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at a plurality of circumferential positions at a second time, after a displacement of the object. The first and second circumferential scans are timed such that the first frame of first image data samples is spatially co-registered with the second frame of second image data samples at least in the circumferential direction and in the catheter longitudinal direction such that a phase change in the optical coherence tomographic image data can be used to determine strain in, and/or elasticity of, the object.

OPTICAL COHERENCE ELASTOGRAPHY IMAGING

This disclosure relates to optical imaging systems suitable for imaging internal structures such as those of the human or animal body. Examples of such optical imaging systems
5 include those which can be used for intravascular, urethral, esophagus, gastrointestinal tract, lung or airway imaging.

Endoscopic Optical Coherence Tomography (Endo-OCT) is a diagnostic imaging technique that can acquire a 2-dimensional (2D) or 3-dimensional (3D) dataset for imaging
10 organs inside patients with micrometre-order resolution. Endo-OCT uses a long and thin catheter to deliver an OCT light beam towards the lumen of an organ inside a patient and collect the reflected light beam. By circumferentially scanning the lumen of the organ, 2D structural OCT images can be reconstructed. Endo-OCT has been widely used in clinical diagnosis with applications in Barrett's oesophagus imaging, gastrointestinal imaging, lung
15 imaging and intracoronary imaging. Endo-OCT is also commercially available from many medical device companies.

Conventional OCT images provide structural information of the patient's organs. The image reading, especially the identification of diseased tissue, relies on image feature
20 interpretation. However, other tissue types or image artefacts may also show similar features, confounding any diagnosis.

Optical Coherence Elastography (OCE), as a functional modality of OCT, makes use of the phase signal of complex OCT data to visualize stress-strain phenomena and to deduce
25 mechanical properties of tissue, such as elasticity. The basic principle of OCE is to apply a mechanical stress to a tissue specimen, detect a resulting displacement of or in the specimen, calculate the strain in the specimen and create a strain image. Stiff tissue with small strain or soft tissue with large strain can be distinguished in the strain image. The strain image data provides an indication of the local elasticity of an object, such as the
30 tissue specimen, being imaged. To induce the stress, various types of mechanical excitation sources have been proposed, such as acoustic radiation force, mechanical load or air pulse. The stress then induces tiny tissue displacements in the nanometre to sub-micrometre range, which will cause a phase changes to the complex OCT data sample.

To provide optimal datasets for clinical use, it would be desirable to be able to compute tissue elasticity images from conventional endoscopic OCT data. This can result in endoscopic OCE data that are spatially co-registered with the OCT data, so that both OCT data (providing structural information) and OCE data (providing stiffness information) can be examined together. Hitherto, it has not been possible to obtain endoscopic OCT data sets that are spatially co-registered with OCE data sets. Most current OCE techniques are restricted to bench-top microscopic imaging and so far, no endoscopic OCE has been able to provide both morphological images and strain images at the same time. This is mainly due to two limiting factors: stability of the imaging and feasibility of a catheter-based excitation source.

It is an object of the invention to provide improvements in OCE imaging. It is another object of the invention to provide a system for endoscopic OCE. It is another object of the invention to provide improved OCE by providing morphological imaging and strain imaging at the same time. Some or all of the objects may be achieved by methods and apparatus as described herein.

According to one aspect, the present invention provides an imaging system comprising:
a catheter-based optical imaging device configured to obtain multidimensional optical coherence tomographic morphological image data of an object disposed around a catheter and including a controller configured to enable successive scans of the morphological image data to be sufficiently spatially co-registered with one another to provide strain or elasticity image data of the object.

The imaging system may include: a catheter defining an optical path structure couplable to a source of optical radiation and a detector. The optical path structure may be configured to direct optical radiation radially outwards from the catheter to an object in which the catheter is disposed and to receive responsive image data radiation signals from the object. A synchronization module may be configured to trigger a first circumferential scan of the optical radiation to obtain a first frame of first image data samples at a plurality of circumferential positions at a first time, and to trigger a second circumferential scan of the optical radiation to obtain a second frame of second image data samples at a plurality of circumferential positions at a second time, after a displacement of the object. The first circumferential scan and the second circumferential scan may be timed such that the first frame of first image data samples is spatially co-registered with the second frame of

second image data samples at least in the circumferential direction and in the catheter longitudinal direction such that a phase change in the optical coherence tomographic image data can be used to determine strain in, and/or elasticity of, the object.

- 5 The spatial co-registration may comprise an at least 50%, 70% or 80% spatial overlap of each of the corresponding first and second image data samples in the circumferential and catheter longitudinal directions. The imaging system may further include a stimulus module configured to deliver a mechanical excitation to the object around the catheter at a time between the first and second circumferential scans. The stimulus module may
- 10 comprise a pump configured to deliver a fluid pressure change to a lumen of the object via the catheter. The pump may be configured to deliver one of a liquid or a gas via a working channel associated with the catheter to a site at a distal region of the catheter. The pump may be configured to deliver a fluid pressure change by changing a flow rate of fluid through the catheter. The synchronization module may comprise a motor drive signal
- 15 generator configured to provide a motor driving signal synchronized with an optical radiation sweep signal of the source of optical radiation that is timed with each scan of the optical radiation through a plurality of wavelengths. The synchronization module may further comprise a frame trigger signal generator configured to generate a frame trigger signal synchronized with predetermined timing positions of the motor driving signal. The
- 20 synchronization module may comprise a motor drive signal generator configured to provide a motor driving signal synchronized to a predetermined constant number of coherence fringes. The imaging system may further include an axial displacement mechanism configured to effect longitudinal displacement of the catheter along its longitudinal axis. The synchronization module may be configured to generate a pullback timing signal to
- 25 control longitudinal displacement of the catheter. The axial displacement mechanism may be configured to effect continuous longitudinal displacement of the catheter during circumferential scans. The longitudinal displacement may be effected at a velocity sufficiently slow that the longitudinal displacement of the optical path structure in the catheter between the first circumferential scan and the second circumferential scan after
- 30 displacement of the object is less than a distance required to maintain at least 50% spatial overlap of the first and second image data samples. The catheter may have an outer diameter of 3 mm or less. The catheter may include a motor in the distal region of the catheter configured to rotate an optical element to direct the optical radiation radially outwards from the catheter in a plurality of angular directions and to receive the responsive
- 35 image data radiation signals. The optical path structure may further include a reflecting

element in the catheter distal of the rotatable optical element. The optical path structure may provide a folded optical path which extends past the motor and rotatable optical element and towards a distal end of the catheter, through the reflecting element and towards the proximal end of the catheter to the rotatable optical element. The optical path structure may include an interferometer having a calibration mirror configured to provide a sharp peak in each A-line dataset and a processor configured to use the coherence fringes of the calibration mirror to correct a sampling offset between different wavelength sweeps of the optical radiation when acquiring the data samples. The stimulus module may comprise a steerable catheter head configured for lateral deflection from a longitudinal axis of the catheter to deliver a mechanical excitation to the object around the catheter at a time between the first and second circumferential scans.

According to another aspect, the invention provides a catheter for optical imaging comprising:

a motor in the catheter coupled to rotate a rotatable optical element about an axis substantially on or parallel to the longitudinal axis of the catheter, the optical element being located on a distal side of the motor relative to the proximal end of the catheter;

the catheter further comprising structures to define an optical path having a first portion extending between a proximal end of the catheter and a distal end of the catheter, past the motor and the rotatable optical element, and a second portion extending between the distal end of the catheter and the rotatable optical element;

the optical path having a third portion extending radially outwards from the rotatable optical element and from the second portion,

the rotatable optical element being configured to effect scanning of the third portion of the optical path about the longitudinal axis of the catheter.

The catheter may further comprise an angular coupling element disposed at the distal end of the catheter and optically coupling the first and second portion of the optical path. The angular coupling element may comprise one or more reflecting interfaces for coupling the first portion of the optical path and the second portion of the optical path. The angular coupling element may comprise a pair of reflecting elements respectively for coupling the first portion of the optical path and the second portion of the optical path by way of an optical path transverse to both the first portion and the second portion and to the longitudinal axis of the catheter. The catheter may further include a focussing element disposed parallel to the motor for conveying the first portion of the optical path past the

motor. The catheter may further include an optical conduit extending along the catheter alongside control wires for the motor, the optical conduit comprising a structure providing at least some of the first portion of the optical path and maintaining separation of the optical path from the control wires of the motor. The first portion of the optical path and the third
5 portion of the optical path may intersect during at least a part of the scanning of the third portion of the optical path about the longitudinal axis of the catheter. The optical path may be folded by less than 180 degrees between the first and second portions. The angular coupling element may comprise a reflecting element orthogonal to the longitudinal axis of the catheter. At least one of the angular coupling element and the rotatable optical element
10 may be a focussing element.

According to another aspect, the invention provides a method of generating multidimensional optical coherence tomographic morphological image data of an object disposed around a catheter comprising:

15 deploying a catheter-based optical imaging device within the object;
 performing successive circumferential scans of the object that are sufficiently spatially co-registered with one another to provide strain or elasticity image data of the object.

20 The method may further comprise: defining, in the catheter, an optical path structure coupled to a source of optical radiation and a detector, the optical path structure directing optical radiation radially outwards from the catheter to the object in which the catheter is disposed and receiving responsive image data radiation signals from the object; triggering a first circumferential scan of the optical radiation to obtain a first frame of first image data
25 samples at a plurality of circumferential positions at a first time, and triggering a second circumferential scan of the optical radiation to obtain a second frame of second image data samples at a plurality of circumferential positions at a second time, after a displacement of the object, the first circumferential scan and the second circumferential scan being timed such that the first frame of first image data samples is spatially co-registered with the
30 second frame of second image data samples at least in the circumferential direction and in the catheter longitudinal direction such that a phase change in the optical coherence tomographic image data can be used to determine the strain in, and/or elasticity of, the object.

Embodiments of the present invention will now be described by way of example and with reference to the accompanying drawings in which:

Figure 1 is a schematic side view of an OCT imaging catheter within a lumen of an object such as a body organ for endoscopic optical coherence tomography;

5 Figure 2 shows Endo-OCT imaging examples of coronary artery, oesophagus, gastrointestinal tract, ureter and lung;

Figure 3 is a schematic diagram of data frames used for signal processing in OCE;

Figure 4 shows an example of using OCE to identify stiff parts of a phantom seen in a dark area of figure 4b compared with an OCT image in figure 4a;

10 Figure 5 is (a) a schematic diagram of an OCT probe used within a phantom to obtain OCE data, (b) a motion-mode image therefrom, and (c), (d), (e) OCT A-line scans and measured displacements at varying distances;

Figure 6 shows in (a) and (b) schematic diagrams of a system using acoustic radiation force to induce excitation for OCE without automated beam scanning, (c) transducer frequency and echo characterisation, (d) transducer axial force field characterisation;

Figure 7 is a schematic diagram of an endoscopic-OCE imaging system with stable imaging and proximal excitation of the structure being imaged;

Figure 7a shows overlapping beams required between two A-lines for OCE signal processing;

Figure 8 shows (a), (b) and (e) schematic diagrams of catheter-based OCT scanning mechanisms and (c), (d) example images therefrom;

Figure 9 is a schematic diagram of timing functions of a synchronization module for an OCE imaging system and results therefrom;

25 Figure 10 is a schematic diagram of phase shift extraction between two frames comparing when stable imaging is, and is not, achieved;

Figure 11 is a schematic diagram illustrating a working principle of proximal flushing for excitation in OCE;

Figure 12 is a schematic diagram illustrating working principles of a calibration mirror to improve phase stability of OCE by compensating a sampling offset where (a) is a plot of A-line amplitude versus depth, (b) shows coherence fringes of four sweeps, (c) shows coherence fringe signals with sampling offsets overlaid, (d) shows the coherence fringe signals overlaid after sampling offsets compensation, (e) and (f) show phase noise before and after compensation;

Figure 13 shows (a) an OCT image and (b) phase shift image and (c), (d) strain images of a phantom acquired by the Endo-OCE apparatus of figure 7 using saline as flushing medium;

Figure 14 shows (a) an OCT image, (b) a phase shift image and (c) a strain image of a phantom acquired by the Endo-OCE apparatus of figure 7 using air as a flushing medium;

Figure 15 shows (a-c) OCT images, (d-f) phase shift images and (g-l) strain images of coronary arteries acquired by the Endo-OCE apparatus of figure 7 using saline as a flushing medium;

Figure 16 shows a schematic timing diagram of a 3D Endo-OCE imaging system illustrating synchronization of pullback with Endo-OCE imaging and proximal infusion;

Figure 17 shows schematic cross-sectional views of an imaging system introduced into the oesophagus with (a) showing an insertion configuration of a steerable head and (b) showing a laterally deflected condition of the steerable head;

Figure 18 shows cross-sectional schematic diagrams of (a) the steerable head, (b) a steering mechanism, and (c) the steering mechanism in position for use.

Throughout the present specification, references to the acquisition and processing of 'image data' and references to imaging devices are intended to encompass acquisition of datasets representative of multi-dimensional (e.g. two- or three-dimensional) spatial distributions of morphological and/or strain / elastic properties of an object structure, which datasets are useful for the creation of images and image processing but without necessarily generating a user viewable representation or image. Thus, the expression 'imaging device' is intended to encompass devices suitable for acquiring datasets from which 2D and 3D images can be produced without necessarily including display devices for the presentation of such images, though such display devices can of course also form part of the described devices if required. The expression 'catheter-based optical imaging device' is intended to encompass devices which can be inserted into a lumen or other cavity of a body or other object to obtain image data representative of the internal structures of the object at least partially surrounding the catheter.

With reference to figure 1, there is shown schematically an OCT imaging catheter apparatus 1 disposed within an object such as a body structure or organ 2 having an organ lumen 3. The catheter 1 has a distal end 4 inserted into the organ lumen 3 and a proximal end 5 outside the body structure 2 for connecting to external apparatus (not shown in figure

- 1). The catheter 1 is configured to emit, from a distal region 6 near the distal end 4 of the catheter, an interrogative light beam 7 which scans the wall 8 of the organ lumen 3 in a circumferential manner as indicated by arrow 9, by rotation of the light beam 7 through successive angular directions around the longitudinal axis 10 of the catheter 1.
- 5 Responsive radiation signals such as back-reflected light that carries information relating to the tissue of the body structure 2 is collected by the catheter optics, and forms a coherence fringe signal by combining it with a reference light beam. The fringe signal is converted into an electronic signal, digitized, and stored as series of discrete data samples.
- 10 The light beam 7 is preferably a laser light beam and is emitted from a source of optical radiation which is operated to scan through a succession of wavelengths (e.g. 1260-1360 nm) at each circumferential position on the body structure 2, such that a succession of data samples, at least one for each circumferential position of the lumen wall 8 around the catheter 1, are captured. Each circumferential position may include multiple data samples,
- 15 each one comprising data corresponding to a one of the various wavelengths of the optical radiation. Alternatively, a broadband light source may be used as the source of optical radiation, while the multiple data samples may be captured by a sensor array or camera mounted as a detector in a spectrometer setup. Using either a wavelength sweep source or a broadband light source and a spectrometer, the multiple data samples can be
- 20 recorded as coherence fringes (also called an interference pattern) that is a function of wavelength.

The coherence fringe signal data samples distributed across a wavelength band, such as 1260 – 1360 nm, are then processed into complex format by a Fourier transform. After

25 Fourier transform, the coherence fringes have become a series of complex data that distribute in axial depth, and the complex data samples corresponding to all the wavelengths at a particular circumferential position of the sweep form an Axial image line, referred to herein as an A-line. More generally, each A-line dataset may be considered as an image data sample for a circumferential position. The scanning of the OCT beam

30 enables A-lines to be generated for multiple radial directions each corresponding to a circumferential position on the organ lumen thereby generating a 2D image of a cross section of the organ lumen. Each 2D image of organ lumen section may be formed by $\geq$ 500 A-lines, corresponding to a full 360 degree circumferential scan of the light beam 7.

A circumferential scan, typically of a full 360 degrees may be referred to herein as a 'frame', although a circumferential scan or 'frame' of less than 360 degrees is possible if desired. 3D imaging of the organ lumen 3 may be achieved by longitudinal translational motion of the catheter along the organ lumen, along the direction of the catheter longitudinal axis 10, typically while the optical beam from the catheter is rotating about the catheter axis. This translational motion may also be referred to herein as "pulling back" the catheter though it is to be understood that the longitudinal translational motion during imaging could be in either longitudinal direction, proximal or distal. The longitudinal translation motion can be a continuous motion or a step-by-step motion. The beam 7 scan might thereby sweep out a helical path of successive A-lines to form a full 3D dataset when a continuous longitudinal motion is applied. Each 360 degree rotation within the helical path may also be referred to as a frame. Conventional Endo-OCT uses the amplitude of the complex data to reconstruct morphological images.

Endo-OCT may be widely used in clinical diagnosis such as intracoronary imaging, oesophagus imaging, gastrointestinal tract (GI) imaging, urethra imaging and lung imaging. Examples of such images are shown in figure 2. Figure 2a illustrates a coronary artery cross-sectional OCT image. Figure 2b illustrates an oesophagus cross-sectional OCT image. Figure 2c illustrates a GI tract cross-sectional OCT image (from "Endomicroscopic optical coherence tomography for cellular resolution imaging of gastrointestinal tracts", Journal of Biophotonics (IF 3.768), 2017-11-20, Yuemei Luo *et al*). Figure 2d illustrates a ureter cross-sectional OCT image ("Optical Coherence Tomography in Urologic Oncology: a Comprehensive Review", J. E. Freund *et al*). Figure 2e illustrates a lung cross-sectional OCT image ("Endobronchial Optical Coherence Tomography for Low-Risk Microscopic Assessment and Diagnosis of Idiopathic Pulmonary Fibrosis In Vivo", Lida P. Hariri, M.D. *et al*). As annotated on figure 2b, it can be understood that the OCT scan acquires image data for multiple positions circumferentially around the lumen wall 8 and multiple positions axially along the lumen walls (into the plane of the drawings) both of which may be referred to as transverse scan directions (i.e. transverse to the beam direction), but also the penetration of the laser light into the organ or body structure 2 yields image data for multiple depths into the lumen wall 8 for each transverse scan position, which may be referred to as the axial scan direction (i.e. the depth along the beam axis into the lumen walls for which image data can be derived).

Determination of a tissue type may depend on structure feature interpretation by the image reader. Sometimes, imaging artefacts or healthy tissue may show similar features to those representative of a tissue clinical condition, thereby confounding a proper diagnosis. To achieve a more accurate diagnosis, other tissue type information such as tissue stiffness
5 can be provided in addition to the morphological information provided by the OCT images shown in figure 2. Detecting the stiffness of tissue can provide diagnostic information since diseased tissue normally has a different stiffness from surrounding healthy tissue. For instance, cancerous tumours are often found to be harder than the surrounding tissue, vulnerable atherosclerosis plaques are often found to be softer than healthy artery walls
10 and lung fibrosis is found to be harder than healthy lung tissue.

