(54) Title: APPARATUS AND METHOD FOR CHARACTERIZATION OF ACUTE OTITIS MEDIA

(57) Abstract: An ultrasound signal processor uses an excitation generator to cause displacement of a tympanic membrane while a series of ultrasound pulses are applied to the tympanic membrane. Phase differences between a transmitted signal and received signal are examined to determine the movement of the tympanic membrane in response to the applied excitation. An examination of the phase response of the tympanic membrane provides a determination as to whether the fluid type behind the tympanic membrane is one of: no fluid, serum fluid, or purulent fluid.

Figure 1
Baseband Signal Processor

110 System Clock
112 Transmit Waveform Generator
114 Transducer Interface
116 Receive Preamplifier
118 Transmit/Receive Switch
120 TM Excitation Generator
122 ADC
128 Mixer
132 ADC
134 ADC
136 Low Pass Filter
142 Mixer
144 ADC
146 Phase Analyzer
148 Controller
150 Data Buffer

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Apparatus and Method for Characterization of Acute Otitis Media

Field of the Invention

The present invention relates to a device for the detection of middle ear effusion with discrimination of fluid type. In particular, the invention relates to the characterization of middle ear effusion behind the tympanic membrane by stimulating the tympanic membrane using a low frequency excitation such as acoustic and measuring the displacement behavior with a comparatively higher frequency excitation such as ultrasound.

Background of the Invention

Acute otitis media (AOM) is an inflammatory process in the middle ear and is the most common clinical condition seen by pediatricians in children fifteen years and
younger. AOM is generally associated with the presence of a middle ear effusion and is considered a middle ear inflammation. Complications of undiagnosed AOM can include hearing loss. Left untreated in children, recurrent AOM can also lead to delays in the development of speech and language skills.

There are two key factors in the diagnosis of AOM: detection of the presence of effusion, and characterization of the type of effusion as either serous, mucoid, purulent or combinations of these. Decision by the health care provider regarding appropriate treatment relies on confirmation of both the presence of effusion and its type. Health care practitioners use a variety of tests to evaluate a patient suspected of having AOM. The only definitive tests for AOM are myringotomy and tympanocentesis, procedures which involve direct aspiration of fluid from the middle ear by puncturing the tympanic membrane and drawing fluid, followed by visual and biochemical analysis of the fluid. These are invasive procedures performed in a surgical setting under anesthesia. Because they are invasive and have significant associated risks of complications, myringotomy and
tympanocentisis are not used as standard diagnostic methods for AOM except in research settings.

Several other non-invasive diagnostic tests are available for evaluating AOM, including acoustic reflectometry, tympanometry, pneumatic otoscopy, and otoscopy, however, none of these tests achieves the diagnostic accuracy of invasive myringotomy and tympanocentisis; the overall likelihood of obtaining an accurate diagnosis using any of the non-invasive methods is no better than 50%. More importantly, the various non-invasive methods are useful only in identifying the presence of middle ear effusion; they provide no information regarding the type of effusion. Because of the risks associated with undiagnosed AOM, and the recognized unreliability of the non-invasive diagnostic tests, patients who are diagnosed with middle ear effusions based on any of these non-invasive tests are often prescribed antibiotics. In many instances, these patients do not have AOM. In addition to the increased cost burden of unnecessary antibiotic treatment, the patients are exposed to the side effects of antibiotics and the attendant and significant risk of developing antibiotic resistance.
Acute otitis media is one of the most common causes of childhood health issues, which include for example, bacterial infections, antibiotic overuse, hearing loss, and surgeries. AOM is responsible for more than 12 million office visits nationwide per year, accounting for over 50 percent of all pediatric antibiotic prescriptions and as much as $5 billion in annual costs. The number of operative procedures performed due to unresolved AOM in the United States is estimated at about 600,000 per year.

The majority of children have at least one episode of AOM by the time they are two years of age. AOM is characterized by ear pain, fever, occasional rupture of the ear drum, and findings of middle ear inflammation, including fluid in the middle ear. About 10 percent of children have recurrent AOM, and these children account for around 40 percent of all AOM episodes. The prevalence of AOM in the United States is increasing. Thus, current diagnostic and treatment methods are not lowering the rate of AOM in the United States.

OM is fundamentally defined by the presence of an effusion in the middle ear. In AOM, the middle ear effusion ("MEE") is induced by infective agents and is often thin or serous with viral infection and thicker and purulent with
bacterial infection. Acute MEE may persist, even with appropriate antimicrobial treatment. After 30 days, the MEE is termed as chronic, and the condition is referred to most commonly as otitis media with chronic effusion or "OME."

Chronic MEE may be thin and watery, purulent, or, most commonly, thick and mucoid. Mucoid effusion is the hallmark of OME and is often called "glue ear" because of its high viscosity. Because each type of MEE has a different prognosis and treatment, the ability to delineate the type of the effusion is of great clinical value.

In spite of decades of research, optimal management of OM remains controversial. In a recent prospective study, antibiotic treatment of OM accounted for more than 90 percent of all antibiotic use during the first two years of life. It has been estimated that distinguishing AOM from OME and deferring antibiotics for OME would avoid 6 to 8 million courses of unnecessary antibiotic therapy annually.

While antibiotics reduce pain symptoms in AOM, their widespread use in AOM has led to an alarming increase in the prevalence of resistant organisms worldwide without any substantial decrease in complications or sequelae of AOM.

Given the high spontaneous resolution rate of AOM, there are serious questions about the need for antibiotics in
most cases. Thus, physicians and parents are frequently uncertain about proper treatment because there are no clear-cut clinical findings that might reliably predict which cases will resolve spontaneously and which cases would be better treated with an oral antibiotic. The recent American Academy of Pediatrics 2014 guideline recommended withholding antibiotic when uncertainty exists but did not discuss ways and means to implement the guideline.

Many children with fever and a red tympanic membrane ("TM") have no MEE and thus do not have AOM. These children do not benefit from antimicrobial therapy, even though many receive it as a precaution.

