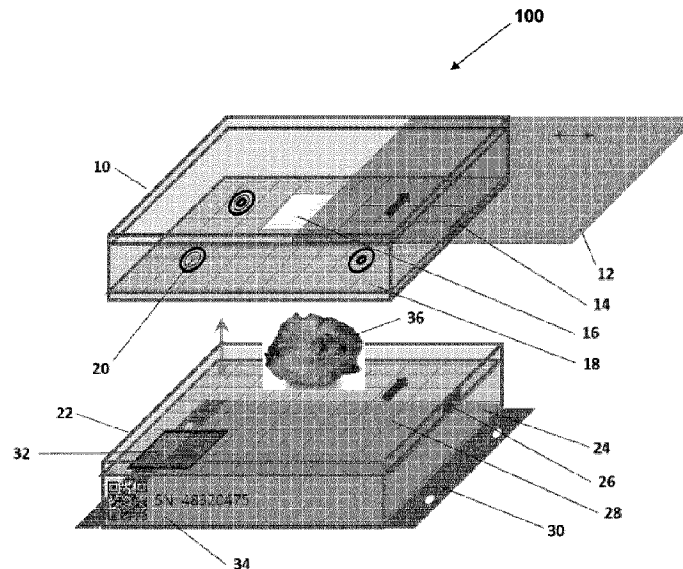




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(54) **Title: BIOPSY CASSETTE FOR MULTI-MODALITY CROSS-SYSTEM DATA CORRELATION**



(57) **Abrégé/Abstract:**

Disclosed herein is a biopsy cassette for multi-modal cross system data correlation. The cassette includes a housing including a top section and a bottom section, the top section being mateable to the bottom section in a fixed orientation with respect to each other when closed. One or both of the top and bottom sections are at least partially transparent to selected imaging modalities of interest which are used to obtain imaging data of tissue enclosed in the housing. A local coordinate system positioned and fixed with respect to the cassette so as to be in a field of view and visible to the selected imaging modalities of interest and configured to provide correlation between the selected imaging modalities of interest.

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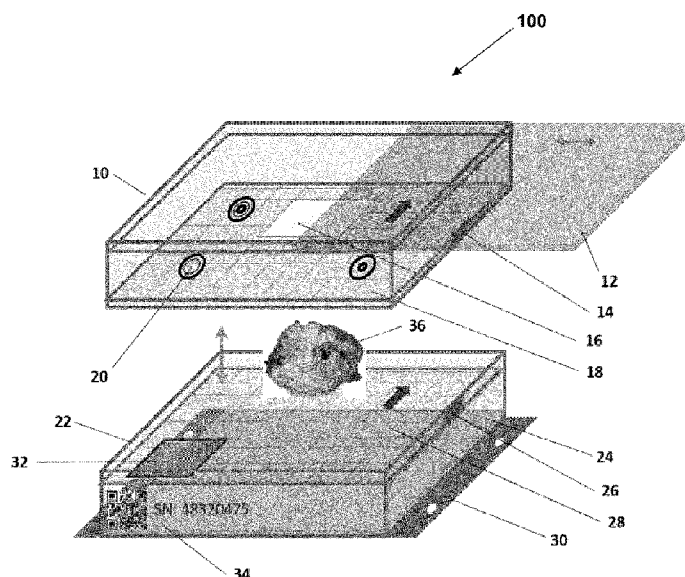


FIGURE 1

(57) Abstract: Disclosed herein is a biopsy cassette for multi-modal cross system data correlation. The cassette includes a housing including a top section and a bottom section, the top section being mateable to the bottom section in a fixed orientation with respect to each other when closed, One or both of the top and bottom sections are at least partially transparent to selected imaging modalities of interest which are used to obtain imaging data of tissue enclosed in the housing. A local coordinate system positioned and fixed with respect to the cassette so as to be in a field of view and visible to the selected imaging modalities of interest and configured to provide correlation between the selected imaging modalities of interest.

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BIOPSY CASSETTE FOR MULTI-MODALITY CROSS-SYSTEM DATA CORRELATION

FIELD

5 The present disclosure relates to a biopsy cassette comprising a local coordinate system to enable cross-system data correlation of a given tissue sample.

BACKGROUND

10 The standard surgical procedure for taking and analyzing biopsy samples is quite primitive. Generally, resection tools, such as the NICO Myriad[®], biopsy needles, or knives are used to remove a sample of tissue from the patient, which is then placed in a plastic container. The container is generally either empty, or comprises solution (e.g. saline and phosphate
15 buffered formalin) to preserve the sample for further analysis, for example, studies in pathology. In all cases, the orientation of the removed tissue sample with respect to the patient, and pre-operative image coordinates are lost.

 As a result, post-operative images and any further analysis performed on the removed tissue cannot be correlated to intra-operative images and videos,
20 or pre-operative images. Further, any imaging or data analysis performed on the removed tissue sample by multiple systems, platforms, or modalities cannot be correlated altogether for analysis.

 One example of a tool presently used in the art to store biopsy samples is the Leica Biosystems Biopsy-Cassette. Such a cassette is in essence a
25 simple plastic container, which offers no mechanisms to provide a local coordinate system visible by the different imaging modalities or system to optimize analysis including those requiring correlation between the different modalities or system.

 Further, current tissue containers with tissue securing features do not
30 contain any local coordinate system readable by an imaging system and does not have any openings to image the tissue. One example of a current tissue container describe would be the CellSafe Biopsy Insert, offered by Fisher Scientific. This device could secures the biopsy tissue between two fabric materials which prevent it from shifting during transportation. However, it does

not have a mechanism to enable imaging of the tissue unless the container securing the tissue is opened which could cause tissue shifting and does not enable the correlation of scans performed on multiple platforms.

Finally, biopsy cassette patent WO2000067639 is similarly limited, in that
5 there are no embedded coordination mechanisms that allow post-op analysis to be correlated across multiple analysis platforms.

Therefore, it would be desirable to achieve a means of storing biopsy samples during surgery such that the orientation of the removed tissue sample is preserved, and such that a local coordinate system are established within the
10 storage unit so sample analysis data can be correlated across multiple platforms.

SUMMARY

The present disclosure relates to a biopsy cassette for multi-modal cross
15 system data correlation. In an embodiment, the biopsy cassette for multi-modal imaging cross system data correlation, comprises:

a housing including a top section and a bottom section, said top section being mateable to said bottom section in a fixed orientation with respect to each other when closed, at least one of said top and bottom sections being at least
20 partially transparent to selected imaging modalities of interest which are used to obtain imaging data of tissue enclosed in said housing; and

a local coordinate system positioned and fixed with respect to said cassette so as to be in a field of view and visible to the selected imaging modalities of interest and configured to provide correlation between the
25 selected imaging modalities of interest.