As mentioned above, Optical Coherence Elastography (OCE) can make use of the phase signal of complex OCT data to visualize stress-strain phenomena and to deduce mechanical property of the tissue specimen. In one aspect, a mechanical stress may be
15 applied to the tissue specimen (or other object), consequential displacement in the specimen detected, and the strain calculated to create a strain image. To induce the stress, various types of mechanical excitation sources may be used such as acoustic radiation force, mechanical load, balloon or air pulse. The stress induces tiny tissue displacements which cause phase changes to the complex OCT data samples.

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To detect such tiny displacements, OCE compares the phase of each complex data sample between two frames, respectively acquired before and after the mechanical excitation. A change in the phase signal (phase-shift) can be converted to displacement.

25 Figure 3 shows the principle of phase-shift extraction between two frames. Figure 3 illustrates schematically the image data of two frames 30 and 31 obtained with a time separation 32 during which stress has been applied to the object being imaged. The data set for each frame 30, 31 comprises a plurality of data samples depicted as the squares 33, after Fourier transform, each of which corresponds to a circumferential position in the
30 frame and a depth into the structure or object being imaged. Thus, each column 34 of samples 33 as shown represents an A-line having depth information. The strain, defined as the gradient of displacement along radius depth (distance of the structure from the catheter axis), can then be calculated, showing the mechanical information of the imaging target object. In such way, a strain image is provided in addition to the conventional OCT
35 images that only show the structure using the amplitude of the complex data.

Figure 4 shows an example of strain imaging of a phantom in a benchtop microscopic setup (Kennedy, Brendan *et al.* "A Review of Optical Coherence Elastography: Fundamentals, Techniques and Prospects", IEEE Journal of Selected Topics in Quantum Electronics 20 (2014): 272-288), where figure 4a shows an OCT image conveying morphological information and figure 4b shows the strain image in which stiff parts 41, 42 show much smaller strain than the surrounding phantom.

Though OCE strain images together with structural OCT images can achieve a joint tissue characterization, applying OCE techniques to endoscopic environments to provide morphological image and strain image at the same time has hitherto proved difficult. This is mainly due to two limiting factors: stability of the imaging and feasibility of the excitation source.

Regarding imaging stability, OCE measures the tissue displacement by comparing the phase signal sample by sample between two frames acquired before and after a mechanical excitation. This means the data samples should be co-located between two frames e.g. the same sample from two frames should correspond to the same radius depth and angular / circumferential position in the tissue specimen or other object as indicated schematically in the A-lines 34 and frames 30, 31 of figure 3. Stable imaging requires not only a stable beam scanning but also a synchronization between data acquisition and beam scanning. A conventional OCT catheter realizes the light beam scanning by rotating a long fiber probe inside the catheter. Rotation distortion of such long fiber probes will affect the beam scanning, leading to spatial mismatch or distortion between different frames 30 31, so that the two different frames 30, 31 are not spatially overlapped. Two corresponding data samples 33 from the two frames 30, 31 would then not correspond to the same location of the imaging target and the phase signal cannot be compared. One compromise solution would be to turn off the beam scanning and extract the phase shift between two A-lines that are in the same position or substantially overlapped. Such a method can, however, only extract the stiffness information of one angular position rather than an entire cross section of the structure and no strain image can be provided. Figure 5 (Kelsey M. Kennedy *et al.*: "Needle optical coherence elastography for tissue boundary detection," Opt. Lett. 37, 2310-2312 (2012)) illustrates an example of such an approach in which, in figure 5a, a probe 60 is inserted into a phantom 61 comprising a soft portion 62 and a hard portion 63. A motion mode image is captured (figure 5b) and the relative

position of the inclusion or hard region 63 to the probe is determined from the displacement measurements (lower graphs of figures 5c, 5d, 5e) to be 570 μm , 450 μm and 300 μm respectively. The red stars denote the locations of interfaces, and the black lines indicate the linear fits used to approximate strain. The determined position of the boundary in the motion image of figure 5b is shown with dashed line 64.

Another limiting factor of catheter-based OCE is the feasibility of the excitation source. The large dimension of excitation sources is an impediment to the minimization of the catheter. One approach has used acoustic radiation force (ARF) to induce tissue displacement. However, the ARF excitation requires a large transducer that is normally several millimetres in size and beam scanning is difficult to realize using such a large transducer. Figure 6 (Yueqiang qu *et al*: "Miniature probe for mapping mechanical properties of vascular lesions using acoustic radiation force optical coherence elastography", scientific report. 2017) shows an example of such approach. Figure 6a shows an overview of the ARFI OCE set up comprising a collimator C, lens L, attenuator A, mirror M, grating G, mechanical stage MS, radio frequency amplifier RFA, probe P, specimen S, function generator FG. Figure 6b shows the probe design having a probe head including a ring transducer (left) and optical elements inside (right). Figure 6c shows the transducer frequency and echo characterization and figure 6d shows the transducer axial force field characterization.

The present disclosure provides methods and apparatus for achieving synchronization of full scans of image data before and after mechanical excitation of the object being imaged. The present disclosure also provides methods and apparatus for achieving mechanical excitation of the object being imaged without adversely impacting the ability of catheter-based optical elements to perform spatially accurate scans. In this way, it is possible to realize endo-OCE with morphological imaging and strain imaging at the same time by achieving a stable imaging and using a proximal excitation source.

Figure 7 shows a schematic diagram of an endoscopic-OCE imaging system. An imaging catheter module 71 comprises a catheter apparatus 1 such as shown in figure 1. The catheter apparatus 1 includes a working channel 11 which can serve to deliver working fluid to a position at or close to a distal region 6 of the catheter apparatus. The distal region 6 also provides an optical scanning mechanism (not shown in figure 7) for generating the light beam 7. The catheter module 71 also includes a connector 12 such as a Y-connector

for coupling a fluid delivery line 13 to the working channel 11 while also allowing the coupling of an optical fibre 14 or other optical path structure into the catheter 1. The expression 'optical path structure' as used herein is intended to encompass one or more structural elements configured to convey an optical beam along an optical path. The working channel 11 may be integrated into the imaging catheter or may be provided as part of a guiding catheter used to guide the imaging catheter towards the imaging position within the organ lumen 3.

The fluid delivery line 13 is connected to an infusion module 73 comprising a fluid delivery mechanism 15 for delivering working fluid to the working channel 11 of the catheter apparatus 1. The fluid delivery mechanism 15 may comprise any suitable device, such as a pump, for controllably delivering fluid to the catheter, e.g. by changing flow rate or pressure of fluid flowing in the fluid delivery line 13. The fluid delivery mechanism may be configured to deliver any suitable fluid medium, including any suitable liquid or gaseous media, such as saline, water, air, inert gas etc. The infusion module 73 is operative to induce intraluminal pressure changes in an object being imaged, such as an organ lumen in a patient in which the catheter 1 is introduced, by changing the infusion rate from the proximal end of the catheter, which is outside the patient and independent of the catheter. In this way, no mechanical or acoustic transducer or other excitation apparatus need be placed in the distal end of the catheter which could otherwise increase the size of the catheter or compromise its imaging stability. The endoscopic OCE image data will be acquired during the pressure changes, e.g. before and after a period of pressure change. In a general aspect, the infusion module 73 may be configured to induce movement or displacement in the object being imaged by either hydraulic excitation or by pneumatic excitation of the object being imaged. More generally, the infusion module exemplifies a stimulus module which is configured to deliver a mechanical excitation to the object being imaged between successive circumferential scans.

Also coupled to the catheter module 71 may be a pullback module 72 which comprises a motor mechanism (not shown) that is configured to effect controlled longitudinal displacement of the catheter in a direction corresponding to the axis of the catheter 1. This longitudinal motion can be synchronized with motion of the optical beam 7 about the longitudinal axis of the catheter 1 to thereby synchronize fast optical scanning around the catheter axis and slow optical scanning along the catheter axis.

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To achieve the synchronization, a synchronization module 74 is connected to the pullback module 72 by way of a pullback control line 74a, and to a motor in the catheter module 71 by way of a motor control line 74b. The motor drives rotation of the optical beam 7 around the catheter longitudinal axis in a manner to be described hereinafter.

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The optical fibre 14 couples into a suitable optical radiation source and detector such as an interferometer module 75 and data acquisition unit 77 for obtaining the OCE imaging data. The light beam 7 is generated by a wavelength sweep laser 76 coupled to the interferometer module 75. The wavelength sweep laser 76 is also coupled to trigger the
10 synchronization module 74 in a manner to be described hereinafter, using control line 76a. The data acquisition unit 77 may comprise a balanced photon detector 770 and a data acquisition device 771.

The catheter module 71 and the synchronization module 74 provide a stable imaging that
15 ensures a phase shift can be extracted between two frames 30, 31 acquired at different intraluminal pressures. The infusion module 73, pullback module 72 and the synchronization module 74 enable 3D Endo-OCE imaging of the organ lumen 3 / walls 8, e.g. by way of a succession of OCE data frame pairs 30, 31 each pair corresponding to different longitudinal positions of the catheter 1. Conventional OCT images showing the
20 morphological information and Endo-OCE strain images showing organ stiffness information can be provided at the same time by this imaging system.

Stable imaging requires stable beam scanning and near perfect synchronization between beam scanning, laser output and data acquisition. Stable beam scanning means that two
25 circumferential beam scans (e.g. frames 30, 31) should be preferably precisely overlaid, or overlapping to such an extent that the transverse spatial mismatch between corresponding A-line data samples 34 before and after an excitation pressure change should be less than 50%, and more preferably less than 30% or even 20% of the spatial size of one A-line data set. The expression 'size' in this context refers to the cross-
30 sectional area of the scanned A-line, which is determined by the optical beam 7 size / cross-sectional profile.

As shown schematically in figure 7a, optical beams 701, 702 comprise Gaussian profile laser beams used respectively to derive the samples 331, 332 of the A-lines 34 from
35 frames 30, 31. In a preferred arrangement, the spatial overlap of the A-line data samples,

i.e. the cross-sectional area spatial overlap of the beams 701, 702 deriving the scanned samples should be at least 50%, preferably at least 70%, and more preferably at least 80%, of the cross-sectional area of the beam or area of the A-line data set samples. The degree of spatial overlap required will depend on the ability to differentiate the phase shift from noise. For a 20 micrometre beam radius, and with little or no noise suppression techniques, an area of overlap of the beams of at least 84% may be preferred; without additional noise suppression techniques, an optimal spatial overlap for ideal results may be greater than 90%. The apparatus as described herein is readily capable of achieving $\geq 90\%$ overlap of beam area.

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More generally, the preferred or minimum overlap may be expressed in terms of beam power, e.g. the overlapping area of two beam spots of Gaussian profile should preferably cover $\geq 43\%$ of the power that is transmitted in the beam, and more preferably the spatial area of overlap should cover $\geq 70\%$ and more preferably $\geq 78\%$ of the power that is transmitted in the beam.

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With advanced noise suppression techniques, the lower figures described above may apply.

Achieving such a degree of overlap means that the successive frames 30, 31 are sufficiently spatially co-registered and therefore the morphological image data and strain data derived therefrom are also spatially co-registered.

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In a conventional catheter design, a long optical fibre probe is rotated on its axis within the catheter causing rotational distortion which affects the precision of the beam scanning and may not enable the co-registration of the frames 30, 31 discussed above. A solution is to place a micro motor at the distal end of the catheter to realize the circumferential beam scanning. Figure 8 illustrates suitable arrangements.

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Figure 8b shows a first arrangement in which a motor 80b is disposed within the catheter 81b towards a distal end 82 thereof. The motor 80b may be a two-phase four-pole synchronous micro motor which can be driven by a two channel sinusoidal current signal that has 90 degree phase shift between the channels. A micro-mirror 83b is attached to a drive shaft 84b of the motor to deflect the light beam 85b that has been focused by a focusing element 86b in a more proximal region of the catheter 81b. The focusing element

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- 86b may be a GRIN lens, a ball lens or a micro convex lens, for example. The micro-mirror 83b deflects the light beam 85b to a radial trajectory to define the circumferentially scanning light beam 7 as seen in figure 1. The scanning light beam 7 passes through transparent walls of the catheter 81b. The micromotor 80b may work in rotating mode to achieve full circumferential beam scanning of the entire section of the organ lumen surrounding the catheter 81b, or work in oscillation mode to scan a circumferential part of the organ lumen. The expression 'circumferential scan' is intended to encompass both options.
- 10 A potential drawback of the design of figure 8b, particularly for full circumferential scanning, is that control wires 87 of the motor 80b that pass along the catheter may partly block the OCT scanning beam and lead to shadow areas in the OCT and OCE images as shown in Figure 8c marked by '*'.
- 15 This potential problem can be avoided by alternative catheter apparatus as shown in figures 8a and 8e. In figure 8a, a motor 80a is disposed within the catheter 81a towards a distal end 82 thereof. The motor 80b may be a two-phase four-pole synchronous micro motor which can be driven by a two channel sinusoidal current signal that has 90 degree phase shift between the channels. A micro-mirror 83a or other rotatable optical element is attached to a drive shaft 84a of the motor 80a. In contrast to the arrangement of figure 8b, in this arrangement the micro-mirror 83a is disposed on a distal side of the motor 80a relative to the proximal end of the catheter 81a. The rotatable optical element exemplified by the micro-mirror 83a is configured to deflect the light beam 85a that has been focused by a focusing element 86a which is disposed in a more proximal region of the catheter 81a, and preferably alongside the motor 80a. The focusing element 86a may be a GRIN lens, a ball lens or a micro convex lens, for example. The micro-mirror 83a deflects the light beam 85a to a radial trajectory, and the micromotor 80a rotates the mirror to direct the light beam radially outwards from the catheter in a plurality of angular directions to thereby define the circumferentially scanning light beam 7 as seen in figure 1. The scanning light beam 7 passes through transparent walls of the catheter 81a. The micromotor 80a may work in rotating mode to achieve full circumferential beam scanning of the entire section of the organ lumen surrounding the catheter 81a, or work in oscillation mode to scan a circumferential part of the organ lumen. The expression 'circumferential scan' is intended to encompass both options.

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To avoid obstruction of the optical beam 7 by the motor control wires, the arrangement of figure 8a provides an optical path structure that includes fibre 89 and focussing element 86a that extend distally past the wires 87 to a region of the catheter 81a that is distal to the motor 80a. The optical path is folded (e.g. through 180 degrees) using a coupling element 88 which serves to define a first portion 14a of the optical path 14 which extends
5 between a proximal end of the catheter and a distal end 82 of the catheter 81a, past the motor 80a and the rotatable optical element 83a, and a second portion 14b of the optical path 14 which extends between the distal end 82 of the catheter 81a and the rotatable optical element 83a. The rotatable optical element 83a serves to define a third portion of
10 the optical path comprising the radially-directed, circumferentially scanning beam 7 that rotates about the axis of the catheter. The coupling element 88 may comprise an angular coupling element as seen in figure 8a comprising a pair of reflecting elements 88a, 88b which respectively couple to the first portion 14a of the optical path and the second portion 14b of the optical path 14 by way of an optical path 14c transverse to both the first portion
15 14a and the second portion 14b and to the longitudinal axis of the catheter.

The reflecting elements of the angular coupling element 88 may comprise two micro-mirrors 88a, 88b. In other arrangements, the coupling element may comprise a plurality of reflecting elements or interfaces for coupling the first portion 14a of the optical path 14
20 to the second portion 14b of the optical path via series of intermediate optical paths at varying angles. As seen in figure 8e, the angular coupling element may comprise a single reflecting element or interface 88c to couple the first portion 14a of the optical path and the second portion 14b of the optical path. Focusing element 86c, motor 80c and rotatable optical element 83c may otherwise have corresponding functions to focusing element 86a,
25 motor 80a and rotatable optical element 83a as described in connection with figure 8a.

The focusing element 86a is preferably alongside and parallel with the micromotor 80a, e.g. so that they can be mounted together in the catheter, though it will be recognised that the position of the focussing element 86a can be adjusted in a distal or proximal direction
30 while still achieving an optical path 14 that passes the motor 80a and the rotatable optical element 83a. In the arrangement of figure 8a, the motor is mounted centrally on the longitudinal axis of the catheter, though it could be laterally offset if required. The light beam from the focusing element 86a is deflected twice by the two mirrors 88a, 88b of the angular coupling element 88 to fold the optical path back to the rotatable optical element
35 83a. The beam finally arrives at the micro-mirror 83a attached to the shaft 84a of the micro-

motor 86a without any physical obstruction such as by wires 87. During the beam scanning, the motor wires 87 will not show up in the optical path and as a result, there will be no shadow areas, as evidenced by the image as shown in figure 8d. An optical fibre 89 may serve as an optical conduit extending along the catheter alongside the control wires 87 thereby maintaining separation of the optical path 14 from the control wires. The folded arrangement of the optical path 14 results in the first portion 14a of the optical path intersecting the third portion 7 during at least a part of a circumferential scanning of the optical beam 7 but there are no structural features involved in this intersection. As with the arrangement of figure 8b, the scanning light beam 7 passes through the transparent walls of the catheter 81a.

The synchronization module 74 synchronizes the output of the wavelength sweep laser 76, the driving of the motor 80a or 80b, the driving of the pullback module 72 and data acquisition by the data acquisition unit 771, using control lines 74a, 74b, 74c and 76a. The synchronization module 74 generates a motor driving signal to the micromotor 80a, 80b directly based on a trigger signal of the laser output from module 76. The synchronization module 74 sends out trigger signals to the data acquisition module 77 on control line 74c to ensure that the data acquisition is synchronized to the beam scanning and laser output.

In the example of figure 7, the synchronization module 74 comprises an Arbitrary Waveform Generator (AWG) 740 and a micro controller 741. In one example, the synchronization module 74 may drive a synchronous micromotor 80a, 80b and trigger frame acquisition based on a 1.5 MHz OCT laser trigger output or sweep signal, where the laser performs 1.5 million wavelength sweeps per second. A wavelength sweep is used to gather the full A-line data set 34 for a position in the circumferential scan direction (the fast mechanical scan direction), e.g. to gather the data samples that can form one A-line data set 34 after Fourier transform. Each wavelength sweep may, for example, comprise 1000 samples which form the coherence fringes distributed upon wavelength. Then after Fourier Transform, these 1000 samples become 1000 complex samples.

