(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 January 2017 (26.01.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/015381 A1

(51) International Patent Classification:
A61B 6/00 (2006.01)

(21) International Application Number:
PCT/US2016/043154

(22) International Filing Date:
20 July 2016 (20.07.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/194,452 20 July 2015 (20.07.2015) US

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

(54) Title: X-RAY PHASE-CONTRAST AND DARK-FIELD INFORMATION EXTRACTION WITH ELECTRIC FRINGE SCANNING AND/OR ACTIVE PIXEL PROCESSING

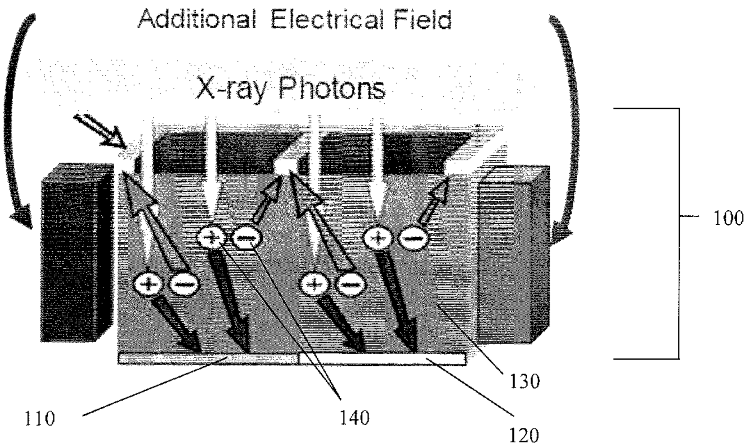

FIG. 2

(57) Abstract: Novel and advantageous systems and methods for performing X-ray imaging by extracting X-ray phase-shift and/or dark-field information through a detector that has built-in G2 functionality are provided. Grating translation can be replaced by an electrical operation in the detection procedure, thereby eliminating the need for the analyzer grating and the typical mechanical stepping process.

WO 2017/015381 A1

X-RAY PHASE-CONTRAST AND DARK-FIELD INFORMATION EXTRACTION WITH ELECTRIC FRINGE SCANNING AND/OR ACTIVE PIXEL PROCESSING

CROSS-REFERENCE TO A RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application Serial No. 62/194,452, filed July 20, 2015, which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

X-ray imaging is a powerful tool in many fundamental and practical applications. As a primary example, X-ray computed tomography (CT) is a cornerstone of modern hospitals and clinics. The dominating theory of X-ray imaging is generally based on the attenuation contrast mechanism.

X-ray gratings have been used for hybrid CT imaging in terms of attenuation, refraction, and small-angle scattering. This grating-based approach represents a paradigm shift in X-ray CT from gray-scale (attenuation) to true-color (attenuation, refraction, and small-angle scattering, which is also referred to as dark-field, and spectral) imaging.

In conventional X-ray imaging, the image contrast arises from varying linear attenuation coefficients. Attenuation-contrast-based imaging exhibits good performance only when strong attenuators are embedded in a weakly absorbing matrix, such as in the cases of bone-tissue and tissue-air interfaces. However, biological soft tissues include mainly light elements (e.g., hydrogen, carbon, nitrogen, and oxygen), and their compositions are quite homogeneous with little density variation. The attenuation-contrast between soft tissue features is often insufficient to reflect pathological changes.

In particular, many healthy tissues display similar characteristics in current X-ray images as those of diseased tissues, such as tumors. For example, fibro-glandular tissue can have a density of 1.035 cm^{-3} and an attenuation coefficient of 0.80 cm^{-1}, and cancerous tissue can have a density of 1.045 cm^{-3} and an attenuation coefficient of 0.85 cm^{-1}. Given inherent measurement noise, it is challenging to discern such cancerous tissue from the healthy tissue, as well as other soft tissue features such as those reflecting musculoskeletal healing. Therefore, attenuation-contrast-based imaging is unable to differentiate early-stage tumors and soft tissues.

X-ray small-angle scattering, or dark-field, imaging acquires photons slightly deflected from the primary beam through an object. Small-angle scattering signals reflect structural texture on length scales between 1 nanometer (nm) to several hundred nm. This imaging mode can reveal subtle texture of tissues. For example, the growth of tumors causes remarkable differences in small-angle scattering patterns from that of healthy tissues. It is clinically important that the structural variation in a tumor modifies the refractive index. The propagation of X-rays in a medium is characterized by the complex index of refraction. The cross section of an X-ray phase shift is one thousand times larger than that of the linear attenuation in the 20 keV – 100 keV range. This implies that phase-contrast imaging has much higher sensitivity for light elements than does attenuation-contrast imaging.

The contrast-to-noise ratio of differential phase contrast CT images is superior to that of its attenuation-contrast CT counterpart. Therefore, phase-contrast imaging can observe unique critical structures of soft biological tissues. Moreover, the refractive index of tissues is inversely proportional to the square of the X-ray energy while the absorption coefficient decreases as the fourth power of the X-ray energy. Hence, X-ray phase-contrast imaging is suitable to operate at higher energies (e.g., > 30 keV) for lower radiation dose than is attenuation imaging. Higher energy X-ray imaging can be useful for imaging and studies on large animals and/or human patients.

In X-ray grating-based imaging, X-ray phase-shift and dark-field information is currently extracted using the fringe scanning method through shifting of the analyzer grating. However, major challenges include the difficulty in making an analyzer grating (often known as G2), the requirement of a high-precision mechanical device, and the long data acquisition time due to the use of the phase stepping procedure.

BRIEF SUMMARY

Embodiments of the subject invention provide novel and advantageous systems and methods for performing X-ray imaging by extracting X-ray phase-shift and/or dark-field information through a detector that has built-in G2 functionality, as well as manipulation thereof. Grating translation can be replaced by an electrical operation in the detection procedure. That is, the typical mechanical stepping process can be omitted and replaced by an electrical steering process and/or mechanism, and the analyzer grating (G2) can be omitted by having its functionality combined with (or incorporated into) the detector itself. The systems and methods of embodiments of the subject invention present new opportunities in phase-contrast X-ray imaging (or X-ray grating-based imaging), shorten X-ray grating-based imaging time, increase dose utilization, and have many applications, including biomedical applications.

In an embodiment, an imaging system can comprise an X-ray radiation source and a detector for detecting X-ray radiation from the radiation source, wherein the detector comprises a semiconductor material and at least one electrode attached to the semiconductor material for providing an electric field. The system can further comprise a phase grating positioned between the radiation source and the detector, and a source grating positioned between the radiation source and the phase grating, and the system can specifically exclude an analyzer grating.

In another embodiment, a system as described herein can be used to perform a method of imaging, the method comprising: providing X-ray radiation to a sample to be imaged using the X-ray radiation source; collecting the X-ray radiation with the detector; and analyzing data from the detector to obtain an image. The electric field can be modulated by increasing or decreasing the voltage of the electric field from a zero voltage to a positive or negative voltage. Differently-shifted moiré-fringe patterns can be detected at a plurality of time intervals while the electric field is modulated, thereby resulting in a recorded intensity measure as a function of voltage. X-ray diffraction fringes, phase-shift information, and dark-field information can be extracted from the data from the detector.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a grating-based X-ray interferometer that can be used in X-ray grating-based imaging.

Figure 2 shows a cross-sectional view of a detector according to an embodiment of the subject invention.

Figure 3A shows an active pixel with according to embodiment of the subject invention.

Figure 3B shows an active pixel with an identical electrode pattern to that of the active pixel in Figure 3A.

Figure 4 shows differential operation of a two-electrode readout pixel according to embodiment of the subject invention.

Figure 5 shows a pixel having multiple electrodes according to an embodiment of the subject invention.

Figure 6A shows configurations of a two-dimensional electrode array that can be implemented in a pixel of a detector according to an embodiment of the subject invention.

Figure 6B shows configurations of a two-dimensional electrode array that can be implemented in a pixel of a detector according to an embodiment of the subject invention.

DETAILED DESCRIPTION

Embodiments of the subject invention provide novel and advantageous systems and methods for performing X-ray imaging by extracting X-ray phase-shift and/or dark-field information through a detector that has built-in G2 functionality, as well as manipulation thereof. Grating translation can be replaced by an electrical operation in the detection procedure. That is, the typical mechanical stepping process can be omitted and replaced by an electrical steering process and/or mechanism, and the analyzer grating (G2) can be omitted by having its functionality combined with (or incorporated into) the detector itself. The systems and methods of embodiments of the subject invention present new opportunities in phase-contrast X-ray imaging (or X-ray grating-based imaging), shorten X-ray grating-based imaging time, increase dose utilization, and have many applications, including biomedical applications. In some embodiments, the detector can be located at a Talbot distance, or fractional Talbot distance, from the phase grating, where the interference fringes are formed.