Similar considerations apply to cases of persistent MEE (OME). Detecting MEE is difficult without expensive equipment, such as a tympanometer or an audiometer. While screening tympanometers are available, they are not widely used in primary care offices where the majority of cases of AOM/OME are first seen. Acoustic reflectometry was introduced 15 years ago as a method for primary physicians and parents to indicate MEE presence. Although the sensitivity and specificity of acoustic reflectometry is similar to that of tympanometry, neither device will predict which cases may resolve spontaneously and which
cases will require treatment. Moreover, neither device is widely used in primary care offices. Chronic MEE is therefore under-diagnosed in primary care practice.

OME may cause hearing loss without other symptoms. The adverse effects of OME on hearing and on the development of cognitive, linguistic, additive, and communicative skills are of concern to parents and physicians alike. National guidelines recommend waiting 3 to 6 months before surgical removal of the MEE and insertion of a ventilation tube.

Some effusions cause substantial hearing loss. Typically, middle ears that are impacted with the characteristic viscous effusion (glue ear) are associated with substantial hearing loss that may persist for years. Primary care physicians, unlike ENT specialists, lack a robust clinical method that can distinguish between a mucoid effusion (glue ear) and one that contains a serous (watery) effusion, which is more likely to resolve spontaneously.

One of the major sources of controversy about OM in clinical practice is accuracy of diagnosis. Otoscopy, the key examination technique, is a visual inspection of the TM by which one may deduce the normal or abnormal middle ear.

The equipment and skills for otoscopy are variable. Although with practice, many physicians become proficient
otoscopists, a monocular examination of the TM of a
struggling infant through a tiny speculum remains a
difficult and challenging maneuver. Often only a glimpse of
the TM is possible. Use of the binocular operating
microscope, which permits a 3D view of the TM, is the most
precise method of otoscopy and is widely used by ear, nose,
and throat specialists. However, this expensive equipment
is rarely found in primary care practices where the
majority of AOM diagnoses are made. Accordingly, only 40
percent of primary care pediatricians are confident about
their otoscopic findings.

The essential elements of otoscopy are a description
of: (1) the static characteristics of the TM (color,
position, translucency), (2) the contents of the middle ear
(air, ear effusion, other), and (3) the mobility of the TM
in response to externally applied air pressure (pneumatic
otoscopy). Determining the presence of effusion (liquid) in
the middle ear is the critical variable in making a
diagnosis of OME. Given that the effusion may vary in
amount and consistency from case to case and may be
obscured by the condition of the TM, it is fair to say that
even when done under ideal conditions (binocular
microscope, pneumatic speculum, and an anesthetized child),
the otoscopic conclusion regarding the presence or absence of ear effusion may vary from observer to observer. Less than half of pediatricians use pneumatic otoscopy. Similar findings have been found in surveys of practicing physicians and residents.

Tympanometry is an objective measure of the condition of the middle ear. It is widely used in specialty clinics for screening and for diagnostic confirmation. The tympanometer displays the change in the acoustic immittance of a 226 Hz transducer tone as the pressure in the ear canal is varied in a range within -300 dekapascals (daPa) to +200 daPa. The classic peaked curve indicates an air-containing middle ear while a classic flat curve is associated with middle ear effusion (assuming an intact TM). Tympanometry is not widely used in primary care offices because of equipment expense and training requirements. The test does require a snug fit between the probe and the ear canal; fitting tightly is not objectionable for older or normal children. However, the pressurization may cause mild discomfort in the presence of an acute infection.

Audiometry often reveals a substantial conductive hearing loss in OME. However, audiometry is expensive and
not widely used in primary care practice. Infants and children are not difficult to test by experienced audiologists. Audiometry is important in surgical planning but is too nonspecific for evaluation of effusion type.

Acoustic reflectometry (measuring response of the TM to a 1.8 to 4.4 kHz frequency sweep spectrum) was introduced to meet the need for an objective, simple, and safe clinical method for evaluating the condition of the middle ear. While acoustic reflectometry is indeed simple, safe, and inexpensive, it is too unreliable for making treatment decisions and is used infrequently by physicians.

Accordingly, a more reliable, non-invasive method of diagnosing Otitis Media with Effusion (OME) is needed.

Objects of the Invention

A first object of the invention is an apparatus and method for detection of acute otitis media (AOM), specifically inflammatory effusion of the middle ear.
A second object of the invention is an apparatus and method for discernment of effusion fluid type in otitis media with effusion (OME) of the middle ear.

A third object of the invention is an apparatus for measurement of fluid viscosity having:

- a speculum having an extent, the speculum having a smaller outer and inner diameter on a first end of the extent and a comparatively larger inner and outer diameter on an opposite end of the extent;

- the speculum having an ultrasound transducer positioned to generate an ultrasound wave directed out of said first end and into an ear canal and also receive reflected ultrasound energy;

- the speculum coupled to an excitation source for displacement of a tympanic membrane with a static or dynamic pneumatic excitation;

- the apparatus actuating the tympanic membrane excitation source and measuring tympanic membrane displacement from a phase shift in ultrasound energy reflected from a tympanic membrane;

thereafter forming an estimate of the viscosity of a fluid which may be present on the far side of the tympanic membrane based on the displacement characteristics of a
tympanic membrane interacting with the pneumatic
excitation.

A fourth object of the invention is an ultrasound
signal processor for measurement of the viscosity of a
fluid behind a tympanic membrane, the measurement including
an excitation resulting in the displacement of the tympanic
membrane using the excitation source, the excitation source
being sub-audible, audible, or super-audible, the
excitation source being either pressure-neutral, pressure-
offset, or periodic, the estimate of fluid viscosity
performed by measuring the phase shift of reflected
continuous wave (CW) or pulsed ultrasound compared to a
transmitted waveform phase.

Summary of the Invention

A speculum tip includes an ultrasound transducer for
sending and receiving ultrasound energy through an ear
canal and a comparatively low frequency tympanic membrane
excitation source. The tympanic membrane excitation source
generates a subtle movement of the tympanic membrane during
an interval coincident with an ultrasound transmitter
delivering acoustic wave ultrasound energy to the tympanic
membrane either in CW form or in pulsed form. A receiver for ultrasound reflected from the tympanic membrane measures displacement of the tympanic membrane as a phase change in the received signal when compared to the transmit frequency, thereby indicating a temporal displacement of the tympanic membrane. An analysis of the temporal displacement of the tympanic membrane, as measured by the phase shifts of the reflected ultrasound in response to the pneumatic excitation coupled to the tympanic membrane, in combination with comparison to the temporal displacement or from templates or metrics associated with the delay in and amplitude of response between the excitation stimulus to and ultrasound response from the tympanic membrane, is used to determine the viscosity of the fluid behind the tympanic membrane. Measurement of the viscosity of the fluid behind the tympanic membrane is thereafter used to characterize the type of effusion fluid present in the middle ear as one of: no fluid, serous fluid, or purulent fluid.

