APPARATUSES AND METHODS FOR SEGREGATING TISSUE SAMPLES FOR MULTIPLE DIAGNOSTIC MODALITIES, AND PACKAGING FOR SAME

BACKGROUND

Priority

[0001] This application claims priority to U.S. Application No. 18/468,416, filed September 15, 2023 and entitled "Methods and Systems for Recovering Assessable Analytes from Core Needle Biopsies", U.S. Application No. 18/514,870, filed November 20, 2023 and entitled "Apparatuses and Methods for Segregating Tissue Samples for Multiple Diagnostic Modalities", U.S. Application No. 18/403,550, filed January 3, 2024 and entitled "Apparatuses and Methods for Segregating Tissue Samples for Multiple Diagnostic Modalities", and U.S. Application No. 18/770,387, filed July 11, 2024 and entitled "Medical Device Packaging Container", the entire contents of each of which is incorporated herein by reference and relied upon.

Technical Field

[0002] The present disclosure generally relates to apparatuses and methods for segregating tissue samples for multiple diagnostic modalities. More specifically, the present disclosure relates to biopsy container apparatuses for recovering solid tissue and dislodged cells from a biopsy and their corresponding methods of use and packaging. The present disclosure generally relates to packaging for such containers.

Background Information

[0003] Biopsies have been used for medical diagnostics for many years, serving as a method to extract and analyze samples of cells or tissues to better understand the nature and extent of a disease. A biopsy can assist in diagnosing a wide array of conditions such as cancers, where a tiny fragment of a suspicious growth or lesion is removed for microscopic examination. Through this scrutiny, pathologists may attempt to detect abnormalities, the presence of malignant cells, infections, or other pathological conditions.

[0004] The procedure to take a biopsy can vary based on the location and nature of the tissue or cells being sampled. Some biopsies, like those for the skin, are straightforward and may only utilize a needle or scalpel, and potentially local anesthesia. However, deeper tissues such as those within organs or bones might require more invasive techniques, including the use of imaging guidance like ultrasound, CT, or MRI.

[0005] Biopsies play a role in the medical decision-making process. While imaging and clinical assessments can provide insight into a patient's condition, the diagnosis can rely on the cellular and molecular details that only a biopsy can provide. It may aid in determining the presence of disease and can provide information on its stage, potential aggressiveness, and other characteristics crucial for tailoring an effective treatment strategy.

[0006] Solid tumor diagnostic procedures typically involve a tissue biopsy. Traditionally, a biopsy involves a substantial amount of tissue being surgically excised from a tumor or suspected affected tissue in a patient. The tissue, once removed from the patient's body, is processed and subsequently can be used for a number of different types of diagnostic tests.

[0007] In recent years, biopsy tools and techniques have advanced to be less invasive, with dramatically smaller tissue samples. Surgically-excised biopsies have largely been replaced by core needle biopsy (CNB) tools. Smaller biopsies are less traumatic for patients, quicker for the clinician to perform, and less expensive for the healthcare system in general. Hence, standard biopsy tissue size has declined significantly between the period before approximately 2010 and the years thereafter. The disadvantage of smaller biopsies is that they provide less tissue for pathologists to examine and analyze to render diagnostic opinions.

[0008] At the same time, diagnostic testing modalities have expanded to include an increased number of tests aimed at identifying molecular changes. The declining tissue biopsy size and the expanding quantity of testing required of the biopsied tissue has created an imbalance between tissue supply and demand. The result is that in some cases, clinicians make treatment decisions for patients with less diagnostic information than they would like. In other cases, patients are subjected to a second biopsy. The risk that a biopsy sample will have insufficient tissue to allow for the clinically-indicated tests to be performed is a big enough problem that it has several unofficial names, with "Tissue Exhaustion" being the most common. Tissue Exhaustion rates for core needle biopsies are reported in literature to be between 22-82% of all biopsies.

[0009] An imbalance therefore exists between the typical amount of tissue yielded from a CNB and the typical amount of tissue needed for testing. Healthcare quality is impacted by the shortfall in the quality and quantity of substrate available for molecular testing. This ultimately affects patient care, with many specimens received in the pathology laboratory not being available for molecular testing, resulting in these patients missing out on the improved

treatment options associated with precision medicine (defined as using molecular testing to find a mutation to guide therapy).

[0010] It is unfortunate that standard tissue biopsy handling practices today result in some of the harvested cells being discarded along with medical waste. These cells come from the patient, unavoidably dislodged (referred to hereafter as D-cells) from the tissue due to the trauma associated with of the sharp edge of the CNB needle cutting through tissue and then pulling back into the metal CNB tube. These cells are not visible to the human eye. They contain valuable genetic information, but they are simply not noticed by the clinician or technician holding the CNB needle handle and placing the tissue into a standard formalin-containing cup-like container after harvesting and then discarding the entire needle and any D-cells on it into a medical waste container. The current standard of care involves fixation of the tissue with formalin, in a process called formalin-fixation, paraffin embedding (FFPE), and which is known to create sub-optimal results when any tissue subjected to it is used as a substrate in molecular testing.

SUMMARY

[0011] The present disclosure provides a biopsy container apparatus that allows a clinician who performs a core needle biopsy to deposit the harvested tissue in such a way that it recovers cells that are dislodged ("D-cells") on the needle from the solid tissue that is procured during the biopsy procedure or from the patient's bodily tissue surrounding the pathway taken by the needle. D-Cells are an unrealized resource for diagnostic testing, mainly because cells are below the acuity of the human eye. This valuable biologic resource is typically discarded, but the apparatuses and methods of the present disclosure enable its recovery for diagnostic testing.

[0012] As discussed in more detail below, the biopsy container apparatus disclosed herein enables a clinician who performs a core needle biopsy to deposit the tissue in such a way that it contains and preserves the microscopic accompanying portions (D-cells) of the biopsied tissue that would otherwise be inadvertently discarded. More specially, the biopsy container apparatus disclosed herein enables cells that are dislodged from tissue that is procured during a biopsy procedure or from the patient's bodily tissue surrounding the pathway taken by the needle to be kept and segregated from the tissue that will be sent for standard pathology laboratory processing, using a specialized removable sieve suspended within a multi-functional watertight container. These recovered cells (D-cells) constitute an unrealized

resource for diagnostic testing. This resource is typically discarded, but the apparatuses and methods of the present disclosure ensure recovery for diagnostic testing.

[0013] A first aspect of the present disclosure is to provide a biopsy container apparatus for recovering solid tissue and D-cells from a biopsy. The biopsy container apparatus includes a sample collection container, a basket sieve, and a buffer container. The sample collection container includes a reagent chamber. The basket sieve is configured for removable attachment at least partially within the sample collection container and includes a sieve surface configured to pass the D-cells from the biopsy but not the solid tissue from the biopsy. The buffer container is configured for removable attachment to the sample collection container and includes a buffer chamber.

[0014] A second aspect of the present disclosure is to provide another biopsy container apparatus for recovering solid tissue and D-cells from a biopsy. The biopsy container apparatus includes a sample collection container, a basket sieve, and a buffer container. The sample collection container includes a reagent. The basket sieve is configured for removable attachment at least partially within the sample collection container and includes a sieve surface configured to pass the D-cells from the biopsy but not the solid tissue from the biopsy. The buffer container is configured for removable attachment to the sample collection container and includes a buffer.

[0015] A third aspect of the present disclosure is to provide another biopsy container apparatus for recovering solid tissue and D-cells from a biopsy. The biopsy container apparatus includes an upper chamber, a lower chamber, a sieve surface and a solid surface. The sieve surface is located between the upper chamber and the lower chamber and is configured to pass the D-cells from the biopsy but not the solid tissue from the biopsy. The solid surface is movably attached with respect to the sieve surface and configured to translate between (i) a first configuration in which the solid surface overlaps the sieve surface to prevent the D-cells from passing through the sieve surface and (ii) a second configuration in which the solid surface is moved away from the sieve surface to permit the D-cells to pass though the sieve surface from the upper chamber to the lower chamber.

[0016] A fourth aspect of the present disclosure is to provide a method of recovering solid tissue and D-cells from a biopsy using a buffer container apparatus including a buffer container, a basket sieve and a sample collection container. The method includes depositing the solid tissue and the D-cells from the biopsy into a buffer solution within the buffer container, removing the buffer container from the basket sieve and the sample collection

container, pouring the solid tissue, the D-cells and the buffer solution into the basket sieve while the basket sieve is located within the sample collection container, removing the basket sieve with the solid tissue from the sample collection container, placing the basket sieve with the solid tissue into a sealed container for tissue processing, and sealing a mixture including the D-cells, the buffer solution and the reagent for diagnostic testing.

[0017] A fifth aspect of the present disclosure is to provide a biopsy container apparatus for recovering solid tissue and D-cells from a biopsy. The biopsy container apparatus includes a sample collection container, a basket sieve, and a buffer container. The sample collection container includes a reagent chamber. The basket sieve is configured for removable attachment at least partially within the sample collection container and includes a sieve surface configured to pass the D-cells from the biopsy but not the solid tissue from the biopsy. The buffer container is configured for removable attachment to the sample collection container and includes a buffer chamber.

[0018] A sixth aspect of the present disclosure is to provide another biopsy container apparatus for recovering solid tissue and D-cells from a biopsy. The biopsy container apparatus includes a sample collection container, a basket sieve, and a buffer container. The sample collection container includes a reagent. The basket sieve is configured for removable attachment at least partially within the sample collection container and includes a sieve surface configured to pass the D-cells from the biopsy but not the solid tissue from the biopsy. The buffer container is configured for removable attachment to the sample collection container and includes a buffer.

[0019] A seventh aspect of the present disclosure is to provide a method of recovering solid tissue and D-cells from a biopsy using a buffer container apparatus including a buffer container, a basket sieve and a sample collection container. The method includes depositing the solid tissue and the D-cells from the biopsy into a buffer solution within the buffer container, removing the buffer container from the basket sieve and the sample collection container, pouring the solid tissue, the D-cells and the buffer solution into the basket sieve while the basket sieve is located within the sample collection container, removing the basket sieve with the solid tissue from the sample collection container, placing the basket sieve with the solid tissue into a sealed container for tissue processing, and sealing a mixture including the D-cells, the buffer solution and the reagent for diagnostic testing.

[0020] The present disclosure also describes a new type of packaging for medical devices. More specifically, the present disclosure provides a new type of packaging for a new medical

device that allows a clinician who performs a core needle biopsy to deposit the harvested tissue in such a way that it recovers cells that are dislodged ("D-cells") on the needle from the solid tissue that is procured during the biopsy procedure or from the patient's bodily tissue surrounding the pathway taken by the needle. The packaging can also be used for other medical devices, for example, which similarly require upright components or liquids or tissue samples that are susceptible to spilling during shipping and/or a medical procedure.

[0021] As discussed in more detail below, the medical device and its packaging container disclosed herein enable a clinician who performs a core needle biopsy to deposit the tissue in such a way that it contains and preserves the microscopic accompanying portions (D-cells) of the biopsied tissue that would otherwise be inadvertently discarded. The medical device disclosed herein enables cells that are dislodged from tissue that is procured during a biopsy procedure or from the patient's bodily tissue surrounding the pathway taken by the needle to be kept and segregated from the tissue that will be sent for standard pathology laboratory processing. The packaging container disclosed herein secures this or other medical devices during shipping while also assisting with a medical procedure involving the medical device.