Figure 1 shows a grating-based X-ray interferometer that can be used in X-ray grating-based imaging (phase-contrast X-ray imaging). Figure 1 is from Burger et al. (Opt. Express 22, 32107-32118 2014; which is hereby incorporated herein by reference in its entirety). Referring to Figure 1, the interferometer can include a phase grating **G1** and an analyzer grating **G2**. The system can also include an X-ray source, a source grating **G0**, and a detector. The specimen being imaged can be placed between the source grating **G0** and the phase grating **G1**. Phase-shift and dark-field information can be extracted using phase stepping, where the analyzer grating **G2** or phase grating **G1** is scanned over one **G2** grating period.

According to embodiments of the subject invention, the analyzer grating **G2** can be omitted by having its functionality combined with (or incorporated into) the detector itself. All the gratings can therefore be kept stationary, thereby decreasing scanning time and inhibiting the chances for mechanical error. The moiré-fringe pattern can be shifted by varying an additional electric field across the detector (e.g., across a semiconductor material in a direct X-ray detector).

Figure 2 shows a cross-sectional view of a detector according to an embodiment of the subject invention. Referring to Figure 2, a detector pixel **100** of the detector **100** can have at least one electrode **110,120** connected to the bulk material **130** (e.g., semiconductor material) of the detector. When X-rays irradiate the semiconductor material **130** in the detector, photo-electrons are generated, producing electron-hole pairs **140** in the semiconductor material **130**. The electrode(s) **110,120** connected to the semiconductor material **130** can acquire a current signal. Though Figure 2 depicts two electrodes **110,120** connected to the bulk material **130** of the detector pixel **100**, embodiments are not limited thereto. Each detector pixel can include a single electrode or a plurality of electrodes; such a plurality of electrodes can include two electrodes, three electrodes, four electrodes, or more. In a certain embodiment, the detector can have one electrode or the plurality of electrodes attached to the entire detector (instead of to each detector pixel).

In many embodiments, each electrode present in the detector can be a micro-electrode. The size of each micro-electrode can be, for example, half of the analyzer grating G2 period (i.e., the period of the analyzer grating G2 that would otherwise be present if its functionality was not combined with the detector).

The additional electric field can steer electron-hole pairs horizontally in the semiconductor material **130**. Homogeneity of the electric field can be advantageous for the moiré-fringe pattern to be shifted consistently; otherwise, further processing may be needed to extract required information. In an embodiment, to improve the homogeneity of the additional electric field, the electric field can be added across only a small number (e.g., 45% or less, 40% or less, 30% or less, 20% or less, 15% or less, 10% or less, or 5% or less) of electrodes attached to the semiconductor material **130** of the detector.

In the data acquisition process, the additional electric field can be modulated by increasing (or decreasing) the voltage of the electric field from a zero voltage to a positive or negative voltage so that differently-shifted moiré-fringe patterns can be detected at various time intervals. The voltage setting can be optimized for a high signal-to-noise ratio. The recorded intensity measure as a function of voltage can be periodic with the same period of G2 (i.e., the period of the analyzer grating G2 that would otherwise be present if its functionality was not combined with the detector). From these data, the X-ray diffraction fringes, and the phase-shift and dark-field information, can be extracted in the same way as with the traditional stepping method.

Specifically, the intensity of the interference pattern in each detector pixel can be written as a Fourier series with negligible contributions of harmonics higher than the first order:

$$I(m,n,x_v) \approx a_0(m,n) + a_1(m,n)\cos(kx_v + \varphi(m,n)). \qquad (1)$$

Using Equation (1), the recorded image $I(m,n,x_v)$ at a given view angle can be used to extract transmission, differential phase shift, and dark-field signals, respectively. This can also be done using a photon-counting detector so that spectral information is included. The phase angle $\varphi(m,n)$ is directly related to the local gradient of the phase shift $\frac{\partial \Phi(m,n)}{\partial x}$, where $\Phi(m,n)$ represents the phase shift of the wave front.

Though two electrodes are depicted in Figure 2, single or multiple electrodes can be used, and their dimensions can be uniform or non-uniform (or some can be uniform while others are non-uniform). Also, in an embodiment, spacing between electrodes can be used, over which some electron-hole pairs may disappear at the cost of dose efficiency.

If electrodes are sufficiently small, no shifting will be needed, because the fringe pattern can be directly recorded. Such small electrodes and associated circuitry can be expensive in certain cases. In many embodiments of the subject invention, cost-effectiveness of the system or method can be optimized, which may not necessarily include using electrodes small enough such that no shifting is needed. Furthermore, the signals directly recorded by the electrodes can be processed for more information as described herein.

In some embodiments, the detector can include active pixel sensors. Active pixel sensors, in which each electrode has its own amplifier(s) and charge-to-voltage converter(s), are applicable in active X-ray phase-contrast imaging applications. Because the photo-electrons from each pixel can be extracted with multiple electrodes independently, the resulting signals can be processed to detect the sub-pixel shift of the X-ray fringes. Here, one pixel can be treated as the smallest unit of the sensor array, and the electrode patterns can be identical for each pixel as an example, though embodiments are not limited thereto (electrode patterns need not be identical for each pixel).

Figures 3A and 3B show two active pixels with identical electrode patterns. Referring to Figures 3A and 3B, each pixel includes two electrodes. Though an asymmetric configuration for the electrodes is depicted in Figures 3A and 3B, the electrodes can be symmetric or asymmetric to capture a sub-pixel intensity change. Each electrode can have its own amplifier and analog-to-digital converter (ADC). The signals from the electrodes after the analog-to-digital conversion can then be processed by an on-chip arithmetic unit to output a pixel value. The arithmetic unit can perform simple calculations, such as addition, subtraction, and multiplication, and it can also serve as a register, which performs a simple arithmetic operation on delayed input values. In various embodiments, each electrode can have its own arithmetic unit, each pixel can have a single arithmetic unit shared by all electrodes thereon, the chip can include a plurality of arithmetic units such that some pixels share the same arithmetic unit, or the chip can have a single arithmetic unit shared by all pixels and all electrodes.

Figure 4 shows an example of a differential operation of a two-electrode **210,220** readout pixel, allowing detection of a sub-pixel phase-shift amplitude and direction. Figure 4 demonstrates that both the sub-pixel phase stepping of the irradiance profile and the direction of the phase stepping (with an asymmetric electrode-pair) can be detected with a difference operation; i.e., the output signal is the difference between the signals from two electrodes **210,220**, as shown in Figure 4. Referring to Figure 4 and assuming that there are two fringe periods on each pixel, the first electrode **210** has three quarters of the total pixel area while the second electrode **220** has one quarter of the pixel area. These proportions are for exemplary purposes only and should not be construed as limiting. At time t0, the applied voltage of the additional electric field **V** is less than 0, and the total signal in the area of the first electrode **210** is 1.5, while that of the second electrode **220** is 0.5. The intensity profile is shown on the left, above the electrodes **210,220**. The readout signal after the arithmetic unit is 1. At time t1, the applied voltage is 0, and the readout signal is 0 as shown in the middle of the "difference signal" row of Figure 4. At time t2, the applied voltage is greater than zero, and the charge at the second electrode **220** can only be partially converted to the readout, resulting in an asymmetric readout function, as shown in the plot at the bottom portion of Figure 4. During the data acquisition process, the shift voltage can drive a scan over one period of the X-ray diffraction fringe, and the phase contrast information can be easily computed.

Figure 5 shows a pixel having multiple electrodes (m electrodes, where m is an integer) according to an embodiment of the subject invention. Though Figure 5 depicts the electrodes having uniform area, embodiments are not limited thereto. Finer sub-pixel shift can be detected by using multiple electrodes, as in Figure 5. If the periodicity of the X-ray fringes and the pixel electrodes matches, a simple difference between signals from two adjacent electrodes can be used to calculate both differential phase-shift and dark-field information.

Figures 6A and 6B show configurations of two-dimensional electrode arrays that can be implemented in pixels of a detector according to embodiments of the subject invention. Referring to Figure 6A, the electrodes of the array can have different areas as depicted, though embodiments are not limited thereto. Also, though Figure 6A depicts four electrodes in the array, this is for exemplary purposes only. Referring to Figure 6B, the areas of the electrodes can be uniform. Also, any reasonable number of electrodes can be present in the array. These two-dimensional configurations can be implemented to measure diffraction fringes on a plane.