Brief Description of the Drawings
Figure 1 is a block diagram of a signal processor system for estimating the characteristics of a fluid behind a tympanic membrane.

Figure 1A is a detail view of the speculum tip of figure 1.

Figure 1B is a cross section view of figure 1A.

Figure 1C shows a view of a tympanic membrane and region of illumination and insonification.

Figure 2 is a block diagram as in figure 1 where the signal processor operates directly on received ultrasound echoes.

Figure 3 shows waveforms for the system of figure 1.

Figure 4A shows a plot for a sinusoidal excitation applied to an ear canal with a tympanic membrane response with a phase delay and amplitude level.

Figure 4B shows a plot for a step excitation applied to an ear canal with a tympanic membrane response having a phase delay and amplitude level.

Figure 4C-1 shows a plot of a sinusoidal TM displacement generating more than +/-180° of phase shift.
Figure 4C-2 shows the acquired data with phase wrapped from the large phase shifts of figure 4C-1.

Figure 4C-3 shows a plot of an unwrapped phase estimate from figure 4C-2.

Figure 5 shows a CW signal processor for continuous interrogation of a tympanic membrane in response to an excitation generator.

Figure 5A shows a detail view of the transmit transducer and receive transducer of figure 5.

Figure 6 shows the waveforms for the CW system of figure 5.

Figure 7A is a plot of a sinusoidal excitation source and associated tympanic membrane displacement response.

Figure 7B is a plot of a step excitation source and associated tympanic membrane displacement response.

Detailed Description of the Invention

Figure 1 shows a signal processor for an example embodiment of a tympanic membrane characterization system.
Region 150 (shown in magnified view figure 1A) includes a cross section view of a middle ear and tympanic membrane 130 of a subject being examined. The tympanic membrane 130 is interrogated by an ultrasound beam 128 from an ultrasound transducer 160 (shown in figure 1A) which is optionally mounted on the inner surface of a speculum tip 124, and is detachable from an otoscope speculum mounting adapter 126. In one embodiment of the invention, an optical source 161 seen in the figure 1B cross section view of figure 1A, generates a visual indication the region of insonification by the ultrasound by illumination of a target or region of the tympanic membrane within the ear canal, as seen in figure 1C. Figure 1C shows the view of the tympanic membrane as seen through the speculum, including the tympanic membrane 174, "cone of light" 176, which is a reflective region of the TM which is normal to incident optical illumination and easily located. The optical source 161 may illuminate a small spot 172 indicating the center of the region of ultrasonic insonification 170, or alternatively the spot 172 may be coincident with the ultrasonically insonified region 170. The primary function of the optical source 161 is to provide guidance to a central region 170 of the TM which is
most likely to provide diagnostic utility in terms of the analysis of TM displacement as a function of the pressure challenge. The optical source 161 may be a visible spectrum semiconductor laser diode, a light emitting diode, or any other optical emitter which indicates the extent of the region insonified by ultrasound energy and reflecting ultrasound energy for measurement. Preferably, the optical source illuminates a region corresponding to the beam profile of the ultrasonic transducer at the tympanic membrane. The otoscope mounting adapter 126 and speculum tip 124 have a common interior volume which provides for coupling of dynamic pressures from tympanic membrane excitation generator 120 through hose 122 to the ear canal where the air pressures result in displacement of the tympanic membrane 130. The excitation generator 120 may generate pressure variations which are coupled into the ear canal through the speculum tip 126. The excitation generator may produce any suitable pressure modulation for displacement of the tympanic membrane, including a sub-audio frequency below 20Hz, an audio frequency from 20Hz to 20Khz, or a super-audio frequency above 20Khz. The nature of the pressure excitation generated by the excitation generator may be an impulsive step or delta (impulse)
generation, a sinusoidal pressure excitation, a square wave excitation, or any combination of these, and the excitation may be a gated burst or continuous. The pressure excitation may be provided with or without a static positive or negative pressure bias. Speculum tip 124 also has an associated ultrasound transducer 160 with electrical leads 162 and 164 coupled to transmit receive switch 118. Ultrasound transducer 160 generates ultrasound beam 128 which is directed to a central region of the tympanic membrane 130. A controller 148 generates a variety of control signals which are distributed through the signal processor 100. A system reference clock 110 may be derived from a temporally stable clock source, and the reference clock 110 may also be used for demodulation of the received signal. System reference clock 110 is coupled to a transmit waveform generator 112 which generates a pulse train at or near the center frequency of transducer 160, transmit transducer interface 114 performs voltage level shifting and any required amplification before coupling to the transmit/receive switch 118, which couples the waveforms from transmit interface 114 to the ultrasonic transducer 160 via leads 162 and 164. The ultrasound transducer 160 generates and directs the ultrasonic energy in beam 128 to
the tympanic membrane. Reflected energy from the tympanic membrane is coupled from the transducer 160 back through leads 162 and 164 to the transmit/receive switch 118, where it is directed to the receive preamplifier 116, which boosts the signal level, and optionally provides automatic gain control through a gain control input from controller 148. The output of the receive preamplifier 116 is applied to quadrature mixers 140 and 142, where a quadrature clock from clock generator 110 at the ultrasound transmitting frequency generates a quadrature output comprising an I (in-phase) baseband channel and Q (quadrature, or 90 degrees separated) baseband channel, which are coupled to identical low pass filters 136 and 138, each of which has a respective analog to digital converter 132 and 134, the output of which is stored in data buffers 144, one for each I and Q channel. The gain control applied to preamplifier 116 is set to place the I and Q signals in an optimum converter range for the A/D converters 132 and 134. When the received signal is mixed with the reference clock in this manner, each transmit pulse generates a single phase value, and over a series of transmit events this sequence of phase differences is used by the phase and amplitude analyzer 146 to estimate the temporal displacement of
tympanic membrane 130. In one embodiment of the invention, the transmit clock coupled to the transducer during the transmit interval is derived from system clock 110, which is substantially at the center frequency of the transducer. In an example embodiment where the phase and amplitude analyzer 146 examines primarily the phase of the returned signal, the system clock, at the transmit rate, is also applied to quadrature mixers 140 and 142 during the receive interval to compare the receive signal phase to the system clock (at the original transmit frequency) to generate a phase difference between the transmitted pulse and the reflected pulse. This phase value may be compared over one or more cycles of the receive signal to establish an average phase value for that particular receive interval, and then each phase value from each receive interval assembled to provide a continuous estimate of tympanic membrane displacement, based on the wavelength of the acoustic wave and the phase value measured. In another example embodiment, the phase and/or amplitude analyzer 146 may operate on the amplitude of the received signal, which may be analyzed to provide information about the quality of the phase estimate made from the data (such as from signal to noise metrics), or the amplitude of the signal may be
analyzed to provide a metric such as dB/MHz-cm falloff, or
the amplitude profile may provide an effusion metric which
indicates whether fluid is present behind the tympanic
membrane based on the strength and characteristic of the
reflection. In general, the effusion metric is any phase
or amplitude derived metric from the data presented to the
amplitude and phase analyzer 146 which provides a
measurement of mobility of the TM, where the mobility is
preferentially associated with the presence or absence of
effusion in the middle ear for diagnosis of OM. Controller
148 which generates the TM excitation 120 also reads the
output of phase and amplitude analyzer 146 over the
duration of excitation generator 120 activity, and
optionally the amplitude of the reflected signal, to derive
a temporal response of the tympanic membrane to the
pneumatic excitation provided through speculum tip 124.
The pneumatic excitation may be any sub-audio, audio, or
super-audio frequency or pulse as previously described.

