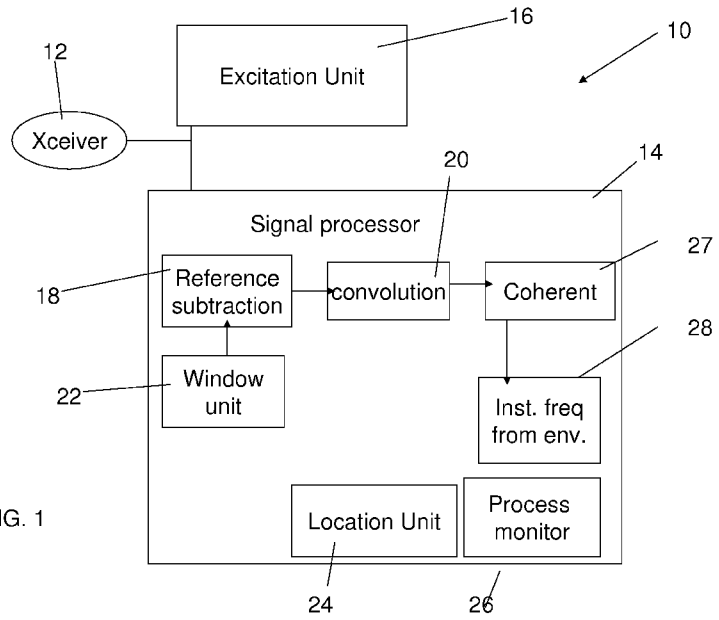


FIG. 1

(57) **Abstract**: An ultrasonic transceiver apparatus for intracorporeal use, comprises an undamped ultrasonic transceiver for placing in a confined intracorporeal space, the transceiver vibrating at an instantaneous frequency and being excited to cause vibration at said instantaneous frequency to produce an ultrasonic ablation beam for ablating surrounding tissues and being further excited to cause vibration by primary echo signals returning from surrounding tissues - from separate excitations during quiet periods between the ablation - to monitor ablation progress. A signal processor isolates the primary echo signals from ringing, secondary echoes and extraneous noise also received from the transceiver and uses presence or absence of the characteristic frequency, or of a body characteristic frequency such as pulse or breathing, as an isolation criterion.

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AN ULTRASOUND TRANSCEIVER AND CONTROL OF A THERMAL DAMAGE PROCESS

FIELD AND BACKGROUND OF THE INVENTION

The present invention, in some embodiments thereof, relates to an ultrasound transceiver and to control of an ablation or thermal damage process to a tissue and, more particularly, but not exclusively, to use of the transceiver in simultaneous monitoring and ablation of nearby tissue by monitoring the distance to the tissue walls, and use of change in distance between tissue walls as an indicator of progress of the thermal damage.

The present application claims priority from U.S. Provisional Patent Application No. 61/393,947 filed October 18, 2010, U.S. Patent Application No. 13/049,022 filed March 16, 2011 and U.S. Provisional Patent Application No. 61/453,239 filed March 16, 2011.

The present application is related to co-filed, co-pending and co-assigned PCT patent applications entitled:

"Therapeutics Reservoir", (attorney docket no. 52341) relating to relates to a method of drug delivery and, more particularly to a method for trapping drugs to form a drug reservoir in tissue.

"Ultrasound Emission element" (attorney docket no. 52344), showing, for example, an apparatus for generating relatively high efficiency ultrasound;

"an ultrasound transceiver and uses thereof" (attorney docket no. 52345), showing for example, a method for feedback and control of the ultrasonic transducer;

"an ultrasound transceiver and cooling thereof" (attorney docket no. 52346), showing for example, a method for blood flow cooling of the ultrasonic transducer;

"tissue treatment" (attorney docket no. 52347) by Ariel Sverdlik, Iiris Szwarcfiter and Or Shabtay, showing for example, a method of selective targeting and treating tissues using ultrasound; and

"separation device for ultrasound element" (attorney docket no. 52348) by Ariel Sverdlik and Or Shabtay, showing for example, a device to prevent the transducer from touching the blood vessel wall.

The disclosures of each of the above are incorporated herein by reference.

For the purposes of ablation of tissue it is desirable to have an ultrasound transmitter which is undamped, because any damping reduced efficiency.

For the purpose of detection of effects, a damped receiver is desirable, since without damping, ringing occurs, making signals hard to read.

In the case where the same device is used both for ablation and detection, the situation is particularly bad, since the transmitted signals cause considerable ringing in the undamped device.

The problem is to detect the wall of an artery, or any other tissue, using an ultrasonic transceiver which is also performing the ablation and which thus must be undamped because damping will reduce efficiency. Low efficiency leads to increased heating, which can be harmful in confined spaces such as blood vessels.

Since the detector is undamped there is considerable noise due to ringing. The ringing is present in the sensor and is also transmitted to the tissues causing reflections of its own, all this interfering with the signal it is intended to detect.

As a consequence, the signal from the artery wall is drowned out by noise due to ringing and the primary echo is hard to discern. Nevertheless, detecting the echo is highly desirable in order to monitor the ablation treatment.

SUMMARY OF THE INVENTION

An embodiment of the present invention may analyze a sequence of sample signals. The primary echo has a fixed relationship to the excitation signal, whereas the ringing signals do not. Typically the primary echo shares a main frequency component with the excitation signal although not the phase and not the amplitude. The relationship is used to distinguish the primary echo from ringing and from secondary echoes.

According to an aspect of some embodiments of the present invention there is provided an ultrasonic transceiver apparatus for intracorporeal use, the apparatus comprising:

an undamped ultrasonic transceiver for placing in a confined intracorporeal space, the transceiver having an instantaneous excitation frequency and for receiving excitation at the excitation frequency to produce an ultrasonic ablation beam for ablating surrounding tissues and being further for receiving excitation by primary echo signals returning from surrounding tissues;

a signal processor connected to the transceiver configured to isolate the primary echo signals from ringing, secondary echoes and extraneous noise also received from the transceiver, the signal processor using presence or absence of the instantaneous excitation frequency as an isolation criterion.

In an embodiment, the signal processor is configured with an instantaneous frequency estimator to obtain an envelope of received signal minus excitation signal from the undamped ultrasonic transceiver and to use a global phase and local slopes thereof as an estimate of the instantaneous frequency, and further comprising an isolator unit for isolating signal segments whose instantaneous frequency approaches the characteristic frequency as segments containing primary echoes.

An embodiment may comprise a window unit for windowing the received signal using a windowing length chosen to provide windows with an expectation of a single primary echo.

In an embodiment, the signal processor is further configured to find a point of appearance of a primary echo in a received signal by successively dividing the curve and fitting to a linear functions and calculating a point at which a corresponding error function is minimized.

An embodiment may be configured with a location unit to determine a distance to a first feature wall from the point of appearance.

In an embodiment, the location unit is configured to use a second point of appearance of a further primary echo to determine a distance to a second feature wall, the signal processor further comprising a monitoring unit for monitoring a distance between the first feature wall and the second feature wall as an indicator of ablation progress.

In an embodiment, the signal processor comprising a convolution unit for convolving an excitation signal with the received signal to carry out the isolation of the primary echo.

In an embodiment, the signal processor comprises a Fourier component analyzer for isolating segments having a principle Fourier component which corresponds to a body-characteristic frequency.

In an embodiment, the signal processor comprises a coherent summation unit for carrying out data summation such as to preserve amplitude and shift signals to a same phase.

In an embodiment, the coherent summation unit is configured to perform coherent summation, the coherent summation comprising building an auxiliary matrix of phase weights, making a Hilbert transform and multiplying to bring all the signal to the same phase, therewith to create an in-phase sum.

An embodiment may comprise a reference subtracting unit configured to subtract a reference from the transceiver signal by averaging several signal samples to eliminate unstable components.

According to a second aspect of the present invention there is provided an ultrasonic transceiver method for intracorporeal use, the method comprising:

placing an undamped ultrasonic transceiver in a confined intracorporeal space, the transceiver having a characteristic frequency

exciting the transceiver at an instantaneous excitation frequency to produce an ultrasonic ablation beam for ablating surrounding tissues using ablation pulses;

at intervals between the ablation pulses providing monitoring excitation to elicit primary echo signals returning from surrounding tissues;

isolating the primary echo signals from ringing, secondary echoes and extraneous noise also received from the transceiver using presence or absence of the instantaneous excitation frequency as an isolation criterion.

In an embodiment, the isolation comprises obtaining an envelope of received signal minus excitation signal from the undamped ultrasonic transceiver and using a global phase and local slopes as an estimate of the instantaneous frequency, and isolating those signal segments whose frequency approaches the instantaneous excitation frequency.

An embodiment may comprise windowing the received signal using a windowing length chosen to provide windows with an expectation of a single primary echo.

An embodiment may be configured to find a point of appearance of a primary echo in a received signal by

successively dividing the curve,

fitting to a linear functions and

calculating a point at which a corresponding error function is minimized.

An embodiment may comprise determining a distance to a first feature wall from the point of appearance.

An embodiment may comprise using a second point of appearance of a further primary echo to determine a distance to a second feature wall, and monitoring a distance between the first feature wall and the second feature wall as an indicator of ablation progress.

An embodiment may comprise convolving an excitation signal with the received signal to carry out the isolation of the primary echo.

An embodiment may comprise isolating segments having a principle Fourier component which corresponds to a body characteristic frequency.

An embodiment may comprise carrying out coherent data summation such as to preserve amplitude and shift signals to a single phase.

In an embodiment, the coherent summation comprises:

making an auxiliary weights matrix evaluation;

carrying out a Hilbert transformation;

multiplication to bring all signals to the same phase; and

performing an in-phase summation.

According to a third aspect of the present invention there is provided an ultrasonic transceiver apparatus for intracorporeal use, the apparatus comprising:

an undamped ultrasonic transceiver for placing in a confined intracorporeal space, the transceiver having a characteristic frequency and for receiving excitation at the characteristic frequency to produce an ultrasonic ablation beam for ablating surrounding tissues and being further for receiving excitation by primary echo signals returning from surrounding tissues;

a signal processor connected to the transceiver configured to isolate the primary echo signals from ringing, secondary echoes and extraneous noise also received from the transceiver, the signal processor using correlation with a body-characteristic frequency as an isolation criterion.

In an embodiment, the body characteristic frequency may be pulse or breathing rate.

In an embodiment, the signal processor is configured to obtain a power spectrum of a signal extracted from the transceiver and to identify the primary echoes from peaks in the power spectrum at the body-characteristic frequency.

An embodiment may comprise a coherent summation unit or a convolution unit or both.

According to a fourth aspect of the present invention there is provided a method of providing controlled thermal damage to a tissue, comprising:

identifying locations of boundary walls of the tissue;

applying energy to the tissue;

during the applying, monitoring changes in locations of the boundary walls as indicators of the application of energy to the tissue, for example thermal shrinkage of the tissue; and

controlling the thermal energy according to the effect, for example, thermal shrinkage.

In an embodiment, the monitoring and applying are carried out from within a blood vessel, and/ or using ultrasonics.

In this fourth aspect of the invention, a known ablation device may be used in conjunction with an ultrasonic detector.

Unless otherwise defined, all technical and/or scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of embodiments of the invention, exemplary methods and/or materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be necessarily limiting.

Implementation of the method and/or system of embodiments of the invention can involve performing or completing selected tasks manually, automatically, or a combination thereof. Moreover, according to actual instrumentation and equipment of embodiments of the method and/or system of the invention, several selected tasks could be implemented by hardware, by software or by firmware or by a combination thereof using an operating system.

For example, hardware for performing selected tasks according to embodiments of the invention could be implemented as a chip or a circuit. As software, selected tasks according to embodiments of the invention could be implemented as a plurality of software instructions being executed by a computer using any suitable operating system. In an exemplary embodiment of the invention, one or more tasks according to exemplary embodiments of method and/or system as described herein are performed by a data processor, such as a computing platform for executing a plurality of instructions. Optionally, the data processor includes a volatile memory for storing instructions and/or data and/or a non-volatile storage, for example, a magnetic hard-disk and/or removable media, for storing instructions and/or data. Optionally, a network connection is provided as well. A display and/or a user input device such as a keyboard or mouse are optionally provided as well.

BRIEF DESCRIPTION OF THE DRAWINGS

Some embodiments of the invention are herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of embodiments of the invention. In this regard, the description taken with the drawings makes apparent to those skilled in the art how embodiments of the invention may be practiced.

In the drawings:

FIG. 1 is a simplified schematic block diagram illustrating ultrasonic transceiver apparatus according to an embodiment of the present invention;

FIG. 2 is a simplified graph showing a raw signal received from the transceiver and the same signal after reference subtraction;

FIG. 3 is a simplified graph showing the signal of FIG. 2 after averaging and after coherent summation;

FIG. 4 is a simplified graph showing the raw signal after noise subtraction and after double coherent summation and convolution;

FIGs. 5A-5B and 6-8 illustrate experimental data for a measured distance of 0.19mm;

FIGs. 9A-9B and 10-12 illustrate experimental data for a measured distance of 1.19mm;

FIGs. 13A-13B and 14-16 illustrate experimental data for a measured distance of 1.69mm;

FIGs. 17A-17B and 18-20 illustrate experimental data for a measured distance of 2.19mm;

FIGs. 21A-21B and 22-24 illustrate experimental data for a measured distance of 2.69mm;

FIGs. 25A-25B and 26-28 illustrate experimental data for a measured distance of 3.19mm;

FIGs. 29A-29B and 30-32 illustrate experimental data for a measured distance of 3.69mm;

FIGs. 33A-33B and 34-36 illustrate experimental data for a measured distance of 4.19mm;

FIGs. 37A-37B and 38-40 illustrate experimental data for a measured distance of 4.69mm;

FIGs. 41A-41B and 42-44 illustrate experimental data for a measured distance of 5.19mm;

FIG. 45 is a correlation graph derived from the experiments of FIGs. 5A to 45, and indicating a very high correlation between actual and measured distances;

FIG. 46 is a simplified flow chart illustrating the process of coherent summation according to an embodiment of the present invention;

FIG. 47 is a flow chart showing in greater detail the actual transceiver frequency evaluation of FIG. 46;

FIG. 48 is a simplified graph illustrating division of envelope sections according to amplitude of the principle Fourier component matching the device resonance, and showing the selection of the sections having the highest amplitude, according to an embodiment of the present invention;

FIG. 49 illustrates ringing following an excitation signal, with primary echoes hidden in the ringing;

FIG. 50 shows sampling to obtain vectors, undamped ringing with echoes included, and a power spectrum graph at the pulse frequency, where peaks in the power spectrum graph indicate features in the primary echo; and

FIG. 51 is a simplified flow chart illustrating a procedure for obtaining the power spectrum graph of FIG. 50.

DESCRIPTION OF SPECIFIC EMBODIMENTS OF THE INVENTION

The present invention, in some embodiments thereof, relates to an ultrasound transceiver, in particular for use in confined spaces such as blood vessel to carry out self-monitored ablation on surrounding tissues.

The problem is to detect the wall of an artery (or any other tissue) using an ultrasonic detector which must be undamped because damping will reduce efficiency.

In general the effectiveness of an ablation process can be determined by measuring the distance between outer and inner walls of a tissue being ablated. Specifically, as the tissue is ablated, the distance between the outer and inner walls falls, so sequential monitoring of the distance is a way of measuring the effectiveness of the ablation process.

Since the detector is undamped there is considerable noise due to ringing. The ringing is present in the sensor and is also transmitted to the tissues causing reflections of its own, all this interfering with the signal it is intended to detect.

The issue is that the signal from the artery wall is drowned out by noise and the ringing. We know however that the signal from the tissue wall has certain characteristics. The primary ringing tends to share a main frequency with the excitation signal, although the phase will differ depending on the distanceThus the frequency can be used to distinguish primary echoes from ringing and from secondary echoes as well as general noise.

Once the primary echoes have been distinguished then it is possible to monitor the thermic effectiveness of the treatment by locating the inner and outer walls and monitoring the change in distance between them.

More generally, detecting the primary echoes allows them to be used in an analysis of the entire artery wall tissue signal, and not only the face of the wall that is touching the blood.

Various methods are given in the disclosure for analyzing the primary echoes.

Since the transceiver is a narrow band device, it irradiates mainly at its Eigen frequency. Furthermore, voltages generated by returned pressure waves are again filtered by the transceiver, so that the primary reflected signal is an almost pure harmonic oscillation, albeit with variable amplitude. It is reasonable to expect that transient-only portions of the signal are characterized by different frequencies.

The present embodiments further include a means of providing controlled thermal damage to a tissue, by identifying locations of boundary walls of the tissue, applying energy to the tissue, and monitoring changes in locations of the boundary walls as indicators of the application of energy to the tissue, for example thermal shrinkage of the tissue; Then the application of the thermal energy can be controlled y according to the detected effect.

In an embodiment, the monitoring and applying are carried out from within a blood vessel, and/ or using ultrasonics. The above may be carried out using the transceiver described herein but alternatively, a known ablation device may be used in conjunction with an ultrasonic detector.

It is noted that the effect on the tissue is not necessarily shrinkage. It may instead be thickening due to heating or to some physiological response. Nevertheless it is the change in size or shape of the tissue, as determined by changes in tissue wall location determined by non-imaging or imaging of tissue, that is used to control the process.

The present embodiments relate to non-focused ultrasound, or to focused ultrasound or to r.f. based systems.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not necessarily limited in its application to the details of construction and the arrangement of the components and/or methods set forth in the following description and/or illustrated in the drawings and/or the Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways.

Referring now to the drawings, Figure 1 illustrates an ultrasonic transceiver apparatus 10 primarily intended for intracorporeal use, according to one embodiment of the present invention. A transceiver 12 is designed to be injected into blood vessels and like confined spaces within the body, particularly with a view to flowing towards

locations where tissue ablation is required, and to direct ultrasound energy towards the tissue to be ablated. In between ablations the transceiver is excited with monitoring signals to use ultrasound energy for a different purpose, the monitoring of the surrounding tissues to make sure that the ablation is being carried out effectively.

As mentioned in the background ablation takes place in the body, where heating of the wrong tissues is undesirable. Thus the transceiver is required to be as efficient as possible and thus to be undamped. Monitoring however requires a damped transceiver since reading the echoes is conventionally only possible once the excitations have died down. Using different transceiver surfaces for monitoring and ablation respectively is also not ideal since it is difficult to guarantee that the tissue being monitored is the same as the tissue being ablated.

The present embodiments thus use a single undamped transceiver for both monitoring and ablation and methods and a structure are provided for isolating the primary reflections from ringing due to the excitation signal and due to secondary reflections from the ringing as well as assorted other noise. The undamped ultrasonic transceiver may be a narrow band transceiver having a characteristic excitation frequency so that all excitations are at that characteristic frequency. The primary echoes tend to share the excitation frequency, albeit at variable phases and amplitudes, whereas general ringing and tend to be at other g frequencies.

A signal processor 14 is connected to the transceiver 12 to isolate the primary echo signals from the ringing, secondary echoes and extraneous noise also received from the transceiver. The signal processor uses presence or absence of the characteristic frequency as an isolation criterion.

An excitation unit 16 provides an excitation signal for the transceiver. The excitation may be high power for the ablation or low power for monitoring.

The signal processor may have reference subtraction unit 18 which subtracts the excitation signal, from the transceiver 12.

As will be discussed in greater detail below, the size of the segments may be chosen so that only one primary echo need be found per segment. Otherwise the presence of multiple reflections makes analysis more difficult. The distances between tissue walls are known in general terms so segment lengths are chosen to represent distances smaller than the distance between walls. Thus a window unit 22 windows the

received signal using a windowing length chosen to provide segments with an expectation of a single primary echo.

There are a number of alternative ways in which the segment isolator can find primary echoes.

A convolution unit 20 convolves an excitation signal with the received signal to isolate only those waveforms having a high coherence with the excitation signals.

Following convolution is coherent summation. A coherent summation unit 27 carries out data summation such as to preserve amplitude and shift signals to the same phase. The coherent summation unit may build an auxiliary matrix and then multiplies it with previously carried out Hilbert transform to shift the obtained complex analytic signals to the same phase and to make in-phase (coherent) summation Coherent summation is discussed in greater detail below.

Although it is possible to use convolution alone or coherent summation alone it is also possible to combine operation of the above units. Fig. 4 below discusses double coherent summation and convolution as a way to obtain the primary echoes.

The above processes may involve obtaining a reference signal, based on the actual excitation. Reference subtracting unit 18 may subtract a reference from the transceiver signal by averaging several signal samples (particular records), simply to eliminate unstable components and obtain the actual excitation. Optionally, one can use as a reference a separate signal where echoes do not arrive until after the ringing dies out. That is, a part of the signal where the ringing has disappeared but echo has not appeared yet can be used as a reference. A separate reference signal is known to be free of echoes in the region of interest. Thus, its subtraction from the particular signal reliably provides us with almost pure echo, except for the noise component.

Finally, after double coherent summation and convolution, an envelope is obtained.

With the envelope, the signal processor may find a point of appearance of a primary echo in the segment by successively dividing the envelope curve while fitting to a linear function and calculating a point at which a corresponding error function is minimized. Such a process is illustrated in Fig. 6 below.

The point of error minimization is most probably the point of onset of the primary echo and indicates the distance to a structure such as a tissue wall. Such an error

minimization is shown in Fig. 7 discussed below. A location unit 24 determines the distance to a first feature wall based on the point of appearance.

The location unit may then use a second point of appearance of a further primary echo to determine a distance to a second feature wall. A process monitoring unit then calculates and monitors the distance between the first feature wall and the second feature wall as an indicator of ablation progress. As the ablation progresses the wall typically shrinks as the tissue dries out.

An alternative to the above is Fourier component analysis, based not on the excitation frequency of the transceiver, but on frequencies characteristic of the body, such as pulse rate or breathing rate.

Using Fourier component analysis, the signal processor uses correlation with a body-characteristic frequency as an isolation criterion. One way of doing this is to obtain a power spectrum of the signal extracted from the transceiver and to identify the primary echoes from peaks in the power spectrum at the body-characteristic frequency.

The Fourier component analysis may be used instead of or in addition to coherent summation and to convolution using a convolution unit.

The above processes are now considered in greater detail.

As mentioned, an envelope of the oscillating signal is obtained, and a global phase and its local slopes are used as estimations of instantaneous frequency (actually, instantaneous frequency is local slope itself). Also instantaneous frequency is estimated from the entire signal in analytical form, as time derivative of phase. The appearance of a primary reflection signal is then recognized within the overall envelope as a transition at an instantaneous frequency of the signal.. The transceiver frequency remains constant.

The Hilbert transform is carried out on a residual signal, after reference subtraction. The results are used for coherent summation of original signals. signal construction the Hilbert transform effectively creates a signal shifted by a quarter of a period with respect to the original signal. For a true harmonic signal, the phase of the obtained complex analytic signal – see Fig. 5B, grows linearly in time. If a new harmonic component appears in the signal, it may be revealed by a change of the phase – time curve slope.

The appearance of a new harmonic component may be taken as the indication of a new feature that is being detected, say the near surface of a tissue in question, and a second new harmonic component may indicate the far surface of the tissue in question artery wall.

Finding the Primary Echo

To find the instant of new component appearance, an algorithm for minimum total error may be used. As illustrated in Fig. 6, the entire curve may be divided in two parts and each part may then be fitted to a linear function. We consider double fitting of the entire error as a function of the separation point. The assumption is that for the true separation point between two frequency regions the overall error reaches its minimum.. In general, a change in best slope indicates the appearance of a new event. The point where the new harmonic is added turns out to be derivable from the error function. The overall error of the two curve fitting operations is a function of the point of appearance of the new harmonic, and minimization of the overall error may indicate the point. Fig. 7 illustrates such an error function with a clear minimization point.

An issue arises in that the result of the above-described procedure is sensitive to the length of the data subjected to analysis. The above-described procedure works best when a stretch of data contains just a single point at which a new harmonic is added. But, in real life there are more, and surfaces have inner and outer walls which each give rise to separate reflections and there are second order reflections and also noise. Thus, the presence of a second reflection or say a long portion of noise, negatively affects the accuracy. The problem may be solved by windowing, analyzing the received data in short chunks, as will be explained in greater detail below.

Correlation approach

The excitation voltage generates mechanical oscillations in the transceiver, which irradiate pressure waves into surrounding media. Return pressure waves generate a reflection voltage signal. It is reasonable to expect that the reflection retains at least a partial correlation with the excitation voltage. An alternative or additional approach is just to convolve part of the excitation signal with the rest of the data. The reflection may thus be amplified according to the correlation and become more recognizable.

Reference is now made to Fig. 8, which illustrates local slopes of a phase – distance curve. Over the full phase – time (distance) curve one can evaluate local standard statistical parameter correlation coefficients. For perfectly linear dependence between two values the correlation coefficient is ±1. For noisy data or for nonlinear dependence, the absolute value is less than 1. A stable and significant decrease of correlation coefficient serves as a reliable sign of useless noisy data and allows the irrelevant signal to be excluded.

The use of correlation coefficients can thus be used to find parts of the data where there are strong echoes and ignore parts where such strong echoes are absent.

Experimental Calibration

The present embodiments were applied experimentally to estimate distance within the interval 0.19 – 5.19 mm.

Two types of experiments were carried out, *in vitro* and *in vivo*.

In *in vitro* experiments, it is possible to control distance between transceiver and reflective object (metal plate) by means of a positioning device with a ruler and set it in parallel to the transceiver surface. Accuracy of 0.1 mm is available.. In the following, in vitro experimentation is used to generate a calibration curve between measured and actual distances. That is, to the experiment finds slope and intercept. The slope is expected to be close to 1. The intercept allows for elimination of systematic error in the ruler reading. Indeed, the intercept is not the interesting point, although technically necessary. The indication of evaluation correctness is that the evaluated points lie on a straight line with a slope close to 1.

Several remote points with reliable separation between transient and reflection were tested and an offset (the above-referred to intercept) was estimated. A true distance can then be used which is the sum of the ruler reading and offset.

Sample Equivalents

In the time domain, the sample equivalent is a reciprocal sampling frequency. For 800 MHz, it is 1.25 ns.

In the space domain, the sample equivalent is half of the sampling period multiplied by sound velocity. Its interpolated value at 23° C is 1489 m/s. Thus, a distance equivalent is 9.306·10-4 mm.

Fig. 2 upper part presents a raw signal and the lower part shows the same after reference subtraction. Fig. 3 upper part shows averaging and gives a ratio of maximum amplitude over noise standard deviation to be 5.86. The signal shown represents results of averaging 11 particular signals. The lower part of Fig. 3 shows coherent summation and manages to achieve a ratio of maximum amplitude over noise standard deviation of 10.2, nearly double the level achieved by averaging.

Fig. 4 presents result of repeated coherent summation of 23 groups (total 11x23=253 processed signals of 256) and convolution with a resonant window.

According to the above considerations, the best improvement of SNR for 11 particular signals is 3.32. It follows from Fig. 3 that the real improvement is 1.74. Specifically, the improvement is the ratio of SNRs after and before processing. SNR after processing is 10.2, and SNR before is 5.96. SNR after processing is greater.

Figures 5A – 8 are as discussed above and illustrate estimated and real distance results for distances of 0.19mm or 0.69mm. Fig. 5A shows the raw signal and Fig. 5B shows the corresponding analytical signal. Fig. 6 shows the curve fitting to find the point at which the primary echo component appears. Fig. 7 illustrates the error function and Fig. 8 illustrates the full phase-distance curve from which local slopes can be obtained.

Figures 9A – 12 illustrate corresponding estimated and real distance data for a distance of 1.19mm. Fig. 9A shows the raw signal and Fig. 9B shows the corresponding analytical signal. Fig. 10 shows the fitting. Fig. 11 illustrates the error function and Fig. 12 illustrates the full phase-distance curve.

Figs 13A – 16 illustrate results for a distance of 1.69mm. Fig. 13A shows the raw signal and Fig. 13B shows the corresponding analytical signal. Fig. 14 shows the fitting. Fig. 15 illustrates the error function and Fig. 16 illustrates the full phase-distance curve.

Figs 17 – 20 illustrate results for a distance of 2.19mm. Fig. 17A shows the raw signal and Fig. 17B shows the corresponding analytical signal. Fig. 18 shows the fitting. Fig. 19 illustrates the error function and Fig. 20 illustrates the full phase-distance curve.

Figs 21A – 24 illustrate results for a distance of 2.69mm. Fig. 21A shows the raw signal and Fig. 21B shows the corresponding analytical signal. Fig. 22 shows the fitting. Fig. 23 illustrates the error function and Fig. 24 illustrates the full phase-distance curve.