In an embodiment there is provided a method of imaging tissue using multiple imaging modalities and performing multi-modal imaging data correlation, comprising:

fixing a tissue sample into a housing made of materials at least partially
30 transparent to selected imaging modalities which are used to obtain imaging data of tissue enclosed in said housing;

imaging, using each of the multiple imaging modalities, a selected volume of the tissue sample and a unique local coordinate system associated with, and visible to, a given imaging modality, the unique local coordinate

system being in a known position on, or in close proximity to the housing thereby obtaining imaging data associated with each imaging modality, the position of each unique local coordinate system for each given imaging modality being known with respect to the unique local coordinate system of all other imaging modalities; and

correlating the imaging data associated with each imaging modality based on the known position of each unique local coordinate system with respect to all other unique local coordinate systems to provide cross correlated multi-modal imaging data of the selected volume of tissue.

In an embodiment the local coordinate system may comprise patterns of fiducials which are visible to non-photon based imaging modalities.

In an embodiment the local coordinate system may comprise any one or combination of

grid patterns, and dot patterns which are visible to photon based imaging modalities, and

a combination of patterns of fiducials which are visible to non-photon based imaging modalities.

The fiducials that are visible to non-photon based imaging modalities may be attached directly to the housing, or located adjacent to the housing, or a combination of being attached directly to the housing and adjacent to the housing.

The multiple imaging modalities may include any combination of visible imaging modalities, X-ray imaging modalities, ultrasound imaging modalities, optical coherence tomography modalities, Raman spectroscopy imaging modalities, computed tomography, terahertz imaging, fluorescence imaging, photoacoustic imaging, multispectral imaging, hyperspectral imaging, thermal imaging, magnetic resonance imaging, diffusion magnetic resonance imaging, 3D imaging including structure light imaging, imaging using photometric stereo technique and/or stereoscopic imaging.

A further understanding of the functional and advantageous aspects of the present disclosure can be realized by reference to the following detailed description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments disclosed herein will be more fully understood from the following detailed description thereof taken in connection with the accompanying drawings, which form a part of this application, and in which:

Figure 1 shows a detailed diagram of a preferred embodiment of the biopsy cassette and its internal components.

Figure 2A shows an image of an empty biopsy cassette in the open position.

Figure 2B shows an image of a biopsy cassette containing a sample in the closed position.

Figure 3 shows a diagram of a warped mesh grid layer overtop a tissue sample.

Figure 4 shows a diagram of an embodiment of the biopsy cassette attached to a slider and being fastened to a biopsy cassette coordinator.

Figure 5 shows a diagram of an embodiment of the biopsy cassette attached to a slider being fastened to a biopsy cassette holder.

Figure 6 shows a preferred embodiment of the biopsy cassette wherein there are arrays of cutouts on the top and bottom frames of the cassette.

Figure 7 shows a diagram of the biopsy cassette with cutouts attached to the biopsy cassette holder, being placed in solution for storage.

Figure 8A shows a diagram of an exemplary multi-modal fiducial based coordinate system.

Figure 8B shows individual panel diagrams of the MRI, the CT, and the IR coordinate system components.

Figure 9A shows an example drawing of orientation marking and alignment with a tissue marking pen before the biopsy sample is removed.

Figure 9B shows a drawing of a biopsy sample post-operation that comprises orientation markings.

Figure 9C shows a drawing of a marked up biopsy sample being placed inside the biopsy cassette for further analysis or storage.

DETAILED DESCRIPTION

Various embodiments and aspects of the disclosure will be described with reference to details discussed below. The following description and drawings are illustrative of the disclosure and are not to be construed as limiting the disclosure. The drawings are not to scale. Numerous specific details are

described to provide a thorough understanding of various embodiments of the present disclosure. However, in certain instances, well-known or conventional details are not described in order to provide a concise discussion of embodiments of the present disclosure.

5 As used herein, the terms “comprises” and “comprising” are to be construed as being inclusive and open ended, and not exclusive. Specifically, when used in the specification and claims, the terms “comprises” and “comprising” and variations thereof mean the specified features, steps or components are included. These terms are not to be interpreted to exclude the
10 presence of other features, steps or components.

 As used herein, the term “exemplary” means “serving as an example, instance, or illustration,” and should not be construed as preferred or advantageous over other configurations disclosed herein.

 As used herein, the terms “about” and “approximately” are meant to
15 cover variations that may exist in the upper and lower limits of the ranges of values, such as variations in properties, parameters, and dimensions.

 As used herein, the expression “fiducials” refers to components that are engineered to be visible by the imaging modalities or systems of interest. They might contain or enable the design of a unique pattern that could be used to
20 identify the coordination of the sample position and orientation.

 As used herein, the phrase “unique local coordinate system” or “local coordinate system” refers to a unique coordinate system fixed to one or more components making up the biopsy cassette and which is visible to all imaging modalities of interest that enables correlations for images taken with the
25 different modalities from the same sample. For photon based imaging modalities (i.e. techniques using wavelength anywhere from deep UV to visible to NIR, mid-IR and Far-IR) , patterns of grids, patterns of dots and the like may be used, which may or may not be annotated can be printed onto one or more components of the cassette which are visible in the visible and near infrared
30 portion of the spectrum. For non-photon based imaging modalities such as ultrasound, x-ray, computed tomography (CT), magnetic resonance imaging (MRI), infrared imaging to mention just a few, patterns of fiducials placed in a fixed position either on the cassette in close proximity to the cassette to be in the field of view of the imaging system may be used to form the unique

coordinate system. Any combination of the photon based coordinate system with the fiducial based coordinate system may be used depending of the anticipated imaging modalities to be employed.

5 The phrases "unique coordinate system" or "coordinate system" refers to all the types of coordinate systems associated with the cassette, not one in particular.

10 This enables correlation between images taken from the different imaging systems/modalities through aligning the unique pattern labelled on the cassette. In one example, to correlate white light images between different systems of different resolution and/or field-of-view and/or different depth-of-view, a grid type of coordinate system with arrows and circles could be used. Images from the different systems could be scaled and translated to match the spacing between the grid and circles to match the scale of the image. The arrows and circles will further be matched to match the orientation of the
15 images. In another example, to correlate between different photon based images, a coordinate system with an orientation unique pattern made out of fiducials for different imaging modality could be used. The shape and size of the fiducials and the pattern will be used to match the scale of the image while matching the unique orientation of the pattern enables matching orientation of
20 the images.

The goal of correlating the imaging data between the various imaging modalities is to ensure that each set of imaging data from the different modalities are of the same volume of tissue. By correlating the location and scale of the images between different modalities, information from the different
25 image can be compared for further analysis including pathology studies which is the gold standard for determining different tissue types and states. This is achieved by knowing the location of the sampling volume of the imaging data set with respect to its particular coordinate system which allows correlation between the different imaging sets since the relationship of each coordinate
30 system with all others is fixed and known.

Referring to **Figure 1**, the present disclosure relates to an enhanced biopsy cassette **100**, that fixes a given biopsy sample **36** (e.g. tissue) in place to maintain a stable local coordinate system, to correlate scans between multiple

analysis systems. Such a cassette will enable multi-modal cross system data correlation for pre-op, intra-op, and post-op phases.