According to embodiments of the subject invention, X-ray phase-shift and dark-field information can be extracted through a specially-designed detector that has built-in analyzer grating G2 functionality and manipulation. Grating translation can be replaced by an electrical operation in the detection procedure. The mechanical stepping process of the conventional art can be replaced by the electric steering mechanism, and the actual analyzer grating G2 can be omitted by having its functionality incorporated into the detector of the imaging system. The detector can be located at a Talbot distance, or a fractional Talbot distance, from the phase grating, where the interference fringes are formed, though embodiments are not limited thereto.

The methods and processes described herein can be embodied as code and/or data. The software code and data described herein can be stored on one or more computer-readable media, which may include any device or medium that can store code and/or data for use by a computer system. When a computer system reads and executes the code and/or data stored on a computer-readable medium, the computer system performs the methods and processes embodied as data structures and code stored within the computer-readable storage medium.

It should be appreciated by those skilled in the art that computer-readable media include removable and non-removable structures/devices that can be used for storage of information, such as computer-readable instructions, data structures, program modules, and other data used by a computing system/environment. A computer-readable medium includes, but is not limited to, volatile memory such as random access memories (RAM, DRAM, SRAM); and non-volatile memory such as flash memory, various read-only-memories (ROM, PROM, EPROM, EEPROM), magnetic and ferromagnetic/ferroelectric memories (MRAM, FeRAM), and magnetic and optical storage devices (hard drives, magnetic tape, CDs, DVDs); network devices; or other media now known or later developed that is capable of storing computer-readable information/data. Computer-readable media should not be construed or interpreted to include any propagating signals. A computer-readable medium of the subject invention can be, for example, a compact disc (CD), digital video disc (DVD), flash memory device, volatile memory, or a hard disk drive (HDD), such as an external HDD or the HDD of a computing device, though embodiments are not limited thereto. A computing device can be, for example, a laptop computer, desktop computer, server, cell phone, or tablet, though embodiments are not limited thereto.

The subject invention includes, but is not limited to, the following exemplified embodiments.

Embodiment 1. An imaging system, comprising:

a radiation source (e.g., an X-ray source); and

a detector for detecting radiation (e.g., X-rays) from the radiation source, wherein the detector comprises a semiconductor material and at least one electrode attached to the semiconductor material for providing an electric field.

Embodiment 2. The system according to embodiment 1, further comprising a phase grating positioned between the radiation source and the detector.

Embodiment 3. The system according to embodiment 2, further comprising a source grating positioned between the radiation source and the phase grating.

Embodiment 4. The system according to embodiment 3, configured such that the subject to be imaged is positioned between the source grating and the phase grating.

Embodiment 5. The system according to embodiment 1, further comprising a source grating positioned between the radiation source and the detector.

Embodiment 6. The system according to any of embodiments 1-5, wherein the system excludes an analyzer grating.

Embodiment 7. The system according to any of embodiments 1-6, wherein the detector comprises a plurality of detector pixels, each comprising the semiconductor material of the detector, and wherein each detector pixel comprises at least one electrode attached to the semiconductor material.

Embodiment 8. The system according to embodiment 7, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material.

Embodiment 9. The system according to embodiment 7, wherein each detector pixel comprises exactly two electrodes attached to the semiconductor material.

Embodiment 10. The system according to any of embodiments 1-9, wherein the detector further comprises an arithmetic unit connected to the at least one electrode.

Embodiment 11. The system according to any of embodiments 1-10, wherein the detector further comprises an amplifier connected to the at least one electrode.

Embodiment 12. The system according to any of embodiments 1-11, wherein the detector further comprises an analog-to-digital convertor (ADC) connected to the at least one electrode.

Embodiment 13. The system according to embodiment 9, wherein the detector further comprises an amplifier connected to the at least one electrode between the arithmetic unit and the at least one electrode.

Embodiment 14. The system according to any of embodiments 9 and 13, wherein the detector further comprises an ADC connected to the at least one electrode between the arithmetic unit and the at least one electrode.

Embodiment 15. The system according to any of embodiments 1-10, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of amplifiers respectively connected to the plurality of electrodes.

Embodiment 16. The system according to any of embodiments 1-10 and 15, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of ADCs respectively connected to the plurality of electrodes.

Embodiment 17. The system according to embodiment 9, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

Embodiment 18. The system according to any of embodiments 9, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

Embodiment 19. The system according to any of embodiments 7-9, wherein each detector pixel further comprises an arithmetic unit connected to the at least one electrode.

Embodiment 20. The system according to any of embodiments 7-9 and 19, wherein each detector pixel further comprises an amplifier connected to the at least one electrode.

Embodiment 21. The system according to any of embodiments 7-9, 19, and 20, wherein each detector pixel further comprises an ADC connected to the at least one electrode.

Embodiment 22. The system according to embodiment 19, wherein each detector pixel further comprises an amplifier connected to the at least one electrode between the arithmetic unit and the at least one electrode.

Embodiment 23. The system according to any of embodiments 19 and 22, wherein each detector pixel further comprises an ADC connected to the at least one electrode between the arithmetic unit and the at least one electrode.

Embodiment 24. The system according to any of embodiments 7-9 and 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes.

Embodiment 25. The system according to any of embodiments 7-9, 19, and 24, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes.

Embodiment 26. The system according to embodiment 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

Embodiment 27. The system according to embodiment 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

Embodiment 28. The system according to any of embodiments 7-9, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of arithmetic units respectively connected to the plurality of electrodes.

Embodiment 29. The system according to embodiment 28, wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the respective arithmetic unit and the respective electrode.

Embodiment 30. The system according to any of embodiments 28-29, wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the respective arithmetic unit and the respective electrode.

Embodiment 31. The system according to any of embodiments 7-30, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material and arranged in an array within said detector pixel.

Embodiment 32. The system according to any of embodiments 7-31, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode within a given detector pixel is the same as that of all other electrodes within said detector pixel.

Embodiment 33. The system according to any of embodiments 1-32, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the same as that of all other electrodes.

Embodiment 34. The system according to any of embodiments 7-31, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode within a given detector pixel is different from that of at least one other electrode within said detector pixel.

Embodiment 35. The system according to any of embodiments 7-31 and 34, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode within a given detector pixel is different from that of all other electrodes within said detector pixel.

Embodiment 36. The system according to any of embodiments 1-31, 34, and 35, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the different from that of at least one other electrode.

Embodiment 37. The system according to any of embodiments 1-31 and 34-36, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the different from that of all other electrodes.

Embodiment 38. The system according to any of embodiments 1-37, wherein the electrode(s) present in the detector provide an electric field that steers electron-hole pairs horizontally (parallel to a detection surface of the detector that faces the radiation source) in the semiconductor material of the detector.

Embodiment 39. The system according to any of embodiments 1-38, wherein the electrode(s) present in the detector provide a homogenous electric field in the semiconductor material of the detector.

Embodiment 40. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 45% or less of the electrodes of the detector.

Embodiment 41. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 40% or less of the electrodes of the detector.

Embodiment 42. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 30% or less of the electrodes of the detector.

Embodiment 43. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 20% or less of the electrodes of the detector.

Embodiment 44. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 15% or less of the electrodes of the detector.

Embodiment 45. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 10% or less of the electrodes of the detector.

Embodiment 46. The system according to any of embodiments 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 5% or less of the electrodes of the detector.

Embodiment 47. The system according to any of embodiments 1-46, wherein each electrode present is a micro-electrode.

Embodiment 48. The system according to embodiment 47, wherein the size (e.g., length, width, or longest dimension in any direction) of each micro-electrode is half of the grating period of the (omitted) analyzer grating whose functionality is incorporated into the detector.

Embodiment 49. The system according to any of embodiments 1-48, wherein the system further comprises a phase grating positioned between the X-ray source and the detector, and wherein the detector is positioned a Talbot distance, or fractional Talbot distance, from the phase grating, where the interference fringes are formed.

Embodiment 50. A method of imaging using the system according to any of embodiments 1-49, the method comprising:

providing radiation (e.g., X-ray radiation) to a sample to be imaged using the radiation source;

collecting the radiation (e.g., X-ray radiation) with the detector; and

analyzing data from the detector to obtain an image.

Embodiment 51. The method according to embodiment 52, further comprising modulating the electric field provided by the at least one electrode attached to the semiconductor material of the detector.

Embodiment 52. The method according to embodiment 51, wherein modulating the electric field comprises increasing (or decreasing) the voltage of the electric field from a zero voltage to a positive (or negative) voltage.

Embodiment 53. The method according to embodiment 52, further comprising detecting differently-shifted moiré-fringe patterns at a plurality of time intervals while the electric field is modulated, thereby resulting in a recorded intensity measure as a function of voltage.

Embodiment 54. The method according to embodiment 53, wherein the recorded intensity measure as a function of voltage is periodic with a period that is the same as the grating period of the (omitted) analyzer grating whose functionality is incorporated into the detector.