Figure 2 shows an alternate embodiment of the signal
processor of figure 1, where the signal processor is
performing direct sampling of the RF signal from the
transducer, rather than using quadrature mixing to baseband
of the RF signal. System clock 210 generates the transmit
clock, which is coupled to transmit waveform generator 112.
The operation of transmit waveform generator 112, transmit transducer interface 114, transmit receive switch 118, receive preamplifier 116, tympanic membrane excitation source 120 and transducer 160 are as previously described for figure 1. The receive preamplifier 116 may be gain controllable, as before, with the gain determined by controller 248 to place the RF signal in optimum A/D converter 232 range. The output of the receive preamplifier 116 is directed to a band pass filter 236 for reduction of the noise bandwidth applied to the ADC 232, which samples at the Nyquist rate of at least 2X faster than the applied signal. For the case of a 1.5Mhz transducer 160, the Nyquist sampling rate is at least 3Mhz plus the skirt falloff associated with the bandwidth of the transducer 160, known in the art of signal sampling as the Nyquist sampling criteria. The single channel output of the ADC 232 is applied to a data buffer 244, and a signal analyzer 246 examines phase shifts in the buffered signal to determine phase changes of the RF signal to discern movement of the tympanic membrane. The sequence of phase measurements used to form the phase measurement may be a series of measurements which are inverse-time weighted to...
increase the effect of recently acquired measurements, or
they may be uniformly weighted over a window of phase
samples. The use of a weighting coefficients applied to
the stream of measurements over a window may provide
favorable noise rejection characteristics, and weighting
may be chosen to favor signals in the excitation source
bandwidth to filter and reduce the effect of noise which is
outside the excitation source bandwidth.

Figure 3 shows example operation of the ultrasound
processor of figure 1. In a pulsed RF mode,
transmit/receive events provide an estimate of the tympanic
membrane position as a series of phase values during a
series of repeated interrogation intervals 340, each of
which provides a single phase value. System clock waveform
302 operates continuously, and is furnished by system clock
generator 110 of figure 1. The duration of the event
interval 340 is determined by the time-of-flight from the
transducer 160 to the tympanic membrane 130 and back to the
transducer 160 of figure 1. The propagation velocity of
ultrasound in air is 330m/s (.33mm/us). Accordingly, for
a 1.5Mhz transducer, the resultant wavelength of this
traveling wave in air is 0.22mm. The total time of flight
for an ultrasound signal 10mm each direction is then 60us,
so duration 340 may be no less than 60 us in this case.