Figure 9 shows a schematic diagram of the synchronization. The sampling rate of the AWG 740 is set to the same value as the sweep rate of the laser as 1.5 million samples per second. The two channel sinusoidal signals 90a, 90b which comprise a motor drive signal for driving the motor 80a, 80b are generated by the AWG 740 of the synchronization module 74. Each cycle of the sinusoidal signal 90a, 90b will realize one rotation of the

motor, which consists of 516 laser wavelength sweeps each corresponding to one A-line data set 34. One circumferential beam scan corresponds to 516 laser sweeps such that each A-line data set 34 corresponds to a circumferential dimension of 0.7 degrees of arc. In a typical application where a lumen of an organ is approximately 3 mm in diameter, the spatial size of a sample in the circumferential direction (i.e. the spatial extent of an A-line data set) is about 20 microns. The micro-controller 741 receives the laser sweep signal 91 and generates a frame trigger signal 92 after 516 laser sweep signal pulses 91 as a frame trigger to the data acquisition module 77. In such way, the laser 76 output, beam scanning and data acquisition is synchronized. Two different frames 93a, 93b are scanned at substantially the same circumferential and lumen longitudinal positions (i.e. with preferably at least 50%, 70% or more preferably at least 80% overlap accuracy as discussed above) respectively giving datasets for respective OCT images 94a, 94b and the phase signal can be compared sample by sample between the two frames to determine any positional changes induced in the object being scanned for each A-line dataset. The two frames 93a, 93b must be sufficiently separated in time that a desired pressure change has induced a consequential change in the position (displacement) of the object being scanned, but this time separation must not be so great as to lose the required degree of overlap of the A-line scan positions. With the high speed rotation of the beam 7, the successive frames 30, 31 used for phase processing may not be adjacent frames (i.e. where one follows immediately after another as the next circumferential scan), but may be selected a number of circumferential scans apart. The expression 'first frame' and 'second frame' or 'successive frames' therefore encompasses frames that can be separated by a number of intervening circumferential scans.

In the alternative arrangement described above using a broadband light source as the source of optical radiation, where multiple data samples may be captured by a sensor array or camera mounted as a detector in a spectrometer setup, the motor driving signal 90a, 90b is synchronized to a predetermined constant number of coherence fringes.

Figure 10 shows the effects of phase processing between two frames acquired at different pressures, shown as dataset 100a and dataset 100b. The imaging is stable enough for phase shift extraction. As a reference, mismatch was created between the two frames with A-line position mismatch clockwise and counter-clockwise. If the mismatch is e.g. one A-line circumferential spatial dimension corresponding to 0.7 degrees of angular mismatch, such a mismatch may lead to between 6 and 18 micrometres circumferential

- mismatch for a typical lumen dimension, which may be still too large compared to the spatial size of one data sample (approximately 20 microns in the circumferential dimension and approximately 10 micrometres in the beam axial dimension (depth into the structure being imaged), and the phase shift cannot be extracted at all as seen in the datasets 101 and 102 corresponding to one A-scan dimension clockwise and anticlockwise respectively. Dataset 103 corresponds to the phase information when stable imaging is achieved, with at least 80% overlap between the A-line spatial locations of the first and second frames 93a, 93b.
- 10 The stimulus module, e.g. infusion module 73, creates a mechanical excitation of the structure 2 being imaged. As depicted in figure 11, a distal intraluminal pressure change 110 at the distal region 6 of the imaging catheter apparatus 1 is induced by a proximal infusion rate modification 111 at the infusion module 73 by the fluid delivery mechanism 15. The infusion media may be liquid such as X-ray contrast media or saline, or may be
- 15 gaseous such as medical grade air, depending on the organ being imaged. The infusion module may comprise a linear motor stage 112 and a syringe 113 that injects saline into the organ lumen 3 through the Y-connector 12 and the working channel 11 (see also figure 7). The barrel of the syringe 113 may be attached to a stable part of the linear motor stage 112 and the plunger 114 is pushed by the moving part of the linear motor stage 112. The
- 20 infusion rate 111 and volume may be controlled by the moving speed and distance of the linear motor stage separately. The intraluminal pressure 110 will increase when increasing the infusion rate and decrease when decreasing the infusion rate. The infusion module 73 produces modulated liquid flushing or modulated air inflation, which are triggered by the synchronization module 74. The air inflation can be realized by using
- 25 medical grade air rather than liquid. The air inflation module can also be realized by modulating the medical compressed air output using a pneumatic valve. In a general aspect, the infusion module comprises a pump configured to deliver a fluid pressure change.
- 30 With further reference to figure 7, in order to improve the phase shift extraction, a calibration mirror 740 can be used in the interferometer module 74 for phase calibration. To achieve a high wavelength sweep, the laser couples part of the output into a long fiber stage that will delay such output compared to the original output. In such way, each wavelength sweep becomes two sweeps thus increasing the sweep rate. However, the
- 35 delay is normally unknown which leads to sampling offset of the OCT dataset, which will

show as a time delay between different coherence fringe signals. As a consequence, the coherence fringe signals of one wavelength sweep may have a shift compared to the fringe signals of another sweep. Such a sampling offset may also induce phase noise and affect the phase shift measurement after the Fourier transform. Figure 12 illustrates working principles of the calibration mirror 740 to improve phase stability of the OCE. Figure 12a shows the amplitude of one A-line signal as a function of depth where the sharp peak corresponds to the location of the calibration mirror 740. Figure 12b shows the coherence fringe signal of the calibration mirror 740 acquired by the data acquisition for four sweeps. Due to the sampling offset, offsets between four coherence fringe signals can be clearly seen. By comparing the offsets between different coherence fringe signals from the calibration mirror, the sampling offset can be found and compensated for. In this example, the sampling offsets were found to be -20.7, -24.5, and -31.5 compared to the first sweep. The compensation can be simply done by shifting the entire coherence fringe signals to make them overlapping with each other. Then after the Fourier transform, the phase noise can be improved. Figures 12c and 12d show the coherence fringe signals before and after the compensation, figure 12c showing the coherence fringe signals overlaid with the sampling offset and figure 12d showing the coherence fringe signals after phase shift compensation. Figures 12e and 12f show the noise of the phase shift before and after the compensation. The phase shift in this case was extracted from two adjacent A-line sweeps and the phase shift should be to zero since there was no mechanically induced displacement in the imaged structure.

To acquire a 2D endo-OCE image of one cross section of the organ lumen, Endo-OCE images have to be acquired when there is pressure change. At least two OCT frames have to be acquired at two different intraluminal pressures with a proper time delay (frame interval ≥ 1). The phase shift can be extracted from these two frames to create a strain image. In the illustrated examples, the OCT images were acquired at approximately 3000 frames per second, corresponding to the motor 80a, 80b rotating at approximately 3000 revolutions per second, when there was pressure change. The frame interval was chosen to be 20 frames meaning that the phase shift was extracted between two frames acquired with a time difference of approximately 6.7 ms which was long enough to induce a strain in the organ structure.

Figure 13 shows Endo-OCE images of a Poly Vinyl Alcohol (PVA) hydrogel phantom with 3 freeze-thaw cycles. An inclusion made of VeroWhitePlus (VWP) was implanted inside

the phantom. The infusion media was saline, and the pressure change was around 2.3 mmHg between the two frames, which was induced by changing the infusion rate. Figure 13a is an OCT image showing the morphological structure of the phantom. Figure 13b is the phase shift extracted from the two frames. Figure 13c is the strain image and figure 13d is the strain image averaged over 20 strain images to suppress noise. The VWP stiff inclusion can easily be identified in the strain image due to its smaller strain compared to the surrounding PVA phantom.

Figure 14 shows strain imaging of the same phantom but using air as the infusion medium.

The stiff inclusion can still be identified.

Figure 15 shows Endo-OCE imaging of three coronary arteries. Intraluminal pressure change was around 8 mmHg. Figures 15(a) to 15(c) show the OCT images that give structural detail of the artery wall. Figures 15(d) to 15(f) show the phase shifts extracted between two frames with a 20-frame interval. Figures 15(g) to 15(i) show the strain images calculated as the gradient of displacement over radius. Figures 15(j) to 15(l) show strain averaged over 20 strain images. The stiff calcified plaque (highlighted with star marks '*') that shows a small strain can clearly be distinguished from the surrounding healthy artery wall.

To realize 3D Endo-OCE imaging of an entire organ lumen or a length thereof, the pullback module 72 can be used to change the longitudinal position of the catheter 1 within the lumen 3. To maintain the required overlap between two frames for phase processing, the pullback could either be implemented as a step-by-step or intermittent pullback at times when no imaging data is being gathered, or as a slow continuous pullback. When using a step-by-step pullback, the pullback is de-activated when the mechanical excitation is activated to allow gathering of data for the at least two frames to be phase compared. During this period, the stress strain phenomena is imaged by Endo-OCE. When the mechanical excitation is deactivated or off e.g. no intraluminal pressure change, the pullback module is activated. In general, the catheter may stop at one location to acquire the strain induced by the infusion and then move to the next longitudinal location in the lumen.

Figure 16 shows a schematic diagram of 3D imaging control using step-by-step pullback.

The infusion and pullback are both triggered by the synchronization module 74 which

suspends pullback with the pullback signal 164 and triggers an infusion pressure / rate change with signal 161, resulting in an intraluminal pressure change 162. During this period, the endo-OCE imaging scans are implemented with, e.g. frame triggers 163.

- 5 Another solution for 3D imaging as mentioned above is to use a slow pullback and acquire data continuously during pullback. In such case, the pullback speed should be slow enough to ensure that the longitudinal distance between two successive frames used for phase processing is <50%, and preferably less than 30%, more preferably less than 20%, of the transverse resolution e.g. the size of the gaussian beam waist of the OCT beam, to
10 ensure that the at least 50%, 70% or at least 80% overlap conditions are met.

Although the apparatus exemplified in figure 7 uses an infusion module 73 as a stimulus module to deliver mechanical excitation to effect displacement in the object being imaged, in some circumstances it may not be necessary to implement such extrinsic displacement,
15 where there is intrinsic displacement in the object being imaged. Such intrinsic displacement could for example, be effected by natural pressure changes in the circulatory system caused by the subject's heart, or natural pressure changes induced by respiration of the subject, e.g. by passive tidal breathing or passive blood pressure change or motion of an organ itself. In such a case, the data of the first and second frames 30, 31 should
20 be separated by an appropriate interval 32 to ensure sufficient displacement of the object to provide an OCE image. The catheter may include a pressure sensor to monitor the natural pressure changes.

Although the apparatus exemplified in figures 7 and 11 illustrates an infusion module 73
25 as a stimulus module, other forms of mechanical excitation device can be used as a stimulus module instead of an infusion module. For example, a remotely controllable, bendable or deflectable, catheter tip arrangement may be deployed, as exemplified in figures 17 and 18. Alternatively, an inflatable balloon could be used, which can also open, e.g. the oesophagus lumen and hold a catheter for imaging. This balloon can also provide
30 the stimulus to induce stress.

With reference to figure 17a, the imaging catheter apparatus 170 comprises a distal region 176 having a steerable head 171 which can be angularly / laterally deflected from the axis of the catheter portion 172 by way of a neck region 173 which is controllable from a
35 proximal end of the catheter. As seen in figure 17b the steerable head 171 can be

angularly / laterally deflected by the neck region 173 so that the head 171 collides with and compresses, distorts and/or deflects a lumen wall 8 or other body structure at wall position 178. The lumen wall 8 may, for example, be that of the oesophagus. The pushing force of the steerable head 171 towards the lumen wall 8 can create the required stress or displacement for elastography imaging, thus capturing an oesophagus cancer (or some other disease)

The steerable head 171 may comprise a rigid capsule containing the optical elements and motor drive mechanism as exemplified in, e.g. figures 8a, 8b, 8e and as seen in figure 18a. A steering mechanism 180 may control the neck region 173 from the proximal end of the catheter, for example as shown in figure 18b. With reference to figure 18b, the steering mechanism 180 may comprise one or more control wires 181 extending along the lumen of the catheter 172 to the neck region 173. The control wires 181 may be coupled to a motor drive unit 182 at the proximal end of the catheter. The motor drive unit 182 is preferably in communication with a synchronization module 74 as exemplified in figure 7 and may serve to provide a coarse displacement function to the neck region to bring the steerable head 171 into pressure contact with the lumen wall portion 178 and may provide a displacement modulation (e.g. pulsed or oscillatory) to vary the pressure applied on or displacement applied to the lumen wall portion in similar manner to the infusion rate modulation 111 described in connection with figure 11. The coarse displacement and displacement modulation may, of course, be combined as a variable displacement.

As seen in figure 18c, the steering mechanism 180 preferably resides outside the body 185 during scanning, at the proximal end 5 of the catheter apparatus 170.

The catheter-based imaging device as described above can be provided within extremely small catheters, e.g. below 3 mm outside diameter and down to 1.2 mm in outside diameter (OD) or less. In particular, the catheter-based imaging device as described herein can be deployed in any suitable catheter. E.g. for coronary artery imaging this may be less than 1.2 mm, e.g. 0.8 mm OD; for lung imaging, the catheter size may be <1.6 mm OD; for GI and oesophagus imaging the catheter size may be < 20 mm e.g. between 1.0 mm and 13 mm OD.

In a general aspect, the synchronization module may drive the motor(s) 80a, 80b and 112 directly to ensure each frame has a constant number of A-line samples corresponding to

the laser output within the same angular scanning range of the catheter. The driving signal of the motors can be varied to be synchronized with the laser output to ensure each frame has a constant number of A-lines that correspond to a constant number of laser outputs with the same angular range of the sample scanned. The catheter has been described
5 with a micro motor and mirror within the catheter at the distal end but could be replaced with a motor at or toward the proximal end driving the mirror at the distal end via a drive fibre.

Other embodiments are intentionally within the scope of the accompanying claims.

CLAIMS

1. An imaging system comprising:
a catheter-based optical imaging device configured to obtain multidimensional
5 optical coherence tomographic morphological image data of an object disposed around a
catheter and including a controller configured to enable successive scans of the
morphological image data to be sufficiently spatially co-registered with one another to
provide strain or elasticity image data of the object.
- 10 2. The imaging system of claim 1 including:
a catheter defining an optical path structure couplable to a source of optical
radiation and a detector, the optical path structure configured to direct optical radiation
radially outwards from the catheter to an object in which the catheter is disposed and to
receive responsive image data radiation signals from the object;
15 a synchronization module configured to trigger a first circumferential scan of the
optical radiation to obtain a first frame of first image data samples at a plurality of
circumferential positions at a first time, and to trigger a second circumferential scan of the
optical radiation to obtain a second frame of second image data samples at a plurality of
circumferential positions at a second time, after a displacement of the object,
20 the first circumferential scan and the second circumferential scan being timed such
that the first frame of first image data samples is spatially co-registered with the second
frame of second image data samples at least in the circumferential direction and in the
catheter longitudinal direction such that a phase change in the optical coherence
tomographic image data can be used to determine strain in, and/or elasticity of, the object.
25
3. The imaging system of claim 2 in which the spatial co-registration comprises an at
least 50%, 70% or 80% spatial overlap of each of the corresponding first and second
image data samples in the circumferential and catheter longitudinal directions.
- 30 4. The imaging system of claim 2 further including a stimulus module configured to
deliver a mechanical excitation to the object around the catheter at a time between the
first and second circumferential scans.
5. The imaging system of claim 4 in which the stimulus module comprises a pump
35 configured to deliver a fluid pressure change to a lumen of the object via the catheter.

6. The imaging system of claim 5 in which the pump is configured to deliver one of a liquid or a gas via a working channel associated with the catheter to a site at a distal region of the catheter.
- 5
7. The imaging system of claim 5 in which the pump is configured to deliver a fluid pressure change by changing a flow rate of fluid through the catheter.
8. The imaging system of claim 2 in which the synchronization module comprises a motor drive signal generator configured to provide a motor driving signal synchronized with an optical radiation sweep signal of the source of optical radiation that is timed with each scan of the optical radiation through a plurality of wavelengths.
- 10
9. The imaging system of claim 8 in which the synchronization module further comprises a frame trigger signal generator configured to generate a frame trigger signal synchronized with predetermined timing positions of the motor driving signal.
- 15
10. The imaging system of claim 2 in which the synchronization module comprises a motor drive signal generator configured to provide a motor driving signal synchronized to a predetermined constant number of coherence fringes.
- 20
11. The imaging system of claim 8 in which the imaging system further includes an axial displacement mechanism configured to effect longitudinal displacement of the catheter along its longitudinal axis and the synchronization module is configured to generate a pullback timing signal to control longitudinal displacement of the catheter.
- 25
12. The imaging system of claim 11 in which the axial displacement mechanism is configured to effect continuous longitudinal displacement of the catheter during circumferential scans, the longitudinal displacement being effected at a velocity sufficiently slow that the longitudinal displacement of the optical path structure in the catheter between the first circumferential scan and the second circumferential scan after displacement of the object is less than a distance required to maintain at least 50% spatial overlap of the first and second image data samples.
- 30

13. The imaging system of claim 2 in which the catheter has an outer diameter of 3 mm or less.

14. The imaging system of claim 2 in which the catheter includes a motor in the distal region of the catheter configured to rotate an optical element to direct the optical radiation radially outwards from the catheter in a plurality of angular directions and to receive the responsive image data radiation signals.

15. The imaging system of claim 12 in which the optical path structure further includes a reflecting element in the catheter distal of the rotatable optical element, the optical path structure providing a folded optical path which extends past the motor and rotatable optical element and towards a distal end of the catheter, through the reflecting element and towards the proximal end of the catheter to the rotatable optical element.

16. The imaging system of claim 2 in which the optical path structure includes an interferometer having a calibration mirror configured to provide a sharp peak in each A-line dataset and a processor configured to use the coherence fringes of the calibration mirror to correct a sampling offset between different wavelength sweeps of the optical radiation when acquiring the data samples.

20

17. The imaging system of claim 4 in which the stimulus module comprises a steerable catheter head configured for lateral deflection from a longitudinal axis of the catheter to deliver a mechanical excitation to the object around the catheter at a time between the first and second circumferential scans.

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18. A catheter for optical imaging comprising:

a motor in the catheter coupled to rotate a rotatable optical element about an axis substantially on or parallel to the longitudinal axis of the catheter, the optical element being located on a distal side of the motor relative to the proximal end of the catheter;

30 the catheter further comprising structures to define an optical path having a first portion extending between a proximal end of the catheter and a distal end of the catheter, past the motor and the rotatable optical element, and a second portion extending between the distal end of the catheter and the rotatable optical element;

35 the optical path having a third portion extending radially outwards from the rotatable optical element and from the second portion,

the rotatable optical element being configured to effect scanning of the third portion of the optical path about the longitudinal axis of the catheter.

5 19. The catheter of claim 18 further comprising an angular coupling element disposed at the distal end of the catheter and optically coupling the first and second portion of the optical path.

10 20. The catheter of claim 19 in which the angular coupling element comprises one or more reflecting interfaces for coupling the first portion of the optical path and the second portion of the optical path.

15 21. The catheter of claim 20 in which the angular coupling element comprises a pair of reflecting elements respectively for coupling the first portion of the optical path and the second portion of the optical path by way of an optical path transverse to both the first portion and the second portion and to the longitudinal axis of the catheter.