Figs 25A – 28 illustrate results for a distance of 3.19mm. Fig. 25A shows the raw signal and Fig. 25B shows the corresponding analytical signal. Fig. 26 shows the fitting. Fig. 27 illustrates the error function and Fig. 28 illustrates the full phase-distance curve.

Figs 29A – 32 illustrate results for 3.69mm. Fig. 29A shows the raw signal and Fig. 29B shows the corresponding analytical signal. Fig. 30 shows the fitting. Fig. 31 illustrates the error function and Fig. 32 illustrates the full phase-distance curve.

Figs 33A – 36 illustrate results for a distance of 4.19mm. Fig. 33A shows the raw signal and Fig. 33B shows the corresponding analytical signal. Fig. 34 shows the fitting. Fig. 35 illustrates the error function and Fig. 36 illustrates the full phase-distance curve.

Figs 37A – 40 illustrate results for a distance of 4.69mm. Fig. 37A shows the raw signal and Fig. 37B shows the corresponding analytical signal. Fig. 38 shows the fitting. Fig. 39 illustrates the error function and Fig. 40 illustrates the full phase-distance curve.

Figs 41A – 44 illustrate the results for a distance of 5.19mm. Fig. 41A shows the raw signal and Fig. 41B shows the corresponding analytical signal. Fig. 42 shows the fitting. Fig. 43 illustrates the error function and Fig. 44 illustrates the full phase-distance curve.

Each estimation is average on 6 sets of 5 times averaged data. Except for one point (4.69 mm), standard deviation is not significant. With outliers excluded, estimation in this point gives 4.61 mm. Absolute RMS error is 0.24 mm.

Referring now to Fig. 45, a correlation curve is obtained by fitting measured results to actual distances. A straight line is fitted to the data points, with slope 0.89 and intercept 0.18 mm. Correlation of known and estimated distances is high, and the observed correlation coefficient is 0.9954.

General description of the problem and requirements

The procedure is now considered in more detail. It is required to estimate distance from a transceiver surface to artery wall. The range of interest lies between 1…5 mm. Allowed error is 0.2 mm. Processing time is not intended to exceed 2s.

Features and difficulties

As mentioned, there is uncertainty in mutual orientation of and artery wall, known as angular uncertainty.

The reflected signal is typically small. That is, first, it is corrupted by noise in general and, second, is distorted by a residual excitation signal, otherwise known as ringing. As mentioned, the ringing can produce second order effects such as echoes of the ringing. The reflected signal is a superposition of multiple similar signals each produced by its own source the source. That is, the shape of reflected signal may vary depending on the angular position of the transceiver.

Within the same *in vivo* experiment, it is possible that a given transceiver surface may be polluted with coagulated blood, causing changes in the characteristic frequency.

Fortunately, in general, applied transceivers are narrow band devices and reflected signals are close to harmonic, however, with variable amplitude. This allows for efficient signal isolation.

Data Averaging

Data are built as a matrix, whose columns represent a reaction wherein a single record maps to a single pulse. Then, columns of the records are divided into groups on which averaging is carried out. Following this, each column is processed on the basis of the averaged groups and overall results are averaged. In the matrix, row size may

represent the total number of points recorded in a single echo response, and the column numbers may represent the total number of echo responses which was recorded.

As an example of the above, in *in vivo* experiments which were carried out, datasets were obtained. Each dataset consisted of 1000 records, each having about 12000 samples, and corresponding to a duration of about 0.15 μs. The PRF was 400 Hz, therefore total duration of the experiment was 2.5 s. Sometimes only the first 256 records were used for processing. The first 1000 samples (about 0.95 mm) were excluded from processing. Data length was restricted to 2^{13}=8192 samples (about 8 mm) to accelerate Fourier transforms. The best case occurs when the number of samples is a power of 2. However, FFT performance it is also good if it is the product of several primes. Optional fine tuning of data length is also carried out.

Reference subtraction

At small distances the entire signal is a superposition of the residual transceiver signal, the free reaction, and the reflected transceiver signal. An apparent solution would be to subtract the pure excitation signal without reflections from the superposition to obtain the reflection, but this fails to take into account noise or second order effects.

Thus in an embodiment, a reference signal is obtained by averaging of several records. Presumably, due to instabilities, phases of reflected signals are randomly different from each other, and averaging weakens this component. Contrary, the excitation pulse is taken as stable so averaging does not cause any deterioration. Thus, in principle the unstable component is more or less efficiently eliminated from the processed signal.

Noise level

Noise levels may be estimated from a remote part of a record where reflections are not expected.

Coherent Summation

Having identified the most relevant windows, the procedure then identifies the primary echo based on coherent summation. Consider a set of signals, which are expected to be similar to each other. Ideally, all signals would be the same, except for

the noise component. Thus summation of N such signals increases the entire signal N times while noise increases only $\sqrt{N}$ times. As a result, the SNR improvement is $\sqrt{N}$ times. In practice, however, due to random phase shifts the described procedure becomes less efficient. This can be solved by means of a Hilbert transform producing a complex analytic signal, in which each signal can be assigned a phase, which, for a true harmonic signal would be the true phase. Thus, phase is defined conventionally as for a usual complex number:

$$\varphi = \arctan \frac{\Im(Hx)}{\Re(Hx)} \qquad (1)$$

Let the k-th signal generate Hilbert phases $\alpha^{(k)}$. We wish to find a transform which preserves amplitude and brings all signals of the set to the same phase or, at least, minimizes phase deviation of each signal from an averaged phase $\overline{\alpha}$. Let $z = x + iy$ be the complex analytic signal generated by the Hilbert transform. Thus new signals are created as follows:

$u = x\cos\gamma - y\sin\gamma$, $v = x\sin\gamma + y\cos\gamma$

which may be expressed as,

$w = z\exp(i\gamma)$.

Such a transform preserves amplitude

$$\sqrt{u^2 + v^2} = \sqrt{x^2 + y^2} = a .$$

We wish to minimize (weighted) error

$$\varepsilon = \sum_k W^{(k)} \left| \frac{z^{(k)} \exp i\gamma_k}{a^{(k)}} - \exp i\overline{\alpha} \right|^2 .$$

For simplicity, summation over elements of each signal is omitted. In equivalent form,

$$\varepsilon = 2\sum_k W^{(k)} - 2\Re \sum_k \frac{W^{(k)}}{a^{(k)}} \left(z^{*(k)} \exp(\overline{\alpha} - i\gamma_k) \right) .$$

Since we wish to have the best agreement for signal but not for noise, weights may be chosen proportional to amplitude. Angles providing minimum error for the *k*-th signal are found from the equation

$$\frac{\partial \varepsilon}{\partial \gamma_k} = 2\Re\left(iz^{*(k)}\exp(i\bar{\alpha} - i\gamma_k)\right) = 0 .$$

In matrix notation,

$$\mathbf{E}_k = \exp(i\gamma_k) = \frac{\mathbf{z}^{H(k)}\mathbf{e}}{\left\|\mathbf{z}^{H(k)}\mathbf{e}\right\|},\ \mathbf{e} = \exp(i\bar{\alpha}) \quad . \qquad (2)$$

The denominator provides proper normalization such that entries of the above weights matrix are true phase exponents. The upper index *H* means matrix Hermit conjugation (or Hermitian conjugation), which is transposition together with complex conjugation. The signal after coherent summation is simply

$$\mathbf{x}_{coh} = \Re(\mathbf{zE}) . \qquad (3)$$

A first factor in equation 3 is the analytic signal corresponding to the entire set of signals. A second factor is an auxiliary phase weight matrix, which provides summation with proper phases.

Step-wise algorithm description

Reference is now made to Fig. 46 which illustrates a possible procedure.

S1 involves carrying out a Hilbert transform on the entire raw data:

$$z = Hx = x + iy$$

to obtain an analytic signal. S 2: Reference signal construction uses

$$z_{ref} = \frac{1}{N}\sum_{k=1}^{N} z^{(k)} .$$

S3: Reference subtraction. In an embodiment, individual subtraction is used. That is to say, for each set of data, the reference signal is multiplied by an individual scaling factor which is close to 1. The scaling factor is evaluated using the initial portion of data (below 1 mm). Individual scaling factors provide the least RMS error being applied to a particular signal, but to a portion, which is not involved in further processing. In the present embodiments, these values are propagated to the remaining portion of the data for more efficient subtraction of the excitation signal.

$$z \rightarrow z - z_{ref}$$

S4: Averaging. Each group of columns is averaged. Members of the group participate in the coherent summation procedure. In an embodiment, an optimal arrangement of groups is used. In this arrangement, within each group, phases are closer to each other.

S5: carrying out a phase evaluation, again based on formula (1).

S6: Construction of particular coherent signal. See formulae (2) and (3).

S7: Actual transceiver frequency evaluation. S8 is shown in greater detail in Fig. 47.

In S7.1, phases of all particular coherent signals are averaged.

In S7.2, the entire phase curve is divided into small pieces (about 100 samples), and for each piece a local strip and a normalized linear fitting error are evaluated. Optionally, local slopes are obtained on overlapping pieces. An instantaneous frequency may be found at each point. Alternatively, instantaneous frequencies may be obtained by usage of a formally exact definition of frequency as a phase time derivative. A Hilbert transform of the derivative may be involved.

In S7.3, for some of the smallest errors (about 10), corresponding local slopes are averaged, to give the actual transceiver frequency.

In S7.4, the actual transceiver frequency is used for resonant window construction. Namely,

$$w_{res}(t) = w(t)\exp(2\pi i f t)$$

A first factor in the above is a standard windowing factor (Hanning, Gauss, Kaiser, etc.). A size of the window may correspond to 2 periods.

Returning now to Fig. 46 and in S8: Convolution with a resonant window is shown. An absolute value of the convolved complex signal (amplitude, or envelope) is used for further analysis.

S9: Thresholds and distance evaluation. It must be emphasized that there is no rigorous rule to choose a threshold for a reflected signal appearance because its shape may change even within the same experiment. Besides, the origin of a transceiver transient reaction may be inherently small and therefore to all intents and purposes are invisible. However, one can set an empirically based value of a threshold and consider

reflection appearance as the point at which a signal firstly falls below the threshold, starting from its maximum. Since signal growth usually occurs rapidly, the result must not be sensitive to the threshold variations or uncertainty. In the current version of the algorithm, two alternate threshold estimations are used:

1. Noise level. A remote section of the data where reflections are not expected is used to estimate noise level. The threshold may then be set as

$$T_1 = k_1 \langle s_{noise\,only} \rangle .$$

Since the final signal is amplitude (envelope), noise level is estimated as its mean.

2. Peak height. A threshold is

$$T_2 = k_2 s_{max} .$$

This second definition is used when the noise level is found to be too high. Sometimes extremely stretched signals are observed. Dimensionless factors in these formulas are established based on visual analysis of the processed signal and may be subjected to fine tuning.

It is possible that reflected signals start at a relatively high level and do not fall below a threshold. Such would be an indication that the origin is closer than 0.95 mm.

Examples

Let us define SNR as a ratio of the largest amplitude of a reflected signal to SD evaluated in the region of pure noise:

$$SNR = \frac{\max(A)}{\sigma_{noise}} .$$

Considering again Figs. 1 to 3, Fig. 1 presents a raw signal and the same after reference subtraction. Fig. 2 presents results of just averaging 11 particular signals vs. coherent summation. Fig. 3 presents the result of repeated coherent summation of 23 groups (total 11x23=253 processed signals of 256) and convolution with a resonant window.

According to the above considerations, the best improvement of SNR for 11 particular signals is 3.32. It follows from Fig. 3 that the real improvement is 1.74 based on the SNR values shown and as discussed above.

Fourier Component Approach

Reference is now made to Figs. 48 - 51 which illustrate an approach based on grouping of samples according to relationships between the echo signals, body frequencies such as pulse or breathing, and the original excitation. The relative position of tissues within the body changes over short times due to breathing and blood pulsation. Ultrasonic echoes from tissues obey such a periodicity whereas ringing artifacts and other types of noises do not. This is specifically true for ultrasonic echoes measured intravascularly. Consequently, the existence of such periodicity can be utilized to separate between tissue reflection and other noise sources in echoes with low signal to noise ratio.

In order to use this information, one must first estimate the periodicity of the echo reflections over consecutive measurements. This periodicity reflects both the movement of the catheter as well as the movement of the tissue.

Several ways can be used to identify the movement profiles of tissue in echo signals. One way is to obtain segments of the echo signals in which a strong reflection is observed. This method is described as follows. Figure 48 (upper left part) shows the echo response of consecutive trials as a function of distance. A clear periodic change in the echo response from the tissue is observed. Since a narrow band transceiver is used, it is possible to quantify the reflection intensity by calculating the Fourier component of the central transceiver frequency Fc in consecutive time windows (Fi) of duration D and overlap OL:

$$F_i = \sqrt{\left(\int \sin(2\pi F_c t) X(t) dt\right)^2 + \left(\int \cos(2\pi F_c t) X(t) dt\right)^2}$$

The response profile in the time domain is illustrated in the lower part of Fig. 48. From the profile, ND windows with the highest values of the central frequency Fourier component are chosen for cross-correlation analysis. The relevant windows are marked by red circles in the lower part of Fig. 48. Using cross correlation analysis between consecutive trials, it is possible to identify the shifts in distance between the tissue and the catheter, as illustrated in the right part of figure 48. Once the movement profile of the tissue is obtained for many tissues samples, this movement profiles can be used to estimate the characteristic frequencies related to breathing and blood pulsation.

Then, the characteristic frequency profiles due to tissue movement are used to separate between the characteristic frequencies and ringing artifacts and other noise signals. In greater detail, owing to the blood pressure, the catheter moves at similar frequencies to the blood pressure, as illustrated in the right part of Fig. 48. On the other hand the echo readings due to catheter ringing as well as other noises are not influenced by the blood pulsation. Thus, the echo signal distance can be distinguished from the background by the fact that it moves backward and forward in correspondence to the blood pulsation. Thus, separating the signals that show the periodicity of the blood pressure movement from other noises may help to identify primary tissue echoes even though their signal to noise ratio is low. This allows accurate detection of the distance to the tissue wall.

To do so, consecutive echo signals are first collected and the power spectrum is calculated for every point in the echo along consecutive trials. This is illustrated in figure 49 which shows the power spectrum of each point of the echo. Each point corresponds to a different distance. The power spectrum intensity is color coded from blue to red. Next, the ratio between the frequency components of breathing and blood pulsation, which were estimated as described earlier, and the frequency components of noise and ringing are calculated for each point of the echo signal. The response ratio is defined as the reflection profile and is used to separate tissue reflections from other noises.

The results of such a process are illustrated in Fig. 50. The upper part of Fig. 50 shows 256 consecutive echo trials as a function of distance. Echo intensity is color coded from blue to red. The middle part shows five superimposed individual trials. Clearly, the variability profile between different signals during the ringing is different from the variability during reflections. These changes in variability are reflected in the power spectrum over consecutive echoes. The lower part of Fig. 50 is a plot of the reflection profile (in blue). A smoothed reflection profile (green) is obtained using a median filter. A rise in this profile indicates reflections from the tissue due to increase in frequencies associated with blood pressure and breathing. Finally, the distance from the artery can be identified using a threshold crossing of the smoothed reflection intensity function, the green line in Fig 50. The threshold is automatically detected by analyzing

the spectrum of points with no tissue reflections, which points are detected using their low kurtosis values.

Referring now to Fig. 51, a summary of the procedure to achieve the above is as follows: Firstly, in 51.1, the power spectrum analysis over the same sample in consecutive echos is performed. In the given example (Fig 50), the echo signal is recorded 256 times, to form 256 records at a sampling frequency of 400 Hz. Within each record, 10000 points are sampled at 800 MHz.

A power spectrum is calculated for each point over the 256 consecutive trials, giving 10000 power spectrum graphs each being 256 samples in length. Following the calculation of the power spectra, the reflection intensity of every point is calculated by using the freq. ratio between the blood pressure frequencies and noise frequencies at each point (S51.2). Tissue reflections are identified by their high reflection intensity (S51.3). The tissue wall location is identified using an automatically detected threshold.

Although in the above, the Fourier component approach is presented as an alternative to coherent summation and convolution, it may also be used together with either or both of coherent summation and convolution to produce improved results.

Rationale

Reliable measurement may require transceiver – tissue boundary distances which are greater than 1 mm and up to 5 mm.

Signal acquisition is performed at 800 MHz/14 bit, and with a suitable oscilloscope such as that produced by Agilent™, the sampling rate may be increased to 2 GHz, but at a modest 8 bit resolution. With transceiver characteristic frequency about 10 and 20 MHz, time resolution is 80 – 40 samples per period.

Current implementations use PRF 400 Hz, which for 1000 repetitions constitutes a measurement duration of 2.5 s. This is enough to observe at least one entire period of heart pulse and therefore a full cycle of an artery dilating and shrinking. This linkage may facilitate distance measurement. In the experiments above there was processing of only 256 repetitions, using about 9000 samples each. At a PRF of 80 kHz, the entire measurement may take 3.2 ms. This time is too short for significant changes in mutual orientation of transceiver and tissue boundary, or distance between the transceiver and

tissue boundary, and thus is expected to improve accuracy. In addition, a long acquisition process provides mutual incoherence of reflected signals which weakens the reflected signal level in the reference.

Currently the transceivers are narrow band. Their advantage is that the main component of their signal is at the Eigen frequency at different excitation shapes. Reflected signal appearance is seen clearly using the Hilbert transform and direct evaluation of local slopes of the phase – time curve. Another possibility is to create a Hilbert transform based instantaneous frequency. A special excitation shape may shorten transient reaction and therefore decrease the low measurement limit.

Due to averaging, a more stable excitation signal is summed almost coherently, while the reflected signal due to random phase variations is weakened with respect to the excitation signal. Thus simple averaging permits the creation of a reference which can be subtracted from a particular signal to almost eliminate the effects of the excitation signal. For better suppression of a (possible) narrow residual spike a low pass filter (LPF) may be applied. As a further point, due to malfunction or the like of an acquisition device, a portion of the signal that is intended for processing may sometimes contain high frequency oscillations between saturation levels. These oscillations are not the same for all particular signals and thus simple averaging is not efficient. In an embodiment, these spikes are identified, cut off, and interpolated with further optional filtration.

Although an Eigen frequency is supplied for the transceiver, it is reasonable to make a data-based estimation. Due to variable amplitude, an instantaneous frequency may change within certain limits even for a pure single-frequency signal. Thus, the frequency may be found from local slopes, which fall within predefined tolerances of the transceiver (say, ±15%) and provide the smallest linear fitting errors. Parts of the data subjected to coherent summation are those which correspond to points which have a frequency that is close to the nominal transceiver frequency. Optionally, all entries of the instantaneous frequency matrix can be subjected to a logical operation which returns true if the frequency falls within the predetermined tolerances and false otherwise. A summation over the rows indicates how suitable a current point may be for coherent summation, and then a predetermined number of the points with largest sums are taken for coherent summation., A resonant window may then amplify true frequency components.

Phase correction of particular signals, that is bringing all signals of interest to the same phase, allows improvement in the SNR. Coherent summation is carried out twice: first, within groups of signals, for example eleven signals may be placed in a group; and then secondly over the groups themselves. Thus in an example of 23 groups, each with eleven signals, the summation would involve 11x23=253 signals. The obtained signal is convolved with a resonant window. Again, as discussed hereinabove, for better efficiency, groups may be arranged such that, within each group mutual closeness is better. ,

The above processing algorithm may provide a rapidly growing envelope signal. Since the slope is large, an error due to uncertainty of the threshold (signal appearance above noise) decreases.

The results of processing may show some cases of multiple reflections, which do not look as though they are reflections from the same object. It is likely that there are different objects with different reflecting properties. However the algorithm of the present embodiments provides a relative height and a length with each peak. The present embodiments may additionally help to classify/recognize detected objects.

It is expected that during the life of a patent maturing from this application many relevant ultrasound devices and transceivers will be developed and the scope of the corresponding terms used herein is intended to include all such new technologies *a priori*.

The terms "comprises", "comprising", "includes", "including", “having” and their conjugates mean "including but not limited to".

The term “consisting of means “including and limited to”.

As used herein, the singular form "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

Whenever a numerical range is indicated herein, it is meant to include any cited numeral (fractional or integral) within the indicated range. The phrases “ranging/ranges between” a first indicate number and a second indicate number and “ranging/ranges from” a first indicate number “to” a second indicate number are used herein interchangeably and are meant to include the first and second indicated numbers and all the fractional and integral numerals therebetween.

It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable subcombination or as suitable in any other described embodiment of the invention. Certain features described in the context of various embodiments are not to be considered essential features of those embodiments, unless the embodiment is inoperative without those elements.

Although the invention has been described in conjunction with specific embodiments thereof, it is evident that many alternatives, modifications and variations will be apparent to those skilled in the art. Accordingly, it is intended to embrace all such alternatives, modifications and variations that fall within the spirit and broad scope of the appended claims.

All publications, patents and patent applications mentioned in this specification are herein incorporated in their entirety by reference into the specification, to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference. In addition, citation or identification of any reference in this application shall not be construed as an admission that such reference is available as prior art to the present invention. To the extent that section headings are used, they should not be construed as necessarily limiting.

WHAT IS CLAIMED IS:

1. An ultrasonic transceiver apparatus for intracorporeal use, the apparatus comprising:

an undamped ultrasonic transceiver for placing in a confined intracorporeal space, the transceiver having an instantaneous excitation frequency and for receiving excitation at said excitation frequency to produce an ultrasonic ablation beam for ablating surrounding tissues and being further for receiving excitation by primary echo signals returning from surrounding tissues;

a signal processor connected to said transceiver configured to isolate said primary echo signals from ringing, secondary echoes and extraneous noise also received from said transceiver, said signal processor using presence or absence of said instantaneous excitation frequency as an isolation criterion.

2. The ultrasonic transceiver apparatus of claim 1, wherein said signal processor is configured with an instantaneous frequency estimator to obtain an envelope of received signal minus excitation signal from said undamped ultrasonic transceiver and to use a global phase and local slopes thereof as an estimate of said instantaneous frequency, and further comprising an isolator unit for isolating signal segments whose instantaneous frequency approaches said characteristic frequency as segments containing primary echoes.

3. The ultrasonic transceiver apparatus of claim 2 further comprising a window unit for windowing said received signal using a windowing length chosen to provide windows with an expectation of a single primary echo.

4. The ultrasonic receiving apparatus of claim 3, wherein said signal processor is further configured to find a point of appearance of a primary echo in a received signal by successively dividing said curve and fitting to a linear functions and calculating a point at which a corresponding error function is minimized.

5. The ultrasonic receiving apparatus of claim 4, further configured with a location unit to determine a distance to a first feature wall from said point of appearance.

6. The ultrasonic receiving apparatus of claim 5, wherein said location unit is configured to use a second point of appearance of a further primary echo to determine a distance to a second feature wall, the signal processor further comprising a monitoring unit for monitoring a distance between said first feature wall and said second feature wall as an indicator of ablation progress.

7. The ultrasonic apparatus of claim 1, wherein said signal processor comprising a convolution unit for convolving an excitation signal with the received signal to carry out said isolation of the primary echo.

8. The ultrasonic apparatus of claim 1, wherein said signal processor comprises a Fourier component analyzer for isolating segments having a principle Fourier component which corresponds to a body-characteristic frequency.

9. The ultrasonic apparatus of claim 1, wherein said signal processor comprises a coherent summation unit for carrying out data summation such as to preserve amplitude and shift signals to a same phase.

10. The ultrasonic apparatus of claim 9, wherein said coherent summation unit is configured to perform coherent summation, said coherent summation comprising building an auxiliary matrix of phase weights, making a Hilbert transform and multiplying to bring the entire signal to the same phase, therewith to create an in-phase sum.

11. The ultrasonic apparatus of claim 1, further comprising a reference subtracting unit configured to subtract a reference from the transceiver signal by averaging several signal samples to eliminate unstable components.

12. An ultrasonic transceiver method for intracorporeal use, the method comprising:

placing an undamped ultrasonic transceiver in a confined intracorporeal space, the transceiver having a characteristic frequency

exciting said transceiver at an instantaneous excitation frequency to produce an ultrasonic ablation beam for ablating surrounding tissues using ablation pulses;

at intervals between said ablation pulses providing monitoring excitation to elicit primary echo signals returning from surrounding tissues;

isolating said primary echo signals from ringing, secondary echoes and extraneous noise also received from said transceiver using presence or absence of said instantaneous excitation frequency as an isolation criterion.

13. The ultrasonic transceiver method of claim 12, wherein said isolation comprises:

obtaining an envelope of received signal minus excitation signal from said undamped ultrasonic transceiver and using a global phase and local slopes as an estimate of said instantaneous frequency,

isolating those signal segments whose frequency approaches said instantaneous excitation frequency.

14. The ultrasonic transceiver method of claim 13 further comprising windowing said received signal using a windowing length chosen to provide windows with an expectation of a single primary echo.

15. The ultrasonic receiving method of claim 14, further configured to find a point of appearance of a primary echo in a received signal by

successively dividing said curve,

fitting to a linear functions and

calculating a point at which a corresponding error function is minimized.

16. The ultrasonic receiving method of claim 15, comprising determining a distance to a first feature wall from said point of appearance.

17. The ultrasonic method of claim 16, comprising using a second point of appearance of a further primary echo to determine a distance to a second feature wall, and monitoring a distance between said first feature wall and said second feature wall as an indicator of ablation progress.

18. The ultrasonic method of claim 12, comprising convolving an excitation signal with the received signal to carry out said isolation of the primary echo.

19. The ultrasonic method of claim 12, comprising isolating segments having a principle Fourier component which corresponds to a body characteristic frequency.

20. The ultrasonic method of claim 12, comprising carrying out coherent data summation such as to preserve amplitude and shift signals to a single phase.

21. The ultrasonic method of claim 20, wherein said coherent summation comprises:
making an auxiliary weights matrix evaluation;
carrying out a Hilbert transformation;
multiplication to bring all signals to the same phase; and
performing an in-phase summation.

22. An ultrasonic transceiver apparatus for intracorporeal use, the apparatus comprising:

an undamped ultrasonic transceiver for placing in a confined intracorporeal space, the transceiver having a characteristic frequency and for receiving excitation at said characteristic frequency to produce an ultrasonic ablation beam for ablating surrounding tissues and being further for receiving excitation by primary echo signals returning from surrounding tissues;

a signal processor connected to said transceiver configured to isolate said primary echo signals from ringing, secondary echoes and extraneous noise also received from said transceiver, said signal processor using correlation with a body-characteristic frequency as an isolation criterion.

23. The apparatus of claim 22, wherein said body characteristic frequency is one member of the group consisting of pulse and breathing rate.

24. The apparatus of claim 22, wherein said signal processor is configured to obtain a power spectrum of a signal extracted from said transceiver and to identify said primary echoes from peaks in said power spectrum at said body-characteristic frequency.

25. The apparatus of claim 22, further comprising a coherent summation unit.

26. The apparatus of claim 22, further comprising a convolution unit.

27. A method of providing controlled thermal damage to a tissue, comprising:

identifying locations of boundary walls of said tissue;

applying energy to said tissue;

during said applying, monitoring changes in locations of said boundary walls as indicators of an effect of said applying said energy on said tissue; and

controlling said thermal energy according to said effect.