This time of flight interval for a transmit pulse to return
as a receive signal after reflection is shown as interval
343 in figure 3. The time of flight provides an upper limit
to the pulse repetition frequency (PRF) corresponding to
the sum of the transmit interval and receive interval. For
this example, the transducer with a 1.5Mhz center frequency
will have a 220u wavelength traveling in air. A
displacement of the TM will result in a shortened path from
the transducer to the TM, and the reflected signal from the
TM back to the transducer will return with a phase shift.
Accordingly, the phase and amplitude analyzer observing a
phase offset of 180 degrees between transmit clock and
received signal compared to a datum phase offset will
correspond to a 55u displacement of the TM. A transmit
interval 342 for the transmission of a longer pulse train
provides improved signal to noise ratio of the receive
signal phase and also extends the return time of flight by
the duration 342 of the transmit pulse stream, at the
expense of decreased axial resolution, which may be
desirable for the case of a discrete moving target such as
the tympanic membrane. For a 10 cycle stream at 1.5Mhz,
transmit interval 342 is 6.6us, and for the reflected
signal from a previous transmit burst to not interfere with
the new transmit burst, the maximum interval 340 is 66.6us,
which implies a pulse repetition frequency (PRF) of 15Khz
or less. In a limiting case where the TM is 30us one way
time-of-flight distant, and most of the signal energy
reflection is at the air/fluid interface of a TM with fluid
behind it, and with minimal signal energy reflected from
structures beyond the TM, the shortest possible repetition
cycle time is 30us (maximum transmit burst length) + 30us
(outgoing time of flight) + 30us (return time of flight).
In this idealized scenario, the transducer starts
transmitting at t=0 of the repetition cycle. At t=30us,
the first cycle of transmit energy reaches the TM at the
same time the transducer is finishing sending the last of
the transmit burst. At t=60us, the first reflected cycle
is reaching the transducer and the last cycle of the burst
is reflecting from the TM, and at t=90us, the last cycle of
the burst has reached the transducer. In an actual
ultrasound system, the PRF will be much lower to account
for the required attenuation of multi-path reflection
energy which will mix with the TM reflections. In a CW
system, separate transmit and receive transducers are used
and multipath considerations are ignored. It may be
preferable for the system to operate in CW mode in some circumstances, and in pulsed mode in others, depending on the nature of the reflected signal energy. For pulsed mode, it is desired to provide many cycles of transmit energy to improve the phase accuracy of each measurement, particularly where a clear TM reflection boundary is present and most of the signal energy is reflected from the TM. The combined transmit interval and receive interval which determine the PRF may be in the repetition period range of 50us to 1ms or more. As multi-path reflections may occur, it may be preferable to reduce the maximum PRF to reduce the effect of ultrasonic reflections from transmit events earlier than the current interval 340, for example. The path length to the TM is also determined by the offset of the transducer from the end of the speculum tip. Although figure 1A shows transducer 160 positioned near speculum 124 tip, this distance may vary, and the transducer may be offset inside or outside the speculum tip. In one example of the invention, the transducer is offset substantially 2.5mm to 5mm inside the end of the speculum tip as shown in detail 150 of figure 1A. For an ultrasound propagation velocity of .33mm/us, when the separation from the transducer to TM is 15mm, the round
trip ultrasound path requires ~90us, and if the separation
distance from transducer to TM is 20mm, the round trip path
requires ~120us. As an example, for the 20mm separation
distance, a transmit burst length of 15 cycles at 1.5Mhz
would add an additional 10us, and adding 20us of settling
time for multipath reflections would result in an interval
340 of 150us, corresponding to a PRF of ~6.67Khz.
Transducer waveform 306 shows the transmit waveform 307
which includes bias and amplitude corrections during the
transmit interval 342, and a reduced amplitude receive
signal 309 from the tympanic membrane. The received signal
309 also includes the effects of tympanic membrane
displacement in the form of a phase change from the system
clock, which must be subtracted from any static phase value
which may be present. Mixer I and Q outputs, after low
pass filtering, are shown as waveforms 308 and 310,
respectively. Each 66us cycle provides a single phase
estimate value, which may be considered in polar
coordinates using the I and Q outputs. This may be done
using a range gate select a time of flight interval
corresponding to the region containing a reflection from
the tympanic membrane to obtain each sample indicating the
instantaneous phase of the tympanic membrane for a
particular sample from a transmit event. Each acquired values within an RX interval 344 is averaged or temporally filtered over the temporal region corresponding to the TM reflected response to reach an average phase estimate shown as 311 and 313, respectively, for I and Q waveforms 308 and 310.] A series of such phase estimates are saved, each of these estimates spanning an extent of the Rx interval 344 and which extent corresponds to a reflection from a particular depth. Across multiple data acquisition Rx intervals 344, the samples of IQ are concatenated to construct a time series describing tympanic membrane motion, since phase change over time is attributed to change in distance from the transducer. A succession of these sampled values are collected and compared against a tympanic membrane excitation waveform which is used to form a characterization of the tympanic membrane for a particular excitation waveform.

Figure 4A shows an example sinusoidal excitation applied to a tympanic membrane, such as a sinusoidal waveform 321 applied using a voice coil diaphragm displacing a volume sufficient to modulate the ear canal pressure by 100daPa (dekapascals) p-p. Sub-sonic frequencies may require sealing the ear canal, whereas
audio frequencies and super-audio frequencies may be sufficiently propagated as audio waves without sealing the ear canal. The sinusoidal ear canal pressure excitation results in a modulation of the tympanic membrane, which is shown as phase plot 332, as the modulation in tympanic membrane position corresponds to a change in the phase of the return signal. Each discrete circle of waveform 332 represents a sample point such as a polar conversion of average values for I 311 and Q 313. In one embodiment of the invention, a series of sinusoidal modulation excitation 321 frequencies are applied, each with a different period 322, and the delay in response 330 and peak phase amplitude are used in combination to estimate the viscosity of the fluid behind the ear. Since each 360 degree phase change of the 1.5Mhz transmit pulse corresponds to lambda / 2 = .11 mm, a phase change of +/- 180 degrees total as shown in plot 332 would correspond to .11mm peak to peak displacement of the tympanic membrane. By applying a series of audio and sub-audio tones with various cycle times 322 and measuring the phase response as shown in plot 332, it is possible to estimate viscosity of the fluid behind the tympanic membrane. For example, an exemplar effusion metric measurement associated with the
changed density or viscosity of the fluid could be an associated change in tympanic response time. In this manner, a frequency domain response of the tympanic membrane may be made using a series of excitations and measuring a series of tympanic membrane responses.

The series of figures 4C-1, 4C-2, and 4C-3 show the effect of reconstructing TM displacements when the received signal phase exceeds \( \lambda/2 \) (180°, corresponding to a \( \lambda/4 \) TM displacement). Figure 4C-1 shows a received signal with displacement-associated phase excursions which exceed \( \lambda/2 \) (180°). Because phase excursions greater than 180° wrap to -180°, the series of samples of figure 4C-2 wrap and produce the series of samples shown, with samples of individual segments. If a sufficiently high sample rate is used, it is possible to "unwrap" the samples as shown in figure 4C-3, to provide the original phase information. These techniques are well known in the prior art of Doppler signal reconstruction.

Whereas figure 4A shows a sinusoidal excitation which may be provided in a series of such excitations to generate a phase vs. frequency response plot of the TM displacement from the series of measurements, Figure 4B shows a time domain step response equivalent of figure 4A, where a step
pressure excitation 362 of 50 daPa peak is applied to the
ear canal, which generates the phase response 372 of the
return signal from the tympanic membrane. It is similarly
possible to characterize the tympanic membrane response
based on a time delay 374 and amplitude response (shown as
180 degrees) for phase response plot 372, corresponding to
.11/2 mm displacement. The phase unwrap techniques
described in the series of figure 4C-1, 4C-2, 4C-3 may
similarly be applied to the samples of waveform 372 of
figure 4B to reconstruct phase shifts in excess of +/-180°.