[0022] An eighth aspect of the present disclosure is to provide a packaging container for one or more medical device. The packaging container includes an inner part and an outer part. The inner part includes a rack surface having at least one cutout configured to hold the one or more medical device both during shipping and upright during use of the one or more medical device. The outer part encloses the inner part and includes a tear line enabling a user to remove a portion thereof and expose the rack surface of the inner part so that the user can use the one or more medical device while the one or more medical device is held upright by the inner part.

[0023] A ninth aspect of the present disclosure is to provide another packaging container for one or more medical device. The packaging container includes an inner part and an outer part. The inner part is formed by a first single sheet of cardboard folded along a plurality of fold lines to form at least a rack surface configured to hold the one or more medical device both during shipping and upright during use of the one or more medical device. The outer part is formed by a second single sheet of cardboard folded along a plurality of fold lines to form an enclosure for the inner part. The outer part includes an upper portion and a lower portion. The upper portion is configured to be separated from the lower portion to expose the inner part.

[0024] A tenth aspect of the present disclosure is to provide a medical package. The medical package includes one or more medical device and a packaging container. The packaging

container contains the one or more medical device therein. The packaging container has at least one cutout configured to hold the one or more medical device both during shipping and upright during use of the one or more medical device.

[0025] An eleventh aspect of the present disclosure is to a method of using a packaging container for one or more medical device before, during, and/or after a medical procedure such as a core needle biopsy.

[0026] Other objects, features, aspects and advantages of the apparatuses and methods disclosed herein will become apparent to those skilled in the art from the following detailed description, which, taken in conjunction with the annexed drawings, discloses exemplary embodiments of the disclosed apparatuses and methods.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] Referring now to the attached drawings which form a part of this original disclosure:

[0028] Figures 1A-1C illustrate a conventional method of performing a core needle biopsy (CNB) on a patient to analyze tissue received from a suspicious area, according to a conventional CNB method;

[0029] Figure 2 illustrates a procedure for recovering an assessable analyte from a tissue sample retrieved via a CNB without exposing the assessable analyte to formalin, according to one or more implementations herein;

[0030] Figure 3 illustrates a core needle biopsy device, according to one or more implementations herein

[0031] Figures 4A-4C illustrate a collection of a tissue sample comprising a tissue core and dislodged cells, according to one or more implementations herein;

[0032] Figure 5 illustrates a system for recovering an assessable analyte from a tissue sample retrieved via a core needle biopsy without exposing the assessable analyte to formalin, according to one or more implementations herein;

[0033] Figure 6 is a flowchart illustrating an example method for recovering an assessable analyte from a tissue sample retrieved via a core needle biopsy, according to one or more implementations herein;

[0034] Figures 7A-7C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations herein, and a tissue specimen processed using conventional methods using formalin;

[0035] Figures 8A-8C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations

herein, and a tissue specimen processed using conventional methods using formalin;

[0036] Figures 9A-9C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations herein, and a tissue specimen processed using conventional methods using formalin;

[0037] Figures 10A-10B are example cellularity images, respectively, of a tissue core and a magnified view of a tissue specimen processed according to one or more implementations herein;

[0038] Figures 11A-11B are example cellularity images, respectively, of a tissue core and a magnified view of a tissue specimen processed according to one or more implementations herein;

[0039] Figures 12A-12F are an example comparison of immunohistochemical antibody-stained tissue specimens from FIGs. 7A-7C and FIGs. 10A-10B at different stages of processing, according to one or more implementations herein;

[0040] Figures 13 illustrates pre-sequencing evaluative electropherogram assessment for degradation of the extracted DNA from a representative sample of washed/recovered dislodged cells demonstrating a bell shaped curve with minimal evidence of degradation, according to one or more implementations herein;

[0041] Figure 14 illustrates post-sequencing qualitative data from all the washed specimens when assessed for Phred score, according to one or more implementations herein;

[0042] Figure 15 illustrates post-sequencing qualitative data from all the washed specimens when assessed for per-base N content, according to one or more implementations herein;

[0043] Figure 16 illustrates a perspective view of a first example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0044] Figure 17 illustrates an exploded view of the biopsy container apparatus of Figure 16;

[0045] Figure 18 illustrates a cross-sectional view of the biopsy container apparatus of Figure 16;

[0046] Figure 19 illustrates a cross-sectional view of a second example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0047] Figure 20 illustrates an exploded view of a third example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0048] Figure 21 illustrates an example embodiment of a method of using a biopsy container apparatus in accordance with the present disclosure;

[0049] Figures 22 to 27 illustrate example embodiments of the steps of the method of Figure 21;

[0050] Figure 28 illustrates a perspective view of a fourth example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0051] Figure 29 illustrates an exploded view of the biopsy container apparatus of Figure 13;

[0052] Figures 30 and 31 illustrate a fifth example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0053] Figure 32 illustrates a perspective view of an example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0054] Figure 33 illustrates a side view of the biopsy container apparatus of Figure 32;

[0055] Figure 34 illustrates a cross-sectional view of the biopsy container apparatus of Figure 1 taken across section line III-III in Figure 33;

[0056] Figure 35 illustrates an exploded view of the biopsy container apparatus of Figure 32;

[0057] Figure 36 illustrates a cross-sectional exploded view of the biopsy container apparatus of Figure 32 taken across lines V-V in Figure 35;

[0058] Figure 37 illustrates an informational view of the biopsy container apparatus of Figure 32;

[0059] Figure 38 illustrates an example embodiment of a method of using the biopsy container apparatus of Figure 32;

[0060] Figures 39 to 48 illustrate example embodiments of the steps of the method of Figure 7;

[0061] Figure 49 illustrates a pictorial summary of the method of Figure 38;

[0062] Figure 50 illustrates a side view of a second example embodiment of a biopsy container apparatus in accordance with the present disclosure;

[0063] Figure 51 illustrates a cross-sectional view of the biopsy container apparatus of Figure 50 taken across section line XX-XX in Figure 50;

[0064] Figure 52 illustrates a perspective view of an example embodiment of a packaging container in accordance with the present disclosure;

[0065] Figure 53 illustrates an outer part of the packaging container of Figure 52 before the outer part is fully constructed and combined with the inner part shown in Figure 54;

[0066] Figure 54 illustrates the inner part of the packaging container of Figure 52 before the inner part is constructed and combined with the outer part shown in Figure 53;

[0067] Figure 55 illustrates a top perspective view of the inner part of the packaging container of Figure 52 with the inner part constructed;

[0068] Figure 56 illustrates a bottom perspective view of the inner part of the packaging container of Figure 52 with the inner part constructed;

[0069] Figure 57 illustrates a top perspective view of the packaging container of Figure 52 after a portion thereof has been removed as described herein;

[0070] Figure 58 illustrates another top perspective view of the packaging container of Figure 52 after a portion thereof has been removed as described herein;

[0071] Figure 59 illustrates another top perspective view of the packaging container of Figure 52 including a plurality of individually packaged medical devices in accordance with the present disclosure;

[0072] Figure 60 illustrates a side plan view an example embodiment of a medical device for use with the packaging container of Figure 52;

[0073] Figure 61 illustrates a cross-sectional view of the medical device of Figure 52 taken across lines X-X in Figure 60;

[0074] Figure 62 illustrates an exploded view of the cross-section for the medical device shown in Figure 61;

[0075] Figure 63 illustrates an example embodiment of a method of using the medical device of Figures 60 to 62 with the packaging container of Figures 52 to 59 in accordance with the present disclosure;

[0076] Figure 64 illustrates a top perspective view of the medical device of Figures 60 to 62 being used with the packaging container of Figures 52 to 59 in accordance with the present disclosure;

[0077] Figure 65 illustrates a top perspective view of the medical device of Figures 60 to 62 being used with the packaging container of Figures 52 to 59 in accordance with the present disclosure;

[0078] Figure 66 illustrates a top perspective view of the medical device of Figures 60 to 62 being used with the packaging container of Figures 52 to 59 in accordance with the present disclosure;

[0079] Figure 67 illustrates a top perspective view of the medical device of Figures 60 to 62 being used with the packaging container of Figures 52 to 59 in accordance with the present disclosure;

[0080] Figure 68 illustrates a top perspective view of another example embodiment of a packaging container in accordance with the present disclosure;

[0081] Figure 69 illustrates another top perspective view of the packaging container of Figure 68;

[0082] Figure 70 illustrates a top perspective view of the inner part of the packaging container of Figure 68 with the inner part constructed;

[0083] Figure 71 illustrates a bottom perspective view of the inner part of the packaging container of Figure 68 with the inner part constructed; and

[0084] Figure 72 illustrates a top perspective view of the constructed parts of the packaging container of Figure 52 and the packaging container of Figure 68.

DETAILED DESCRIPTION OF EMBODIMENTS

[0085] Selected embodiments will now be explained with reference to the drawings. It will be apparent to those skilled in the art from this disclosure that the following descriptions of the embodiments are provided for illustration only and not for the purpose of limiting the invention as defined by the appended claims and their equivalents.

[0086] A biopsy is a diagnostic procedure in which a sample of tissue is removed from the body and examined under a microscope to determine the presence, cause, or extent of a disease. Conventional biopsy techniques are used in diagnosing a variety of conditions, including cancer.

[0087] Conventional excisional and incisional biopsies can involve the surgical removal of tissue. In an excisional biopsy, the entire lump or suspicious area is removed, often with a margin of surrounding normal tissue. On the other hand, an incisional biopsy only removes a portion of the suspicious area. These techniques are useful for larger lumps or lesions that cannot be easily accessed with a needle. The removed tissue is then examined under a microscope by pathologists to determine its nature.

[0088] Another conventional technique includes endoscopic biopsies. Endoscopic biopsies are conducted using an endoscope, a flexible tube with a light and camera attached to its end. Tiny instruments can be passed through the endoscope to take tissue samples from areas of interest.

[0089] Another, less-invasive conventional technique is the needle biopsy, which uses a sharp, hollow needle to extract a core of tissue from the suspicious area. Depending on the size and location of the lesion, different types of needle biopsies may be used, such as

fine-needle aspiration (FNA) and core needle biopsy (CNB). The former, FNA, uses a thin needle to withdraw cells or fluid, whereas the latter, CNB, uses a slightly larger needle to remove a 'core' of tissue. These methods can be guided by imaging techniques like ultrasound, CT scan, or MRI to ensure the correct placement of the needle and accurate sampling of the target tissue.

[0090] FNA is a diagnostic procedure that involves using a thin, hollow needle to extract cells or fluids from a lump or mass within the body for microscopic examination. This minimally invasive technique is conventionally used to investigate and diagnose various conditions, especially in the context of tumors or cysts.

[0091] During the FNA procedure, the clinician inserts a fine needle, often attached to a syringe, into the suspicious area. The needle's positioning can be guided by palpation, especially if the lump is just under the skin. For deeper or less palpable masses, imaging modalities like ultrasound, computerized tomography (CT) scan, or magnetic resonance imaging (MRI) can be used to ensure accurate needle placement.

[0092] Once the needle is in the desired position, a slight vacuum may be created using the syringe, helping to draw cells or fluid into the needle. The collected sample is then spread onto microscope slides and sent to a pathology lab. There, it may be stained and examined under a microscope by a pathologist to determine the nature of the cells, whether they're benign, malignant, inflammatory, or related to other conditions.