28. The method of claim 27, wherein said monitoring and said applying are carried out from within a blood vessel.

29. The method of claim 27, wherein said monitoring and said applying are carried out using ultrasonics.

30. The method of claim 27, wherein said effect on said tissue is thermal shrinkage.

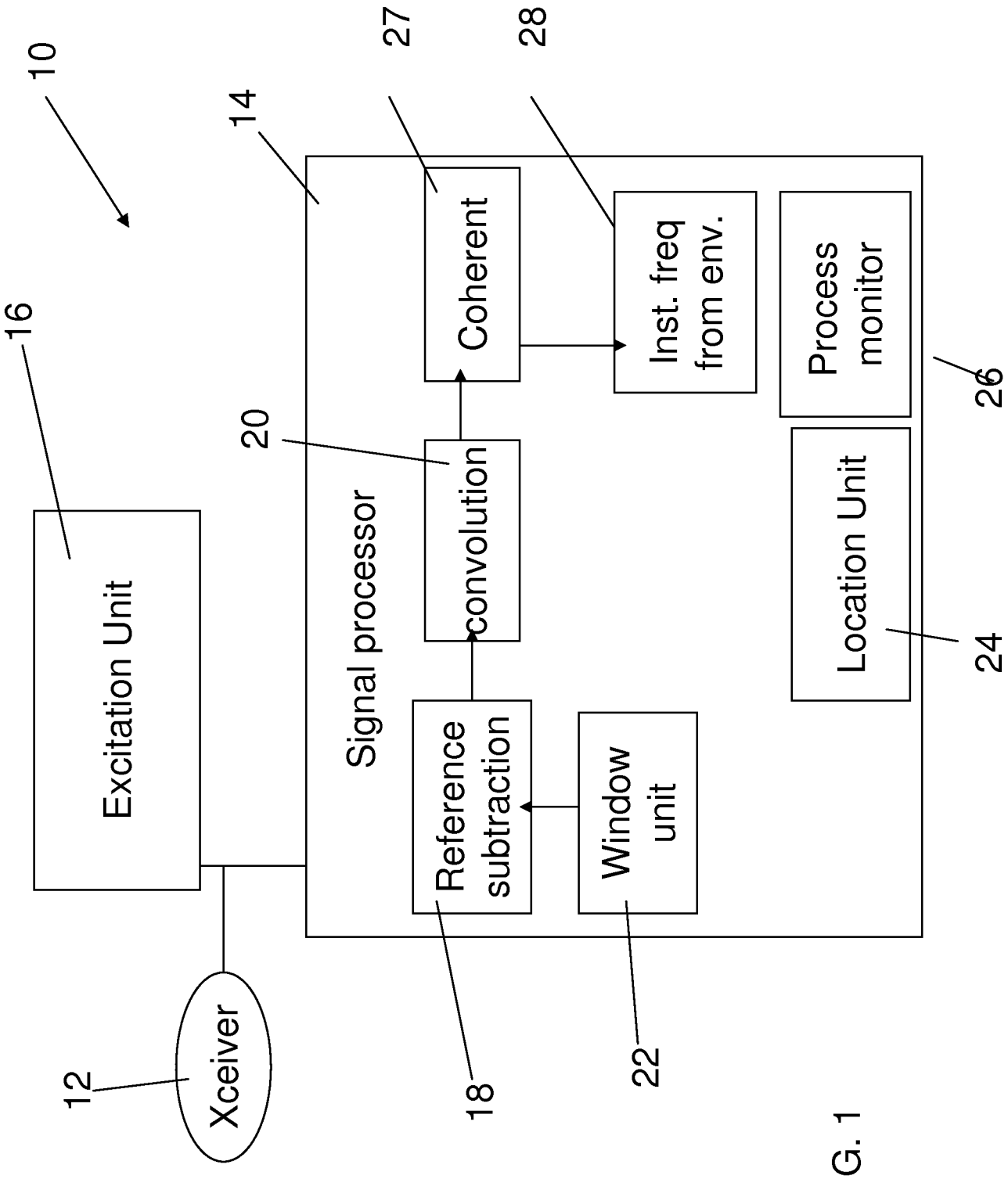

10
14
27
28
16
Coherent
Inst. freq from env.
Process monitor
26
20
convolution
Signal processor
Excitation Unit
Location Unit
24
Reference subtraction
Window unit
Xceiver
12
18
22

FIG. 1

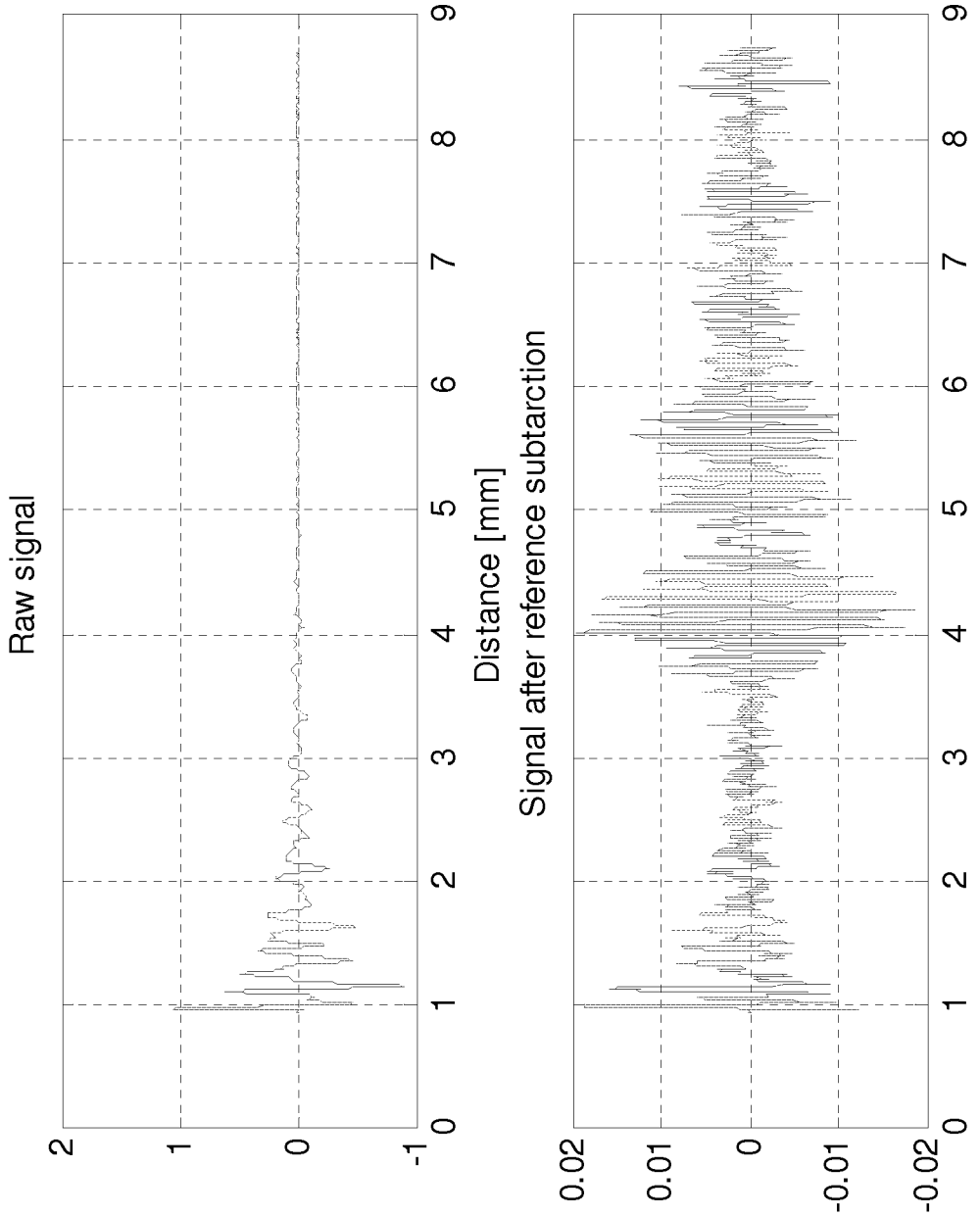

Raw signal
2
1
0
-1
0
1
2
3
4
5
6
7
8
9
Distance [mm]
Signal after reference subtarction
0.02
0.01
0
-0.01
-0.02
0
1
2
3
4
5
6
7
8
9

FIG. 2

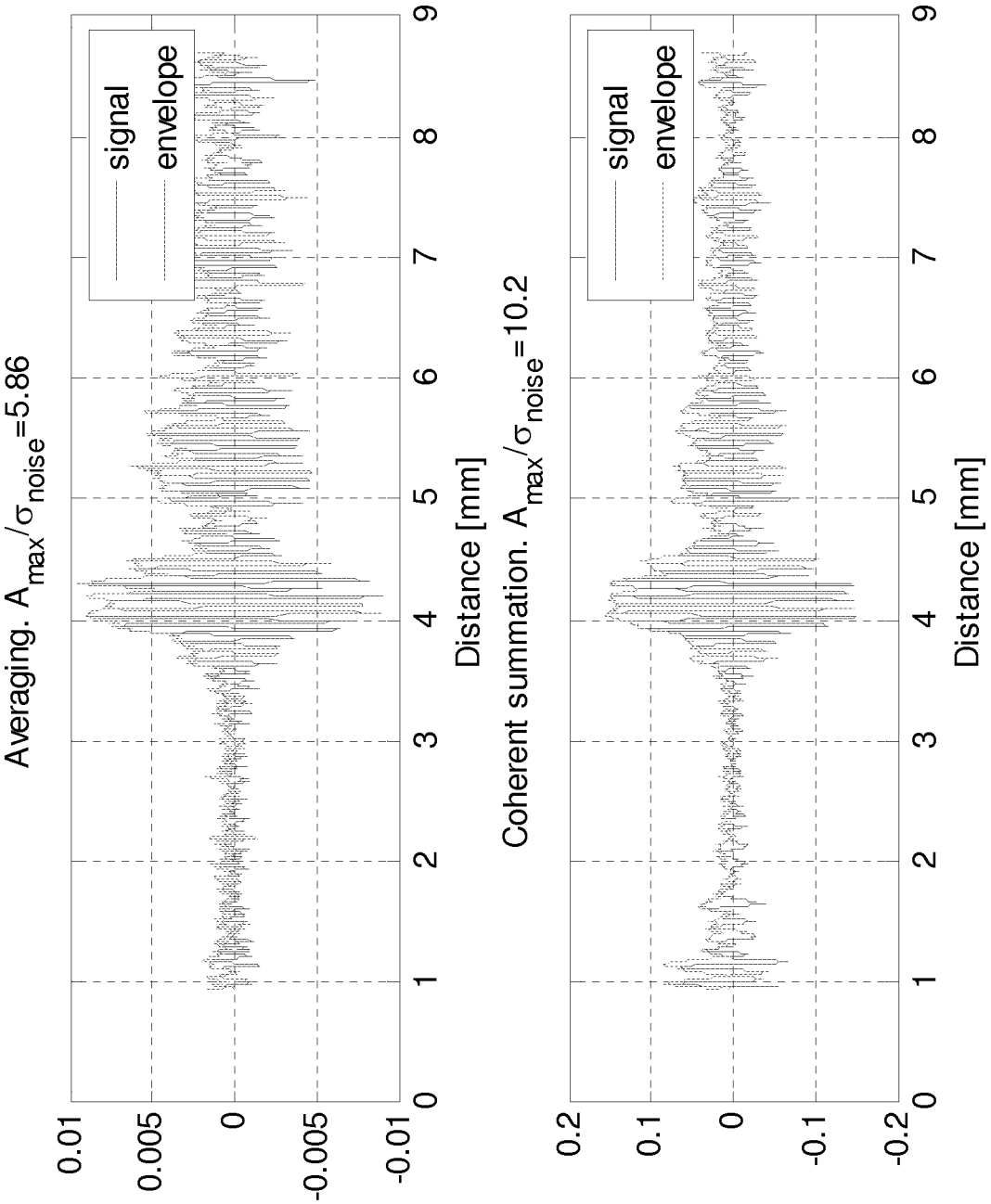

Averaging. A_{max}/σ_{noise}=5.86
signal
envelope
0.01
0.005
0
-0.005
-0.01
0
1
2
3
4
5
6
7
8
9
Distance [mm]
Coherent summation. A_{max}/σ_{noise}=10.2
signal
envelope
0.2
0.1
0
-0.1
-0.2
0
1
2
3
4
5
6
7
8
9
Distance [mm]

FIG. 3

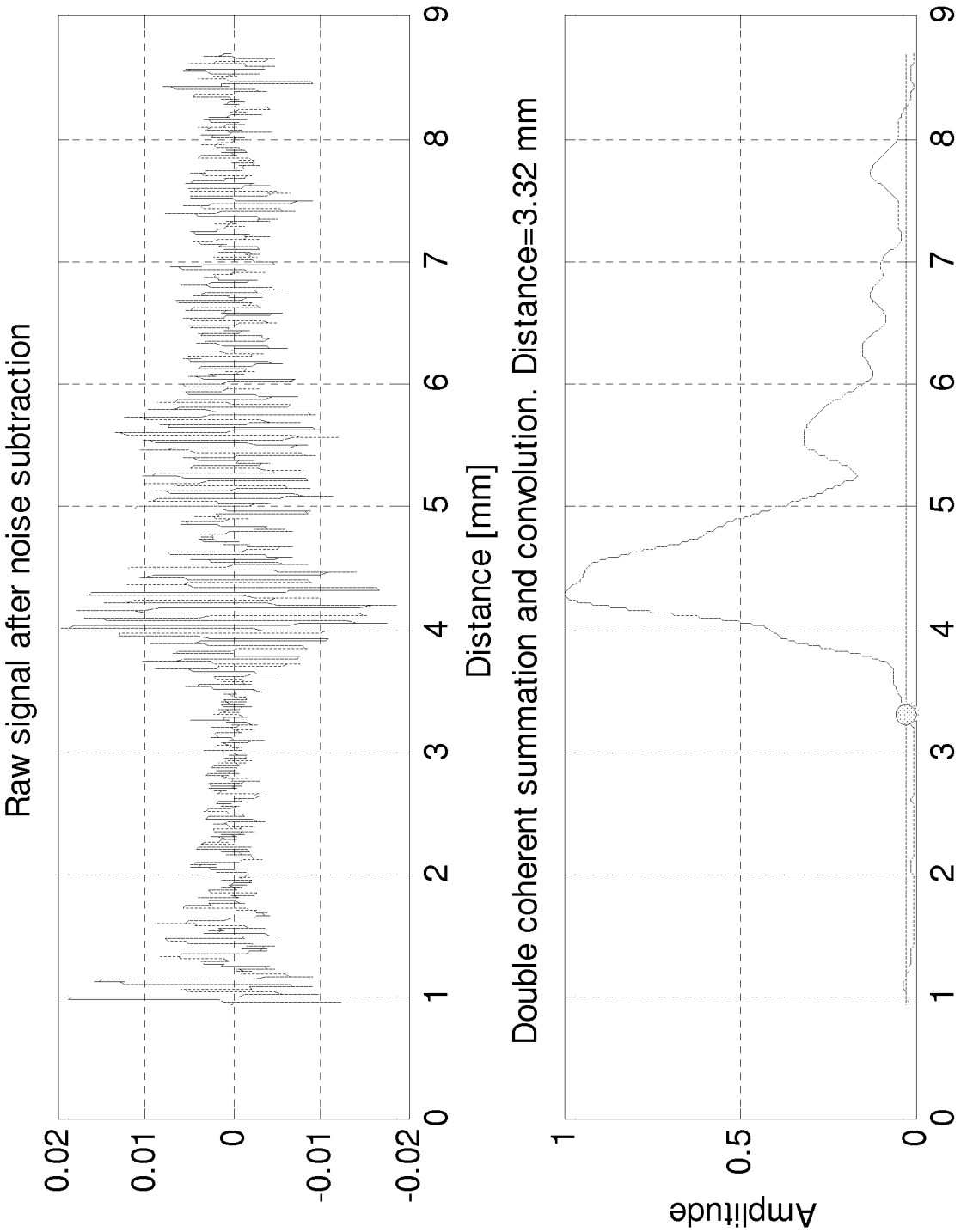
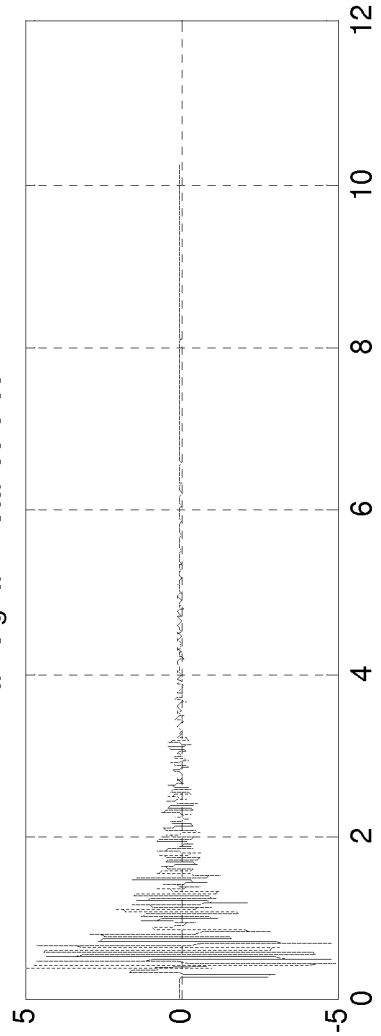

Raw signal after noise subtraction
0.02
0.01
0
-0.01
-0.02
0
1
2
3
4
5
6
7
8
9
Distance [mm]
Double coherent summation and convolution. Distance=3.32 mm
Amplitude
1
0.5
0
0
1
2
3
4
5
6
7
8
9

FIG. 4

0.69 mm

FIG. 5A



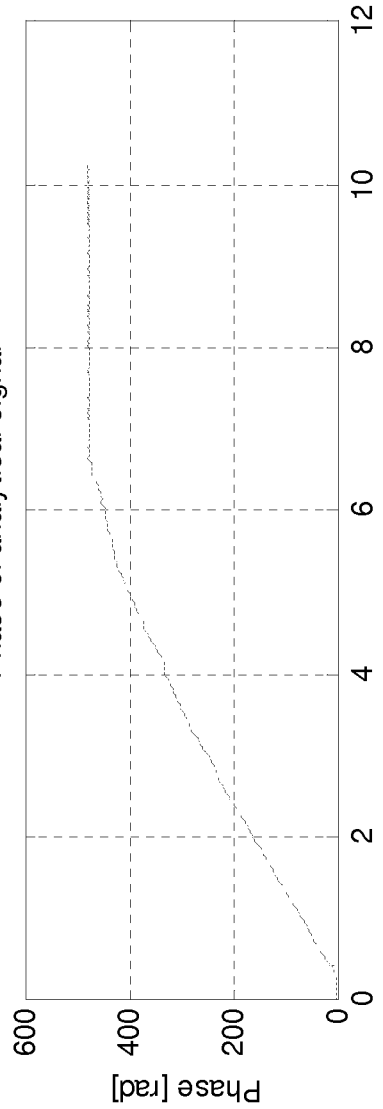


FIG. 5B

Two slopes. Estimated distance 0.88 mm vs. Actual 0.69 mm

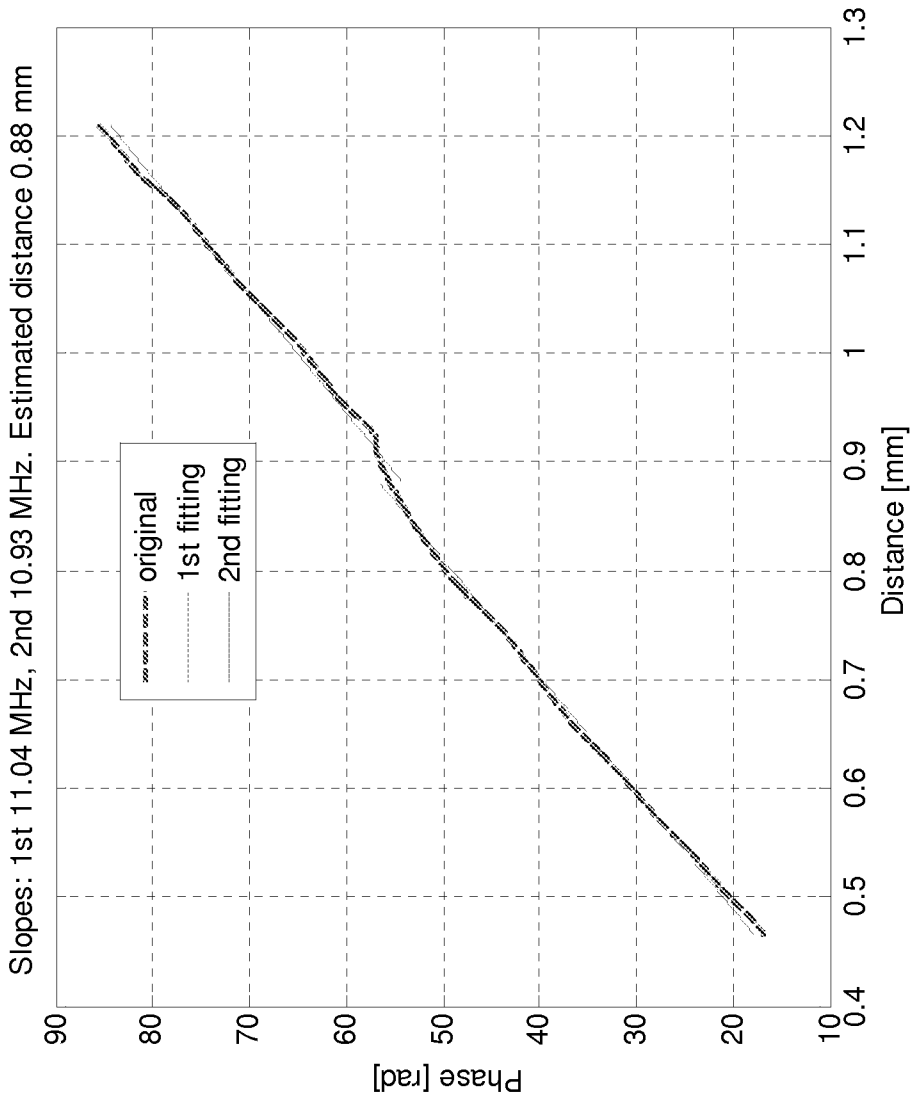


FIG. 6

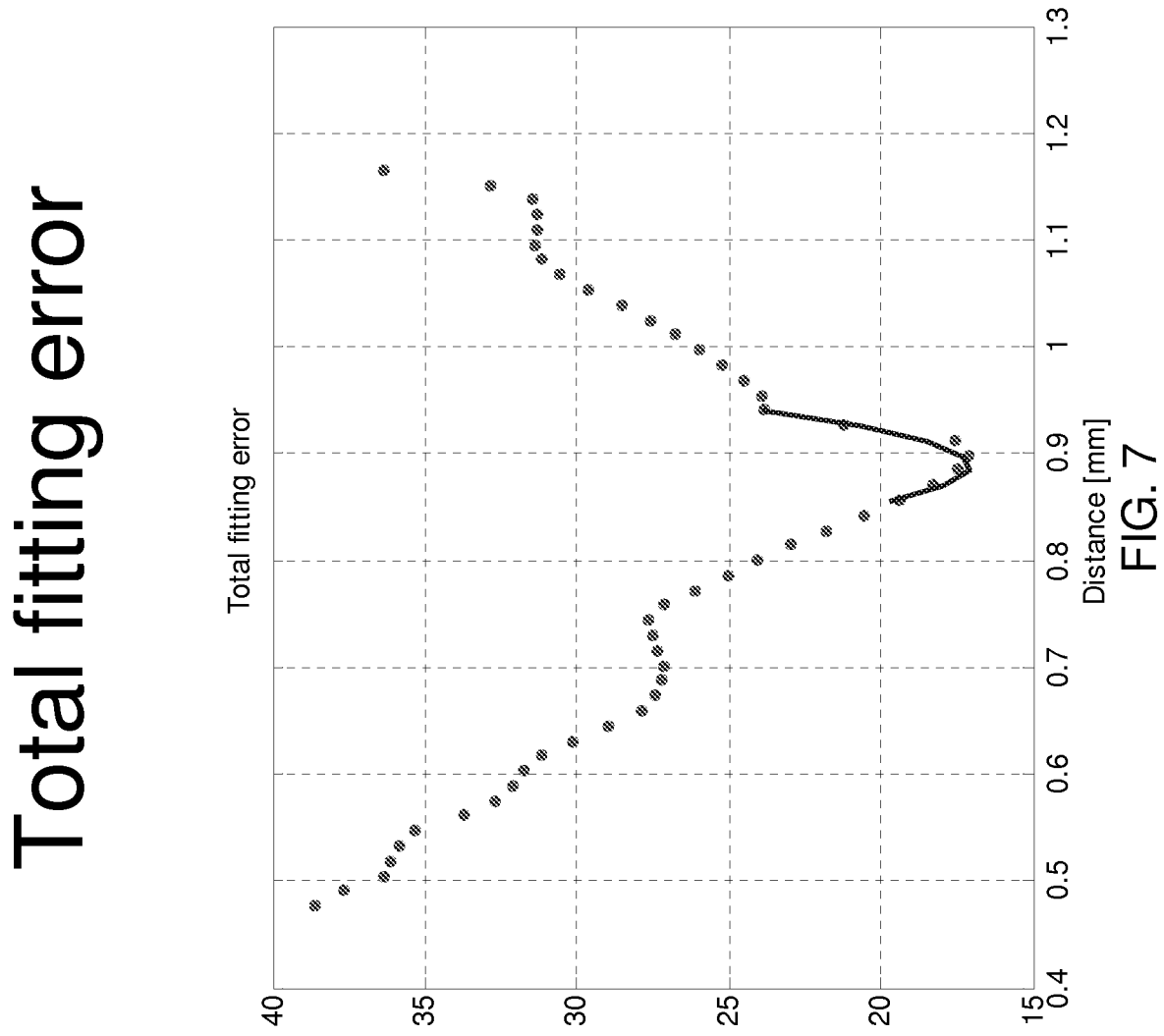

Total fitting error
Total fitting error
Distance [mm]
40
35
30
25
20
15
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3