The signal processing of figure 2 operates in a
similar manner as was described for figure 3, however the
transducer reflection 306 is directly sampled and compared
with a reference clock to determine the phase changes
associated with the tympanic membrane movement, for example
by multiplying the reference clock with the received signal
over a receive signal averaging time, and integrating this
value over the duration of the receive signal to estimate a
phase value for one receive interval. In a similar manner,
this will result in the generation of response waveform 332
from excitation source 321 interacting with the tympanic
membrane, as described for figure 4A, or response waveform
372 from excitation source 362 interacting with the tympanic membrane.

Figure 5 shows another embodiment of the invention for CW operation. The signal processor of figure 5 operates as in figure 1, and with the same block descriptions operative as was present in figure 1, however the transmit interface 114 is directly coupled via leads 502/504 to a transmit transducer shown in detail view of figure 5A as 524 and generating transmit beam 526, which is coincident on the tympanic membrane with the receive beam profile 528 of receive transducer 530, which conveys the receive signal using leads 506/508 to receive amplifier 116, where the signal processing occurs as described previously for figure 1, however, the system of figure 5 operates continuously, with the transmitter continuously transmitting, and the receiver baseband signal being continuously received. This operation is advantageous for detection of signal bandwidth which exceeds the pulsed transmit configuration described in figure 3. Because the CW transmit signal results in a standing DC offset at the receive mixers 140 and 142, it is desired to provide electronic isolation between transmit element 524 and receive element 530.
Figure 6 shows waveform plots for the baseband CW system of figure 5. The system clock 110, transmit waveform generator 112, and transmit transducer interface 114 generate a biased transducer CW signal waveform 602 of figure 6, which is applied to the transmit transducer 524 of figure 5, and the receive transducer 530 of figure 5 generates receive signal 608 of figure 6. The outputs of the I and Q channel low pass filters 136 and 138, respectively, are shown as waveforms 614 and 616. The phase unwrapping techniques described previously may be applied to these waveforms as well, where the detected phase crosses the +/- 180° boundary and wraps to the opposite boundary.

Figures 7A and 7B show CW output 714 for an excitation 702, and the sample points of 332 and 372 of figures 4A and 4B are not present, as the CW system of figure 5 is not subject to the baseband Nyquist sampling limitations of the pulsed dopper system of figures 2 and 3, provided that the mixer output is sampled at a sufficiently high rate to satisfy the Nyquist criteria for phase changes at the mixer output.

The transducer types for 130 of figures 1 & 2, and 524 and 530 of figure 5A may be any of capacitive micromachined
ultrasonic transducer (cMUT), or piezoelectric transducers, for example, formed with the piezoelectric material PZT.

The example embodiments for the signal processors have shown embodiments of a pulsed Doppler system of figures 1 and 2, and a CW Doppler system of figure 5. Each of these systems can be practiced using direct RF sampling, as shown in figure 2, where a bandpass filter is operative to reduce the noise bandwidth of the system to \( e_n = \sqrt{4kTBR} \), commonly expressed as nanovolts per root hertz, where:

\[
K \text{ is the Boltzmann constant } 1.38 \times 10^{-23};
\]

\[
T \text{ is the temperature of the system, assumed to be } 300^\circ \text{K;}
\]

\[
B \text{ is the bandwidth of the sampled signal (either the bandwidth of the bandpass filter 236 of figure 2, or bandwidth of the low pass filter 136/138 of figures 1 and 5;}
\]

\[
\text{and } R \text{ is the resistance generating the Johnson noise, typically } 50 \text{ ohms.}
\]

In an ideal system Johnson noise is generated by transducer 160 and preamplifier 120 of figure 1, and this noise is frequency-limited to reduce its effect on system measurements. The noise floor for a 50 ohm system is
0.9nV/√Hz. It is typically easier to perform narrowband filtering on a baseband signal such as the low pass filters 136 and 138 of figure 1 than the bandpass filter 236 of figure 2. For example, a first order band pass filter 236 for a 1.5Mhz system might have a 3db bandwidth of 1 Mhz, whereas the desired signal content is below 1Khz, which is difficult to incorporate into bandpass filter 236, but simple to incorporate into low pass filter 136. Accordingly, the sample noise floor for 1Khz baseband system would 28nV rms whereas the 1Mhz bandwidth direct sampling system would be 30x higher, or 900nV rms with the same signal energy. The noise factor of the system (typically governed by the first few elements in the receive chain) is managed separately, as it would scale the noise floor by the noise factor, so a 6dB noise factor would approximately double both of the above rms noise floor values.

The invention may be practiced many different ways. In one embodiment, the phase and amplitude analyzer produces an effusion metric which is a characterization of the sequence of phase measurements from the ultrasound reflection from the tympanic membrane in combination with the displacement of the tympanic membrane from the tympanic
membrane excitation source. The effusion metric which is derived from the response of the tympanic membrane may provide an indication of whether the tympanic membrane has an air boundary indicating no effusion, a watery fluid boundary, or a purulent fluid boundary. When fluid is detected, one effusion metric may be a viscosity estimate, another effusion metric may be a scattering metric.

The components of the system are shown in block diagram form for clarity in understanding the invention. Certain components are indicated as present in a speculum tip, for clarity of understanding the operation of the invention. It should be understood that these components may be located anywhere, including inside or outside the speculum tip, or alternatively the objects of the invention may be accomplished with the described structures and no speculum tip at all. Alternatively, the speculum tip may be removable with the various structures stationary or removable, including any optical element for viewing of a tympanic membrane, ultrasound transducer, or optical source. The particular arrangement of the elements with respect to the speculum tip is shown for clarity and to illustrate one example of the invention.
The excitation generator may be a manual bulb operated by a clinician, an air displacement generator producing alternating pressure, step pressure, or air puffs. The excitation generator output may be sealed to the ear canal or unsealed and using a puff of gas such as atmospheric air or other suitable gas.

The estimate of tympanic membrane deflection may be derived from a velocity, an acceleration, or any other metric associated with deflection over time.