[0093] A shortcoming of FNA is that the small sample size can sometimes limit the pathologist's ability to make a definitive diagnosis. The procedure might not always retrieve an adequate number of cells, leading to inconclusive or indeterminate results. This limitation often necessitates repeat procedures or alternative tests, making it less efficient in certain cases. Additionally, while FNA can identify malignancy, it might fall short in determining the specific type or subtype of cancer, a critical aspect for tailored treatments. As a result, if the findings from the FNA are inconclusive or contradictory to other clinical evidence, a more extensive biopsy method might become needed for further evaluation.

[0094] Furthermore, the accuracy of FNA depends significantly on the skill of the operator. Inexperienced operators might increase the risk of inconclusive or inaccurate results. There's also a minimal but present risk of complications like bleeding, infection, or unintentional injury to nearby structures, especially when aspirating from deeply seated organs. Another concern with FNA is the theoretical risk that the procedure might inadvertently spread cancerous cells due to the need to aspirate the target cells.

Additionally, FNA only provides cellular samples, unlike biopsies that offer larger tissue samples. This distinction means FNA can't assess the architectural organization of the tissue, which is essential for some diagnoses. Furthermore, FNA is purely diagnostic, lacking therapeutic benefits like draining or lesion removal. As a result, while FNA is a valuable tool, its limitations require careful consideration by medical professionals.

[0095] A conventional alternative to FNA is to perform a core needle biopsy (CNB). CNB is a medical procedure used to extract a small sample of tissue from a suspicious area within the body, often from masses or lumps that a medical provider suspects might be cancerous.

[0096] FIGs. 1A-1C illustrate a conventional method of performing a CNB on a patient 110 to analyze tissue received from a suspicious area 120, according to a conventional CNB method.

[0097] To perform a CNB, at 100a, a clinician may use a hollow needle 130 to retrieve a slender *(e.g.,* cylindrical or other shape) sample—a tissue core—of tissue from suspicious area 120. The procedure can involve the use of imaging guidance, such as ultrasound, mammography, or MRI, to help position the needle precisely. After numbing the area with a local anesthetic, the doctor may insert hollow needle 130 through the skin and into suspicious area 120. At 100b, hollow needle 130 may be extracted from patient 110 with the tissue sample disposed therein. Then, at 100c, the tissue sample may be extracted from needle 130 and placed in a cassette 140 for processing. Once the tissue sample is obtained and fixed in cassette 140, it may then be sent to a pathology laboratory for examination under a microscope.

[0098] Once the sample reaches the pathology laboratory, a pathologist may examine it to determine the nature of the cells and the type of disease present, if any. The results can typically be expected within a few days to a week, depending on the complexity of the case and the specific protocols of the medical facility.

[0099] One of the main advantages of a CNB is that it is less invasive than surgical biopsies, which often require larger incisions and a longer recovery time. This biopsy method offers quicker recovery, less scarring, and is generally safer than surgical alternatives. However, there are also limitations to core needle biopsies, including a possibility that the needle might not capture the tissue that best represents the entire abnormality. Consequently, the results might be inconclusive or not entirely accurate, potentially leading to a need for further testing or a surgical biopsy.

[0100] While conventional-technique CNBs may be valuable for diagnosing many conditions, they may not provide sufficient tissue for certain molecular or genetic tests that could be usable in modern targeted therapies. One of the reasons for this shortcoming is the conventional way tissue derived from a CNB is preserved.

[0101] Tissue samples derived using CNBs are conventionally preserved in a formalin *(e.g.,* formaldehyde-containing) solution. Formalin may be used as a fixative for the preservation of tissue samples derived from CNBs, acting by creating cross-links between proteins, which stabilizes cellular structures and preserves the morphological and cellular details of the tissue. When a CNB is performed, the tissue sample is conventionally promptly immersed in formalin to prevent autolysis and degradation of the cellular components. The preserved tissue can then be processed, embedded in paraffin, and sectioned for microscopic examination, for example, using hematoxylin and eosin staining. The use of formalin is conventionally justified as ensuring that the histopathological features of the tissue core are maintained, allowing for accurate diagnostic interpretation by pathologists.

[0102] However, the conventional use of formalin in the preservation of tissue samples is also the cause of one of the shortcomings of conventional-technique CNBs, since that it easily damages certain analytes, such as nucleic acids. Thus, any remaining analyte which could be derived from a tissue sample may not be usable for provision of reliable diagnostic or molecular testing data due to its exposure to formalin.

[0103] Beyond the tissue core taken during the biopsy, additional diagnostic material, in the form of dislodged cells, can be released from the tissue. Because these dislodged cells cannot be seen by the naked eye, they are routinely discarded, either attached to the needle itself, or to a gauze pad the physician places the visible piece of tissue on.

[0104] Implementations herein enable the preservation of both the tissue core and the dislodged cells are separated from the needle by swirling them in a buffered solution. Then, the solution may be filtered to separate the tissue core from the dislodged cells. The tissue core, which can be seen, may then be separated *(e.g.,* extracted) and placed into a container such as a cassette for routine processing. A reagent may be added to the dislodged cells to lyse them and stabilize their nucleic acids.

[0105] Implementations pertain to methods and systems for efficiently and effectively recovering assessable analytes, potentially including but not limited to DNA, RNA, exosomes, or proteins, from a tissue sample obtained by CNB. This process may include

providing a core needle embedded with a tissue sample, immersing the needle in a buffer solution, such as a sterilized phosphate buffered saline solution, and swirling to dislodge the tissue and cells, thereby forming an intermediate mixture. This mixture may be filtered using a designated strainer into a sample tube, serving to separate the tissue core and generate a second intermediate mixture of dislodged cells within the buffer solution.

[0106] A volume of a cell lysis and nucleic acid stabilization reagent, for example, equal in volume to the volume of the second intermediate mixture, may be combined with the second intermediate mixture, resulting in cell lysis and the creation of a third mixture. The analyte can subsequently be extracted from this mixture. Different from conventional-technique CNB and sample preparation, implementations operate without exposure of the analyte to formalin. The method may be facilitated by a system comprising a core needle, as well as a container for the buffer solution, a sample tube, a strainer, and a receptacle for the removed tissue core, all or some of which may be presented as a kit. The method may also optionally involve tube centrifugation *(i.e.,* spinning) for mixture separation to facilitate removal of the supernatant from the sample tube, and storage of the sample tube in temperatures near 4 degrees C, alleviating the need for deep-freezing the analyte.

[0107] Implementations may thus enable recovery of the dislodged cells for analysis of an analyte contained therein *(e.g.,* DNA, RNA, exosomes, proteins), without having been exposed to formalin.

[0108] Implementations may provide for simpler CNB and sample preparation procedures, lowering the skill requirement and the effects of variance thereof, and may reduce the time needed to provide the sample to a laboratory for diagnostics or molecular study *(e.g.,* nucleic acid sequencing)

[0109] Creating two specimens from one means there is a reduced chance of exhausting the parent tissue, thus allowing the pathologist to abide by regulatory and credentialing agencies, and provide for improved patient experience.

[0110] Shortened pre-analytics additionally reduces a risk that false negative or false positive changes will be encountered from the specimen. The pre-analytics in proof-of-principle studies by the inventor was kept to 15 minutes. Although regulations are inconsistent or unavailable on pre-analytics for most types of specimens—using conventional methods, molecular breakdowns and other issues can start as early as 1 hour.

[0111] FIG. 2 illustrates a procedure 200 for recovering an assessable analyte from a tissue sample retrieved via a CNB without exposing the assessable analyte to formalin, according to one or more implementations herein. The assessable analyte may be, for example, DNA, RNA, an exosome, or a protein.

[0112] At 200a, a core needle 230 having the tissue sample disposed therein retrieved via the CNB may be provided. The tissue sample may include both a tissue core 242 and dislodged cells 272.

[0113] At 200b, a portion of core needle 230 having the tissue sample disposed therein may be immersed in a buffer solution in a container 250, and swirled until the tissue core 242 and the dislodged cells 272 dislodge from core needle to form a first intermediate mixture in container 250 comprising the buffer solution, the tissue core 242, and the dislodged cells. The buffer solution may comprise a phosphate buffered saline solution. The buffer solution may be sterilized prior to immersing the core needle 230 therein.

[0114] The first intermediate mixture in container 250 may be filtered using a strainer into a sample tube 270 *(e.g.,* a container) to separate the tissue core 242 from the first intermediate mixture, yielding the tissue core 242—which may be disposed within a container such as cassette 240 at 200c, and a second intermediate mixture comprising the buffer solution and the dislodged cells 272. The strainer may be disposed at least partially in sample tube 270.

[0115] A cell lysis and stabilization reagent may be added to the second intermediate mixture in sample tube 270 to yield a third mixture comprising lysed dislodged cells 272 from which the assessable analyte can be retrieved. The cell lysis and stabilization reagent may be equal in volume to the second intermediate mixture. In some implementations, the cell lysis and stabilization reagent may comprise from 2 mL to 5 mL of the cell lysis and stabilization reagent. The cell lysis and stabilization reagent may be a concentrated, dual action cell lysis and nucleic acid stabilization reagent.

[0116] The assessable analyte may then be isolated from the third mixture contained in sample tube 270, and analysis may be performed using the assessable analyte *(e.g.,* DNA/RNA/protein/gene analysis).

[0117] Sample tube 270 having the third mixture disposed therein may be stored within a freezer, for example, at an internal temperature of 4 deg C. Thus, the need for storage in a deep freezer is obviated by implementations herein.

[0118] FIG. 3 illustrates a core needle biopsy device 300, according to one or more implementations herein. Core needle biopsy device 300 may include a core needle, handle,

sheath, and components necessary for covering the core needle with the sheath and be configured for performance of a CNB on a patient and/or specified for a particular CNB to be performed.

[0119] FIGs. 4A-4C illustrate a collection of a tissue sample 414 comprising a tissue core and dislodged cells, according to one or more implementations herein. Particularly, FIGs. 4A-4C illustrates the capture of the dislodged cells in addition to the tissue core in a target tissue area 412 using a core needle 430 and retracting core needle 430 into a core needle sheath 432, and may be similar to the capture of the tissue specimen at 200a. The basis for the collection of dislodged cells in the CNB may occur when core needle sheath 432 is released and covers the biopsy needle. A tissue sample 414 comprising the tissue core and dislodged cells *(e.g.,* dislodged tumor cells) remain in the space between core needle 430 and core needle sheath 432.

[0120] Since individual cells and small groups of cells cannot be visualized by the human eye, they are conventionally not accounted for when transferring the specimen for processing. However, according to implementations herein, disposing the core needle 430 and core needle sheath 432 in a buffer solution may create a liquid biopsy specimen, from which the tissue can be separated and sent for traditional processing and the dislodged cells kept and retained for later use. Further processing of implementations herein of filtering, followed by lysing and stabilization herein provides for long-term, economical storage of the dislodged cells.

[0121] FIG. 5 illustrates a system 500 for recovering an assessable analyte from a tissue sample retrieved via a core needle biopsy without exposing the assessable analyte to formalin, according to one or more implementations herein. All or part of system 500 may be provided as a kit. The assessable analyte may be, for example, DNA, RNA, an exosome, or a protein.

[0122] System 500 may include a core needle *(e.g.,* a core needle of core needle biopsy device 300), which may be configured to collect a tissue sample therein retrieved via the core needle biopsy, wherein the tissue sample comprises a tissue core and dislodged cells.

[0123] System 500 may include a buffer container 502 configured to contain a buffer solution and receive the core needle having the tissue sample disposed therein such that a portion of the core needle having the tissue sample disposed therein may be immersed in the buffer solution and swirled until the tissue core and the dislodged cells dislodge from the core needle to form a first intermediate mixture within the buffer container comprising the buffer solution, the tissue core, and the dislodged cells.