FIG. 7

Local slopes

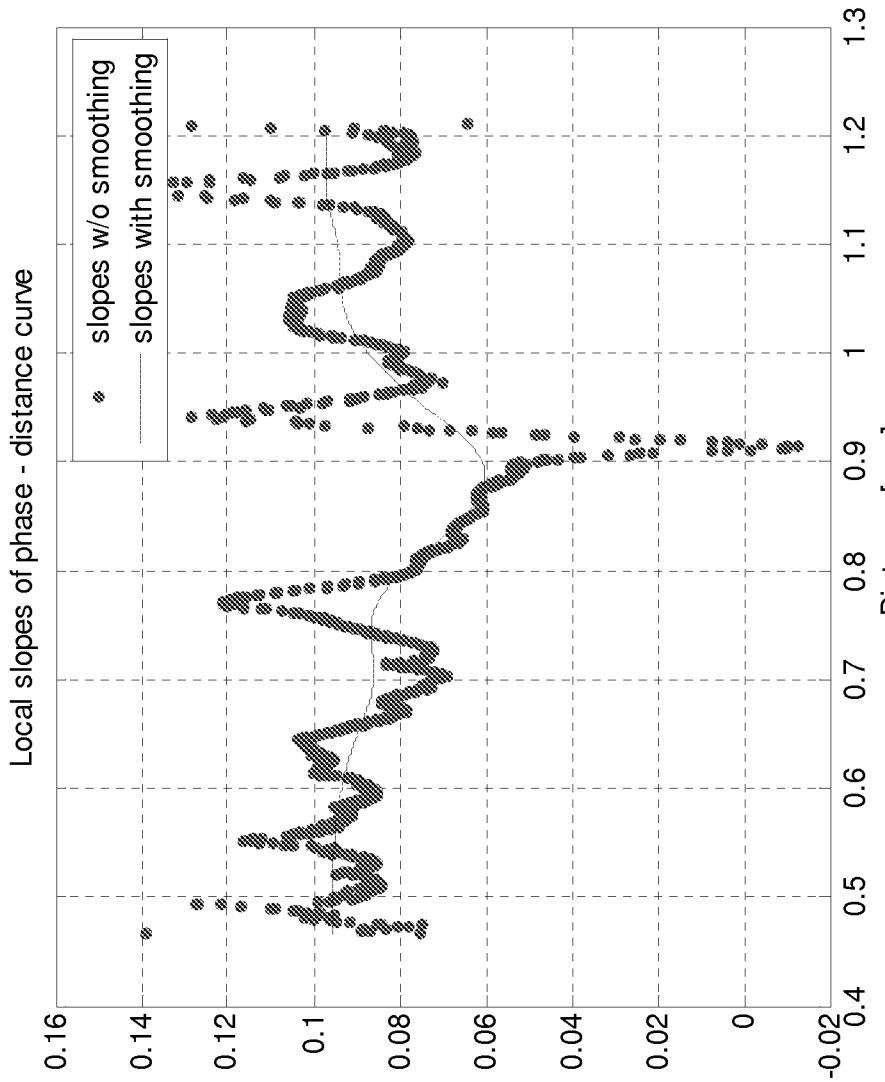


FIG. 8

1.19 mm

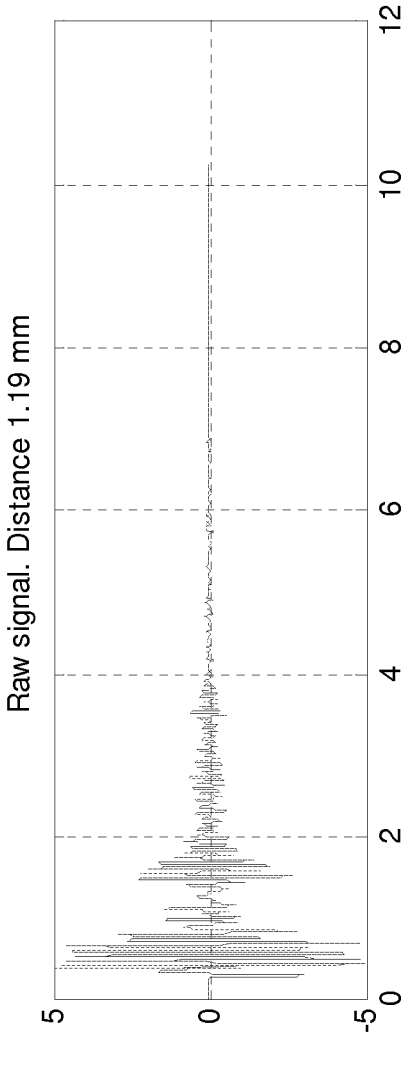


FIG. 9A

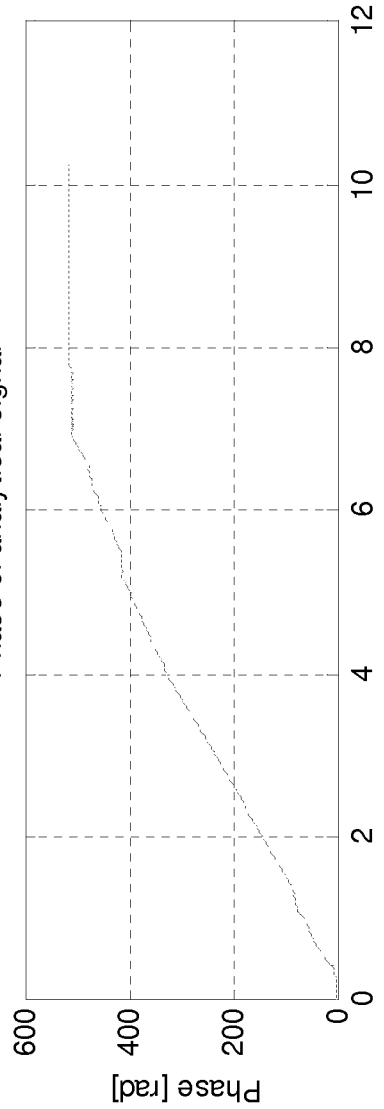


FIG. 9B

Estimated1.25 mm vs. Actual1.19 mm

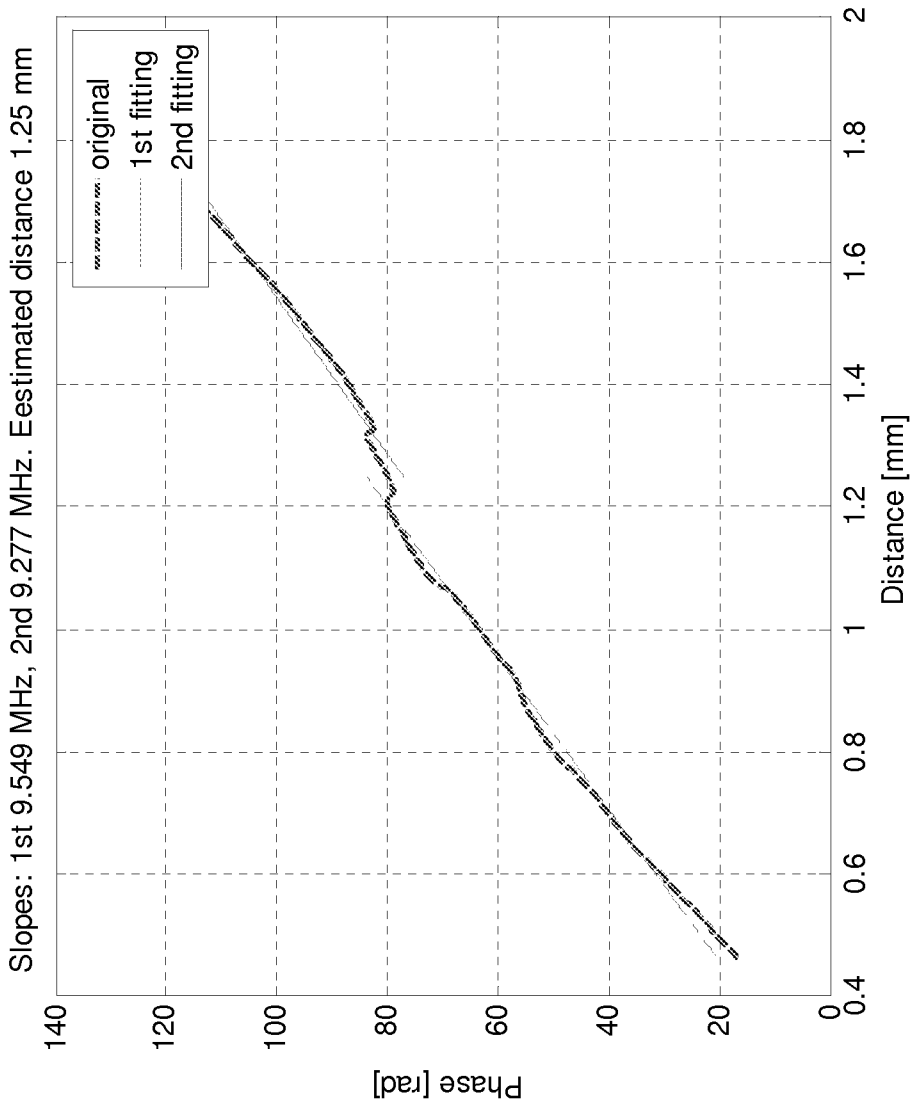


FIG. 10

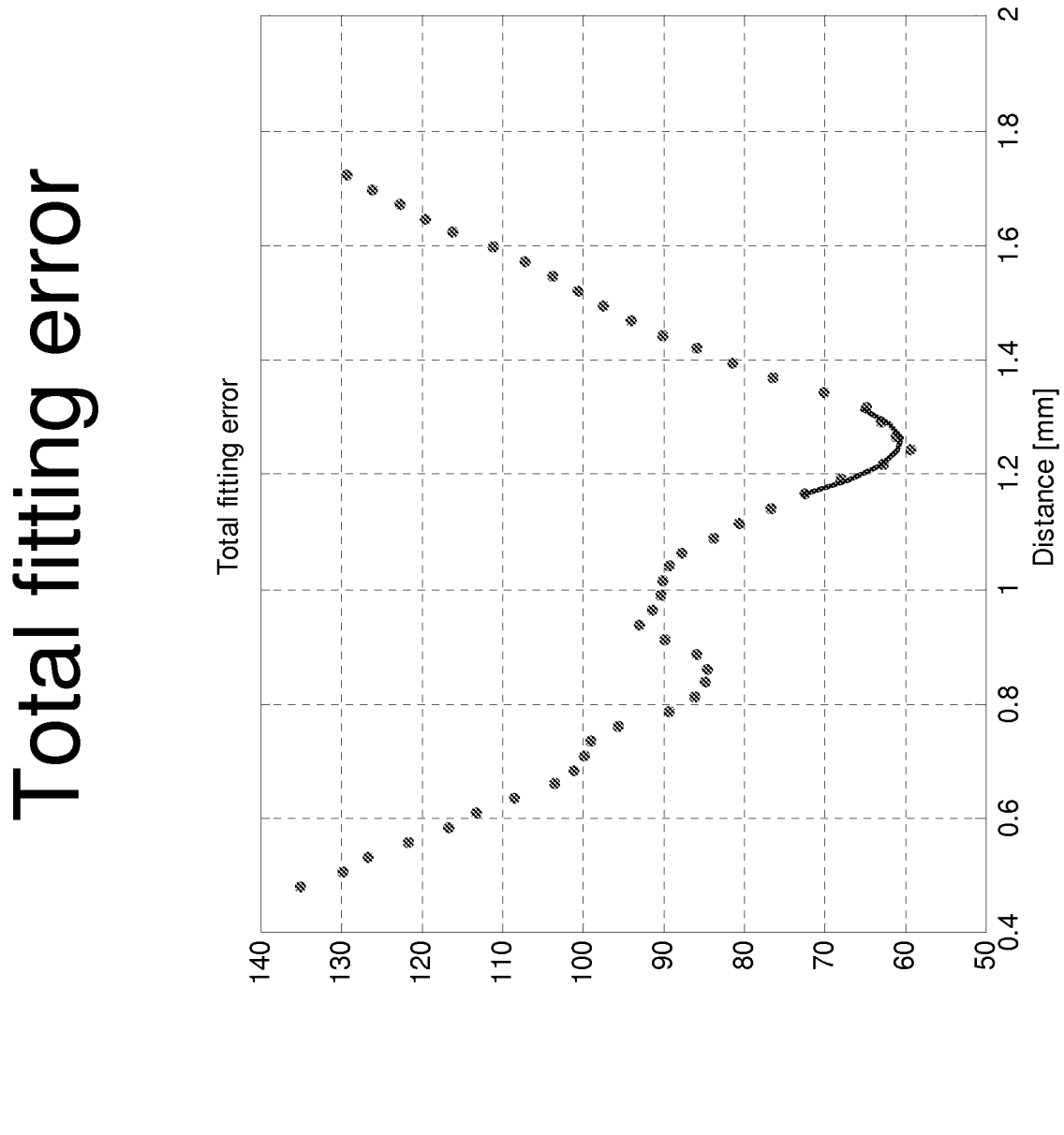

Total fitting error
Total fitting error
Distance [mm]
140
130
120
110
100
90
80
70
60
50
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2

FIG. 11

Local slopes

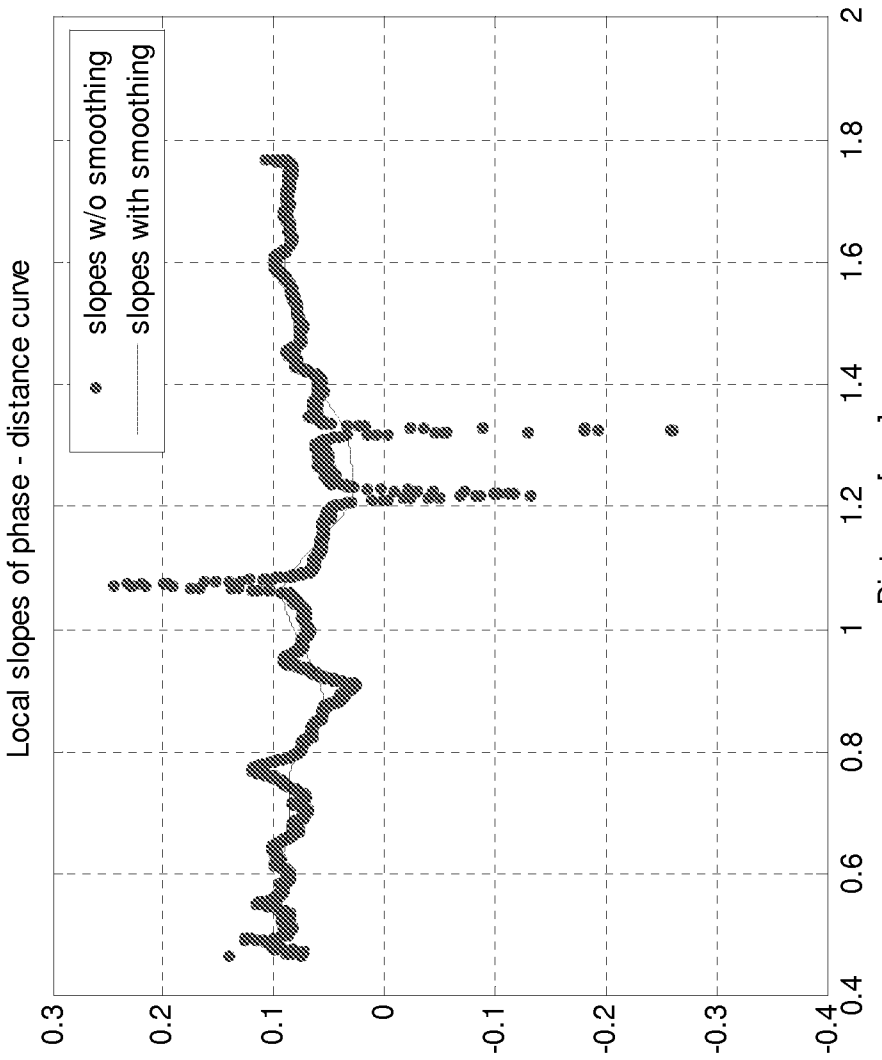


FIG. 12

1.69 mm

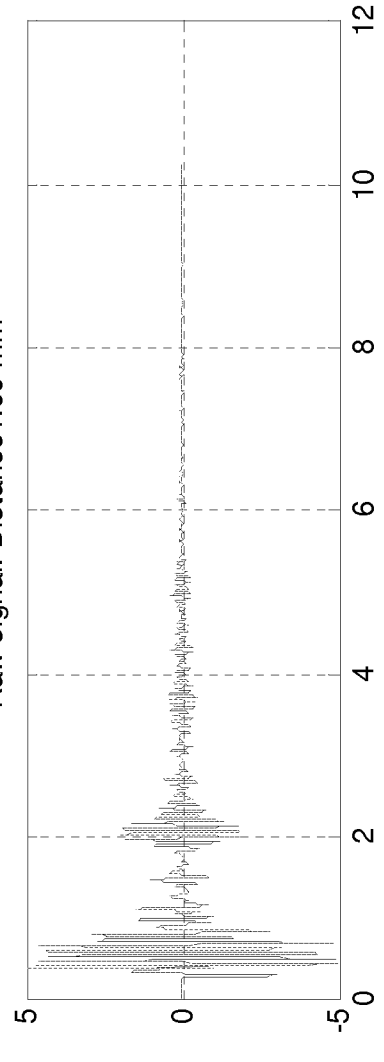


FIG. 13A

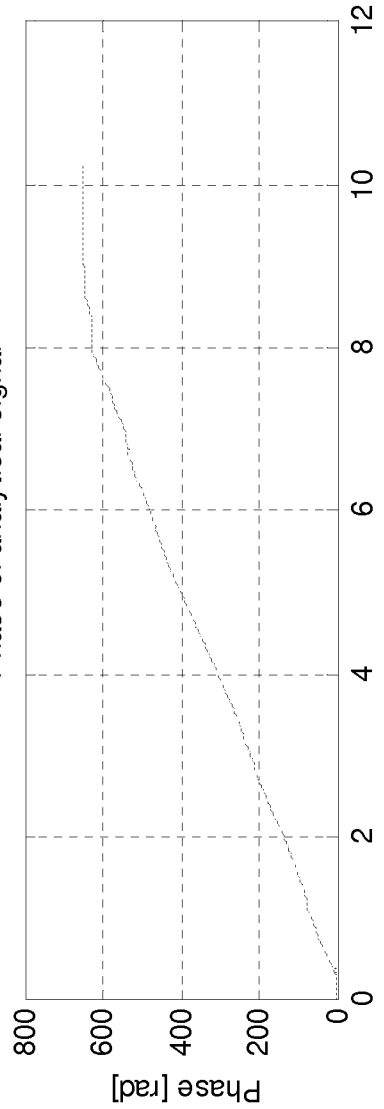


FIG. 13B

Estimated 1.61 mm vs. Actual 1.69 mm

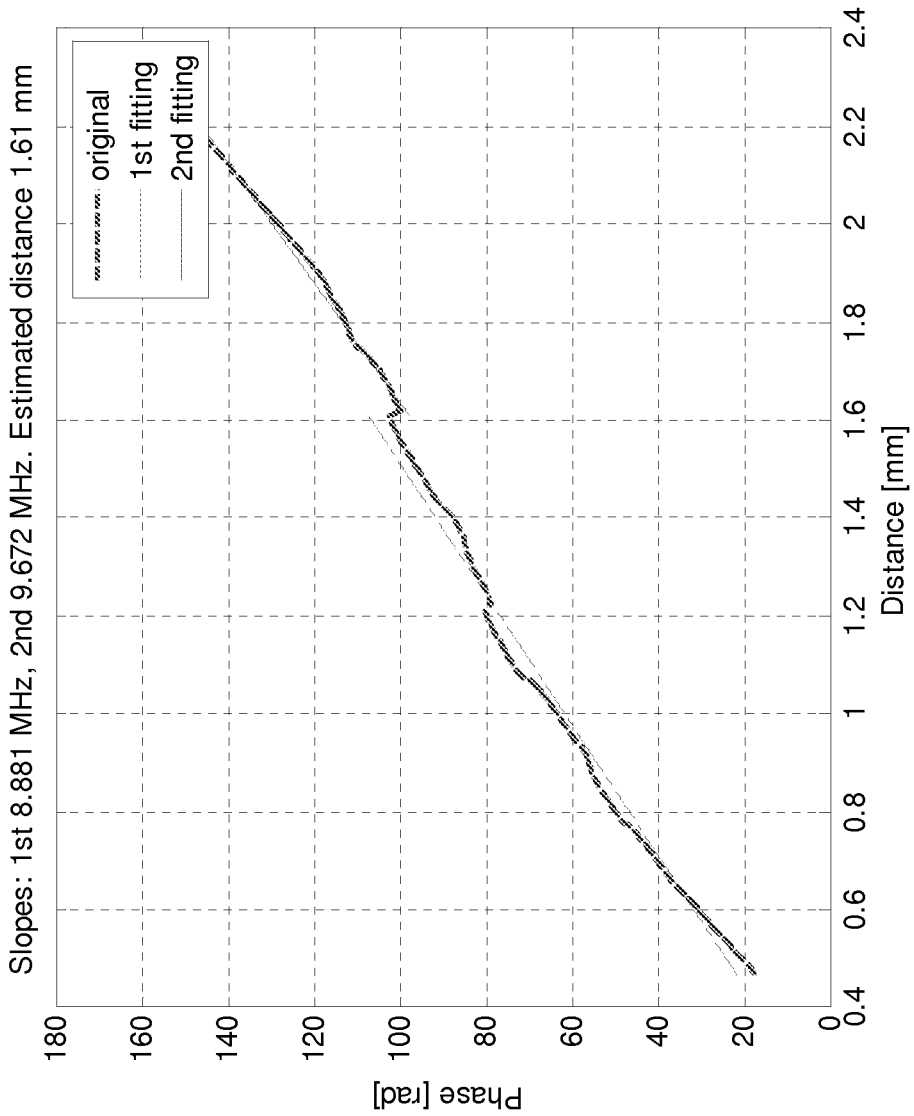


FIG. 14

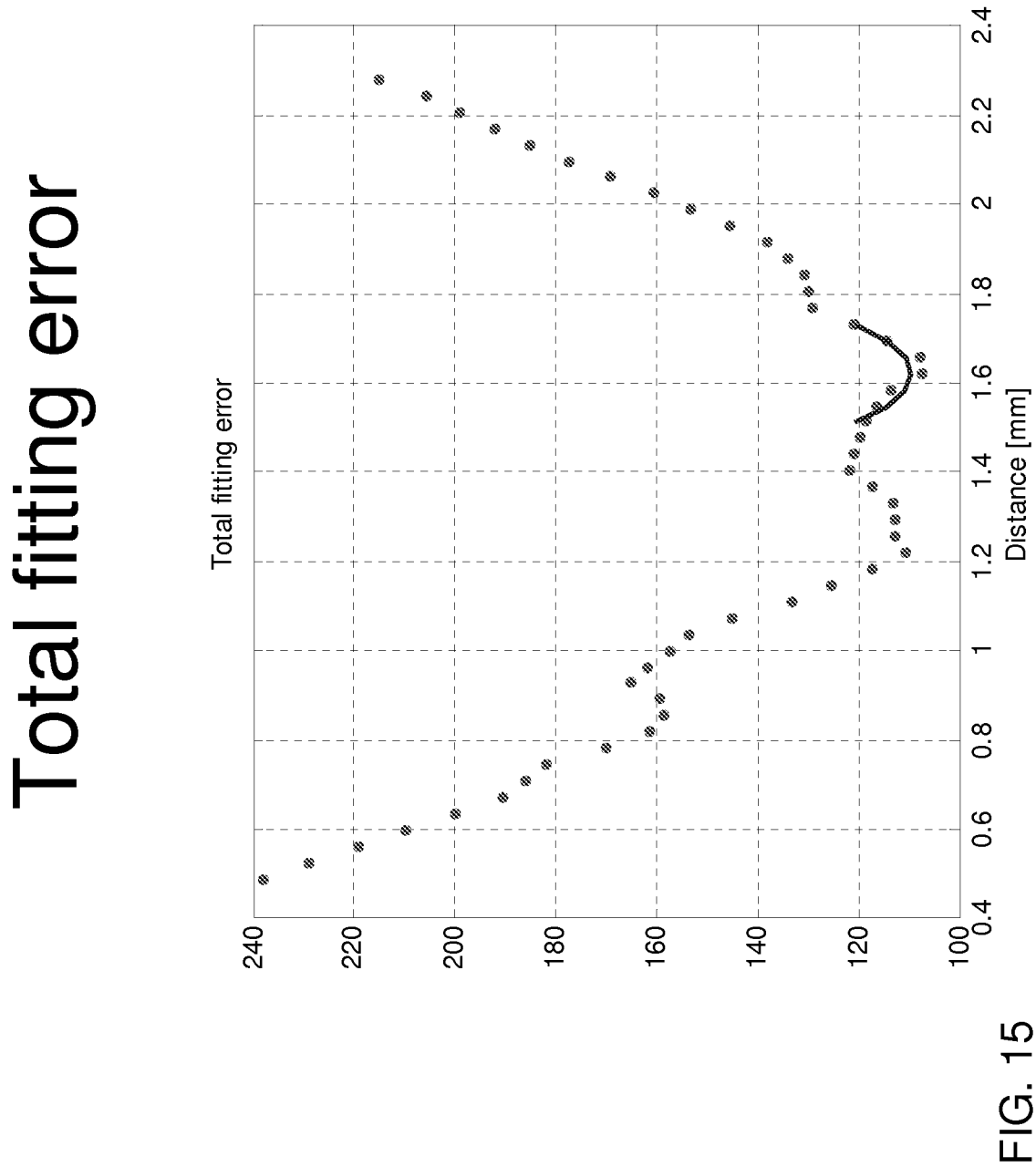

Total fitting error
Total fitting error
Distance [mm]
240
220
200
180
160
140
120
100
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
2.2
2.4