Embodiment 55. The method according to any of embodiments 50-54, wherein analyzing data from the detector to obtain an image comprises extracting diffraction fringes (e.g., X-ray diffraction fringes), phase-shift information, and dark-field information from the data from the detector.

Embodiment 56. The method according to any of embodiments 50-55, wherein the detector comprises a plurality of detector pixels, and wherein analyzing data from the detector to obtain an image comprises using the recorded image intensity measure $I(m,n,x_v)$ at a given view angle to extract transmission, differential phase shift, and dark-field signals, respectively, where $I(m,n,x_v)$ is represented by the following Fourier series:

$$I(m,n,x_v) \approx a_0(m,n) + a_1(m,n)\cos(kx_v + \varphi(m,n)).$$

Embodiment 57. The method according to embodiment 56, wherein the phase angle $\varphi(m,n)$ is directly related to the local gradient of the phase shift $\frac{\partial\Phi(m,n)}{\partial x}$, where $\Phi(m,n)$ represents the phase shift of the wave front.

Embodiment 58. The system according to any of embodiments 1-49, further comprising a (non-transitory) machine readable medium (e.g., computer readable medium) having machine-executable (e.g., computer executable) instructions (stored thereon) for performing the step of analyzing data from the detector according to the method of any of embodiments 50-57, wherein the machine readable medium is in operable communication with the detector.

Embodiment 59. The system according to any of embodiments 1-49 and 58, or the method according to any of embodiments 50-57, wherein the detector is a photon-counting detector, such that spectral information is included in data of the detector.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application.

All patents, patent applications, provisional applications, and publications referred to or cited herein (including those in the "References" section) are incorporated by reference in their entirety, including all figures and tables, to the extent they are not inconsistent with the explicit teachings of this specification.

REFERENCES

Shi et al., An edge-on charge-transfer design for energy-resolved x-ray detection, Physics in Medicine and Biology, Volume 61, Number 11, 2016

Wang et al., International Patent Application Publication No. WO2016/106348

Wang et al., U.S. Patent Application Publication No. 2015/0157286

Wang et al., U.S. Patent Application Publication No. 2015/0170361

Wang et al., U.S. Patent Application Publication No. 2015/0193927

Wang et al., International Patent Application Publication No. WO2015/164405

Wang et al., U.S. Patent Application Publication No. 2016/0113602

Wang et al., U.S. Patent Application Publication No. 2016/0135769

Wang et al., U.S. Patent Application Publication No. 2016/0166852

Wang et al., International Patent Application Publication No. WO2016/106348

Wang et al., International Patent Application No. PCT/US2016/014769

Wang et al., International Patent Application No. PCT/US2016/023460

Wang et al., International Patent Application No. PCT/US2016/036057

Burger et al., "Regularized iterative integration combined with non-linear diffusion filtering for phase-contrast x-ray computed tomography," Opt. Express 22, 32107-32118 (2014); http://www.opticsinfobase.org/oe/abstract.cfm?uri=oe-22-26-32107

U.S. Provisional Application Serial No. 62/197,301

CLAIMS

What is claimed is:

1. An imaging system, comprising:

an X-ray radiation source; and

a detector for detecting X-ray radiation from the radiation source, wherein the detector comprises a semiconductor material and at least one electrode attached to the semiconductor material for providing an electric field.

2. The system according to claim 1, further comprising a phase grating positioned between the radiation source and the detector.

3. The system according to claim 2, further comprising a source grating positioned between the radiation source and the phase grating.

4. The system according to claim 3, configured such that the subject to be imaged is positioned between the source grating and the phase grating.

5. The system according to claim 1, further comprising a source grating positioned between the radiation source and the detector.

6. The system according to any of claims 1-5, wherein the system excludes an analyzer grating.

7. The system according to any of claims 1-6, wherein the detector comprises a plurality of detector pixels, each comprising the semiconductor material of the detector, and wherein each detector pixel comprises at least one electrode attached to the semiconductor material.

8. The system according to claim 7, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material.

9. The system according to claim 7, wherein each detector pixel comprises exactly two electrodes attached to the semiconductor material.

10. The system according to any of claims 1-9, wherein the detector further comprises an arithmetic unit connected to the at least one electrode.

11. The system according to any of claims 1-10, wherein the detector further comprises an amplifier connected to the at least one electrode.

12. The system according to any of claims 1-11, wherein the detector further comprises an analog-to-digital convertor (ADC) connected to the at least one electrode.

13. The system according to claim 9, wherein the detector further comprises an amplifier connected to the at least one electrode between the arithmetic unit and the at least one electrode.

14. The system according to any of claims 9 and 13, wherein the detector further comprises an ADC connected to the at least one electrode between the arithmetic unit and the at least one electrode.

15. The system according to any of claims 1-10, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of amplifiers respectively connected to the plurality of electrodes.

16. The system according to any of claims 1-10 and 15, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of ADCs respectively connected to the plurality of electrodes.

17. The system according to claim 9, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector

further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

18. The system according to any of claims 9, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein the detector further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

19. The system according to any of claims 7-9, wherein each detector pixel further comprises an arithmetic unit connected to the at least one electrode.

20. The system according to any of claims 7-9 and 19, wherein each detector pixel further comprises an amplifier connected to the at least one electrode.

21. The system according to any of claims 7-9, 19, and 20, wherein each detector pixel further comprises an ADC connected to the at least one electrode.

22. The system according to claim 19, wherein each detector pixel further comprises an amplifier connected to the at least one electrode between the arithmetic unit and the at least one electrode.

23. The system according to any of claims 19 and 22, wherein each detector pixel further comprises an ADC connected to the at least one electrode between the arithmetic unit and the at least one electrode.

24. The system according to any of claims 7-9 and 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes.

25. The system according to any of claims 7-9, 19, and 24, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material,

and wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes.

26. The system according to claim 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

27. The system according to claim 19, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the arithmetic unit and the respective electrode.

28. The system according to any of claims 7-9, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein each detector pixel further comprises a plurality of arithmetic units respectively connected to the plurality of electrodes.

29. The system according to claim 28, wherein each detector pixel further comprises a plurality of amplifiers respectively connected to the plurality of electrodes between the respective arithmetic unit and the respective electrode.

30. The system according to any of claims 28-29, wherein each detector pixel further comprises a plurality of ADCs respectively connected to the plurality of electrodes between the respective arithmetic unit and the respective electrode.

31. The system according to any of claims 7-30, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material and arranged in an array within said detector pixel.

32. The system according to any of claims 7-31, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein

an area of each electrode within a given detector pixel is the same as that of all other electrodes within said detector pixel.

33. The system according to any of claims 1-32, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the same as that of all other electrodes.

34. The system according to any of claims 7-31, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode within a given detector pixel is different from that of at least one other electrode within said detector pixel.

35. The system according to any of claims 7-31 and 34, wherein each detector pixel comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode within a given detector pixel is different from that of all other electrodes within said detector pixel.

36. The system according to any of claims 1-31, 34, and 35, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the different from that of at least one other electrode.

37. The system according to any of claims 1-31 and 34-36, wherein the detector comprises a plurality of electrodes attached to the semiconductor material, and wherein an area of each electrode is the different from that of all other electrodes.

38. The system according to any of claims 1-37, wherein the at least one electrode of the detector provides an electric field that steers electron-hole pairs horizontally in the semiconductor material of the detector.

39. The system according to any of claims 1-38, wherein the at least one electrode of the detector provides a homogenous electric field in the semiconductor material of the detector.

40. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 45% or less of the electrodes of the detector.

41. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 40% or less of the electrodes of the detector.

42. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 30% or less of the electrodes of the detector.

43. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 20% or less of the electrodes of the detector.

44. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 15% or less of the electrodes of the detector.

45. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 10% or less of the electrodes of the detector.

46. The system according to any of claims 1-39, wherein the detector comprises a plurality of electrodes, and wherein the electric field is added across 5% or less of the electrodes of the detector.

47. The system according to any of claims 1-46, wherein each electrode present is a micro-electrode.

48. The system according to claim 47, wherein a length of each micro-electrode is half of the grating period of the analyzer grating whose functionality is incorporated into the detector.

49. The system according to any of claims 1-48, wherein the system further comprises a phase grating positioned between the X-ray source and the detector, and wherein the detector is positioned a Talbot distance, or fractional Talbot distance, from the phase grating, where the interference fringes are formed.

50. A method of imaging using the system according to any of claims 1-49, the method comprising:

providing X-ray radiation to a sample to be imaged using the X-ray radiation source;

collecting the X-ray radiation with the detector; and

analyzing data from the detector to obtain an image.

51. The method according to claim 50, further comprising modulating the electric field provided by the at least one electrode attached to the semiconductor material of the detector.