22. The catheter of claim 18 further including a focussing element disposed parallel to the motor for conveying the first portion of the optical path past the motor.

20 23. The catheter of claim 18 further including an optical conduit extending along the catheter alongside control wires for the motor, the optical conduit comprising a structure providing at least some of the first portion of the optical path and maintaining separation of the optical path from the control wires of the motor.

25 24. The catheter of claim 18 in which the first portion of the optical path and the third portion of the optical path intersect during at least a part of the scanning of the third portion of the optical path about the longitudinal axis of the catheter.

30 25. The catheter of claim 19 in which the optical path is folded by less than 180 degrees between the first and second portions.

26. The catheter of claim 25 in which the angular coupling element comprises a reflecting element orthogonal to the longitudinal axis of the catheter.

27. The catheter of claim 19 in which at least one of the angular coupling element and the rotatable optical element is a focussing element.

28. A method of generating multidimensional optical coherence tomographic morphological image data of an object disposed around a catheter comprising:

5 deploying a catheter-based optical imaging device within the object;

performing successive circumferential scans of the object that are sufficiently spatially co-registered with one another to provide strain or elasticity image data of the object.

10

29. The method of claim 28 comprising:

defining, in the catheter, an optical path structure coupled to a source of optical radiation and a detector, the optical path structure directing optical radiation radially outwards from the catheter to the object in which the catheter is disposed and receiving responsive image data radiation signals from the object;

15

triggering a first circumferential scan of the optical radiation to obtain a first frame of first image data samples at a plurality of circumferential positions at a first time, and triggering a second circumferential scan of the optical radiation to obtain a second frame of second image data samples at a plurality of circumferential positions at a second time, after a displacement of the object, the first circumferential scan and the second circumferential scan being timed such that the first frame of first image data samples is spatially co-registered with the second frame of second image data samples at least in the circumferential direction and in the catheter longitudinal direction such that a phase change in the optical coherence tomographic image data can be used to determine the strain in, and/or elasticity of, the object.

20

25

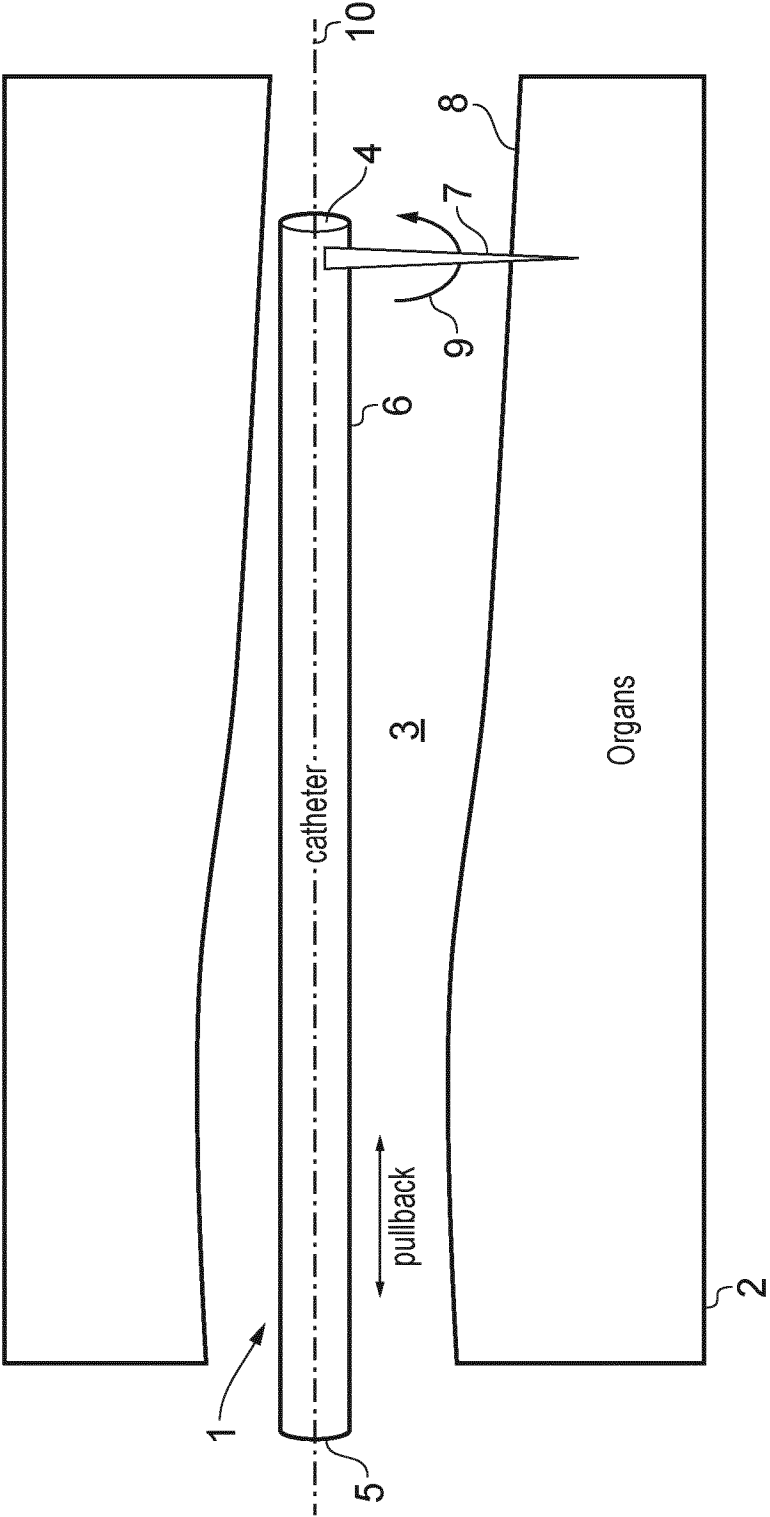


FIG. 1

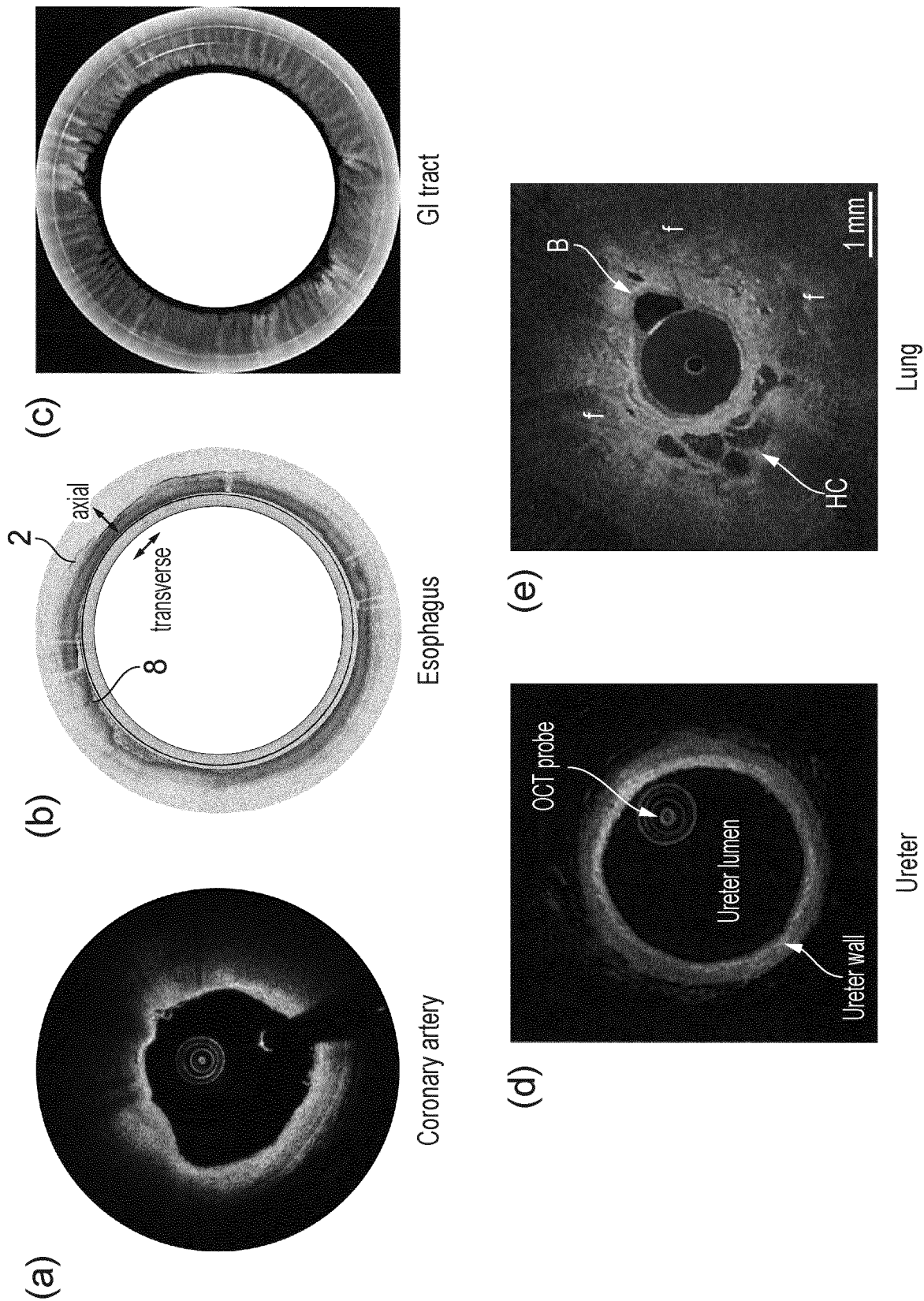


FIG. 2

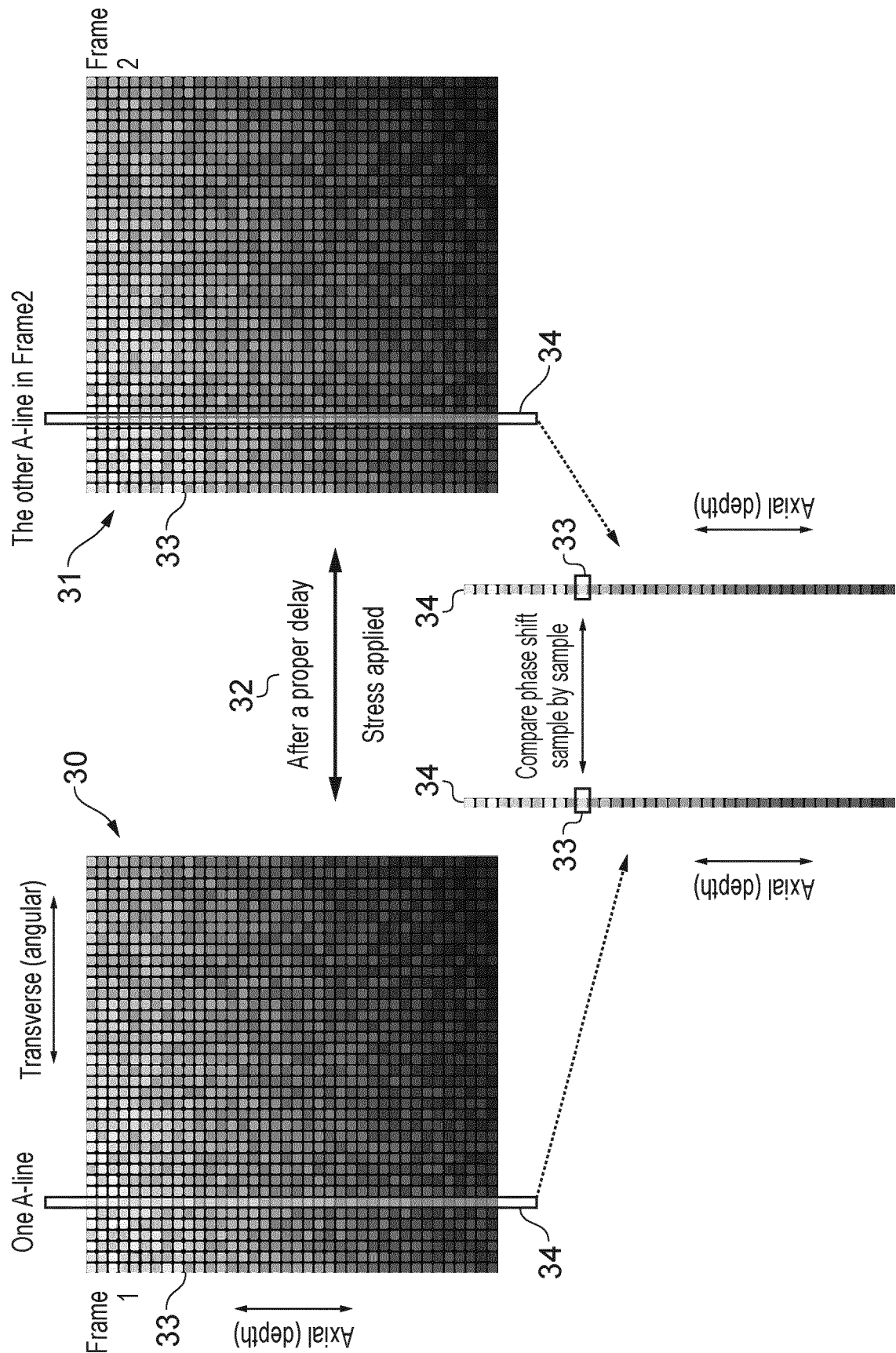
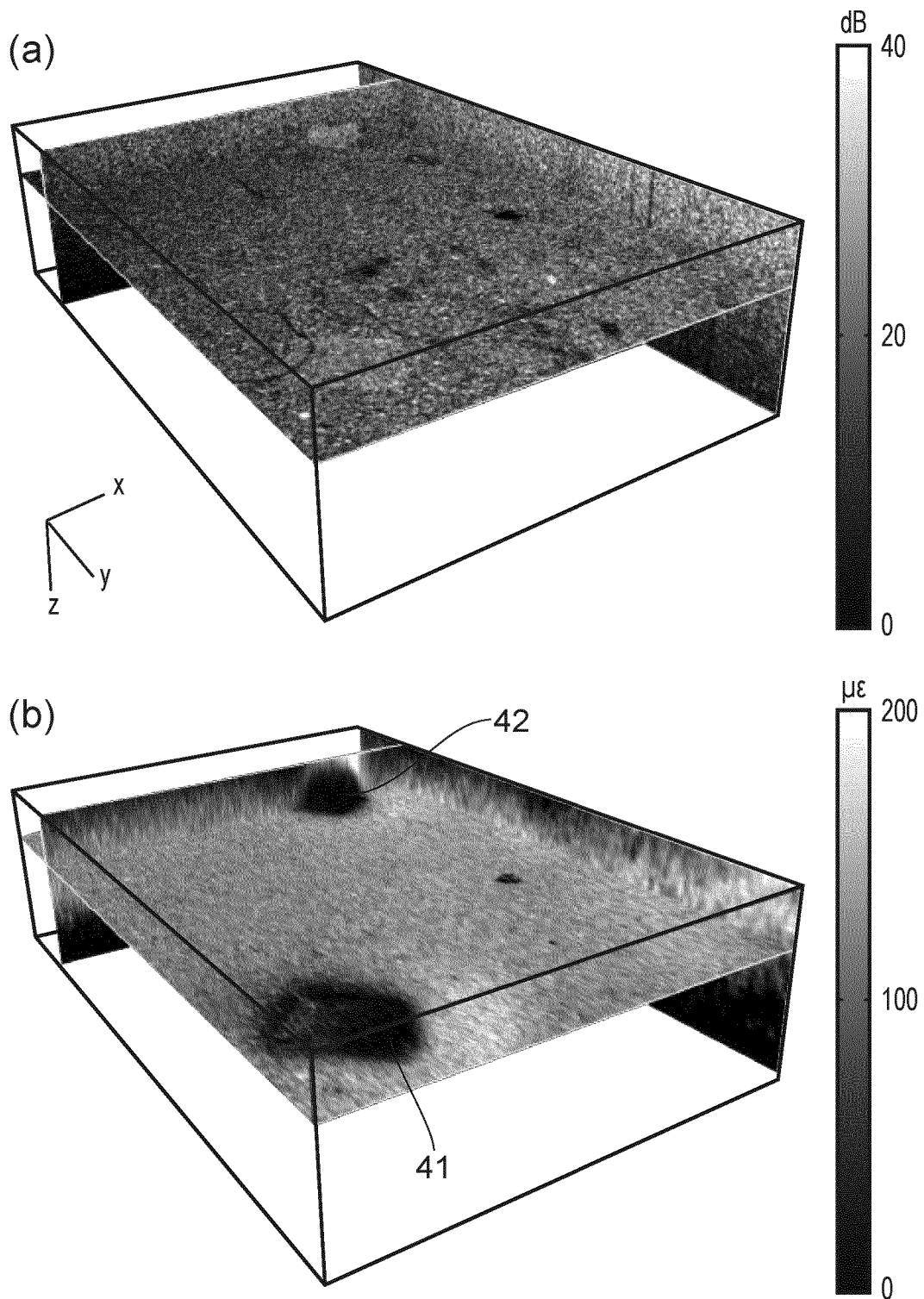


FIG. 3

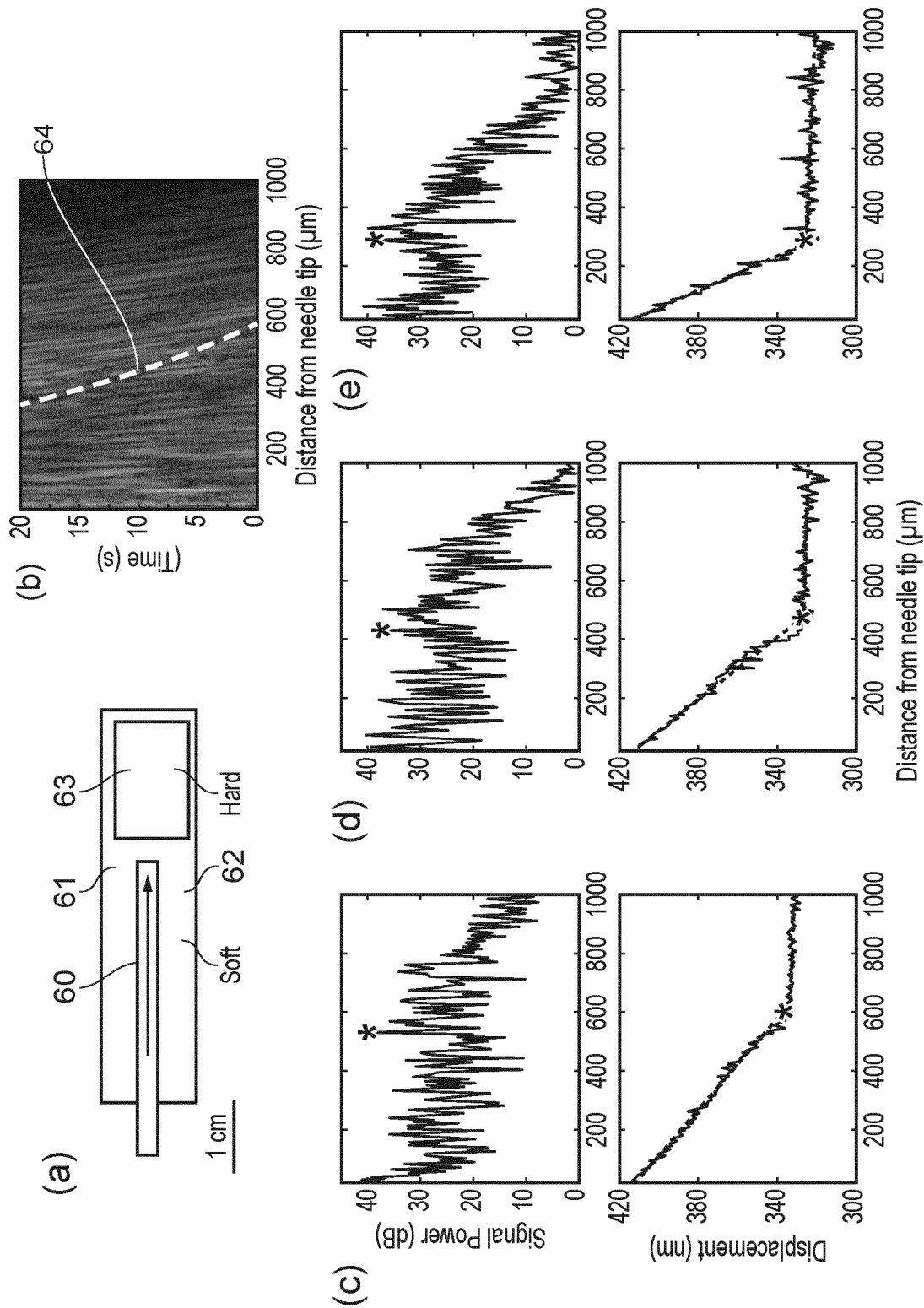
4/24



(a) Is conventional OCT image showing the structure of the phantom and (b) is the strain image shows the stiffness information, where the stiff area shows much smaller strain - dark area.