FIG. 15

Local slopes

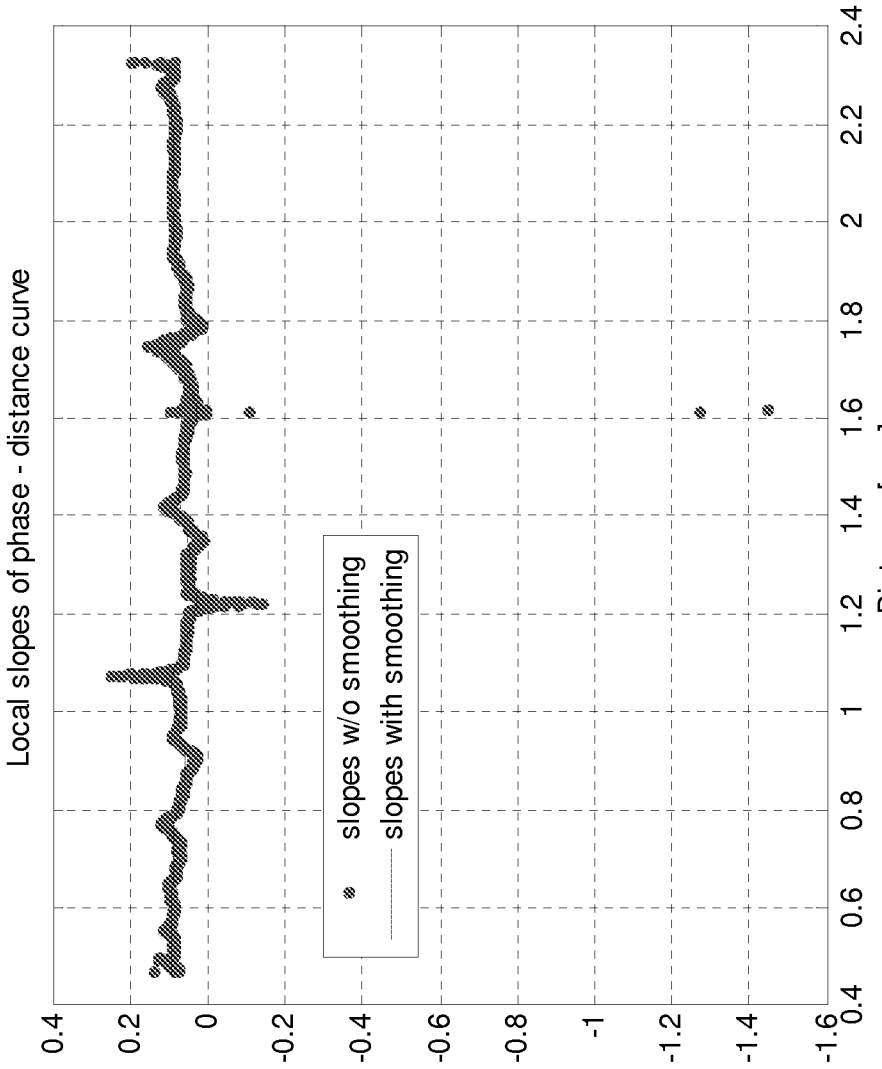


FIG. 16

2.19 mm

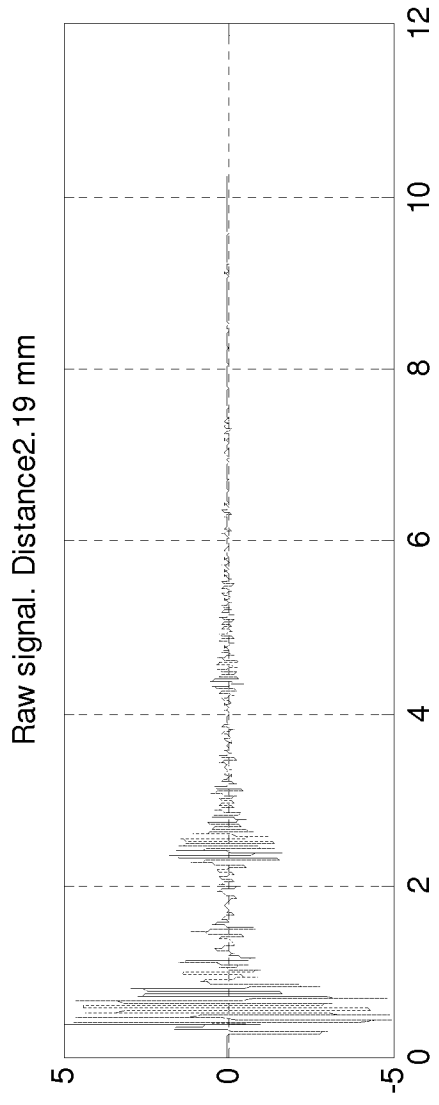


FIG. 17A

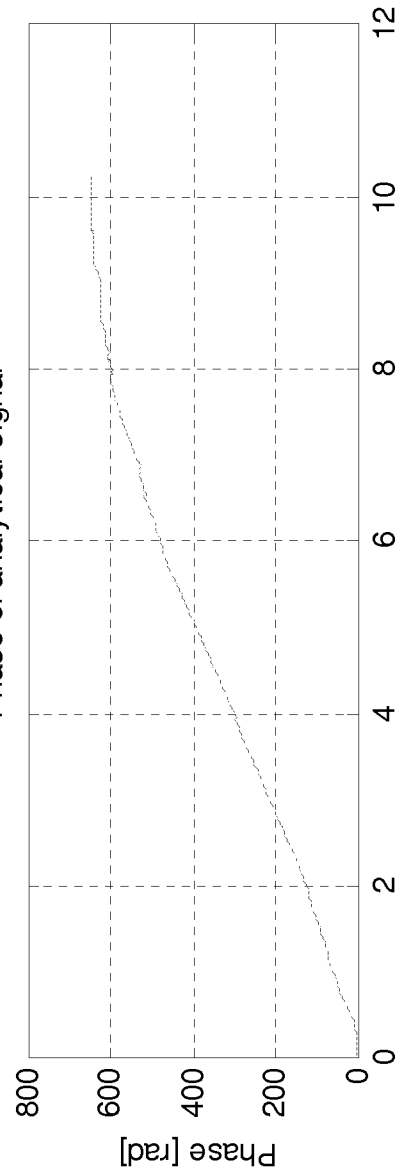


FIG. 17B

Estimated distance 1.96 mm vs. Actual 2.19 mm

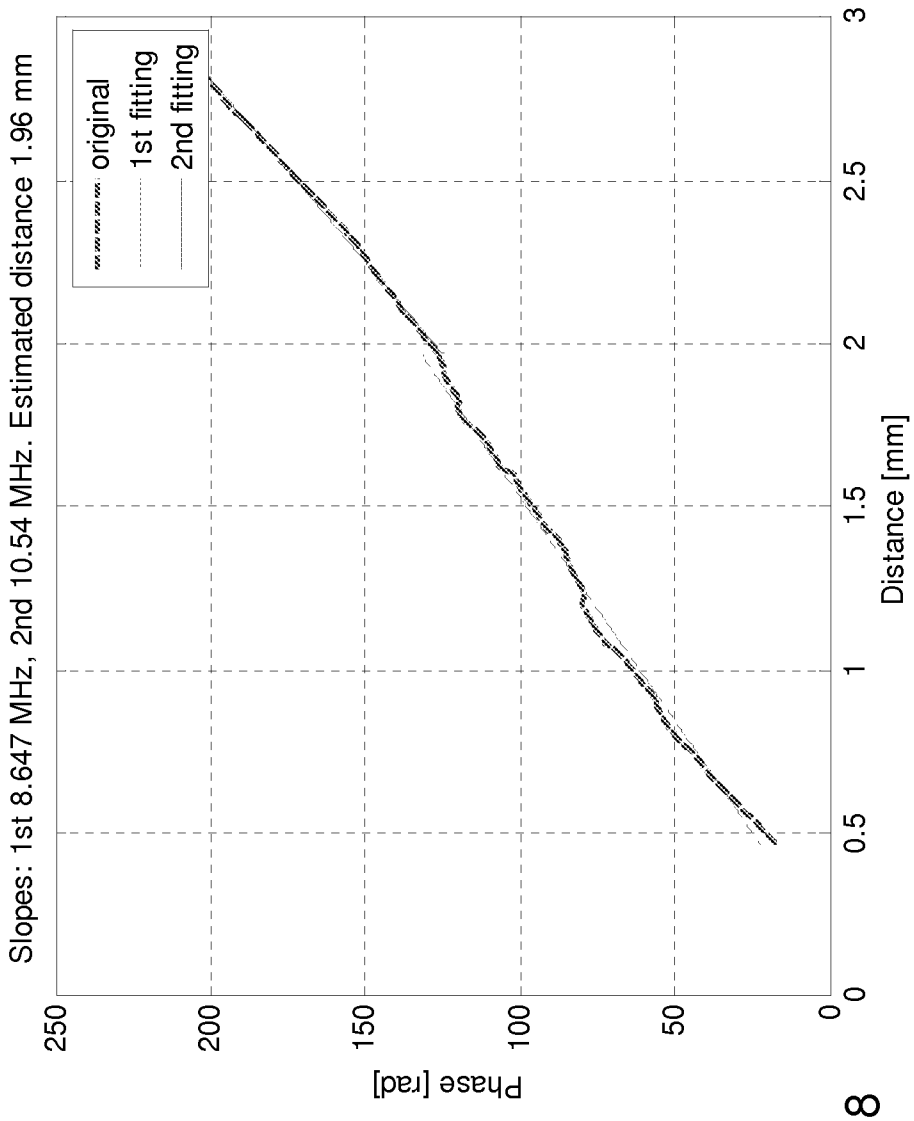


FIG. 18

Total fitting error

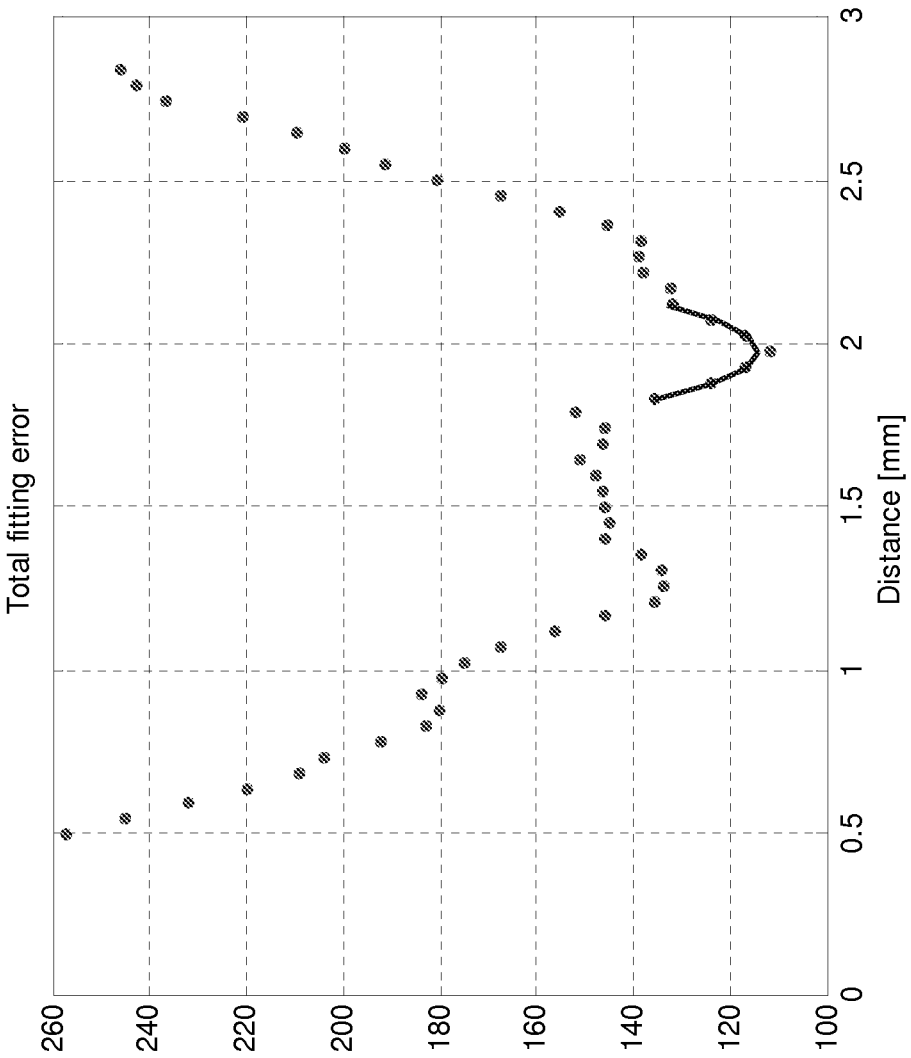


FIG. 19

Local slopes

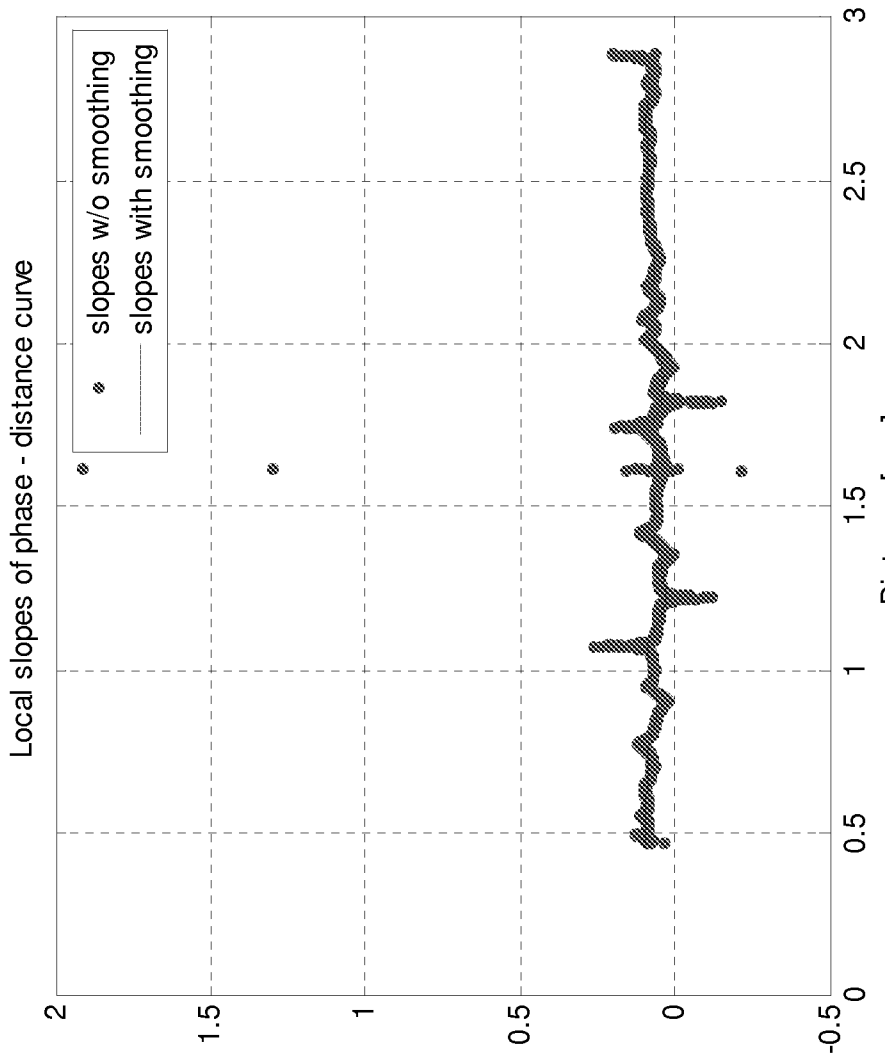


FIG. 20

2.69 mm

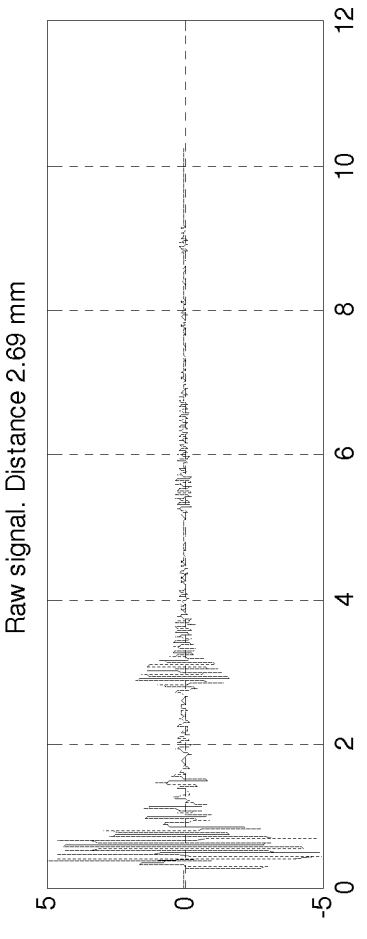


FIG. 21A

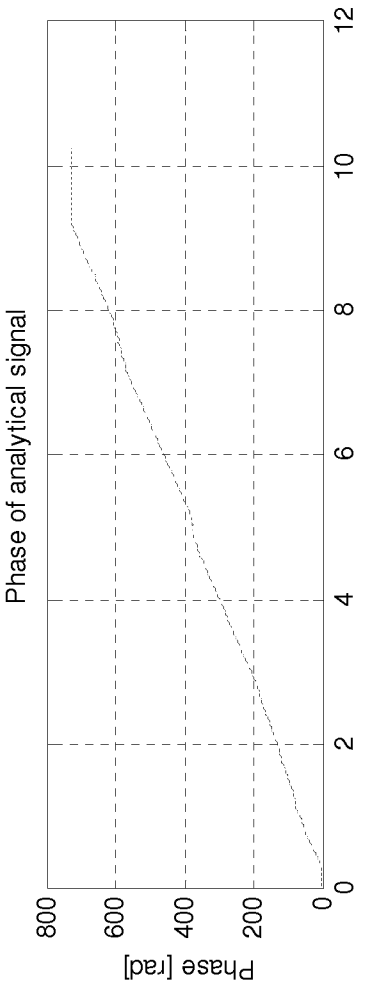


FIG. 21B

Estimated distance 2.77 mm vs. Actual 2.69 mm

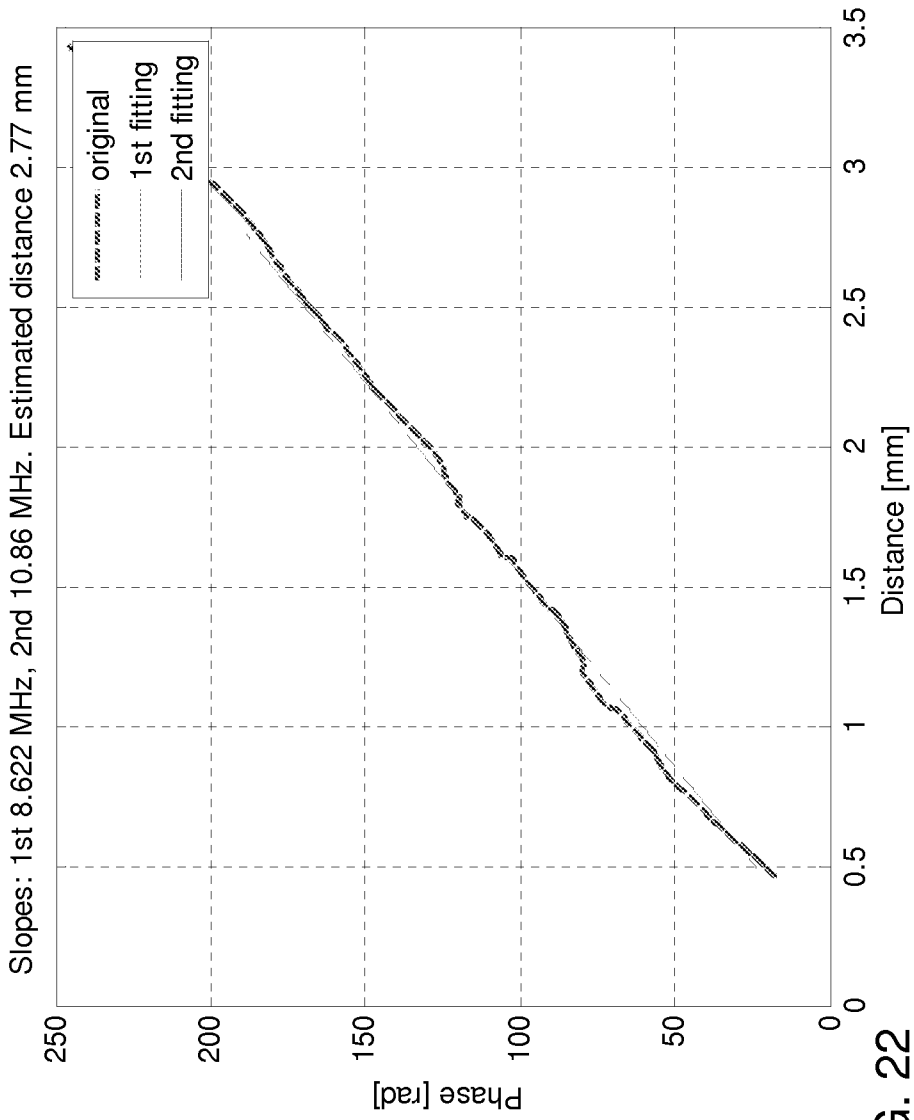


FIG. 22

Total fitting error

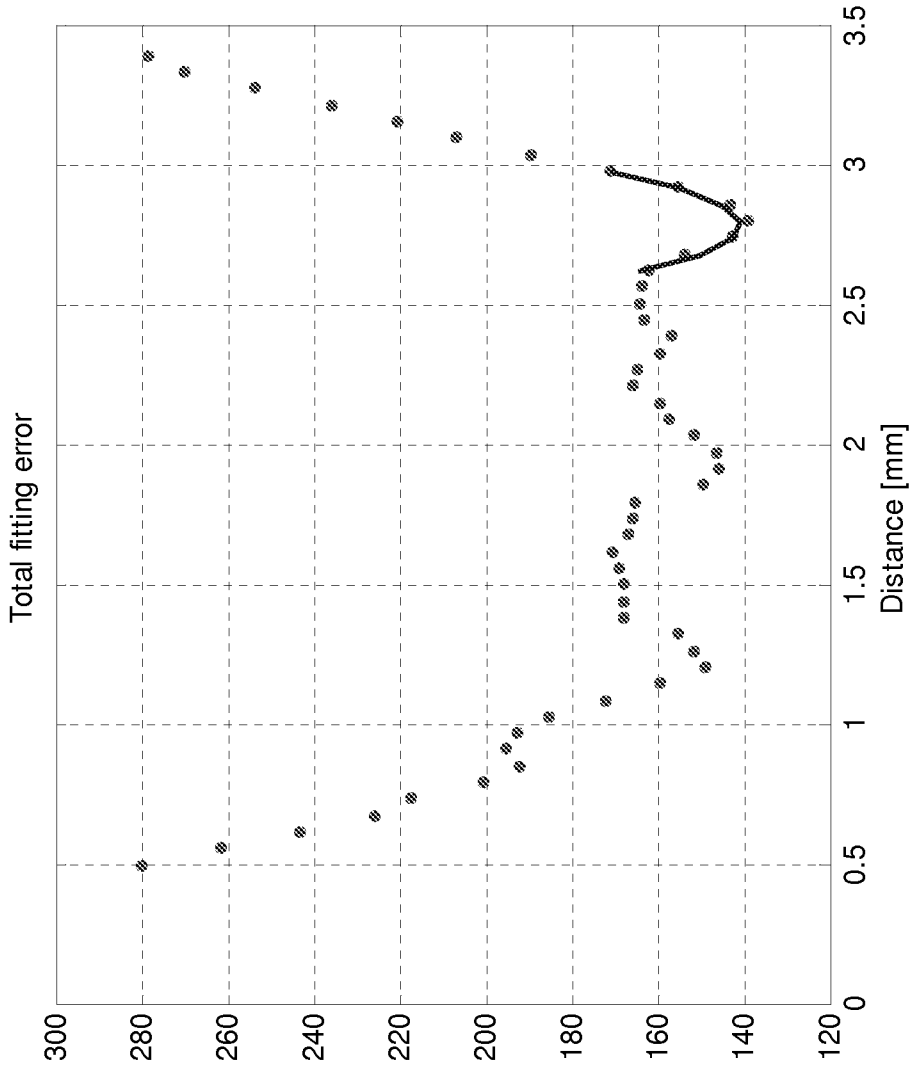


FIG. 23

Local slopes

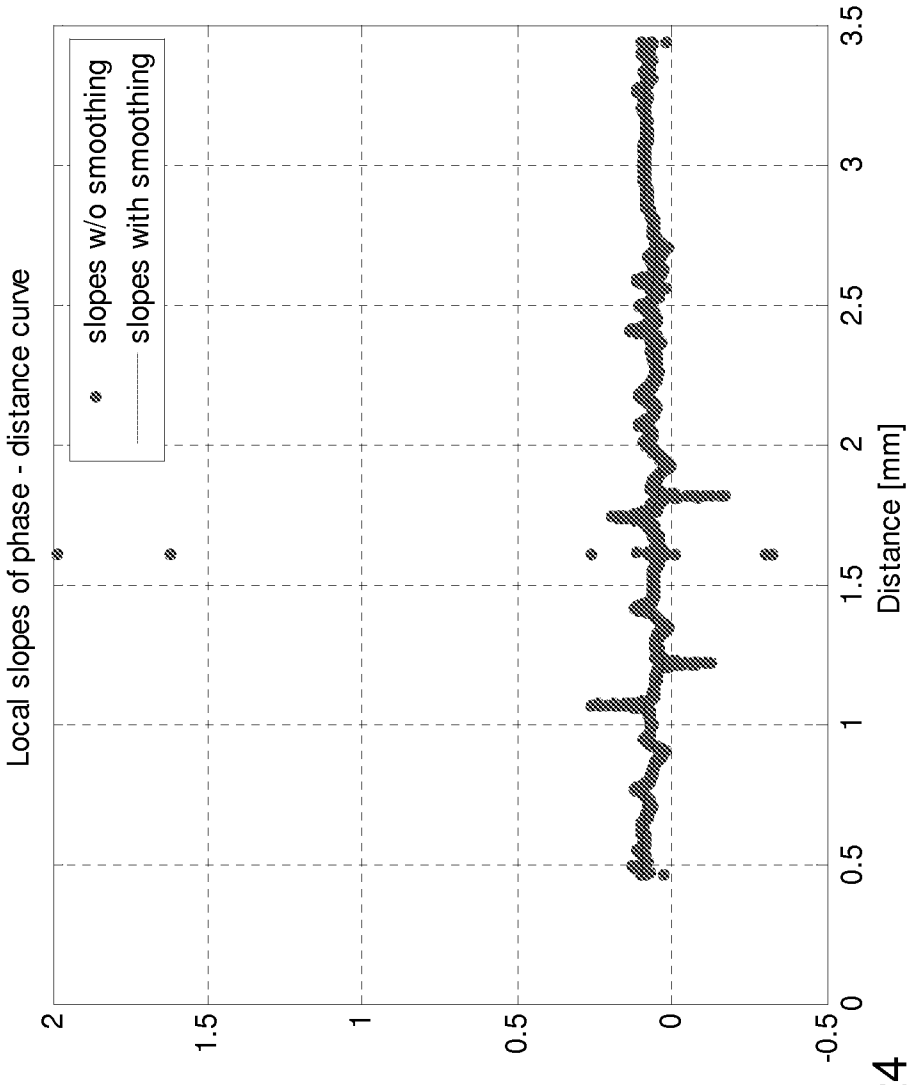


FIG. 24

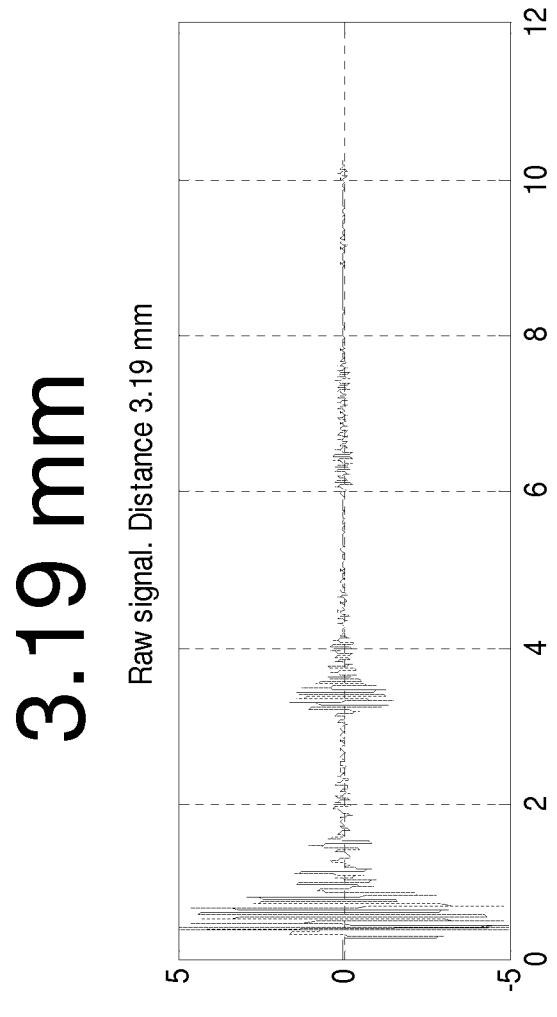


FIG. 25A

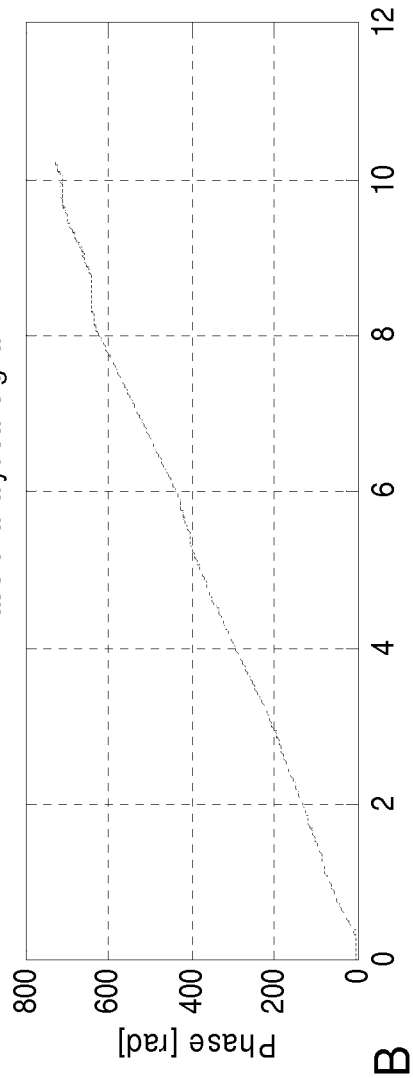


FIG. 25B

Estimated distance 2.85 mm vs. Actual 3.19 mm

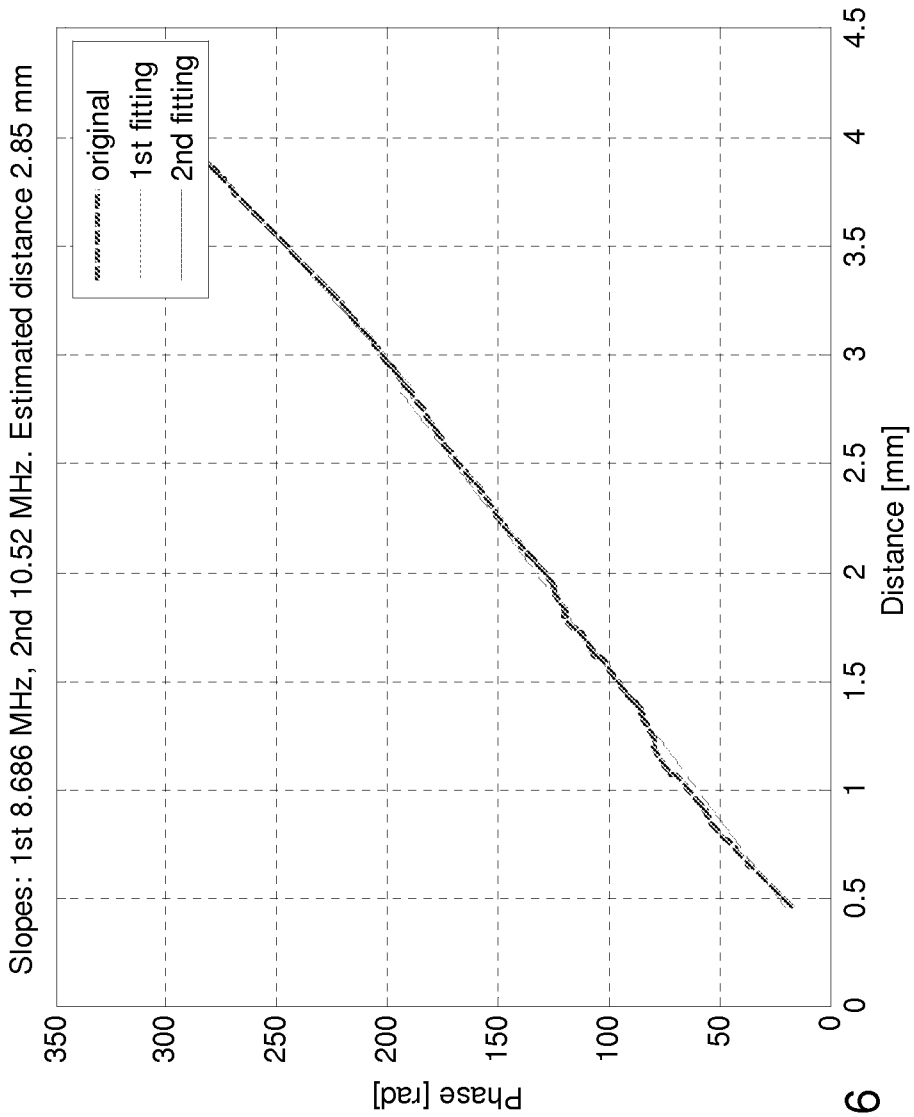


FIG. 26

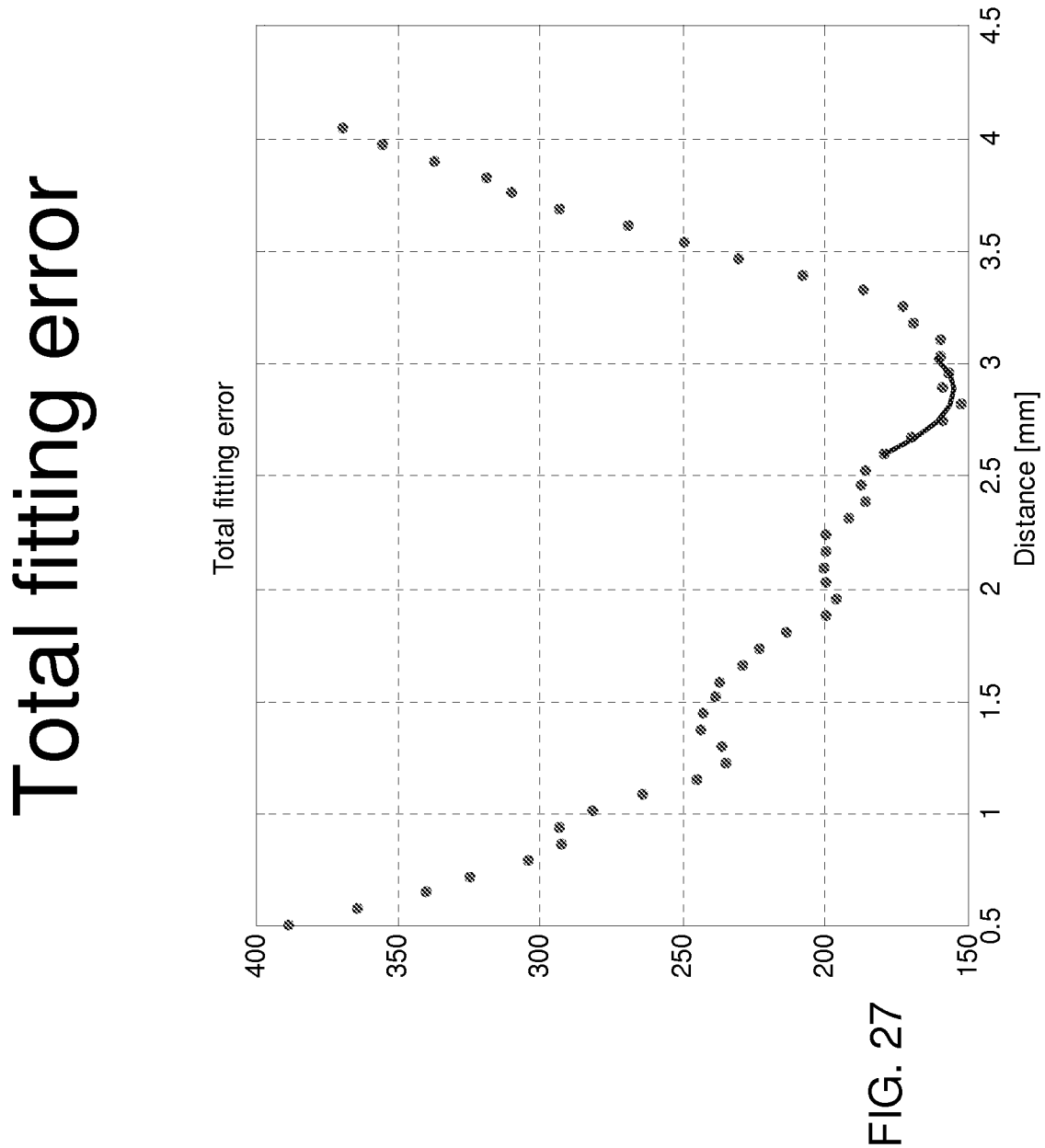

Total fitting error
Total fitting error
Distance [mm]
400
350
300
250
200
150
0.5
1
1.5
2
2.5
3
3.5
4
4.5