In an embodiment, the cassette **100** may include a transparent quadrilateral top frame **10**, comprising: four side walls, a removable top window plate **12**, and a top membrane layer **18** orthogonal to the four side walls while parallel to the top window plate **12**. There is further included a transparent quadrilateral bottom frame **22**, comprising: four side walls, a non-removable bottom window plate **24**, and a bottom membrane layer **28** orthogonal to the four side walls while parallel to the bottom window plate **24**. It will be appreciated that the above description of the cassette is exemplary, and certainly the cassette housing components are not restricted to being quadrilateral or any other shape.

The transparent quadrilateral top housing frame **10** is mateable to the transparent quadrilateral bottom housing frame **22** such that the top membrane layer **18** and the bottom membrane layer **28** are face-to-face. Such mating is enabled by notches **14** and **26** provided on the top and bottom frames **10** and **22** of the cassette which are configured to lock the top and bottom housing sections **10** and **22** together. This mating feature enables the establishment of a local coordinate system by fixing a given sample **36** in place in between the two membrane layers **18** and **28**.

In an embodiment of such a cassette **100**, the top and bottom membrane layers **18** and **28** are comprised of thin highly elastic transparent polyether polyurethane, but any other transparent membrane material may be used. In order for the layers **18** and **28** to accommodate varying sample types and thicknesses, in various embodiments the top membrane layer **18** and the bottom membrane layer **28** can be spaced at varying distances from each other so to best preserve any given sized sample **36**. The morphology of such membranes **18** and **28** can be generally a thin mesh arranged in a repeating pattern, or further a thin mesh that additionally comprises a variation of shapes, openings, or divots therein. In certain embodiments, it may be beneficial for the top and bottom membrane layers **18** and **28** to include a number of thin supportive wires.

Alternatively, flat transparent rigid plates of a material such as highly transparent quartz can be optionally included or used instead of the membrane

on one or both sides of the cassette **100** in any such embodiment to further support samples during **36** examination. The inclusion of such rigid plates will further reduce imaging or spectroscopic artifacts, (e.g. Raman and Ultrasound imaging). Further, it flattens the sample surface which improve image visibility
5 for techniques with shallow depth of field such as high resolution microscopy or OCT.

The choice of whether to use flexible membranes or rigid plates as tissue engaging members will depend on the type of tissue being imaged. The use of flexible membranes may be more appropriate when the tissue being imaged is
10 very hard, such as hardened tumors or bone that are not prone to being compressed. On the other hand, when dealing with soft compressible tissues, the use of the hard tissue engaging plates will flatten the tissue to some extent which may be beneficial for holding the soft tissue in one compressed position for the duration of the imaging sequences.

In another embodiment, the top membrane layer **18** (or bottom membrane **28**) may include a center opening **16**, in addition to comprising the removable plastic window **12**. This combination of features enables in-contact imaging with the window **12** removed, and prevents artifact generation from the membrane **18** , e.g. strong light reflection. For example, Fuel 3D Scanify® 3D
20 scanner could be used on a sample in such a cassette without experiencing distortion caused by the membrane **18** or plastic window **12**. Further, the window **12** could also be designed to accommodate the optical requirements for different imaging techniques. For example, in Raman spectroscopy with 785 nm laser, quartz could be used to eliminate artifacts or fluorescence signals from
25 the window while maximizing the throughput of the laser. In another example, a coated NBK7 window could be used to maximize light throughput; thus maximizing imaging sensitivity, while reducing artifacts results from back reflections of the window. In another example. multi-spectral and hyperspectral imaging might require imaging wavelength from ultraviolet (UV) to visible and
30 near infrared (NIR); thus a material with high throughput in all these wavelength should be utilized to maximize imaging sensitivity.

Alternatively, in another embodiment the top window plate is fixed on the cassette, such that it exhibits a contact angle of 8 degrees or less and is coated

with an anti-reflective coating. An embodiment such as this enables optical imaging while avoiding intense reflection from the window.

A unique coordinate system is generally provided as well to correlate scans between multiple sample analysis systems and this local coordinate
5 system may be affixed onto any component of the cassette **100**, including one or both of the top and bottom housing sections **10** and **22**, one or both of the membrane layers **18** and **28**, or any combination of these components.

In an embodiment, the local coordinate system to correlate scans across multiple imaging platforms may be provided in part by designing the top
10 membrane layer **18** to include markings **20**. Examples of such markings **20** include three or more printed points on the top membrane layer **18**, or providing it with a printed grid pattern. Such a grid pattern enables 3D imaging of the biopsy sample (e.g. tissue) based on white light images (or structured light). An example with a warped grid layer is shown at **38** in **Figure 3**. There is also
15 provided an embodiment wherein the bottom membrane layer **28** and sides of the bottom frame **22** are provided with markers as well (e.g. printed coordinates or a grid) for the purpose of imaging.

As noted above, in another embodiment, for non-photon based imaging modalities, the coordinate system may be provided by a multi-modal fiducial
20 based coordinate system (or fiducial identifier) shown at **32** in **Figure 1**, in addition to the above mentioned markers. **Figure 8A** shows a diagram of an exemplary multi-modal fiducial based coordinate system **32** which is placed either inside cassette **100**, as shown in **Figure 1**, or it may be placed in a fixed position just outside of cassette **100**, depending on size constraints. **Figure 8B**
25 shows individual panel diagrams of the MRI, the CT, and the IR based coordinate system components to give some non-limiting examples. Each of these non-photon based fiducials for each imaging modality is placed in a unique pattern separate from the patterns of the other fiducials.

The fiducial identifier/coordinate system may be provided between the
30 bottom membrane **28** and the bottom housing section **22** as shown in **Figure 1**. As shown in **Figure 5**, fiducials may be attached to the cassette **200** itself as shown at **210**, or they may be attached to the inner surface of holder **44** adjacent to cassette **200**, or a combination of both so long as they are in the field of view of the imaging device. As previously noted, these fiducial based

coordinate systems serve the purpose of coordinating correlation between the scans of various modalities (i.e., the fiducials shown in a scan should match between scans in the right orientation). Images from different modalities may then be overlaid for analysis, and the fiducials shown in the image of the
5 different modality could be combined and matched together if coordinates and orientation are matched. The fiducials can be 2D or 3D (for MRI for example). If the size of this device cannot be made small enough, then it could be used on the “biopsy cassette coordinator” shown at **40** in **Figure 4**. Note that the fiducial used in this coordinate system is not limited to any particular modality and can
10 be used with any fiducial used with the modality of interest or any parts or device that gives contrast to the modality of interest.

Figures 4, 5 and 6 show that cassette **200** is configured differently than cassette **100** in **Figure 1**, such that cassette **200** is comprised of a plastic container having a rigid top housing section **202** and a rigid bottom housing
15 section **204** which have a living hinge along one side connecting them together and with the two sections configured to be snapped shut when the tissue sample is inserted into cassette **200**. In this embodiment, the rigid top **202** and rigid bottom **204** are the tissue engaging members so that cassette **200** does not require additional flexible or rigid tissue engaging members.

20 The top housing section **202** as shown in **Figure 4** is produced to have an open grid or lattice structure (along with the bottom section **204**) to provide apertures **46** (**Figure 6**) so that when the tissue is enclosed in the cassette, fixing or preservation fluid can easily fill the cassette, and the various imaging techniques can still penetrate through the open lattice structure. As shown the
25 coordinate system for non-photon based imaging includes fiducials **42** shown at the corners of coordinator **40**, but they may be placed anywhere on coordinator **40** or affixed to cassette **200**.