FIG. 4

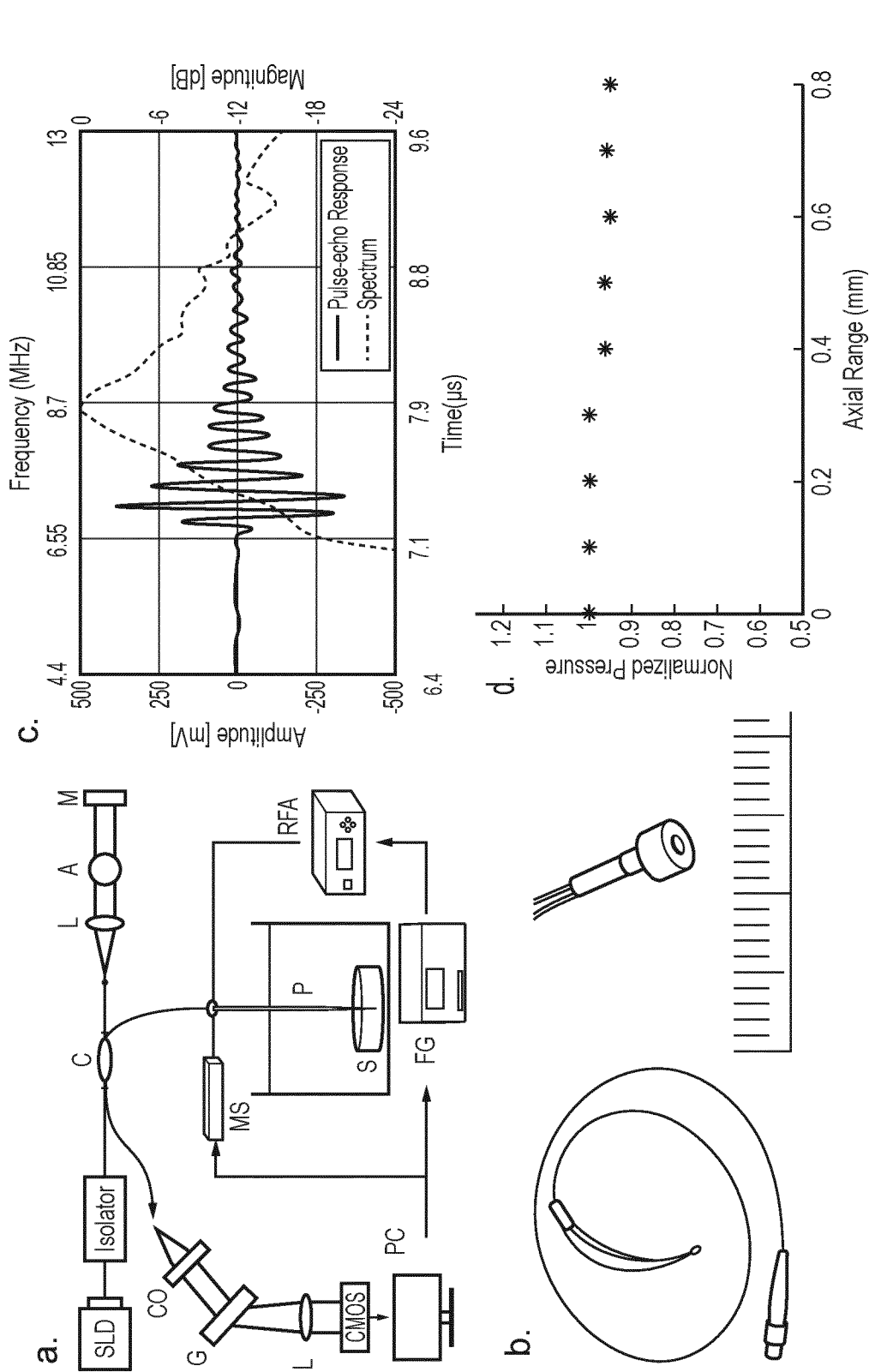
5/24



(a) Schematic of probe insertion into phantom; (b) motion-mode image (dashed line indicates interface); OCT A-scans and measured displacements at distances (c) 570 μm; (d) 450 μm; and (e) 300 μm from the inclusion. The stars denote the locations of interfaces, and the black lines indicate the linear fits used to approximate strain.

FIG. 5

6/24



(a) Overview of ARFI OCE system set up. C: collimator, L: lens, A: attenuator, M: mirror, G: grating, MS: mechanical stage, RFA: radio frequency amplifier, P: probe, S: sample, FG: function generator. (b) Probe design (left). probe head including a rink transducer and optical elements inside (right). (c) Transducer frequency and echo characterization. (d) Transducer axial force characterization.

FIG. 6

7/24

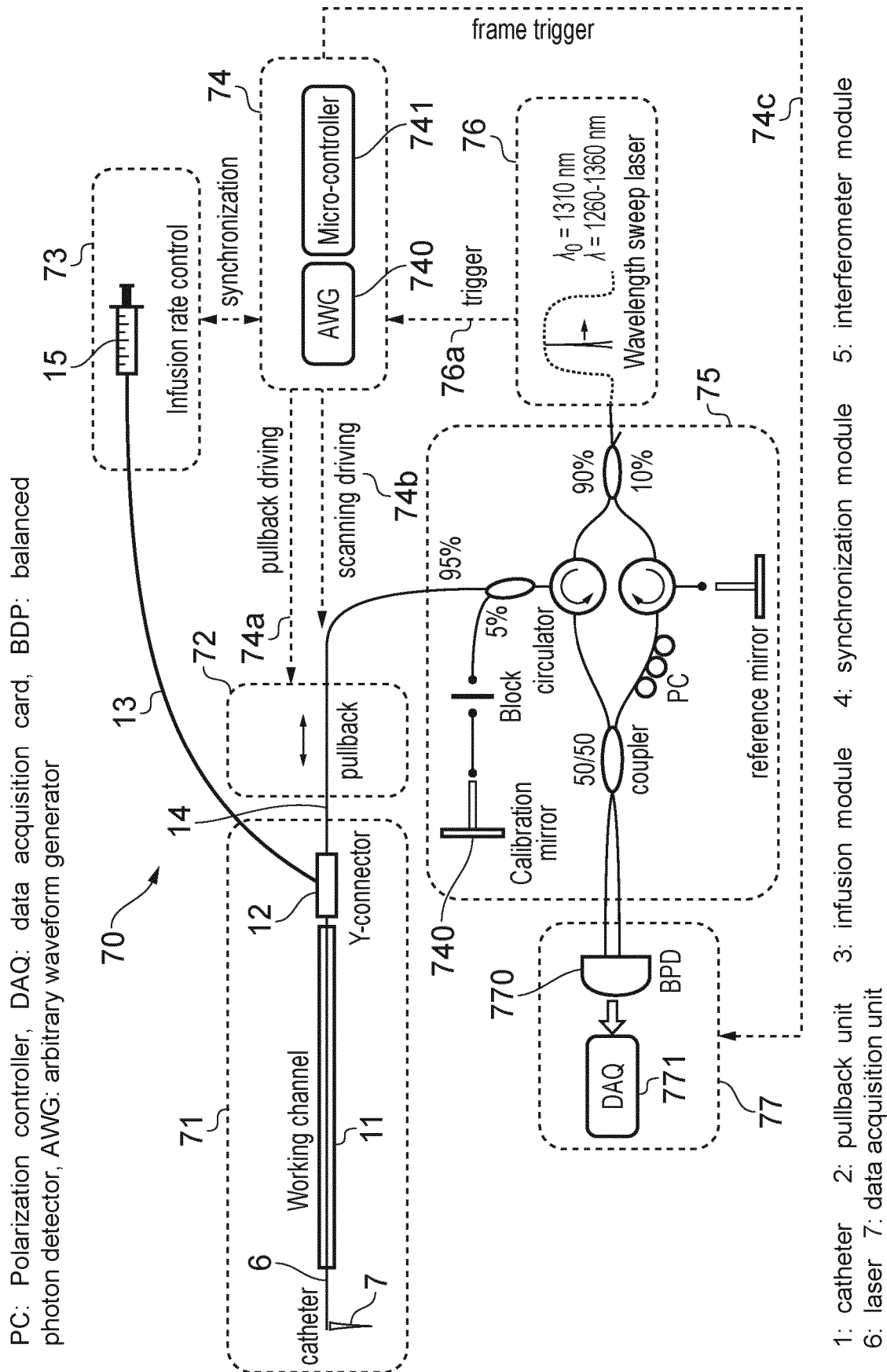
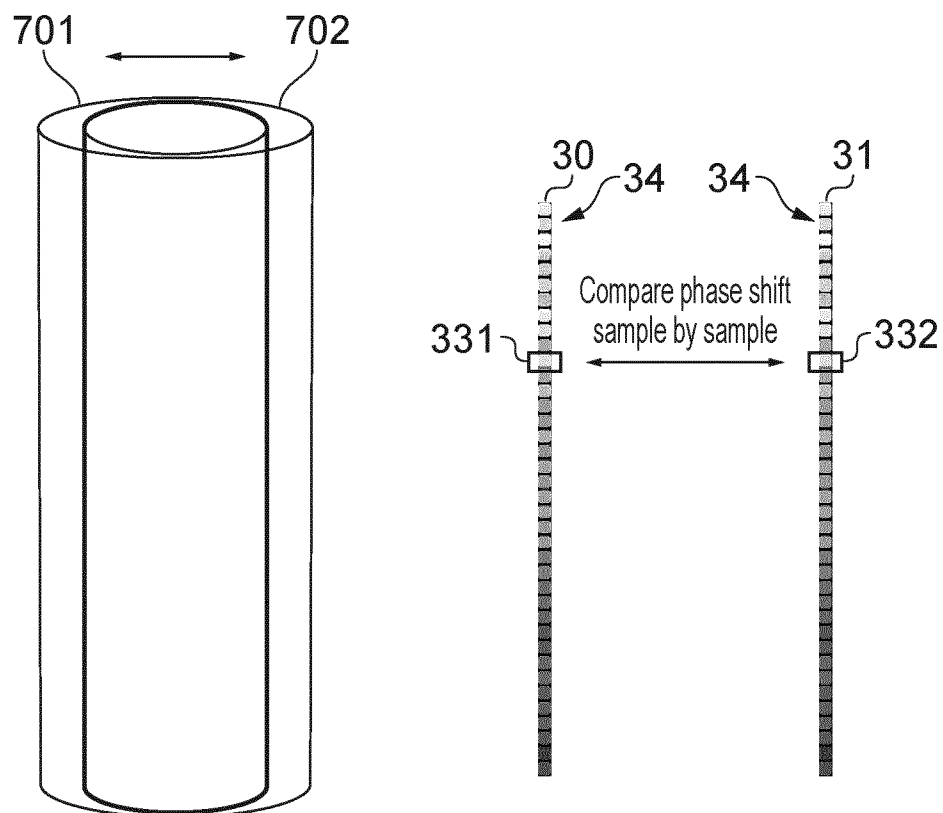


FIG. 7

8/24



These two A-lines corresponds to two Gaussian beam that should be overlapped, then you can compare the phase shift