FIG. 27

Local slopes

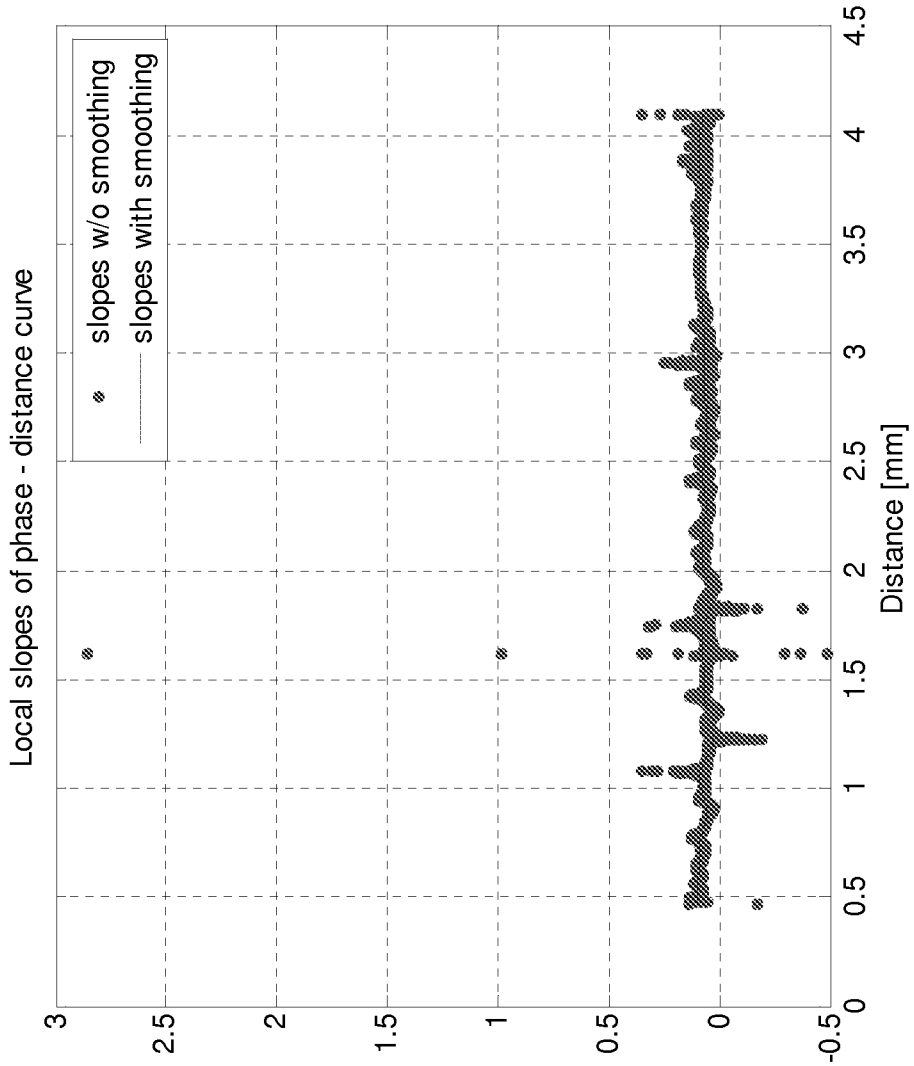


FIG. 28

3.69 mm

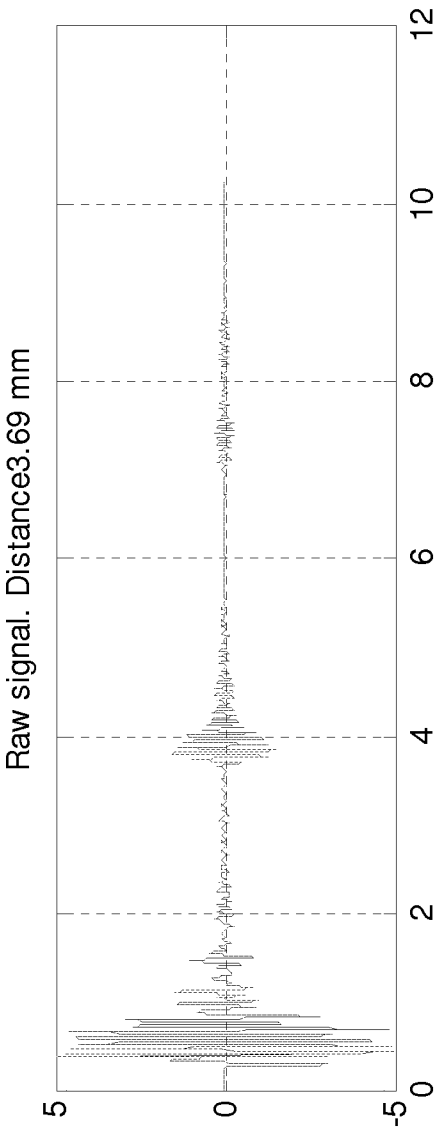


FIG. 29A

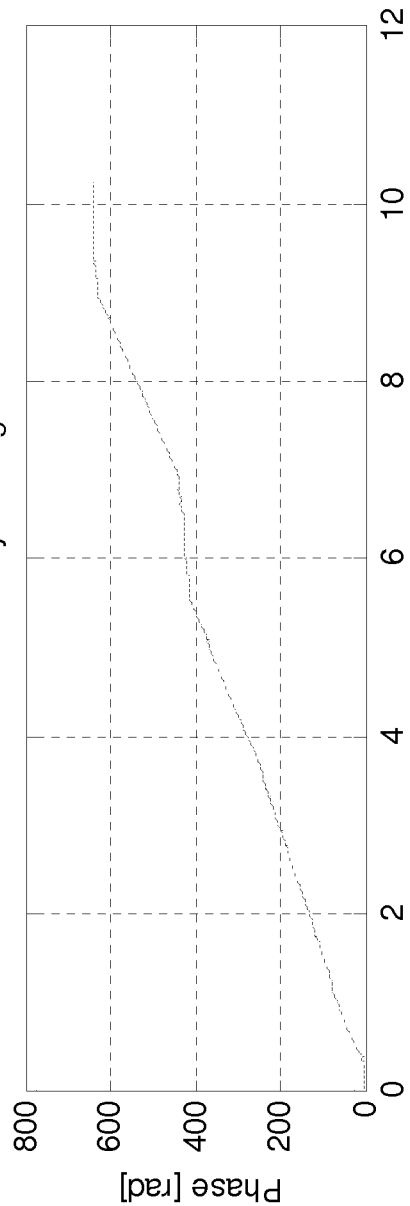


FIG. 29B

Two slopes. Estimated distance 3.66 mm vs. 3.69 mm

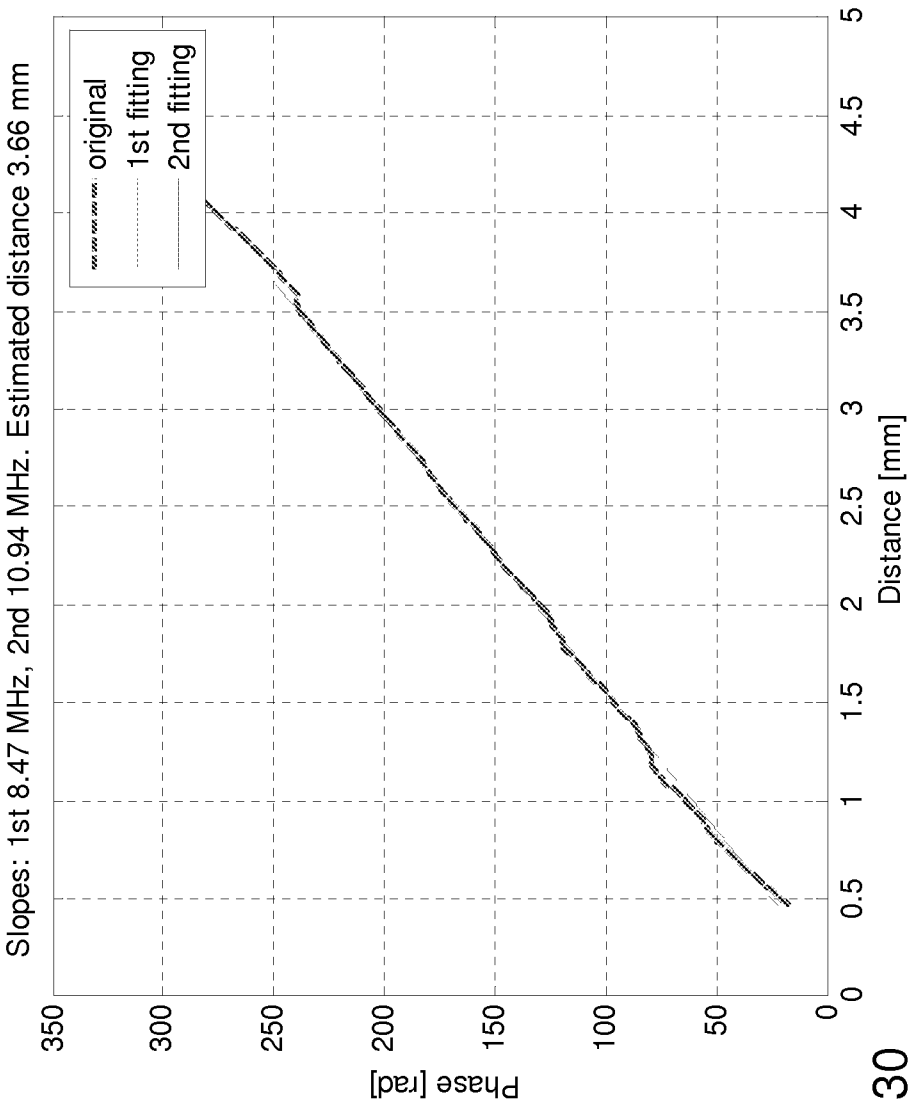


FIG. 30

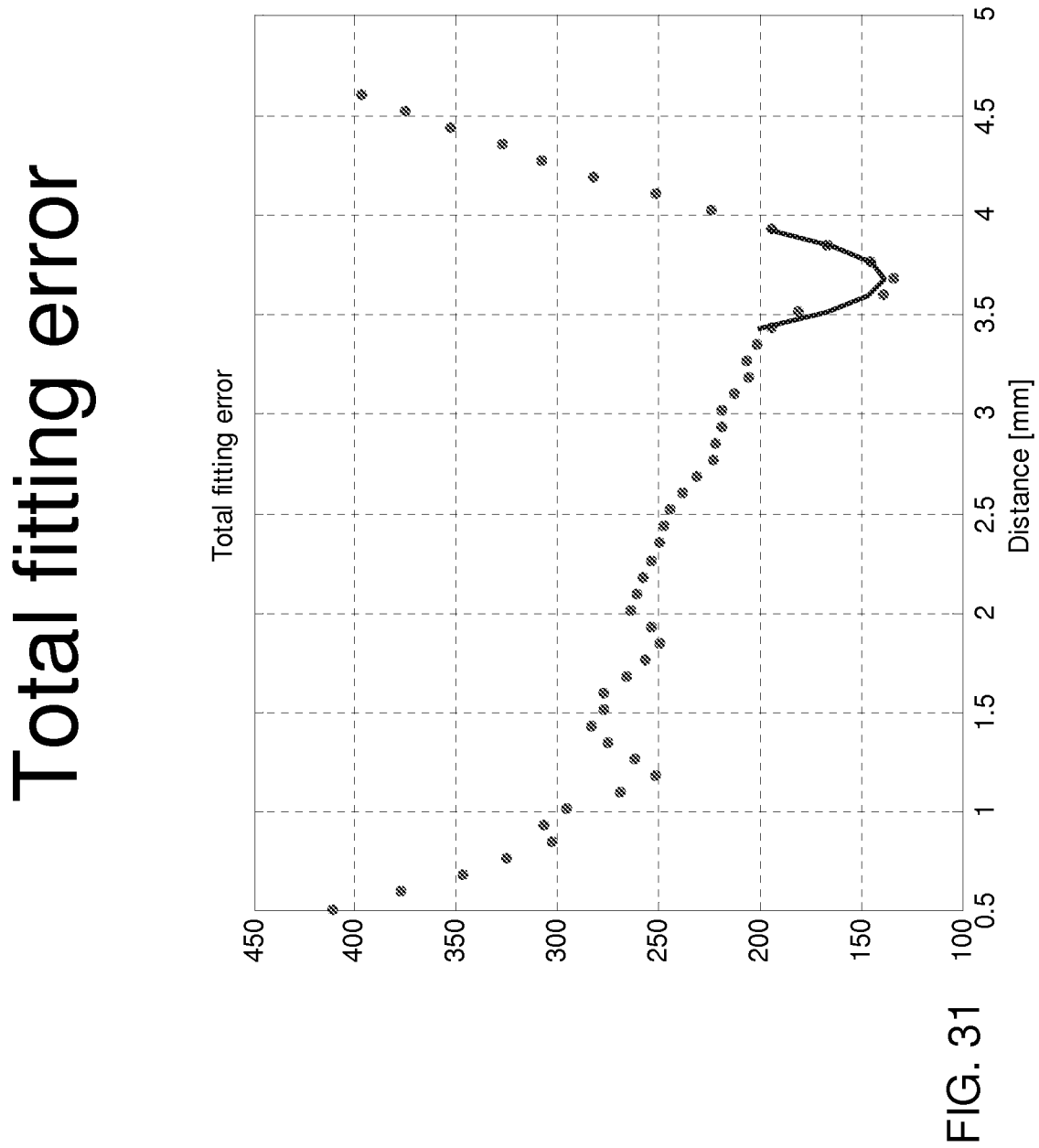

Total fitting error
Total fitting error
Distance [mm]
450
400
350
300
250
200
150
100
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5