The cassette **200** may have the photon based coordinate system printed on the lattice structure. **Figures 4, 5 and 7** also shows the different
30 embodiments in which the cassette could be attached to other containers or adapters to an imaging system or for storage. Figure 4 shows an adaptor plate that contains a fixed coordinate system for an imaging system that could be used in conjunction with the correlate system on the cassette so that the two coordinate system between the cassette and the imaging system can be fixed

and correlated. The same design could be used for coordinate system used between a coordinate system for different imaging modalities in which the cassette coordinate system is visible for visible imaging system and/or ultrasound, and the coordinate system on the plate is for infrared navigation or imaging system and/or MRT and CT as an example.

Figure 5 shows an example that the cassette could be attached to a petri dish that could be loaded into an imaging system such as the biopsy imaging system provided by Synaptive Medical Inc.. An example of a platform to perform such imaging is disclosed in International PCT Patent Publication WO2017/185161, which is PCT Serial No. PCT/CA2016/050502.

The petri dish could further contain liquid to better preserve the tissue during imaging or improve the imaging sensitivity. **Figure 7** shows an example of a cassette that could be slide into a side of a container that contains liquid for long term preservation and/or imaging with greater sensitivity.

After storing a sample, the cassette **100 or 200** can be either quickly sealed with a glue (e.g. UV cure glue or fast cured epoxy), or remain closed shut with a rubber seal and mechanical locking mechanism.

In order for an embodiment of the cassette **100** to slide onto a biopsy cassette coordinator **40** (or alternatively, a biopsy cassette holder **44** in **Figure 5**, and **Figure 7**), the cassette **100** is attached to a "slider" **30**, that being a thin rectangular platform comprising holes **31** that are mateable with the various pins **33** mounted on the various attachment bases (e.g. holder **44** as shown in **Figure 5** but coordinator **40** may also contain such mounting pins as shown in **Figure 4**). All previously described embodiments of the mated biopsy cassette (one of which is shown at **48** in **Figure 7**) can be attached to slider **30** (**Figure 4**), and joined to an associated biopsy cassette coordinator **40** (**Figure 4**).

Figure 4 shows fiducials **42** mounted at the corners of coordinator **40** rather than inside cassette **100**. In this example, the coordinator **40** serves the purpose of reference tracking and coordinate linking with MR (**52**), CT (**54**), and NIR (**56**) coordinate system components (shown in **Figure 8A** and **8B**) using their respective fiducials. Note that this is not limited to just MRI, CT and IR modalities but could be made with any fiducials that could be imaged within the imaging distance of the system used. For example, a pattern formed by near infrared (NIR) reflective balls (i.e. NIR fiducials) could be used to locate the

overall coordinates of the object in 3D space in the room. By design, the CT and MR's unique fiducial patterns are set to be at a fixed coordinate transform to the NIR fiducial pattern; therefore, the image coordinate determined by the respective CT and MR images linked to location and orientation of the entire sample in the room with a navigation system. Moreover, the images in CT and MR containing their respective patterns formed by their respective fiducial patterns can be correlated to other images through the designed fixed coordinate transform. Since the printed/labeled coordinate system on the cassette is fixed in a particular position to the fiducial patterns on the coordinator **40**, the coordinate system between the two can be determined through a pre-designed or pre-set fixed coordinate transformed. This system enables coordinate linking between a photon based imaging system (i.e. imaging system using wavelength from deep UV to visible to NIR, mid-IR and Far-IR) and a non-photon imaging system that includes all the others including and not limited to ultrasound, microwave, radio, and wave used in MRI, CT and X-ray. An example of a platform to perform such imaging is disclosed in International PCT Patent Publication WO2017/185161, which is PCT Serial No. PCT/CA2016/050502.

Another embodiment includes a cassette **48** comprising a sample **36** attached to slider **30** and mated to holder **44** for sample storage, wherein the holder **44** comprises a preservation or fixation solution **50**, e.g. saline, formaldehyde, formalin and buffered formalin, or any combination thereof. Any other known preservative solution may be used as well.

The biopsy cassette holder **44** containing the preservation or fixation solution **50** could be used for long term storage of the cassettes, if needed, after sealing the cassette **100**. Alternatively, the cassette **100** could contain a small amount of liquid for tissue preservation or fixation which is sealed together with the tissue in the cassette **100**. A large amount of solution might cause the tissue position to drift and lose its coordinate.

A barcode and serialized label **34** in **Figures 1, 4-6** is generally provided on the cassette's side in all embodiments for tracking and tissue correlation. The term barcode here refers to an information or part tracking system and is not limited to traditional barcode labels with vertical or horizontal black bars.

The barcode may also include radio frequency identification (RFID) and quick response (QR) codes.

Finally, there are several additional methods that could be used in conjunction with any of the previously described embodiments to help link the orientation of the biopsy sample **36** from the surgical field to the biopsy cassette **100**.

One method comprises recording the coordinate in the navigation system before the biopsy is removed from the patient, and after the biopsy tissue sample has been removed and placed in the cassette **100**. The cassette coordinate and orientation are recorded through the fiducials on the cassette coordinator **40**.

Further, in order to orient samples with respect to a patient, marking techniques may be employed, e.g. with a sterile surgical marking pen, before taking the biopsy to mark the top and orientation of the tissue sample **36** relative to the imaging camera. Examples of how a patient could be marked are provided in **Figures 9A, 9B, and 9C**. The marking **94** of the biopsy sample before removal can be aligned with the arrow on the cassette **100** sample to link orientation between surgical site **90** and cassette coordinate. An example of a pre-op marked surgical site is shown in **Figure 9A**. The marker need only be temporary, but is preferably waterproof. A potential example of the marker includes any from the line of Aspen Surgical's patient identification and marking pens, however any sterile surgical marking pen could also be used. An image of a post-op marked sample of tissue **96** is shown in **Figure 9B**.

An ablative laser could also be used to make markings on tissue before it is taken out of the patient to identify orientation when the marked tissue **96** is placed into the biopsy cassette **100**, as shown in **Figure 9C**.

Note that pre-op image coordinates are linked to intra-op imaging coordinate through the use of a navigation system. The biopsy cassette coordinator **40** will further link the pre-op and intra-op coordinates to post-op ex-vivo imaging coordinates. The post-op ex vivo imaging technique is not limited to conventional techniques such as white light microscopy. Advanced techniques such as, but not limited to, fluorescence, life time fluorescence, OCT, Raman, mass spectroscopy, multi-photon imaging can also be used to

obtain imaging that links to pre-op and intra-op images using the present biopsy cassette **100**.