[0124] System 500 may include a sample tube 504. The sample tube may be further configured for adding an equal volume to the second intermediate mixture of a cell lysis and stabilization reagent to the second intermediate mixture yielding a third mixture comprising lysed dislodged cells from which the assessable analyte can be retrieved from.

[0125] System 500 may include a strainer 506 *(e.g.,* a 40 pm to 100 pm strainer) configured to be disposed at least partially within sample tube 504 such that the first intermediate mixture may be filtered into sample tube 504 using strainer 506 to separate the tissue core from the first intermediate mixture, yielding the tissue core and a second intermediate mixture comprising the buffer solution and the dislodged cells.

[0126] System 500 may include a container 508 configured for storage of the tissue core.

[0127] System 500 may include a container 510 for provision of the cell lysis and stabilization reagent.

[0128] FIG. 6 is a flowchart illustrating an example method 600 for recovering an assessable analyte from a tissue sample retrieved via a core needle biopsy, according to one or more implementations herein. In some implementations, one or more process blocks of FIG. 6 may be performed by components similar to one or more of the devices or components of FIGs. 3-5, or other components or devices. The assessable analyte may be, for example, DNA, RNA, an exosome, or a protein.

[0129] An operation 602 may include providing a core needle having the tissue sample disposed therein retrieved via the core needle biopsy, and may be performed alone or in combination with one or more other operations depicted in FIG. 6. The tissue sample may comprise a tissue core and dislodged cells.

[0130] An operation 604 may include providing a buffer solution, and may be performed alone or in combination with one or more other operations depicted in FIG. 6. The buffer solution may be sterilized and not comprise formalin.

[0131] An operation 606 may include immersing a portion of the core needle having the tissue sample disposed therein in the buffer solution, and may be performed alone or in combination with one or more other operations depicted in FIG. 6.

[0132] An operation 608 may include swirling the core needle within the buffer solution until the tissue core and the dislodged cells dislodge from the core needle to form a first intermediate mixture comprising the buffer solution, the tissue core, and the dislodged cells, and may be performed alone or in combination with one or more other operations depicted in FIG. 6.

[0133] An operation 610 may include filtering the first intermediate mixture into a sample tube using a strainer disposed at least partially in the sample tube to separate the tissue core from the first intermediate mixture, yielding the tissue core and a second intermediate mixture comprising the buffer solution and the dislodged cells, and may be performed alone or in combination with one or more other operations depicted in FIG. 6. The tissue core may be extracted and disposed within a container configured for conventional tissue processing of the tissue core.

[0134] An operation 612 may include adding an equal volume, to the second intermediate mixture, of a cell lysis and stabilization reagent to the second intermediate mixture yielding a third mixture comprising lysed dislodged cells from which the assessable analyte not exposed to formalin can be retrieved, and may be performed alone or in combination with one or more other operations depicted in FIG. 6. The cell lysis and stabilization reagent may be a concentrated, dual action cell lysis and nucleic acid stabilization reagent.

[0135] An operation 614 may include isolating the assessable analyte not exposed to formalin from the third mixture, and may be performed alone or in combination with one or more other operations depicted in FIG. 6.

[0136] An operation 616 may include assessing the assessable analyte not exposed to formalin, and may be performed alone or in combination with one or more other operations depicted in FIG. 6.

[0137] Although FIG. 6 depicts example method 600, respectively, and operations thereof, in some implementations, a method illustrated herein may include additional operations, fewer operations, differently arranged operations, or different operations than the operations depicted in FIG. 6. Moreover, or in the alternative, two or more of the operations depicted in FIG. 6 may be performed at least partially in parallel.

[0138] EXPERIMENTATION

[0139] *Methodology*

[0140] At the time of the procedure, an interventional radiologist was given a container with phosphate buffered saline (PBS) for each of five cases. For the first three cases, the interventional radiologist made one to two passes to obtain tissue, and then transferred them into an empty container by scraping off the tissue with a scalpel blade on to a saline soaked gauze pad that was then filled with formalin. For the final pass, the tissue in the needle was immersed in the container with PBS and gently agitated, so as to separate both

the tissue and any dislodged cells from the needle that may have been loosened by the procedure.

[0141] By placing and agitating the tip of the needle after a procedure into a container with fluid, both the targeted tissue and the unseen cells could be recovered and separately processed for their disparate needs, as illustrated in FIG. 2. In the first three cases of this experimentation, the wash step was done as the last pass performed by the interventional radiologist so as not to introduce a possibly contaminated needle reentering the patient. For the final two cases, the PBS solution and container were sterilized prior to the procedure. This allowed the interventional radiologist to release the tissue and any dislodged cells from all the passes into the PBS solution.

[0142] The initial approach in the first three cases inadvertently permitted testing as to whether the washed tissue specimen—processed slightly different from the initial passes, and therefore may have incurred some pre-analytical changes—resulted in any downstream differences in evaluation, such as, for example morphologic and immunohistochemically, from the unwashed tissue that was processed in a conventional manner.

[0143] Antibodies to proteins known to be expressed on the cell membrane, the cytoplasm, and nucleus in the tumor sample biopsies as part of the first three cases were evaluated to ascertain if the pre-processing wash step altered protein expression compared to the traditional, unwashed approach.

[0144] Once the last pass was completed, formalin was added to the container containing the unwashed tissue. All tissue cores—washed and unwashed—were placed in separate cassettes for subsequent embedding and sectioning.

[0145] The washed specimen—the specimen deposited in PBS in the interventional radiology suite—was filtered through a disposable, 100 pm sieve strainer. The tissue core that was recovered in the sieve was then placed into a cassette, placed in formalin and processed using formalin-fixed paraffin-embedded (FFPE) procedures. The filtered solution was transferred to a microcentrifuge tube and spun down until all the fluid was processed. At this point 500 pl of the lysis and preservative reagent was added to the microcentrifuge tube and pipetted repeatedly so as to lyse the cells. This mixture of only dislodged cells from the parent tissue and of no tissue fragments, was then placed in a 20 deg C freezer and kept there until all cases in this study cohort were collected. Time stamps were recorded as to the acquisition of the tissue from the interventional radiologist,

time to transport to the lab, and time at which point the preservative reagent was added to the pelleted dislodged cells and were compiled as the time before stabilization (TABLE 1).

[0146] **TABLE 1:** Tumor type, cellularity, and nucleic acid quantitative and qualitative metrics associated with each specimen.

[0147]

Case #	Diagnosis	Biopsy site	Total number of passes	Number of passes washed/tissue core length (cm)	Number of tissue cores not washed	Cellularity
1	Small cell carcinoma	Liver	3	1/1.3	2	moderate
2	Normal liver	Liver	3	1/0.5	2	moderate
3	Cholangiocarcinoma	Liver	3	1/0.7	2	moderate
4	Prostatic adenocarcinoma	Patella	3	3/4.6	N/A	high
5	Cirrhosis	Liver	5	5/4.0	N/A	moderate

[0148] TABLE 1 (continued)

Case #	Time before stabilization (minutes)	A260/280	Average size of recovered DNA (bp)	Recovered DNA (ng) Quibit/ Nanodrop	Genomic Quality Number
1	15	1.76	23,351	1600/1325	10
2	14	1.67	28,330	151/550	10
3	16	1.63	19,694	395/445	9.9
4	55	1.81	18,806	2605/1745	9.9
5	15	1.88	24,581	102/540	9.9

[0149] The parent core tissue was examined by bright field examination and evaluated for cellularity, with consideration given to whether there were areas of normal tissue and/or necrosis present in the specimen to determine impact on nucleic acid recovery.

[0150] Once all of the cases had been collected, DNA was extracted. Quantification was done in duplicate, and obtained using a fluorometer and a spectrophotometer. The latter was used to obtain an A260/280 absorbance ratio for assessment of DNA purity. Amounts of recovered DNA were calculated from the given concentration from the fluorometer multiplied by the eluted volume. Qualitative metrics were derived from a fragment analyzer and included both specimen size and the Genomic Quality Number (GQN). The latter was obtained at a threshold of 500 base pairs, a size previously used as the standard for assessment of DNA from FFPE tissue blocks. A score of 10 is optimal while 1 is considered highly degraded. The DNA from each case was then subjected to library preparation. An input of 200 ng of sample up to a volume of 30 microliters was used for each sample.

[0151] Sequencing of each sample was performed and quality metrics of the sequencing run for each case was evaluated. In particular, evaluation of the Phred score, a measure of the quality of the identification of nucleotides generated during automated DNA sequencing, and the percentage of nucleotides that could not be identified (per base N content), were assessed. For a Phred score, values can range from 4 to 60, with a score of 20 corresponding to a 99% probability that the base call is correct, a score of 30 equivalent to an accuracy of 99.9%, and a score of 40 corresponding to a 99.99% rate of accuracy. For the Phred scores, the scores from each sample at each nucleotide were taken and a plot generated with scores in the lower quartile (Q1), the middle quartiles (Q2—Q3), and upper quartile (Q4). Average quality scores typically demonstrate a steady drop over the length of the read. The "per base N content" analysis reflects the percentage that a particular base was ambiguous and could not be given a designation of being an A, T , C or G nucleotide. In this metric, a very low proportion of N's appearing in the sequence is not to be unexpected, specifically near the end of the sequence.

[0152] However, concerns about quality arise when the proportion of N's rise above a few percentage points. These variables were examined as an indirect assessment of the originating DNA, following the principle that poor originating template quality is the most common cause of any subsequent, problematic sequencing result.

[0153] *Results*

[0154] The time from tissue specimen procurement in the interventional radiology suite, transport to the pathology laboratory, separation of the dislodged daughter cells from the

parent tissue core, and stabilization of the former in the DNA/RNA preservative reagent was under twenty minutes for four of the five cases (TABLE 1).

[0155] For the outlier, the pre-analytical time frame was still under sixty minutes and was due to transport related issues. This delay however, did not result in an appreciable difference in the evaluated qualitative metrics. The effort in processing the specimen required less than five minutes of hands-on time, and could be done by one individual.

[0156] Four of the five biopsied sites came from the liver, with the fifth coming from bone. The diagnosis for each case is given in TABLE 1. The tissue core that was washed in PBS as previously described was then placed in formalin, and along with the other tissue cores that were not washed, underwent FFPE processing to generate tissue blocks. The length of the single tissue core that was washed ranged from 0.5 to 1.3 cms (cases 1 to 3), and for cases 4 and 5, in which all the tissue from all the passes was washed, 4.0 and 4.6 cm in aggregate (TABLE 1). Upon examination, no notable discrepancies could be identified between the tissue specimens at the morphologic level, in terms of both architecture and cytology when stained by hematoxylin and eosin, between those tissue cores that had been washed and those that had not (FIGs. 7A11 B). The cellularity between the washed cores and the unwashed cores were similar as well, with no noticeable diminution in cellularity. The problem of core cell depletion that is associated with aggressive touch preparation was not noted in this study, probably because gentle agitation of the tissue core was sufficient to recover any loose cells, but not sufficient to cause significant depletion of the core's cellularity. The cellularity in each specimen was considered to be either moderate or highly cellular (TABLE 1). Immunohistochemistry for proteins present at the cell membrane *(e.g.,* CD-56), the cytoplasm *(e.g.,* PSA), and the nucleus *(e.g.,* NKX3.1) showed no appreciable differences in intensity (FIGs. 12A-12F). Variability in staining within the tumor tissue was noted in both matched tissue cores.