FIG. 31

Local slopes

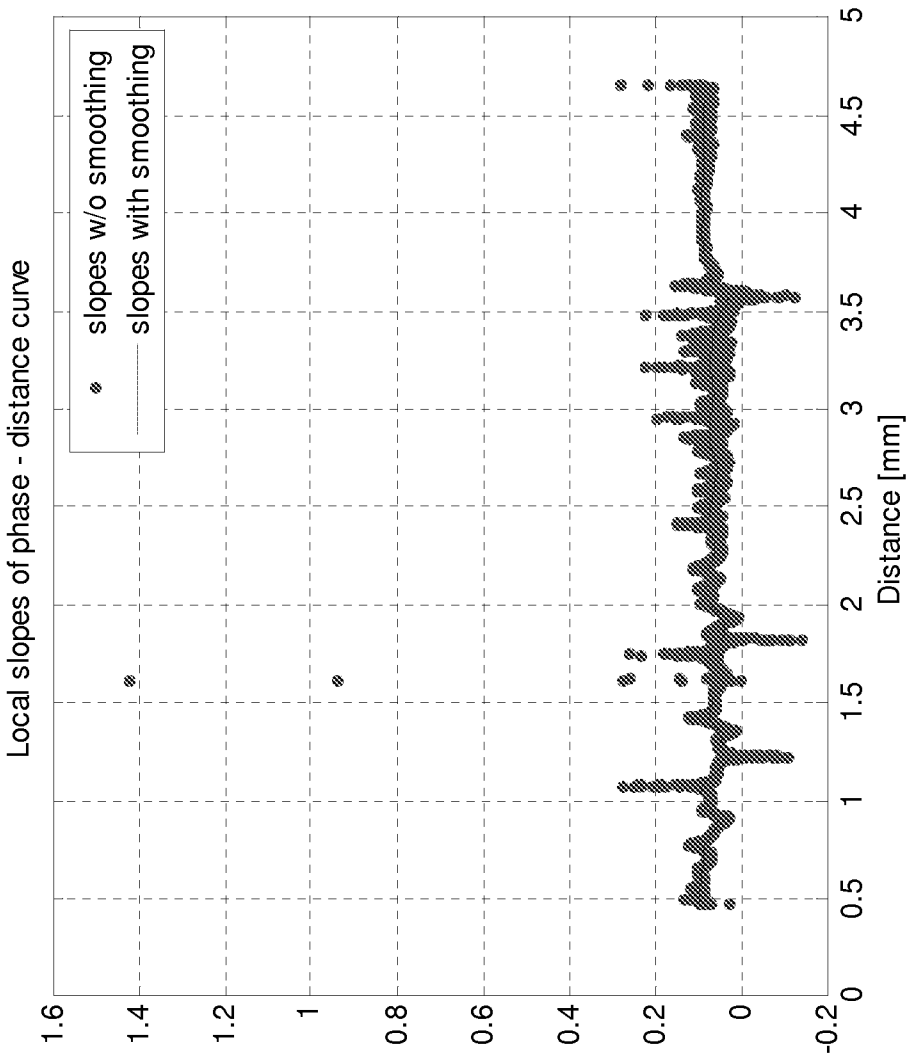


FIG. 32

Distance 4.19 mm

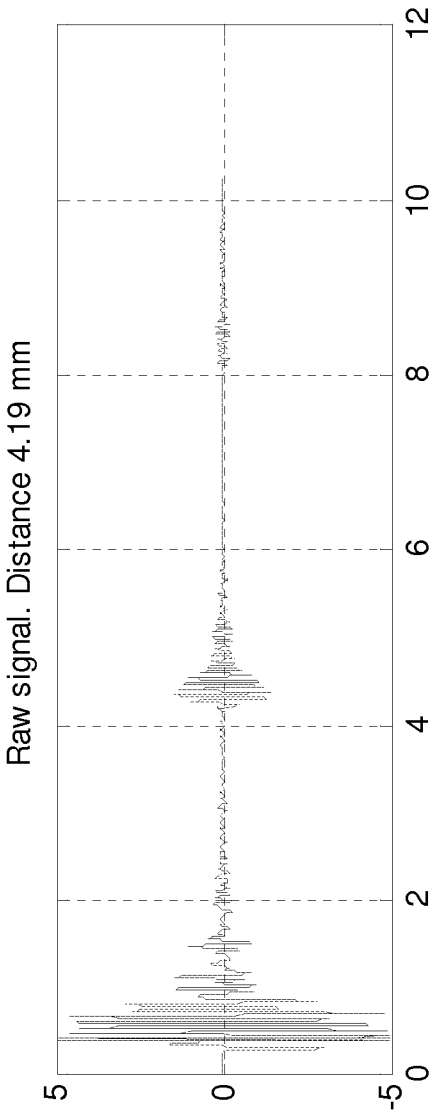


FIG. 33A

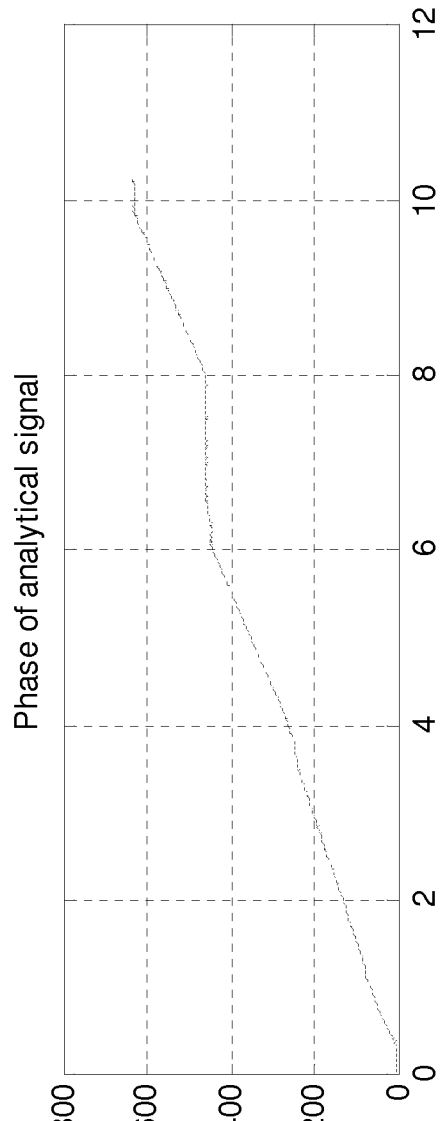


FIG. 33B

Estimated distance 3.83 mm vs. actual 4.19 mm

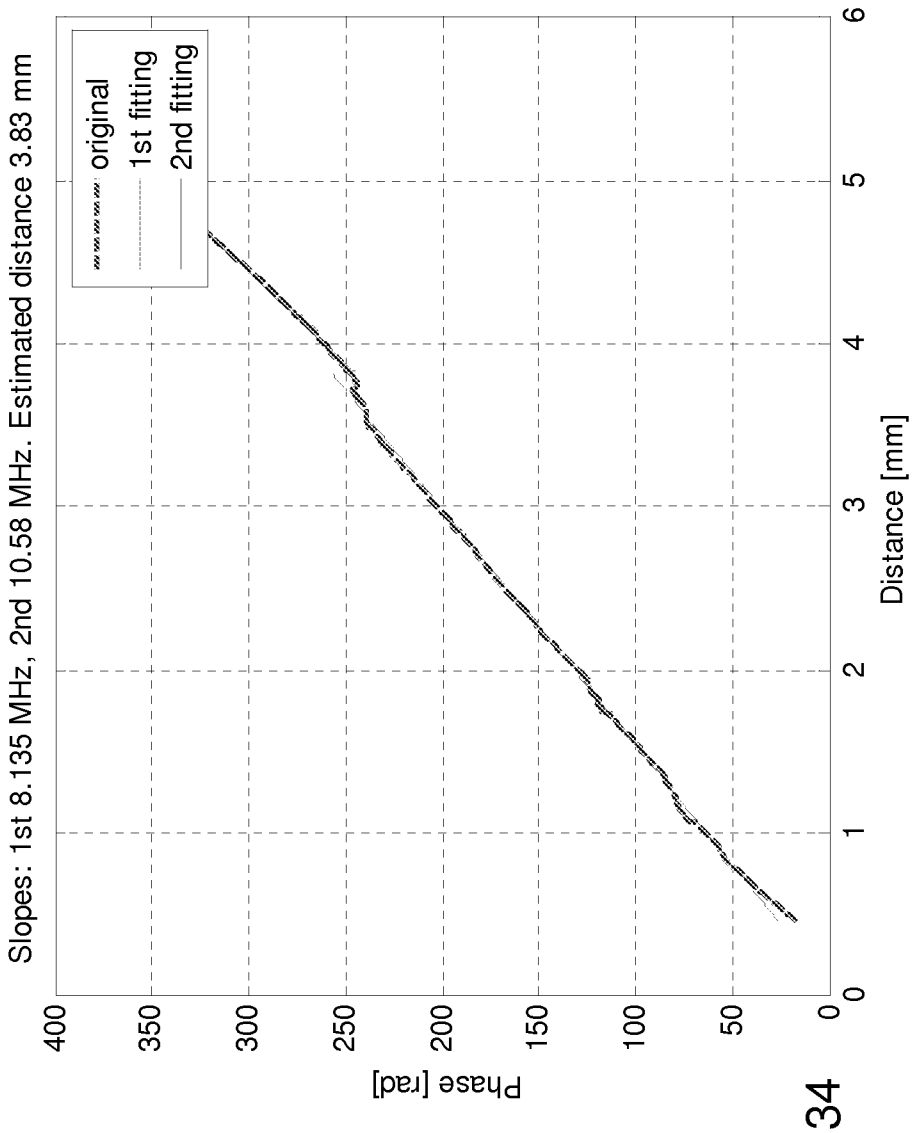


FIG. 34

Total fitting error

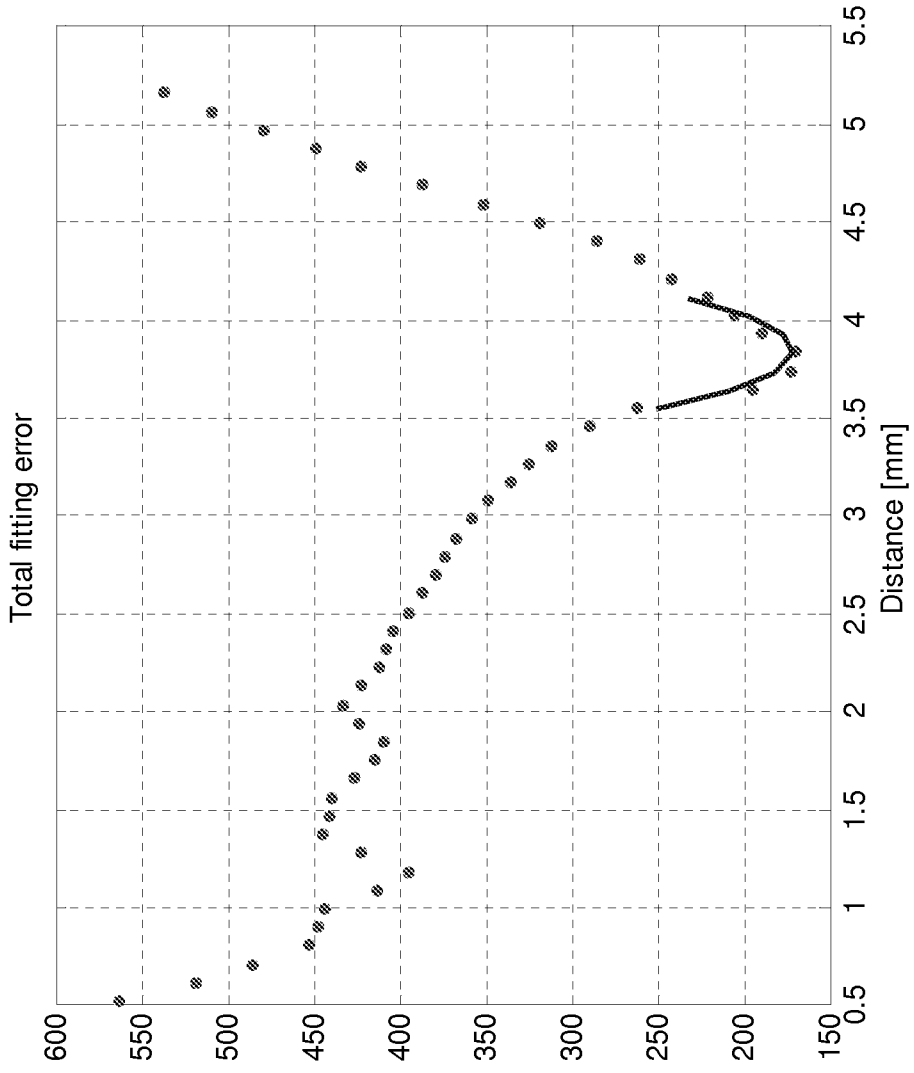


FIG. 35

Local slopes

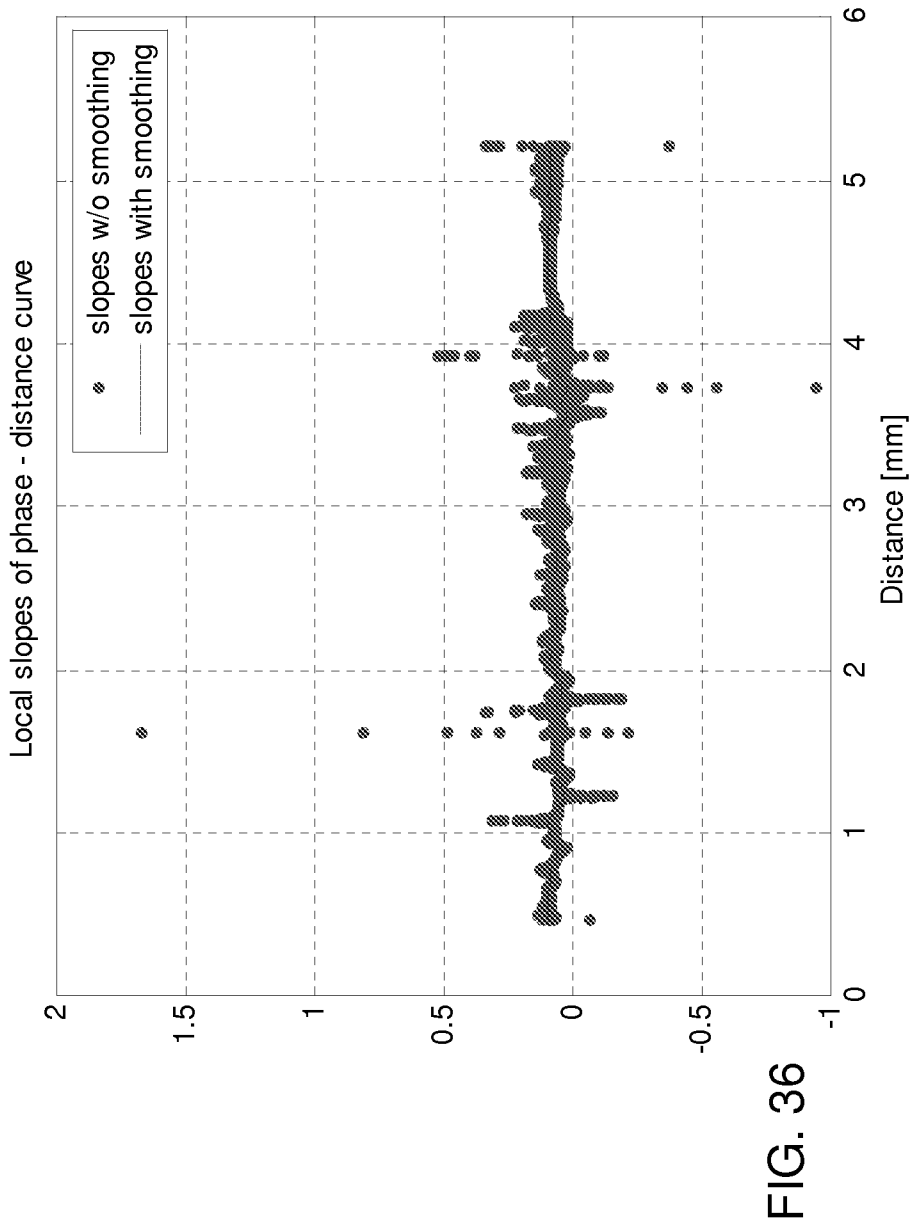


FIG. 36

4.69 mm

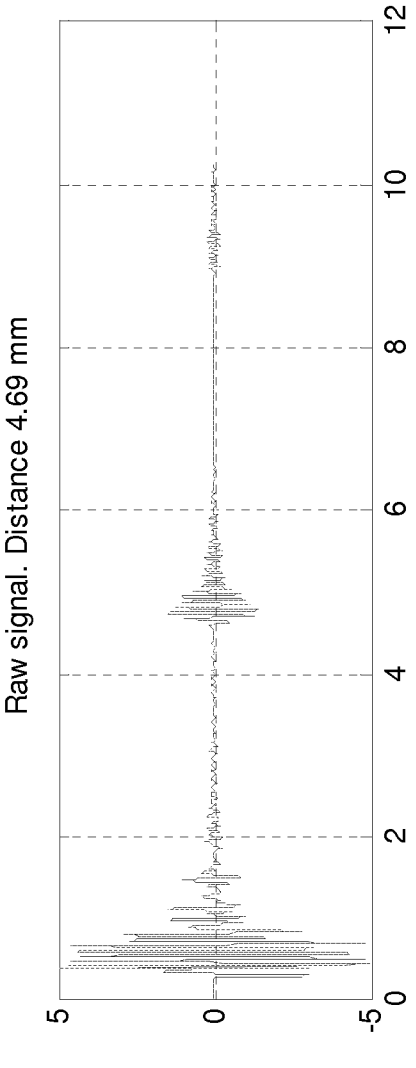


FIG. 37A

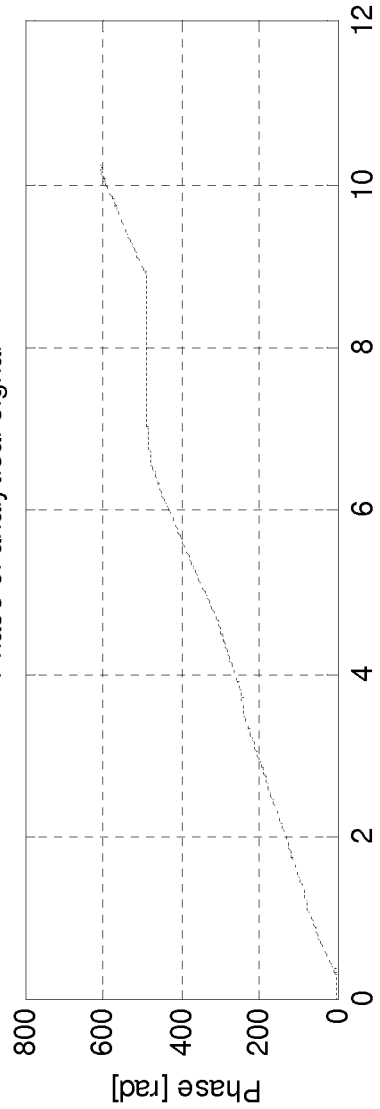


FIG. 37B

. Estimated distance 4.36 mm vs. Actual 4.69 mm
w/o outliers: 4.61 mm

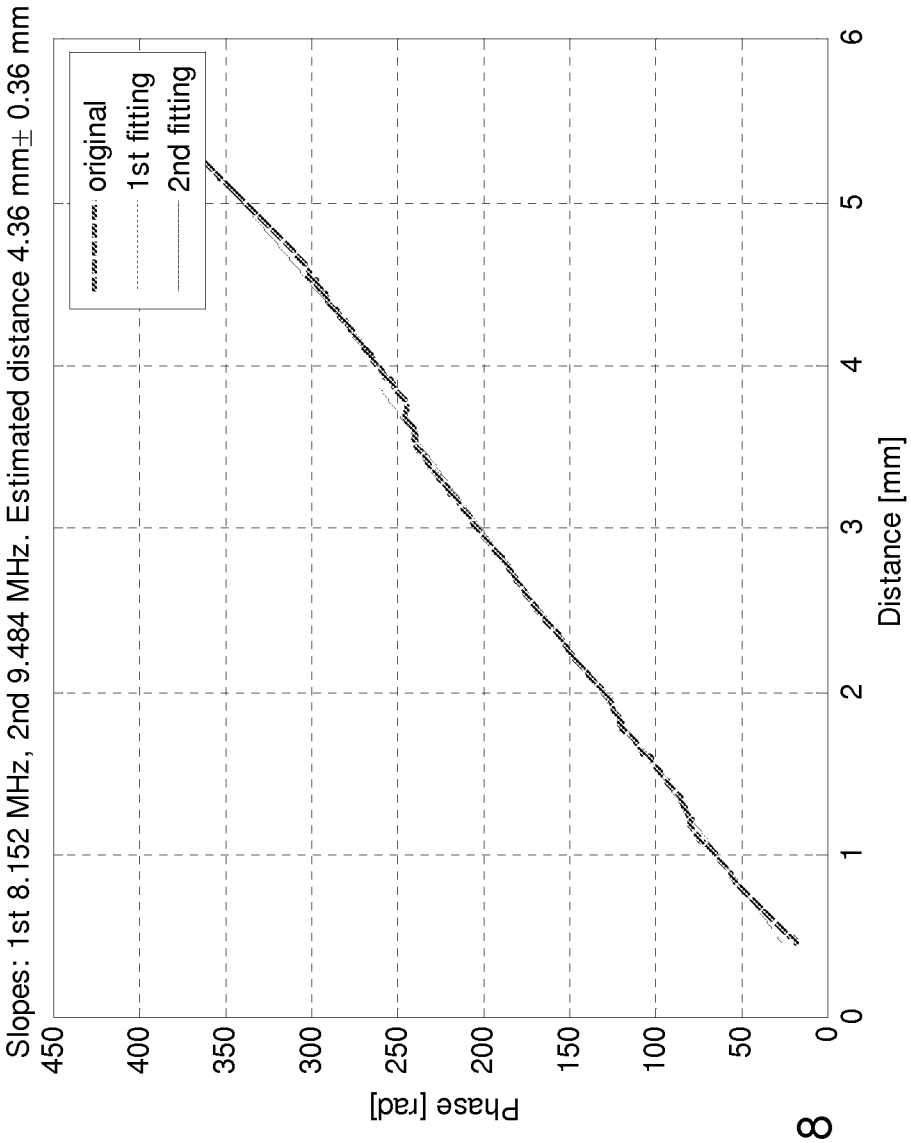


FIG. 38

Total fitting error

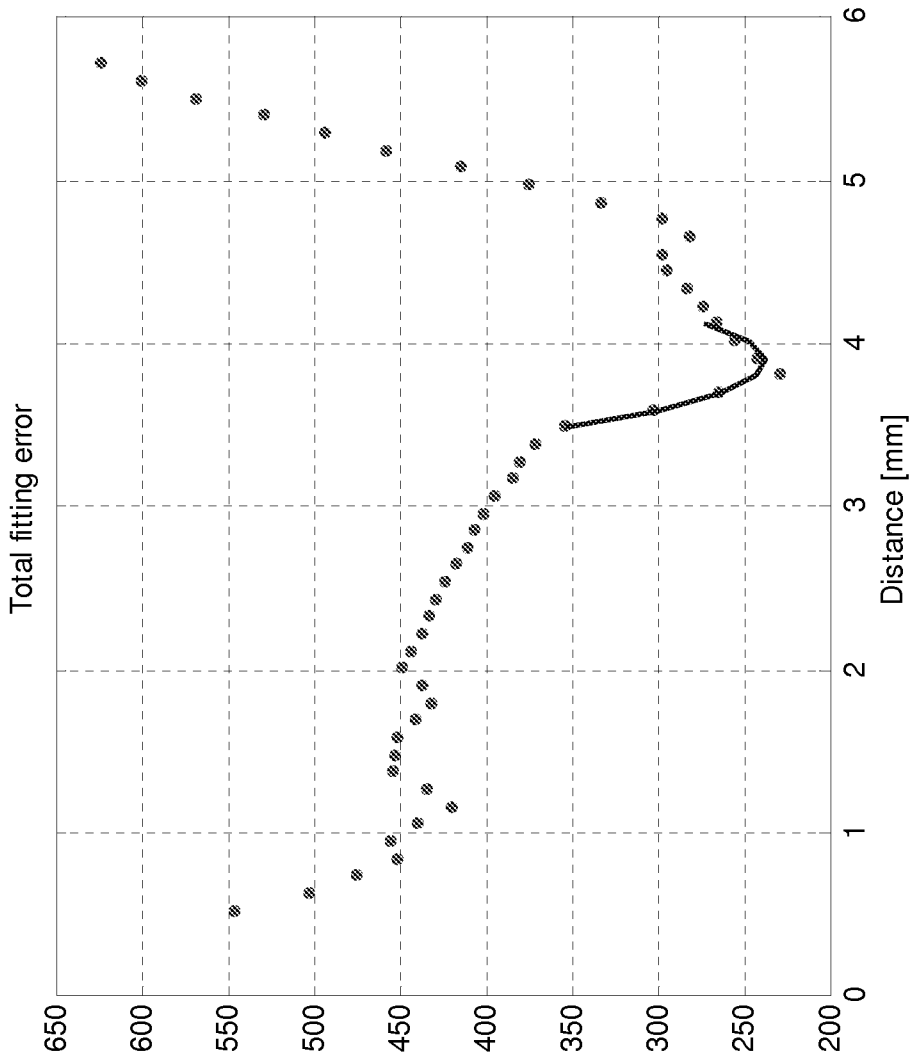


FIG. 39

Local slopes

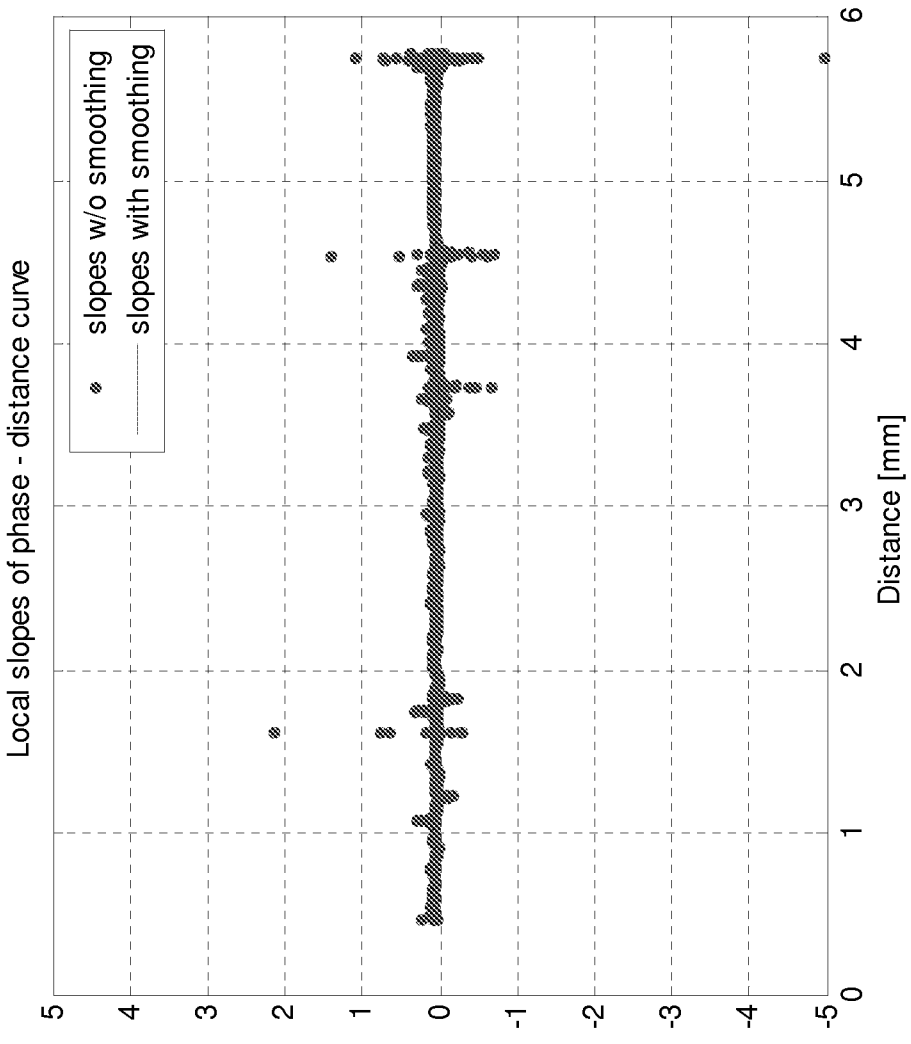


FIG. 40

5.19 mm

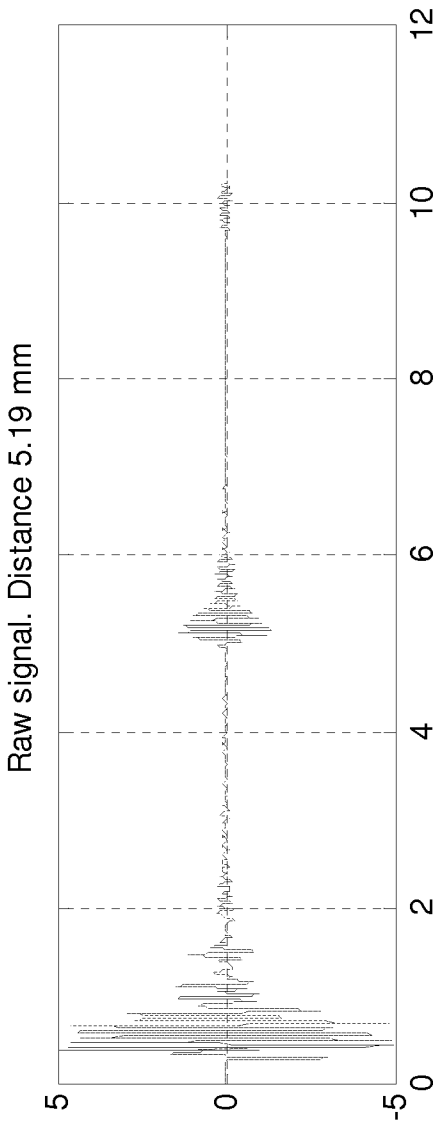


FIG. 41A

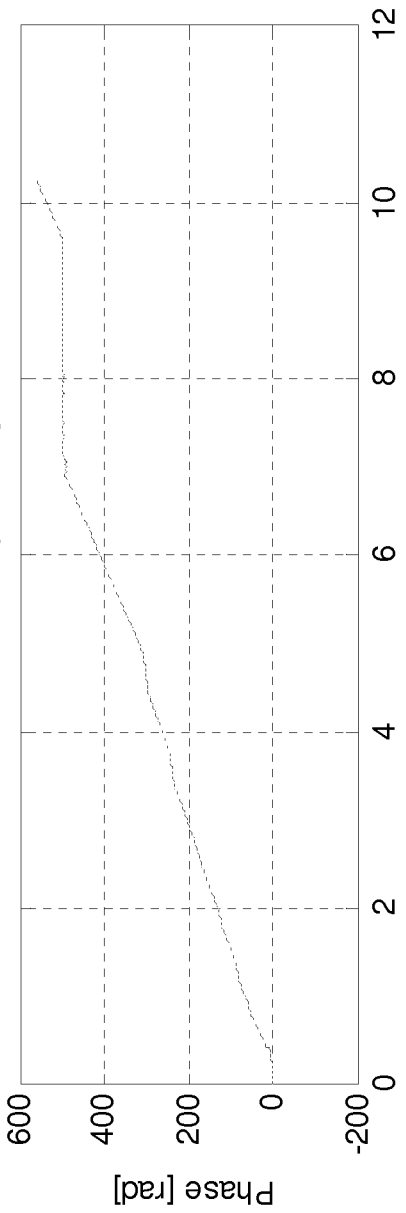


FIG. 41B

Estimated distance 4.83 mm vs. Actual 5.19 mm

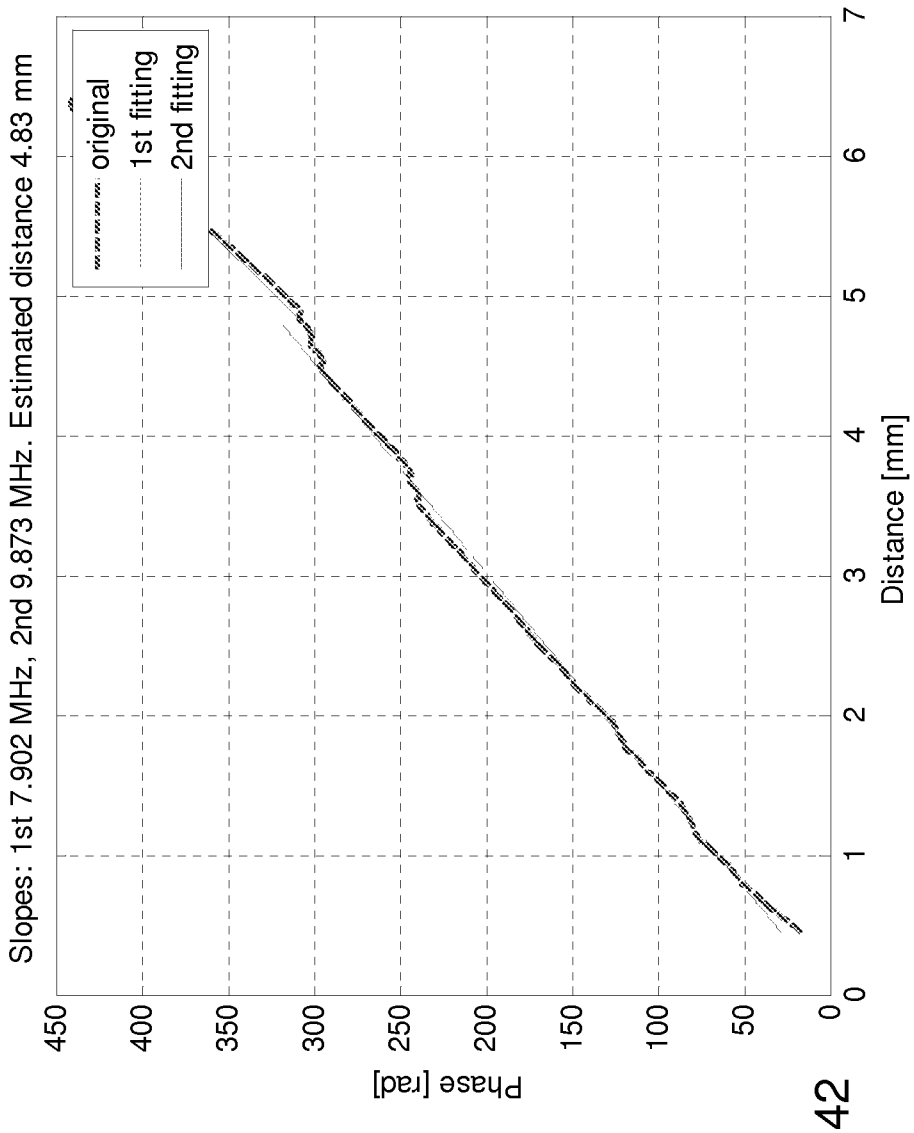


FIG. 42

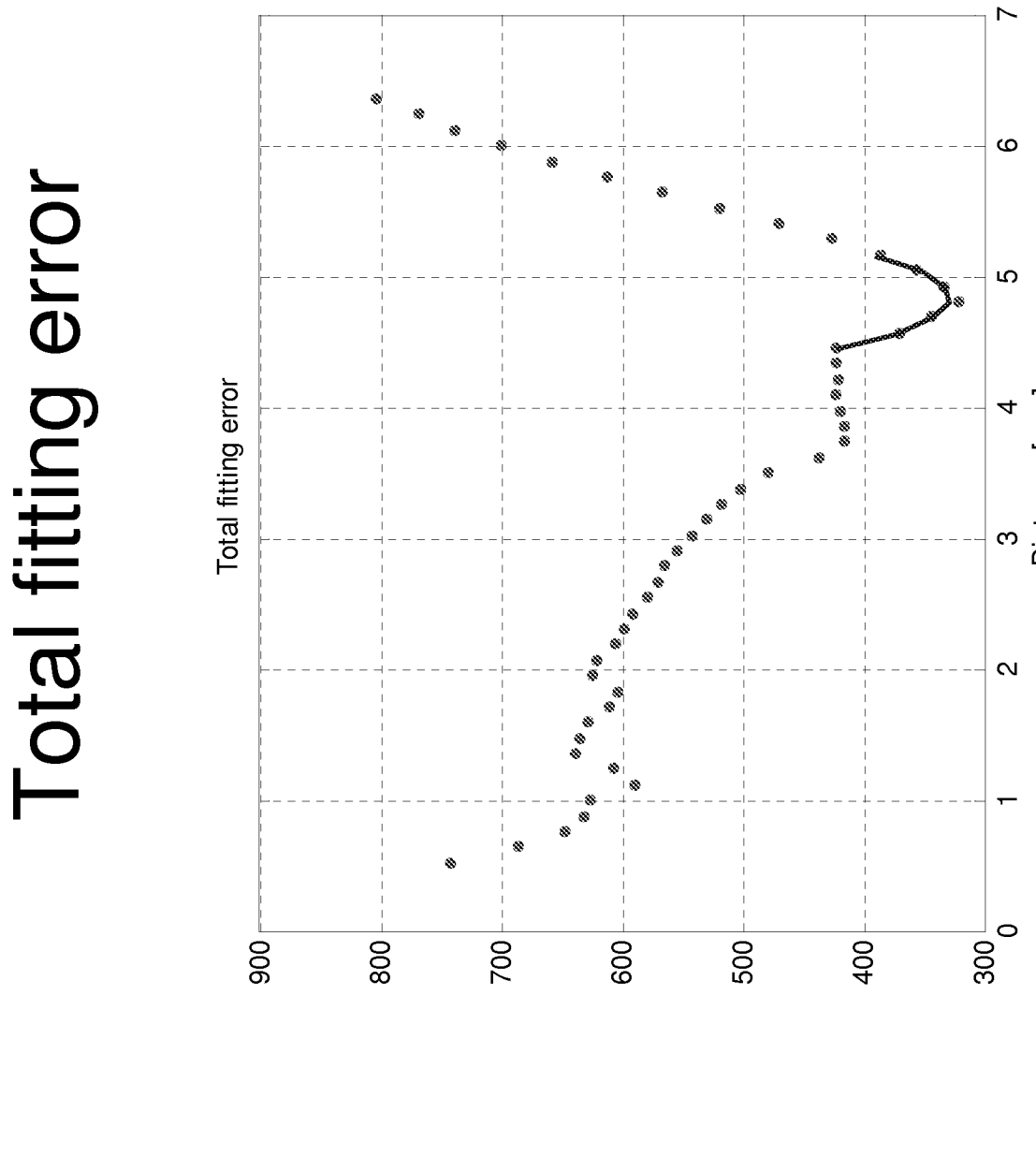

Total fitting error
Total fitting error
900
800
700
600
500
400
300
0
1
2
3
4
5
6
7
Distance [mm]