FIG. 7a

9/24

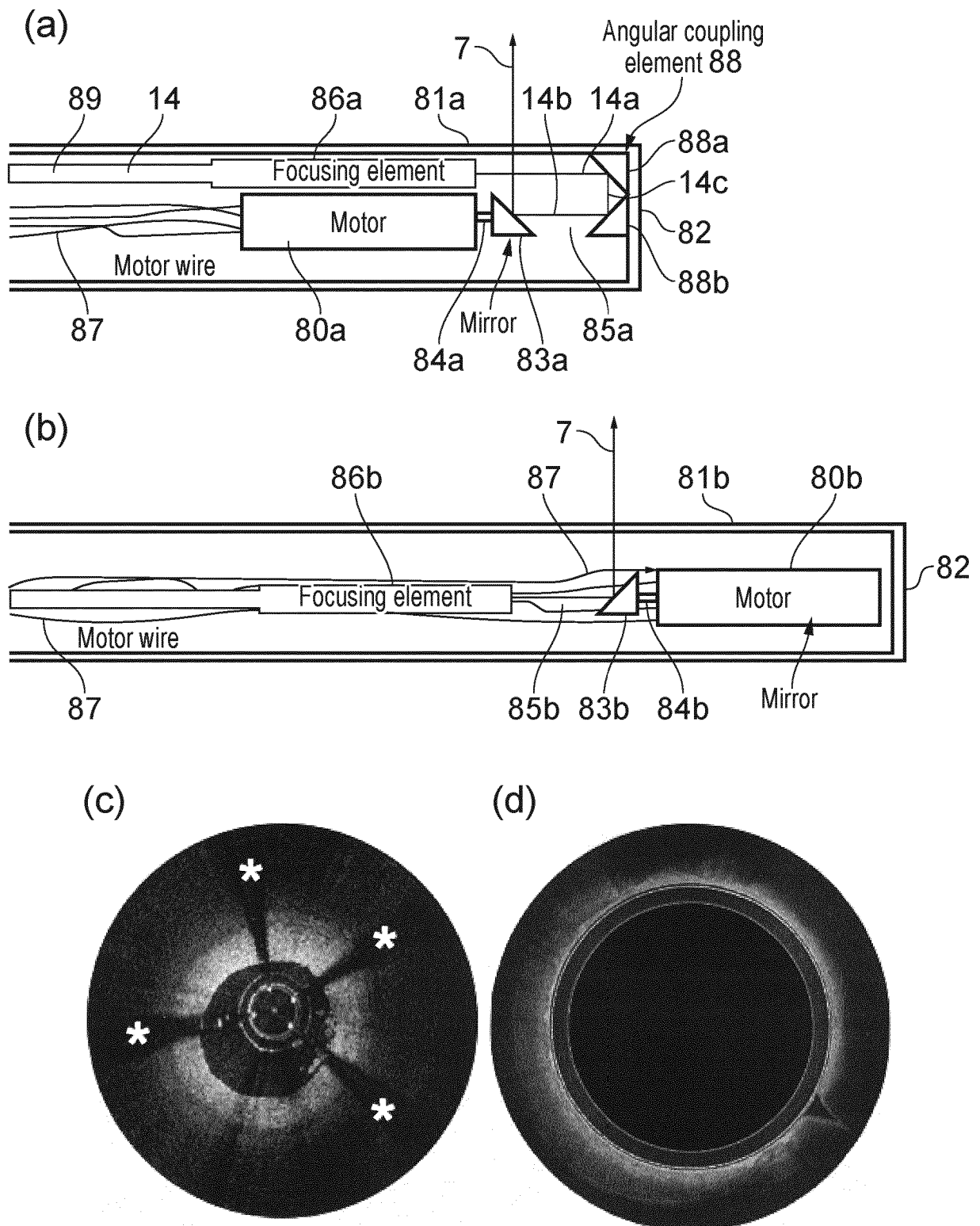


FIG. 8

10/24

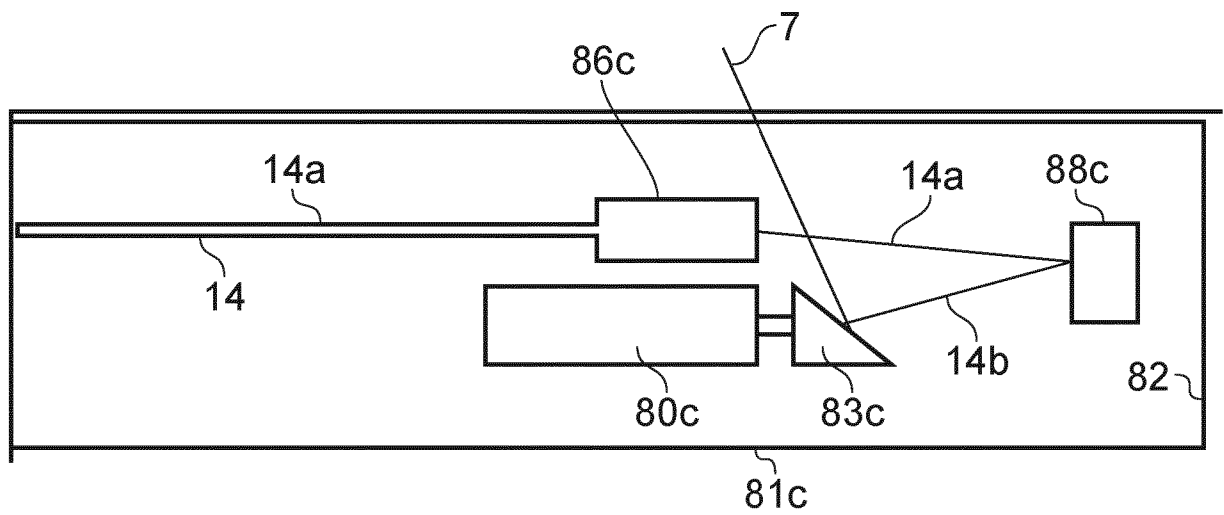


FIG. 8e

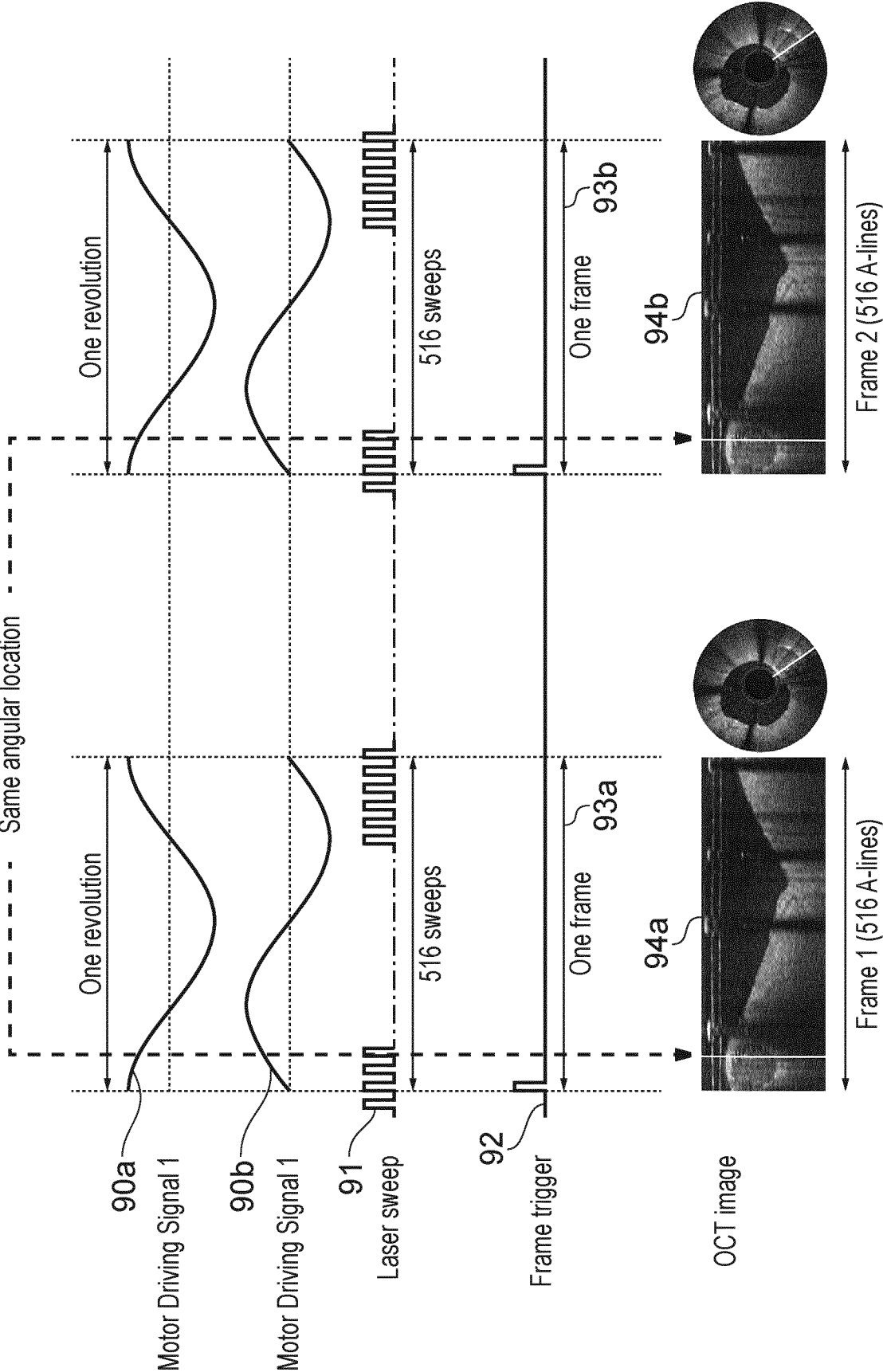


FIG. 9

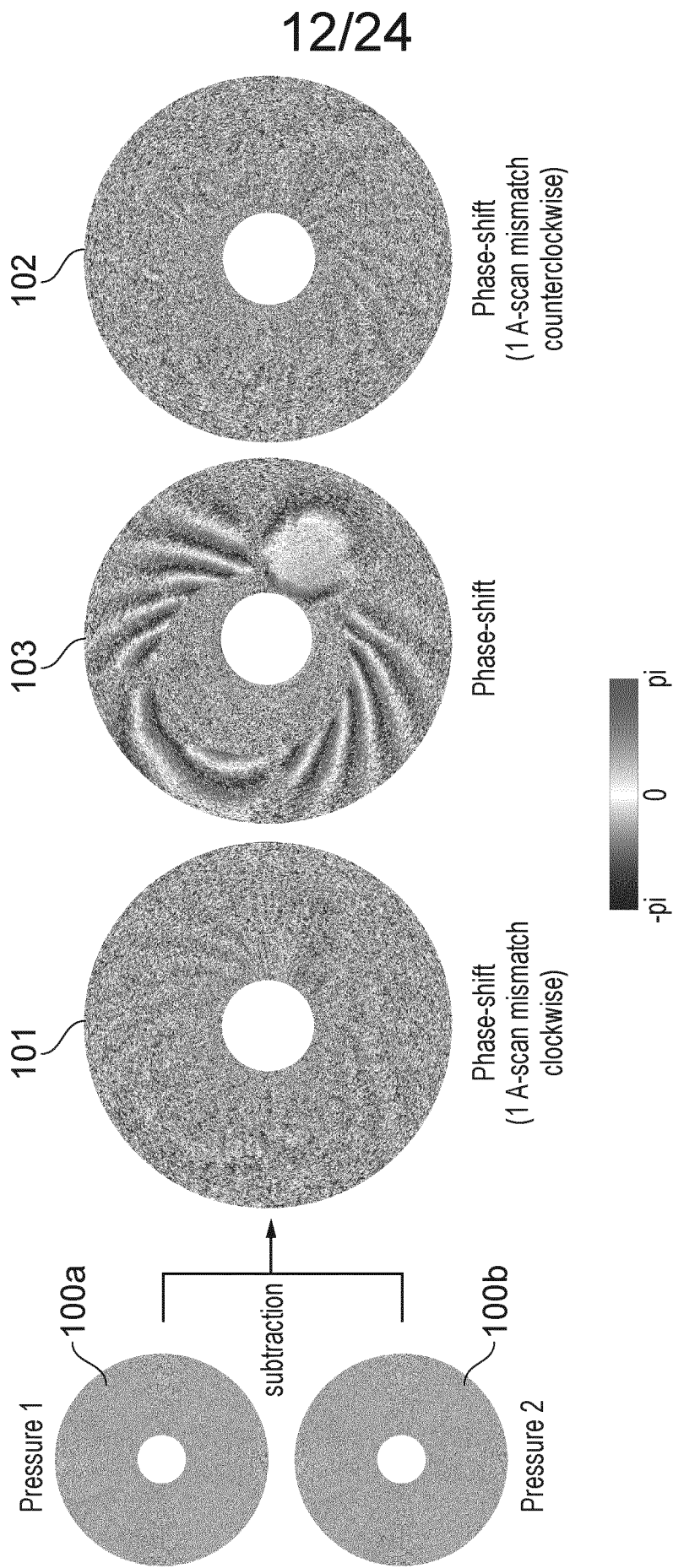


FIG. 10

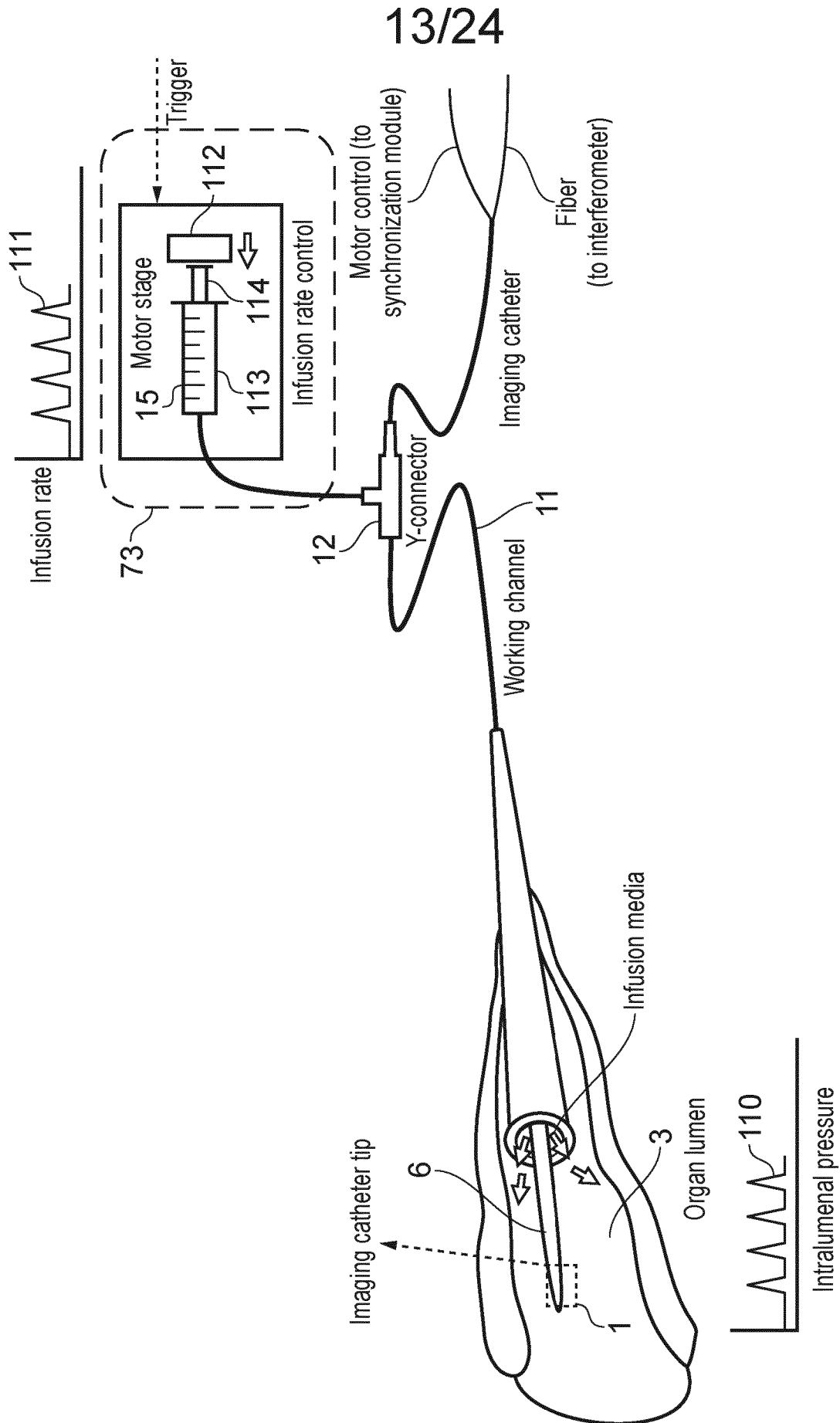
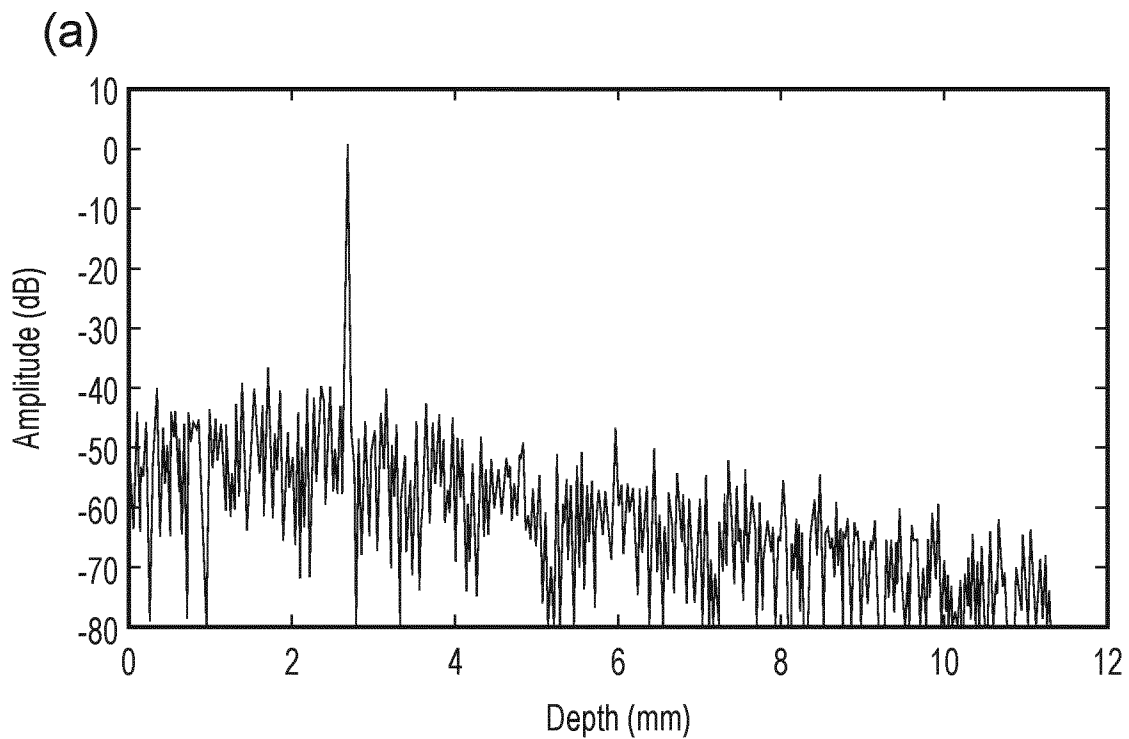
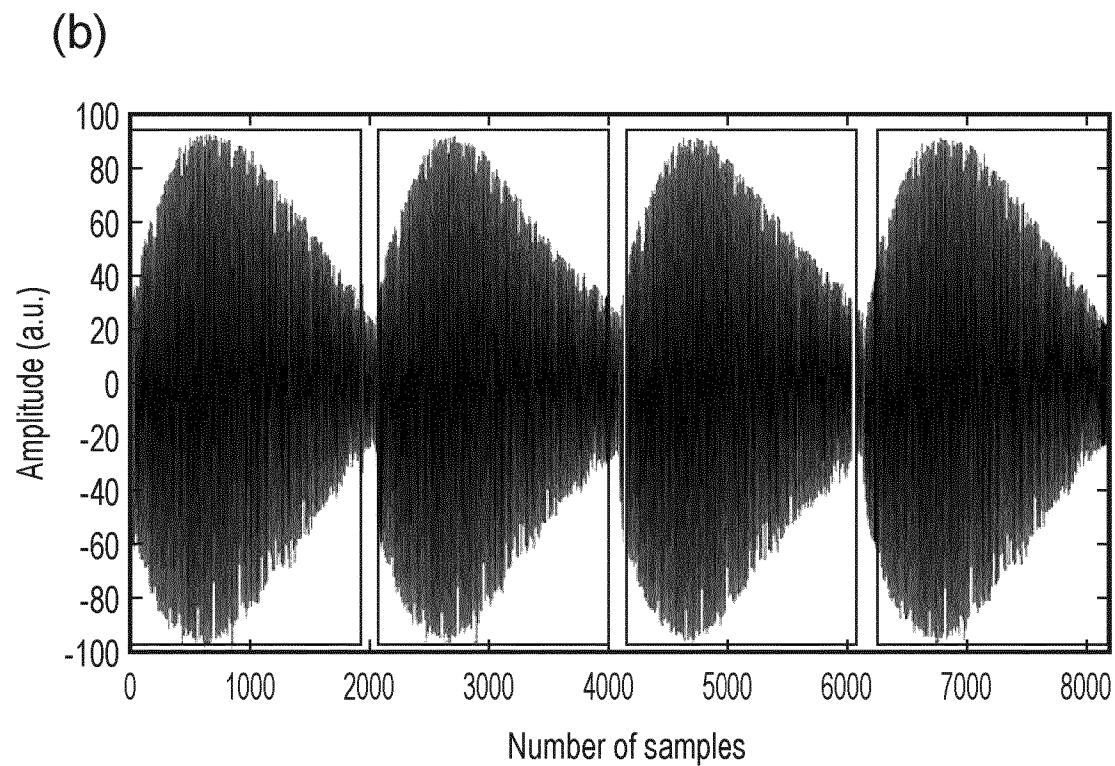


FIG. 11

14/24



Plot of the amplitude of one Aline. Peak shows the location of the calibration mirror,



Coherence fringes signal of four sweep.