52. The method according to claim 51, wherein modulating the electric field comprises increasing or decreasing the voltage of the electric field from a zero voltage to a positive or negative voltage.

53. The method according to claim 52, further comprising detecting differently-shifted moiré-fringe patterns at a plurality of time intervals while the electric field is modulated, thereby resulting in a recorded intensity measure as a function of voltage.

54. The method according to claim 53, wherein the recorded intensity measure as a function of voltage is periodic with a period that is the same as the grating period of the analyzer grating whose functionality is incorporated into the detector.

55. The method according to any of claims 50-54, wherein analyzing data from the detector to obtain an image comprises extracting X-ray diffraction fringes, phase-shift information, and dark-field information from the data from the detector.

56. The method according to any of claims 50-55, wherein the detector comprises a plurality of detector pixels, and wherein analyzing data from the detector to obtain an image comprises using the recorded image intensity measure $I(m,n,x_v)$ at a given view angle to extract transmission, differential phase shift, and dark-field signals, respectively, where $I(m,n,x_v)$ is represented by the following Fourier series:

$$I(m,n,x_v) \approx a_0(m,n) + a_1(m,n)\cos(kx_v + \varphi(m,n)).$$

57. The method according to claim 56, wherein the phase angle $\varphi(m,n)$ is directly related to the local gradient of the phase shift $\frac{\partial\Phi(m,n)}{\partial x}$, where $\Phi(m,n)$ represents the phase shift of the wave front.

58. The system according to any of claims 1-49, further comprising a machine readable medium having machine-executable instructions stored thereon for performing the step of analyzing data from the detector according to the method of any of claims 50-57, wherein the machine readable medium is in operable communication with the detector.

59. The system according to any of claims 1-49 and 58, or the method according to any of claims 50-57, wherein the detector is a photon-counting detector, such that spectral information is included in data of the detector.

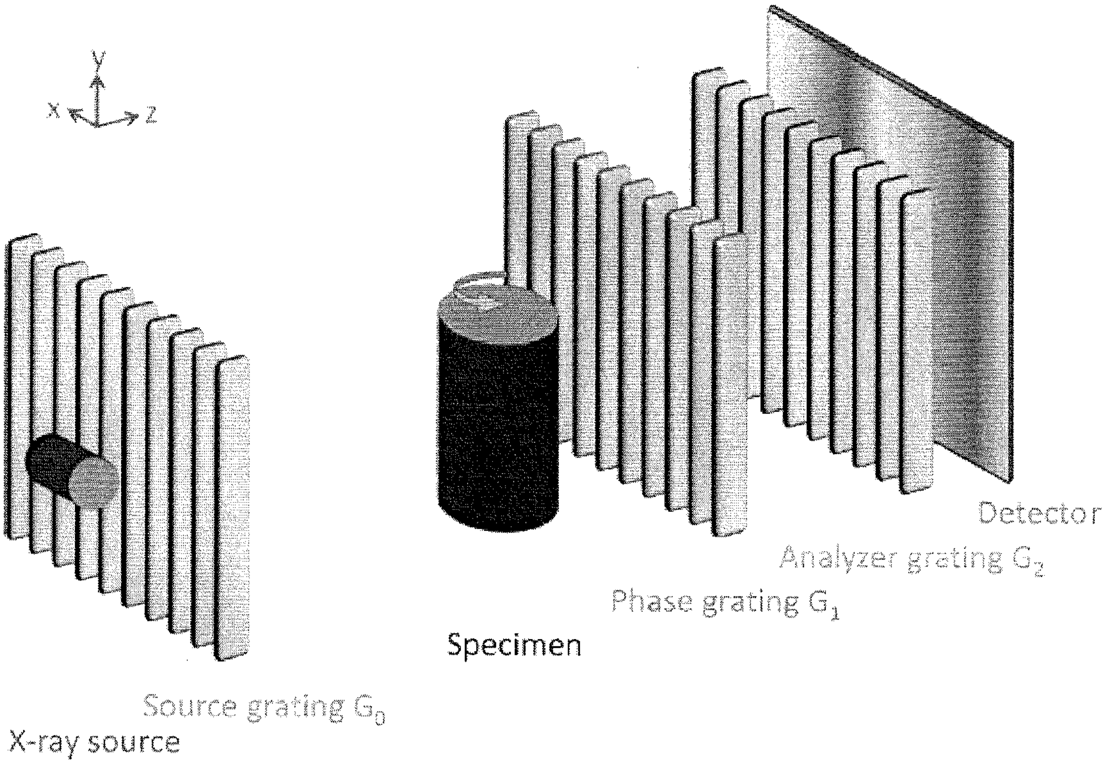
y
x
z
Detector
Analyzer grating G_2
Phase grating G_1
Specimen
Source grating G_0
X-ray source

FIG. 1

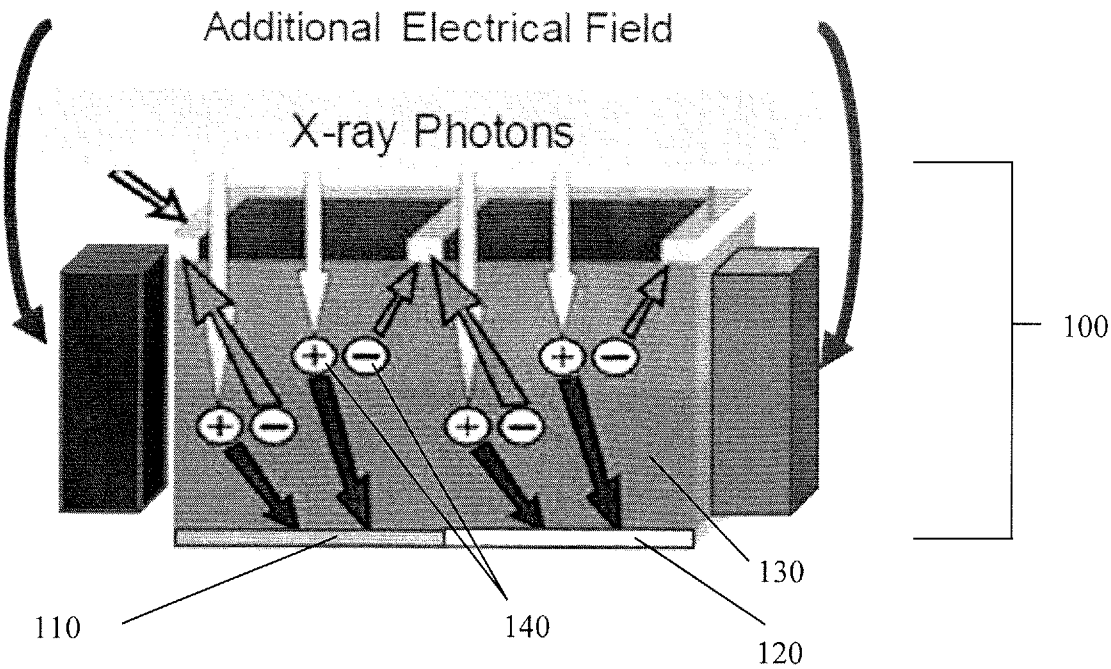
Additional Electrical Field
X-ray Photons
100
130
110
140
120