FIG. 43

Local slopes

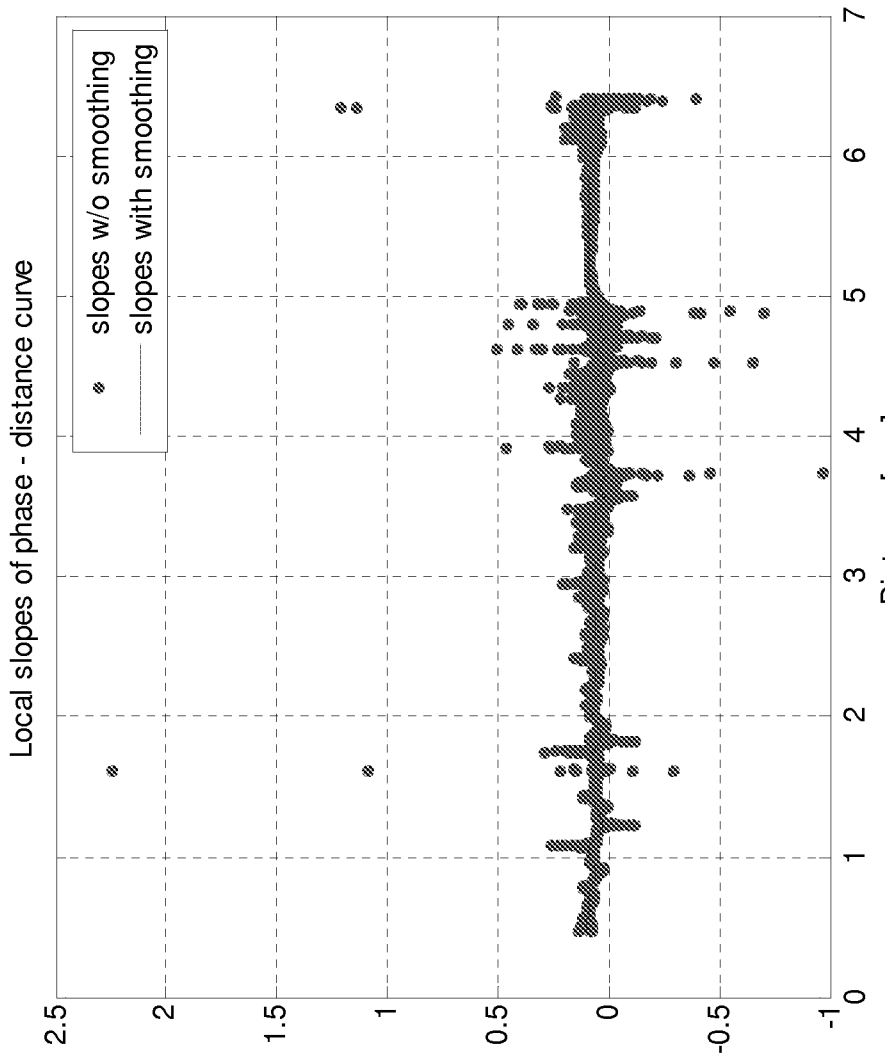


FIG. 44

Summary

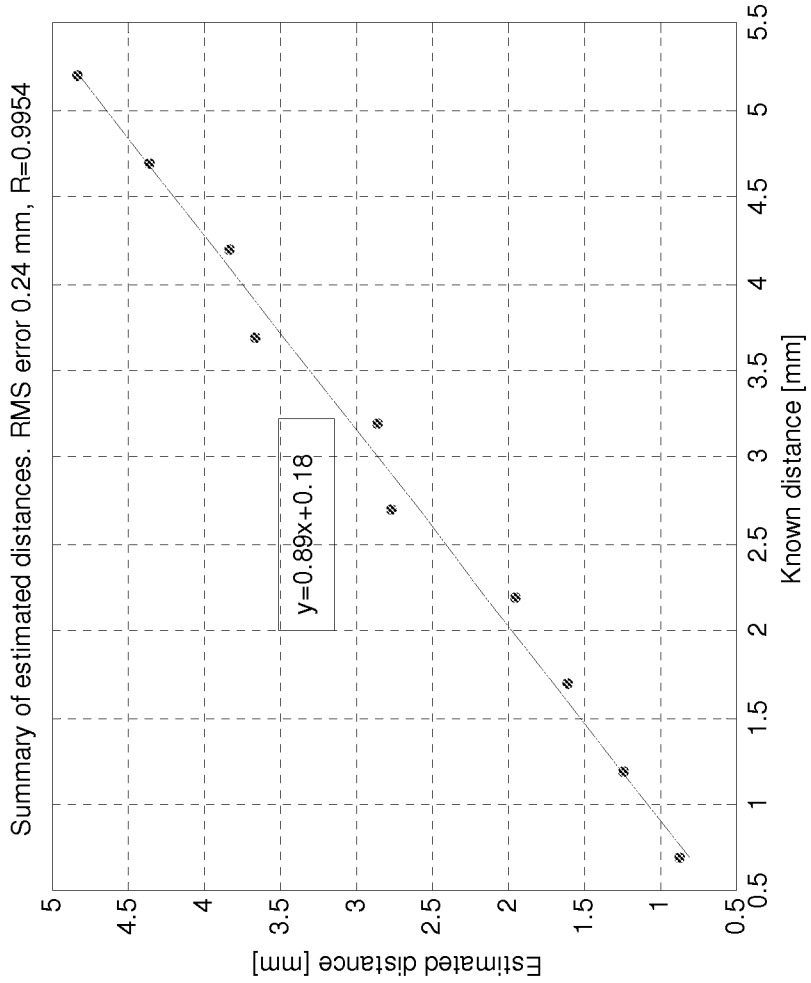
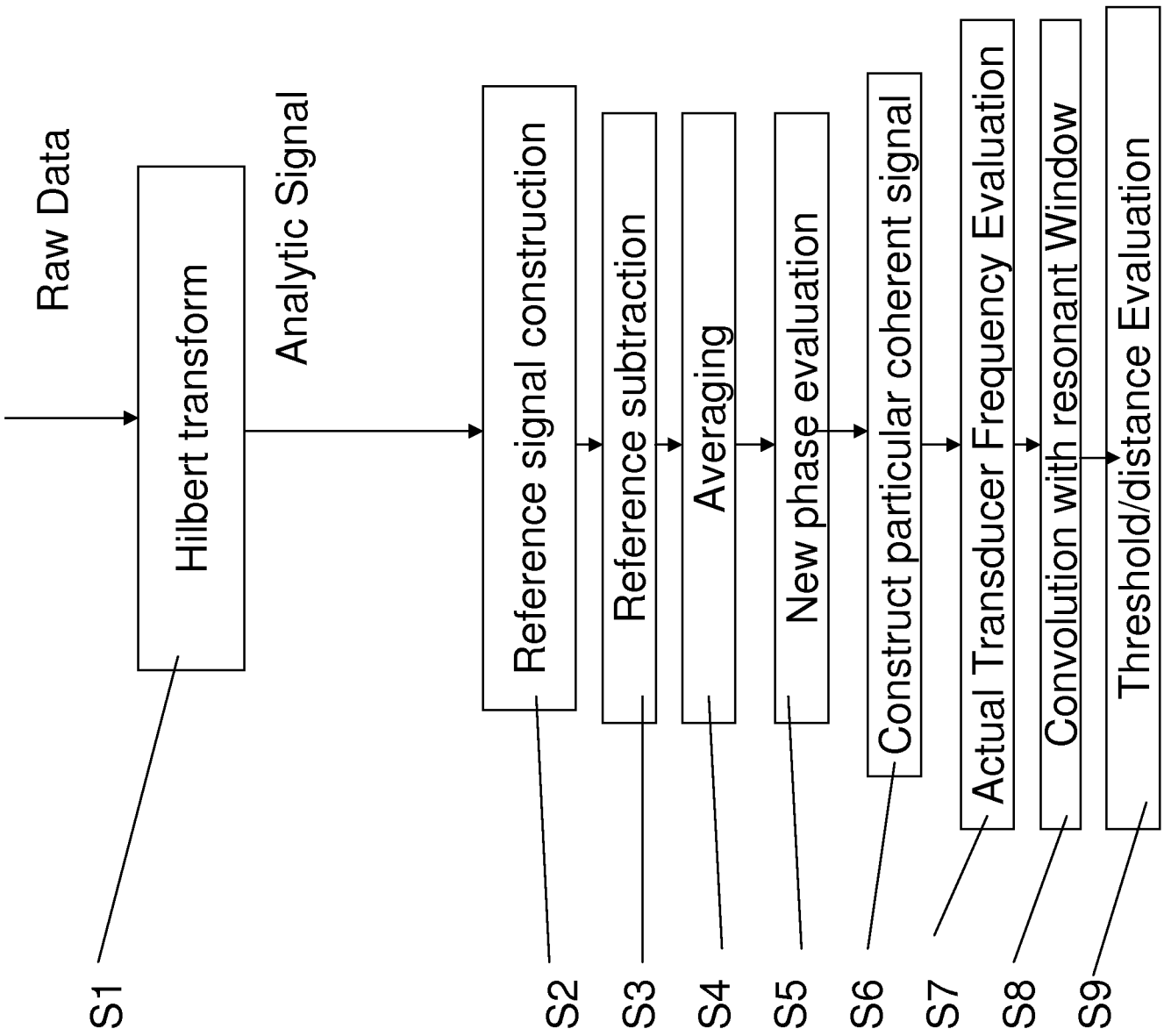


FIG. 45

FIG. 46


Raw Data
Hilbert transform
Analytic Signal
Reference signal construction
Reference subtraction
Averaging
New phase evaluation
Construct particular coherent signal
Actual Transducer Frequency Evaluation
Convolution with resonant Window
Threshold/distance Evaluation
S1
S2
S3
S4
S5
S6
S7
S8
S9

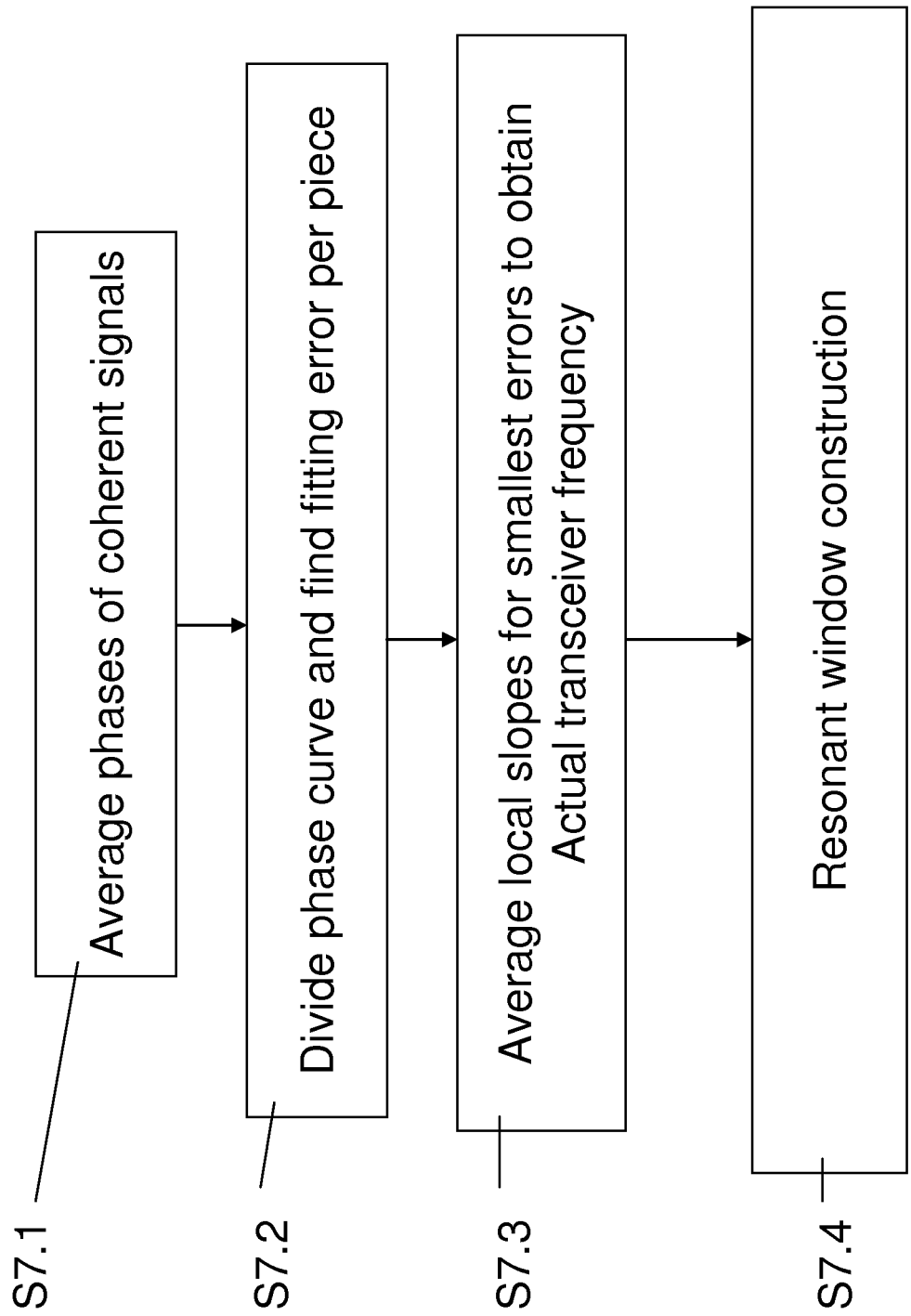

Average phases of coherent signals
Divide phase curve and find fitting error per piece
Average local slopes for smallest errors to obtain Actual transceiver frequency
Resonant window construction
S7.1
S7.2
S7.3
S7.4

FIG. 47

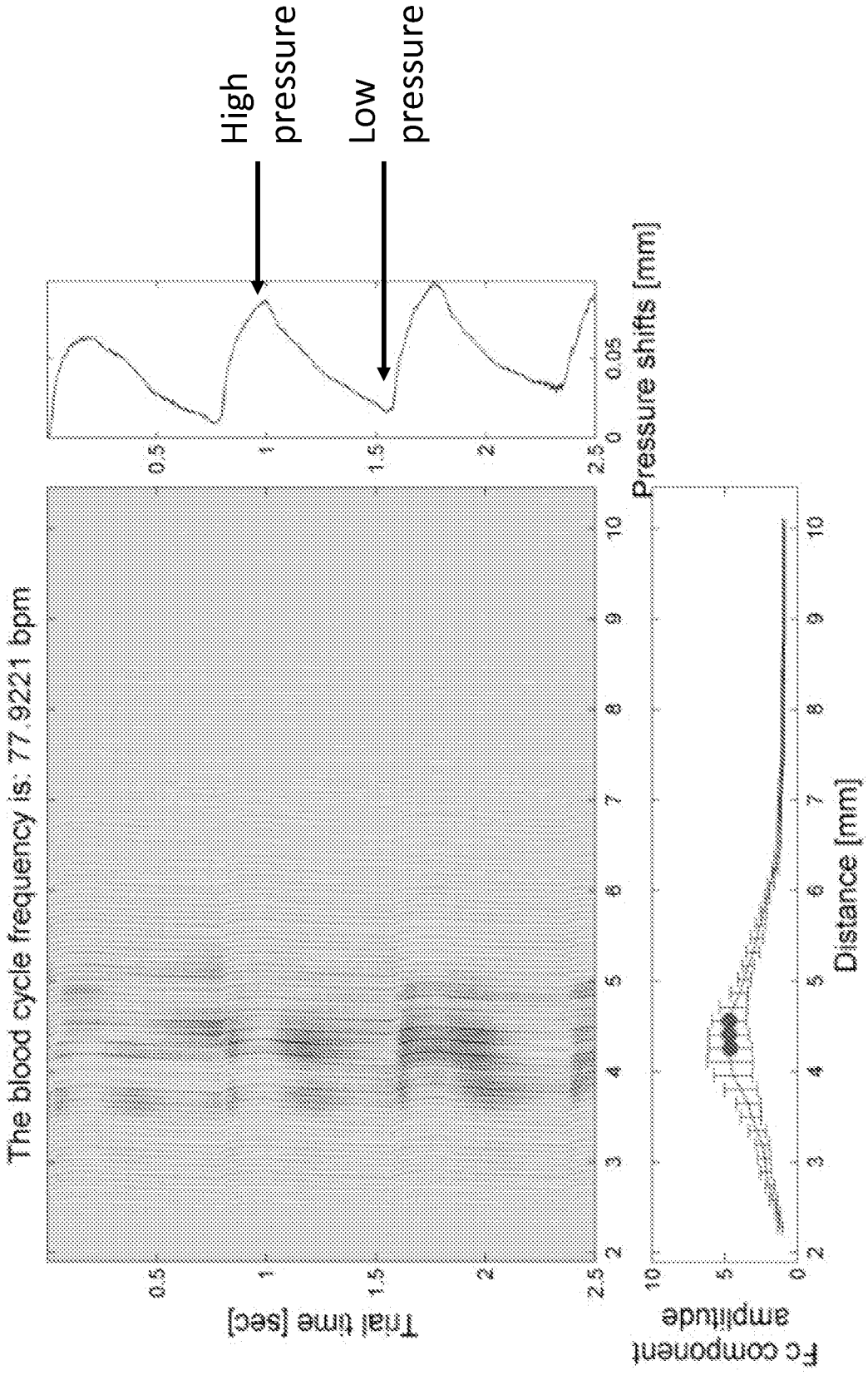

High pressure
Low pressure
Pressure shifts [mm]
The blood cycle frequency is: 77.9221 bpm
Tmal time [sec]
Distance [mm]
Fc component amplitude

FIG. 48

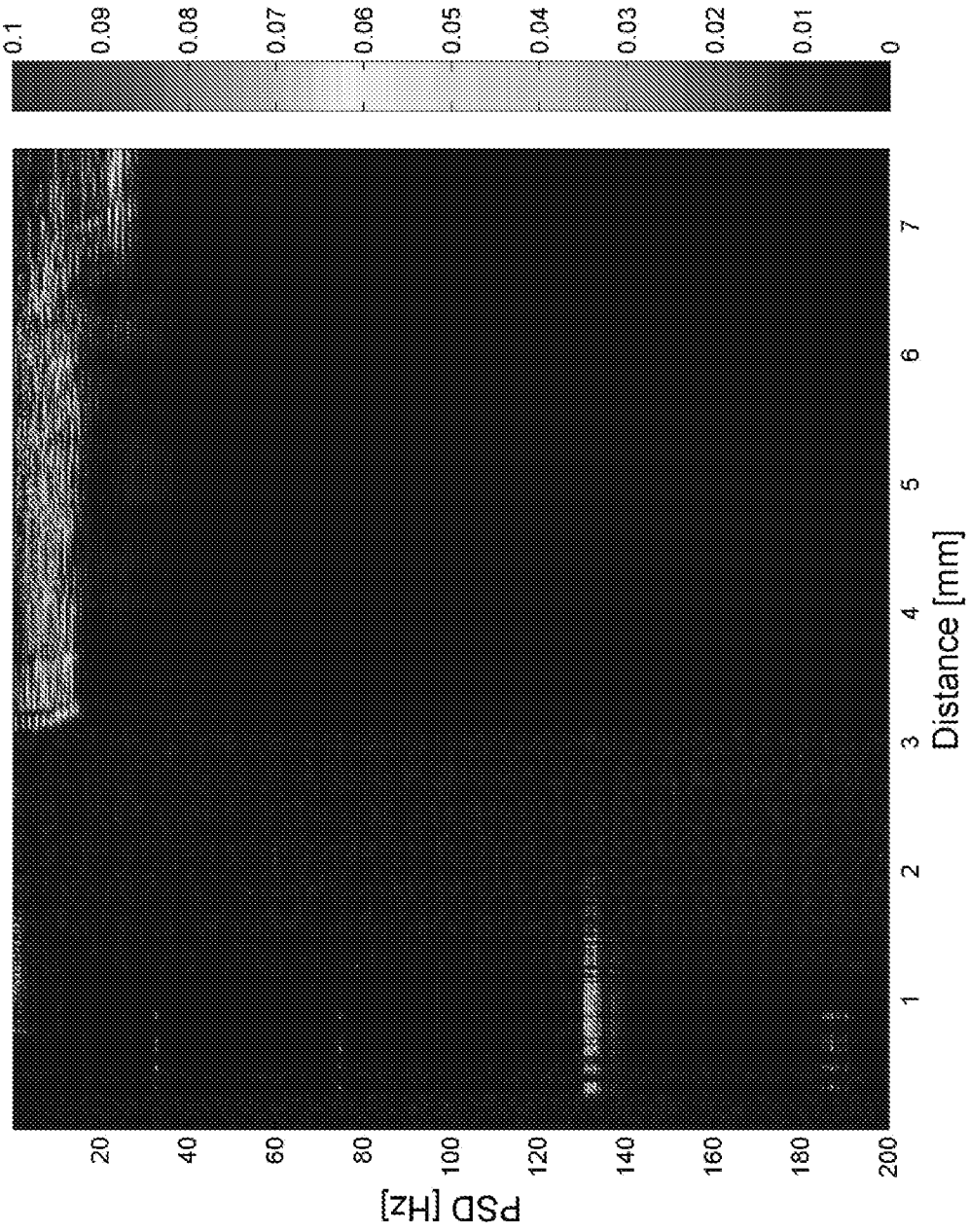

0.1
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
20
40
60
80
100
120
140
160
180
200
PSD [Hz]
1
2
3
4
5
6
7
Distance [mm]

FIG. 49

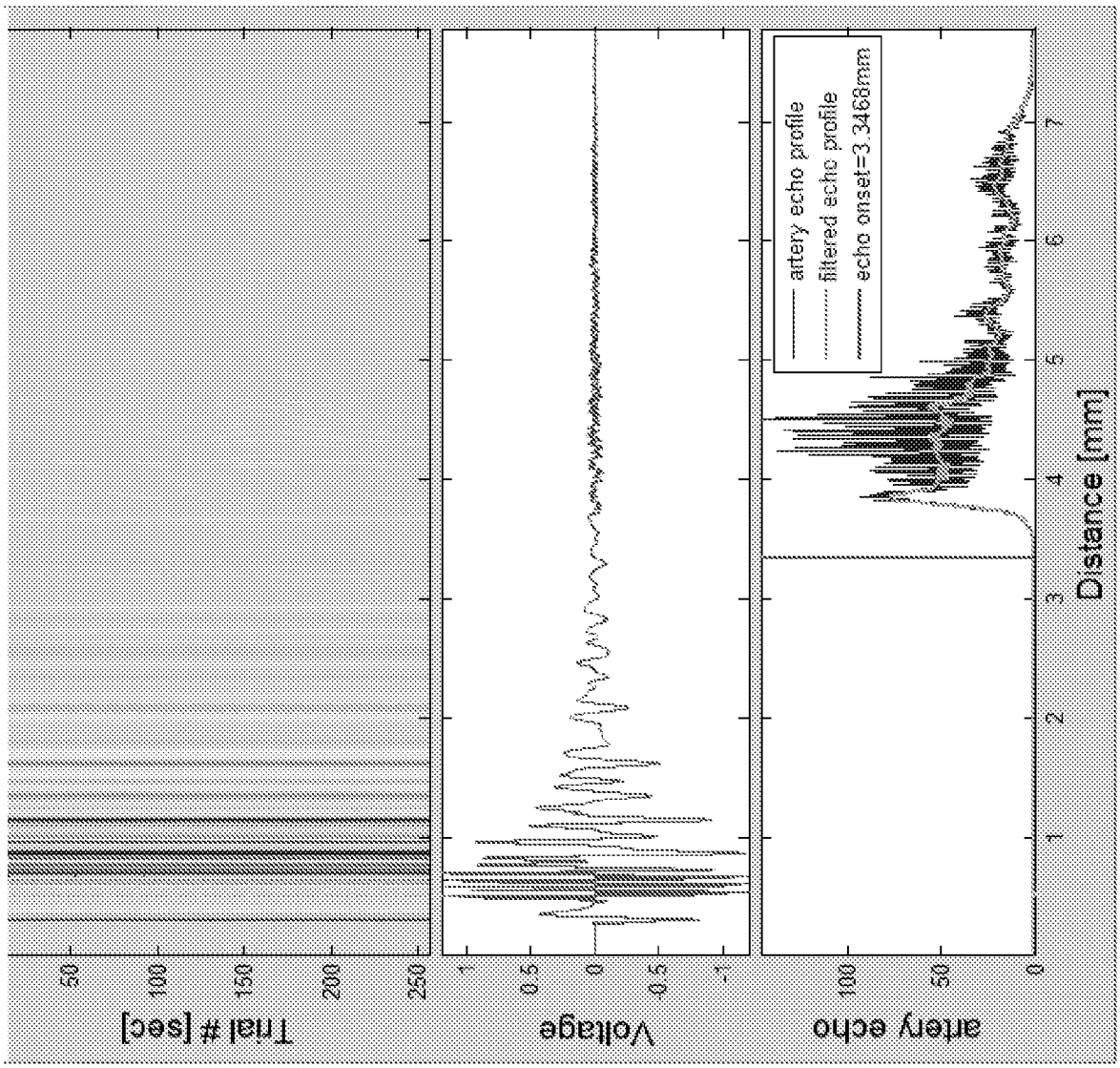

Trial # [sec]
50
100
150
200
250
Voltage
1
0.5
0
-0.5
-1
artery echo
100
50
0
1
2
3
4
5
6
7
Distance [mm]
artery echo profile
filtered echo profile
echo onset=3.3468mm

FIG. 50

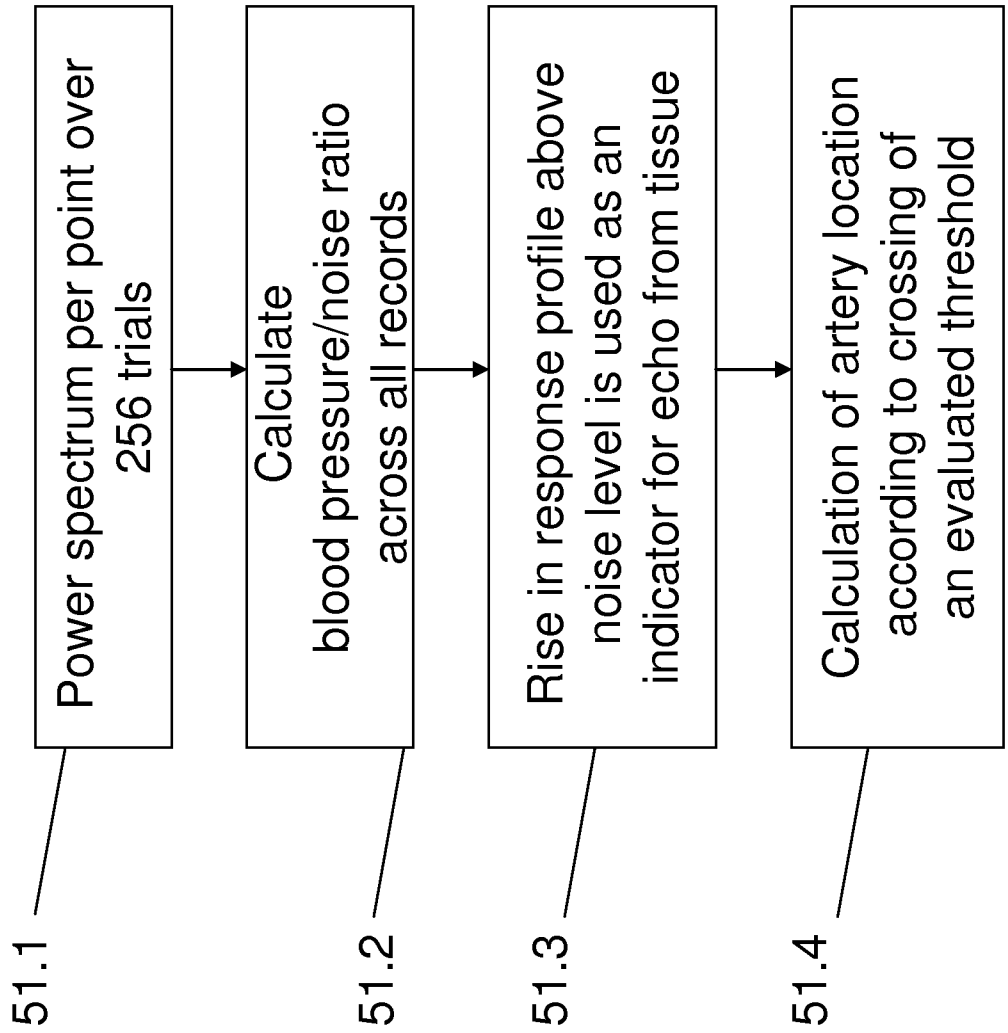

Power spectrum per point over 256 trials
Calculate blood pressure/noise ratio across all records
Rise in response profile above noise level is used as an indicator for echo from tissue
Calculation of artery location according to crossing of an evaluated threshold
51.1
51.2
51.3
51.4

FIG. 51

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2011/054639

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N7/00 A61M25/00 G01N29/44 G01N29/46 G01S7/52 G01S7/536
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N A61M G01N G01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BAILEY M R ET AL: "Cavitation detection during shock-wave lithotripsy", ULTRASOUND IN MEDICINE AND BIOLOGY, NEW YORK, NY, US, vol. 31, no. 9, 1 September 2005 (2005-09-01), pages 1245-1256, XP027605630, ISSN: 0301-5629 [retrieved on 2005-09-01] abstract; figure 1 page 1246 page 1247, right-hand column page 1249, right-hand column	1-11, 22-26
A	US 5 657 760 A (YING HAO [US] ET AL) 19 August 1997 (1997-08-19) column 22, line 39 - line 59	8,22-24

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 January 2012	31/01/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Kajzar, Anna

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2011/054639

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CATTAFESTA L N ET AL: "Acoustic proximity ranging in the presence of secondary echoes", IEEE TRANSACTIONS ON INSTRUMENTATION AND MEASUREMENT, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 52, no. 5, 1 October 2003 (2003-10-01), pages 1593-1605, XP011102759, ISSN: 0018-9456, DOI: 10.1109/TIM.2003.817907 page 1593 -----	5,6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2011/054639

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 12-21, 27-30
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy/surgery

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2011/054639

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5657760 A	19-08-1997	NONE	