Various aspects of the invention may be practiced, as recited below:

A signal processor for detection of air or fluid behind a tympanic membrane, and further estimating an effusion metric of a fluid when present, the signal processor comprising:

a speculum tip having an ultrasound transducer for coupling ultrasound energy into an ear canal and to a tympanic membrane;

an excitation generator producing sub-audio, audio, or super-audio excitation coupled into said speculum tip and having sufficient amplitude to cause a measurable deflection in a tympanic membrane;
a transmitter coupled to said ultrasound transducer
during a transmit interval;
a receiver coupled to said ultrasound transducer
during a receive interval which follows said transmit
interval;
a phase and/or amplitude analyzer comparing the phase
of a transmit signal of said transmit interval to a phase
and/or amplitude of a receive signal during said receive
interval to estimate a tympanic membrane deflection;
said signal processor deriving a metric from said
phase and amplitude analyzer by comparing said tympanic
membrane deflection with said excitation generator output;
said effusion metric indicating whether said receive
signal is a reflection from a membrane structure which
includes reflections from air or from fluid, and
optionally characterizing a fluid when detected.

A signal processor where said speculum tip includes an
optical source which indicates a region of insonification
of ultrasound from said ultrasound transducer.

A signal processor where said speculum tip provides at
least one optical element for direct viewing of a tympanic
membrane to be characterized.
A signal processor where said speculum tip provides an aperture through which image capture may be performed for providing a captured image to a display.

A signal processor where a camera is positioned in said aperture.

A signal processor where said aperture provides an optical path to an optical viewing port.

A signal processor where said speculum tip is removable.

A signal processor where said speculum tip includes said ultrasound transducer.

A signal processor where said excitation generator generates at least one of: sinusoidal, impulse, steady state, or periodic sub-audio, audio, or super-audio excitation.

A signal processor where said phase and amplitude analyzer is operative on received acoustic energy from said transducer at a natural center frequency of said transducer.

A signal processor where said phase and amplitude analyzer is operative on received acoustic energy from said...
transducer at a baseband frequency spectrum, said baseband
frequency spectrum formed by mixing said receive signal
with a carrier frequency which is at substantially the
center frequency of said transmitter.

A signal processor where said transmitter generates a
transmit waveform which includes an excitation voltage
signal at a center frequency of said transducer during said
transmit interval.

A signal processor where the sum of said transmit
interval and said receive interval is greater than 50
microseconds and less than 1 millisecond.

A signal processor where said phase and amplitude
analyzer determines a weighted or unweighted average phase
with respect to a transmit clock.

A signal processor where said metric is a temporal
phase change between a received signal from said transducer
during said receive signal interval and a transmit clock
which is operative during said receive interval.

A signal processor where said metric is a phase
relationship between a mixer output baseband signal and
said excitation generator output.
A signal processor of claim 1 where said metric is derived from a temporal phase change in said receive signal and said excitation generator output.

A signal processor where said ultrasound transducer generates a periodic burst of transmit signal energy.

A signal processor where said ultrasound transducer generates continuous transmit signal energy.

A signal processor where said phase and amplitude analyzer is operative on received signals to identify a region of first reflection from a tympanic membrane, and thereafter characterizes a fluid behind said identified region as either air or liquid.

A The signal processor where, when said fluid behind said identified region is liquid, determines a viscosity of said fluid using a phase and amplitude response associated with said measurable deflection.

A signal processor for characterizing a temporal response from an eardrum, the signal processor having:

an excitation generator producing sub-audio, audio, or super-audio excitation for application to a tympanic membrane to cause a displacement;
a transducer for launching acoustic waves towards a
tympanic membrane and receiving reflections from a tympanic
membrane;

a visual indicator to allow the direction of acoustic
waves from said transducer to a region of interest on a
tympanic membrane;

an ultrasound transmitter operative during a transmit
interval and coupling a gated frequency burst to said
transducer;

an ultrasound receiver operative during a receive
interval and coupled to said transducer;

a phase and amplitude detector comparing the phase of
a transmit clock to a receive signal from said ultrasound
receiver and generating a phase output;

a response analyzer comparing said phase output to the
excitation generator output, said response analyzer
determining a viscosity of a fluid adjacent to a tympanic
membrane by comparison of said phase output and said
excitation generator output.
A signal processor where said transducer is at least one of a capacitive micro-machined ultrasound transducer (cMUT) or a piezoelectric transducer.

A signal processor where said excitation generator is at least one of a voice coil actuator, or a moving diaphragm.

A signal processor where said visual guide is at least one of: a laser diode, light emitting diode, or optical indicator which illuminates a region corresponding to a beam profile from said ultrasonic transducer.

A signal processor where said ultrasound transmitter has a repetition rate of less than 15Khz.

A signal processor where said phase and amplitude detector is a baseband mixer generating an output after a low pass filter.

A signal processor where said phase and amplitude detector is operative at a center frequency of said transducer.

A signal processor where said response analyzer compares said phase output and said excitation generator output over a plurality of sample points over a duration of time when said excitation generator is operative.
A signal processor where said receive interval and said transmit interval are concurrent intervals.

A signal processor where said receive interval and said transmit interval are exclusive intervals.
We claim:

1. A signal processor for detection of air or fluid behind a tympanic membrane, and further estimating an effusion metric of a fluid when present, the signal processor comprising:
   - a speculum tip having an ultrasound transducer for coupling ultrasound energy into an ear canal and to a tympanic membrane;
   - an excitation generator producing sub-audio, audio, or super-audio excitation coupled into said speculum tip and having sufficient amplitude to cause a measurable deflection in a tympanic membrane;
   - a transmitter coupled to said ultrasound transducer during a transmit interval;
   - a receiver coupled to said ultrasound transducer during a receive interval which follows said transmit interval;
   - a phase and/or amplitude analyzer comparing the phase of a transmit signal of said transmit interval to a phase
and/or amplitude of a receive signal during said receive interval to estimate a tympanic membrane deflection;
said signal processor deriving a metric from said phase and amplitude analyzer by comparing said tympanic membrane deflection with said excitation generator output;
said effusion metric indicating whether said receive signal is a reflection from a membrane structure which includes reflections from air or from fluid, and optionally characterizing a fluid when detected.

2) The signal processor of claim 1 where said speculum tip includes an optical source which indicates a region of insonification of ultrasound from said ultrasound transducer.