[0157] Nuclear material from the dislodged cells for the tissue core and corresponding needle was recovered from each case. No cell pellet was identified in any of the supernatant washes from any of the specimens. These two observations indicate that cellular material is present in the supernatant wash, but too few to form a visible pellet. This held true for even cases 4 and 5, when all the tissue from the passes were included in one wash container. The amount of DNA present in the supernatant was variable, with the fewest amount in the non-neoplastic liver tissue (cases 2 and 5), and higher in the neoplastic tissue (TABLE 1). This is consistent with previous observations that in normal

tissue there are fewer dislodged cells as a by-product of the procedure. The limited time frame and the unknown underlying diagnosis in each case prevented the investigators from selecting only biopsied tumor tissue to test. The largest amount of recovered DNA was from a neoplasm in which the tissue from all the passes had been washed (case 4). The purity of the DNA, as assessed by the A260/280 was above 1.8 in only two of the five cases, indicative of some possible residual contaminants in three of the specimens. No further purification was performed prior to generating the libraries as the GQN was at or close to 10 in each case. The range in the size of the extracted DNA was between 15,000 to a little under 24,000 base pairs (FIG. 13). Typical features of fragmentation, as in the presence of smearing at the lower end of each electropherogram, were not present or minimal in all of the cases. No effort was made to recover higher molecular weight DNA (>50kbp), as the recovered DNA was fit for purpose *(e.g.,* the sequencing platform used works with short reads). Enough DNA was recovered for sequencing using a sequencer having input requirements of 200 ng of total DNA. The resulting sequencing metrics were indicative of high confidence data, with Phred scores consistently at or above 35 and no dipping at the tail end of the read (FIG. 14). Additionally, per base N content never reached a level of 1% in any of the reads of any of the samples (FIG. 15).

[0158] FIGs. 7A-7C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations herein, and a tissue specimen processed using conventional methods using formalin.

[0159] FIGs. 8A-8C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations herein, and a tissue specimen processed using conventional methods using formalin.

[0160] FIGs. 9A-9C are example cellularity images, respectively, of a tissue core, a magnified view of a tissue specimen processed according to one or more implementations herein, and a tissue specimen processed using conventional methods using formalin.

[0161] FIGs. 10A-10B are example cellularity images, respectively, of a tissue core and a magnified view of a tissue specimen processed according to one or more implementations herein.

[0162] FIGs. 11A-11B are example cellularity images, respectively, of a tissue core and a magnified view of a tissue specimen processed according to one or more implementations herein.

[0163] FIGs. 12A-12F are an example comparison of immunohistochemical antibody-stained tissue specimens from FIGs. 7A-7C and FIGs. 10A-10B at different stages of processing, according to one or more implementations herein.

[0164] FIGs. 12A and 12B illustrate immunohistochemical staining results for antibodies to a membranous *(e.g.,* CD-56) protein in the tissue core. FIGs. 12C and 12D illustrate immunohistochemical staining results for antibodies to a nuclear *(e.g.,* NKX3.1) protein in the tissue core. FIGs. 12E and 12F illustrate immunohistochemical staining results for antibodies to a cytoplasmic *(e.g.,* PSA) protein in the tissue core.

[0165] FIGs. 12A, 12C, and 12E have not completed processing *(e.g.,* washing). FIGs. 12B, 12D, and 12F have completed processing *(e.g.,* washing).

[0166] FIG. 13 illustrates pre-sequencing evaluative electropherogram assessment for degradation of the extracted DNA from a representative sample of washed/recovered dislodged cells demonstrating a bell shaped curve with minimal evidence of degradation, according to one or more implementations herein.

[0167] FIG. 14 illustrates post-sequencing qualitative data from all the washed specimens when assessed for Phred score, according to one or more implementations herein.

[0168] FIG. 15 illustrates post-sequencing qualitative data from all the washed specimens when assessed for per-base N content, according to one or more implementations herein.

[0169] Figures 16 to 18 illustrate an example embodiment of a biopsy container apparatus 1010 for recovering solid tissue and D-cells from a biopsy in accordance with the present disclosure. In the illustrated embodiment, the biopsy container apparatus 1010 includes a buffer container 1012, a basket sieve 1014 and a sample collection container 1016, which are three separable elements that can be attached prior to a biopsy and then separated during the method of use disclosed herein. As illustrated, the buffer container 1012 and basket sieve 1014 are configured for removable attachment to the sample collection container 16. Figure 16 illustrates the buffer container 1012, the basket sieve 1014 and the sample collection container 1016 attached together, while Figure 17 shows the buffer container 1012, the basket sieve 1014 and the sample collection container 1016 detached from each other.

[0170] The buffer container 1012 includes a buffer chamber 1020 for storing or receiving buffer solution 1021. The bottom edge 1023 of the buffer chamber 1020 is sealed and watertight so that the inner space 1022 of buffer chamber 1020 retains the buffer solution 1021. In an embodiment, the buffer chamber 1020 is pre-filled with the buffer solution 1021 within the inner space 1022. In an embodiment, the buffer solution 1021 is a sterile

phosphate-buffered saline (PBS) buffer solution. In an embodiment, the buffer chamber 1020 includes between 1 and 2 mL of buffer solution. In an embodiment, the buffer chamber 1020 is pre-filled with approximately 1-2 ml of buffer solution. While PBS is the most likely choice of buffer, any similar buffer solution, such as Buffer Roswell Park Memorial Institute ("RPMI 1640 Media") Buffer Solution, would serve the same purpose.

[0171] In the illustrated embodiment, the buffer container 1012 has a funnel shape to assist a user in depositing a biopsy sample from a core needle into the buffer solution 1021 within the buffer chamber 1020. More specifically, the buffer container 1012 includes a funnel portion 1024. The funnel portion 1024 flares outwardly from bottom to top, while the buffer chamber 1020 has a generally cylindrical shape for insertion into the basket sieve 1014 and/or the sample collection container 1016 as shown in Figure 18. The funnel portion 1024 is configured to guide the solid tissue and the D-cells from the biopsy into the buffer chamber 1020 when ejected from a core needle, as discussed in more detail below.

[0172] In the illustrated embodiment, the buffer container 1012 includes a top opening 1026 and a lid 1028. The lid 1028 attaches to the top of the funnel portion 1024 to cover the top opening 1026 and enclose the inner space 1022 so that the buffer solution 1021 does not spill if the biopsy container apparatus 1010 is inverted. The lid 1028 can be attached by being screwed onto the top of the funnel portion 1024, or by another suitable attachment mechanism. In an embodiment, the lid 1028 is configured to attach to both the buffer container 1012 and the sample collection container 1016, so that a user can remove the lid 1028 form the buffer container 1012 when beginning use of the biopsy collection apparatus 1010 and then later place the lid 1028 on the sample collection container 1016 to seal its contents, as discussed in more detail below.

[0173] In the illustrated embodiment, the buffer container 1012 also includes a first attachment mechanism 1030 to enable attachment to a second attachment mechanism 1032 of the sample collection container 1016. More specifically, the outer surface of the buffer chamber 1020 includes the first attachment mechanism 1030. In the illustrated embodiment, the second attachment mechanism 1032 is located on the inner surface of the sample collection container 1016. The first attachment mechanism 1030 and the second attachment mechanism 1032 enable removable attachment of the buffer container 1012 to the sample collection container 1016, with the buffer container 1012 located at least partially within the sample collection container 1016. As shown in Figure 18, the first attachment mechanism 30 and the second attachment mechanism 1032 create a watertight seal between the outer surface

of the buffer container 1012 and the inner surface of the sample collection 1016 container so that liquid will not spill from the sample collection container 1016 if the biopsy container apparatus 1010 is inverted. In the embodiment illustrated in Figures 16 to 18, the first attachment mechanism 1030 and the second attachment mechanism 1032 are corresponding screw threads that enable the buffer container 1012 to screw into the sample collection container 1016. In an alternative example embodiment of a biopsy container apparatus 1010b illustrated in Figure 20, the first attachment mechanism 1030b includes a rubber sleeve on the outer surface of the buffer chamber 1020b of the buffer container 1012b, and the second attachment mechanism 1032b includes a rubber sleeve on the inner surface of the sample collection container 1016b.

[0174] The sample collection container 1016 includes a reagent chamber 1038 for storing or receiving a reagent 1039. In Figure 18, the sample collection container 1016 includes an upper portion 1040 and a lower portion 1042, with the reagent chamber 1038 located within and/or formed by the lower portion 1042. The bottom edge 1044 of the sample collection container 1016 is sealed and watertight so that the reagent chamber 1038 retains the reagent 1039. In the illustrated embodiment, the reagent chamber 1038 is pre-filled with the reagent 1039 within the inner space 1046. In an embodiment, the reagent 1039 is a solution for lysing cells and preserving nucleic acids that is approximately 2x the normal concentration of an off-the-shelf cell lysing reagent. In an embodiment, the reagent 1039 is Zymo DNA/RNA Shield™ reagent, or an equivalent for lysing cells and preserving nucleic acids which is 2x the normal concentration defined by and provided by Zymo. In an embodiment, the reagent chamber 1038 includes between 1 and 2 mL of reagent 39. In an embodiment, the reagent chamber 1038 is pre-filled with 1-2 ml of double-concentration cell lysis/nucleic acid stabilization reagent 1039. In an embodiment, the reagent chamber 1038 includes a first amount of reagent 1039, and the buffer chamber 1020 includes a second amount of buffer solution 1021 that is approximately equal in volume to the first amount of reagent.

[0175] In the illustrated embodiment, both the upper portion 1040 and the lower portion 1042 of the sample collection container are generally cylindrical, with the lower portion 1042 having a smaller inner diameter than the upper portion 1040, as shown in Figure 18. As also shown in Figure 18, the sample collection container 1016 can include an internal ledge 1050 between the upper portion 1040 and the lower portion 1042 which is configured to support the basket sieve 1014. In an alternative embodiment, the upper portion 1040 and the lower portion 1042 can be approximately the same diameter, and the sample collection container

1016 can include an internal ridge line between the upper portion 1040 and the lower portion 1042 which is configured to support the basket sieve 1014.

[0176] The basket sieve 1014 includes a sieve surface 1054 configured to pass the D-cells from a biopsy but not solid tissue from the biopsy. The pore size of the sieve is approximately 40-100 microns in diameter per pore (the pore aperture size) to allow D-cells 1062 to fall through. In the illustrated embodiment, the sieve surface 1054 is the lower surface of the basket sieve 1014. As seen in Figure 3, the basket sieve 1014 also includes a lip 1056 that rests on the ledge 1050 or ridge line of the sample collection container 1016 so that the basket sieve 1014 is suspended within the sample collection container 1016 above the reagent chamber 1038 and below the buffer container 1012. As seen in the alternate example embodiment of a biopsy container apparatus 1010a in Figure 19, the basket sieve 1014a can also include loop-like or hook-like vertical members 1058 to assist a user in lifting the basket sieve 1014a upward to remove the basket sieve 1014a (and the tissue it carries) from the sample collection container 1016 during use.

[0177] As seen in Figure 18, when the buffer container 1012, the basket sieve 1014 and the sample collection container 1016 are attached, the basket sieve 1014 is suspended above the reagent chamber 1038 of the sample collection container 1016, and the buffer container 1012 is suspended above the basket sieve 1014 by attachment of the first attachment mechanism 1030 to the second attachment mechanism 1032. Those of ordinary skill in the art will recognize from this disclosure that there are other ways of attaching the elements so that they are generally arranged as shown in Figure 18.