FIG. 2

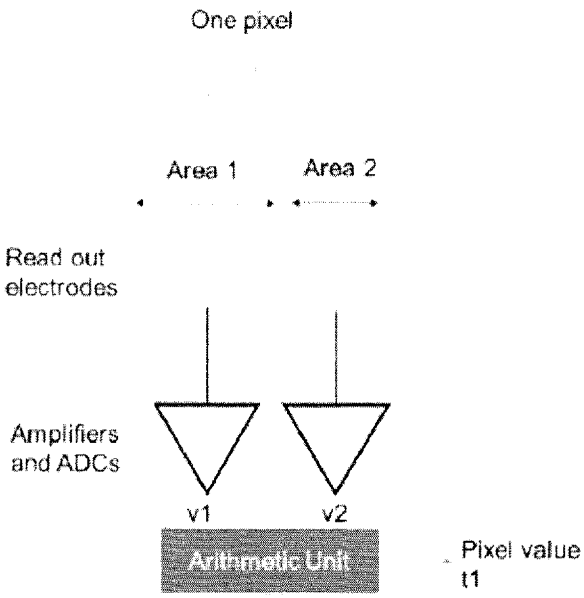

FIG. 3A

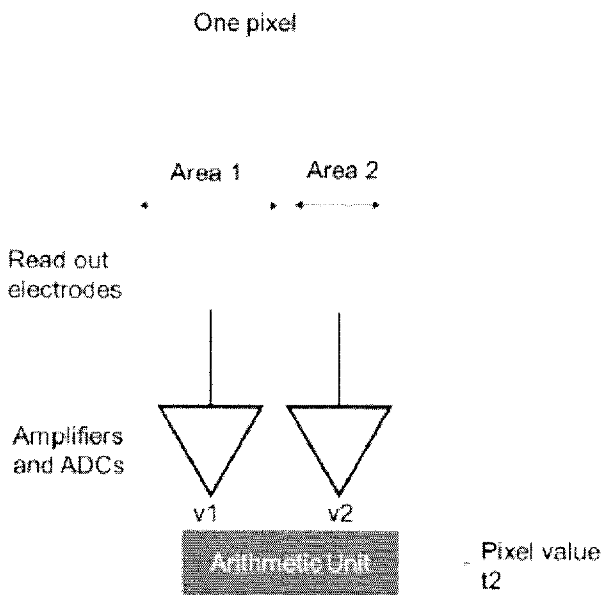

FIG. 3B

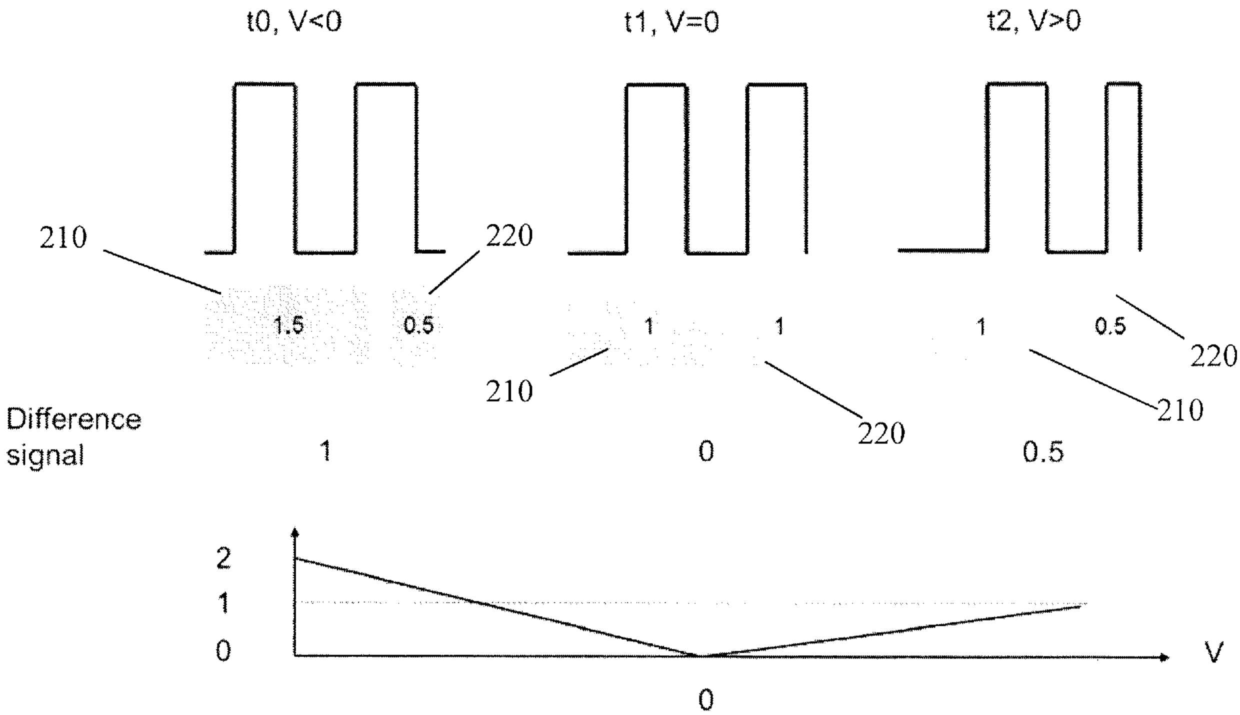

FIG. 4

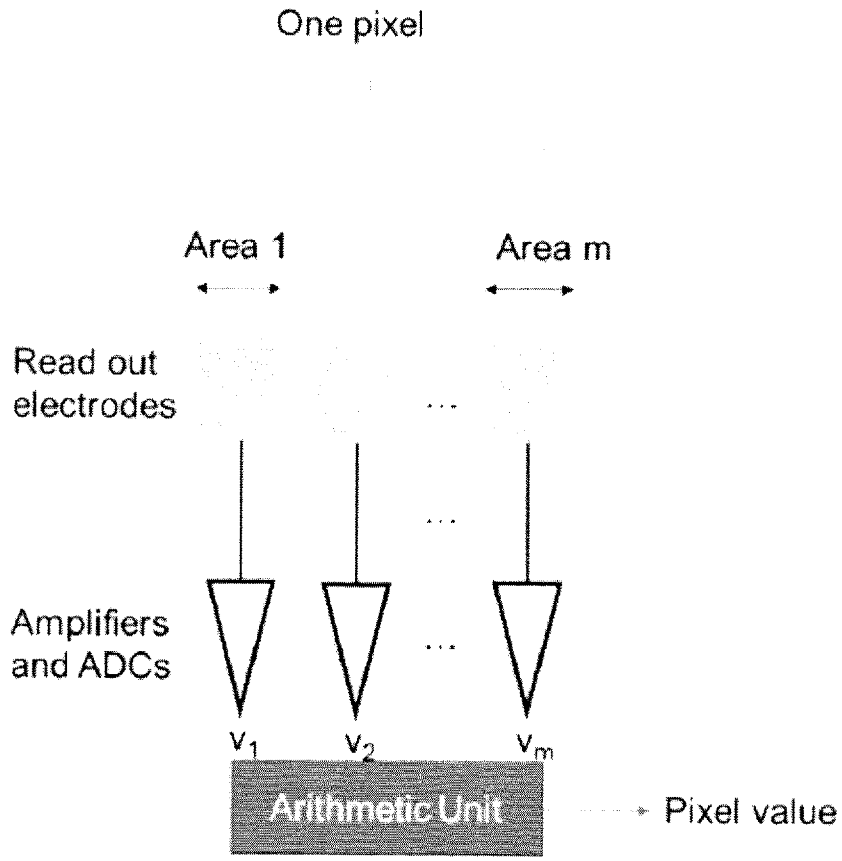

FIG. 5

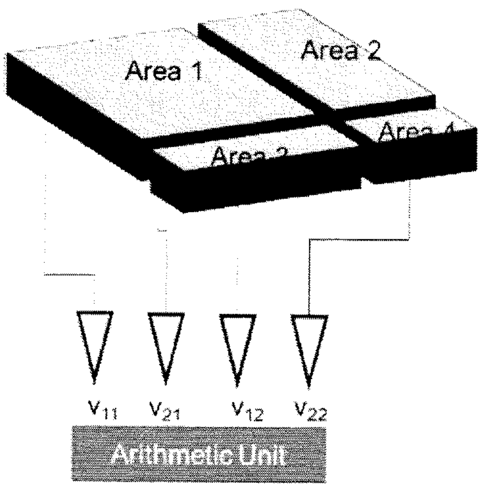

FIG. 6A

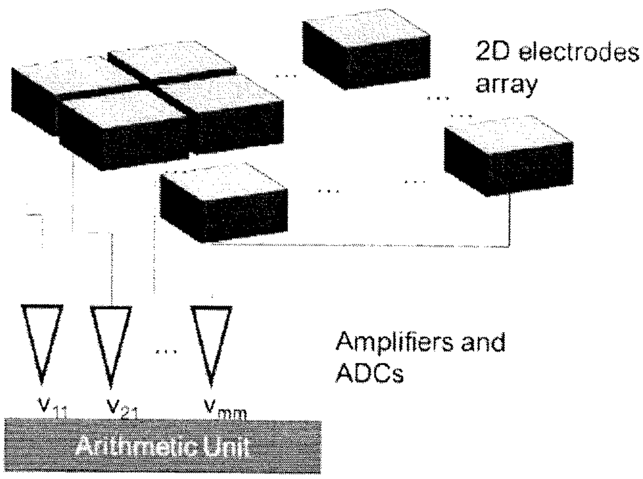

FIG. 6B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/043154

A. CLASSIFICATION OF SUBJECT MATTER

A61B 6/00(2006.01)i

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 6/00; A61B 6/03; G01N 23/04; G21K 1/12; G21K 1/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: Xray, radiation, detector, semiconductor, phase, grating

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 0161324 A1 (MATSUSHITA ELECTRIC INDUSTRIAL CO., LTD.) 21 November 1985 See abstract, claims 1,2 and figures 1-3.	1 2-6
Y	US 9066649 B2 (ROESSL et al.) 30 June 2015 See abstract, claims 1,3 and figures 1a-1c.	2-6
A	WO 2014-154188 A1 (INSTITUTE OF EXPERIMENTAL AND APPLIED PHYSICS) 02 October 2014 See abstract, claims 1-7 and figure 1(a).	1-6
A	US 7492871 B2 (POPESCU et al.) 17 February 2009 See abstract, claims 1-37 and figure 1.	1-6
A	US 7453981 B2 (BAUMANN et al.) 18 November 2008 See abstract, claims 1-30 and figure 3.	1-6

☐ 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
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 October 2016 (31.10.2016)	**01 November 2016 (01.11.2016)**

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/043154

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.: 50-57, 59
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 50-57 and 59 pertain to a diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required to search under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv).