FIG. 12

15/24

(c)

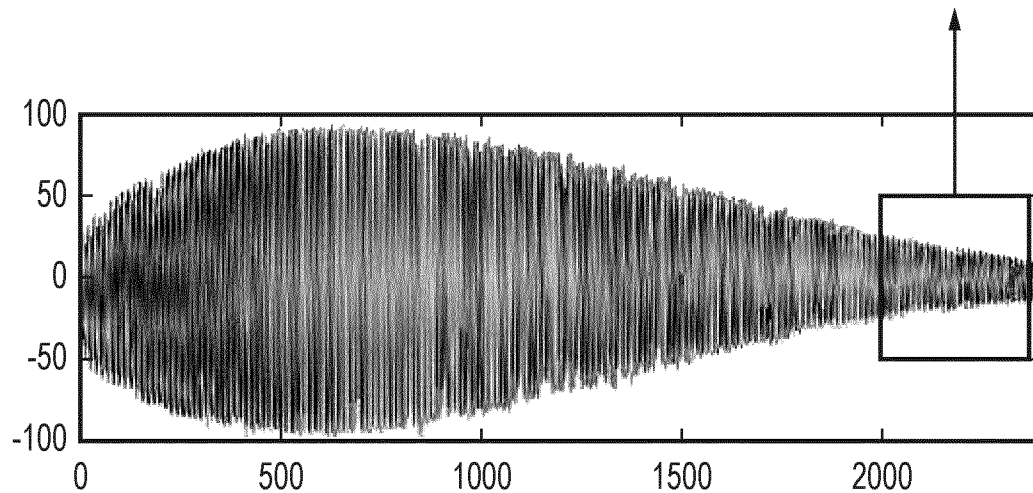
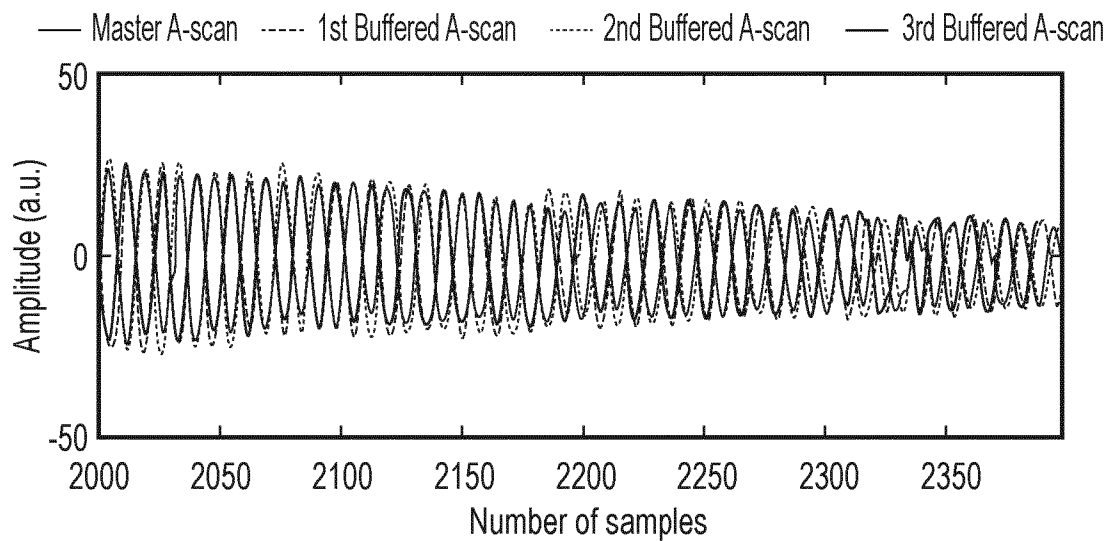
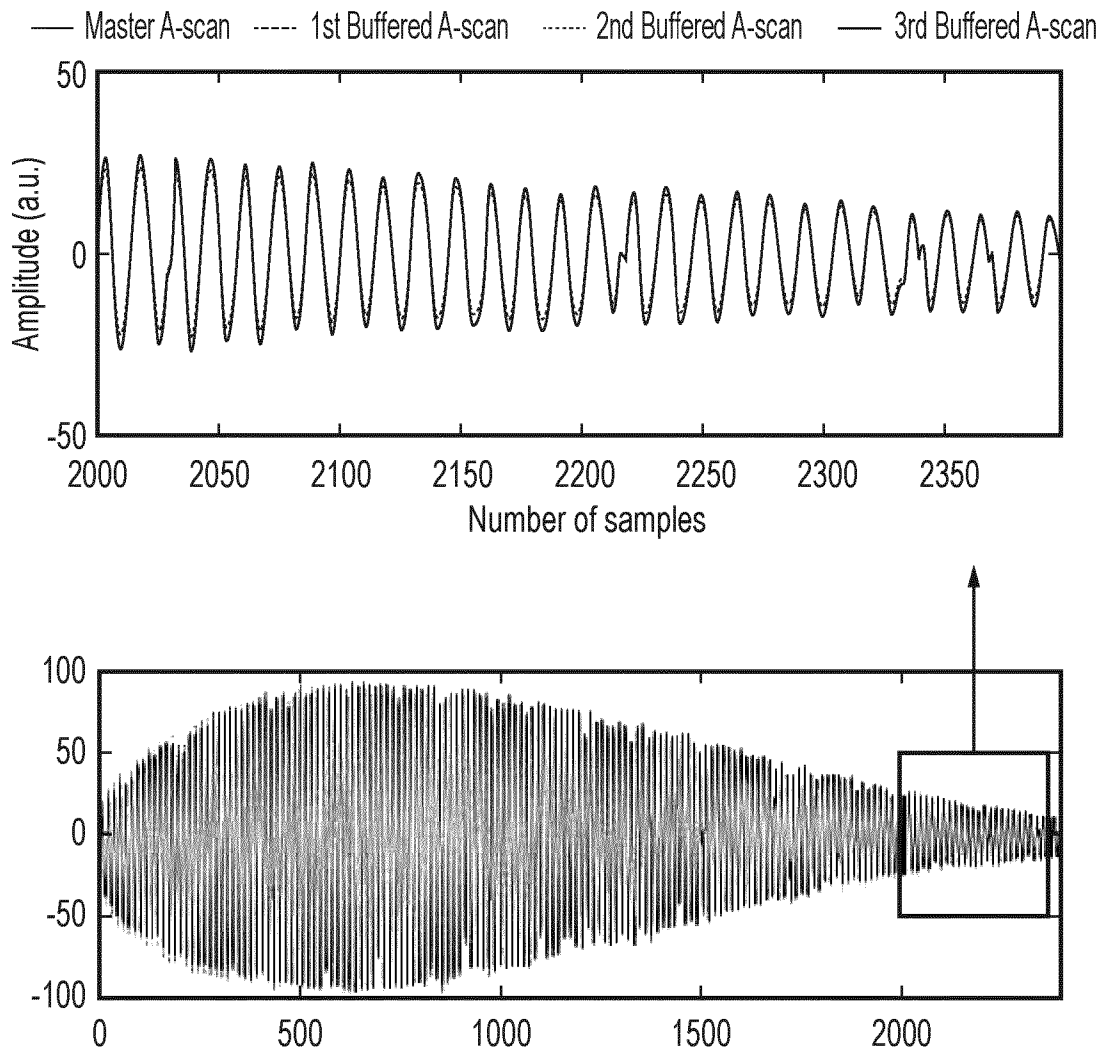


FIG. 12 (Continued)

16/24

(d)

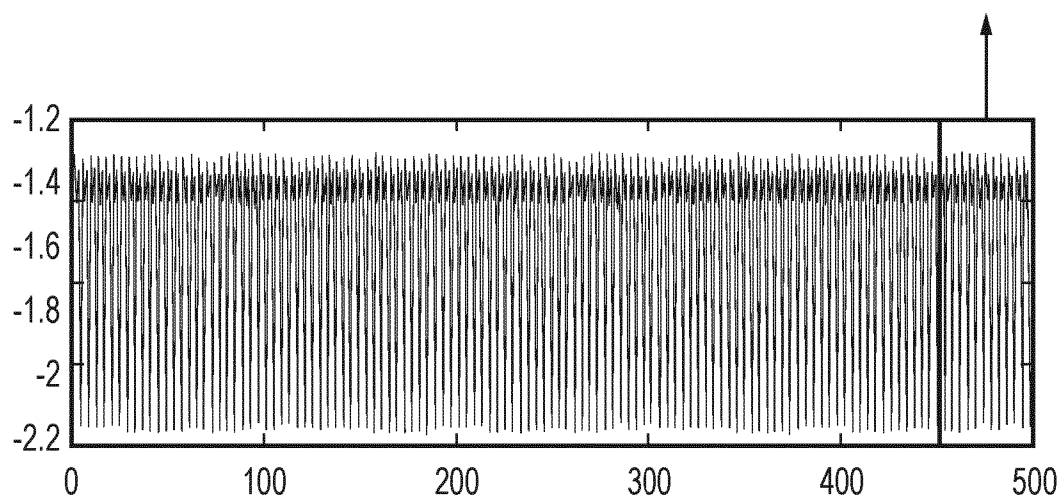
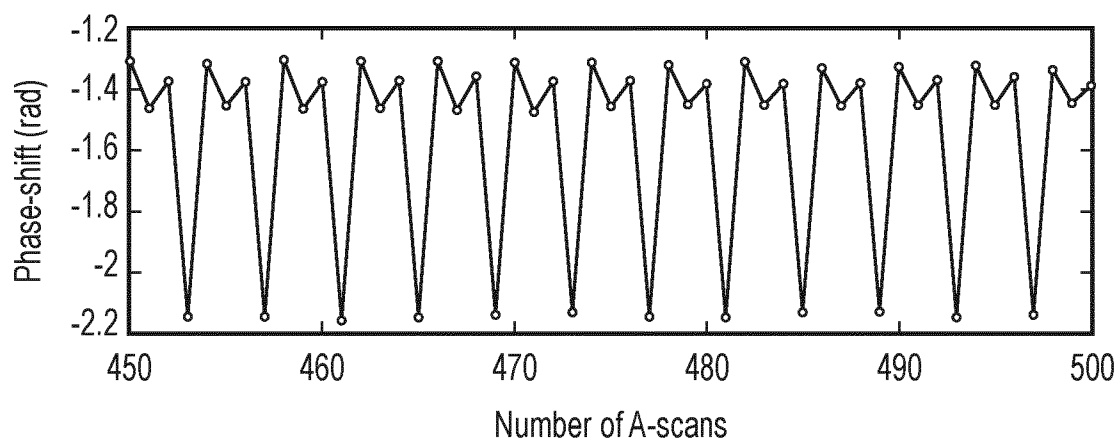


Coherence fringe signal overlaid after the phase shift compensation.

FIG. 12 (Continued)

17/24

(e)

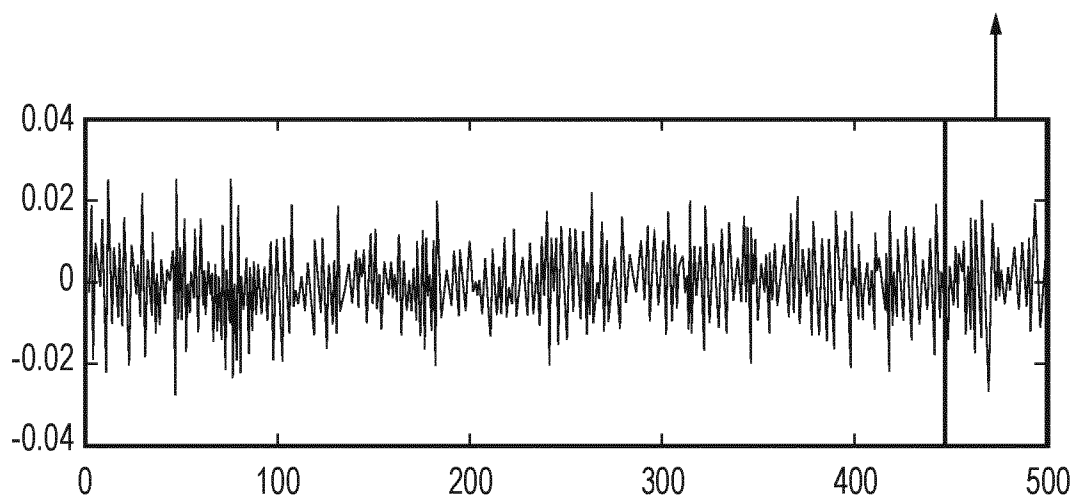
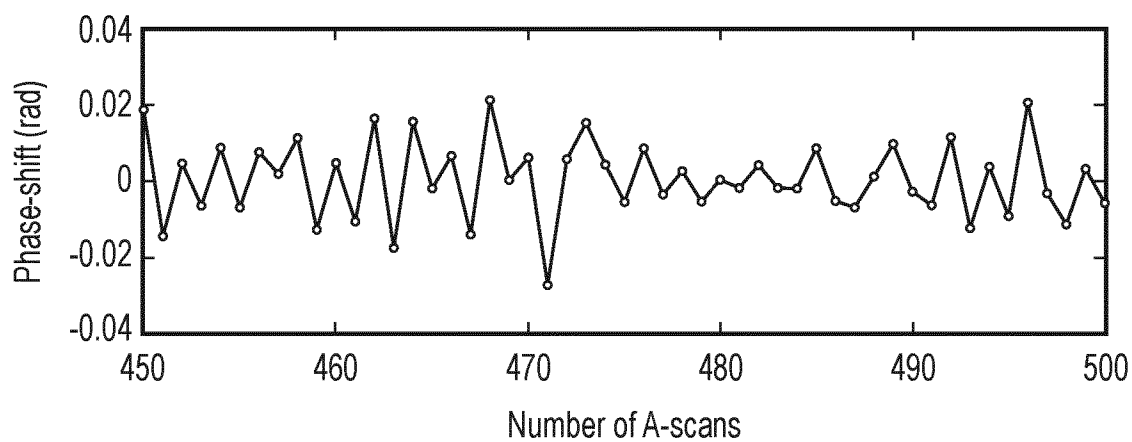


Phase shift noise before the compensation.

FIG. 12 (Continued)

18/24

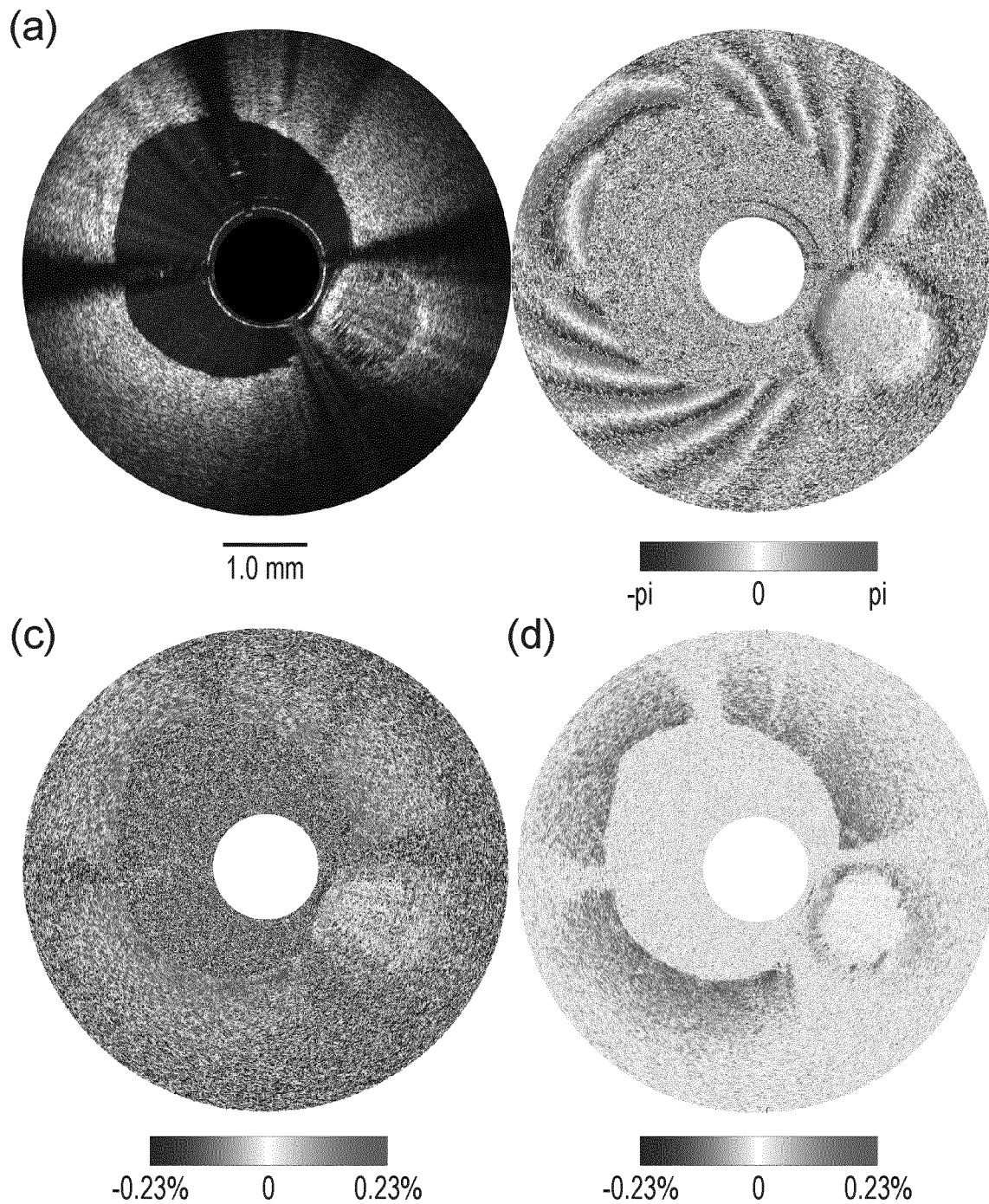
(f)



Phase noise after the compensation which is much smaller.

FIG. 12 (Continued)

19/24



- (a) Intensity image of the PVA phantom that has a VWP inclusion.
(b) Phase shift extracted.
(c) Strain image.
(d) Strain image after averaging over 20 strain images.