While various imaging modalities have been mentioned above, it will be appreciated that the present biopsy cassette may be used with a multitude of imaging techniques/systems, including but not limited to The multiple imaging modalities may include any combination of visible imaging modalities, X-ray imaging modalities, ultrasound imaging modalities, optical coherence tomography modalities, photoacoustic imaging, Raman spectroscopy imaging modalities, computed tomography, terahertz imaging, fluorescence imaging, multispectral imaging, hyperspectral imaging, thermal imaging, magnetic resonance imaging, diffusion magnetic resonance imaging, 3D imaging including structure light imaging, imaging using photometric stereo technique and/or stereoscopic imaging.

While the teachings described herein are in conjunction with various embodiments for illustrative purposes, it is not intended that these teachings be limited to such embodiments. On the contrary, the teachings described and illustrated herein encompass various alternatives, modifications, and equivalents, without departing from the embodiments, the general scope of which is defined in the appended claims.

Except to the extent necessary or inherent in the processes themselves, no particular order to steps or stages of methods or processes described in this disclosure is intended or implied. In many cases the order of process steps may be varied without changing the purpose, effect, or import of the methods described.

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WHAT IS CLAIMED IS:

1. A biopsy cassette for multi-modal imaging cross system data correlation, comprising:
 - a housing including a top section and a bottom section, said top section being mateable to said bottom section in a fixed orientation with respect to each other when closed, at least one of said top and bottom sections being at least partially transparent to selected imaging modalities of interest which are used to obtain imaging data of tissue enclosed in said housing; and
 - a local coordinate system positioned and fixed with respect to said cassette so as to be in a field of view and visible to the selected imaging modalities of interest and configured to provide correlation between the selected imaging modalities of interest.
2. The biopsy cassette according to claim 1, wherein said local coordinate system comprises any one or combination of grid patterns, and dot patterns overlaid on at least one of said top and bottom sections which are visible to photon based imaging modalities.
3. The biopsy cassette according to claim 1, wherein said local coordinate system comprises patterns of fiducials which are visible to non-photon based imaging modalities.
4. The biopsy cassette according to claim 1, wherein said local coordinate system comprises any one or combination of
 - grid patterns, and dot patterns which are visible to photon based imaging modalities, and
 - a combination of patterns of fiducials which are visible to non-photon based imaging modalities.

5. The biopsy cassette according to claims 3 or 4, wherein said fiducials which are visible to non-photon based imaging modalities are attached directly to said housing, or located adjacent to said housing, or a combination of being attached directly to said housing and adjacent to said housing.
6. The biopsy cassette according to any one of claims 1 to 5, wherein said top and bottom sections are comprised of a lattice structure having holes extending therethrough to permit fluid to flow into said housing.
7. The biopsy cassette according to any one of claims 1 to 6, wherein one or both of said top and bottom sections include said local coordinate system printed thereon visible by a photon based imaging modality.
8. The biopsy cassette according to any one of claims 1 to 7, wherein one or both of said top and bottom sections have removable sections adjacent to a position of the fixed tissue to permit imaging through one or both of said top and bottom sections.
9. The biopsy cassette according to any one of claims 1 to 7, wherein one or both of said top and bottom sections have optical window sections made of selected optical materials adjacent to a position of the fixed tissue to permit imaging through said optical windows.
10. The biopsy cassette according to any one of claims 1 to 9, further comprising a transparent top tissue engaging support member affixed to said top section and a transparent bottom tissue engaging support member affixed to said bottom section and configured such that said top and bottom tissue engaging support members are face to face and spaced from each other in said housing to sandwich a tissue sample therebetween when said biopsy cassette is closed thereby fixing the tissue sample with respect to the biopsy cassette when said biopsy cassette is closed.

11. The biopsy cassette according to claim 10, wherein said transparent top tissue engaging support member and transparent bottom tissue engaging support member are comprised of sheets of flexible polymer material.
12. The biopsy cassette according to claim 11, wherein said flexible polymer material is highly elastic transparent polyether polyurethane.
13. The biopsy cassette according to claims 11 or 12 wherein the each sheet of polymer material are in the form of any one or combination of a continuous sheet, an open lattice structure having a repeating mesh pattern, a lattice structure comprising a variation of lattice patterns.
14. The biopsy cassette according to any one of claims 11, 12 or 13, wherein one or both of said transparent top and bottom tissue engaging members include a plurality of thin reinforcing supporting wires.
15. The biopsy cassette according to claim 10, wherein said transparent top tissue engaging support member and transparent bottom tissue engaging support members are comprised of two rigid flat plates to compress the tissue sample therebetween during scanning by the selected imaging modalities of interest.
16. The biopsy cassette according to claim 15, wherein the two rigid flat plates are comprised of transparent quartz or glass material.
17. The biopsy cassette according to any one of claims 10 to 16, wherein one or both of said transparent top and bottom tissue engaging members include said local coordinate system printed thereon which is visible by a photon based imaging modality.
18. The biopsy cassette according to any one of claims 1 to 17, further comprising a cassette holder having dimensions suitable to receive therein said biopsy cassette.

19. The biopsy cassette according to claim 18 wherein said cassette holder is configured to be sealed closed with a leak-tight seal, and including a sample preservation solution sealed therein enveloping the sample sealed in said biopsy cassette.

20. The biopsy cassette according to any one of claims 1 to 19, further comprising a planar biopsy cassette coordinator, said biopsy cassette being configured to be affixed to a top surface of said planar biopsy cassette coordinator, said planar biopsy cassette coordinator being configured to receive imaging modality specific fiducials adjacent to said biopsy cassette said planar biopsy cassette coordinator being configured for reference tracking and coordinate linking with fiducials associated with each imaging modality using their respective imaging modality specific fiducials between an imaging coordinate and biopsy cassette coordinates.

21. The biopsy cassette according to claims 18, 19 or 20, further comprising a planar slider platform having a surface area larger than a surface area of said bottom surface of said transparent bottom section and being affixed thereto such that at a peripheral edge of said slider platform extends beyond said bottom surface, and wherein said peripheral edge includes alignment apertures.

22. The biopsy cassette according to claim 21 wherein said cassette holder and said planar biopsy cassette coordinator include alignment features which align with said alignment apertures, and wherein said alignment apertures and said alignment features are configured such that said biopsy cassette can be secured to said cassette holder and said planar biopsy cassette coordinator in a fixed position and orientation.

23. The biopsy cassette according to any one of claims 1 to 22 further comprises means for identifying and tracking affixed to said biopsy cassette.

24. The biopsy cassette according to claim 23 wherein said means for identifying, tracking and tissue correlation comprises any one or combination of barcode, quick response (QR) code, radio frequency identification (RFID).

25. A method of imaging tissue using multiple imaging modalities and performing multi-modal imaging data correlation, comprising:

fixing a tissue sample into a housing made of materials at least partially transparent to selected imaging modalities which are used to obtain imaging data of tissue enclosed in said housing;

imaging, using each of the multiple imaging modalities, a selected volume of the tissue sample and a unique local coordinate system associated with, and visible to, a given imaging modality, the unique local coordinate system being in a known position, or in close proximity to the housing thereby obtaining imaging data associated with each imaging modality, the position of each unique local coordinate system for each given imaging modality being known with respect to the unique local coordinate system of all other imaging modalities; and

correlating the imaging data associated with each imaging modality based on the known position of each unique local coordinate system with respect to all other unique local coordinate systems to provide cross correlated multi-modal imaging data of the selected volume of tissue.