[0178] As also seen in Figure 18, when the basket sieve 1014 is attached to the sample collection container 1016, the basket sieve 1014 is located at least partially within the sample collection container 1016. In Figure 18, the basket sieve 1014 is located entirely within the sample collection container 1016. Similarly, the buffer container 1012 can be located at least partially or fully within the sample collection container 1016 when attached to the sample collection container 1016. In Figure 18, the buffer container 1012 is located partially within the sample collection container 1016, with the reagent chamber 1020 located within the sample collection container 1016 but the funnel portion 1024 located outside of the sample collection container 1016. More specifically, the buffer chamber 1020 of the buffer container 1012 is at least partly located within the sample collection container 1016, and the funnel portion 1024 of the buffer container 1012 is at least partially located outside of the sample collection container 1016. Those of ordinary skill in the art will recognize from this

disclosure that there are various ways to arrange the buffer container 1012, the basket sieve 1014 and the sample collection container 1016 without departing from the spirit and scope of the present disclosure. In other embodiments, the buffer container 1012 and/or basket sieve 1014 can be removably attached outside of the sample collection container 1016.

[0179] Figure 21 shows an example embodiment of a method 1100 of recovering solid tissue and D-cells from a biopsy using a biopsy container apparatus 1010 in accordance with the present disclosure. Figures 22 to 27 illustrate various steps of the method 1100. Those of ordinary skill in the art will recognize from this disclosure that certain steps can be added, removed or altered without departing from the spirit and scope of the present disclosure.

[0180] At step 1102 (Figures 22 and 23), a user (e.g., interventional radiologist or other clinical user) uses a core needle 1060 to harvest an image guided biopsy from a patient with suspicious mass lesion inside his or her body (e.g., liver, lung, kidney, etc). The core needle 1060 removes both solid tissue 1062 and dislodged cells 1064 (D-cells) from the patient. The funnel portion 1024 makes it easy for the user to spacially coordinate the CNB needle tip and the target area and provides a convenient way to for the user to place the tip of the needle (and therefore the tissue sample) into the buffer solution 1021. Since the user's hand is approximately eight (8) inches away from the needle tip (holding the handle; not the tip), and the other hand is holding a buffer container or a conventional tray or rack in which the container is placed (not pictured) or otherwise unavailable and generally not used to guide the tip of the needle, maneuvering the tip of the needle into a small target is not easy. The larger funnel shape 24 of the present disclosure makes the target easier to hit.

[0181] At step 1104 (Figure 24), the user removes the lid 1028 and places the tip of the core needle 1060 within the funnel portion 1024 of the buffer container 1012. The user deposits the contents of the core needle 1060 including the solid tissue 1062 and the D-cells 1064 into the buffer solution 1021 within the buffer-containing closed end of the funnel shape 1024. The user may swirl the CNB needle tip to deposit the harvested tissue sample by moving the needle in a roughly circular fashion in the closed distal end of the funnel shape 1024, somewhat like the motion one would use with a manual egg beater, if the egg beater were a hollow-bore needle.

[0182] At step 1106 (Figures 25 and 26), the user removes the buffer container 1012 from the sample container 1016. The user removes the buffer container 1012 from the sample collection container 1016, for example, by detaching the first attachment mechanism 1030 and the second attachment mechanism 1032. The user then pours the contents of the buffer

container 1012 (the solid tissue 1062, the D-cells 1064 and the buffer solution 1021) into the basket sieve 1014 that is located within the sample collection container 1016. As seen in Figure 26, the solid tissue 1062 is captured by the sieve floor 1054 and remains within the basket sieve 1014, while the buffer solution 1021 and the D-cells 64 fall through the sieve floor 1054 and mix with the reagent 1039 in the reagent chamber 1038 of the sample collection container 1016. Since the reagent 1039 is 2x concentrated, the additional volume of buffer solution 1021 and dislodged cells 1062 restores the reagent concentration to normal.

[0183] At step 1108 (Figure 27), the user removes the basket sieve 1014 containing the solid tissue 1062 from the sample collection container 1012. The user places the basket sieve 1014 containing the solid tissue 1062 into a specimen cup 1066 containing formalin. The specimen cup 1062 is sealed and sent to a tissue pathology lab. Thereafter the tissue core can undergo traditional tissue processing, for example, to create a glass slide image for the pathologist to make a diagnosis.

[0184] At step 1110 (Figure 27), the user seals the sample collection container 1016 including the dislodged cells 1064, the buffer solution 1021 and the reagent 1039 for diagnostic testing. For example, the user can send the sealed sample collection container 1016 and its contents to a molecular lab for molecular diagnostic testing. At this point the buffer container 1012 and basket sieve 1014 have been removed and the sealed sample collection container 1016 includes the mixed buffer solution 1021, reagent 1039 and D-cells 1064.

[0185] Figures 28 and 29 illustrate an alternative embodiment of a biopsy container apparatus 1010c in accordance with the present disclosure. Those of ordinary skill in the art will recognize that various elements of the biopsy container apparatus 1010c can be modified with various elements of the other embodiments of biopsy containers discussed herein, and vice versa. In Figures 28 and 29, the same reference numbers are used to describe the same elements as biopsy container apparatus 1010.

[0186] In the illustrated embodiment, the biopsy container apparatus 1010c includes a buffer container 1012c, a basket sieve 1014c and a sample collection container 1016c. As with the biopsy container apparatus 1010, the buffer container 1012c and basket sieve 1014c are configured for removable attachment to the sample collection container 1016c.

[0187] In the illustrated embodiment, the buffer container 1012c is generally similar to the buffer container 1012 discussed herein. The buffer container 1012c includes a buffer chamber 1020c, a funnel portion 1024c, a top opening 1026c and a lid 1028c. As seen in Figure 29, the lid 1028c is configured to fit both the buffer container 1012c and the sample collection

container 1016c, so that a user can remove the lid 1028c from the buffer container 1012c when beginning to use the biopsy container apparatus 1010c, and then later place the lid 1028c on the sample collection container 1016c to seal the D-cells 1064 within the sample collection container 1016c. More specifically, as seen in Figure 29, the buffer container 1012c includes threads 1070c at the top of the funnel portion 1024c, and the sample collection container 16c includes threads 1072c near its top rim. The threads 1070c and the threads 1072c are the same size so that the lid 1028c is configured to screw onto both the threads 1072c of the buffer container 1012c and the threads 1072c of the sample collection container 1016c.

[0188] In the illustrated embodiment, the buffer container 1012c also includes a skirt 74c with threads 1076c on its inner surface. The threads 1076c on the inner surface on the skirt 1074c are configured to mate with the threads 1072c of the sample collection 1016b. So the threads 1076c on the inner surface on the skirt 1074c attach to the threads 1072c of the sample collection 1016c when the lid 1028c is threaded onto the threads 1070c at the top of the funnel portion 1024c, and the lid 1028c is then threaded onto the threads 1072c of the sample collection container 1016c once the threads 1076c on the inner surface on the skirt 1074c are unthreaded from the threads 1072c of the sample collection 1016c.

[0189] In the illustrated embodiment, the buffer container 1012c also includes a handle 1078c protruding from skirt 1074c. The handle 1078c enables the user to (i) hold the biopsy container apparatus 1010c with one hand while the other hand unscrews the lid 1028c, (ii) hold the biopsy container apparatus 1010c steady with one hand while the other hand operates a core needle 1060 containing a tissue sample, maneuvering it into the funnel portion 1024c and depositing its contents therein, (3) unscrew the buffer container 1012bc from the sample collection container 1016c, and (4) lift and pour the contents of the buffer container 1012c (e.g., the solid tissue 1062, the D-cells 1064 and the buffer solution 1021) into the basket sieve 1014c and sample collection container 1016c.

[0190] In the illustrated embodiment, the basket sieve 1014c is generally similar to the basket sieve 1014 discussed herein. The basket sieve includes a sieve surface 1054c and a lip 1056c. The sieve surface 1054c is configured to pass the D-cells 1064 from a biopsy but not solid tissue 1062 from the biopsy. The lip 1056c is configured to rest on a corresponding ledge or ridge line of the sample collection container 1016c. As illustrated, the lip 1056c can be wider on one side of the basket sieve 1014c than another. As seen in Figure 29, the basket sieve 1014c is sized and shaped to be sealed within a corresponding specimen cup 1066 with the solid tissue 1016 and sent to a tissue pathology lab.

[0191] Figures 30 and 31 illustrate an alternative example embodiment of a biopsy container apparatus 1200. Those of ordinary skill in the art will recognize that various elements of the biopsy container apparatus 1200 can be modified with various elements of the other embodiments of biopsy containers discussed herein, and vice versa.

[0192] In the illustrated embodiment, the biopsy container apparatus 1200 includes an upper chamber 1202 and a lower chamber 1204 which are separated by a sieve surface 1206 and a solid surface 1208. The sieve surface 1206 is located between the upper chamber 1202 and the lower chamber 1204 and is configured to pass the dislodged cells 1064 from a biopsy but not the solid tissue 1062 from the biopsy. The solid surface 1208 is movably attached with respect to the sieve surface 1206 and configured to translate between (i) a first configuration in which the solid surface 1208 overlaps the sieve surface 1206 to prevent the D-cells 1064 from passing through the sieve surface 1206 and (ii) a second configuration in which the solid surface 1208 is moved away from the sieve surface 1206 to permit the D-cells 1064 to pass though the sieve surface 1206 from the upper chamber 1202 to the lower chamber 1204.

[0193] In the illustrated embodiment, the biopsy container apparatus 1200 includes a handle 1210 attached to the solid surface 1208. The handle 1210 enables a user to translate the solid surface 1208 in a perpendicular direction with respect to the height of the biopsy container apparatus 1200 as shown in Figures 30 and 31. More specifically, the handle 1210 enables a user to pull the solid floor 1208 out from between the upper chamber 1202 and the lower chamber 1204 and away from the sieve surface 1206, and then to push the solid floor 1208 back in between the upper chamber 1202 and the lower chamber 1204 so that it overlaps with the sieve surface 1206 in the vertical direction of Figures 30 and 31. When the solid floor 1208 is pulled to the side, the sieve surface 1206 allows the dislodged cells 64 to pass into the lower chamber 1204, but retains the solid tissue 1062 in the upper chamber 1202. As illustrated, the biopsy container apparatus 1200 also includes a lid 208 that attaches to the upper chamber 1202.

[0194] In use, a radiologist user who takes a needle biopsy unscrews the lid 1228 from the upper chamber 1202, places the core needle 1060 including solid tissue 1062 and D-cells 1064 into upper chamber 1202, and swirls the core needle 1060 to dislodge the solid tissue 62 and D-cells 1064. The user then pulls the handle 1210 to pull the solid surface 1208 from between the upper chamber 1202 and the lower chamber 1204 and away from the sieve surface 1206, releasing the D-cells 1064 into buffer solution into the lower chamber 1204, where they mix with a reagent (e.g. Zymo DNA/RNA Shield™ reagent) in the lower chamber

1204. The user then pushes handle 1210 back to its original position, sealing the D-cells 1064 in solution in the lower chamber 1204, then tilts the biopsy container apparatus 1200 upside down to release the solid tissue 1062 from the upper chamber 1202 into a standard formalin-containing vial for transport to paraffin preparation lab. The user the screws the lid 1228 back on, and sends the biopsy container apparatus 1200 containing the D-cells 1064 in solution for molecular testing. As seen in Figure 30, the biopsy container apparatus 200 can also include vertical projections 1212 that enable the sieve surface 1206 holding the solid tissue 1062 to be removed from the biopsy container apparatus 1200 and placed into the standard formalin-containing vial for transport to paraffin preparation lab.