2. ☒ Claims Nos.: 8,9,13,14,17,18,22,26,27,29,48,51-54,57
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:
Claims 8,9,13,14,17,18,22,26,27,29,48,51-54,57 are unclear, because they refer to multiple dependent claims which do not comply with PCT Rule 6.4(a).

3. ☒ Claims Nos.: 7,10-12,15,16,19-21,23-25,28,30-47,49,50,55,56,58,59
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

1. ☐ As all required addtional 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 any additional fees.

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

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

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/043154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0161324 A1	21/11/1985	EP 0161324 B1	25/11/1987
		US 4794257 A	27/12/1988
US 9066649 B2	30/06/2015	CN 102655809 A	05/09/2012
		CN 102655809 B	17/06/2015
		EP 2509503 A1	17/10/2012
		JP 2013-513414 A	22/04/2013
		JP 5759474 B2	05/08/2015
		RU 2012128794 A	20/01/2014
		RU 2562879 C2	10/09/2015
		US 2012-0307966 A1	06/12/2012
		WO 2011-070493 A1	16/06/2011
WO 2014-154188 A1	02/10/2014	EP 2978377 A1	03/02/2016
US 7492871 B2	17/02/2009	AU 2004-202581 A1	06/01/2005
		AU 2004-202581 B2	14/08/2008
		AU 2005-200687 A1	01/09/2005
		AU 2005-200687 B2	16/07/2009
		AU 2005-201357 A1	20/10/2005
		AU 2005-201357 B2	08/03/2007
		AU 2005-201523 A1	01/12/2005
		AU 2005-201523 B2	12/11/2009
		AU 2005-201776 A1	08/12/2005
		AU 2005-201776 B2	19/04/2007
		AU 2005-201851 A1	24/11/2005
		AU 2005-202048 A1	01/12/2005
		AU 2005-202048 B2	03/03/2011
		AU 2005-202743 A1	19/01/2006
		AU 2005-202743 B2	06/09/2007
		AU 2005-218063 A1	27/04/2006
		AU 2005-248980 A1	03/08/2006
		AU 2005-248980 B2	09/12/2010
		AU 2006-203203 A1	15/03/2007
		AU 2006-203203 B2	03/01/2008
		AU 2006-222653 A1	19/04/2007
		AU 2006-222653 B2	10/06/2010
		AU 2006-241389 A1	21/06/2007
		AU 2006-241389 B2	13/10/2011
		AU 2006-256876 A1	14/12/2006
		AU 2006-256876 B2	01/12/2011
		AU 2007-200058 A1	09/08/2007
		AU 2007-200058 B2	08/01/2009
		AU 2007-219311 A1	17/04/2008
		CA 2470740 A1	13/12/2004
		CA 2491986 A1	09/07/2005
		CA 2493338 A1	23/07/2005
		CA 2493494 A1	30/07/2005
		CA 2497319 A1	18/08/2005

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/043154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CA 2502846 A1	02/10/2005
		CA 2503294 A1	28/09/2005
		CA 2506307 A1	07/11/2005
		CA 2506365 A1	07/11/2005
		CA 2506941 A1	12/11/2005
		CA 2507331 A1	14/11/2005
		CA 2508131 A1	26/11/2005
		CA 2509310 A1	08/12/2005
		CA 2509893 A1	05/01/2006
		CA 2510771 A1	02/01/2006
		CA 2511994 A1	24/02/2006
		CA 2512331 A1	22/01/2006
		CA 2512555 A1	23/01/2006
		CA 2517866 A1	02/03/2006
		CA 2518149 A1	09/03/2006
		CA 2518768 A1	13/03/2006
		CA 2519497 A1	14/03/2006
		CA 2520234 A1	20/03/2006
		CA 2521208 A1	29/03/2006
		CA 2521684 A1	01/04/2006
		CA 2522256 A1	05/04/2006
		CA 2522489 A1	11/04/2006
		CA 2524558 A1	29/04/2006
		CA 2524833 A1	03/05/2006
		CA 2529114 A1	06/06/2006
		CA 2529264 A1	07/06/2006
		CA 2529415 A1	10/08/2006
		CA 2530998 A1	13/07/2006
		CA 2533050 A1	19/07/2006
		CA 2536704 A1	24/08/2006
		CA 2541226 A1	27/11/2006
		CA 2542569 A1	14/10/2006
		CA 2546030 A1	11/11/2006
		CA 2546403 A1	19/11/2006
		CA 2547732 A1	27/11/2006
		CA 2549206 A1	03/12/2006
		CA 2550700 A1	21/12/2006
		CA 2551975 A1	25/02/2007
		CA 2554445 A1	17/02/2007
		CA 2555927 A1	12/02/2007
		CA 2557693 A1	16/03/2007
		CA 2560164 A1	30/03/2007
		CA 2567433 A1	10/05/2007
		CA 2567539 A1	10/05/2007
		CA 2568076 A1	10/05/2007
		CA 2570085 A1	05/06/2007
		CA 2572763 A1	26/07/2007
		CA 2576626 A1	02/08/2007
		CA 2579987 A1	25/09/2007
		CA 2585305 A1	04/05/2006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CA 2602999 A1	28/03/2008
		CA 2614993 A1	28/09/2005
		CA 2625331 A1	19/04/2007
		CA 2669952 A1	05/01/2006
		CN 1532780 A	29/09/2004
		CN 1538159 A	20/10/2004
		CN 1550788 A	01/12/2004
		CN 1572356 A	02/02/2005
		CN 1572356 B	26/01/2011
		CN 1572928 A	02/02/2005
		CN 1580617 A	16/02/2005
		CN 1597411 A	23/03/2005
		CN 1608752 A	27/04/2005
		CN 1608984 A	27/04/2005
		CN 1610027 A	27/04/2005
		CN 1610027 B	15/06/2011
		CN 1611425 A	04/05/2005
		CN 1621587 A	01/06/2005
		CN 1621587 B	12/05/2010
		CN 1622543 A	01/06/2005
		CN 1626710 A	15/06/2005
		CN 1627567 A	15/06/2005
		CN 1629523 A	22/06/2005
		CN 1636905 A	13/07/2005
		CN 1636905 B	16/05/2012
		CN 1637111 A	13/07/2005
		CN 1637111 B	27/10/2010
		CN 1637341 A	13/07/2005
		CN 1637356 A	13/07/2005
		CN 1637356 B	13/07/2011
		CN 1637439 A	13/07/2005
		CN 1637715 A	13/07/2005
		CN 1638595 A	13/07/2005
		CN 1638596 A	13/07/2005
		CN 1640580 A	20/07/2005
		CN 1640634 A	20/07/2005
		CN 1640716 A	20/07/2005
		CN 1641084 A	20/07/2005
		CN 1641084 B	26/05/2010
		CN 1641304 A	20/07/2005
		CN 1641304 B	17/07/2013
		CN 1641990 A	20/07/2005
		CN 1644966 A	27/07/2005
		CN 1648393 A	03/08/2005
		CN 1648518 A	03/08/2005
		CN 1648518 B	06/10/2010
		CN 1649209 A	03/08/2005
		CN 1651601 A	10/08/2005
		CN 1654918 A	17/08/2005
		CN 1657332 A	24/08/2005