3) The signal processor of claim 2 where said speculum tip provides at least one optical element for direct viewing of a tympanic membrane to be characterized.
4) The signal processor of claim 2 where said speculum tip provides an aperture through which image capture may be performed for providing a captured image to a display.

5) The signal processor of claim 4 where a camera is positioned in said aperture.

6) The signal processor of claim 4 where said aperture provides an optical path to an optical viewing port.

7) The signal processor of claim 4 where said speculum tip is removable.

8) The signal processor of claim 4 where said speculum tip includes said ultrasound transducer.

9) The signal processor of claim 1 where said excitation generator generates at least one of: sinusoidal, impulse, steady state, or periodic sub-audio, audio, or super-audio excitation.
10) The signal processor of claim 1 where said phase and amplitude analyzer is operative on received acoustic energy from said transducer at a natural center frequency of said transducer.

11) The signal processor of claim 1 where said phase and amplitude analyzer is operative on received acoustic energy from said transducer at a baseband frequency spectrum, said baseband frequency spectrum formed by mixing said receive signal with a carrier frequency which is at substantially the center frequency of said transmitter.

12) The signal processor of claim 1 where said transmitter generates a transmit waveform which includes an excitation voltage signal at a center frequency of said transducer during said transmit interval.

13) The signal processor of claim 1 where the sum of said transmit interval and said receive interval is greater than 50 microseconds and less than 1 millisecond.
14) The signal processor of claim 1 where said phase and amplitude analyzer determines a weighted or unweighted average phase with respect to a transmit clock.

15) The signal processor of claim 1 where said metric is a temporal phase change between a received signal from said transducer during said receive signal interval and a transmit clock which is operative during said receive interval.

16) The signal processor of claim 1 where said metric is a phase relationship between a mixer output baseband signal and said excitation generator output.

17) The signal processor of claim 1 where said metric is derived from a temporal phase change in said receive signal and said excitation generator output.

18) The signal processor of claim 1 where said ultrasound transducer generates a periodic burst of transmit signal energy.
19) The signal processor of claim 1 where said ultrasound transducer generates continuous transmit signal energy.

20) The signal processor of claim 1 where said phase and amplitude analyzer is operative on received signals to identify a region of first reflection from a tympanic membrane, and thereafter characterizes a fluid behind said identified region as either air or liquid.

21) The signal processor of claim 20 where, when said fluid behind said identified region is liquid, determines a viscosity of said fluid using a phase and amplitude response associated with said measurable deflection.

22) A signal processor for characterizing a temporal response from an eardrum, the signal processor having:

an excitation generator producing sub-audio, audio, or super-audio excitation for application to a tympanic membrane to cause a displacement;
a transducer for launching acoustic waves towards a tympanic membrane and receiving reflections from a tympanic membrane;

a visual indicator to allow the direction of acoustic waves from said transducer to a region of interest on a tympanic membrane;

an ultrasound transmitter operative during a transmit interval and coupling a gated frequency burst to said transducer;

an ultrasound receiver operative during a receive interval and coupled to said transducer;

a phase and amplitude detector comparing the phase of a transmit clock to a receive signal from said ultrasound receiver and generating a phase output;

a response analyzer comparing said phase output to the excitation generator output, said response analyzer determining a viscosity of a fluid adjacent to a tympanic membrane by comparison of said phase output and said excitation generator output.
23) The signal processor of claim 22 where said transducer is at least one of a capacitive micro-machined ultrasound transducer (cMUT) or a piezoelectric transducer.

24) The signal processor of claim 22 where said excitation generator is at least one of a voice coil actuator, or a moving diaphragm.

25) The signal processor of claim 22 where said visual guide is at least one of: a laser diode, light emitting diode, or optical indicator which illuminates a region corresponding to a beam profile from said ultrasonic transducer.

26) The signal processor of claim 22 where said ultrasound transmitter has a repetition rate of less than 15Khz.

27) The signal processor of claim 22 where said phase and amplitude detector is a baseband mixer generating an output after a low pass filter.
28) The signal processor of claim 22 where said phase and amplitude detector is operative at a center frequency of said transducer.

29) The signal processor of claim 22 where said response analyzer compares said phase output and said excitation generator output over a plurality of sample points over a duration of time when said excitation generator is operative.

30) The signal processor of claim 22 where said receive interval and said transmit interval are concurrent intervals.

31) The signal processor of claim 22 where said receive interval and said transmit interval are exclusive intervals.
Figure 3
Waveform Plots (baseband processor)

Figure 4A
Figure 4B
Figure 4C-1
Input signal phase

Figure 4C-2
Sampled TM Displacement w/phase wrap

Figure 4C-3
Unwrapped phase estimate
Figure 6
Waveform Plots (CW baseband processor)

Figure 7A
Figure 7B
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/12; G01H 15/00, 17/00 (2016.01)
CPC - A61B 5/12, 5/126; G01H 15/00, 17/00

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)
IPC(8) - A61B 10/00, 5/12; G01H 15/00, 17/00 (2016.01)
CPC - A61B 5/12; G01H 15/00, 17/00

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 practicable, search terms used)
Patent (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google Patent; Google, Google Scholar; EBSCO; ScienceDirect. actuate, canal, center, clock, coil, concurrent, diaphragm, drum, ear, effusion, excite, fluid, frequency, illuminate, image, light, liquid, media, optic, phase, receive, signal, simultaneous, sonic, sound, time, transducer, transmit, transonic, ultrasonic, visual

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>US 2007/012632; A1 (VOIE, A H et al.) 7 June 2007; figures 1-3, 5-7; paragraphs [0022], [0027], [0037-0039], [0043], [0045], [0051], [0053], [0058], [0062-0070], [0073].</td>
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<td>US 6043820 A (KRAINARD, ERIC J) 11 April 2000; figure 1; column 2, lines 13-21; column 3, lines 10-29; column 8, lines 1-2</td>
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<td>US 2010/0191144 A1 (ZOTHE, P et al.) 29 July 2010; figure 3; paragraphs [0021], [0023], [0028-0030], [0036], [0037], [0049].</td>
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</table>

Further documents are listed in the continuation of Box C. See patent family annex.

"A" Special categories of cited documents:
"D" Document defining the general state of the art which is not considered to be of particular relevance
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"Z" Document member of the same family

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