[0195] The embodiments described herein provide improved apparatuses and methods for segregating tissue samples for multiple diagnostic modalities. An advantage of the disclosed apparatuses and methods is that D-cells can be collected at the site of the procedure, in an easy to perform process that almost completely eliminates pre-analytic variation and more importantly, before exposure to formalin fixation. This front-end approach, where the collection and stabilization occurs before fixation, is in contrast to other proposed biopsy substrate shortage solutions that seek to improve the substrate after it has already been fixed in formalin and damaged (back-end approaches). Prototype testing has shown that the specimen collected as D-cells by using this method result in more than sufficient amounts of nucleic acids, that are also of high quality, for molecular studies.

[0196] Figures 32 to 37 illustrate a first example embodiment of a biopsy container apparatus 2010 for recovering solid tissue and D-cells from a biopsy in accordance with the present disclosure. In the illustrated embodiment, the biopsy container apparatus 2010 includes a buffer container 2012, a basket sieve 2014 and a sample collection container 2016, which are three separable elements that can be attached prior to a biopsy and then separated during the method of use disclosed herein. As illustrated, the buffer container 2012 and basket sieve 2014 are configured for removable attachment to the sample collection container 2016. Figures 32 to 34 illustrate the buffer container 2012, the basket sieve 2014 and the sample collection container 2016 attached together, while Figures 35 and 36 show the buffer container 2012, the basket sieve 2014 and the sample collection container 2016 detached from each other.

[0197] The buffer container 2012 includes a buffer chamber 2020 for storing or receiving buffer solution 2021. The bottom edge 2023 of the buffer chamber 2020 is sealed and watertight so that the inner space 2022 of buffer chamber 2020 retains the buffer solution

2021. In an embodiment, the buffer chamber 2020 is pre-filled with the buffer solution 2021 within the inner space 2022. In an embodiment, the buffer solution 2021 is a sterile phosphate-buffered saline (PBS) buffer solution. In an embodiment, the buffer chamber 2020 includes between 1 and 2 mL of buffer solution. In an embodiment, the buffer chamber 2020 is pre-filled with approximately 1-2 ml of buffer solution. While PBS is the most likely choice of buffer, any similar buffer solution, such as Buffer Roswell Park Memorial Institute ("RPMI 1640 Media") Buffer Solution, would serve the same purpose.

[0198] In the illustrated embodiment, the buffer container 2012 includes a funnel to assist a user in depositing a biopsy sample from a core needle into the buffer solution 2021 within the buffer chamber 2020. More specifically, the buffer container 2012 includes a funnel portion 2024 leading into the buffer chamber 2020. The funnel portion 2024 flares outwardly from bottom to top, while the buffer chamber 2020 has a generally cylindrical shape for insertion into the basket sieve 2014 and/or the sample collection container 16 as shown in Figure 34. The funnel portion 2024 is configured to guide the solid tissue and the D-cells from the biopsy into the buffer chamber 2020 when ejected from a core needle, as discussed in more detail below.

[0199] In the illustrated embodiment, the buffer container 2012 includes a top opening 2026 and a lid 2028. The lid 2028 attaches at or near the top of the funnel portion 24 to cover the top opening 2026 and enclose the inner space 2022 so that the buffer solution 2021 does not spill if the biopsy container apparatus 2010 is inverted. The lid 2028 can be attached by being screwed onto the buffer container 2012 at or near the top of the funnel portion 2024, or by another suitable attachment mechanism. In the illustrated embodiment, the lid 2028 is configured to attach to both the buffer container 2012 and the sample collection container 2016, so that a user can remove the lid 2028 from the buffer container 2012 when beginning use of the biopsy collection apparatus 2010 and then later place the lid 2028 on the sample collection container 2016 to seal its contents, as shown in Figure 48.

[0200] In the illustrated embodiment shown in Figures 35 and 36, the lid 2028 includes a first attachment mechanism 2029 to enable removable attachment to a second attachment mechanism 2030 of the buffer container 2012. As seen in Figure 48, the first attachment mechanism 2029 also enables removable attachment to a third attachment mechanism 2031 of the sample collection container 2016, enabling the lid 2028 to be attached to the sample collection container 2016 after being removed from the buffer container 2012. In the illustrated embodiment, the buffer container 2012 also includes a fourth attachment

mechanism 2032 to enable removable attachment to the third attachment mechanism 2031 of the sample collection container 2016. In the illustrated embodiment, the inner surface of the lid 2028 includes the first attachment mechanism 2029, the outer surface of the buffer container 2012 includes the second attachment mechanism 2030, the outer surface the sample collection container 2016 includes the third attachment mechanism 2031, and the inner surface of the buffer container 2012 includes the fourth attachment mechanism 2032. When attached as shown in Figures 32 to 34, the first attachment mechanism 2029 and the second attachment mechanism 2030 create a watertight seal between the buffer container 2012 and the lid 2028, and the third attachment mechanism 2031 and the fourth attachment mechanism 2032 create a watertight seal between the buffer container 2012 and the sample collection container 2016, so that liquid will not spill from the buffer container 2012 or the sample collection container 2016 if the biopsy container apparatus 2010 is inverted. When attached as shown in Figure 48, the first attachment mechanism 2029 and the third attachment mechanism 2031 create a watertight seal between the lid 2028 and the sample collection container 2016 so that liquid will not spill from the sample collection container 2016 if the biopsy container apparatus 2010 is inverted

[0201] In the illustrated embodiment, the attachment mechanisms 2029, 2030, 2031, 2032 are screw threads. The screw threads of the first attachment mechanism 2029 and the fourth attachment mechanism 2032 have approximately the same size, and the screw threads of the second attachment mechanism 2030 and the third attachment mechanism 2031 have approximately the same size. Those of ordinary skill in the art will recognize from this disclosure that other attachment mechanisms are possible.

[0202] In the illustrated embodiment, the buffer container 2012 includes a skirt 2034 with the fourth attachment mechanism 2032 on its inner surface. As seen in Figures 34 and 36, the skirt 2034 encircles the buffer chamber 2020. The buffer container 2012 also includes a handle 2036 protruding from the skirt 2034. The handle 2036 enables the user to (i) hold the biopsy container apparatus 2010 with one hand while the other hand unscrews the lid 2028, (ii) hold the biopsy container apparatus 2010 steady with one hand while the other hand operates a core needle 2060 containing a tissue sample, maneuvering it into the funnel portion 2024 and depositing its contents therein, (3) unscrew the buffer container 2012 from the sample collection container 2016, and (4) lift and pour the contents of the buffer container 2012 (e.g., solid tissue 2062, D-cells 2064 and buffer solution 2021) into the basket sieve 2014 and sample collection container 2016.

[0203] The sample collection container 2016 includes a reagent chamber 2038 for storing or receiving a reagent 2039. In Figure 34, the sample collection container 2016 includes an upper portion 2040 and a lower portion 2042, with the reagent chamber 2038 located within and/or formed by the lower portion 2042. The bottom edge 2044 of the sample collection container 2016 is sealed and watertight so that the reagent chamber 2038 retains the reagent 2039. In an embodiment, the reagent chamber 2038 is pre-filled with the reagent 2039 within the inner space 2046. In an embodiment, the reagent 2039 is a solution for lysing cells and preserving nucleic acids that is approximately 2x the normal concentration of an off-the-shelf cell lysing reagent. In an embodiment, the reagent 2039 is Zymo DNA/RNA Shield™ reagent, or an equivalent for lysing cells and preserving nucleic acids which is 2x the normal concentration defined by and provided by Zymo. In an embodiment, the reagent chamber 38 includes between 1 and 2 mL of reagent 2039. In an embodiment, the reagent chamber 2038 is pre-filled with 1-2 ml of double-concentration cell lysis/nucleic acid stabilization reagent 39. In an embodiment, the reagent chamber 2038 includes a first amount of reagent 2039, and the buffer chamber 2020 includes a second amount of buffer solution 2021 that is approximately equal in volume to the first amount of reagent.

[0204] In the illustrated embodiment, the upper portion 2040 of the sample collection container 2016 is cylindrical, and the lower portion 2042 of the sample collection container 2012 tapers inwardly from top to bottom, with the lower portion 2042 near the bottom edge 2044 having a smaller inner diameter than the upper portion 2040. As seen in Figures 36 and 37, the upper portion 2040 of the sample collection container 2016 includes a rim 2050 configured to support the basket sieve 2014. In an alternative embodiment, the upper portion 2040 and the lower portion 2042 can be approximately the same diameter, and the sample collection container 2016 can include an internal ridge line within or between the upper portion 2040 and the lower portion 2042 which is configured to support the basket sieve 2014.

[0205] The basket sieve 2014 includes a sieve surface 2054 configured to pass the D-cells from a biopsy but not solid tissue from the biopsy. The pore size of the sieve is approximately 40-100 microns in diameter per pore (the pore aperture size) to allow D-cells to fall through. In the illustrated embodiment, the sieve surface 2054 is the lower surface of the basket sieve 2014. As seen in Figures 35 and 36, the basket sieve 2014 also includes a lip 2056 sized to rest on the rim 2050 of the sample collection container 2016 so that the basket sieve 2014 is suspended within the sample collection container 2016 above the reagent chamber 2038 and below the buffer chamber 2020 when the biopsy container apparatus 2010 is assembled as

shown in Figure 34. In an alternate example embodiment, the basket sieve 2014 can include loop-like or hook-like vertical members to assist a user in lifting the basket sieve 2014 upward to remove the basket sieve 2014 (and the tissue it carries) from the sample collection container 2016 during use. As seen in Figure 48, the basket sieve 2014c is sized and shaped to be sealed within a corresponding specimen cup 2066 and sent to a tissue pathology lab.

[0206] As seen in Figure 34, when the buffer container 2012, the basket sieve 2014 and the sample collection container 2016 are attached to each other, the basket sieve 2014 is suspended above the reagent chamber 2038 of the sample collection container 2016, and the buffer chamber 2020 is suspended above sieve surface 2054 by attachment of the third attachment mechanism 2031 to the fourth attachment mechanism 2032. Those of ordinary skill in the art will recognize from this disclosure that there are other ways of attaching and/or arranging the elements besides as shown in the example embodiment of Figures 32-37.

[0207] As also seen in Figure 34, when the basket sieve 2014 is attached to the sample collection container 2016, the basket sieve 2014 is located at least partially within the sample collection container 2016. In Figure 34, the basket sieve 2014 is located almost entirely within the sample collection container 2016 besides the lip 2056 protruding from the top of the sample collection container 2016. Similarly, the buffer container 2012 can be located at least partially or fully within the sample collection container 2016 when attached to the sample collection container 2016. In Figure 34, the buffer container 2012 is located partially within the sample collection container 2016, with the reagent chamber 2020 located partially within the sample collection container 2016 but the funnel portion 2024 located outside of the sample collection container 2016. More specifically, the buffer chamber 2020 of the buffer container 2012 is at least partly located within the sample collection container 2016, and the funnel portion 2024 of the buffer container 2012 is at least partially located outside of the sample collection container 2016. Those of ordinary skill in the art will recognize from this disclosure that there are various ways to arrange the buffer container 2012, the basket sieve 2014 and the sample collection container 2016 besides as shown in the example embodiment of Figures 32-37. In other embodiments, the buffer container 2012 and/or basket sieve 2014 can be removably attachable outside of the sample collection container 2016.