26. The method according to claim 25, wherein said local coordinate system comprises any one or combination of grid patterns, and dot patterns overlaid on at least one of said top and bottom sections which are visible to photon based imaging modalities.

27. The method according to claim 25, wherein said local coordinate system comprises patterns of fiducials which are visible to non-photon based imaging modalities.

28. The method according to claim 25, wherein said local coordinate system comprises any one or combination of
grid patterns, and dot patterns which are visible to photon based imaging modalities, and
a combination of patterns of fiducials which are visible to non-photon based imaging modalities.

29. The method according to claims 27 or 28, wherein said fiducials which are visible to non-photon based imaging modalities are attached directly to said housing, or located adjacent to said housing, or a combination of being attached directly to said housing and adjacent to said housing.

30. The method according to any one of claims 25 to 29, wherein the multiple imaging modalities include any combination of visible imaging modalities, X-ray imaging modalities, ultrasound imaging modalities, optical coherence tomography modalities, photoacoustic imaging, Raman spectroscopy imaging modalities, computed tomography, terahertz imaging, fluorescence imaging, multispectral imaging, hyperspectral imaging, thermal imaging, magnetic resonance imaging, diffusion magnetic resonance imaging, 3D imaging including structure light imaging, imaging using photometric stereo technique and/or stereoscopic imaging.

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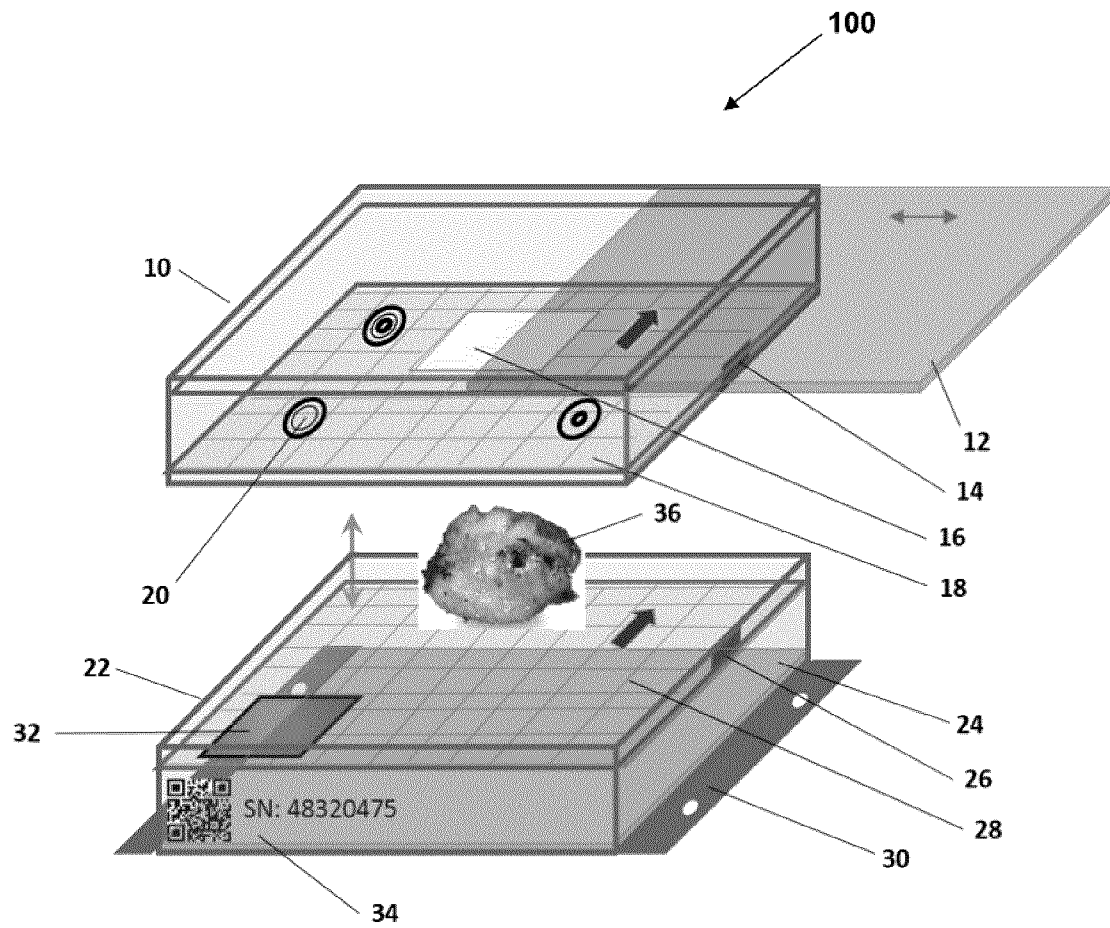
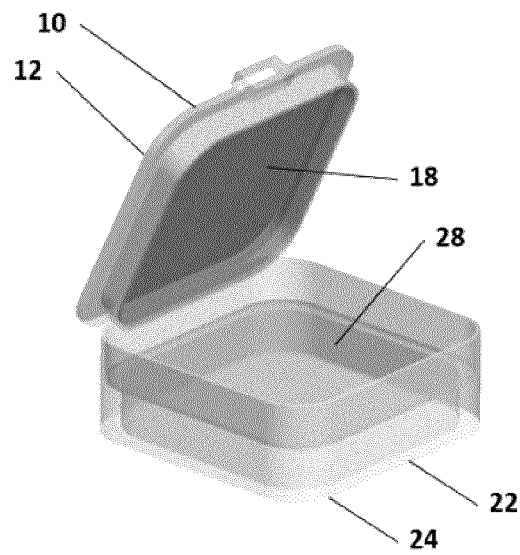


FIGURE 1

2/10**FIGURE 2A**

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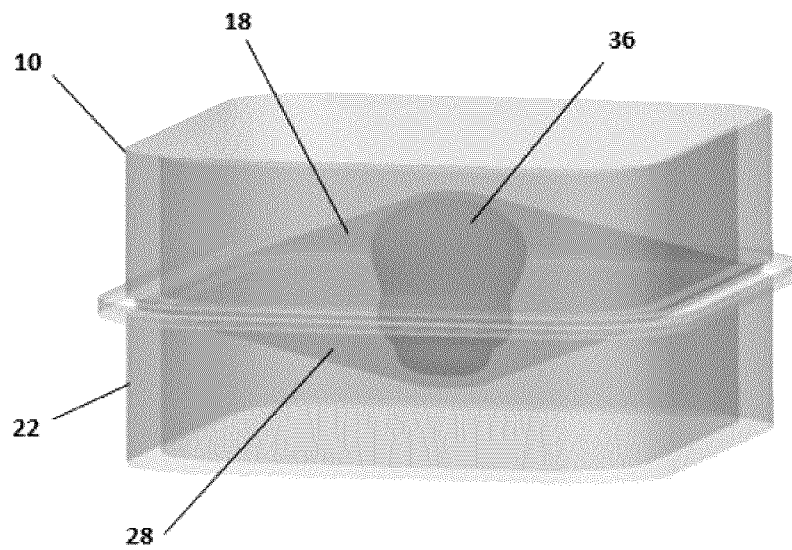