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/043154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CN 1657646 A	24/08/2005
		CN 1660561 A	31/08/2005
		CN 1661340 A	31/08/2005
		CN 1661585 A	31/08/2005
		CN 1661585 B	14/04/2010
		CN 1664514 A	07/09/2005
		CN 1664514 B	12/05/2010
		CN 1669520 A	21/09/2005
		CN 1669676 A	21/09/2005
		CN 1673409 A	28/09/2005
		CN 1680127 A	12/10/2005
		CN 1680127 B	28/04/2010
		CN 1680128 A	12/10/2005
		CN 1680128 B	15/09/2010
		CN 1690247 A	02/11/2005
		CN 1692866 A	09/11/2005
		CN 1692896 A	09/11/2005
		CN 1694310 A	09/11/2005
		CN 1694312 B	04/08/2010
		CN 1702913 A	30/11/2005
		CN 1702913 B	01/12/2010
		CN 1707242 A	14/12/2005
		CN 1748833 A	22/03/2006
		CN 1789793 A	21/06/2006
		CN 1789793 B	19/10/2011
		CN 1796356 A	05/07/2006
		CN 1798465 A	05/07/2006
		CN 1799799 A	12/07/2006
		CN 1799799 B	26/05/2010
		CN 1918427 A	21/02/2007
		CN 1918427 B	02/06/2010
		CN 1928027 A	14/03/2007
US 7453981 B2	18/11/2008	AU 2004-202581 A1	06/01/2005
		AU 2004-202581 B2	14/08/2008
		AU 2005-200687 A1	01/09/2005
		AU 2005-200687 B2	16/07/2009
		AU 2005-201357 A1	20/10/2005
		AU 2005-201357 B2	08/03/2007
		AU 2005-201523 A1	01/12/2005
		AU 2005-201523 B2	12/11/2009
		AU 2005-201776 A1	08/12/2005
		AU 2005-201776 B2	19/04/2007
		AU 2005-201851 A1	24/11/2005
		AU 2005-202048 A1	01/12/2005
		AU 2005-202048 B2	03/03/2011
		AU 2005-202743 A1	19/01/2006
		AU 2005-202743 B2	06/09/2007
		AU 2005-218063 A1	27/04/2006
		AU 2005-248980 A1	03/08/2006

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2016/043154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		AU 2005-248980 B2	09/12/2010
		AU 2006-203203 A1	15/03/2007
		AU 2006-203203 B2	03/01/2008
		AU 2006-222653 A1	19/04/2007
		AU 2006-222653 B2	10/06/2010
		AU 2006-241389 A1	21/06/2007
		AU 2006-241389 B2	13/10/2011
		AU 2006-256876 A1	14/12/2006
		AU 2006-256876 B2	01/12/2011
		AU 2007-200058 A1	09/08/2007
		AU 2007-200058 B2	08/01/2009
		AU 2007-219311 A1	17/04/2008
		CA 2470740 A1	13/12/2004
		CA 2470740 C	01/05/2012
		CA 2491986 A1	09/07/2005
		CA 2493338 A1	23/07/2005
		CA 2493494 A1	30/07/2005
		CA 2497319 A1	18/08/2005
		CA 2502846 A1	02/10/2005
		CA 2503294 A1	28/09/2005
		CA 2503294 C	17/06/2008
		CA 2506307 A1	07/11/2005
		CA 2506365 A1	07/11/2005
		CA 2506365 C	28/06/2011
		CA 2506941 A1	12/11/2005
		CA 2507331 A1	14/11/2005
		CA 2507331 C	04/09/2012
		CA 2508131 A1	26/11/2005
		CA 2509310 A1	08/12/2005
		CA 2509893 A1	05/01/2006
		CA 2509893 C	01/02/2011
		CA 2510771 A1	02/01/2006
		CA 2511994 A1	24/02/2006
		CA 2511994 C	18/09/2012
		CA 2512331 A1	22/01/2006
		CA 2512555 A1	23/01/2006
		CA 2512555 C	26/03/2013
		CA 2517866 A1	02/03/2006
		CA 2518149 A1	09/03/2006
		CA 2518768 A1	13/03/2006
		CA 2519497 A1	14/03/2006
		CA 2520234 A1	20/03/2006
		CA 2521208 A1	29/03/2006
		CA 2521684 A1	01/04/2006
		CA 2522256 A1	05/04/2006
		CA 2522256 C	07/12/2010
		CA 2522489 A1	11/04/2006
		CA 2524558 A1	29/04/2006
		CA 2524558 C	24/04/2012
		CA 2524833 A1	03/05/2006

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CA 2529114 A1	06/06/2006
		CA 2529264 A1	07/06/2006
		CA 2529264 C	11/08/2015
		CA 2529415 A1	10/08/2006
		CA 2529415 C	08/06/2010
		CA 2530998 A1	13/07/2006
		CA 2530998 C	29/11/2011
		CA 2533050 A1	19/07/2006
		CA 2533050 C	04/06/2013
		CA 2536704 A1	24/08/2006
		CA 2541226 A1	27/11/2006
		CA 2542569 A1	14/10/2006
		CA 2546030 A1	11/11/2006
		CA 2546403 A1	19/11/2006
		CA 2547732 A1	27/11/2006
		CA 2549206 A1	03/12/2006
		CA 2550700 A1	21/12/2006
		CA 2551975 A1	25/02/2007
		CA 2551975 C	01/09/2009
		CA 2554445 A1	17/02/2007
		CA 2555927 A1	12/02/2007
		CA 2557693 A1	16/03/2007
		CA 2557693 C	19/07/2011
		CA 2560164 A1	30/03/2007
		CA 2560164 C	11/02/2014
		CA 2567433 A1	10/05/2007
		CA 2567539 A1	10/05/2007
		CA 2568076 A1	10/05/2007
		CA 2570085 A1	05/06/2007
		CA 2570085 C	10/07/2012
		CA 2572763 A1	26/07/2007
		CA 2572763 C	21/04/2015
		CA 2576626 A1	02/08/2007
		CA 2576626 C	03/08/2010
		CA 2579987 A1	25/09/2007
		CA 2579987 C	06/04/2010
		CA 2585305 A1	04/05/2006
		CA 2602999 A1	28/03/2008
		CA 2614993 A1	28/09/2005
		CA 2614993 C	05/04/2011
		CA 2625331 A1	19/04/2007
		CA 2669952 A1	05/01/2006
		CN 1532780 A	29/09/2004
		CN 1538159 A	20/10/2004
		CN 1550788 A	01/12/2004
		CN 1572356 A	02/02/2005
		CN 1572356 B	26/01/2011
		CN 1572928 A	02/02/2005
		CN 1580617 A	16/02/2005
		CN 1597411 A	23/03/2005

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CN 1608752 A	27/04/2005
		CN 1608984 A	27/04/2005
		CN 1610027 A	27/04/2005
		CN 1610027 B	15/06/2011
		CN 1611425 A	04/05/2005
		CN 1621587 A	01/06/2005
		CN 1621587 B	12/05/2010
		CN 1622543 A	01/06/2005
		CN 1626710 A	15/06/2005
		CN 1627567 A	15/06/2005
		CN 1629523 A	22/06/2005
		CN 1636905 A	13/07/2005
		CN 1636905 B	16/05/2012
		CN 1637111 A	13/07/2005
		CN 1637111 B	27/10/2010
		CN 1637341 A	13/07/2005
		CN 1637356 A	13/07/2005
		CN 1637356 B	13/07/2011
		CN 1637439 A	13/07/2005
		CN 1637715 A	13/07/2005
		CN 1638595 A	13/07/2005
		CN 1638596 A	13/07/2005
		CN 1640580 A	20/07/2005
		CN 1640634 A	20/07/2005
		CN 1640716 A	20/07/2005
		CN 1641084 A	20/07/2005
		CN 1641084 B	26/05/2010
		CN 1641304 A	20/07/2005
		CN 1641304 B	17/07/2013
		CN 1641990 A	20/07/2005
		CN 1644966 A	27/07/2005
		CN 1648393 A	03/08/2005
		CN 1648518 A	03/08/2005
		CN 1648518 B	06/10/2010
		CN 1649209 A	03/08/2005
		CN 1651601 A	10/08/2005
		CN 1654918 A	17/08/2005
		CN 1657332 A	24/08/2005
		CN 1657646 A	24/08/2005
		CN 1660561 A	31/08/2005
		CN 1661340 A	31/08/2005
		CN 1661585 A	31/08/2005
		CN 1661585 B	14/04/2010
		CN 1664514 A	07/09/2005
		CN 1664514 B	12/05/2010
		CN 1669520 A	21/09/2005
		CN 1669676 A	21/09/2005
		CN 1673409 A	28/09/2005
		CN 1680127 A	12/10/2005
		CN 1680127 B	28/04/2010

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/043154

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		CN 1680128 A	12/10/2005
		CN 1680128 B	15/09/2010
		CN 1690247 A	02/11/2005
		CN 1692866 A	09/11/2005
		CN 1692896 A	09/11/2005
		CN 1694310 A	09/11/2005
		CN 1694312 B	04/08/2010
		CN 1702913 A	30/11/2005
		CN 1702913 B	01/12/2010
		CN 1707242 A	14/12/2005
		CN 1748833 A	22/03/2006
		CN 1789793 A	21/06/2006
		CN 1789793 B	19/10/2011
		CN 1796356 A	05/07/2006
		CN 1798465 A	05/07/2006
		CN 1799799 A	12/07/2006
		CN 1799799 B	26/05/2010
		CN 1918427 A	21/02/2007
		CN 1918427 B	02/06/2010
		CN 1928027 A	14/03/2007