[0208] The dimensions of a biopsy container apparatus 2010 in accordance with the present disclosure can vary. In Figures 32-34, the total height of the biopsy container apparatus 2010 is approximately 12.4 cm, the height of the sample collection container 2016 is approximately 7.6 cm, the outer diameter of the upper portion 40 of the sample collection container 2016 is

approximately 3.0 cm, the outer diameter of the basket sieve 2014 is approximately 2.7 cm with the rim 56 having an outer diameter of approximately 2.9 cm, and the outer diameter of the lid 2028 is approximately 3.3 cm. Referring to Figures 34 and 36, the buffer chamber 2020 has an approximate inner diameter of 10 mm and an approximate height of 30 mm. Those of ordinary skill in the art will recognize from this disclosure that these dimensions are an example only and can change with different embodiments.

[0209] Figure 38 shows an example embodiment of a method 2100 of recovering solid tissue and D-cells from a biopsy using a biopsy container apparatus 2010 in accordance with the present disclosure. Figures 39 to 48illustrate various steps of the method 2100, and Figure 2018 illustrates an example pictorial summary of the method 2100. Those of ordinary skill in the art will recognize from this disclosure that certain steps can be added, removed or altered without departing from the spirit and scope of the present disclosure.

[0210] At step 2102 (Figures 39 and 40) a user (e.g., interventional radiologist or other clinical user) uses a core needle 2060 to harvest an image guided biopsy from a patient with suspicious mass lesion inside his or her body (e.g., liver, lung, kidney, etc). The core needle 2060 removes both solid tissue 2062 and dislodged cells 2064 (D-cells) from the patient.

[0211] At step 2104, (Figure 41), the user removes the lid 2028 from the buffer container 2012. The lid 2028 can be set aside and later reused to seal the sample collection container 2016 at step 2118.

[0212] At step 2106 (Figure 42), the user deposits the contents of the core needle 2060 including the solid tissue 2062 and the D-cells 2064 into the buffer solution 2021 within the buffer-buffer chamber 2020. The user may swirl the CNB needle tip to deposit the harvested tissue sample by moving the needle in a roughly circular fashion in the closed distal end of the funnel shape 2024, somewhat like the motion one would use with a manual egg beater, if the egg beater were a hollow-bore needle. The funnel portion 2024 makes it easy for the user to spacially coordinate the CNB needle tip and the target area and provides a convenient way to for the user to place the tip of the needle (and therefore the tissue sample) near or into the buffer solution 2021. That is, the larger funnel shape 2024 of the present disclosure makes the buffer chamber 2020 easier to hit since the user's hand is approximately eight (8) inches away from the needle tip (holding the handle; not the tip), and the other hand is holding the buffer container 2012 or a conventional tray or rack in which the buffer container 2012 is placed (not pictured) or otherwise unavailable and generally not used to guide the tip of the needle.

[0213] At step 2108 (Figure 43), the user removes the buffer container 2012 from the sample container 2016. The user removes the buffer container 2012 from the sample collection container 2016, for example, by detaching (e.g., unscrewing) the third attachment mechanism 2031 and the fourth attachment mechanism 2032.

[0214] At step 2110 (Figure 44), the user pours the contents of the buffer container 2012 (the solid tissue 2062, the D-cells 2064 and the buffer solution 2021) into the basket sieve 2014 that is located within the sample collection container 2016. As seen in Figure 44, the solid tissue 2062 is captured by the sieve floor 2054 and remains within the basket sieve 2014, while the buffer solution 2021 and the D-cells 2064 fall through the sieve floor 2054 and mix with the reagent 2039 in the reagent chamber 2038 of the sample collection container 2016. Since the reagent 2039 is 2x concentrated, the additional volume of buffer solution 2021 and dislodged cells 2064 restores the reagent concentration to normal.

[0215] At step 2112, (Figure 45), the user can discard the buffer container 2012.

[0216] At step 2114 (Figure 46), the user removes the basket sieve 2014 containing the solid tissue 2062 from the sample collection container 2012 containing the buffer solution 2021, reagent 2039 and dislodged cells 2064.

[0217] At step 2116 (Figure 47), the user places the basket sieve 2014 containing the solid tissue 2062 into a specimen cup 2066 containing formalin. The specimen cup 2062 is sealed and sent to a tissue pathology lab. Thereafter the tissue core can undergo traditional tissue processing, for example, to create a glass slide image for the pathologist to make a diagnosis.

[0218] At step 2118 (Figure 48), the user seals the sample collection container 2016 including the dislodged cells 2064, the buffer solution 2021 and the reagent 2039 for diagnostic testing. The user can seal the sample collection container 2016 by attaching the lid 2028 that was previously removed from the buffer container 2012. The user can send the sealed sample collection container 2016 and its contents to a molecular lab for molecular diagnostic testing. At this point the buffer container 2012 and the basket sieve 2014 have been removed and the sealed sample collection container 2016 includes the mixed buffer solution 2021, reagent 2039 and D-cells 2064.

[0219] Figures 50 and 51 illustrate an alternative second example embodiment of a biopsy container apparatus 2010' for recovering solid tissue and D-cells from a biopsy in accordance with the present disclosure. The biopsy container apparatus 2010' includes all of the elements of the biopsy container 2010, besides that the buffer container 2012 includes a concave outer surface 2070 surrounding the buffer chamber 2020 instead of a handle. The concave outer

surface 2070 reduces the size of the biopsy container apparatus 2010' and can be gripped by a user when handling the biopsy container apparatus 2010 in accordance with the method 2100.

[0220] The embodiments described herein provide improved apparatuses and methods for segregating tissue samples for multiple diagnostic modalities. An advantage of the disclosed apparatuses and methods is that D-cells can be collected at the site of the procedure, in an easy to perform process that almost completely eliminates pre-analytic variation and more importantly, before exposure to formalin fixation. This front-end approach, where the collection and stabilization occurs before fixation, is in contrast to other proposed biopsy substrate shortage solutions that seek to improve the substrate after it has already been fixed in formalin and damaged (back-end approaches). Prototype testing has shown that the specimen collected as D-cells by using this method result in more than sufficient amounts of nucleic acids, that are also of high quality, for molecular studies.

[0221] Any of the elements of any of the embodiments described herein can also be included in any of the other embodiments described herein.

[0222] It should be understood that various changes and modifications to the apparatuses and methods described herein will be apparent to those skilled in the art and can be made without diminishing the intended advantages.

GENERAL INTERPRETATION OF TERMS

[0223] In understanding the scope of the present invention, the term "comprising" and its derivatives, as used herein, are intended to be open-ended terms that specify the presence of the stated features, elements, components, groups, and/or steps, but do not exclude the presence of other unstated features, elements, components, groups, integers and/or steps. The foregoing also applies to words having similar meanings such as the terms, "including", "having" and their derivatives. Also, the terms "part," "section," or "element" when used in the singular can have the dual meaning of a single part or a plurality of parts.

[0224] The term "configured" as used herein to describe a component, section or part of a device includes hardware that is constructed to carry out the desired function.

[0225] While only selected embodiments have been chosen to illustrate the present invention, it will be apparent to those skilled in the art from this disclosure that various changes and modifications can be made herein without departing from the scope of the invention as defined in the appended claims. For example, the size, shape, location or orientation of the various components can be changed as needed and/or desired. Components that are shown

directly connected or contacting each other can have intermediate structures disposed between them. The functions of one element can be performed by two, and vice versa. The structures and functions of one embodiment can be adopted in another embodiment. It is not necessary for all advantages to be present in a particular embodiment at the same time. Every feature which is unique from the prior art, alone or in combination with other features, also should be considered a separate description of further inventions by the applicant, including the structural and/or functional concepts embodied by such features. Thus, the foregoing descriptions of the embodiments according to the present invention are provided for illustration only, and not for the purpose of limiting the invention as defined by the appended claims and their equivalents.

WHAT IS CLAIMED IS:

1. A method for recovering an assessable analyte potentially including DNA, RNA, an exosome or a protein from a tissue sample retrieved via a core needle biopsy, the method comprising:

obtaining the tissue sample via a core needle having the tissue sample disposed therein retrieved via the core needle biopsy, wherein the tissue sample comprises a tissue core and dislodged cells;

providing a buffer solution, wherein the buffer solution does not comprise formalin;

immersing a portion of the core needle having the tissue sample disposed therein in the buffer solution;

swirling the core needle within the buffer solution to form a first intermediate mixture comprising the buffer solution, the tissue core, and the dislodged cells;

filtering the first intermediate mixture into a sample tube using a strainer to separate the tissue core from the first intermediate mixture, yielding the tissue core and a second intermediate mixture comprising the buffer solution and the dislodged cells;

adding a cell lysis and stabilization reagent not including formalin to the second intermediate mixture, yielding a third mixture comprising lysed dislodged cells from which the assessable analyte can be retrieved;

extracting the assessable analyte from the third mixture; and

assessing the assessable analyte;

wherein the assessable analyte has not been exposed to formalin.

2. The method of claim 1, further comprising extracting the tissue core and disposing the tissue core within a container.

3. A method for recovering an assessable analyte potentially including DNA, RNA, an exosome or a protein from a tissue sample retrieved via a core needle biopsy, comprising:

obtaining the tissue sample via a core needle having the tissue sample disposed therein retrieved via the core needle biopsy, wherein the tissue sample comprises a tissue core and dislodged cells;

immersing a portion of the core needle having the tissue sample disposed therein in a buffer solution;

swirling the core needle within the buffer solution to form a first intermediate mixture comprising the buffer solution, the tissue core, and the dislodged cells;

filtering the first intermediate mixture using a strainer into a sample tube to separate the tissue core from the first intermediate mixture, yielding the tissue core and a second intermediate mixture comprising the buffer solution and the dislodged cells; and

adding a cell lysis and stabilization reagent not including formalin to the second intermediate mixture yielding a third mixture comprising lysed dislodged cells from which the assessable analyte can be retrieved;

wherein the assessable analyte has not been exposed to formalin.

4. The method of claim 3, wherein the cell lysis and stabilization reagent is equal in volume to the second intermediate mixture.

5. The method of claim 3, wherein the cell lysis and stabilization reagent comprises from 2 mL to 5 mL of the cell lysis and stabilization reagent.

6. The method of claim 3, further comprising storing the sample tube having the third mixture disposed therein within a freezer.

7. The method of claim 3, further comprising extracting the assessable analyte from the third mixture.

8. The method of claim 3, wherein the buffer solution comprises a phosphate buffered saline solution.

9. The method of claim 3, further comprising sterilizing the buffer solution prior to immersing the core needle therein.

10. The method of claim 3, wherein the assessable analyte is DNA, RNA, an exosome, or a protein.

11. The method of claim 1, wherein the buffer solution comprises a sterilized phosphate buffered saline solution.

12. The method of claim 1, wherein the cell lysis and stabilization reagent is equal in volume to the second intermediate mixture.

13. The method of claim 1, wherein the cell lysis and stabilization reagent comprises from 2 mL to 5 mL of the cell lysis and stabilization reagent.

14. The method of claim 1, wherein assessing the assessable analyte includes using a fluorometer.

15. The method of claim 1, wherein assessing the assessable analyte includes using a spectrophotometer.

16. The method of claim 1, wherein the assessable analyte is DNA, RNA, an exosome, or a protein