FIGURE 2B

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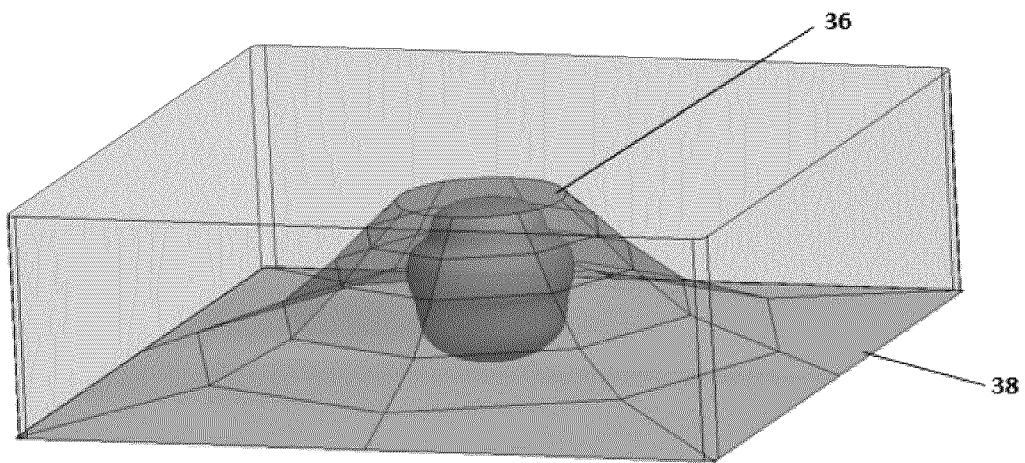


FIGURE 3

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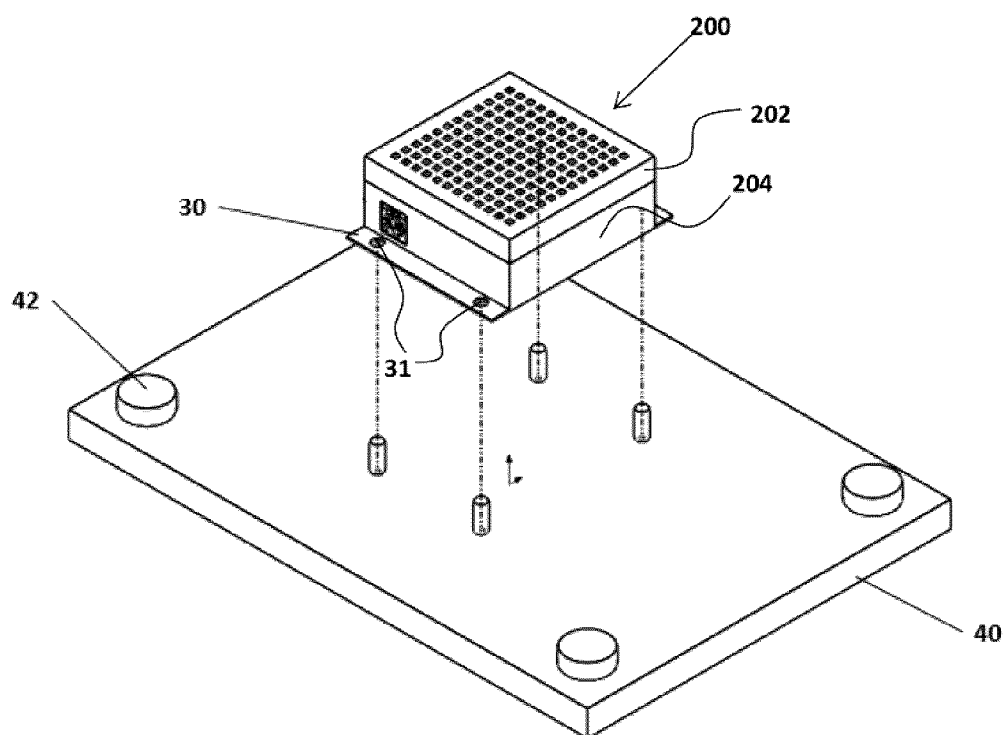


FIGURE 4

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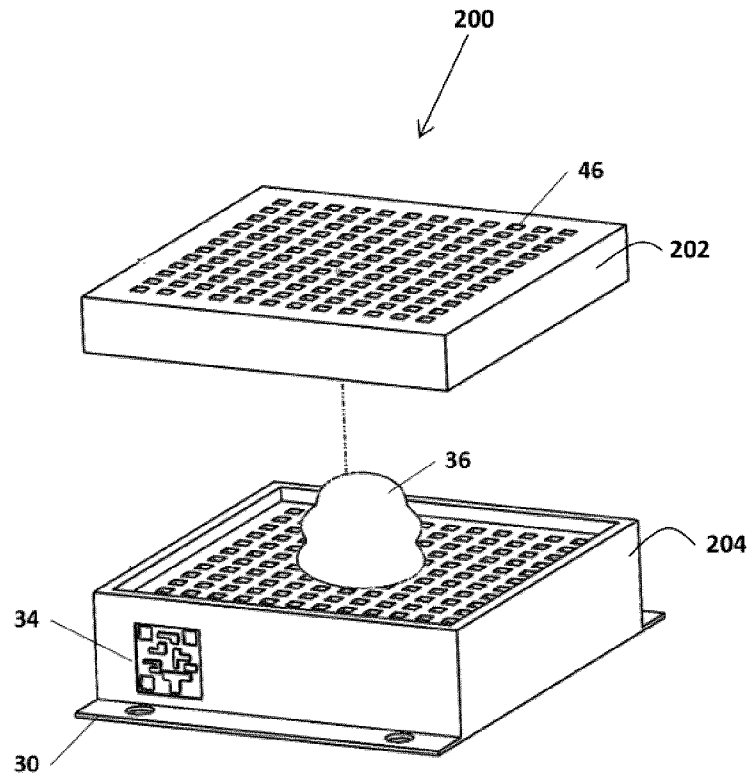


FIGURE 6

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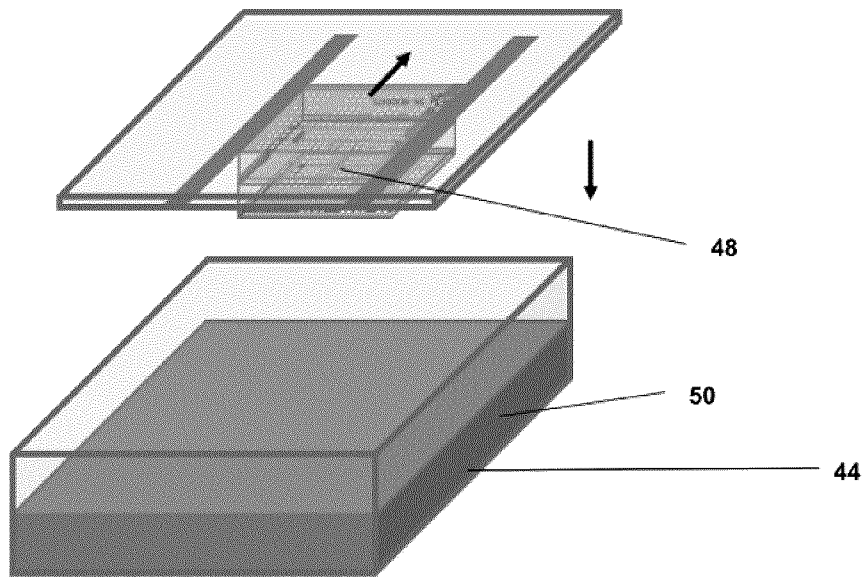