FIG. 13

20/24

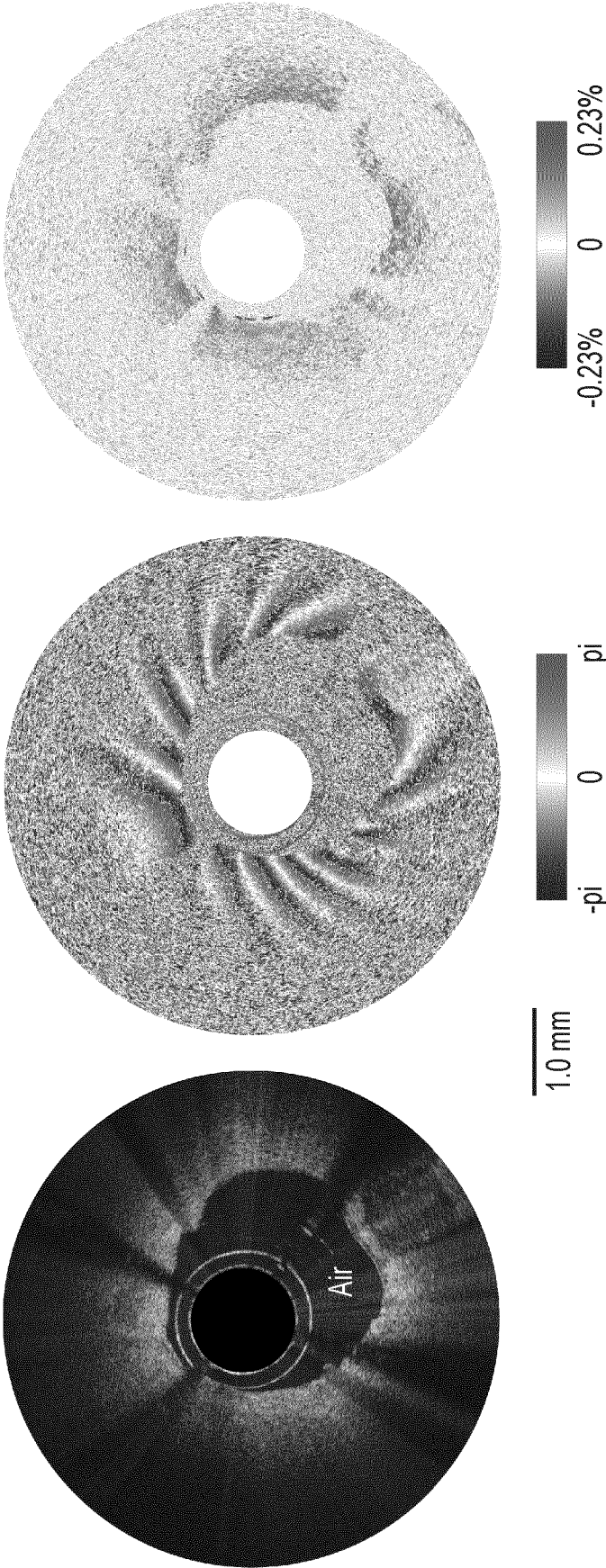


FIG. 14

21/24

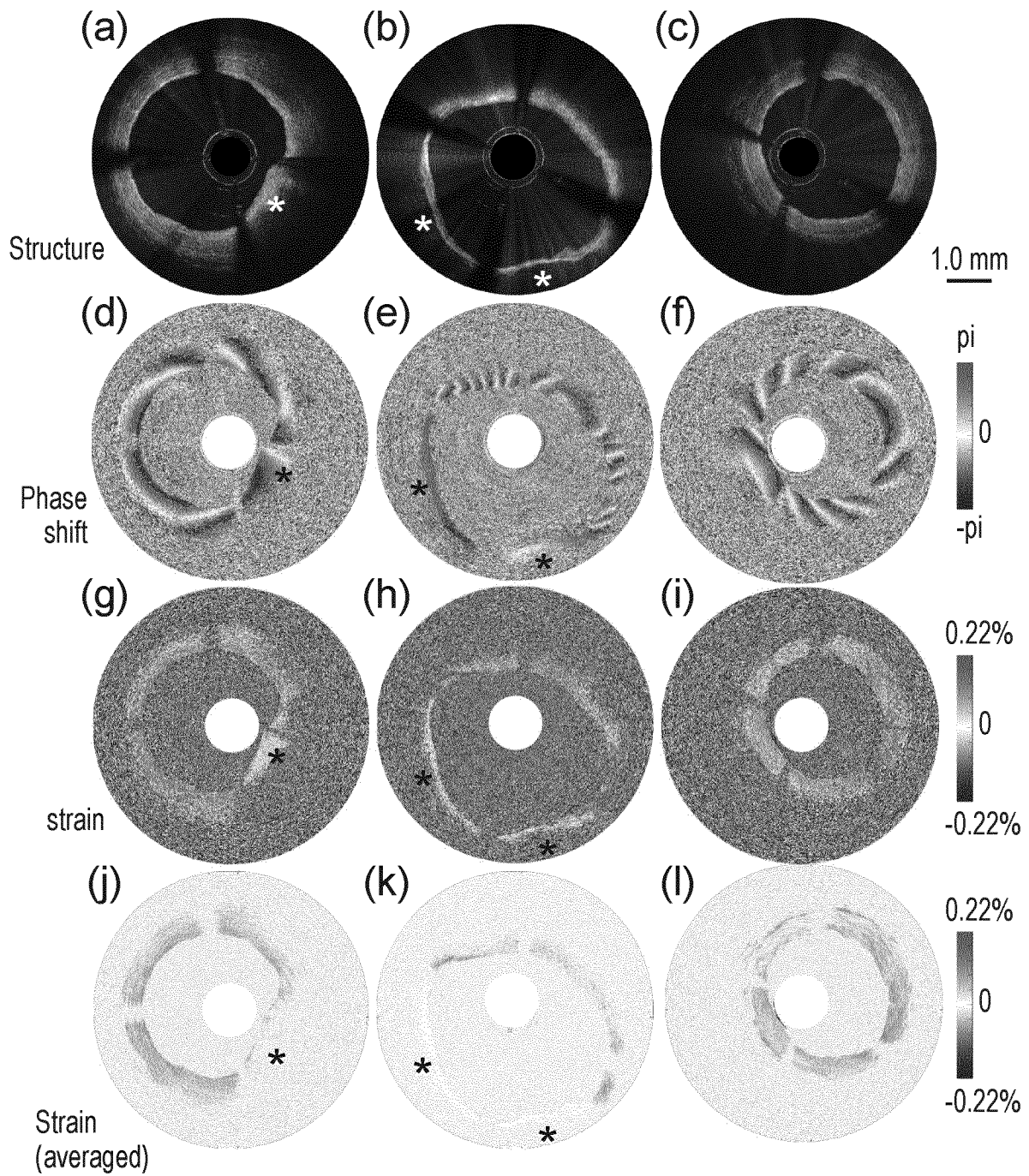


FIG. 15

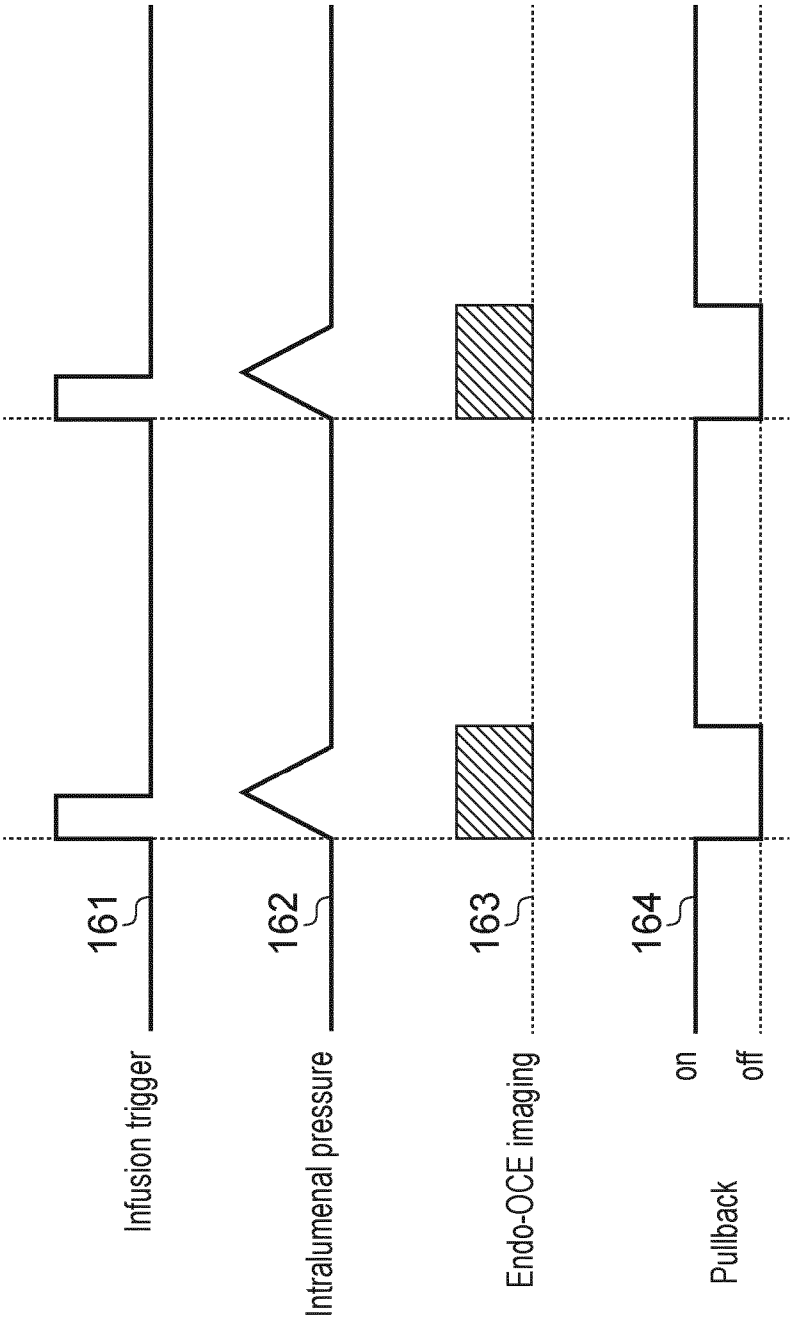


FIG. 16

23/24

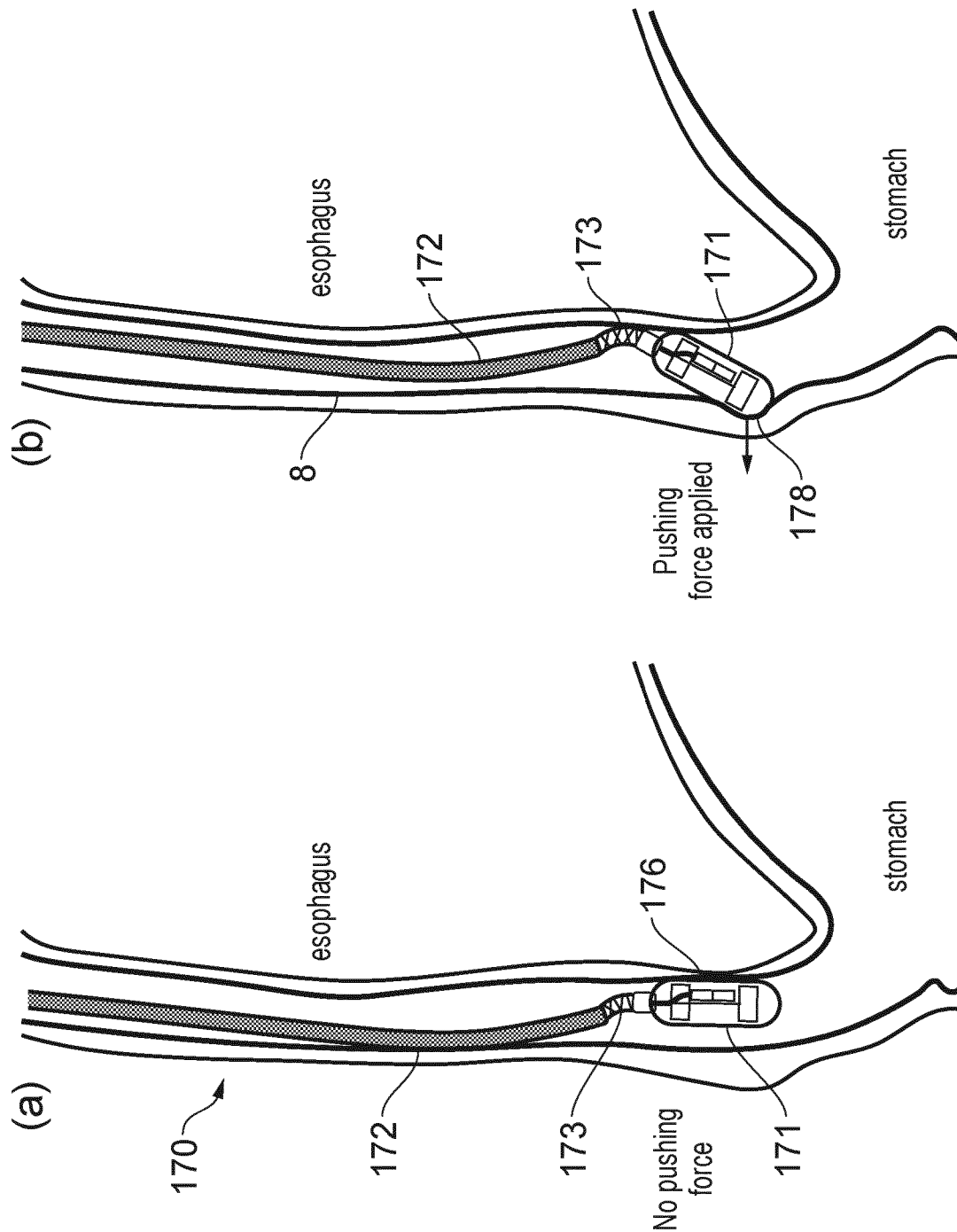


FIG. 17

24/24

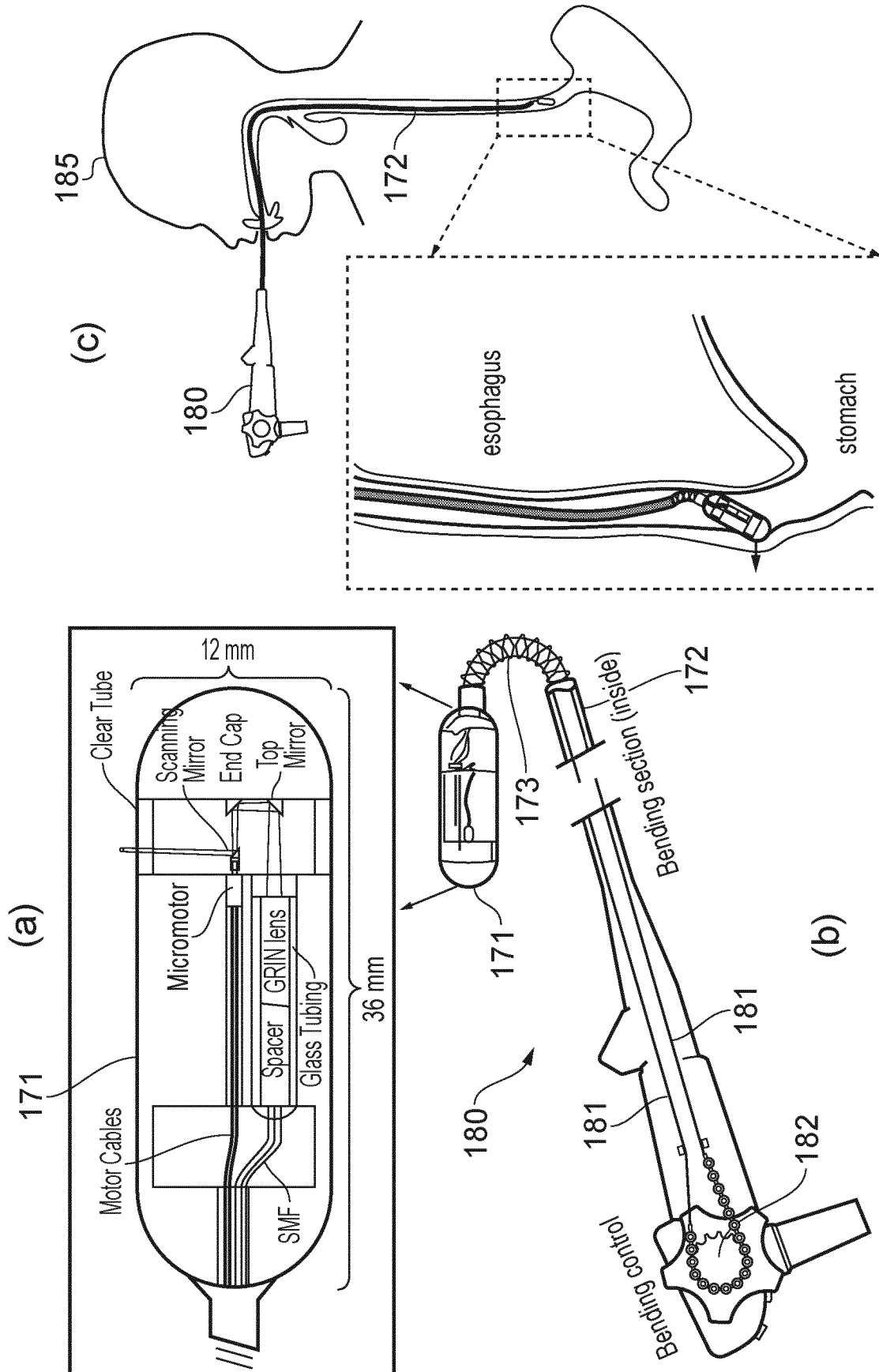


FIG. 18

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/052510

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00
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)
A61B

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)

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	US 2015/351722 A1 (CHEN ZHONGPING [US] ET AL) 10 December 2015 (2015-12-10)	1-4, 8-14,16, 17
Y A	paragraphs [0008], [0010], [0013], [0062], [0066], [0068], [0080], [0084] - [0089], [0099]; figures 6-8,15A-15B,17A-17B -----	15 18-27
X	US 2012/265061 A1 (SLIWA JOHN [US] ET AL) 18 October 2012 (2012-10-18)	1-14,16, 17
Y A	paragraphs [0002], [0005], [0006], [0008] - [0010], [0025] - [0034]; figures 2,2A ----- -/--	15 18-27



Further documents are listed in the continuation of Box C.



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

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"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

22 April 2020

Date of mailing of the international search report

06/05/2020

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Lommel, André

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/052510

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANG TIANSHI ET AL: "Micro motor OCT enables catheter based assessment of vascular elasticity(Conference Presentation)", PROGRESS IN BIOMEDICAL OPTICS AND IMAGING, SPIE - INTERNATIONAL SOCIETY FOR OPTICAL ENGINEERING, BELLINGHAM, WA, US, vol. 9710, 9 March 2016 (2016-03-09), pages 97100U-97100U, XP060066558, ISSN: 1605-7422, DOI: 10.1117/12.2216847 ISBN: 978-1-5106-0027-0	1-14,16,17
Y	the whole document	15
A		18-27
X	----- Tianshi Wang et al.: "Micro motor OCT enables catheter based assessment of vascular elasticity", YouTube, 27 April 2016 (2016-04-27), page 14 pp., XP054980401, Retrieved from the Internet: URL: https://www.spiedigitallibrary.org/conference-presentations/9710/97100U/Micro-motor-OCT-enables-catheter-based-assessment-of-vascular-elasticityConference/10.1117/12.2216847.4848678011001 [retrieved on 2020-04-22]	1-14,16,17
Y	the whole document	15
A		18-27
A	----- TIANSHI WANG ET AL: "Heartbeat OCT: superfast imaging and elasticity detection", PROCEEDINGS OF BIOMEDICAL OPTICS CONGRESS 2016, "OPTICS AND THE BRAIN 2016", FORT LAUDERDALE, FL, USA, 1 January 2016 (2016-01-01), pages 1-3, XP55688248, Washington, D.C. DOI: 10.1364/OTS.2016.OTu4C.2 ISBN: 978-1-943580-10-1 the whole document	1-27
X	----- US 2017/143196 A1 (LIANG KAICHENG [US] ET AL) 25 May 2017 (2017-05-25)	18-27
Y	paragraph [0078]; figure 9 -----	15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2020/052510

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. ☒ Claims Nos.: 28, 29
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 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:

see additional sheet

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27

optical imaging catheter

1.1. claims: 1-17

A catheter-based OCT system providing spatial co-registered successive scans

1.2. claims: 18-27

A catheter for optical imaging having a folded optical path.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2020/052510

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2015351722	A1	10-12-2015	NONE

US 2012265061	A1	18-10-2012	EP 2696747 A1 19-02-2014
			JP 6023788 B2 09-11-2016
			JP 2014514092 A 19-06-2014
			US 2012265061 A1 18-10-2012
			US 2012265062 A1 18-10-2012
			US 2015351642 A1 10-12-2015
			WO 2012142373 A1 18-10-2012

US 2017143196	A1	25-05-2017	US 2017143196 A1 25-05-2017
			WO 2015168594 A1 05-11-2015