FIGURE 7

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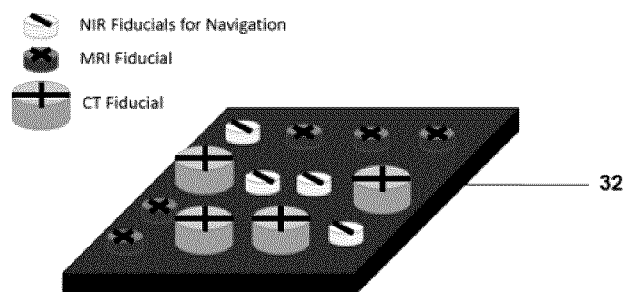


FIGURE 8A

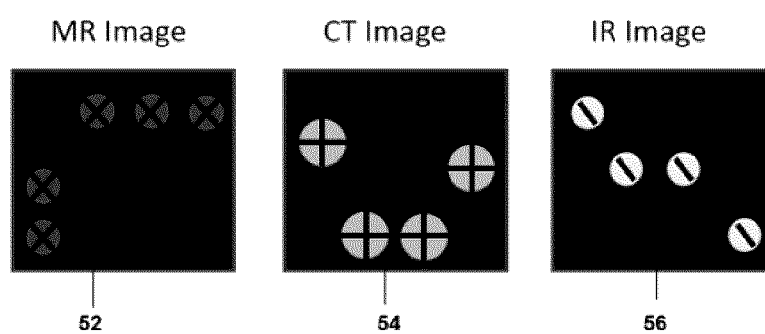
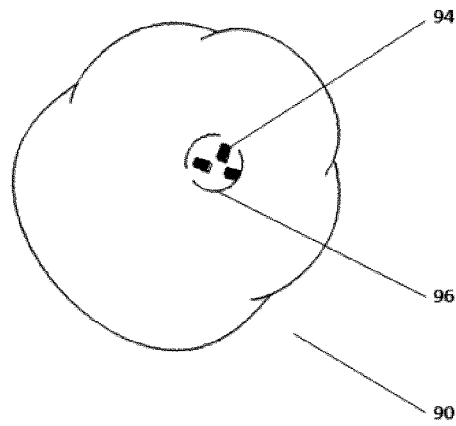
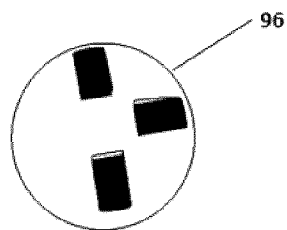
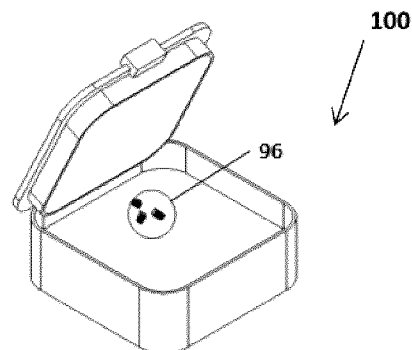


FIGURE 8B

10/10**FIGURE 9A****FIGURE 9B****FIGURE 9C**

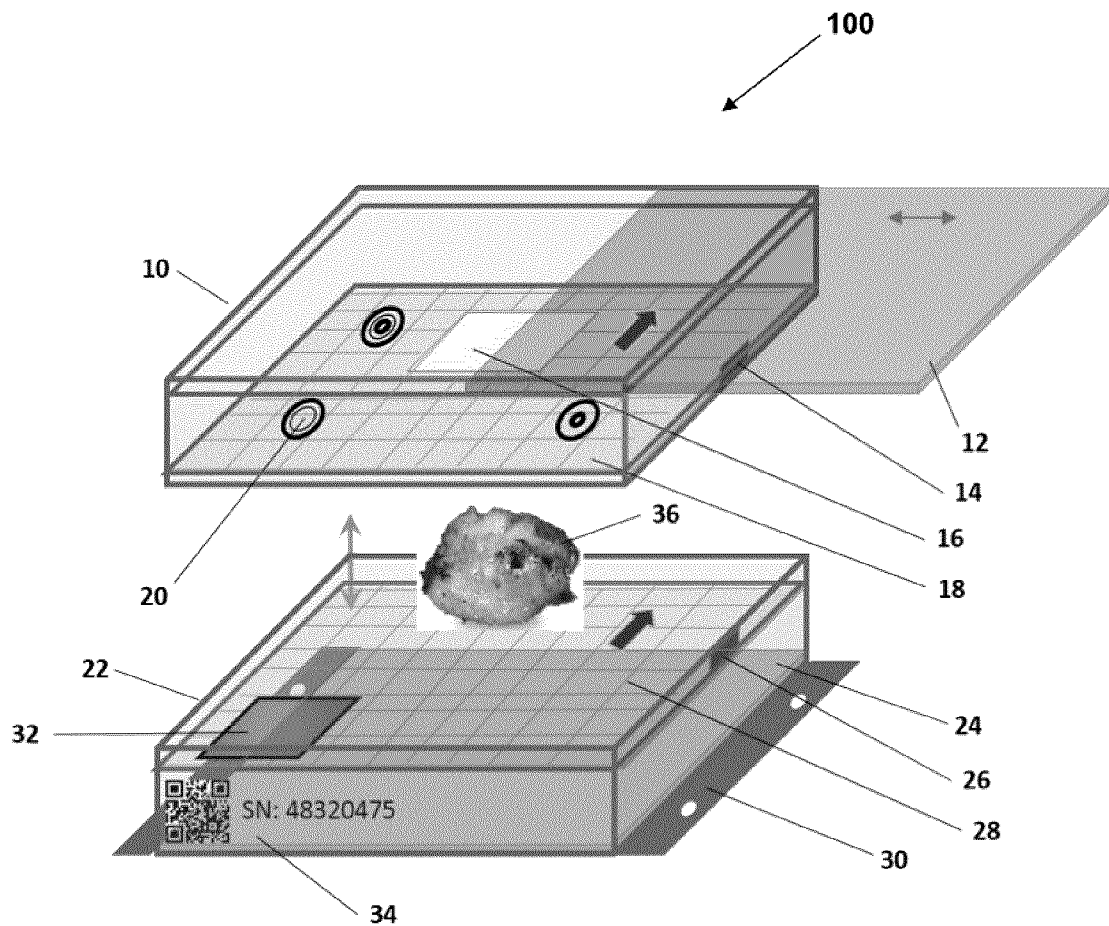


FIGURE 1